EBMed's Great GI Debates: Welcome to Our Second Meeting!

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Welcome!

Philip Schoenfeld, MD

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EBMed Vision

1. Advance the careers of women and under-represented minorities in academic GI careers through mentorship and sponsorship opportunities.

2. EBMed is the acronym for "***Evidence-Based Medicine education***" Our goal is to improve GI patient care through CME education emphasizing EBM principles.

3. EBMed is a 501(c)3 non-profit organization

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Education Should Be Fun-Interactive Talks

1. How I Do It - Experts discussing their approach to common problems.

2. Two experts debate opposite sides of a controversial management issue.

3. Guideline Updates

4. Best of Evidence - Based GI: An ACG Publication

5. ”Ask the Expert”- Case studies of complicated patients are presented to faculty.

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Our EBMed Team

Philip Schoenfeld, MD, MSEd, MSc (Epi), AGAF, FACG

Linda Nguyen, MD, AGAF, FACG

Aline Charabaty, MD, AGAF, FACG

Joseph Sleiman, MD

Christine Tebben, CME Manager

Amber Tresca, Patient Advocate

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Have Fun and Meet New Friends

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EBMed's Great GI Debates

February 28 - March 2, 2025

Complete this card to WIN extra EBMed swag!

1. Visit all 12 sponsor booths
2. Have each sponsor place a sticker on their logo
3. Once completed, turn in at hospitality desk for drawing

MUST BE PRESENT TO WIN!

Name: _____

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Housekeeping

- PDF Download of Slides
  - Conference > Slides https://ebmed.net/slides
- Wi-Fi Network
  - Convention_Wireless Access Code: EBMed2025
- Continuing Education Evaluation for Credit
  - The CE Link and QR code will be live on Sunday, March 2nd, at 12pm through Wednesday, April 2nd
  - You can claim up to 6.25 hours of total credit for both Saturda and Sunday sessions. Your certificates will be emailed to you. https://akhinc.formstack.com/forms/250018l
- Please complete post-meeting evaluation before leaving

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Our Industry Partners

The KL Logistics Team

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Inflammatory Bowel Disease

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Simplifying the Algorithm: Treating Moderate-Severe IBD with Advanced Therapies

Stephen B. Hanauer, MD

Professor of Medicine

Medical Director, Digestive Health Center

Northwestern University Feinberg School of Medicine

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Conflicts

- Abbvie
- Amgen
- Boerhinger-Ingelheim
- BMS
- Celltrion
- Johnson & Johnson
- Lilly
- Merck
- Pfizer
- Samsung-Bioepis
- Takeda

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What is Moderate-Severe UC or CD?

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Disease *Activity* vs Disease *Severity*

Activity

Reflects cross-sectional assessment of biologic inflammatory impact on symptoms, signs, endoscopy, histology, and biomarkers

How is your patient TODAY?

Severity

Includes longitudinal (disease course) and historical factors that provide a more complete picture of the prognosis and overall "burden" of disease

What has your patient's disease course been like over their history since diagnosis?

Peyrin-Biroulet L, et al. *Clin Gastroenterol Hepatol*. 2016;14(3):348-54.e17.

Clinical Trials ≠ Clinical Practice

- Clinical Trials Enroll Patients with Moderate-Severe “Activity”
  - Mayo Score
  - CDAI, SES

- Clinical Practice Patients with Moderate-Severe Severity
- Newly diagnosed moderately ill patient
- Patient failing mesalamine (UC) or budesonide (CD)
- Patient failing corticosteroids + Thiopurine/MTX
- Steroid-dependent
- Hospitalized patient failing IV steroids

Singh S, et al. *Gastroenterology*. 2024;167(7):1307-1343.

Risk Stratification in IBD

Risk for Colectomy/Surgery

Extensive Disease

Deep ulcers

Age <40

High CRP and ESR

EIMs, Anemia, Etc.

Steroid-requiring disease

History of hospitalization

C. Difficile or CMV infection

Mod-Sev Disease can be Diagnosed at Presentation!

Dassopoulos T, et al. *Gastroenterology*. 2015;149(1):238-245; Sandborn WJ. *Gastroenterology*. 2014;147(3):702-705.

Other Considerations in Moderate-Severe IBD

- Disease Activity (Hospitalized vs Outpatient)
- Prior Therapies (Response/LOR/AE's)
- Age (Young vs Old)
- Gender (Fertility)
- Family History (other IMIDs suggesting genetic dispositions)
- EIMs
- Risk Tolerance
- Convenience (IV, SC, Oral/Dosing Frequency)
- Insurance & Cost to Patients
- Accessibility (not just Access)

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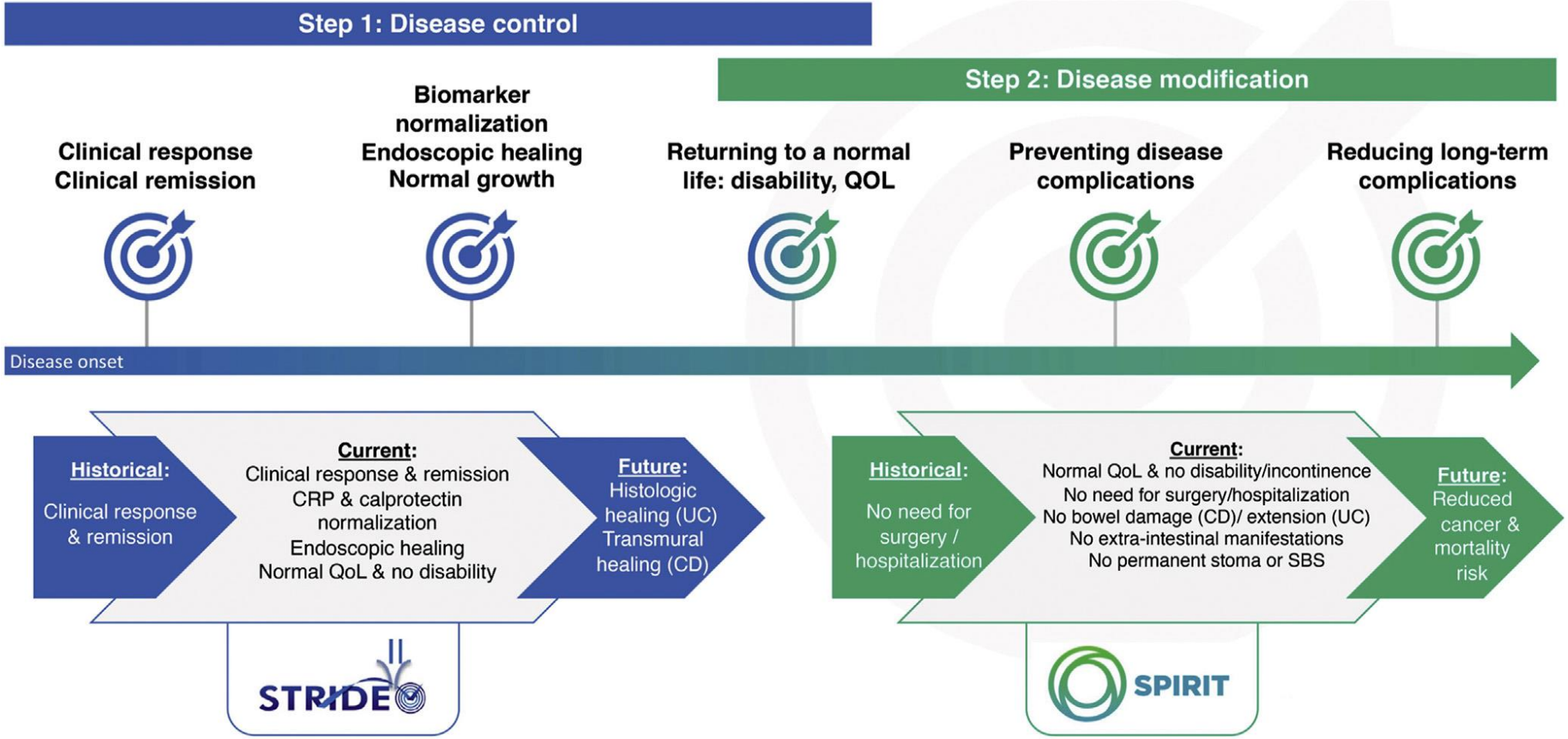
Impact of an Aging Population=Comorbidities

- Metabolic Syndrome
- Cardiovascular Disease
- Arthritis
- Neoplasia
- Socioeconomic (Medicare)
- Frailty

Evolving Short-Term and Long-Term Goals in IBD



Le Berre C, et al. *Gastroenterology*. 2022;162(5):1424-1438.

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Mod-Severe IBD is both a Sprint and a Marathon

- How Sick
- How Fast
- How Accessible

- How Safe
- How Durable

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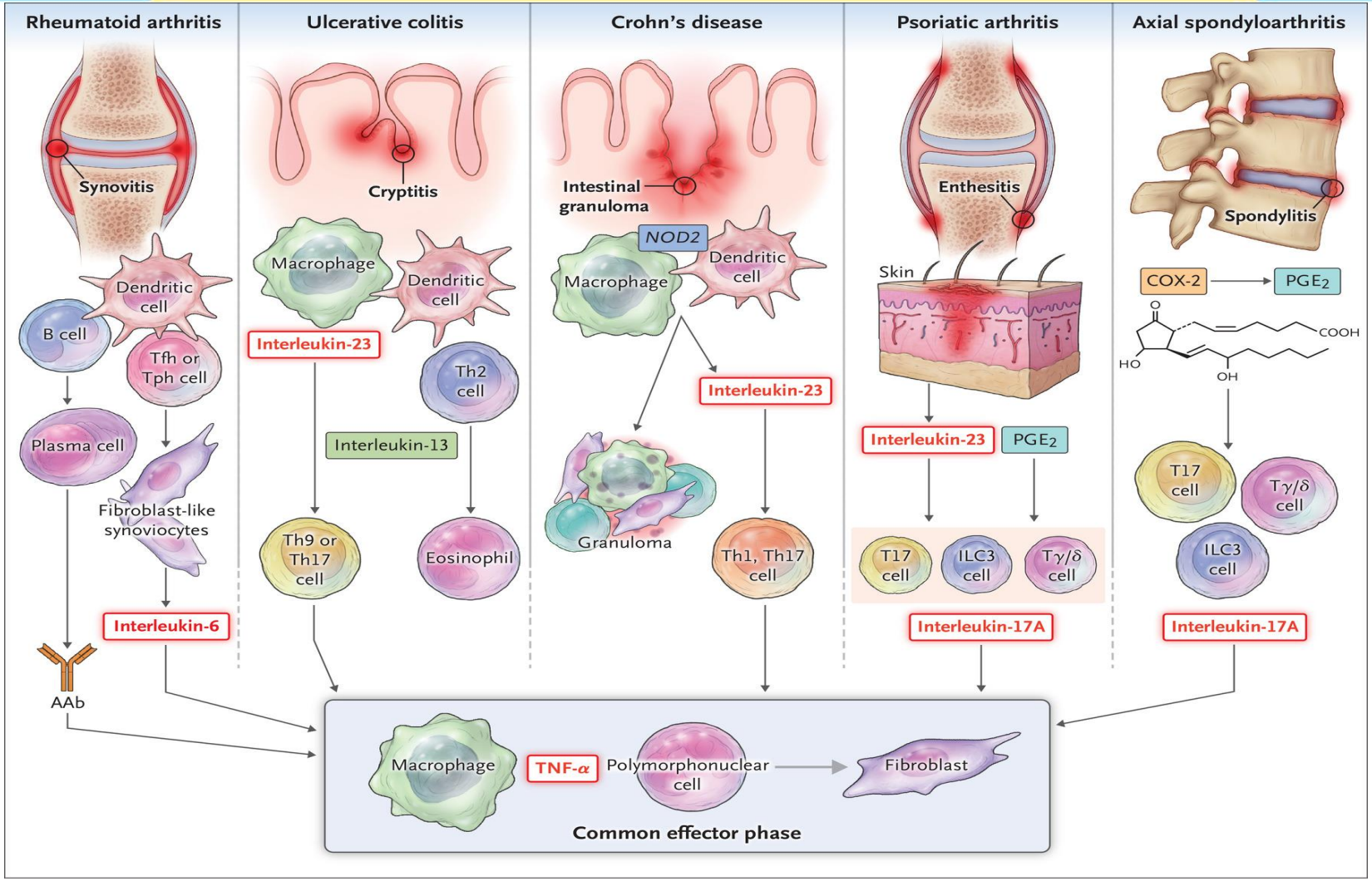
Current “Advanced-Therapy” Armamentarium in IBD

- Corticosteroids + Thiopurines
- TNF blockers (+ Biosimilars)
- Anti-α4 / α4β7 antibodies
- IL-12/23 & IL-23 Blockers
- JAK inhibitors
- S1P Modulators (UC)

Feuerstein JD, et al. *Gastroenterology*. 2020;158(5):1450-1461; Rubin DT, et al. *Am J Gastroenterol*. 2019;114(3):384-413.

Signature Cytokines and Their Functions in the Inflammatory Process of Arthritis and Colitis



Schett G, et al. *N Engl J Med*. 2021;385(7):628-639.

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Anti-IL-23 Antibodies in IBD

- Effective options as first- or second-line advanced therapies in IBD, and safer than TNFi
- As with all agents, slightly lower absolute efficacy in bio-experienced patients, though similar efficacy when placebo-adjusted
- Efficacy advantage over anti-IL-12/23 (ustekinumab) in CD may be ~10% margin
  - Access will be determined by the market

JAKs in IBD: Practical Implications

- Black box warning “necessitates” second-line *marketing* position after failure of TNFi
  - FDA regulates marketing
  - Clinicians are “regulated” by standard of care
- Whether positioned after IL-12/23i, IL-23i, or vedolizumab, or after S1P receptor modulator, depends upon risk-benefit considerations for individual patient (symptom severity, risk factors for MACE, cancer, thrombosis, risk aversion)
- Note: *Greatest risk for C-V and Thromboembolic events in IBD is ACTIVE IBD*

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Ozanimod/Etrasimod
Practical Implications

- Best positioned as first-line advance therapy for moderate activity
  - E.g. After mesalamine
- Despite “precautions” Cardiovascular Effects are minimal
  - <1 beat/minute reduced heart rate
- If used as second-line advanced therapy, efficacy similar in those who failed 1 biologic
- Patients who failed ≥2 biologics may still respond but may take longer

Key Safety Considerations With IBD Therapies

Cytopenias
Thiopurines
Methotrexate

Cardiovascular Disease
Anti-TNF/JAK/S1P

Hepatotoxicity
Thiopurines
Methotrexate

Osteoporosis
Corticosteroids

Infection
Anti-TNF
Corticosteroids
Thiopurines
JAK (*H. zoster*)

Malignancy
Anti-TNF/JAK
(lymphoma?)
Corticosteroids
Thiopurines

Immunogenicity
Anti-TNF

1. Lichtenstein GR, et al. *Am J Gastroenterol*. 2009;104(2):465-484; 2. Lichtenstein GR, et al. *Am J Gastroenterol*. 2012;107(9):1409-1422; 3. Yadav S, et al. *Mayo Clin Proc*. 2015;90(6):738-746.

Combination Therapy is Common in Moderate-Severe UC

- Steroids + Thiopurines/Calcineurin inhibitors
- Calcineurin inhibitors + Thiopurines
- Steroids + All Advanced Therapies
  - (Phase III trials)
- TNFi + Thiopurines
- Other mAbs + Thiopurines

Cornet N, et al. *Inflamm Bowel Dis*. Published online August 29, 2024.

Combining Advanced Therapies: Practical Implications

- Golimumab + guselkumab in UC at least additive in efficacy
- Not feasible at present due to cost; a future concept
- While current combinations consist of what we have now, future combinations may include non-immune targets (barrier, microbiome, other)

Feagan BG, et al. *Lancet Gastroenterol Hepatol*. 2023;8(4):307-320.

Advanced Therapy Options in IBD

Individual Patient Characteristics

Pregnancy

Young woman with steroid-dependent UC planning to start a family

Any Biologic (Anti-TNF w/robust data)

Lifestyle Considerations

Businesswoman who travels often for work

S1P, SC TNFi, Il 12/23 or 23

Failed Anti-TNF

Young man with pan-UC who is a primary non-responder to anti -TNF

Uste, Tofa, Upa, Surgery

Shared Decision-making

Unfavorable Pharmacokinetics

Older woman with pan-UC in whom you want to avoid immunomodulator, who has HLA-DQA1*05 genotype

Vedo, Uste, or S1P

Newly Diagnosed

Newly diagnosed male with moderate with personal history of lymphoma

Vedo, Uste, Il-23

Perianal Disease

Woman admitted with severe rectal Crohn's with perirectal abscess s/p drainage and seton placement

Anti-TNF (+Azathioprine)

Courtesy Millie Long, MD. (Modified.)

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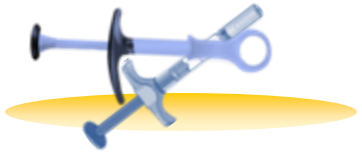
Access vs Accessible

- Time to Access is Important Determinant of First-Line Therapies
  - Time to Infusion/Injection/Ingestion
  - Insurance Hurdles/Delays
  - Infusion Center Scheduling
  - Starter Kits
- Treatment Delays=Prolonged Suffering or Steroids

Positioning Therapies in Moderate to Severe IBD



TNF antagonists

- IV vs SC options
- Rapid onset of action (IV hospitalized patients)
- Best with immunomodulator
- Infection risk
- Lymphoma risk (with immunomodulator)

Lymphocyte trafficking (Vedolizumab)

- IV option or SC
- Low rate of immunogenicity
- Onset of action?
- Better results in TNF naïve patients
- Monotherapy or combination therapy?
- "Gut-Selective"
- Long-term safety

Anti-IL12/23(Ustekinumab) Anti-IL/23 (Risankizumab, Mirikizumab, Guzelkumab)

- Similar induction success as TNFi agents
- Efficacy in TNFi-naïve and -failure patients
- Safety superior to anti-TNF therapies
- Low rate of immunogenicity
- Good use if concomitant psoriasis

JAK inhibitors (Tofacitinib, Upatacitinib)

- Oral
- Rapid onset of action
- Monotherapy, indicated after anti-TNF failure
- Maintenance dosing vs transition?
- Infection risk (zoster)
- MACE
- Lymphoma

S1P Modulator (Ozanimod, Etrasimod)

- Oral
- Rapid onset of action
- Monotherapy
- Best for moderate activity after 5-ASA
- Cardiac conduction

Avoid in Pregnancy

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Debate:
Stride II: Should We Treat to Target or Treat to Symptom Response?

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IL-23p19 Monoclonal Antibodies Should be First-Line Therapy for Moderate to Severe Crohn's disease

Aline Charabaty, MD, AGAF, FACG
Associate Professor of Medicine
Johns Hopkins School of Medicine
Medical Director of the Division of Gastroenterology and Hepatology and
Clinical Director of the IBD Center, Johns Hopkins-Sibley Memorial Hospital
Washington DC

@DCharabaty
@MondayNightIBD
@ScrubsNHeels

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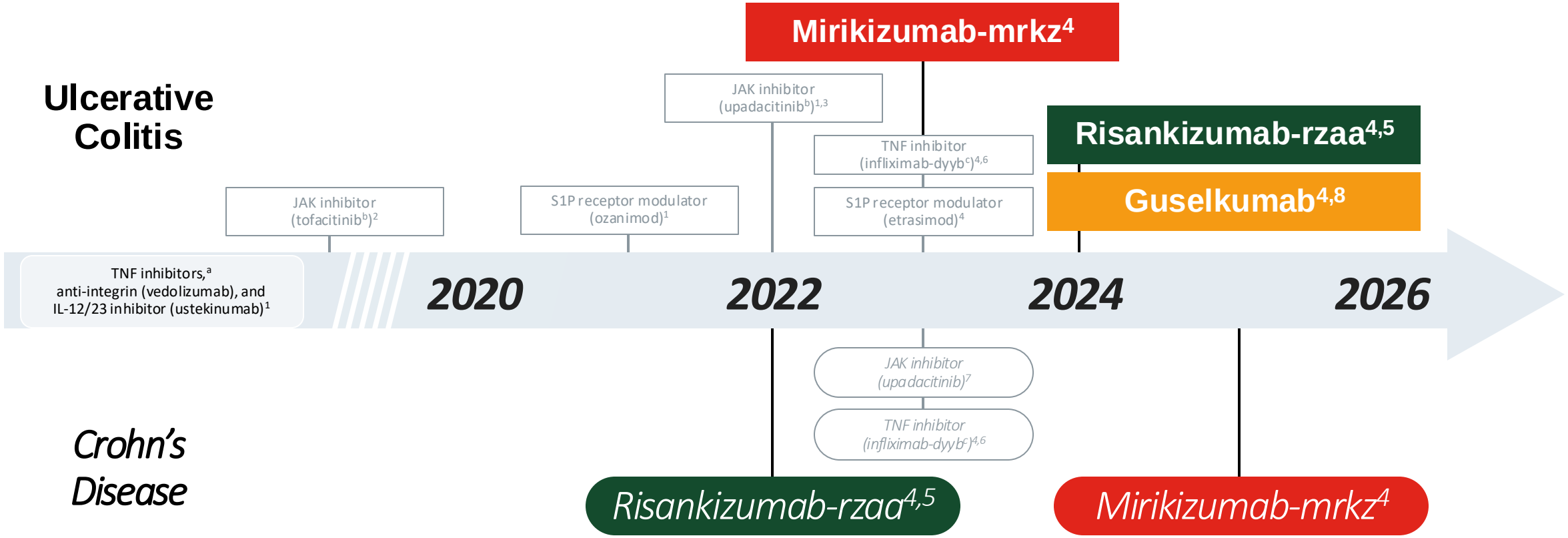
IL-23p19 Treatment Landscape in IBD



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Out with the Old, In with the New !

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Out with the Old, In with the New !
Let's Embrace the Future NOW !

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What Do We Want from a Crohn's Therapy

- Work fast
- Effective in most people, Durable Effectiveness
- Safe
- Convenient : Minimal need for monitoring, Easy to take, monotherapy
- Prevent disease progression (Endoscopic healing)

Anti-TNF

The good

- Easy access
- Works quickly
- Effective for EIM

The bad and the ugly

- 30% primary non-responders
- 30%-50% secondary LOR
- High risk for anti-drug antibodies
- Combo with thiopurines = increased risk infection and lymphoma

- Infectious risk, TB risk, reactivation of HepB
- Infusion reaction, drug-induced lupus, paradoxical psoriasis
- Skin cancer/ Melanoma

- Inconvenient: IV Center, frequent SQ, lab monitoring levels and dose adjustments

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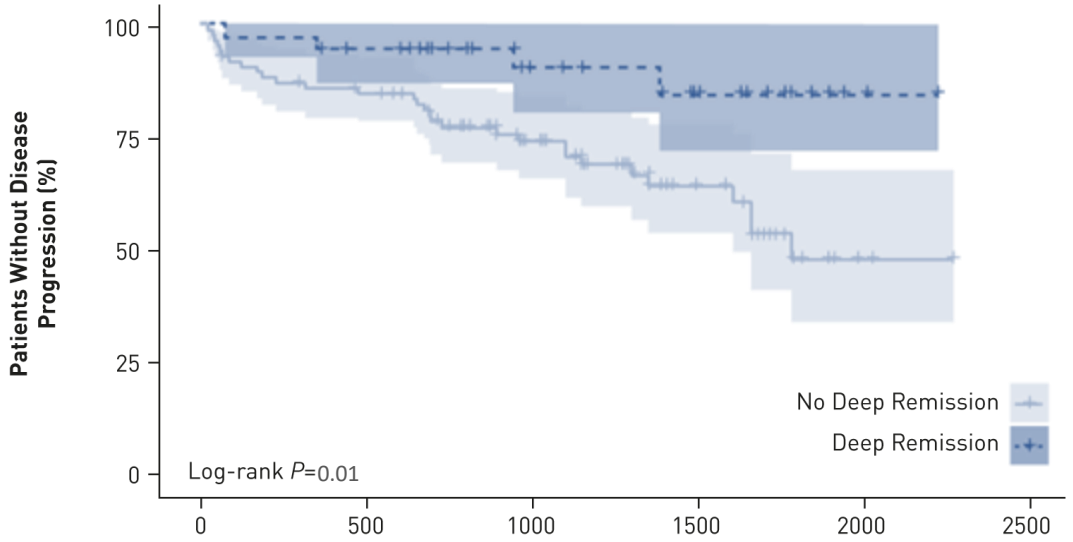
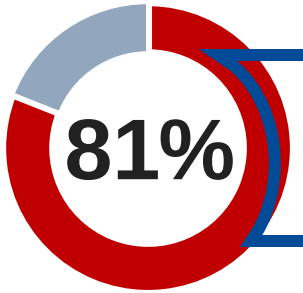
Endoscopic Remission Plus Clinical Remission

- **Odds of Avoiding Disease Progression in Patients With CD**



Number at risk:						
Deep Remission	36	32	19	12	2	0
No Deep Remission	86	70	46	21	2	0



Clinical remission[a] + endoscopic remission[b] + no steroids for ≥8 weeks

(aHR: 0.19; 95% CI: 0.08-0.31)

Data from CALM (N=122)

Ungaro RC et al, *Gastroenterology*. 2020;159(1):139-147

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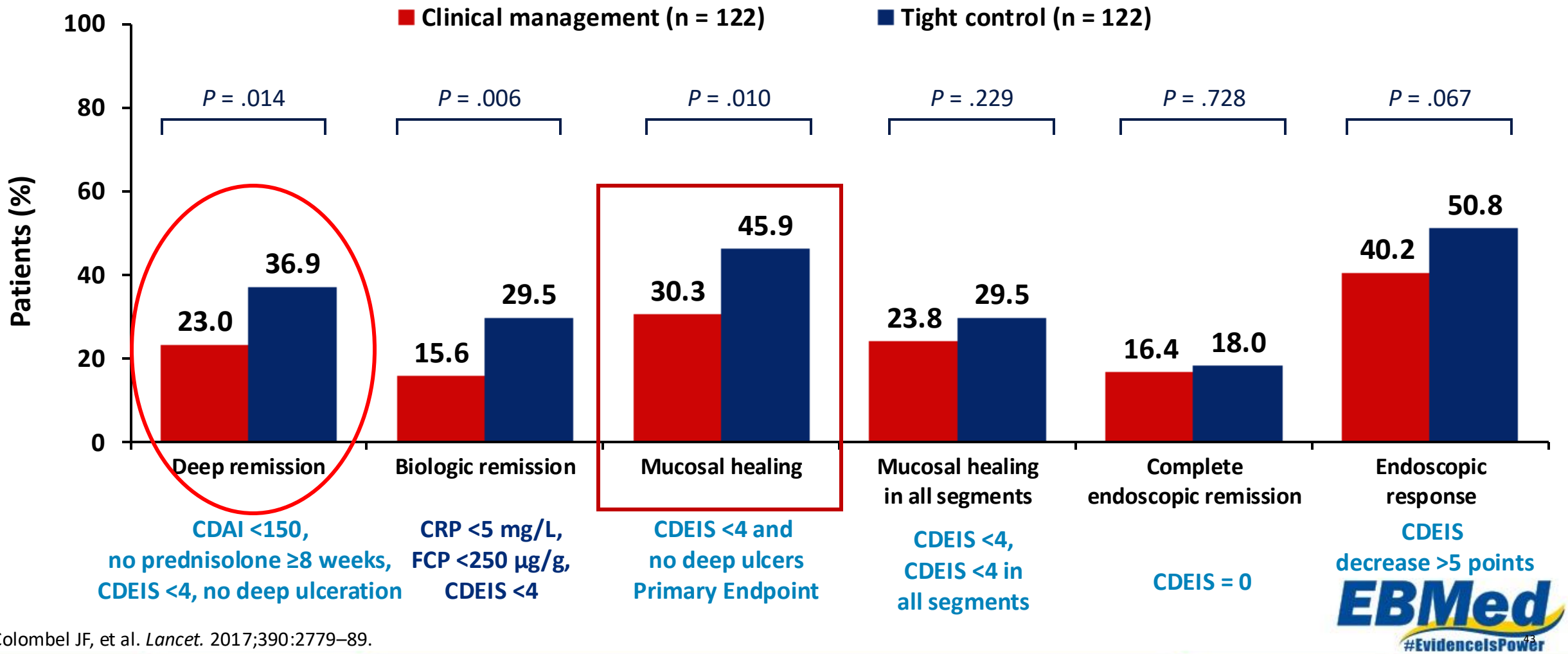
Therapeutic Ceiling in Clinical and Endoscopic Remission Results from CALM (Anti-TNF +/- AZA)



Colombel JF, et al. *Lancet.* 2017;390:2779–89.

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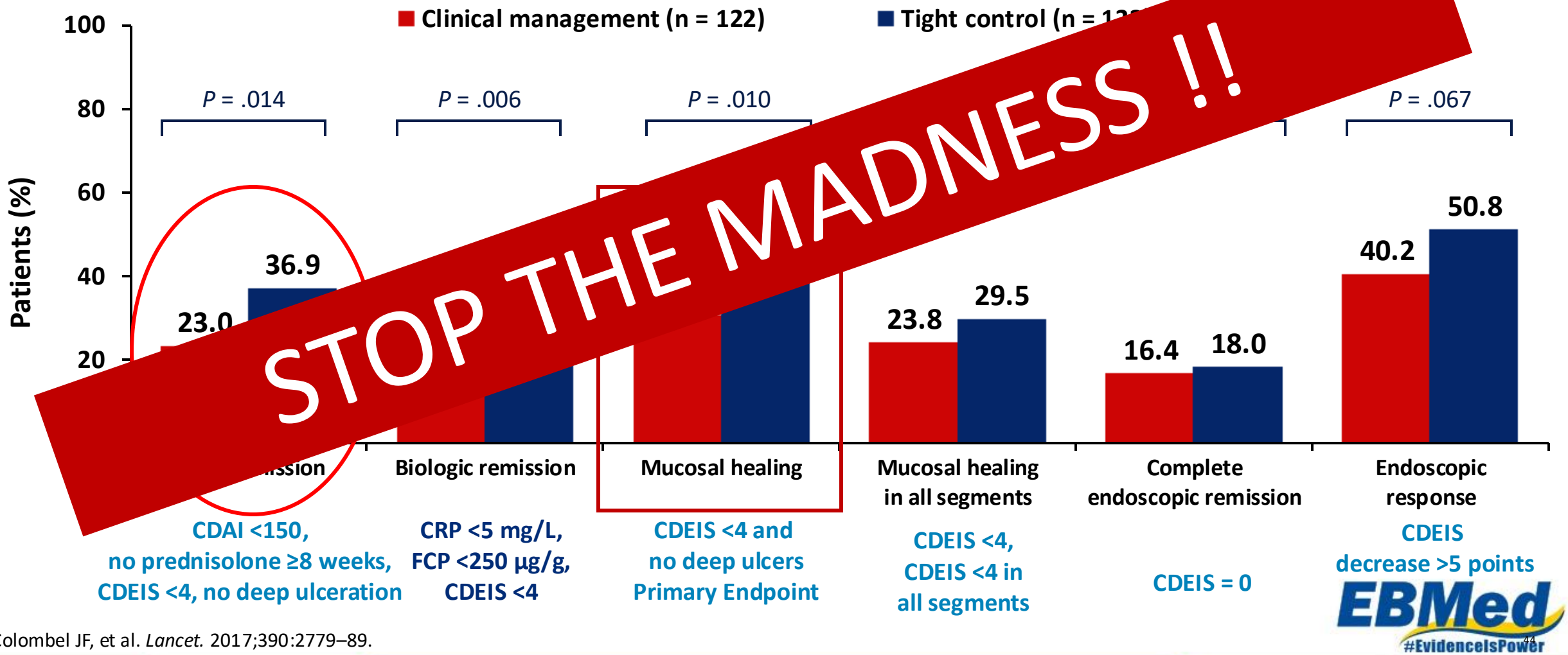
Therapeutic Ceiling in Clinical and Endoscopic Remission Results from CALM (Anti-TNF +/- AZA)



STOP THE MADNESS !!

Colombel JF, et al. *Lancet.* 2017;390:2779–89.

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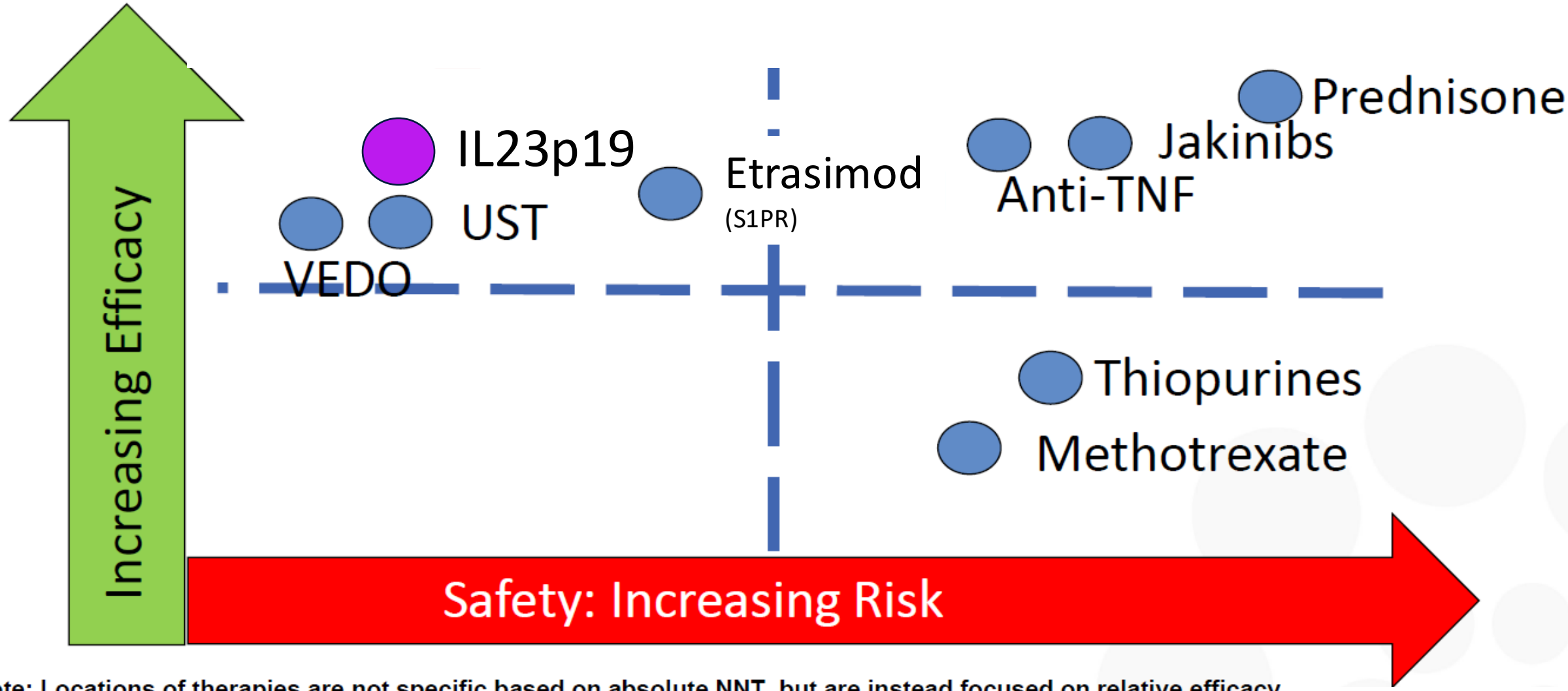
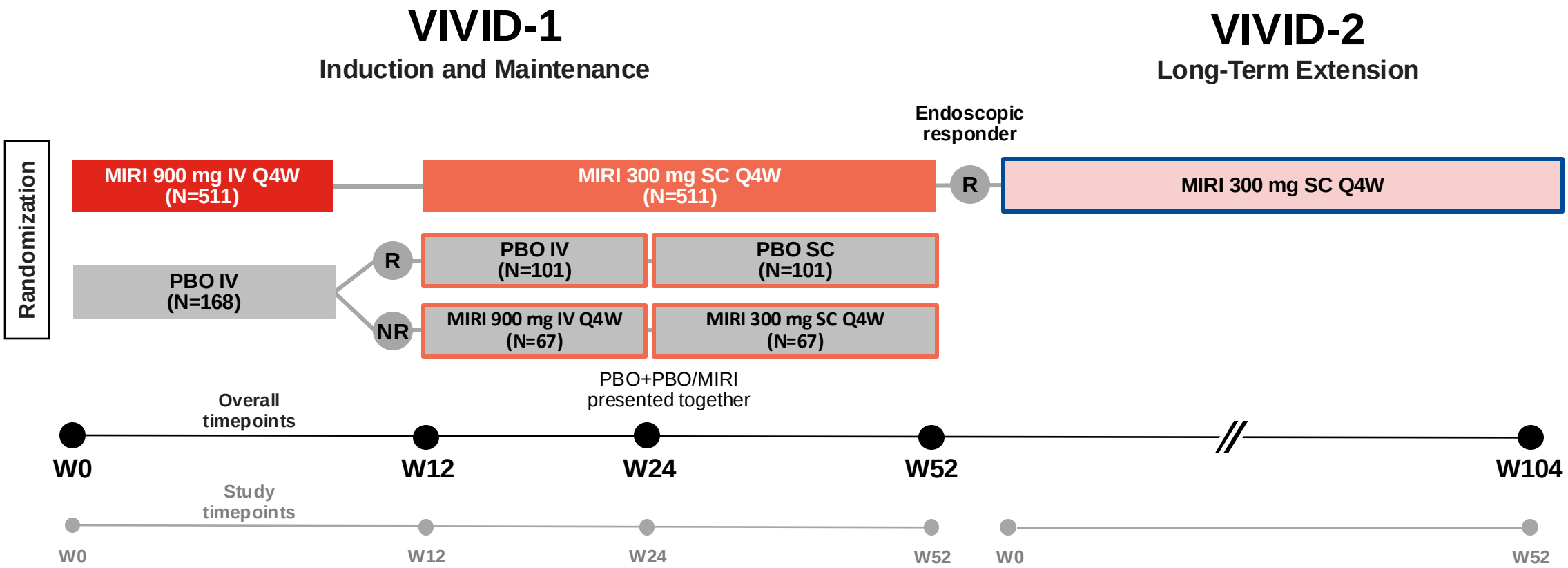
The Sweet Spot: High Efficacy AND Safety



Note: Locations of therapies are not specific based on absolute NNT, but are instead focused on relative efficacy in quadrants.
Slide courtesy of Millie Long, MD.

Mirikizumab in CD: VIVID 1-2 Study Design (Treat-Through Design and No suffering on placebo for a year !)



Ferrante M, et al. The Lancet 2024; 404: 2423 – 2436
Vermeire S, et al. JCC 2025;19: i91–i93

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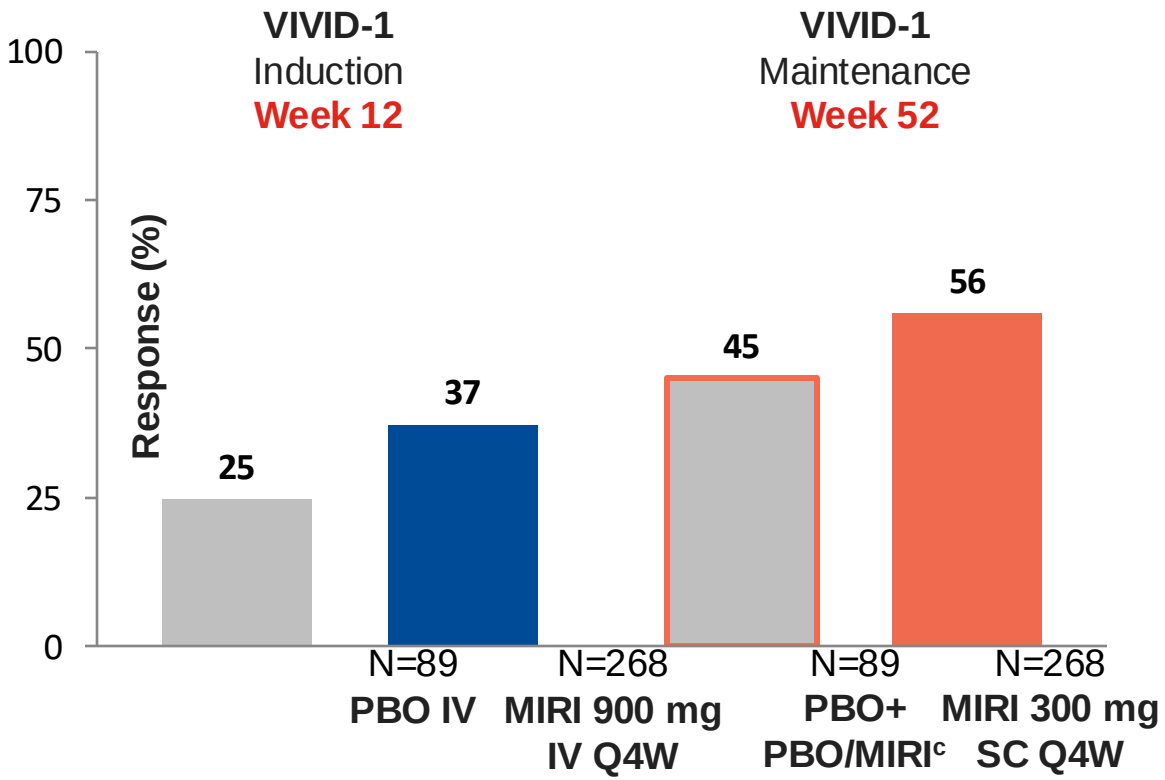
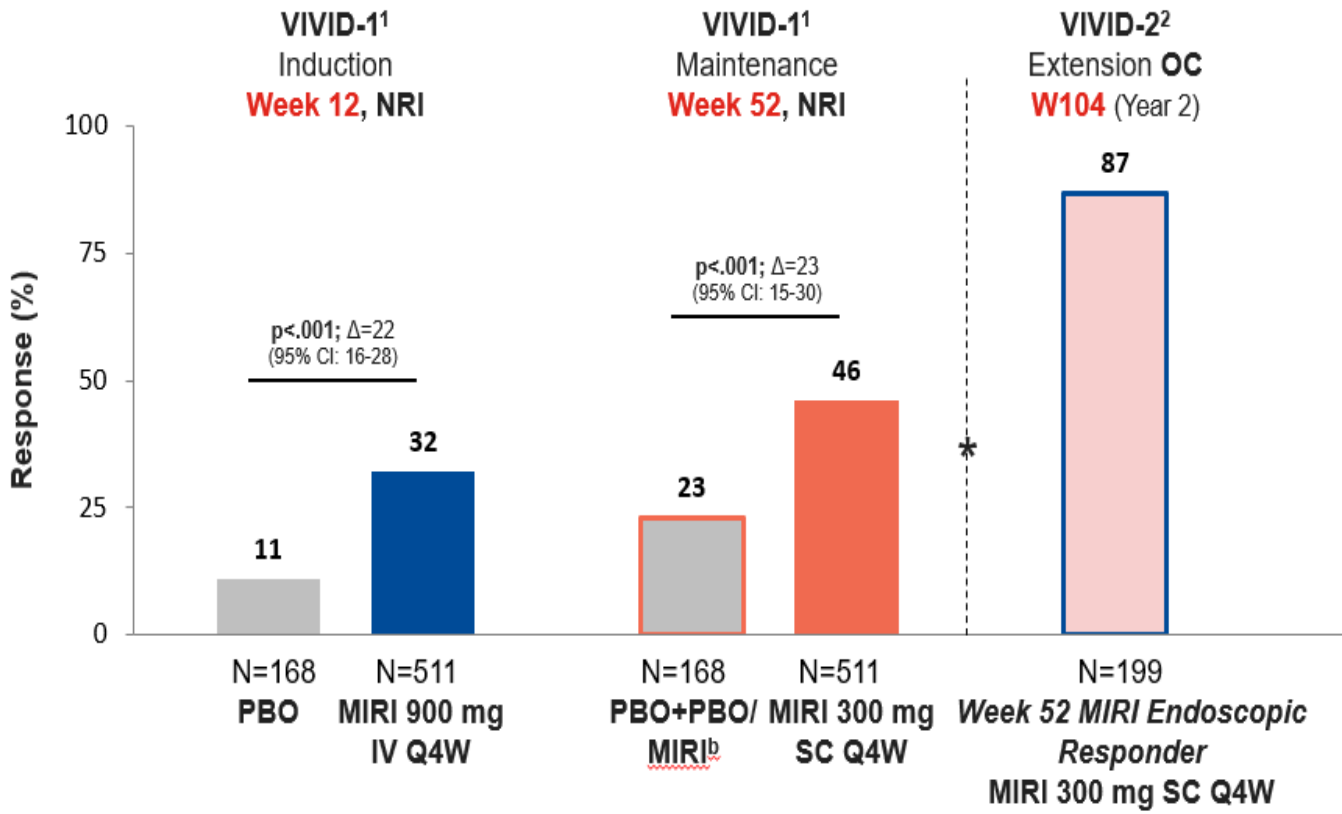
Mirikizumab in CD: VIVID 1-2: Weeks 12 and 52

Clinical Remission in Bio-Naive



Endoscopic Response



Clinical Remission: CDAI score < 150
Endoscopic Response: >50% reduction from baseline in SES-CD total score

Ferrante, MarcTron, Emiliano et al. The Lancet 2024; 404: 2423 – 2436
Vermeire S et al. J Crohns Colitis 2025;19: i91–i93

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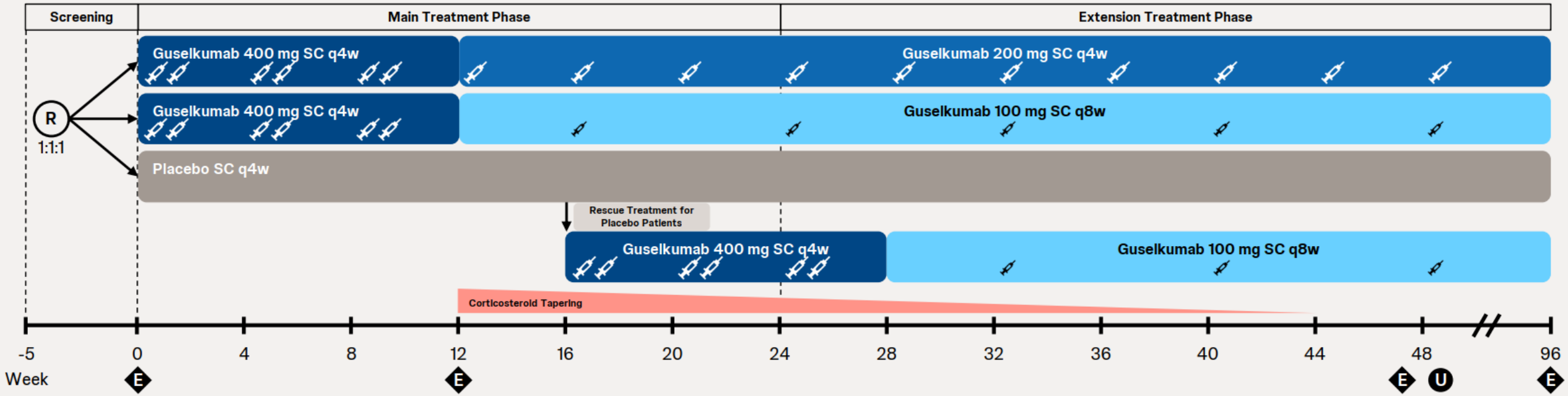
Mirikizumab in CD: Safety Data

	VIVID-1 and VIVID-2 MIRI 300 mg SC N=287, PY=589.7 n [EAIR][a]
Patients with ≥1 AE	249 [140.6]
Serious AE	32 [5.8]
AEs leading to discontinuation	4 [0.7]
Deaths	0
AEs of special interest	
Hepatic event (narrow)	31 [5.6]
Immediate hypersensitivity reaction	13 [2.3]
Serious infections	8 [1.4]
Opportunistic infections (narrow)	4 [0.7]
Adjudicated cerebrocardiovascular events	4 [0.7]
Adjudicated MACE	1 [0.2]
Malignancies	1 [0.2]
NMSC	1 [0.2]

Guselkumab in CD: GRAVITI (SQ induction)
(Treat-Through Design and No suffering on placebo for a year !)



Randomization stratified by:
- CDAI score (≤300 or >300)
- SES-CD (≤12 or >12)
- Prior BIO-failure status

: Guselkumab 100 mg

: Guselkumab 200 mg

E : Endoscopy

U : Study unblinding

Rescue Treatment Criteria
- CDAI score > 220 and < 70-point reduction from baseline CDAI at both Weeks 12 and 16 **OR**
- SES-CD score increase by ≥ 50% from baseline at Week 12

Rescue Treatment for Guselkumab Arms: Sham matching placebo SC to maintain the blind

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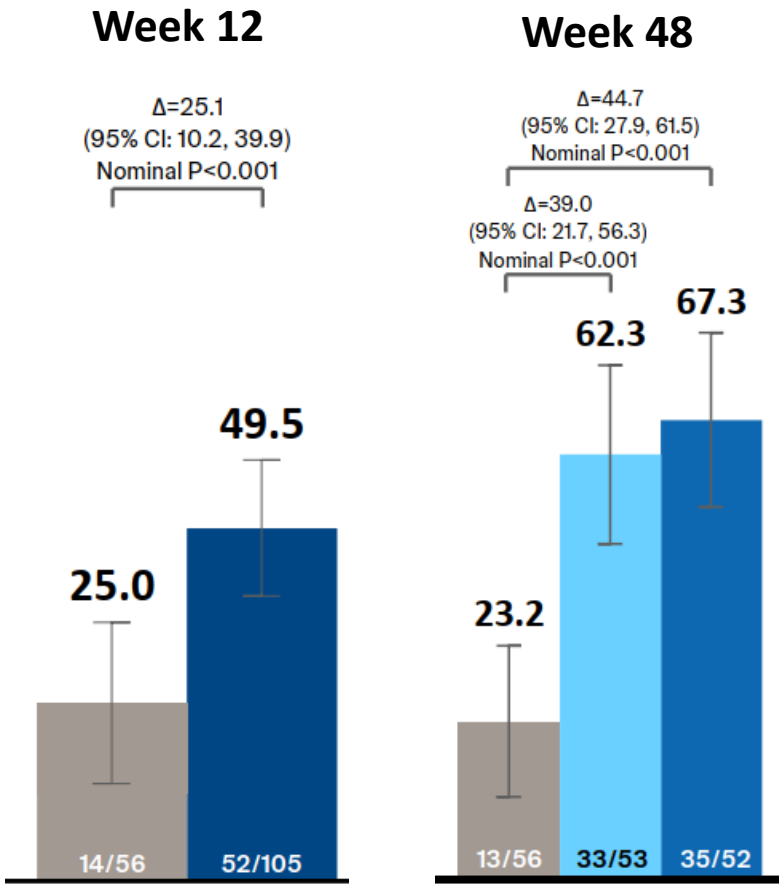
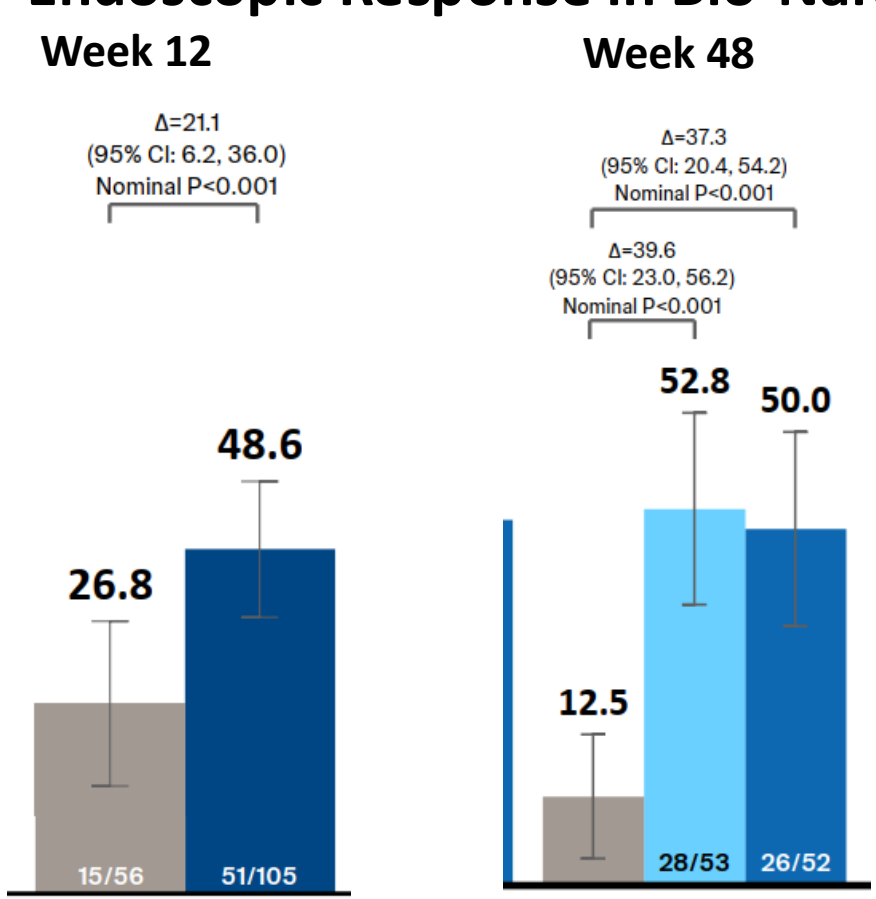
Guselkumab in CD: GRAVITI Weeks 12 and 48

Clinical Remission in Bio-Naive



Endoscopic Response in Bio-Naive



Placebo SC | GUS 400 mg SC q4w → GUS 100 mg SC q8w | GUS 400 mg SC q4w → GUS 200 mg SC q4w

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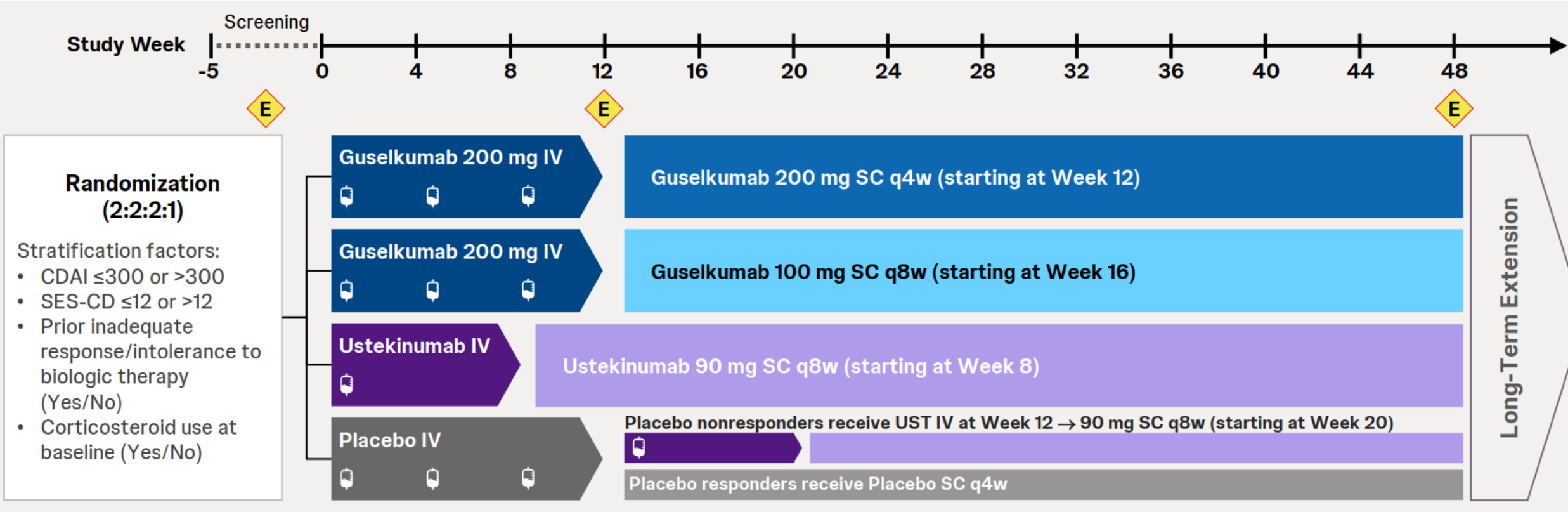
Guselkumab in CD: GALAXI 2-3 (IV induction) (Treat-Through Design and no suffering on placebo x 1 year)



Danese S, et al. *The Lancet*. 2024;9:133-146

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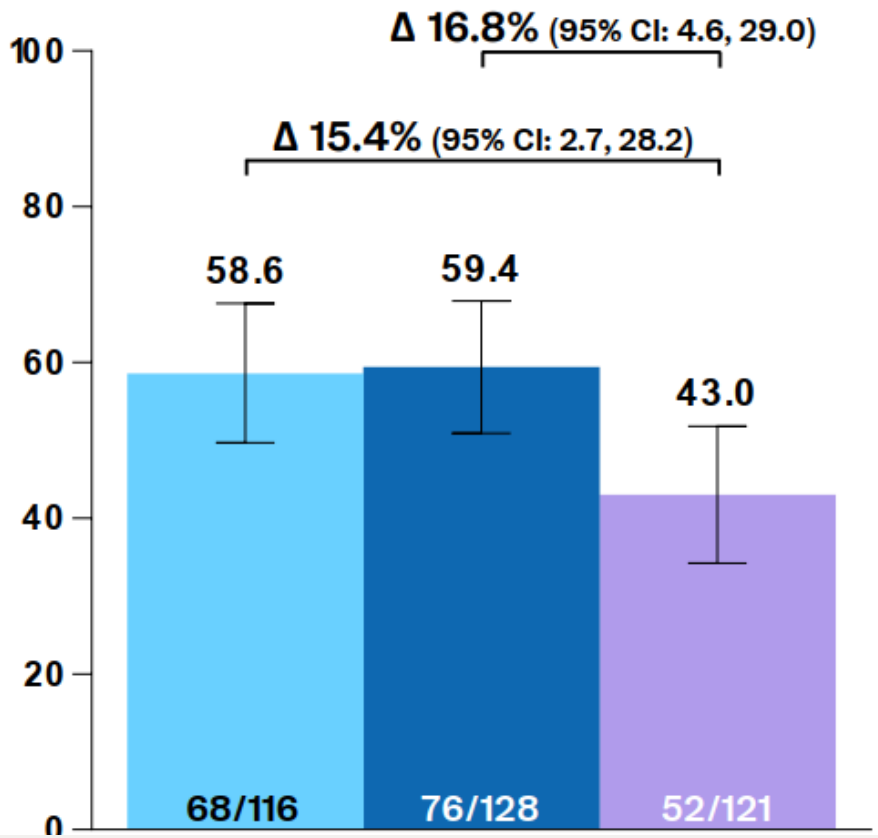
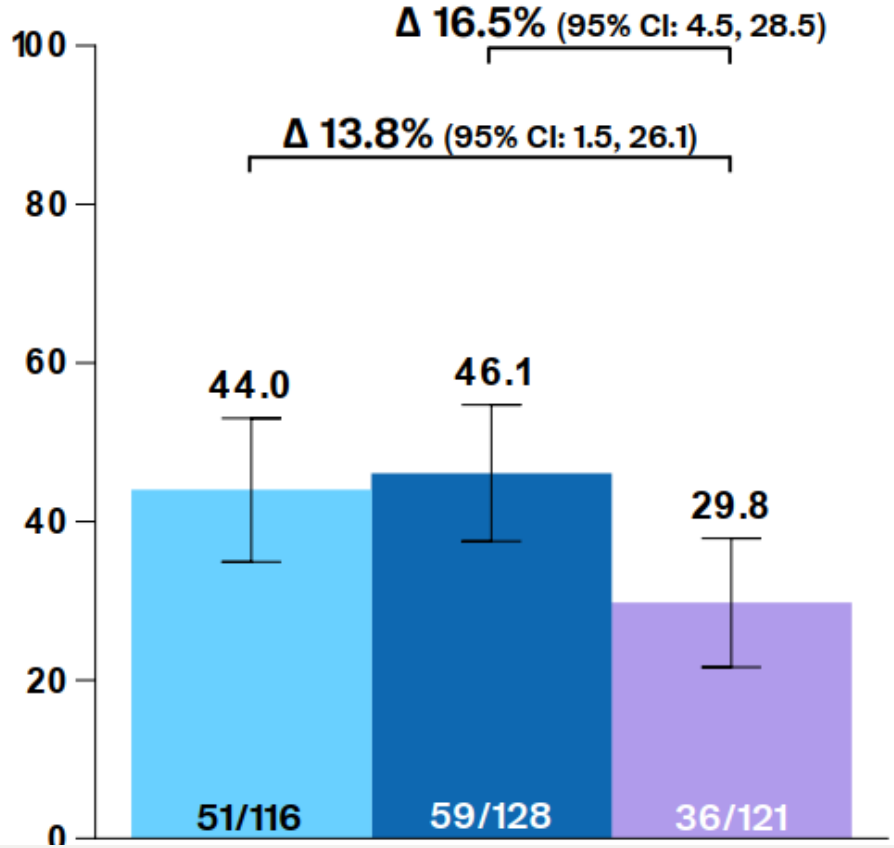
GUS vs UST in Bio-Naïve: Week 48

Endoscopic Response



Endoscopic Remission



Guselkumab 200 mg IV q4w → 100 mg SC q8w | Guselkumab 200 mg IV q4w → 200 mg SC q4w | Ustekinumab ~6 mg/kg IV → 90 mg SC q8w

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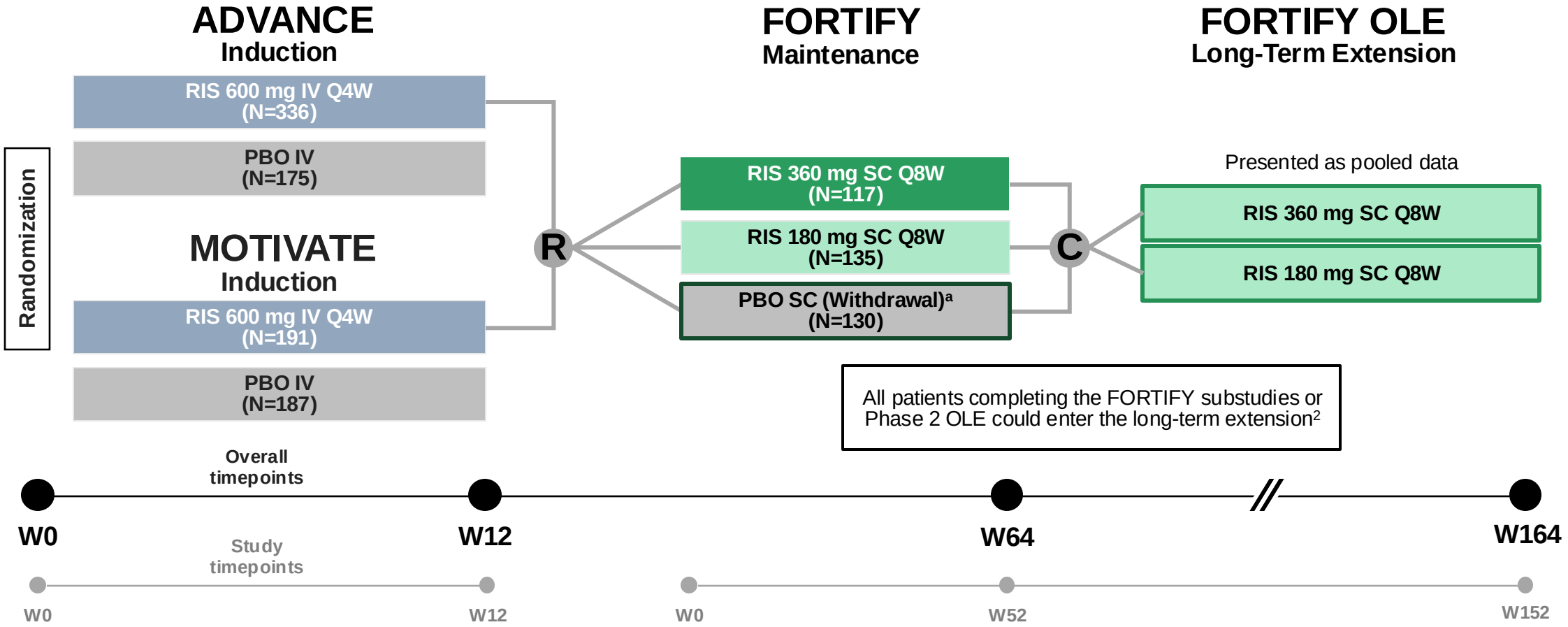
Risankizumab in CD: Study Design



D'Haens, Geert et al. The Lancet 2022;399:2015 – 2030
Ferrante M et al. J Crohns Colitis 2024;18:168-170

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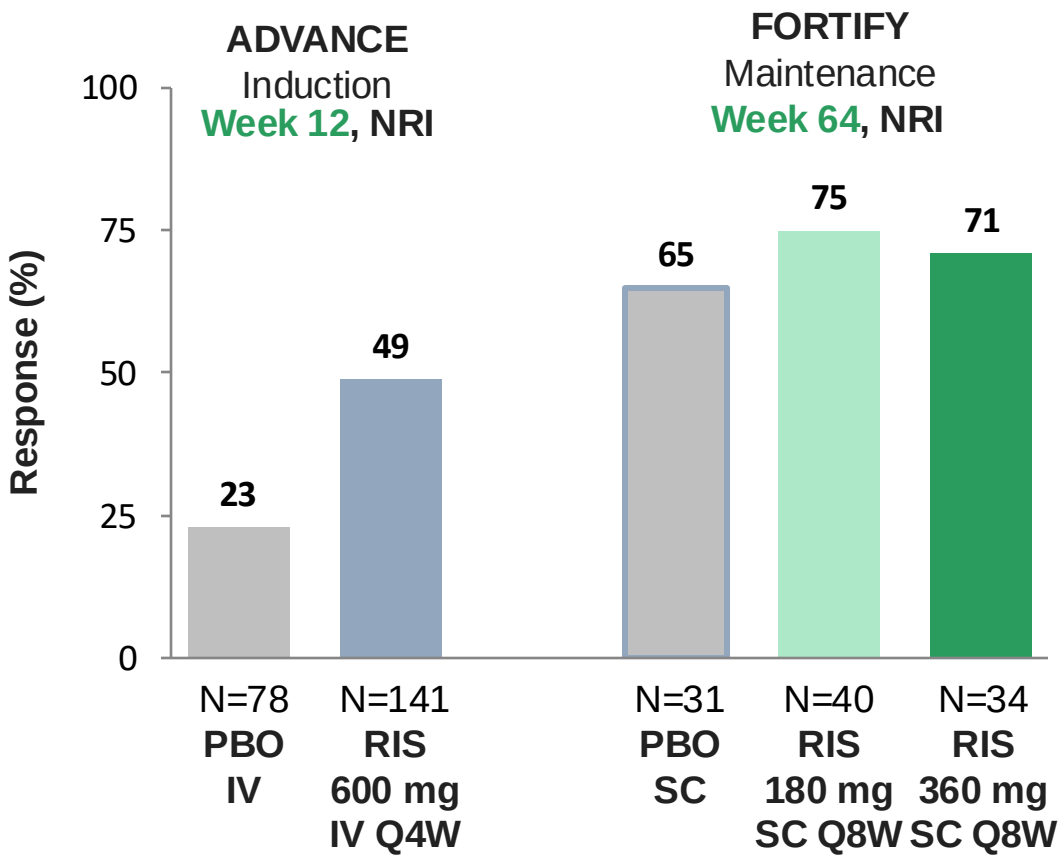
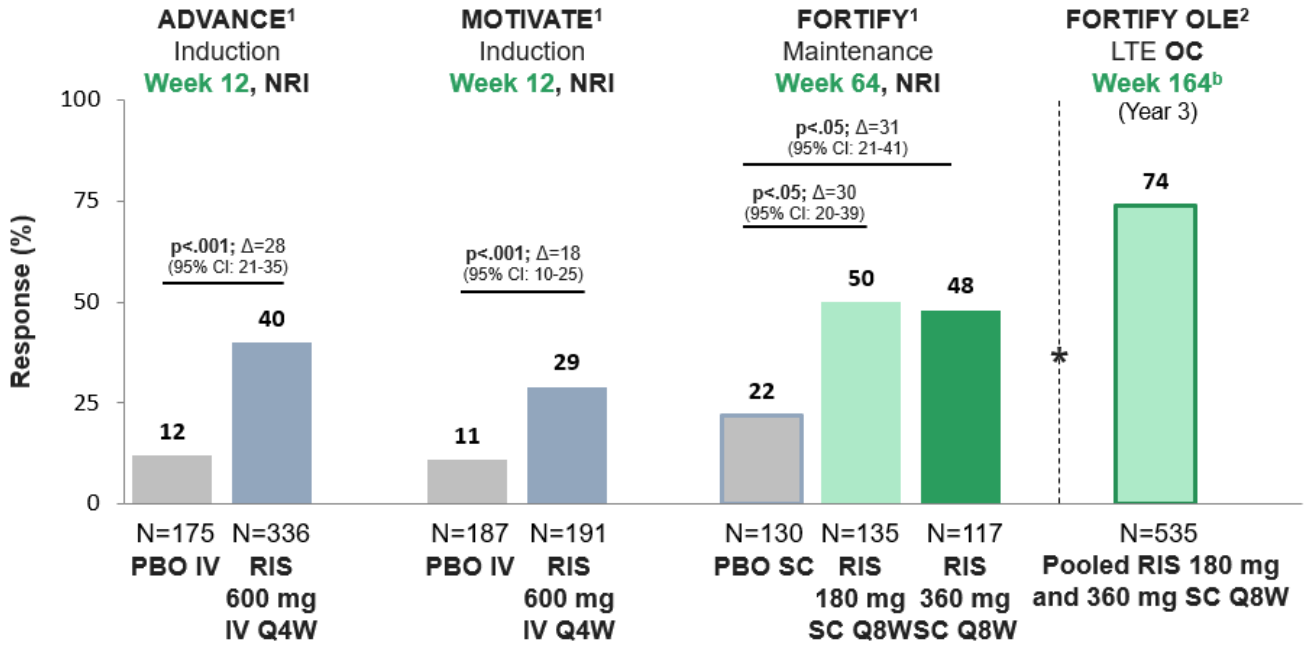
Risankizumab in CD: Weeks 12 and 64

Clinical Remission in BioNaive



Endoscopic Response



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D'Haens, Geert et al. The Lancet 2022;399:2015 – 2030
Ferrante M et al. J Crohns Colitis 2024;18:168-170

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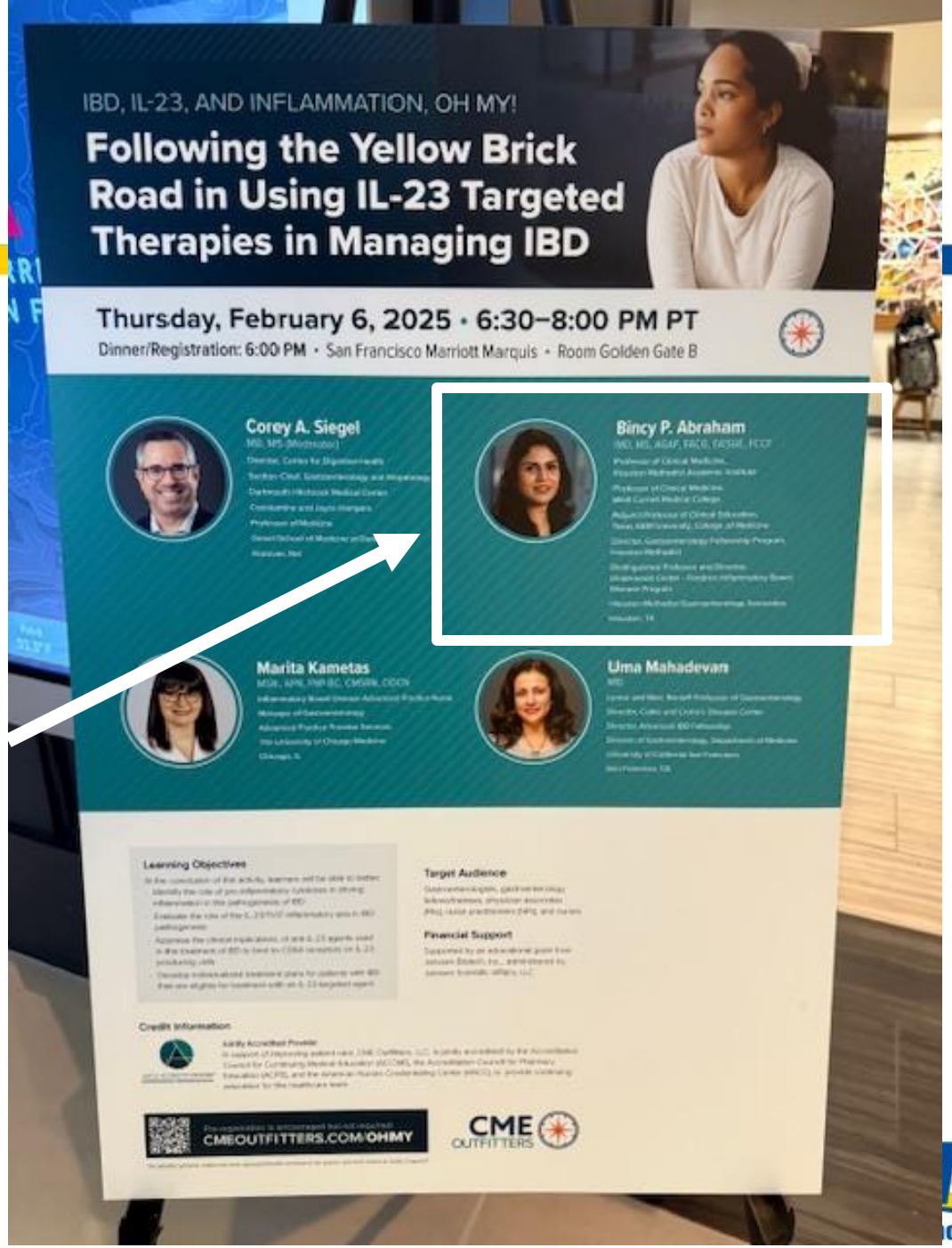
Here Come the IL-23p19 Inhibitors:
Exploring New Treatments in IBD
THURSDAY, FEBRUARY 6, 2025 | 7:00 – 8:00 PM PST
SAN FRANCISCO MARRIOTT MARQUIS | SALON 7
Faculty
Vipul Jairath
Aline Charabaty
Agenda
Learning Objectives


IBD, IL-23, AND INFLAMMATION, OH MY!
Following the Yellow Brick Road in Using IL-23 Targeted Therapies in Managing IBD
Thursday, February 6, 2025 · 6:30–8:00 PM PT
Dinner/Registration: 6:00 PM · San Francisco Marriott Marquis · Room Golden Gate B
Corey A. Siegel
Bincy P. Abraham
Marita Kametas
Uma Mahadevan
Learning Objectives
Target Audience
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Aline Charabaty,...
@DCharabaty

Promote

Attending #CCCongress25? Join me & @vipuljairath to review what #IL23p19 can do for your #IBD pts!

✅Risa, Miri, Gus
✅Clin remission in bio-exposed & naive CD & UC
✅Endo Response

🗓️Thurs Feb6, 6.45pm
📌Mariott Marquis Salon7
🌮Dinner included

😉Matching outfits not required

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Uma Mahadevan
@UmaMahadevanIBD

Or you could come to the better one! @DrCoreySiegel @IBD_Houston 😀😀

Aline Charabaty, MD... · 2/6/25
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Bincy Abraham, MD, MS
@IBD_Houston

I second that! Unshameful plug. No bias!! Please come see us tonight!!

Uma Mahadevan @U... · 2/6/25
Or you could come to the better one! @DrCoreySiegel @IBD_Houston 😀😀 pic.x.com/QBFf2S1U04 x.com/DCharabaty/sta...

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So…. Let’s Vote Honest – No Bias

- IL23 are the FIRST line therapy for mod-severe Crohn’s disease
  - Safe, Effective, Convenient (and bonus: ethical RCT design !)

- Everything I learned about debating …. I learned it from Dr Bincy Abraham

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Anti-Integrin (Vedo) & Anti-IL12/23 (UST)

The good

VEDO

- Good safety profile
- No increased risk of infection, TB, skin cancer

UST

- Good Safety profile
- Convenient

The bad and ugly

VEDO

- Infusion access
- Or SQ every 2 weeks
- Slower onset of action in Crohns?
- Decreased efficacy in TNFi-exposed

UST

- Not covered by Medicare
- Often need to change from SQ every 8 weeks to every 4 weeks = insurance battle

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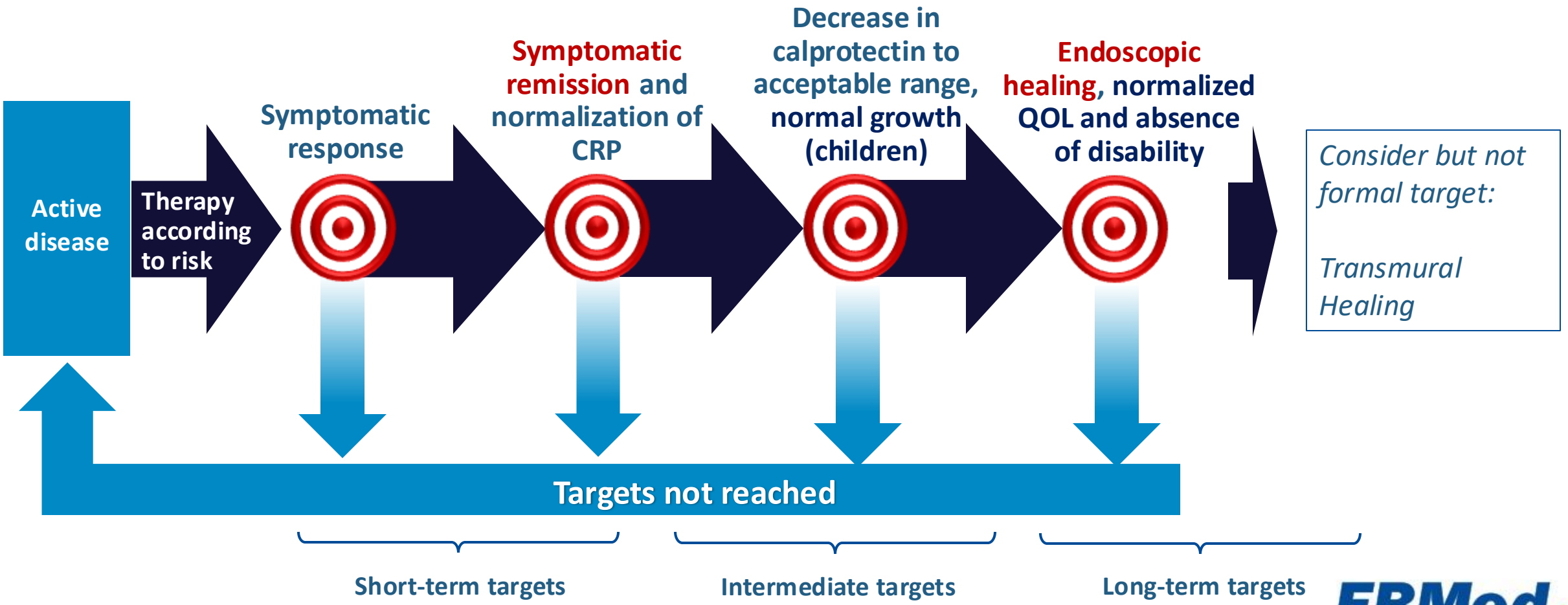
STRIDE II: Selecting Therapeutic Targets in Crohn's Disease



Turner D, et al. *Gastroenterology.* 2021 Apr;160(5):1570-1583.

IL-23 Should NOT be First Line for Moderate-Severe Crohn's Disease

Why you should listen to what Aline has to say:

"The Dr. Aline Charabaty"

- IL-23 monoclonal antibodies
  - Excellent efficacy
  - Targeted treatment
  - Excellent safety profile
  - Prior data from psoriasis & psoriatic arthritis
  - …

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Moderate to Severe Crohn's Disease Patients

Come in all shapes and sizes

- No one size fits all!
- Multiple FDA options for treatment
- Some have comorbidities
- Some have perianal / fistulizing disease

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The IBD Treatment Landscape

Conventional Therapies

Corticosteroids
Budesonide
Prednisone

Aminosalicylates (5-ASA)
Balsalazide
Mesalamine
Sulfasalazine
Olsalazine

Immunomodulators
Methotrexate
6-Mercaptopurine
Azathioprine
Tacrolimus
Cyclosporine

Advanced Therapies

TNF-α Inhibitors
Adalimumab
Certolizumab pegol
Golimumab
Infliximab

Integrin Inhibitors
Natalizumab
Vedolizumab

IL-23 Inhibitors
Risankizumab
Guselkumab
Mirikizumab

IL-12/23 Inhibitors
Ustekinumab

JAK Inhibitors
Tofacitinib
Upadacitinib

S1PR1/5 Agonists
Ozanimod
Etrasimod

FDA. www.accessdata.fda.gov. Accessed 9/21/2022.

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The Evolving IBD Therapeutic Landscape: FDA-Approved and Late-Stage Targeted Therapies

Type	Class	Therapy	Target	Crohn's Disease	Ulcerative Colitis
Biologic	TNF-α blockers	Adalimumab	TNF-α	6 yrs and older	5 yrs and older
		Certolizumab pegol		Adults	
		Golimumab			Adults
		Infliximab		6 yrs and older (IV) Adults (SC)	6 yrs and older (IV) Adults (SC)
	Integrin blockers	Natalizumab	α4β1	Adults with IR to TNFi or conventional treatment	
		Vedolizumab	α4β7	Adults (IV and SC)**	Adults (IV and SC)**
	Interleukin inhibitors	Guselkumab	IL-23	Phase 3	Approved 2024 for adults
		Mirikizumab	IL-23	Approved 2025 for adults	Approved 2023 for adults
		Risankizumab	IL-23	Approved 2022 for adults	Approved 2024 for adults
		Ustekinumab	IL-12/23	Adults	Adults
Small Molecule	JAK inhibitors	Tofacitinib	JAK1/3		Adults with TNFi-IR
		Upadacitinib	JAK1	Approved 2023 for adults with TNFi-IR	Approved 2022 for adults with TNFi-IR
		Ivarmacitinib	JAK1		Phase 3
	S1PR agonists	Etrasimod	S1PR 1,4,5	Phase 3	Approved 2023 for adults
		Ozanimod	S1PR 1,5	Phase 3	Approved 2021 for adults

**SC administration approved in 2023 as maintenance therapy following IV induction; IR = Inadequate Response; IL = Interleukin; JAK = Janus Kinase; TNF = Tumor Necrosis Factor; S1PR = Sphingosine 1-Phosphate Receptor.
FDA. www.accessdata.fda.gov. Accessed 7/24/24.

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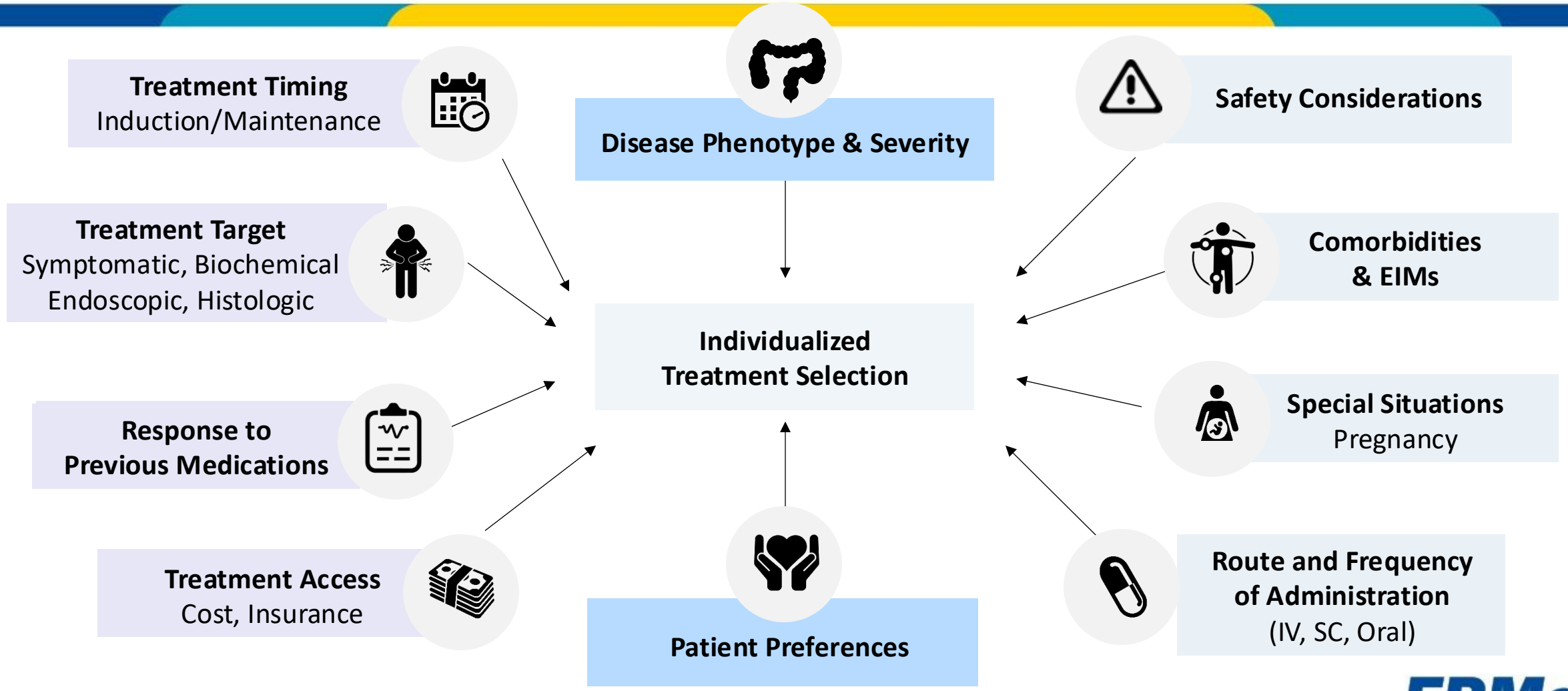
Factors to Consider in Treatment Selection for IBD



EIM = Extra-Intestinal Manifestation; IV = Intravenous; SC = Subcutaneous

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Extra-Intestinal Manifestations (EIMs) Can Influence Treatment Selection

EIMs		First-Line Therapy	Second-Line Therapy	Third-Line Therapy
Musculo-skeletal	**Axial SpA**	COX-2 inhibitors; **TNFi**	**TNFi**	
	Peripheral SpA	Systemic/local steroids; SSZ; MTX; COX-2 inhibitors	**TNFi**	anti-IL-12/23; JAKi
Cutaneous	**Psoriasis**	Topical steroids, Vitamin D derivatives, TAC	MTX; CYC	TNFi; anti-IL-12/23; anti-IL-23
	Erythema nodosum	Steroids	Systemic management of IBD	
	Pyoderma gangrenosum	Topical steroids or TAC	Systemic steroids; Calcineurin inhibitor; **TNFi;** CYC or TAC; AZA or MTX	
	Hidradenitis suppurativa	Topical antibiotics; Oral tetracycline	Antibiotics; **TNFi**	
Ocular	**Episcleritis**	Self-limiting	Topical steroids	
	Scleritis	Dexamethasone eye drops	Systemic steroids	
	Anterior uveitis	Topical/systemic steroids	**TNFi**	

In all cases, active intestinal disease activity, if present, should have priority in the management of EIMs.

AZA = Azathioprine; COX = Cyclooxygenase; CYC = Cyclosporine; IL = Interleukin; JAKi = Janus Kinase inhibitor; MTX = Methotrexate; SpA = Spondyloarthritis; SSZ = Sulfasalazine; TAC = Tacrolimus; TNFi = Tumor Necrosis Factor inhibitor; FDA. www.accessdata.fda.gov. Accessed 9/18/2021. Jansen FM, et al. *United European Gastroenterology Journal.* 2020; 8(9):1031-1044.

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Characteristics of TNF Inhibitors for IBD

Class	Therapy	IBD Indication	Route	Dosing Schedule*	Additional Indications
TNF-α Blockers	Adalimumab	CD/UC	SC (pre-filled pen or syringe)	Q2W	**RA, JIA, PsA, PsO, AS, HS, uveitis**
	Certolizumab pegol	CD	SC (pre-filled syringe)	Q4W	**RA, polyarticular JIA, PsA, PsO, AS, nr-AxSpA**
	Golimumab	UC	SC (autoinjector or prefilled syringe)	Q4W	**RA, PsA, AS**
	Infliximab	CD/UC	IV	Q8W	**RA, PsA, PsO, AS**
	Infliximab	CD/UC	SC (pre-filled pen or pre-filled syringe)	Q2W**	–

*Consult prescribing information for full dosing instructions, warnings, and contraindications; **Maintenance treatment only, starting at week 10; all patients must first complete an IV induction regimen with infliximab first; RA = rheumatoid arthritis; JIA = juvenile idiopathic arthritis; PsA = psoriatic arthritis; PsO = psoriasis; AS = ankylosing spondylitis; HS = hidradenitis suppurativa; nr-AxSpA = nonradiographic axial spondyloarthritis

FDA. www.accessdata.fda.gov. Accessed 11/11/24; Feig VR, et al. *Lancet*. 2024;77:102850.

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So why are you trying to put a square peg in a round hole?

IL23 inhibitors

"Dr. Aline Charabaty"

Moderate to Severe CD Patients

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Show us the data Aline!

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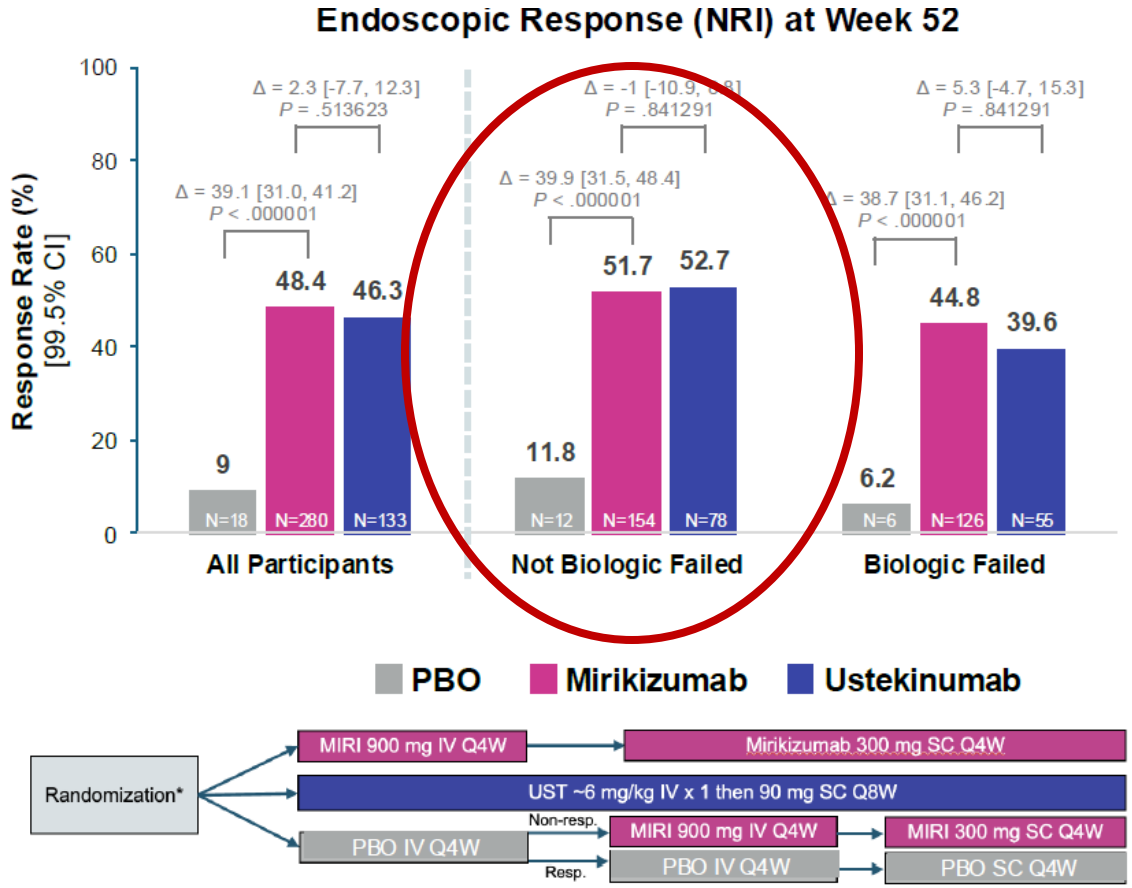
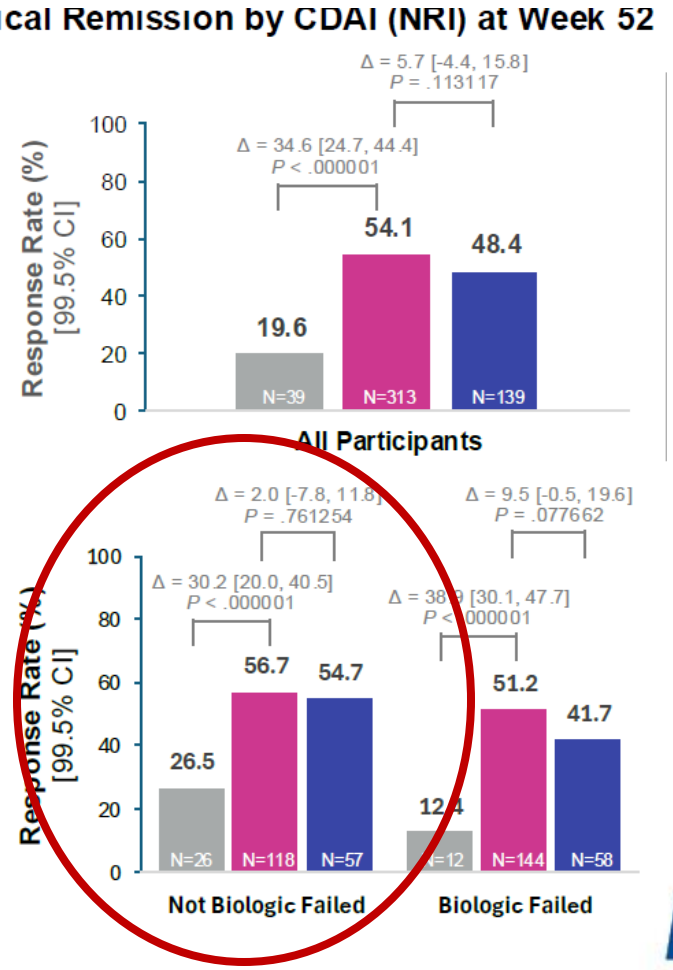
I don’t have the data!
There are NO head to head studies of IL23 inhibitors vs antiTNFs, anti-integrins, other MOAs.

Are IL23i Better?

VIVID-1: MIRI vs UST in Moderate to Severe CD





Ferrante M, et al. *Lancet*. 2024;404(10470):2423-2436.

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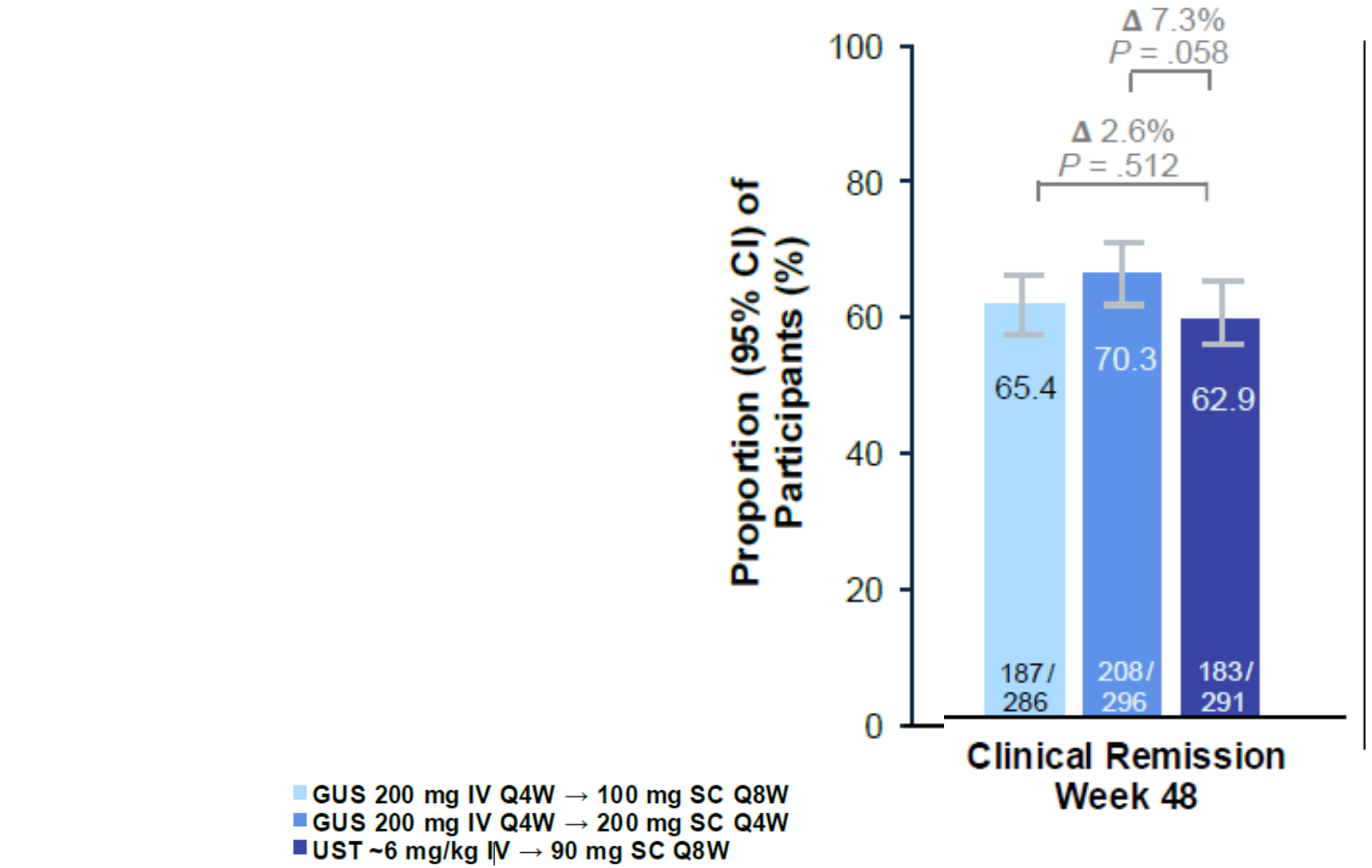
Are IL23i Better?

GUS vs UST in CD at 48 Weeks: GALAXI 2,3



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Benefits of Other Medications:

ACG & AGA GUIDELINES:

ANTI-TNFS RECOMMENDED FOR PERIANAL FISTULIZING CROHN'S DISEASE

LOWER COSTS

BIOSIMILARS!

EASIER INSURANCE COVERAGE

DOSE OPTIMIZATION & PERSONALIZATION:

THERAPEUTIC DRUG MONITORING AVAILABLE FOR ANTI-TNFS, VDZ, UST.

DECADES OF DATA!!:

INFLIXIMAB APPROVED IN 1998 !

KNOWN SAFETY AND EFFICACY:

MAJORITY OF OUR PATIENTS ARE DOING WELL!

REDUCE RISKS:

VACCINATIONS

LAB MONITORING,

PRE-TEST FOR INFECTIONS (TB, HBV)

TREAT IF FOUND.

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Many Options: But ~~A~~IL23i is Not Always the Best

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Many Options: But A~~line~~ IL23i is Not Always the Best

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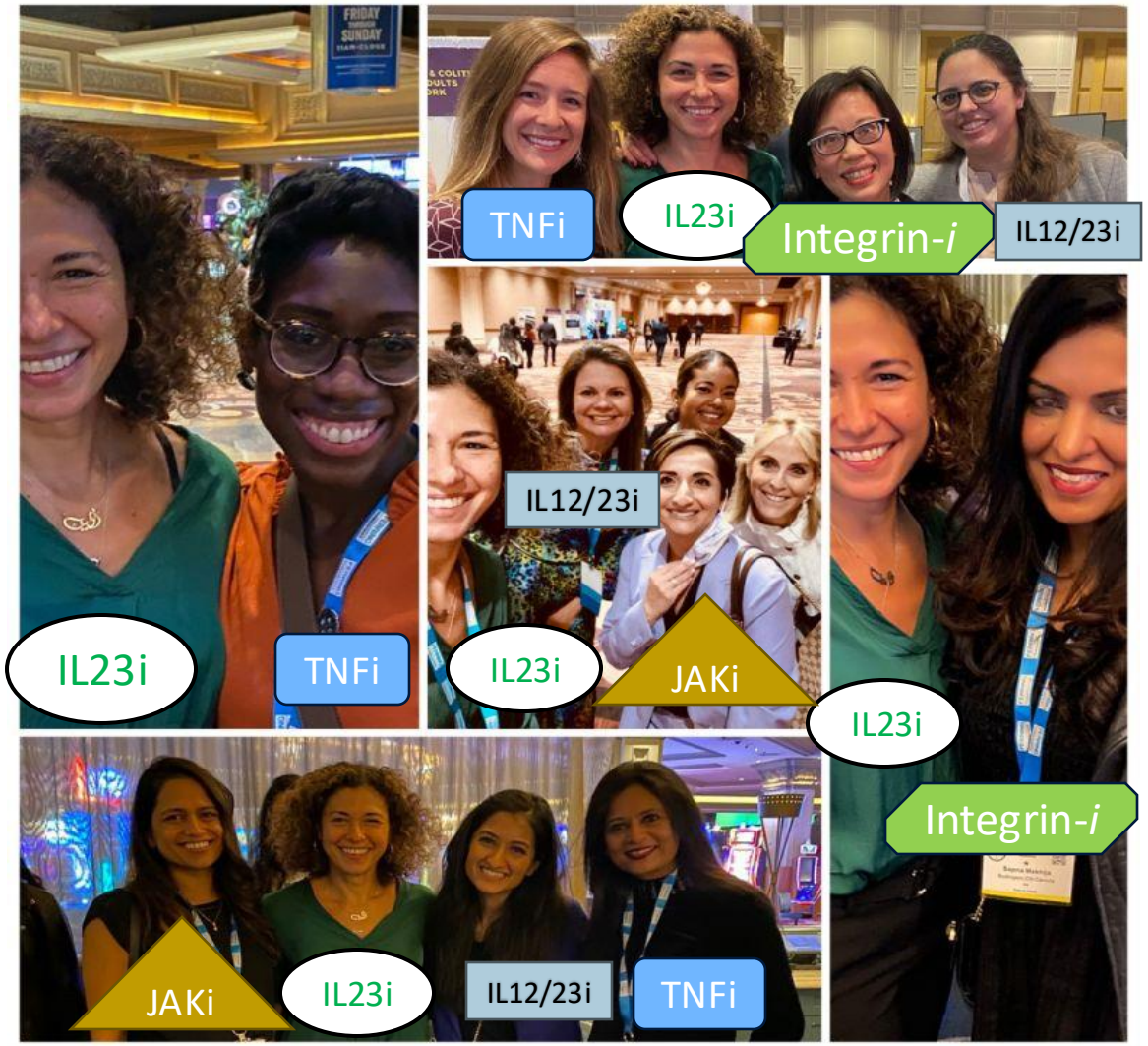
Many Options: But ~~A~~line is Not Always the Best

IL23i



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Choosing Therapy in CD: CALL to ACTION!

Just because you have a new toy…

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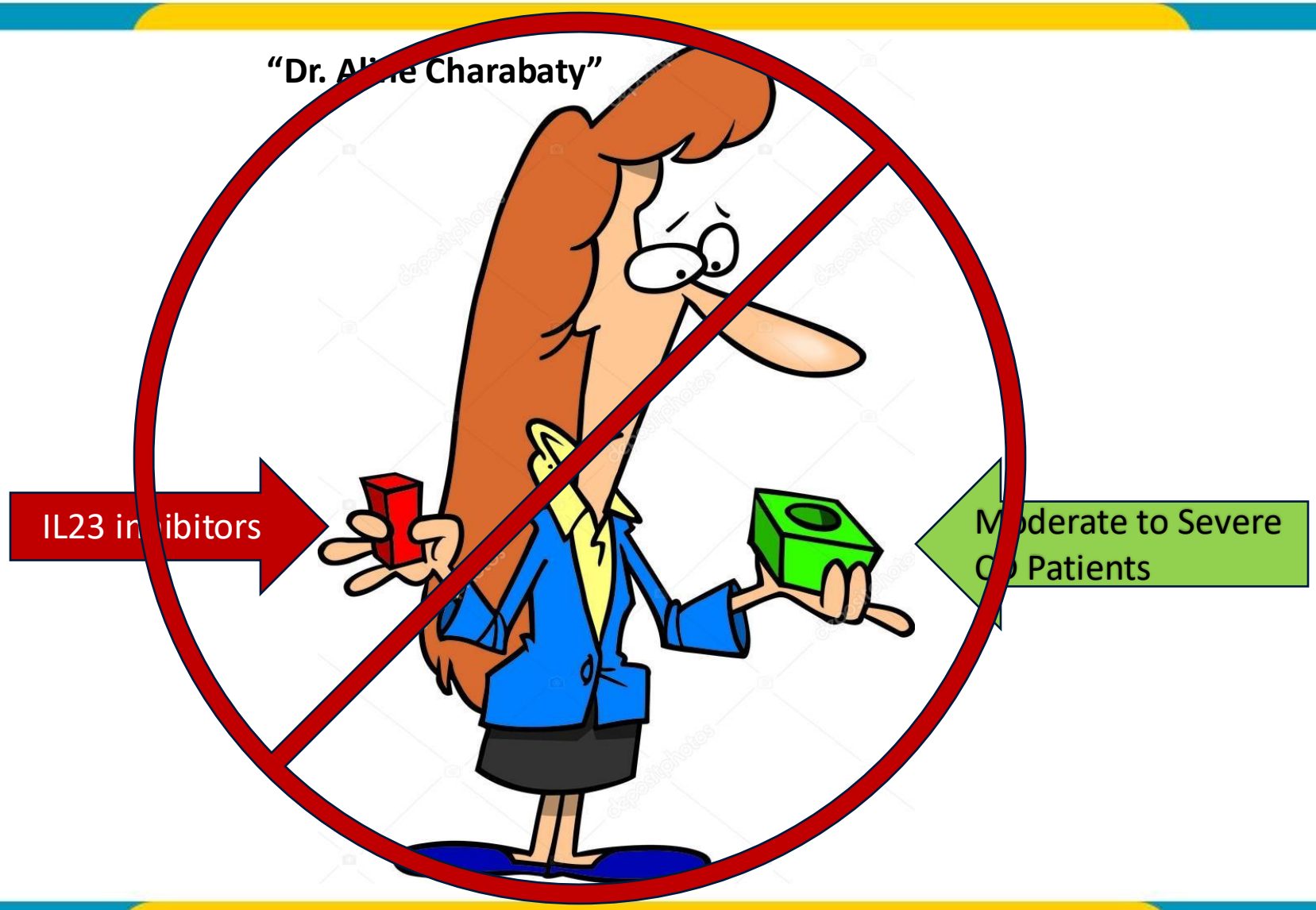
Choosing Therapy in CD: Don’t be like Aline:



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Choosing Therapy in CD: Fit the Puzzle Well

DRUG

Efficacy

Indication

Safety

Infection
Cancer
Specific concerns by agent or mechanism

PATIENT

Individual Characteristics

CD extent
Disease behavior/complication
Disease severity
Early vs late
EIMs
Prior treatment success or failure

Choose the BEST drug for your patient!
IL-23i should NOT ALWAYS be First-Line Therapy

EIM = extraintestinal manifestations; TDM = therapeutic drug monitoring.

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Case Studies in IBD

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POUCH FUNCTION & COMPLICATIONS

Katie Dunleavy, MB BCh BAO

Advanced Inflammatory Bowel Disease Fellow

Mayo Clinic, Rochester, MN

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CONFLICTS OF INTEREST

None

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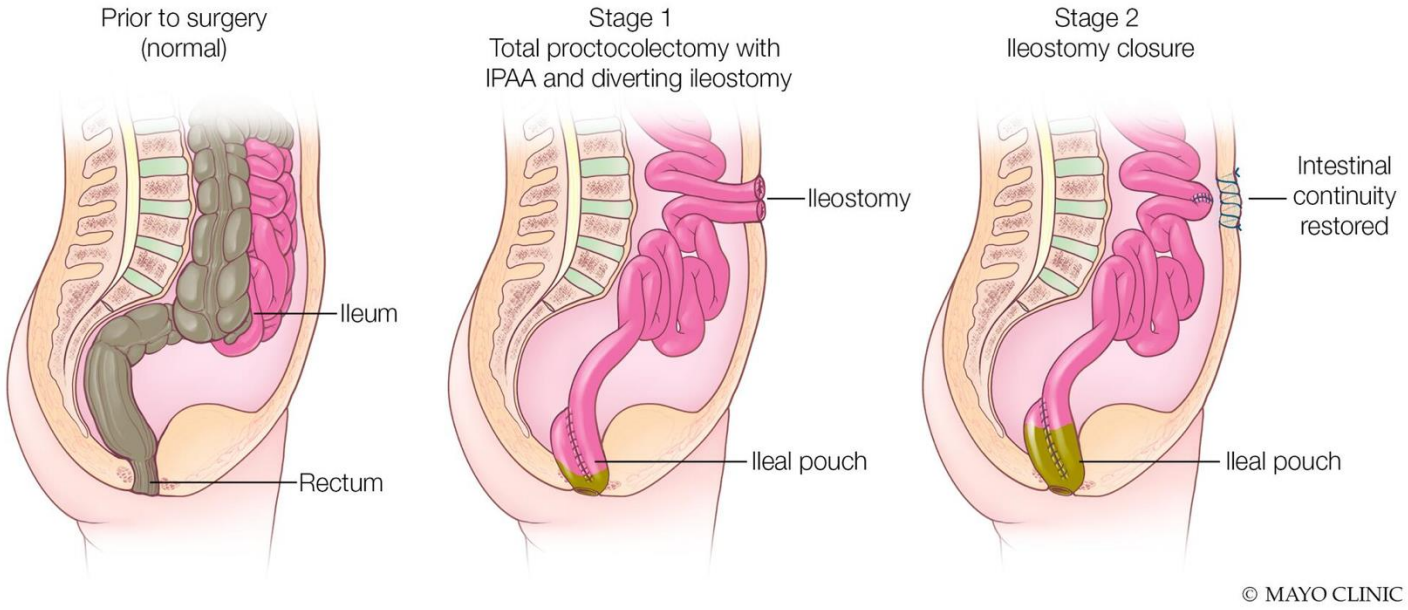
MEET SARAH

- 27-year-old woman with history of ulcerative colitis
- 8-10 BM daily, loose, moderate urgency, hematochezia
- She is hospitalized. Infections rule out. On hospital day 3 no response to steroids.
- Prior meds: 5-ASA, infliximab, upadacitinib, ustekinumab, vedolizumab
- Patient decides to have surgery and undergoes a total proctocolectomy with ileal pouch anal anastomosis (IPAA)

QUESTION 1

How do you counsel patients on function and complications after total proctocolectomy with IPAA?



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POUCH COMPLICATIONS

Inflammatory/ Infectious

- Pouchitis
- Crohn's
- Cuffitis
- C difficile

Surgical/ Mechanical

- Leak
- Abscess
- Sinus
- Fistula
- Stricture
- SBO
- Prolapse

Functional

- Dyssynergic defecation
- Irritable pouch syndrome
- Pouchalgia fugax

Dysplasia/ Neoplasia

- Dysplasia or cancer of pouch
- Dysplasia or cancer of anal transition zone

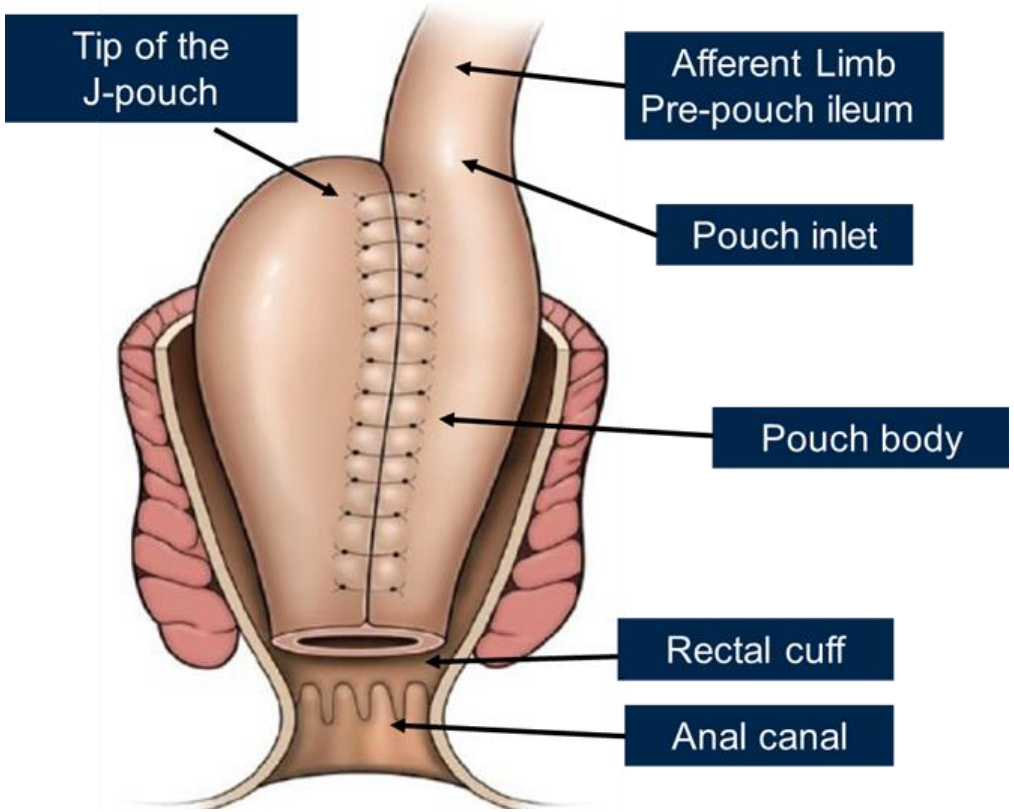
Quinn KP, et al. *Inflamm Bowel Dis*. 2019;25(3):460-471.

3 YEARS LATER, SARAH RETURNS TO IBD CLINIC

- She is now having 12-15 BM daily (3-4 nocturnal)
  - Bristol 7, occasional blood
  - Moderate urgency, fecal incontinence during the daytime
  - Straining, incomplete evacuation
- She's had 3 episodes of similar symptoms, and her surgeon prescribed antibiotics which helped. Recently antibiotics are not helping.
- Testing: Fecal calprotectin is 600 ug/g. Negative GI pathogen panel.
- Patient undergoes pouchoscopy…

QUESTION 2

Describe your typical approach to pouchoscopy including extent, photo documentation and biopsies?



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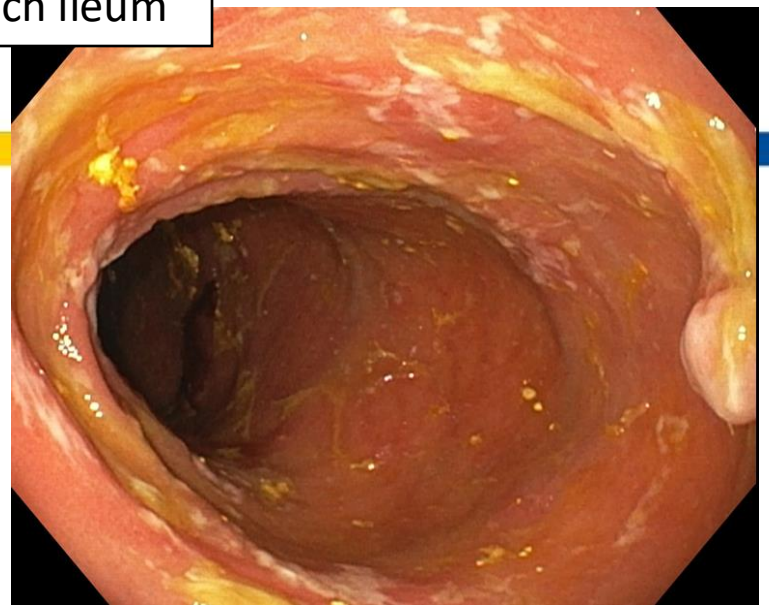
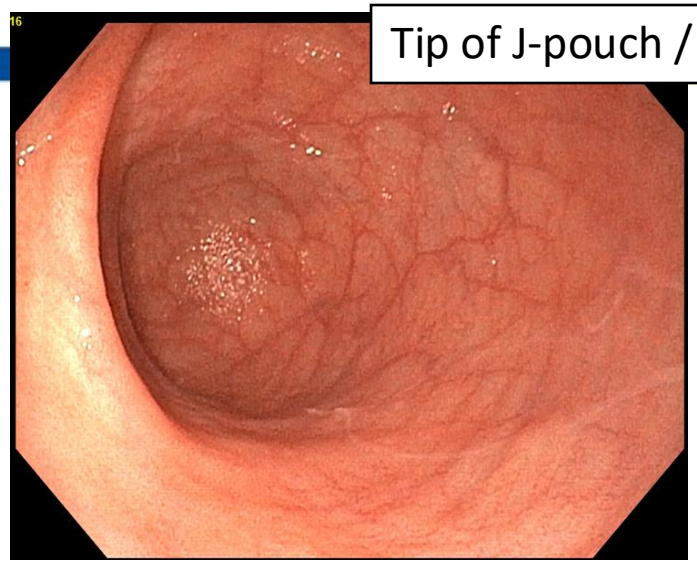
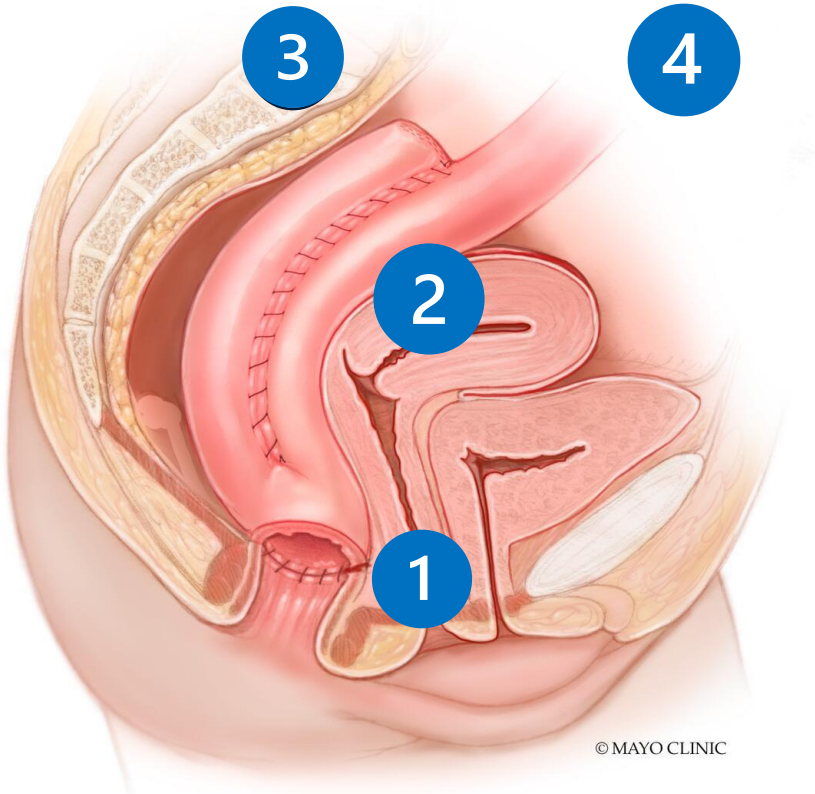
POUCHOSCOPY

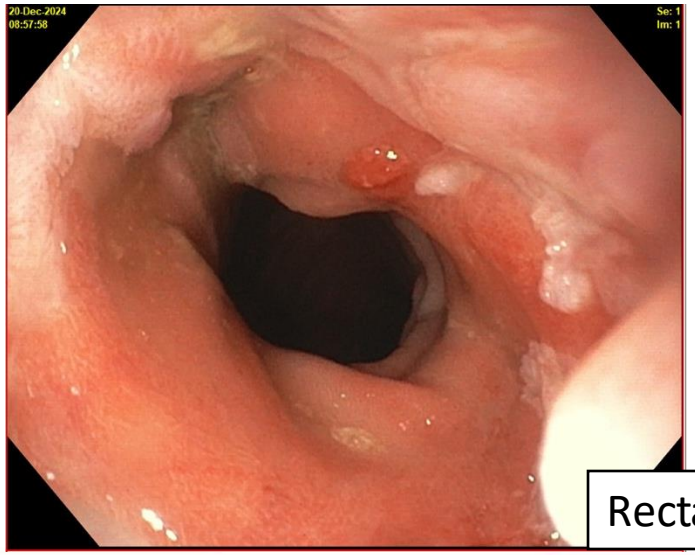
4 Pre-pouch ileum



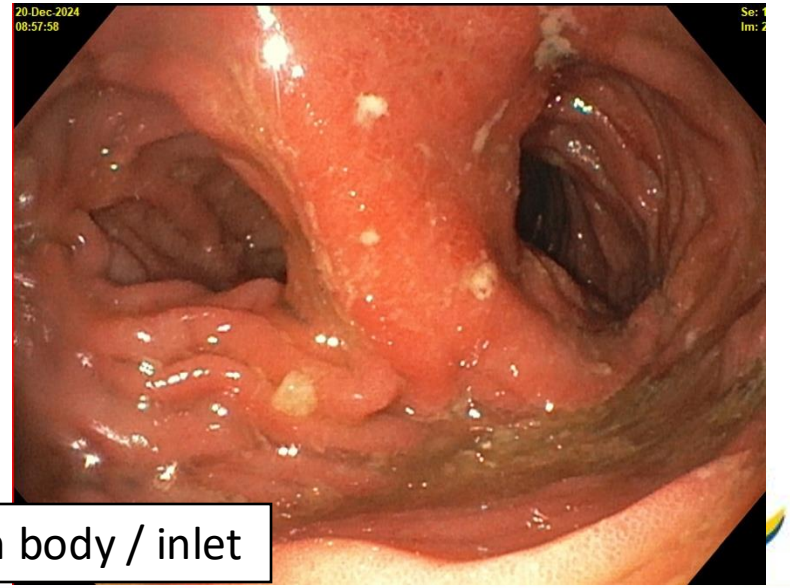
Tip of J-pouch / Blind end 3







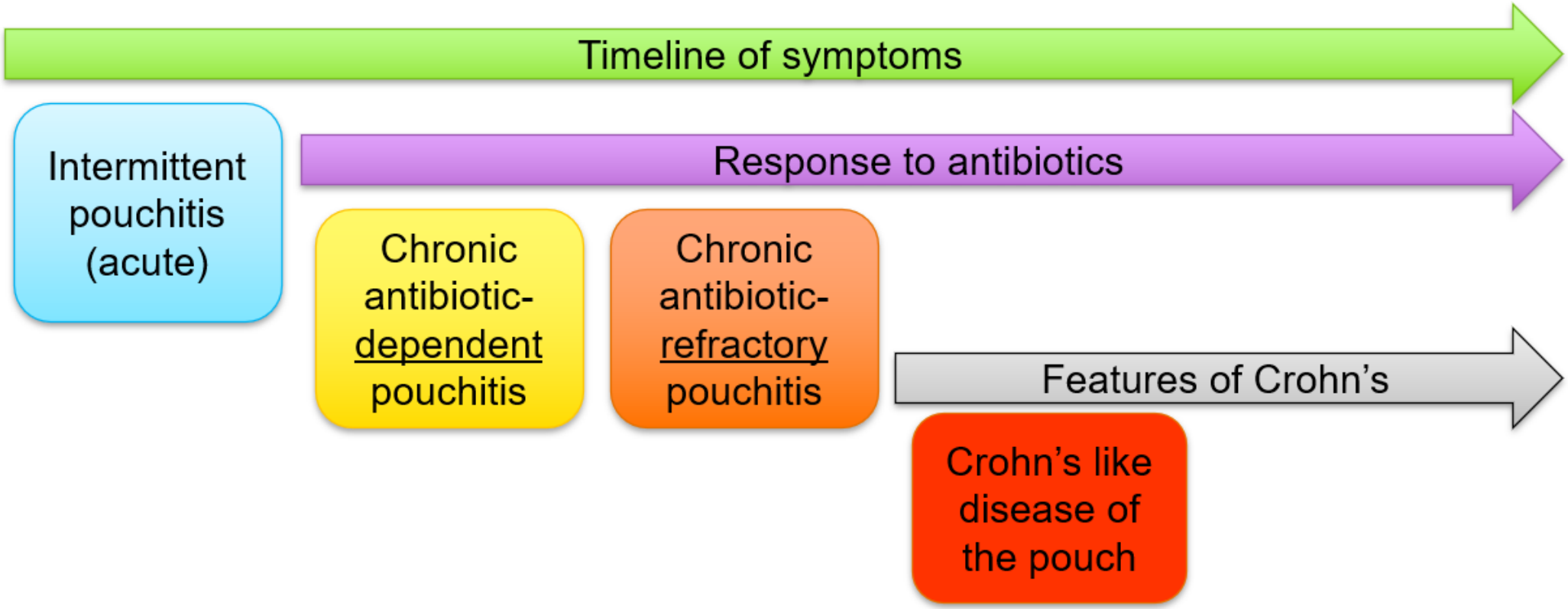
Rectal cuff 1



2 Pouch body / inlet

QUESTION 3

How do you define inflammatory conditions of the pouch, and when should you do further testing?



Barnes EL, Agrawal M, et al. *Gastroenterology*. 2024;166:59-85.

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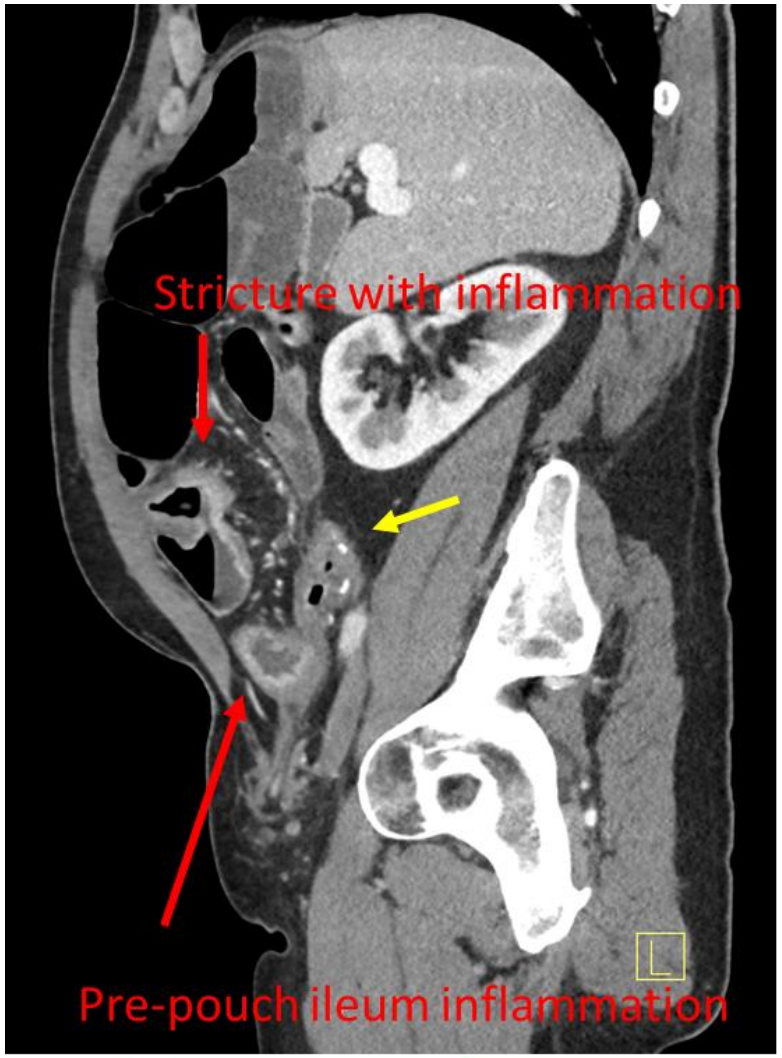
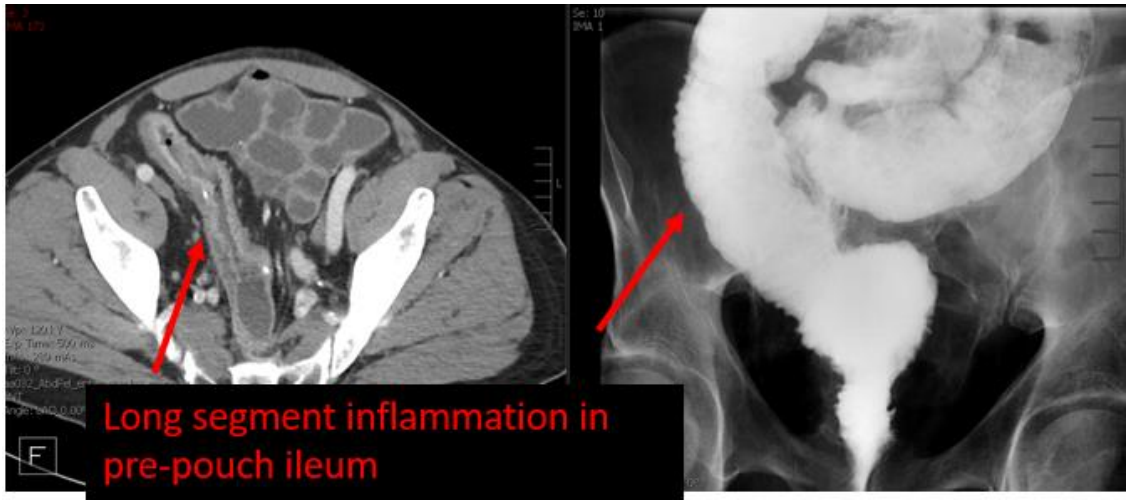
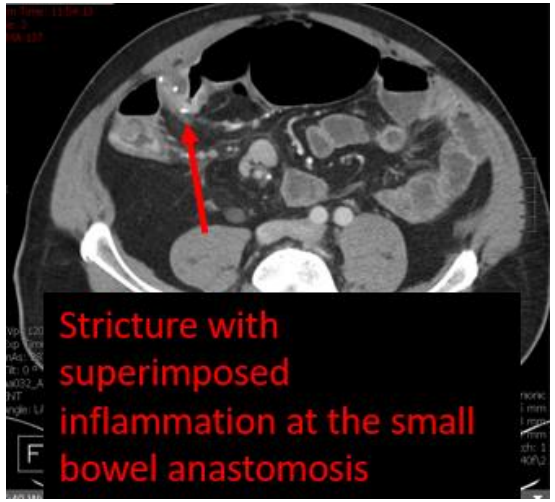
CROHN'S LIKE DISEASE OF THE POUCH







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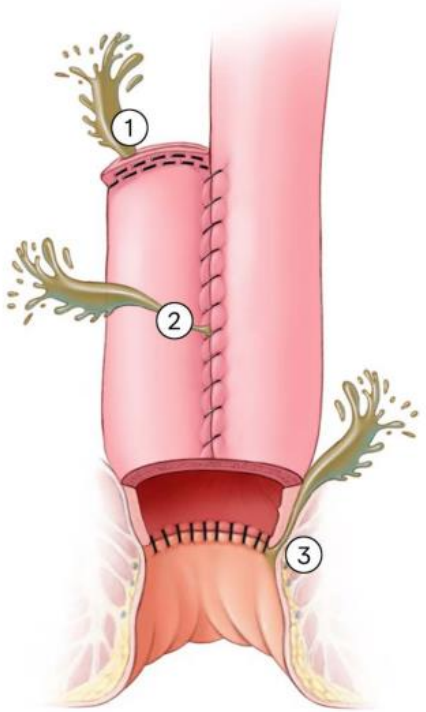
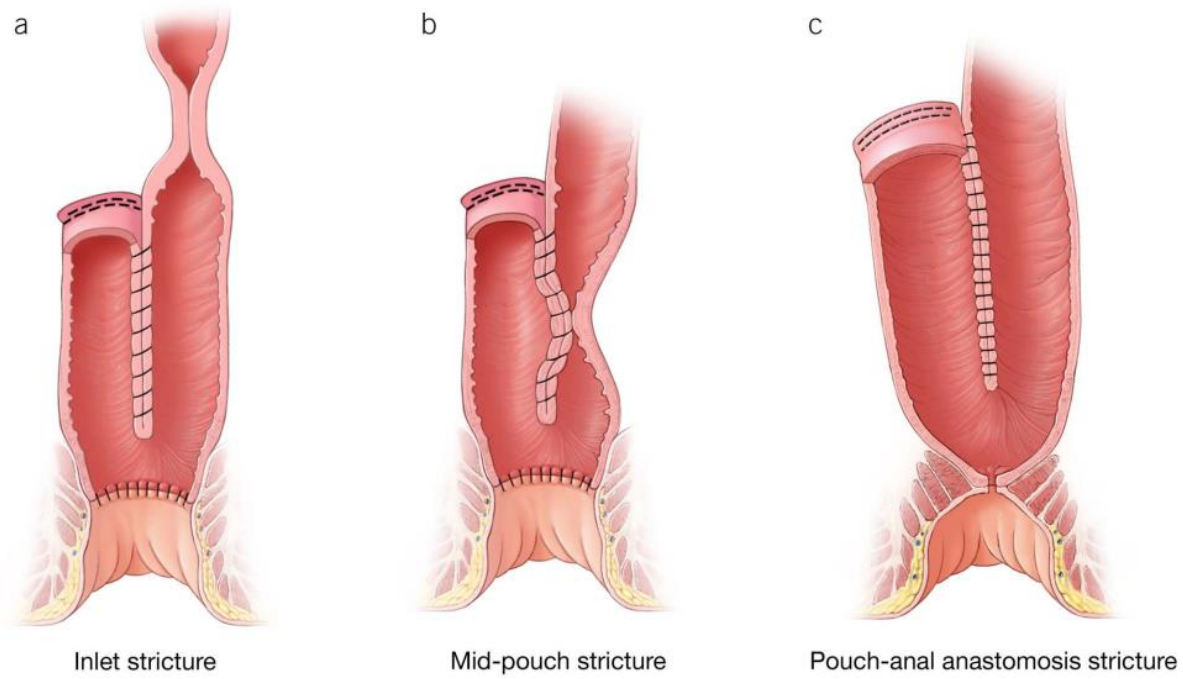
QUESTION 4

Why is it important to review the operative report in pouchitis?

LEAKS	STRICTURES





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Inflammatory Bowel Disease & Endoscopy Case

Sara Ghoneim, MD

March 1st, 2025

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Case

- A 26-year-old female presents to the IBD clinic for evaluation of ongoing symptoms of ulcerative colitis (UC).
- She was diagnosed with UC 2 years ago after presenting with bloody diarrhea, abdominal cramping, and urgency.
- Managed by local GI specialist.

Case (continued)

- She has been on mesalamine (5-ASA) 4.8 g/day and intermittent courses of oral prednisone (most recently a 6-week taper starting at 40 mg daily) but reports incomplete symptom resolution.

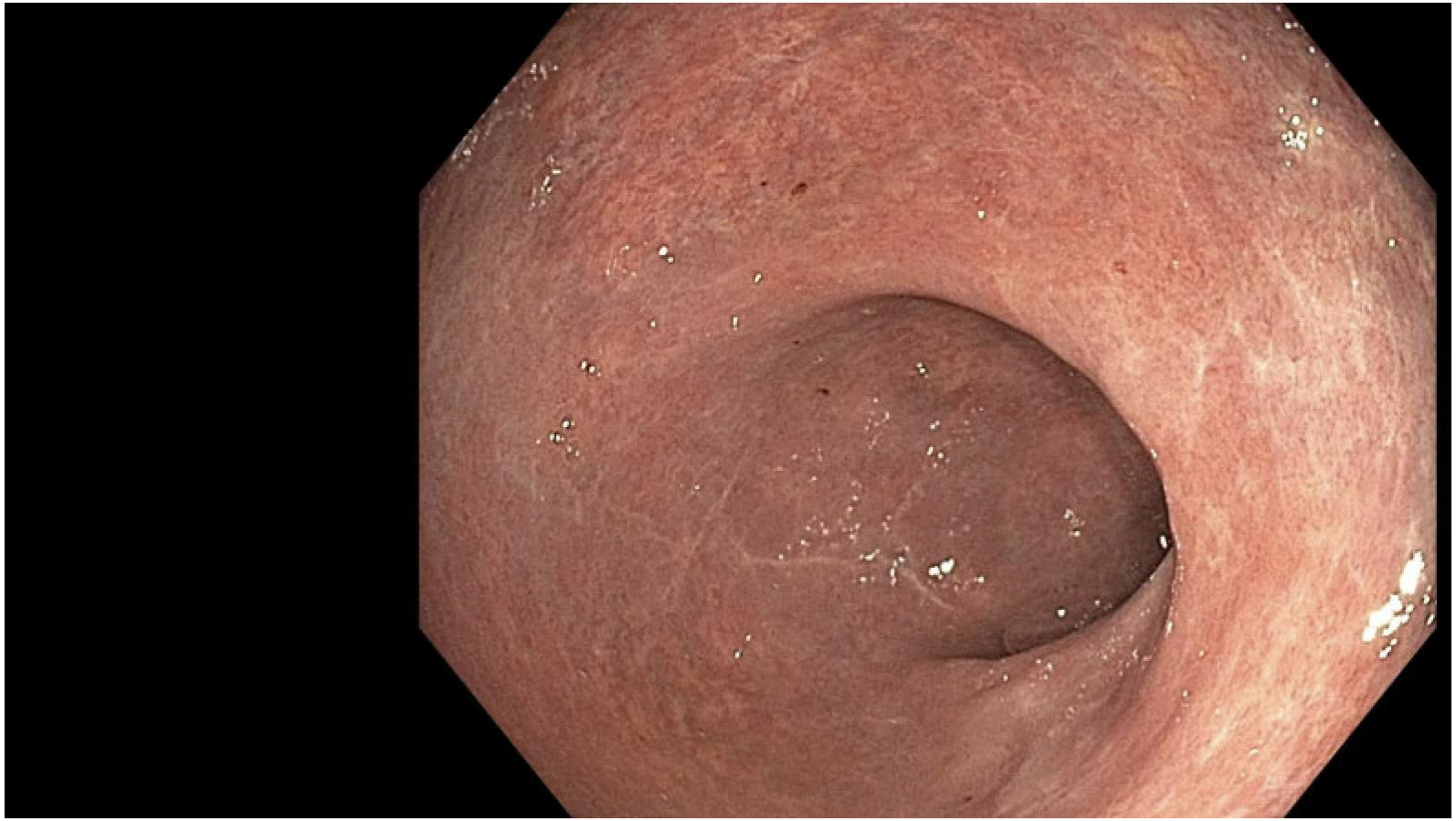
- She continues to have 4-6 bloody bowel movements per day, mild abdominal pain, and fatigue. She has no prior exposure to biologics, immunomodulators, or small molecule therapies.

Work-up

- **Laboratory Findings:**
  - Hemoglobin: 10.5 g/dL (low)
  - CRP: 32 mg/L (elevated)
  - Albumin: 3.2 g/dL (low)
  - Fecal calprotectin: 850 µg/g (elevated)

Colonoscopy

- Moderate inflammation characterized by erythema, loss of vascular pattern, and friability.
- No deep ulcers or spontaneous bleeding
- Involvement is continuous and extends from the rectum to the cecum.
- Biopsies confirm active chronic colitis with crypt abscesses and no evidence of dysplasia or CMV.



Questions

- Would you choose **vedolizumab** (anti-integrin), an **anti-IL-23 agent** (e.g., ustekinumab or mirikizumab), or an **S1P modulator** (e.g., ozanimod)?

- How would you factor in her disease distribution and endoscopic severity (Mayo 2) when making this decision?

- How important is it to aim for **histologic remission**?

Best of Evidence-Based GI: IBD, Endoscopy, Obesity

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

Panel: Oriana Damas, MD, Mohammad Bilal, MD, and James Leavitt, MD

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Risankizumab is Superior to Ustekinumab for Induction and Maintenance of Crohn's Disease: The SEQUENCE Trail

Original Article

EBGI Summary

Article Covered: Risankizumab versus Ustekinumab for Moderate-to-Severe Crohn's Disease. N Engl J Med. 2024;391(3):213-223. doi:10.1056/NEJMoa2314585

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Study Question

Is risankizumab, a p19 subunit-specific interleukin (IL)-23 monoclonal antibody, as efficacious and safe as ustekinumab, a dual IL-12/23 inhibitor, in the treatment of patients with moderate-to-severe Crohn's disease who previously had unacceptable side effects or an inadequate response to at least one anti-tumor necrosis factor (TNF) therapy?

Why is This Important?

Head-to-Head Therapeutic Trials in IBD

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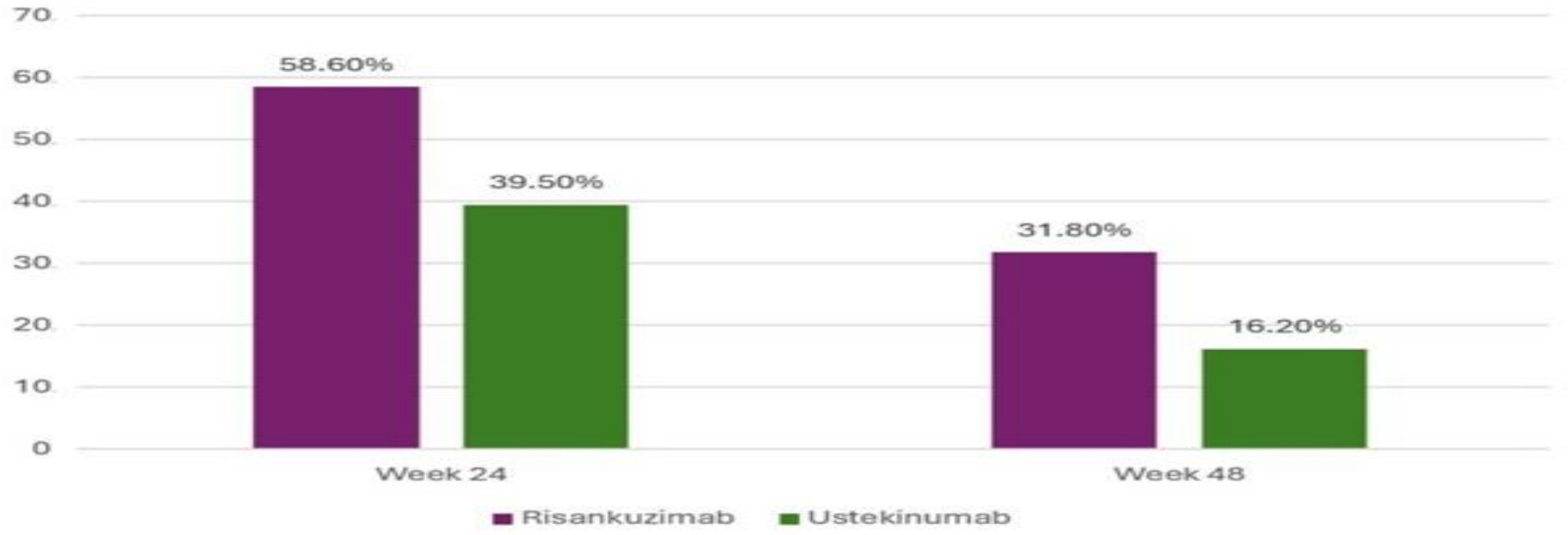
Results

Clinical remission-
24 weeks

Endoscopic remission-
48 weeks



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How Should We Apply This to Our Practice?

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

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

"[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 in patients with ulcerative colitis (VEGA): a randomized, double blind, controlled phase 2, proof of concept trial. Lancet Gastroenterol Hepatol 2023; 8: 307-20]

Multiple new medications for Ulcerative Colitis

Clinical remission rate still LOW!

Combination Biologics Better?

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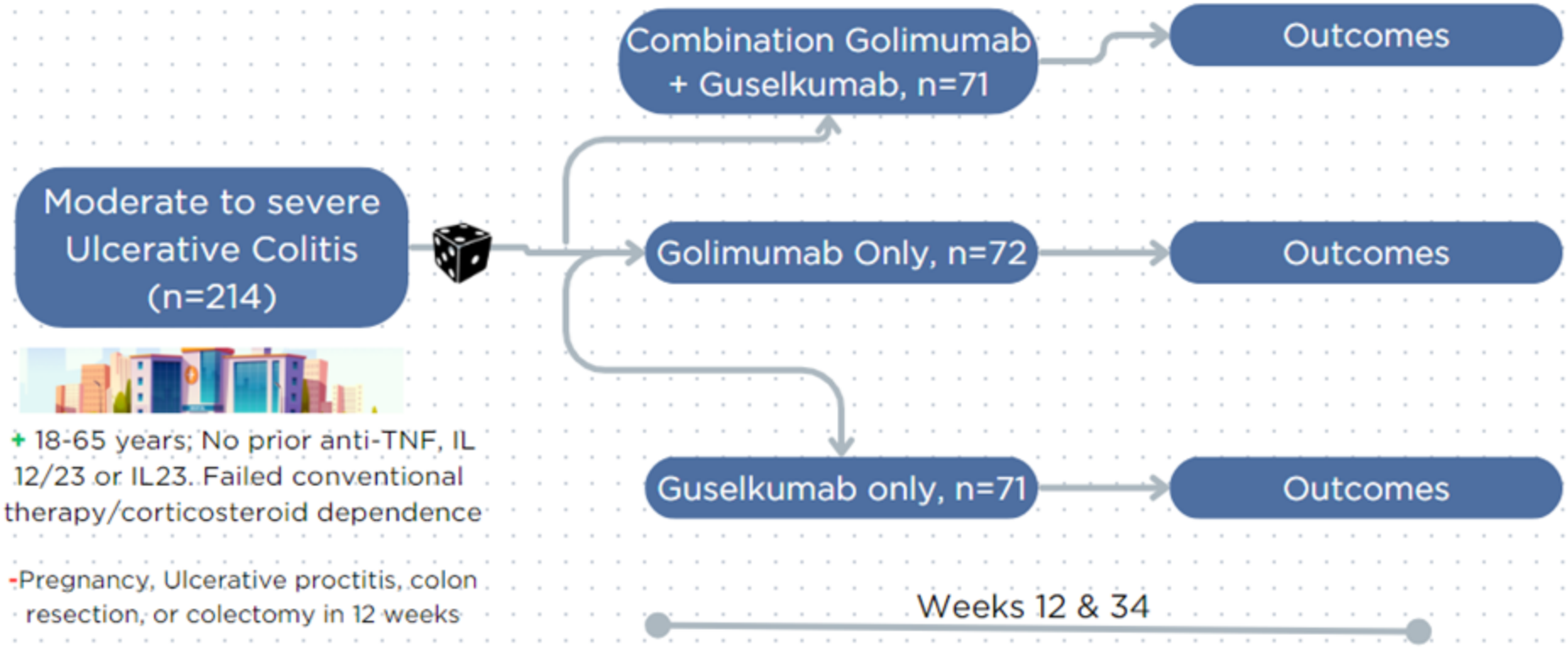

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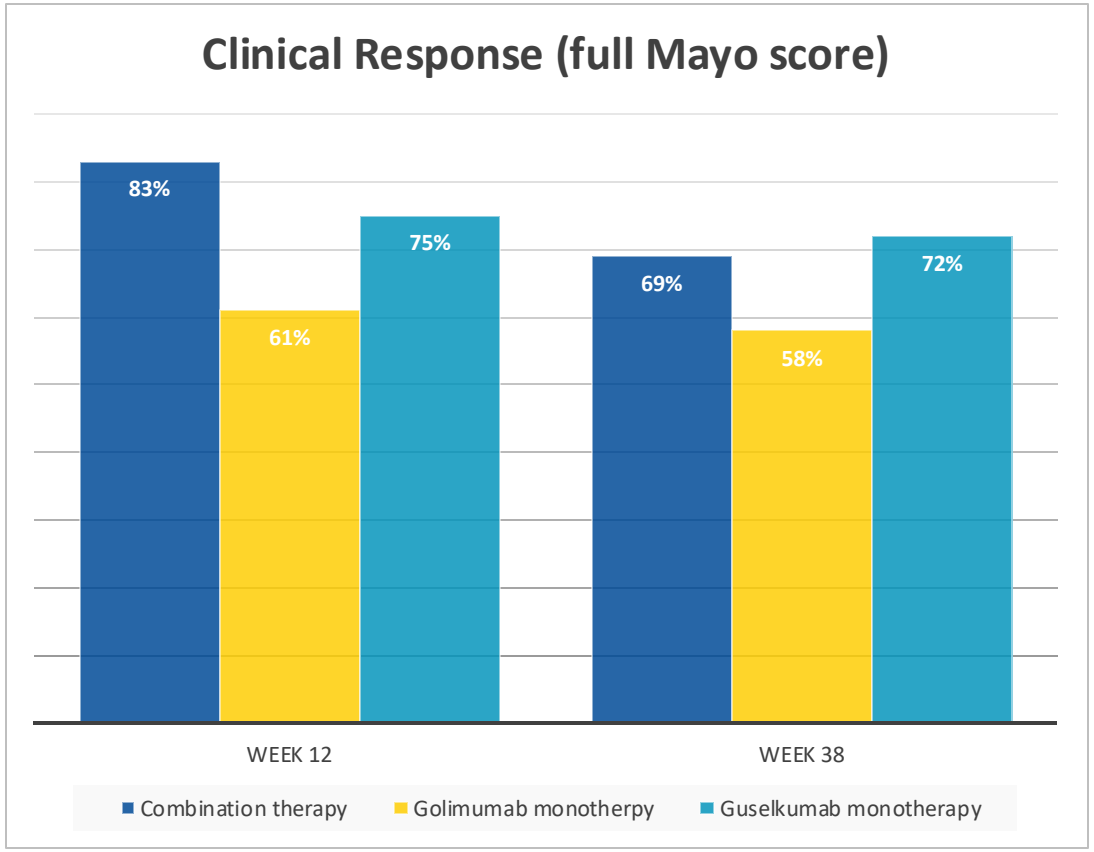

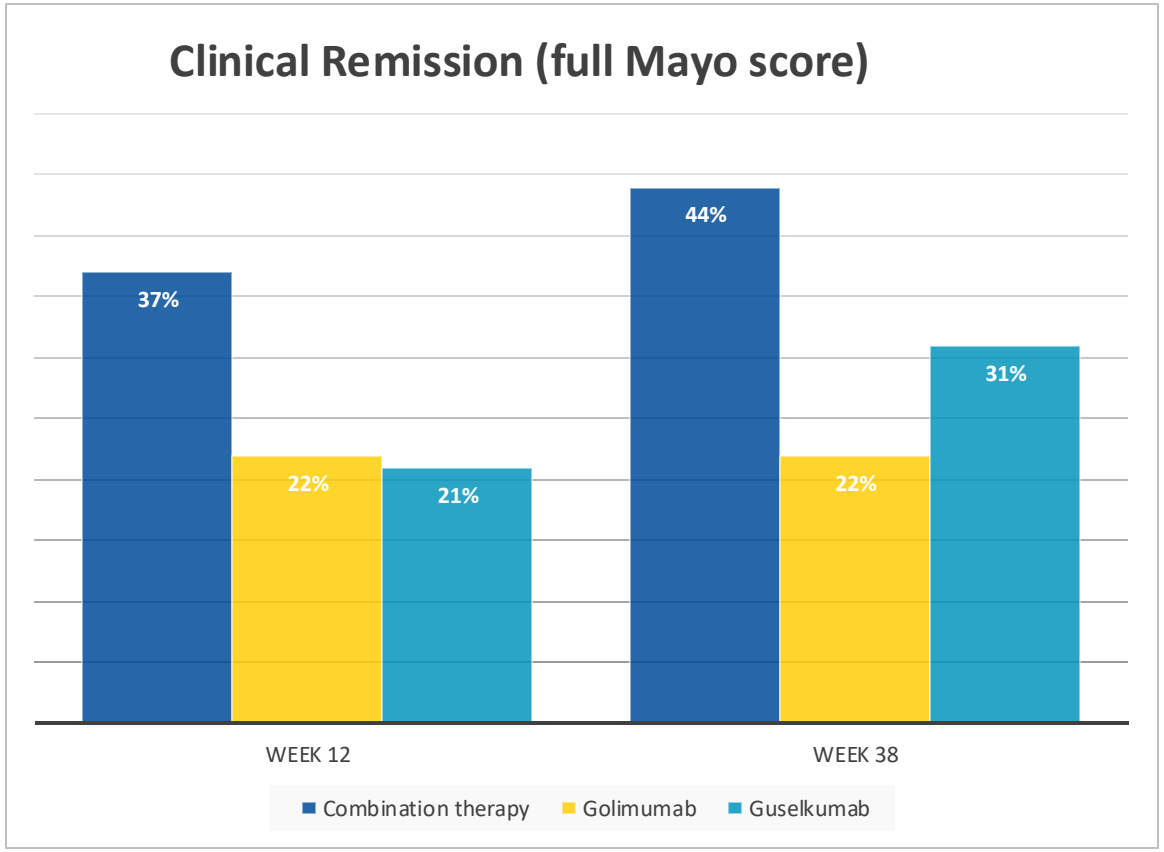

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Questions

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?

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Time to Increase Adenoma Detection Rate Benchmarks for Screening Colonoscopies

Article covered: Schottinger JE, Jensen CD, Ghai NR, et al. Association of Physician Adenoma Detection Rates With Postcolonoscopy Colorectal Cancer. JAMA 2022; 7;327(21):2114-2122. DOI:10.1001/jama.2022.6644

Original Article

EBGI Summary

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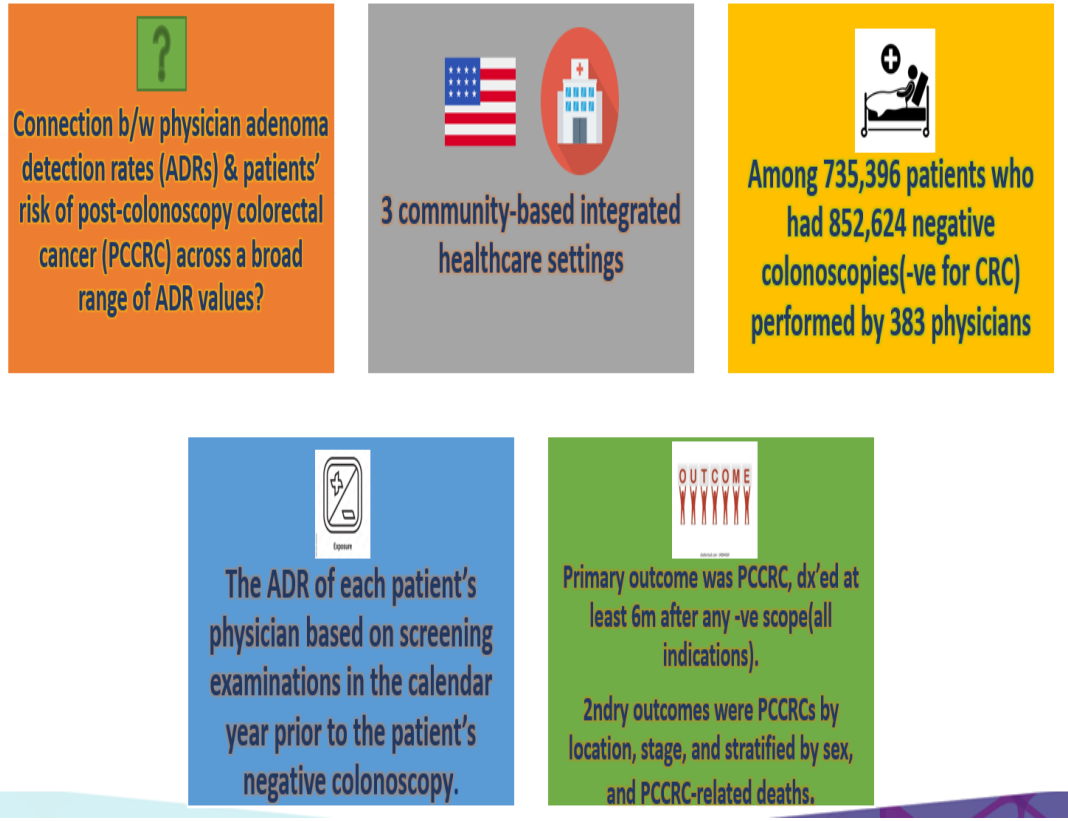
Study Question

- What are the associations between physician adenoma detection rates (ADRs) and patients' risk of post-colonoscopy colorectal cancer (PCCRC) across a broad range of ADR values?

Study Design

- Design: Retrospective cohort study.
- Setting: Three community-based healthcare systems in the U.S. (Kaiser Permanente Northern and Southern California, and Washington).
- Patients: Included 735,396 individuals with 852,624 CRC-negative colonoscopies by 383 physicians; 51.6% were female, median age 61.4 years (IQR: 55.5-67.2).



https://jamanetwork.com/journals/jama/fullarticle/2792977
https://gi.org/journals-publications/ebgi/lee_september_2022/

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References

Results

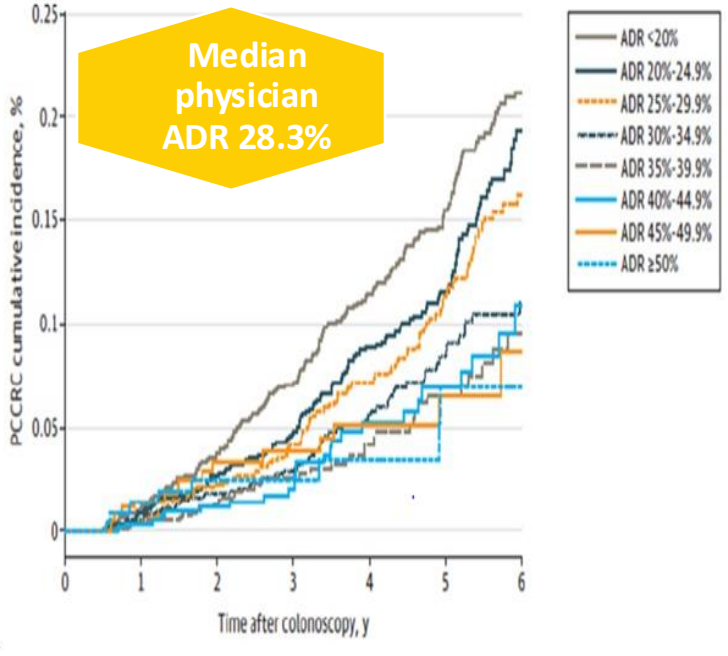

Figure 1. Cumulative Incidence of PCCRC Stratified by ADR

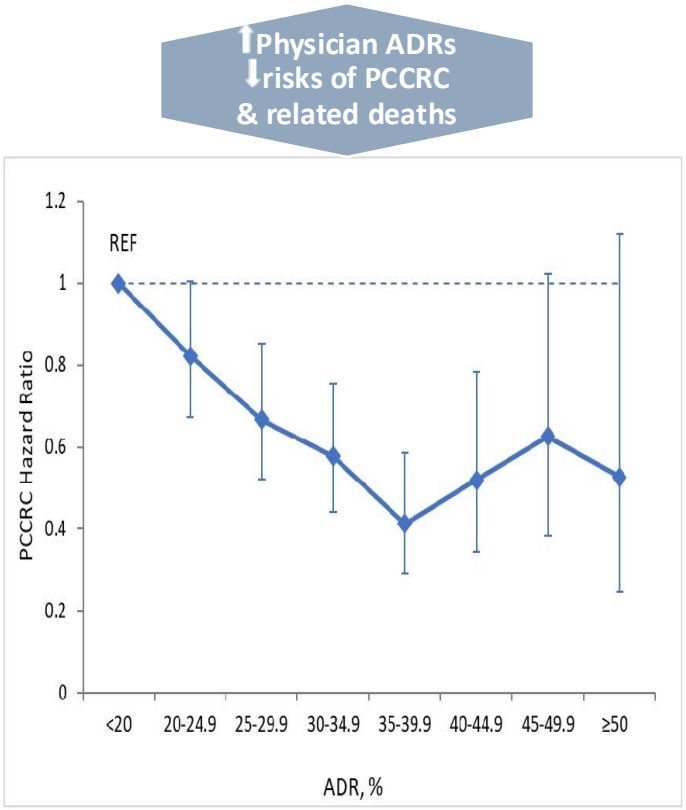

Figure 2: Risk of Post-Colonoscopy Colorectal Cancer (PCCRC) According to Adenoma Detection Rates (ADR)

Primary Outcome: Over a median follow-up of 3.25 years, higher physician ADRs were linked to a significantly lower risk of PCCRC (HR: 0.97 per 1% ADR increase) and related deaths (HR: 0.95 per 1% ADR increase).

Key Finding: Physicians with ADRs at or above the median (28.3%) had reduced PCCRC risk (HR: 0.61) and lower related mortality (HR: 0.26) compared to those with ADRs below the median.

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Key Study Findings

- Increased ADR Lowers PCCRC Risk: Each 1% increase in ADR reduces PCCRC risk by 3% and PCCRC-related death by 5%.
- Optimal ADR Range: ADRs of 35%-39.9% showed the greatest reduction in PCCRC risk, compared to ADRs below 20%.
- Implication for Guidelines: Findings suggest raising the minimum and aspirational ADR targets in future guidelines.

How Should We Apply This to Our Practice?

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

"Which Endoscopists Benefit from Using Computer-Aided Detection of Polyps During Colonoscopy?"
Summary of Shaukat, A., Lichtenstein, D.R., Chung, D.C.,, et al. Am J Gastroenterol
. 2023 Oct 1;118(10):1891-1894

Which Endoscopists Benefit from Using Computer-Aided Detection of Polyps During Colonoscopy?

Philip Schoenfeld, MD, MSEd, MSc (Epi)

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

This summary reviews Shaukat A, Lichtenstein DR, Chung DC, et al. Endoscopist-level and procedure-level factors associated with increased adenoma detection with the use of a computer-aided detection device. Am J Gastroenterol 2023; 118: 1891-94.

Dr. Schoenfeld & Dr. Prince have no conflicts of interest to report.

Tweetorial Provided by:

Sean-Patrick Prince, MD, MPH

@seanpattyp

Internist, AdventHealth Orlando

"Which Endoscopists Benefit from Using Computer-Aided Detection of Polyps During Colonoscopy?"
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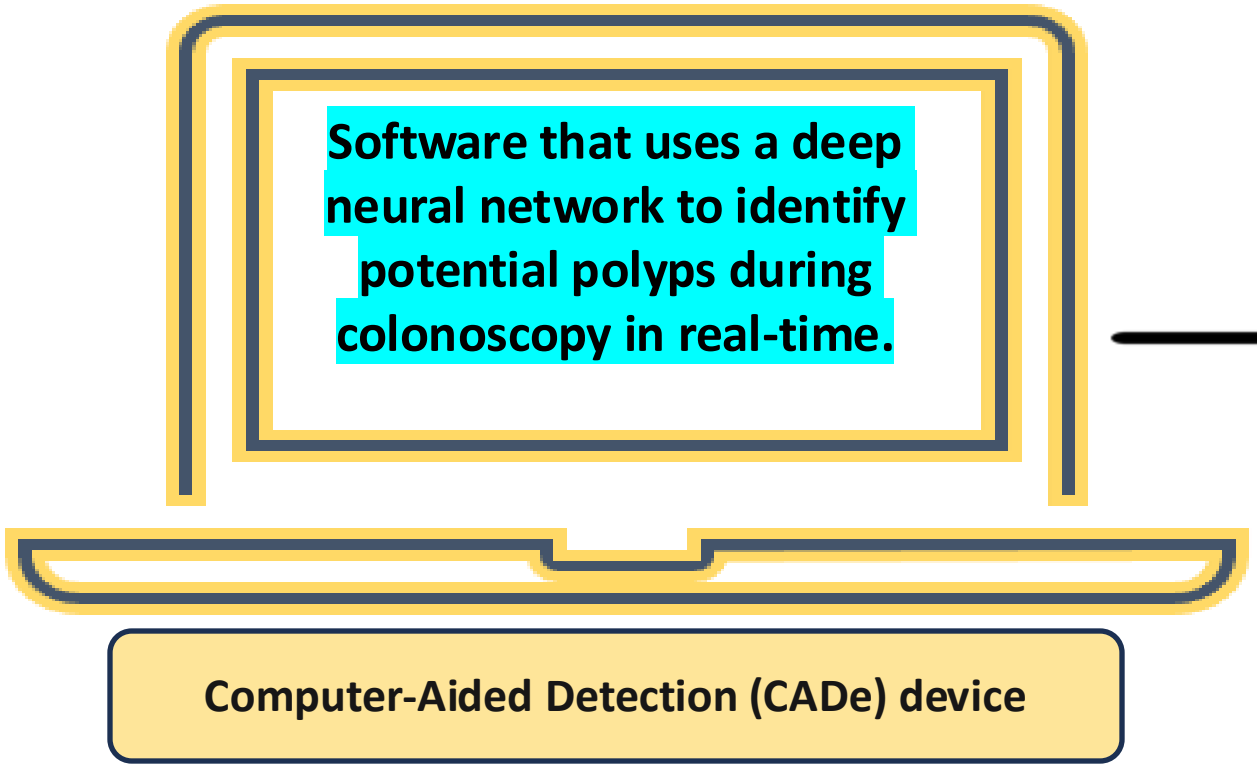
. 2023 Oct 1;118(10):1891-1894

CURRENT RESEARCH = VARIABLE ADR BENEFIT



Computer-Aided Detection (CADe) device

<u>Adenoma Detection Rate BENEFIT</u>

- Endoscopists with low ADR (GI Fellows)
- Patient population with lower adenoma prevalence
- Endoscopists committed to using it in most cases

<u>NO ADR BENEFIT</u>

- High prevalence of adenomas
- FIT-positive individuals
- Endoscopists with high ADRs (>45%)

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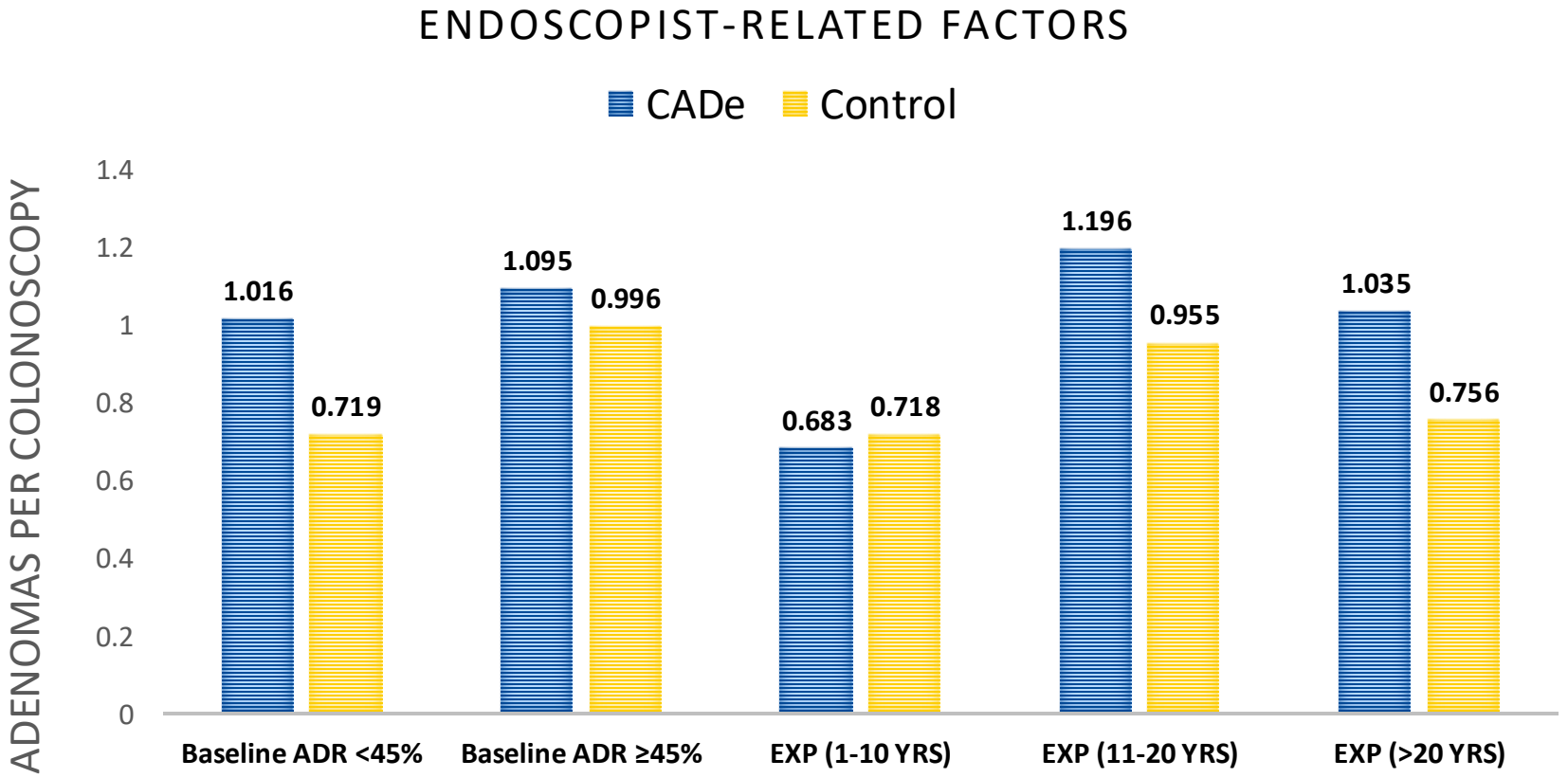

NUMERICALLY IMPROVED APC

- ADR < 45%
- WT > 8 MINUTES
- > 20 YRS OF EXP

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How Should We Apply This to Our Practice?

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

Tirzepatide For Obesity: "Mounting" Evidence for Substantial Weight Loss

Sonali Paul, MD, MS

Assistant Professor of Medicine, Division of Gastroenterology, Hepatology & Nutrition, Pritzker School of Medicine, University of Chicago, Chicago, Illinois

Sonali Paul, MD, MS
Associate Editor

This summary reviews: Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med 2022;387(3):205-216. https://pubmed.ncbi.nlm.nih.gov/35658024/

Correspondence to Sonali Paul, MD, MS, Associate Editor. Email: EBGI@gi.org

Tweetorial Provided By:

Aimen Farooq, MD
@AimenKhanMD
IM Physician, AdventHealth Orlando

Conflicts of Interest

Dr. Paul and Dr. Farooq have no conflicts of interest.

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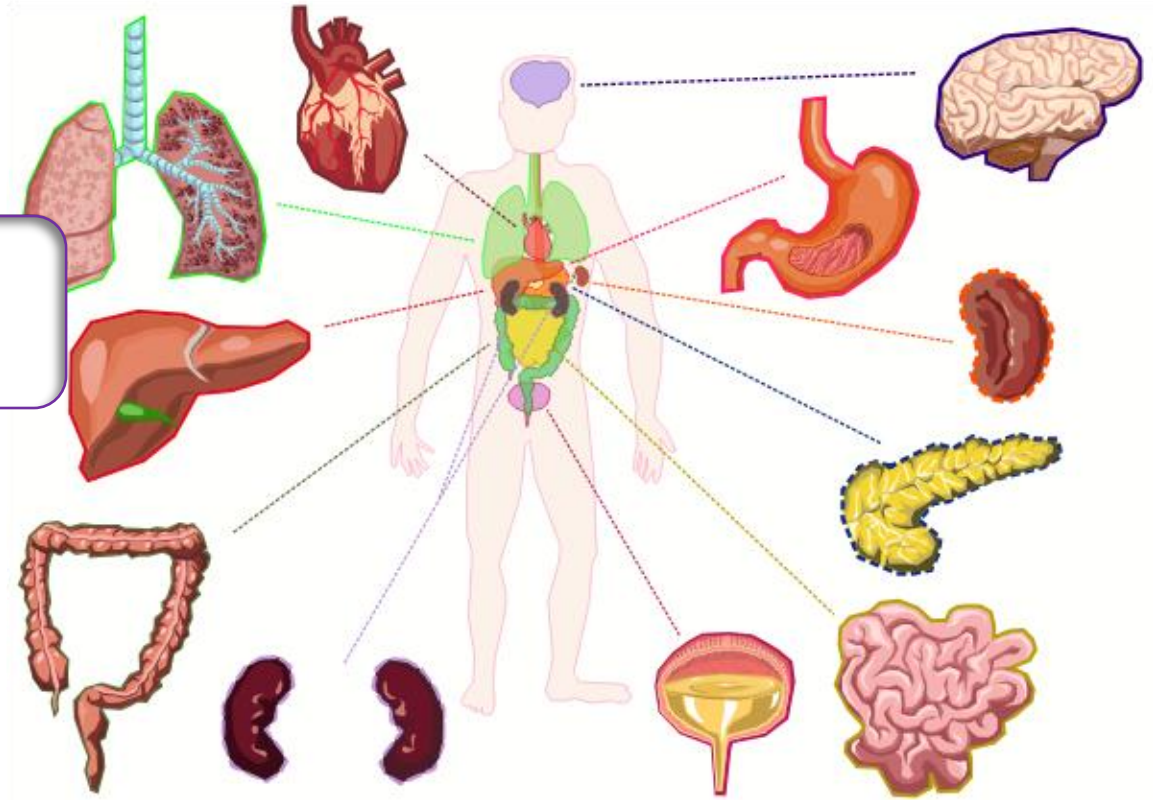
Multiple Effects of Obesity

- Cardiovascular Disease
- Non-Alcoholic Fatty Liver Disease
- Multiple Malignancies
- Mental Health Disorders
- Type 2 Diabetes Mellitus
- Musculoskeletal Diseases



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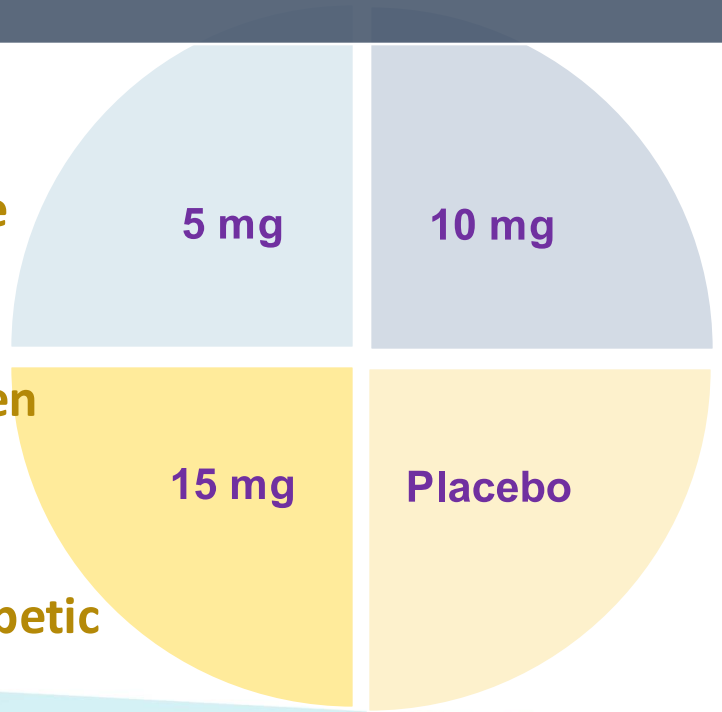
n=2539

Lifestyle Interventions plus once weekly subcutaneous Tirzepatide (increments of 2.5 mg weekly) for 72 weeks

71% White

67% Women

41% Prediabetic



Inclusion Criteria

BMI >30

OR

BMI >27 + one weight-related condition

Exclusion Criteria

- Diabetes
- Change in body weight of >5kg within 90 days of enrollment

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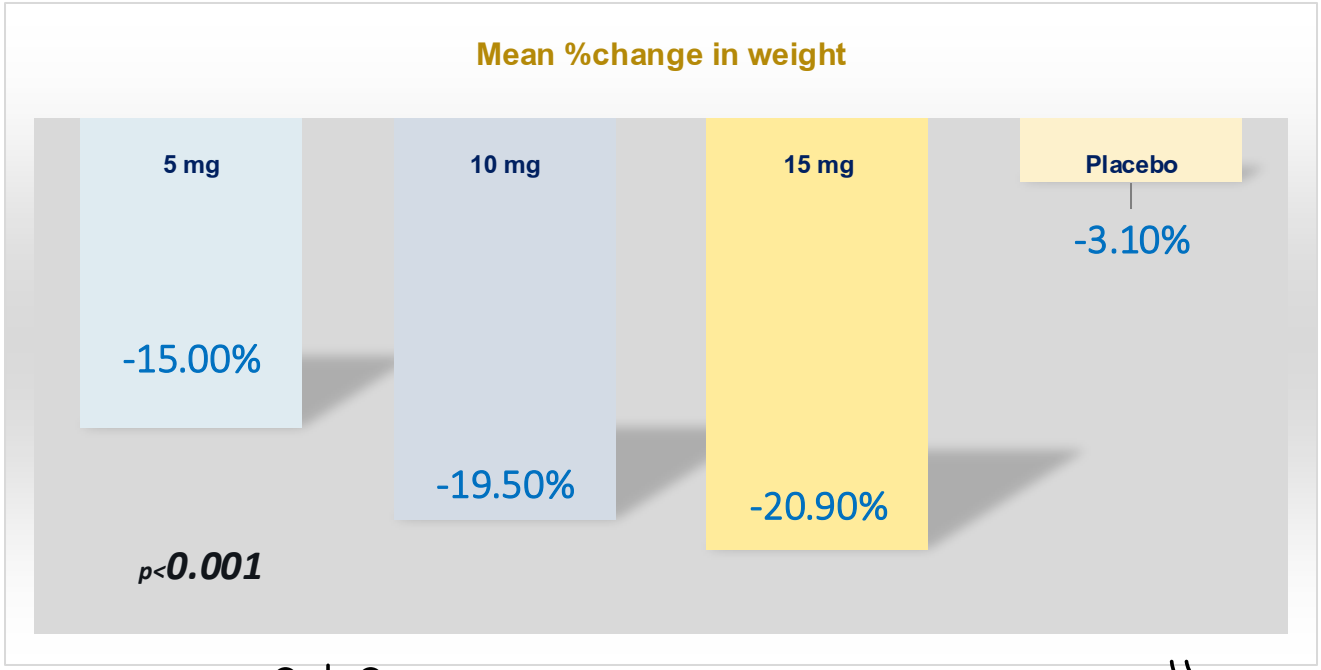

Improved Cardiovascular parameters

Mean reduction in total body fat mass

Dose-dependent Gastrointestinal side effects

Tirzepatide Improves NASH and Reduces Fibrosis: Findings From the SYNERGY-NASH Trial

Original Article

EBGI Summary

Article covered: Loomba R, Hartman ML, Lawitz EJ, et al. Tirzepatide for metabolic-dysfunction associated steatohepatitis with liver fibrosis. NEJM 2024;391:299-310.

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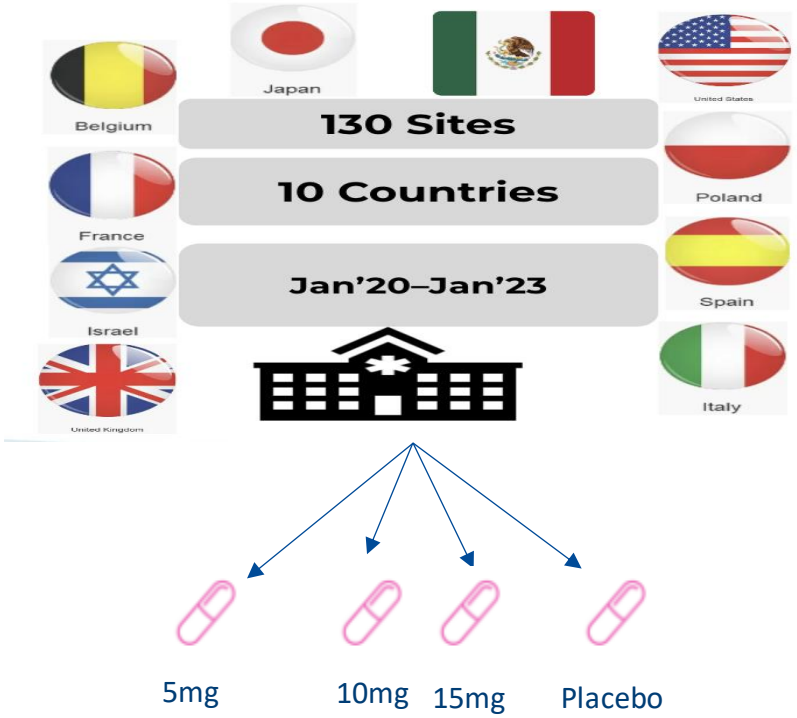
Study Design

- Design: Phase II, multicenter, placebo-controlled, dose-finding, double-blind, randomized controlled trial (RCT).

- Sites: 10 countries (Belgium, France, Israel, Italy, Japan, Mexico, Poland, Spain, UK, USA).

- Duration: January 2020 - January 2023.



Loomba R, et al. NEJM 2024; Rich N. EBGI July 2024

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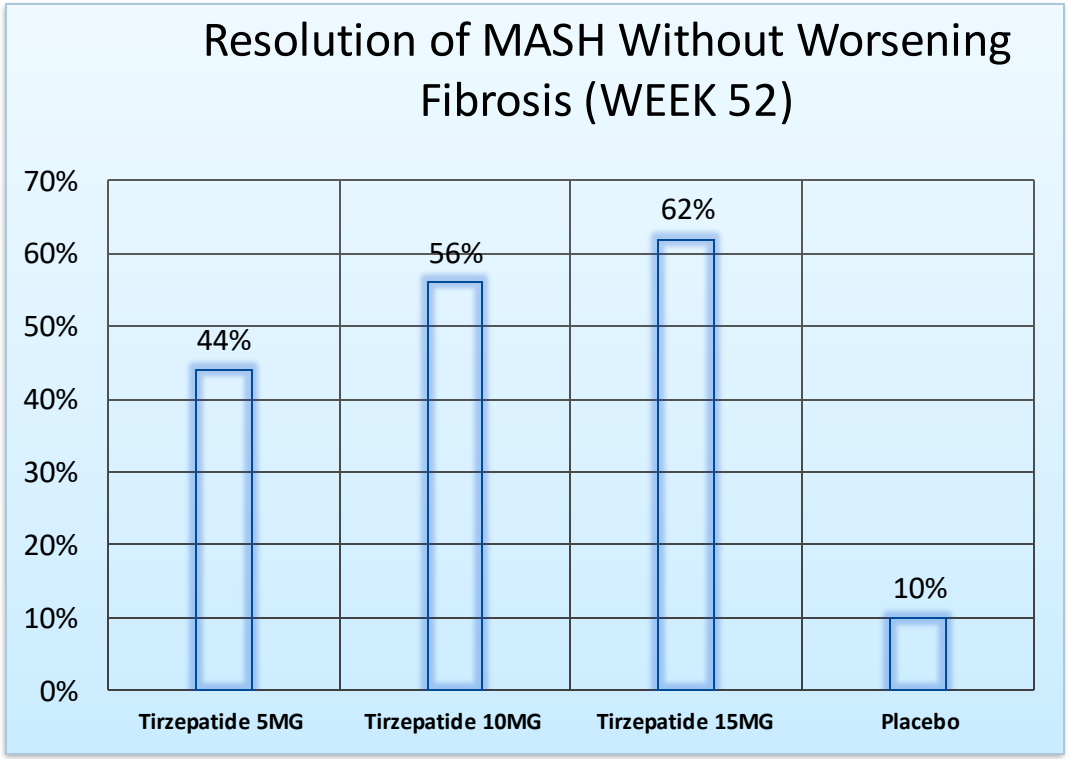
Results

	Tirzepatide 5MG	Tirzepatide 10MG	Tirzepatide 15MG	PLACEBO
SECONDARY OUTCOMES				
IMPROVEMENT OF AT LEAST 1 FIBROSIS STAGE	55%	51%	51%	30%
MEAN PERCENTAGE CHANGE IN BODY WEIGHT	-10.7%	-13.3%	-15.6%	-0.8%
ADVERSE EVENTS				
NAUSEA	36%	34%	44%	12%
DIARRHEA	32%	36%	27%	23%
CONSTIPATION	23%	19%	15%	6%



Loomba R, et al. NEJM 2024; Rich N. EBGI July 2024

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Endoscopic Sleeve Gastroplasty Is Effective for Patients With Obesity Who MERIT Intervention

Jennifer M. Kolb MD, MS[1] and Austin L. Chiang, MD, MPH[2]

[1]*Assistant Professor of Medicine, Division of Gastroenterology, Hepatology and Parenteral Nutrition, VA Greater Los Angeles Healthcare System, David Geffen School of Medicine at UCLA, Los Angeles, CA*

[2]*Assistant Professor of Medicine, Division of Gastroenterology and Hepatology, Thomas Jefferson University Hospital, Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, PA*

This summary reviews Dayyeh BKA, Bazerbachi F, Vargas EJ, et al. Endoscopic sleeve gastroplasty for treatment of class 1 and 2 obesity (MERIT): a prospective, multicentre, randomised trial. Lancet 2022; 400: 441–51.

Tweetorial provided by:

Mouhand Mohamed, MD

@MouhandMD

EBGI Ambassador

PGY-2 Brown University

Dr. Kolb reports no potential conflict of interest. Dr. Chiang is an employee of Medtronic.

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Abu Dayyeh BK et al. *Lancet*. 2022;400(10350):441-451.
doi:10.1016/S0140-6736(22)01280-6

21-65 years old + BMI 30-40 kg/m2+ previous 🚫 response to non-surgical weight loss interventions

ESG & lifestyle modifications (n=85)

1:1.5 randomization

Lifestyle modifications only (n=124)

1. Excess weight loss (EWL) =(weight loss / baseline excess weight*) x 100

2. Total body weight loss (TBWL)

*EWL Baseline excess weight= Index weight minus ideal weight based on BMI of 25 kg/m2

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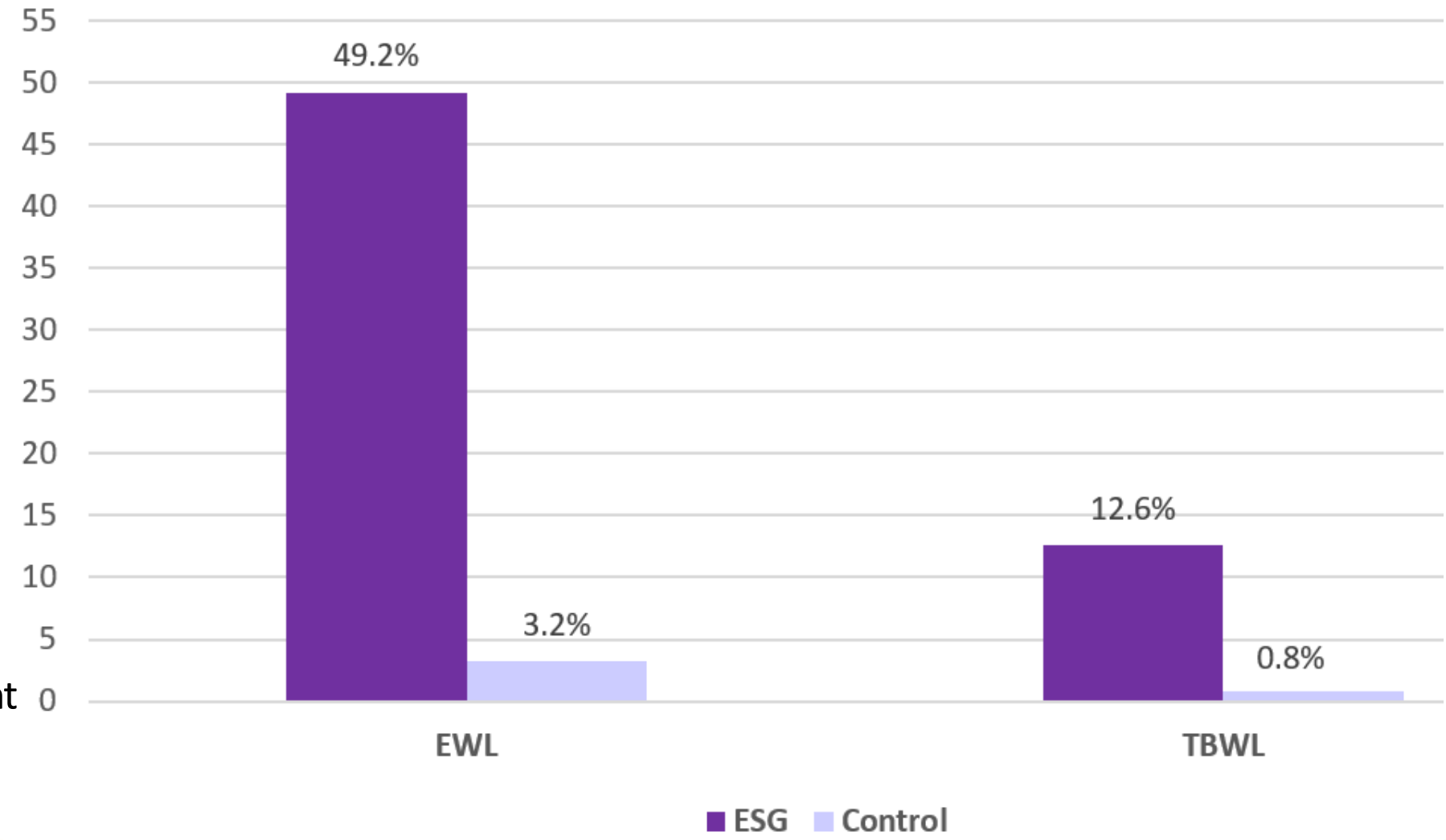

Figure:

Percent of excess weight loss (EWL) and mean total body weight loss (TBWL) at week 52

How Should We Apply This to Our Practice?

Questions & Answers

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Break

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Esophageal and GI Motility Disorders

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Esophagology in the Endoscopy Suite

How I Do it: Diagnostics

EndoFLIP, Bravo and Manometry

John Pandolfino

Northwestern Medicine

Northwestern Memorial Hospital

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Esophageal Symptoms: Understanding the Diagnostics

- No test is perfect
  - EGD
    - A large proportion of patients with reflux and motility disorders have a normal exam
  - HRM
    - Requires another test to make the diagnosis in up to 30-50% of cases
      - Up to 25% of normal HRM have abnormal esophagram findings
      - Up to 25% of normal HRM have abnormal FLIP findings
  - Esophagram
    - Focuses on defining abnormalities- but not the diagnosis
    - Requires endoscopy and motility testing to make the diagnosis- not a single test
  - FLIP Panometry
    - Great screening test for esophageal motility disorders and obstructive disease, but requires HRM or esophagram in 30-50%
  - *These tools complement each other and can be used in various sequences based on presentation, availability and patient preference*

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Esophageal Symptoms: Diagnostic Approach

- Heartburn, regurgitation, dysphagia, chest pain and food impaction.
- Differential Diagnosis:
  - *GERD, EoE, Obstruction, Motor Disorder, Functional Esophageal Disorder*

- All roads lead to endoscopy
  - r/o mechanical obstruction, reflux injury, EoE
  - Negative- NERD, motility disorder, functional

Diagnostic Algorithm for Esophageal Symptoms

Patient with Esophageal Symptoms

Patient with Dysphagia (*warning sign*)

No

Chest Pain, Heartburn, Globus

May attempt PPI Trial if no warning signs on History and Physical Exam to suggest Cardiac issue or GI malignancy

2-3 months PPI Trial

response

Yes

Evaluate and treat accordingly

Consider **endoscopy** for screening and **esophageal function testing** to confirm diagnosis

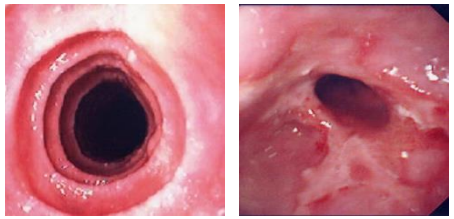
No

1-2 months

Yes

Endoscopic Visualization

- Isolated Chest Pain –EGD
  - *With eating-add Biopsy*
- Dysphagia- EGD with Biopsy
- Heartburn- EGD

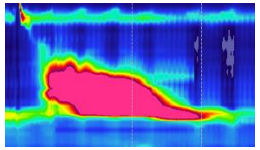


Yes

Stop and treat accordingly

Abnormality Identified

No



Esophageal Function Testing

- Reflux Testing- using Lyon 2.0
  - Wireless/24 hour pH-Impedance
- Motility Testing using Chicago Classification 4.0
  - HRM +/- (FLIP/TBE)

1-3 months

Esophageal Disorder of Gut-Brain Interaction

No

Abnormality Identified

Yes

Evaluate and treat accordingly

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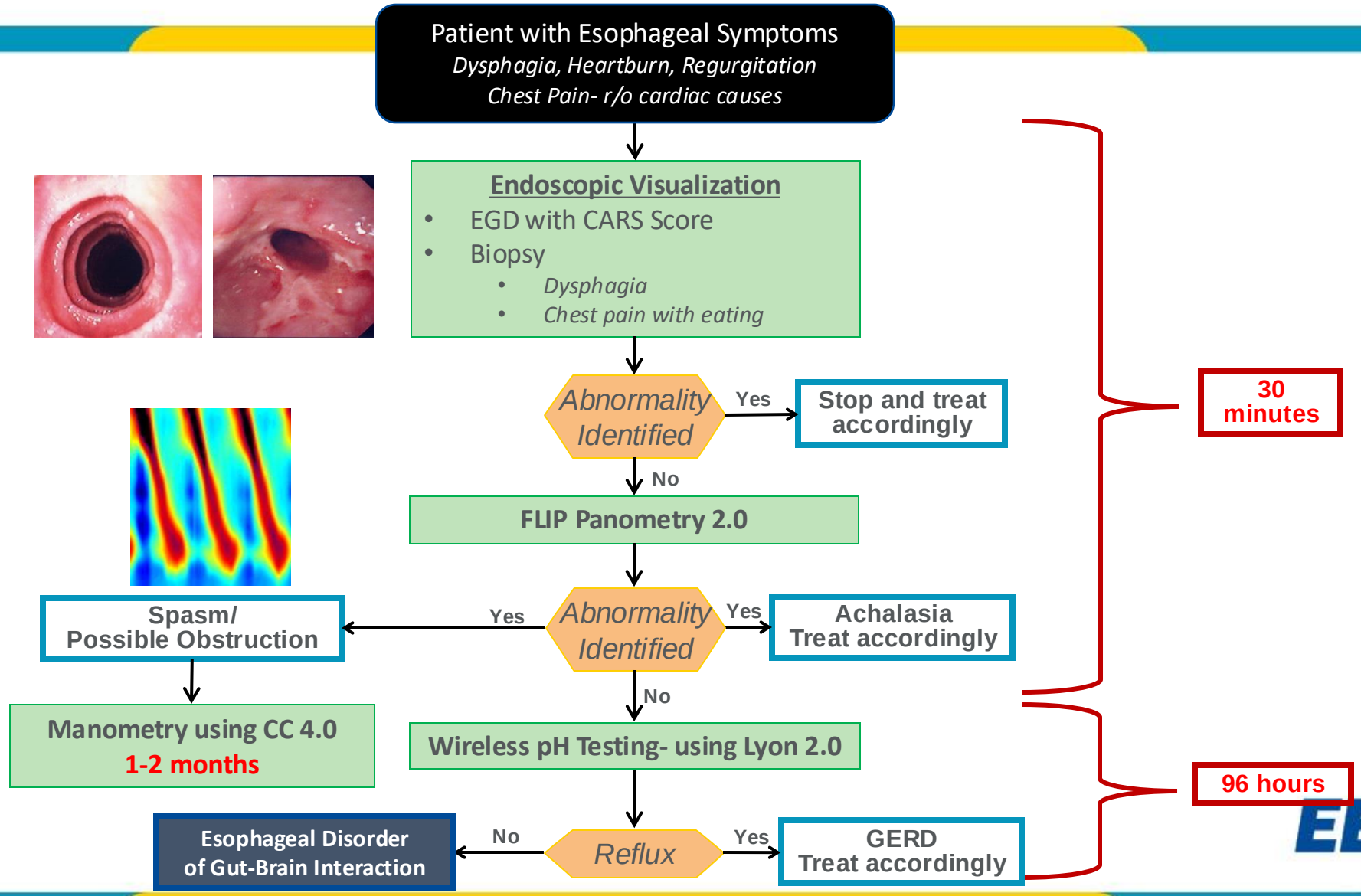
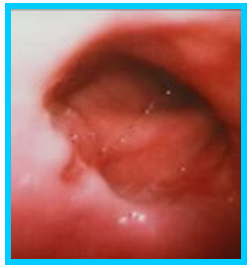
NEW - Diagnostic Algorithm for Esophageal Symptoms



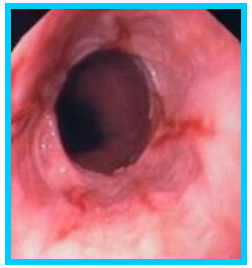
The Los Angeles Classification System for Esophagitis
The "Flap Valve" Concept of EGJ Disruption

Los Angeles Grade A



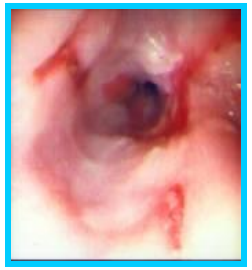
One or more mucosal breaks no longer than 5 mm, not bridging the tops of mucosal folds

Los Angeles Grade B



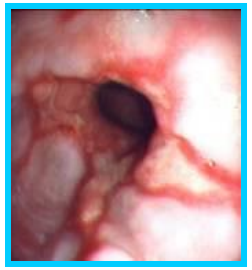
One or more mucosal breaks longer than 5 mm, not bridging the tops of mucosal folds

Los Angeles Grade C

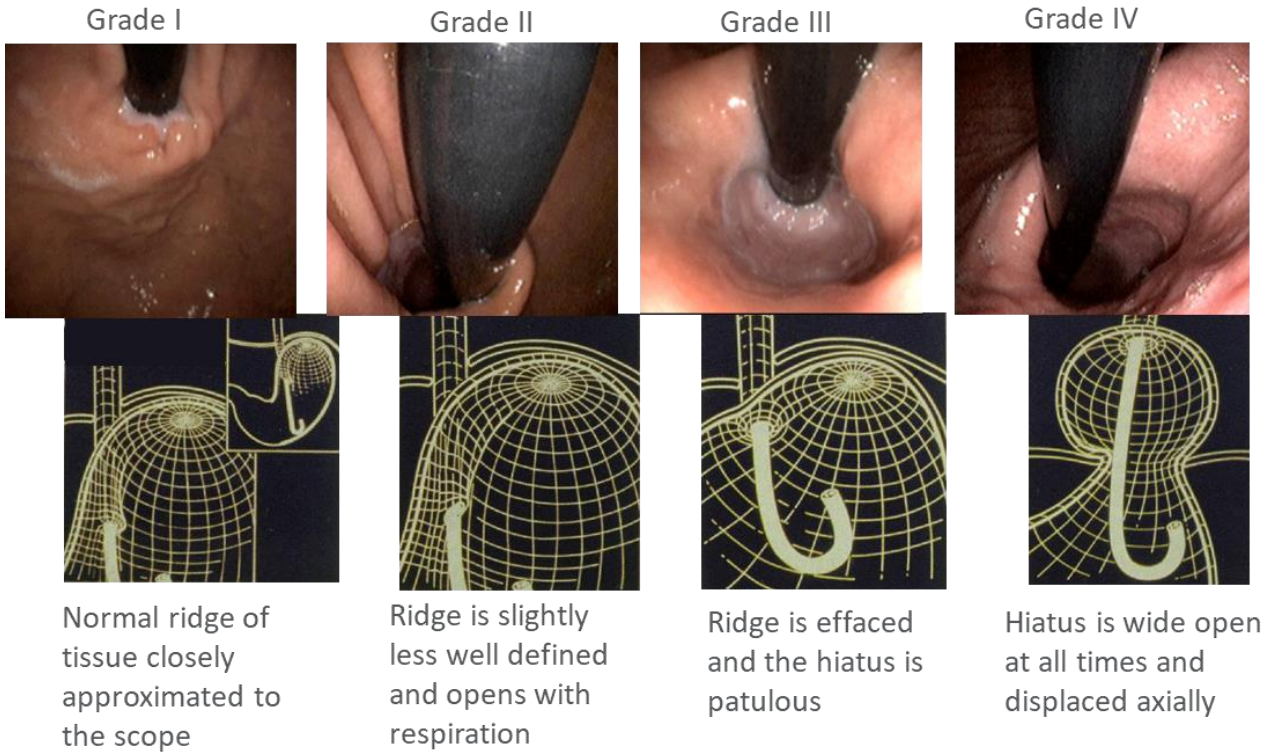


One or more mucosal breaks bridging the tops of mucosal folds involving <75% of the circumference

Los Angeles Grade D



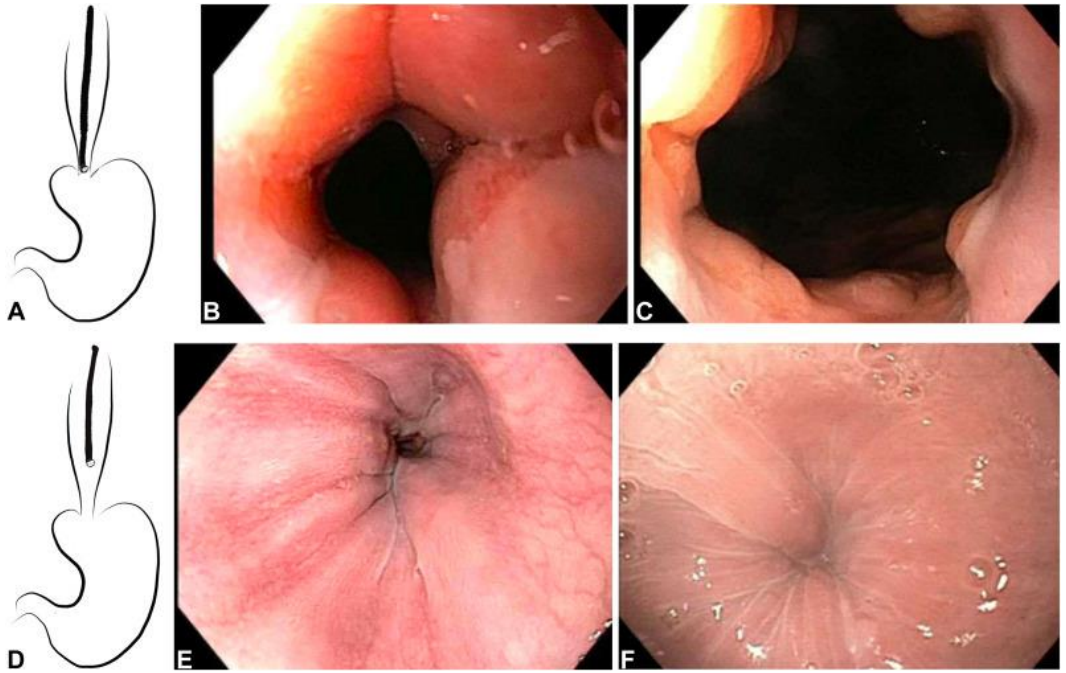
One or more mucosal breaks bridging the tops of mucosal folds involving >75% of the circumference

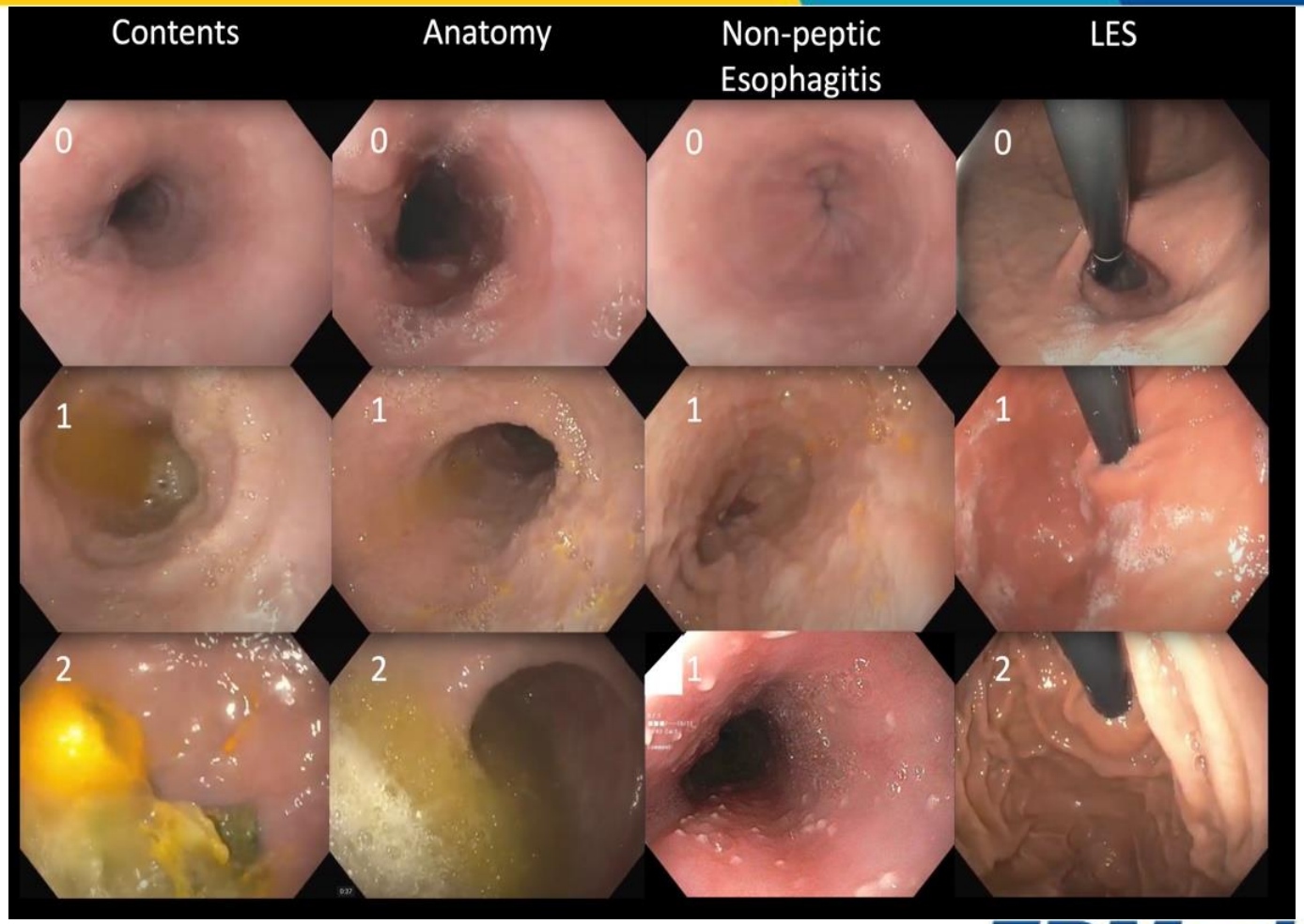


Lundell LR, et al. *Gut*. 1999;45:172-180; Armstrong D, et al. *Gastrenterology*. 1996;111:85-92; Hill LD, et al. *Gastrointest Endosc*. 1996;44:541-547.

Clinical Impression of the EGD: Motility Assessment

Assessing EGJ and Body
25% will have a normal EGD





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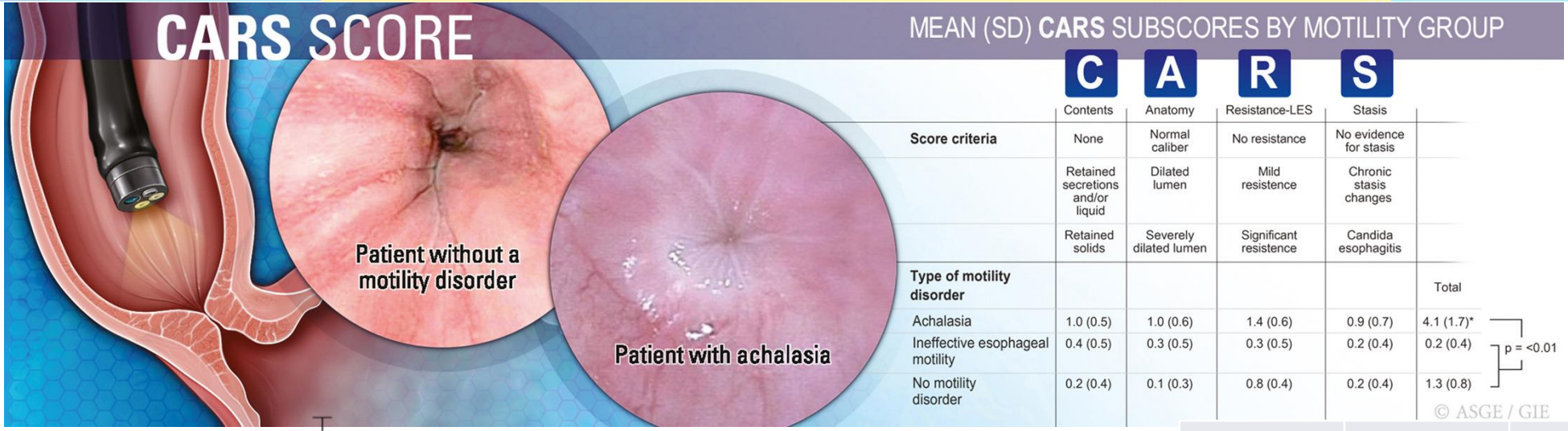
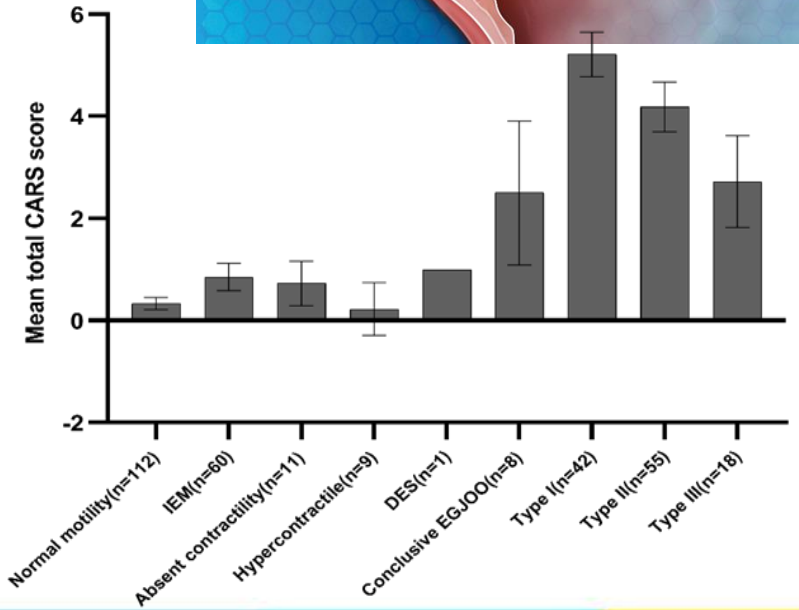
An Endoscopic Scoring System for Achalasia: The CARS Score

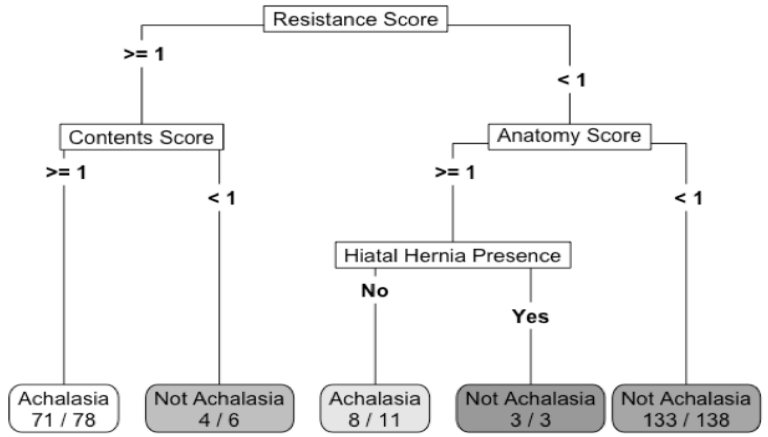


MEAN (SD) **CARS** SUBSCORES BY MOTILITY GROUP

	C Contents	A Anatomy	R Resistance-LES	S Stasis	
Score criteria	None	Normal caliber	No resistance	No evidence for stasis	
	Retained secretions and/or liquid	Dilated lumen	Mild resistence	Chronic stasis changes	
	Retained solids	Severely dilated lumen	Significant resistence	Candida esophagitis	
Type of motility disorder					Total
Achalasia	1.0 (0.5)	1.0 (0.6)	1.4 (0.6)	0.9 (0.7)	4.1 (1.7)*
Ineffective esophageal motility	0.4 (0.5)	0.3 (0.5)	0.3 (0.5)	0.2 (0.4)	0.2 (0.4)
No motility disorder	0.2 (0.4)	0.1 (0.3)	0.8 (0.4)	0.2 (0.4)	1.3 (0.8)

p = <0.01





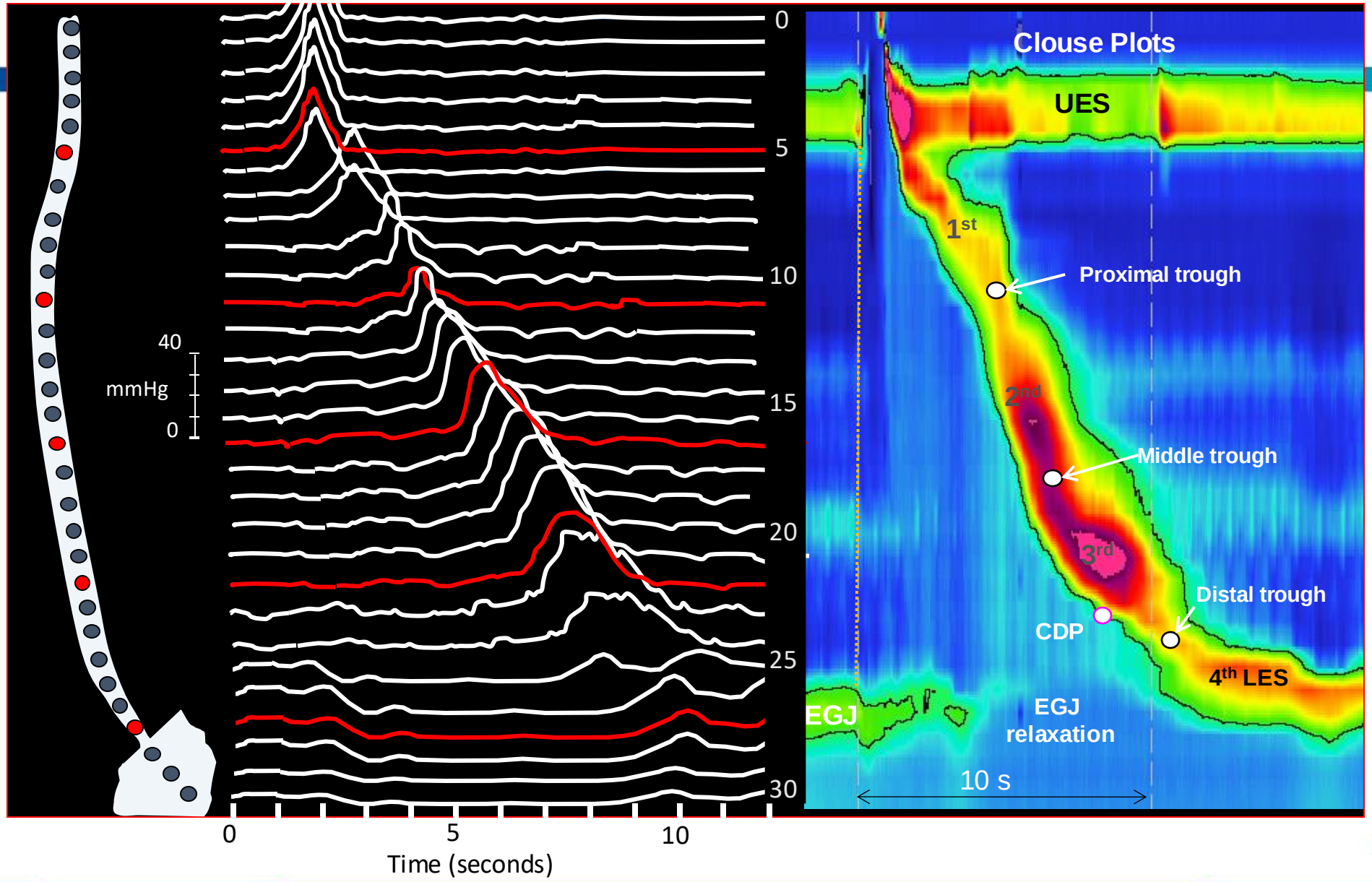
CARS score	Positive Within Interval	Negative Within Interval	Interval LR
≥4	83	3	48.36
3	13	6	3.79
2	6	15	0.70
1	9	56	0.28
0	4	121	0.06

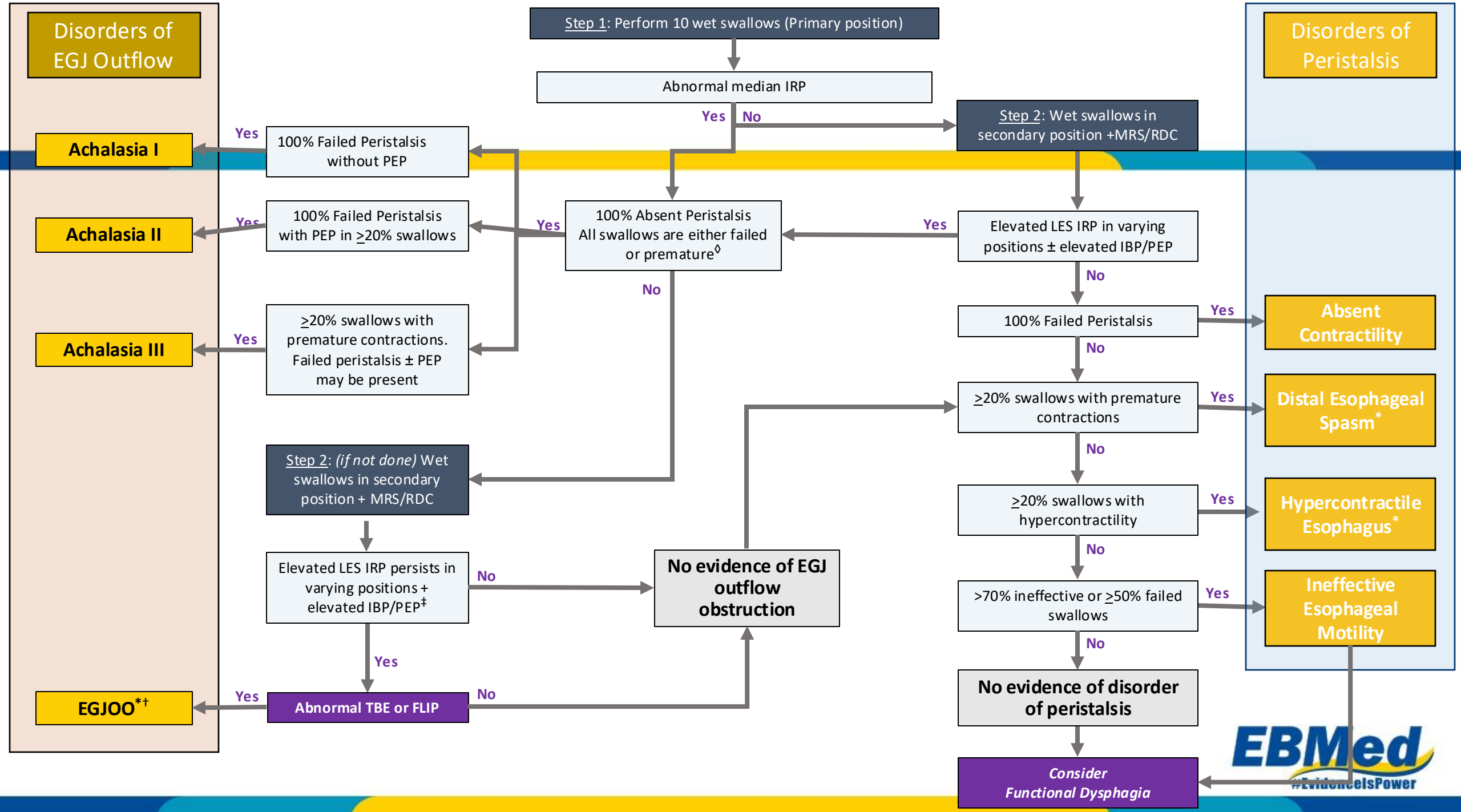
Ellison A, et al. *Gastrointest Endosc*. 2024;100:417-428.e1.

Catheter Configuration

Line Plots (pressure vs time) of Conventional and High Resolution Manometry

HRM Plotted in Esophageal Pressure Topography




Disorders of EGJ Outflow
Step 1: Perform 10 wet swallows (Primary position)
Abnormal median IRP
Yes
No
Step 2: Wet swallows in secondary position +MRS/RDC
Disorders of Peristalsis
Achalasia I
Yes
100% Failed Peristalsis without PEP
Achalasia II
Yes
100% Failed Peristalsis with PEP in ≥20% swallows
Yes
100% Absent Peristalsis All swallows are either failed or premature◊
Yes
Elevated LES IRP in varying positions ± elevated IBP/PEP
Achalasia III
Yes
≥20% swallows with premature contractions. Failed peristalsis ± PEP may be present
No
No
100% Failed Peristalsis
Yes
Absent Contractility
No
≥20% swallows with premature contractions
Yes
Distal Esophageal Spasm*
Step 2: (if not done) Wet swallows in secondary position + MRS/RDC
No
≥20% swallows with hypercontractility
Yes
Hypercontractile Esophagus*
Elevated LES IRP persists in varying positions + elevated IBP/PEP‡
No
No evidence of EGJ outflow obstruction
No
>70% ineffective or ≥50% failed swallows
Yes
Ineffective Esophageal Motility
Yes
No
EGJOO*†
Yes
Abnormal TBE or FLIP
No
No evidence of disorder of peristalsis
Consider Functional Dysphagia
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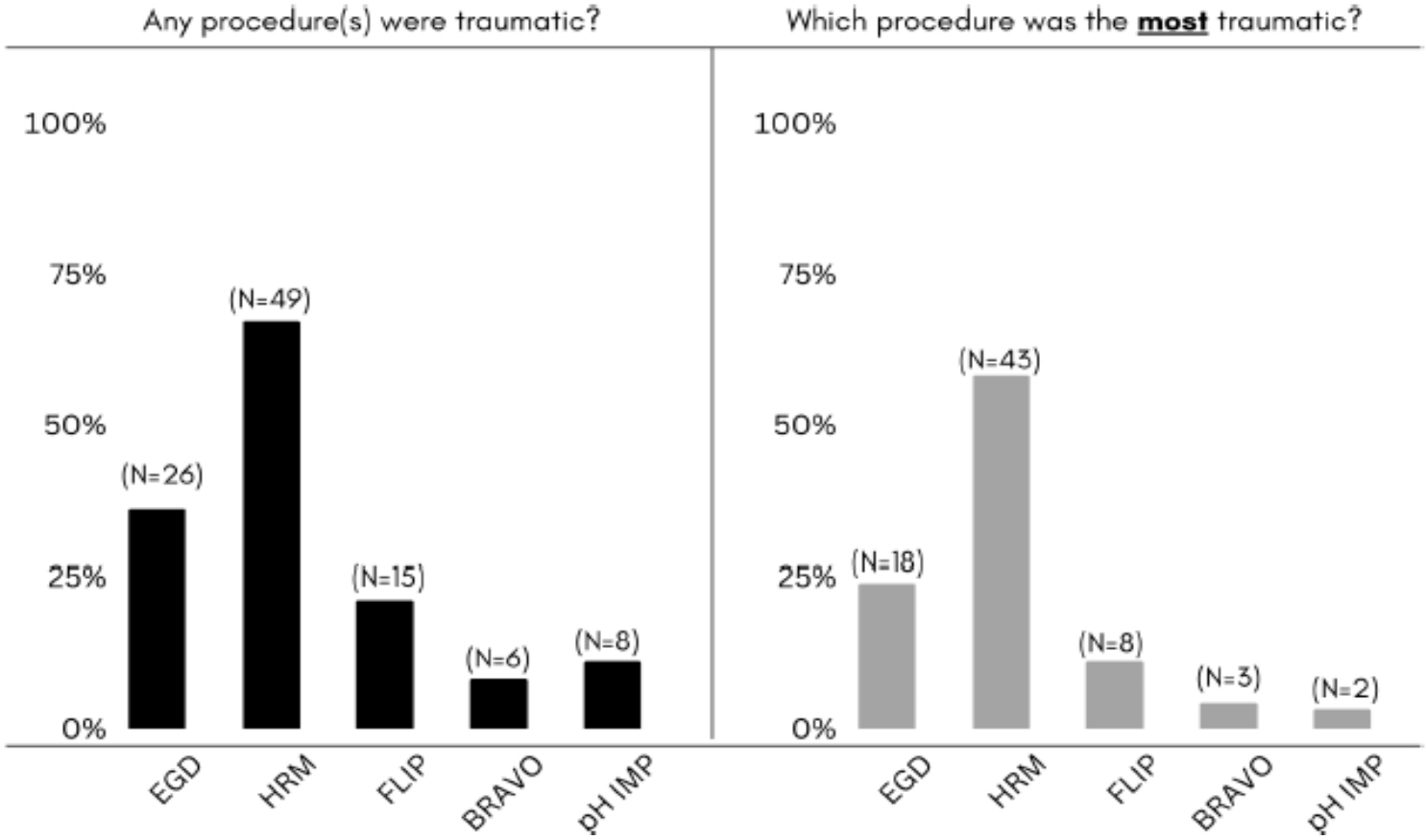
Tolerability of Esophageal Diagnostics

Of the 5 esophageal procedures included, only HRM was significantly associated with the likelihood of having a traumatic experience ($\chi 2 = 8.92$, $p = 0.003$).



Taft TH, et al. *Neurogastroenterol Motil*. 2023;35:e14540.

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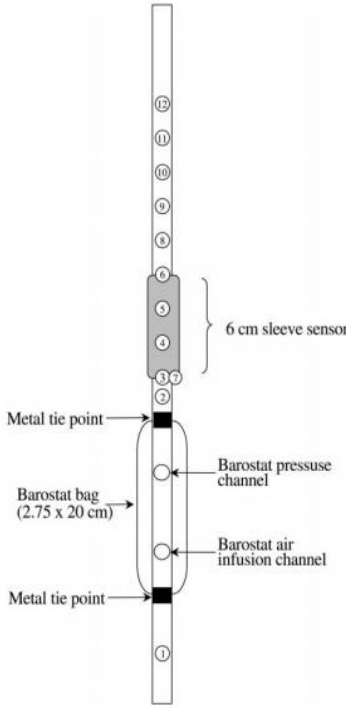
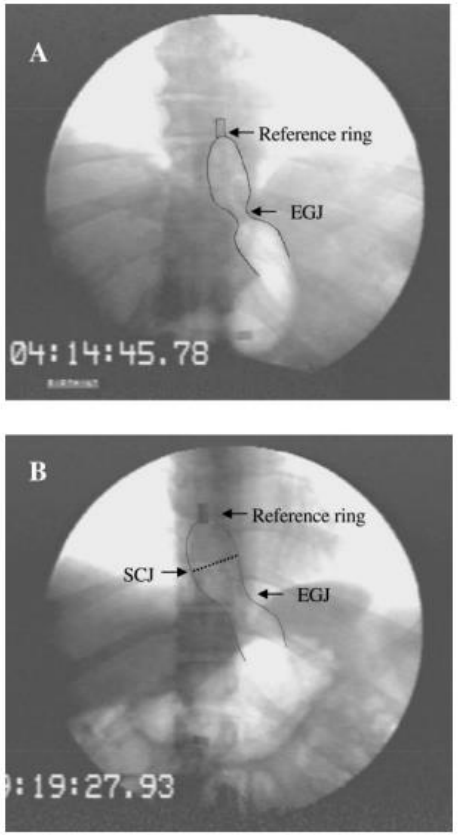
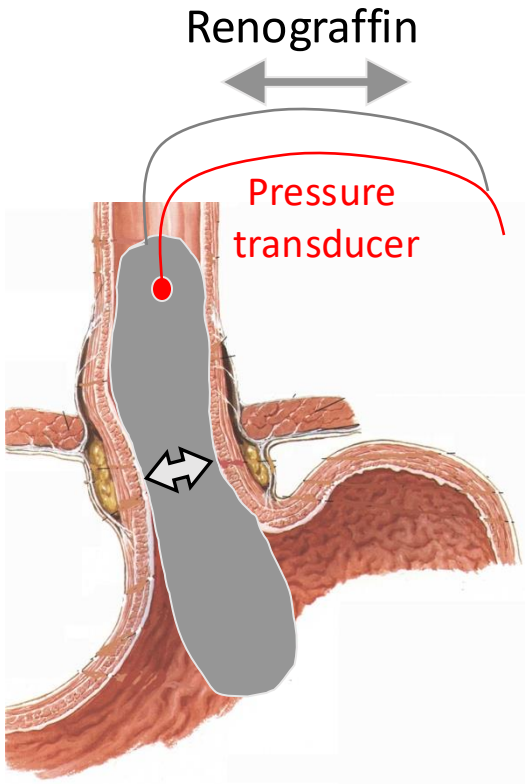
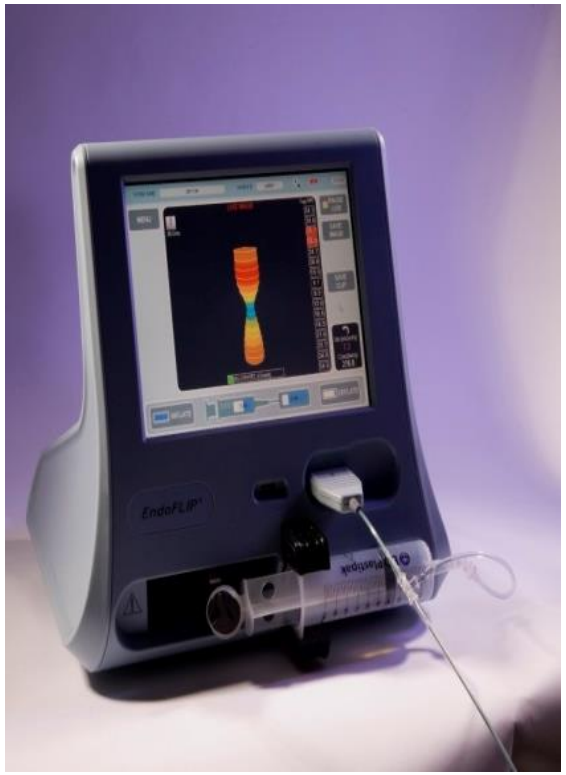
Response to Volumetric Distention - Distensibility - Measuring Mechanical Properties of the Esophagus

Barostat → Hydrostat → Functional Lumen Imaging Probe









Esophageal Center at Northwestern

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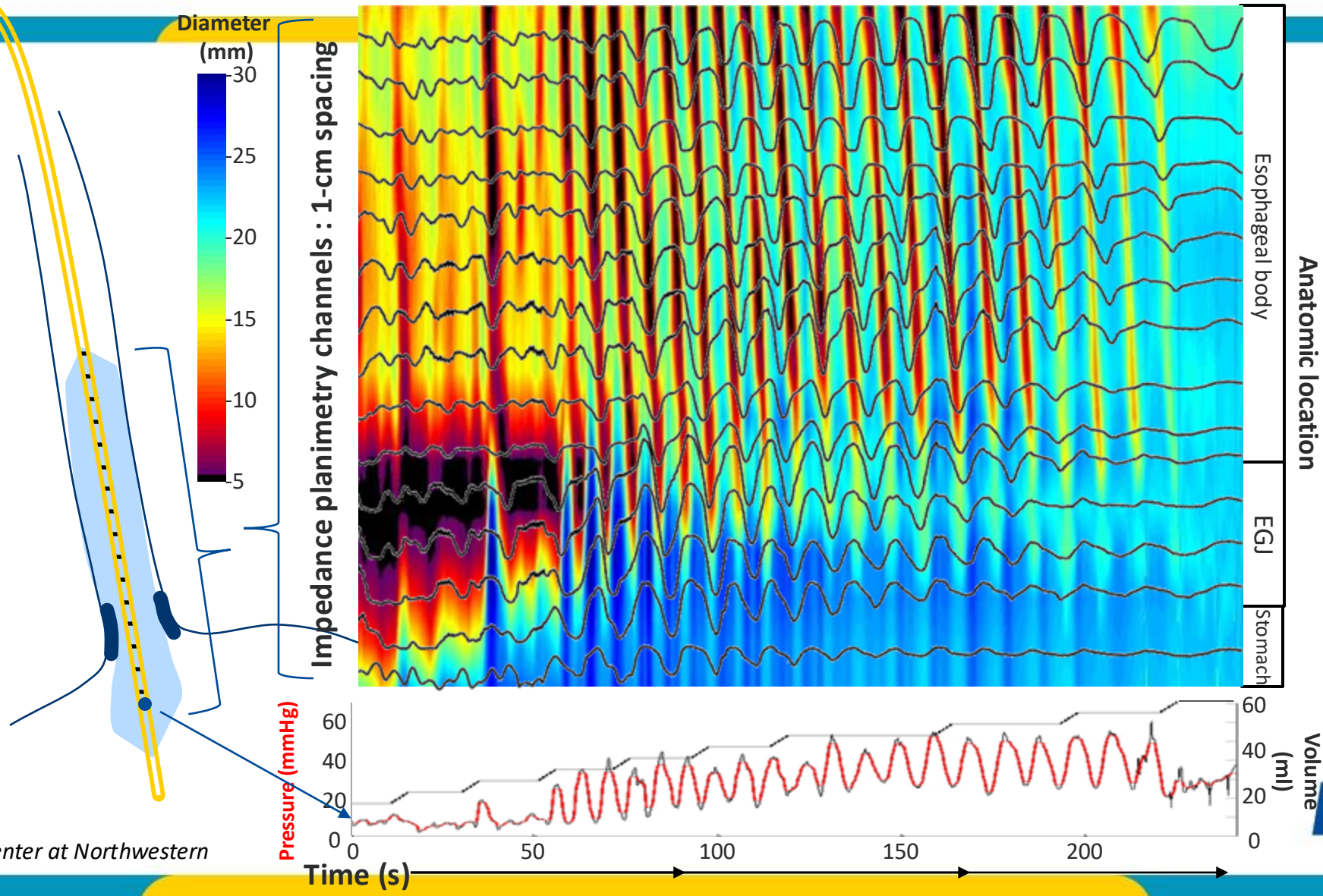
Flip Panometry: Esophageal Diameter Topography



Esophageal Center at Northwestern

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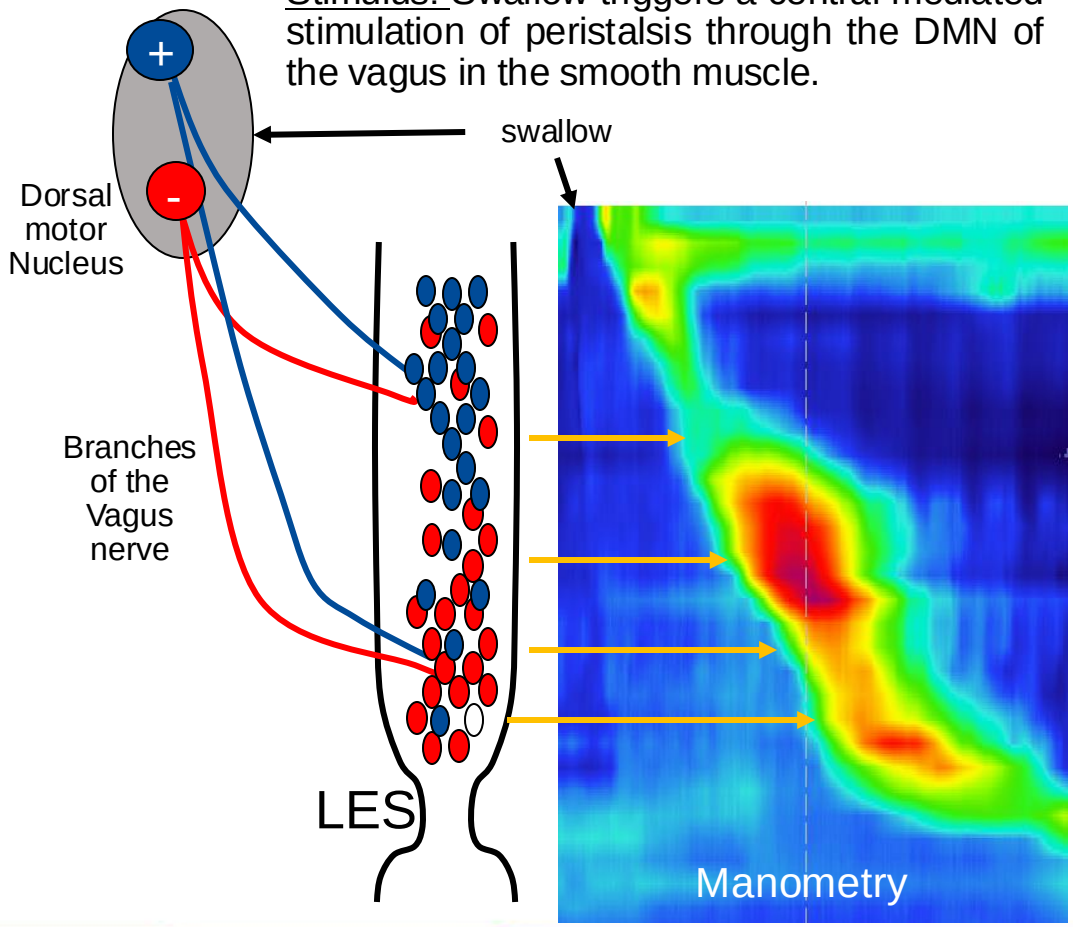
Assessing Neuromyogenic Function of the Esophagus

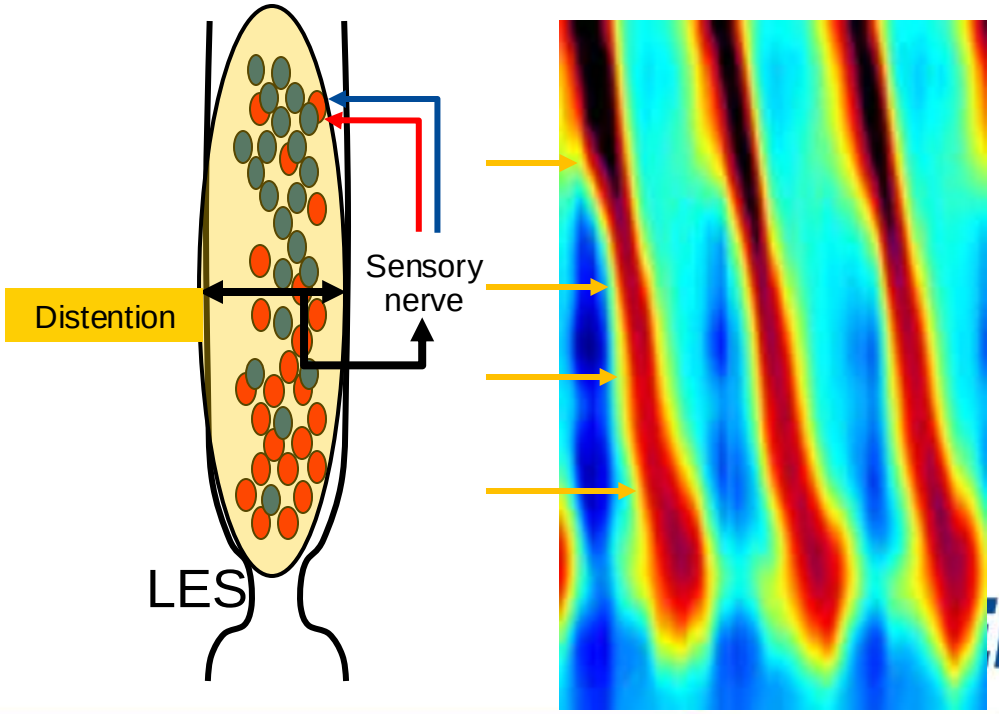
Primary Peristalsis

Stimulus: Swallow triggers a central mediated stimulation of peristalsis through the DMN of the vagus in the smooth muscle.

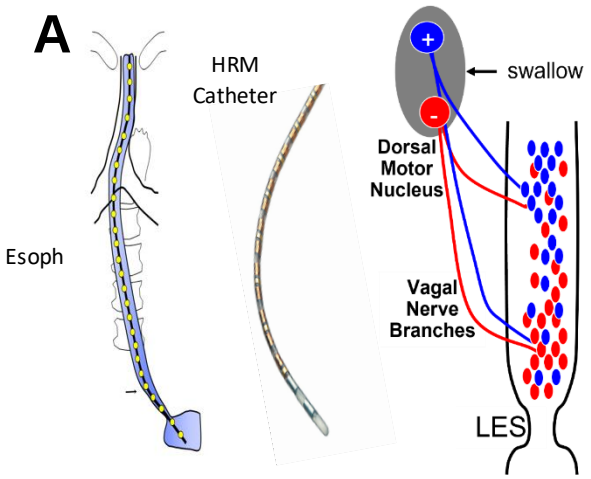


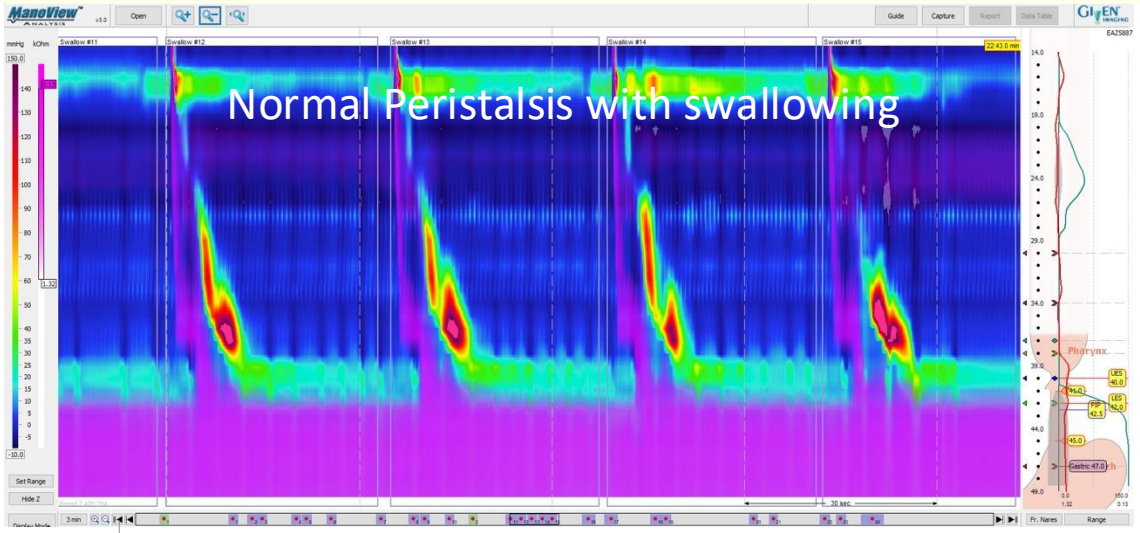
Secondary Peristalsis

Stimulus: Balloon Distention mediates a local reflex that causes contraction above the distention and relaxation below. Sustained axial contraction with **FLIP** will elicit simultaneous stimulation of the intrinsic enteric nerves and the direction and timing of the contraction will follow the intrinsic latency gradient.

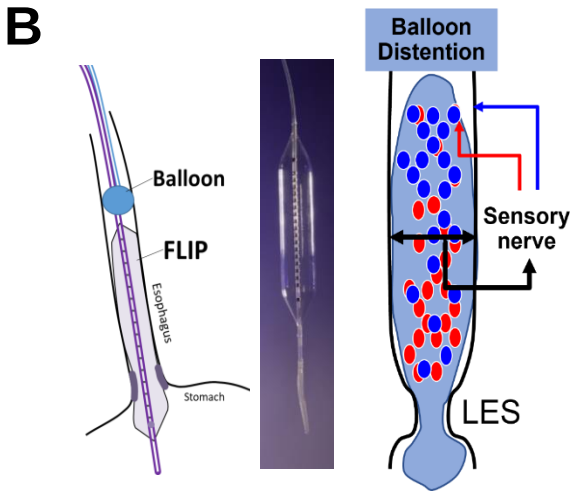


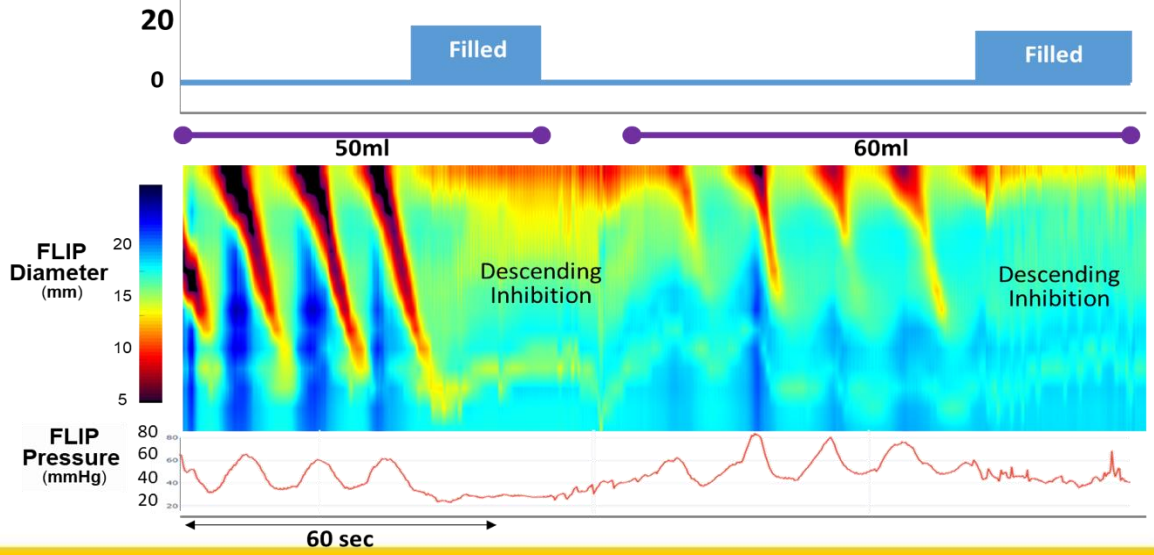
Background: Differences Between Manometry (A) and FLIP (B)





- High-resolution manometry
- Done unsedated- but need an endoscopy first to make sure there is no mechanical obstruction.
- 10- 20 swallows and make measurements of pressure
- Can determine if the esophageal muscles are working appropriately





- FLIP Panometry
- Done sedated while the patient is getting their endoscopy
- A bag is filled and triggers peristalsis and rate and strength of the contraction can be measured.
- The protocol is 40-70 ml distentions for 1 minute

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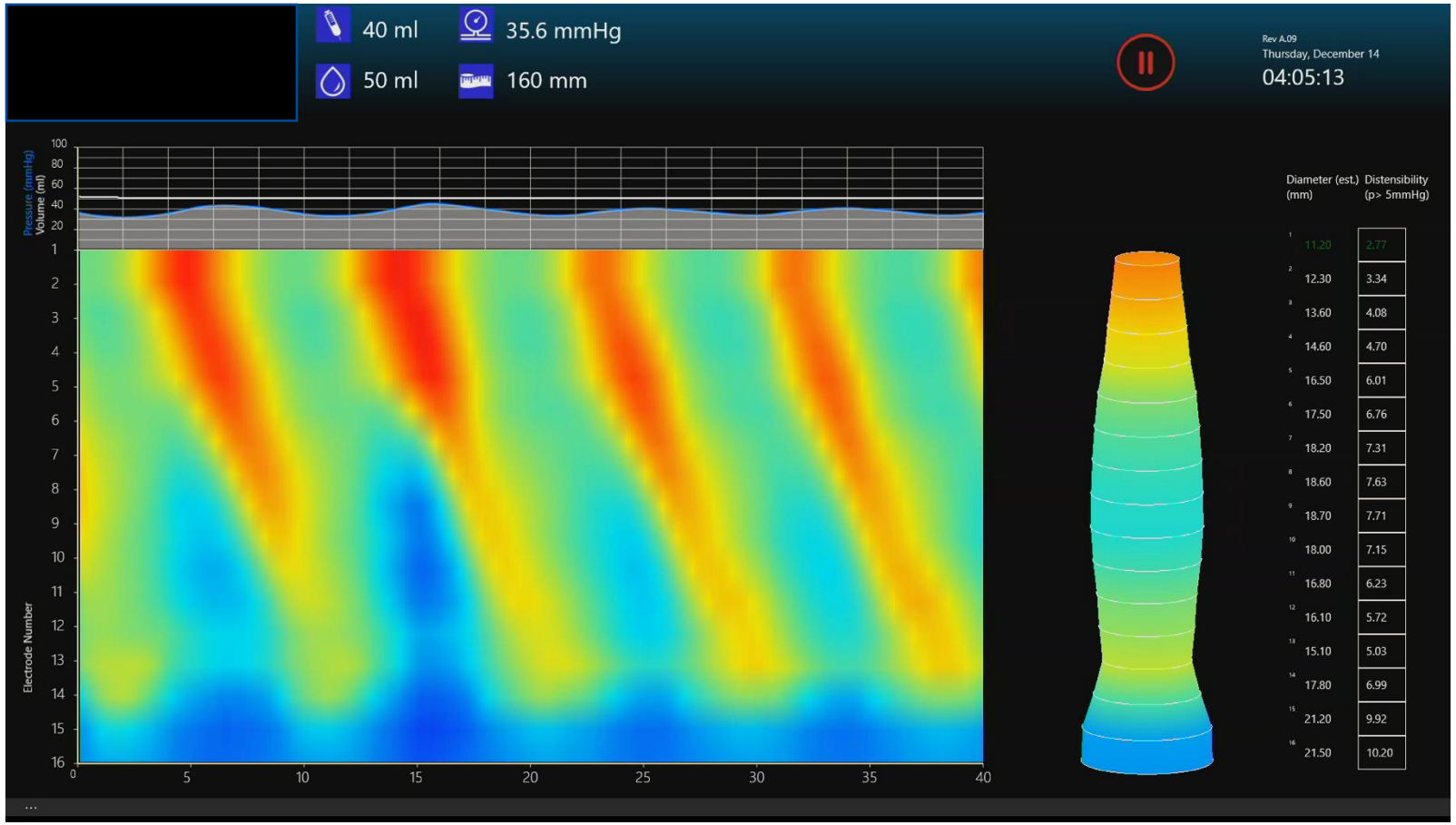
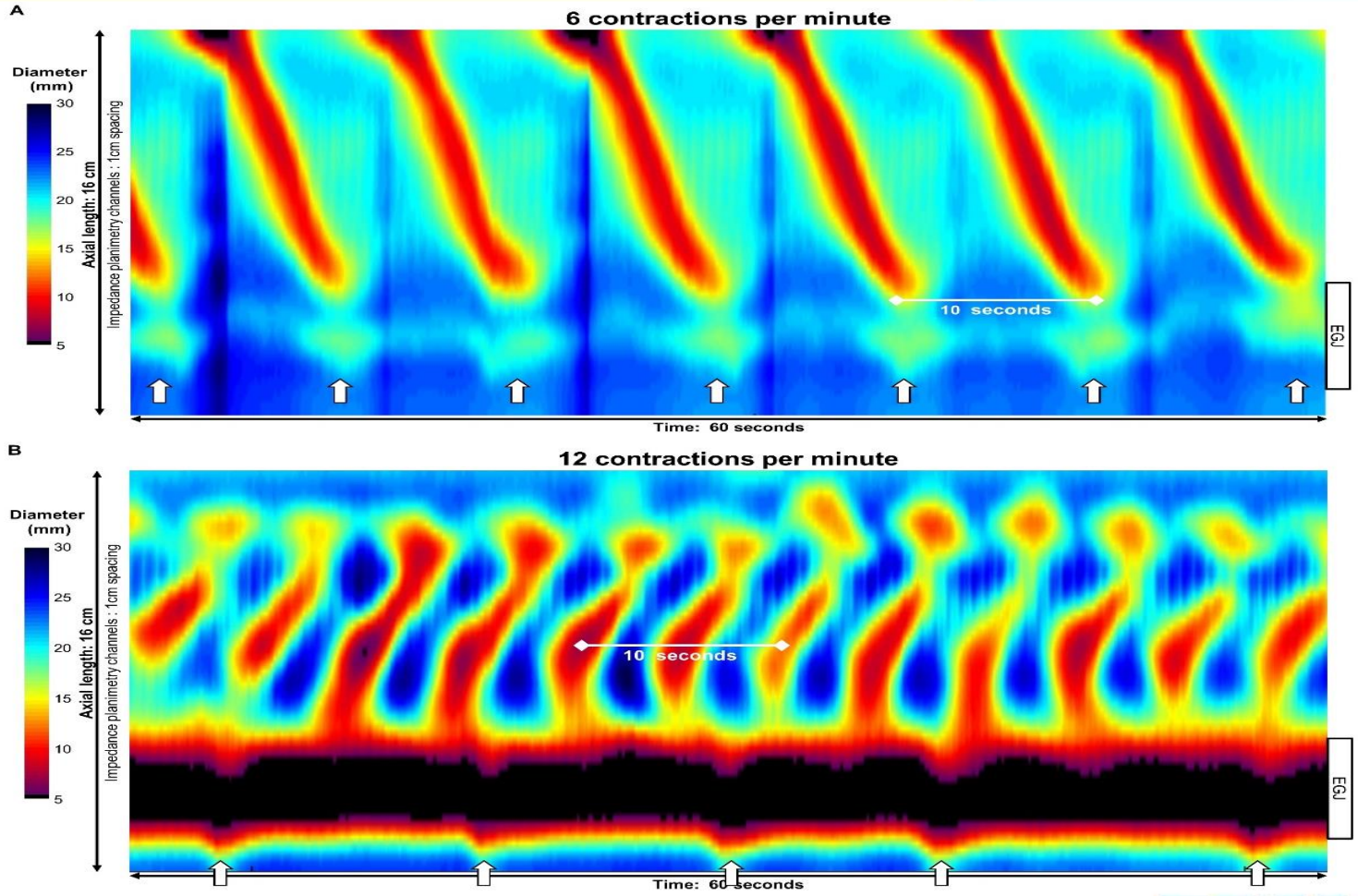
Flip Panometry: Assessing Esophageal Function using Topography



Rate of RACS: *Rule of 6*

- At least 6 repeating lumen occlusions longer than 6 cm at a consistent rate of 6 (+/- 3) per minute
- Governed by the inhibitory gradient and refractory period of the esophagus
- ?Pacemaker



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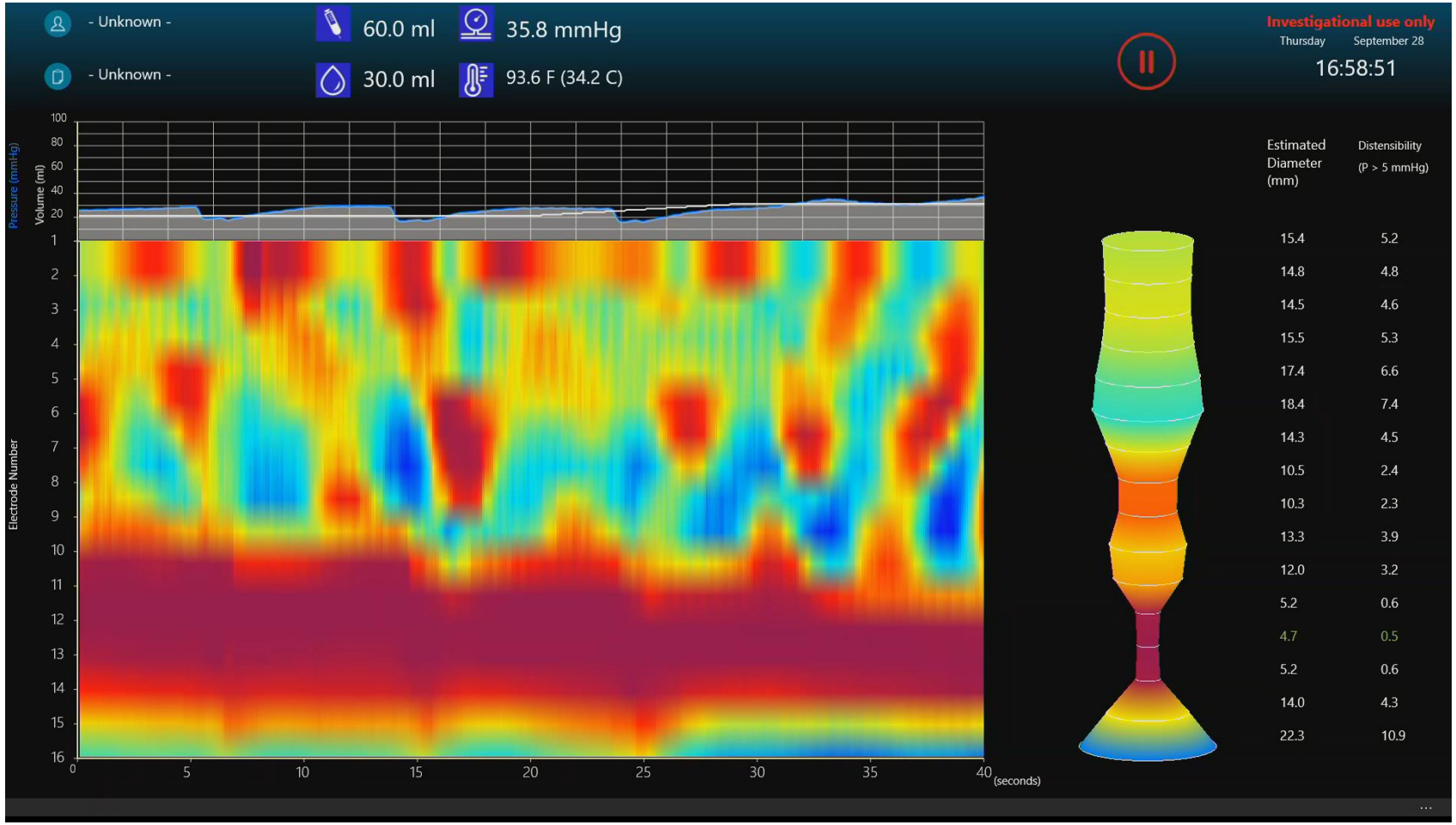
FLIP Cases: Achalasia Type III



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Esophageal Symptoms

What FLIP Panometry can do during the index EGD

- Assess peristalsis by triggering secondary peristalsis.
  - Can separate motility into physiologic and clinically relevant patterns to assess peristaltic function [Swallow type, DCI on HRM] POWER/WORK
- Assess EGJ Opening dynamics.
  - IRP on HRM, EGJ opening on TBE EGJ-DI/MAXD- Probability
- Provide an estimate of esophageal stiffness and determine the minimal diameter for impaction risk for EoE patients and strictures.
  - Determine minimal diameter similar to esophagram and compliance of the esophagus
- Potentially guide esophageal surgery.
  - Intraoperative and post-operative evaluation

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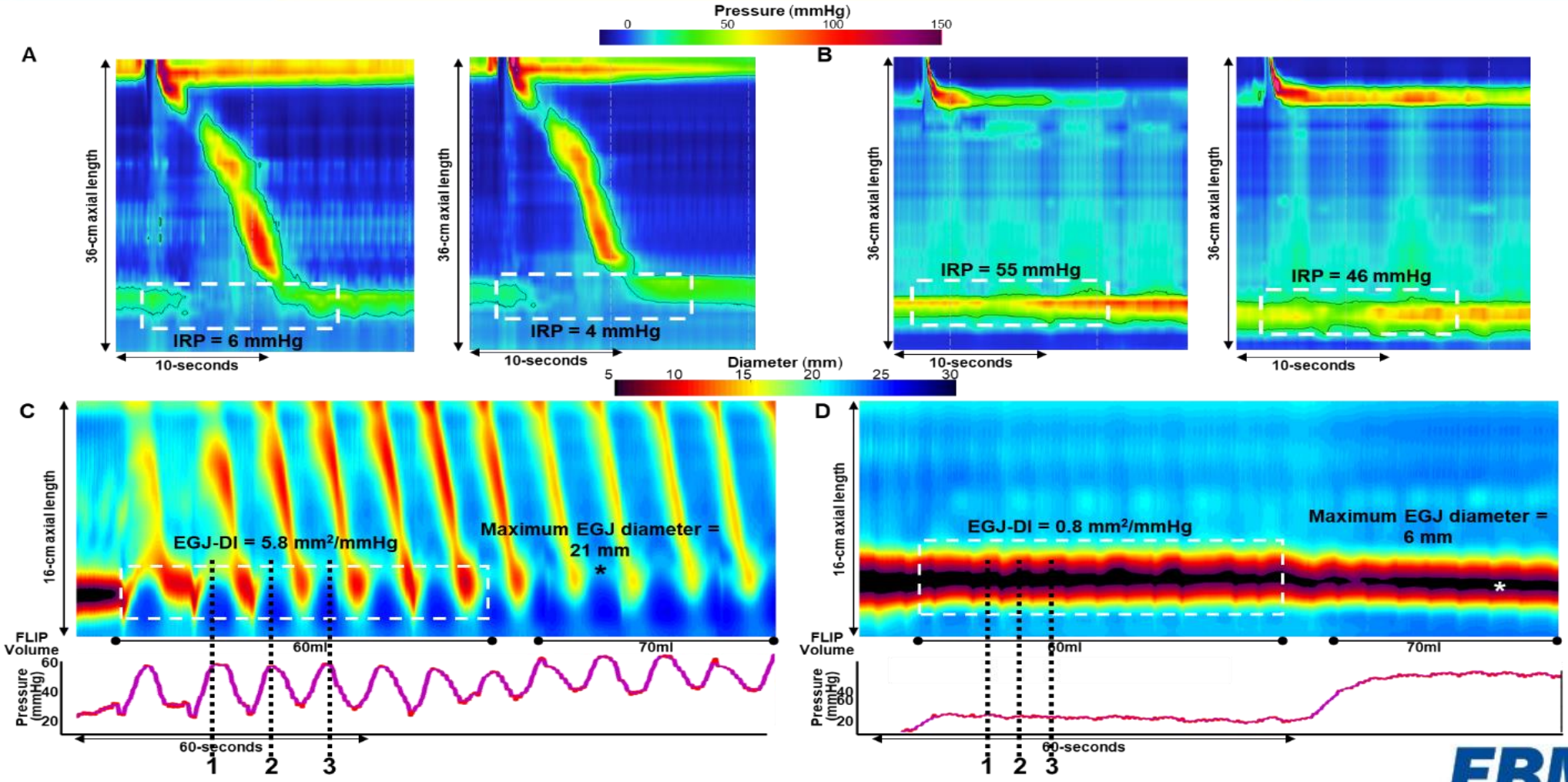
Assessing EGJ Opening Dynamics in the Context of Peristalsis
Balancing EGJ-DI and Max Diameter



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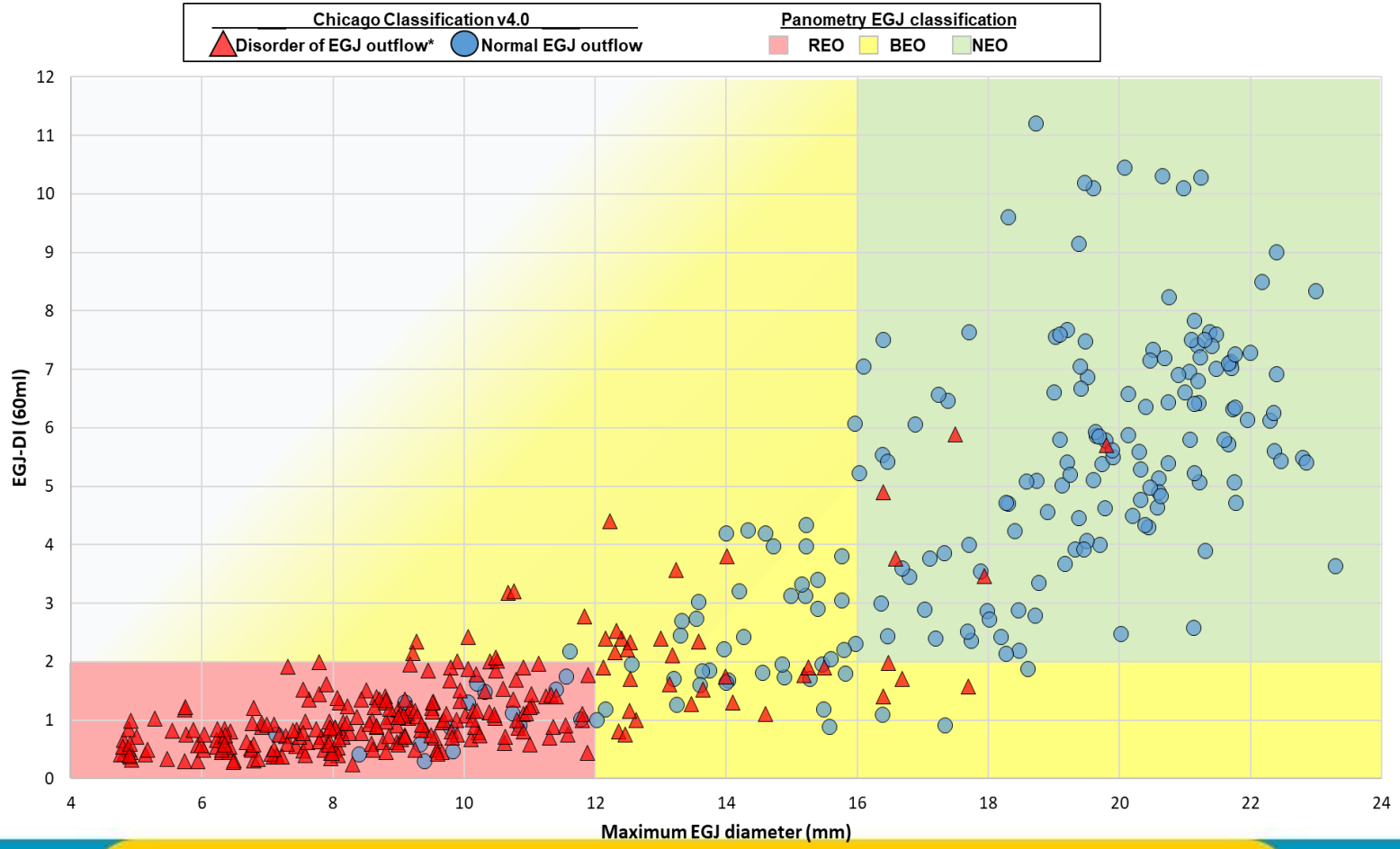
Assessing EGJ Opening Dynamics in the Context of Peristalsis Balancing EGJ-DI and Max Diameter

Association of FLIP Panometry esophagogastric junction (EGJ) opening parameters with esophagogastric junction (EGJ) obstruction based on the Chicago Classification v4.0.



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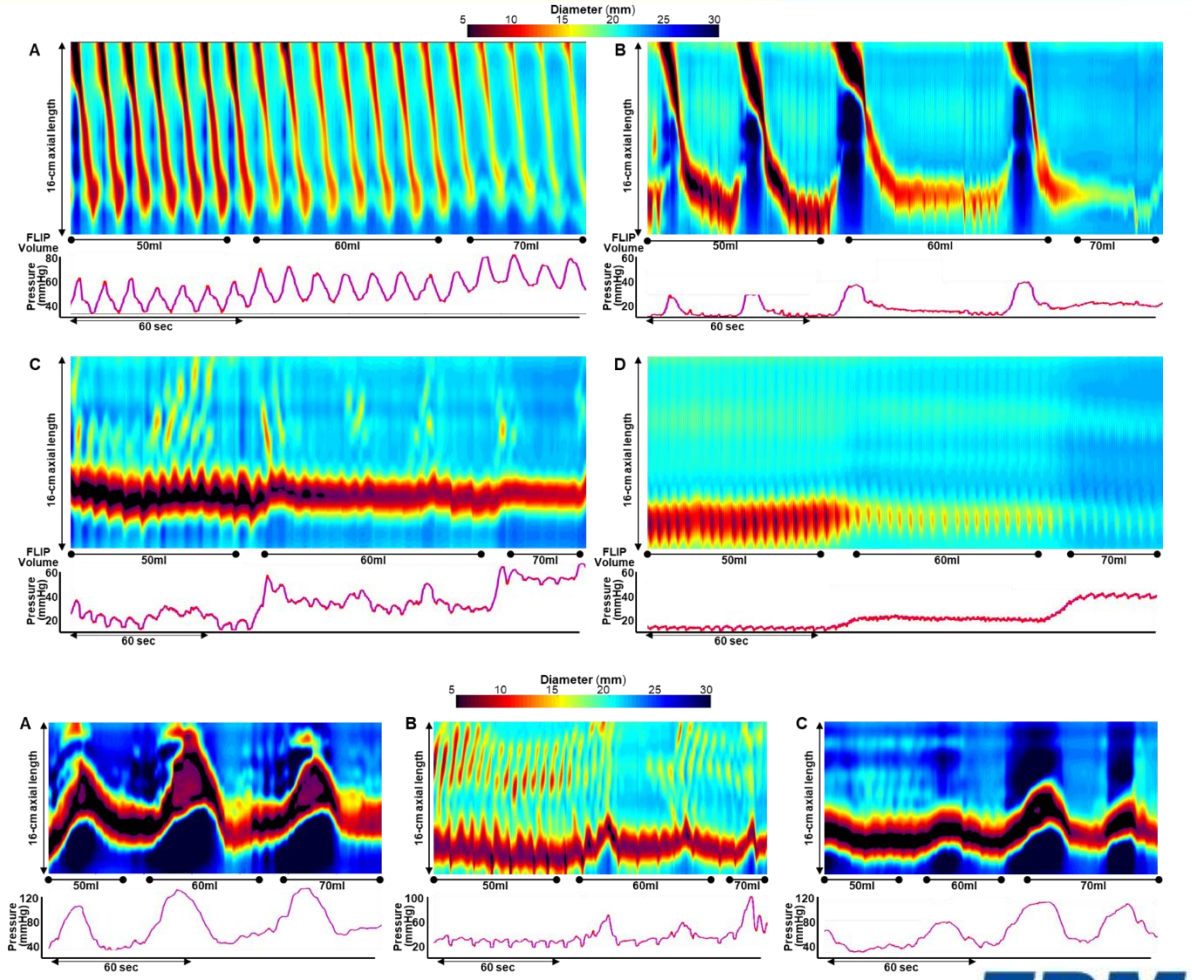
FLIP Panometry Contractile Patterns

Panometry Contractile Response Patterns	Definition
Normal Contractile Response **NCR**	RAC-Rule of 6s (Ro6s) ▪ ≥6 consecutive AC's of ▪ ≥6 cm in axial length occurring at ▪ 6+/-3 AC per minute regular rate
Borderline Contractile Response **BCR**	▪ Not meeting RAC Ro6 ▪ Distinct AC of at least 6-cm axial length present ▪ May have RCs - but not RRCs ▪ No SOCs or sLESCs
Impaired/Disordered Contractile Response **IDCR**	▪ No distinct ACs ▪ May have sporadic or chaotic contractions not meeting ACs ▪ May have RCs- but not RRCs ▪ No SOCs
Absent Contractile Response **ACR**	▪ No contractile activity in the esophageal body
Spastic-Reactive Contractile Response **SRCR**	▪ SOC or ▪ sLESC or ▪ RRCs- at least 6 RCs at rate > 9 RCs per minute ▪ May have sporadic AC's



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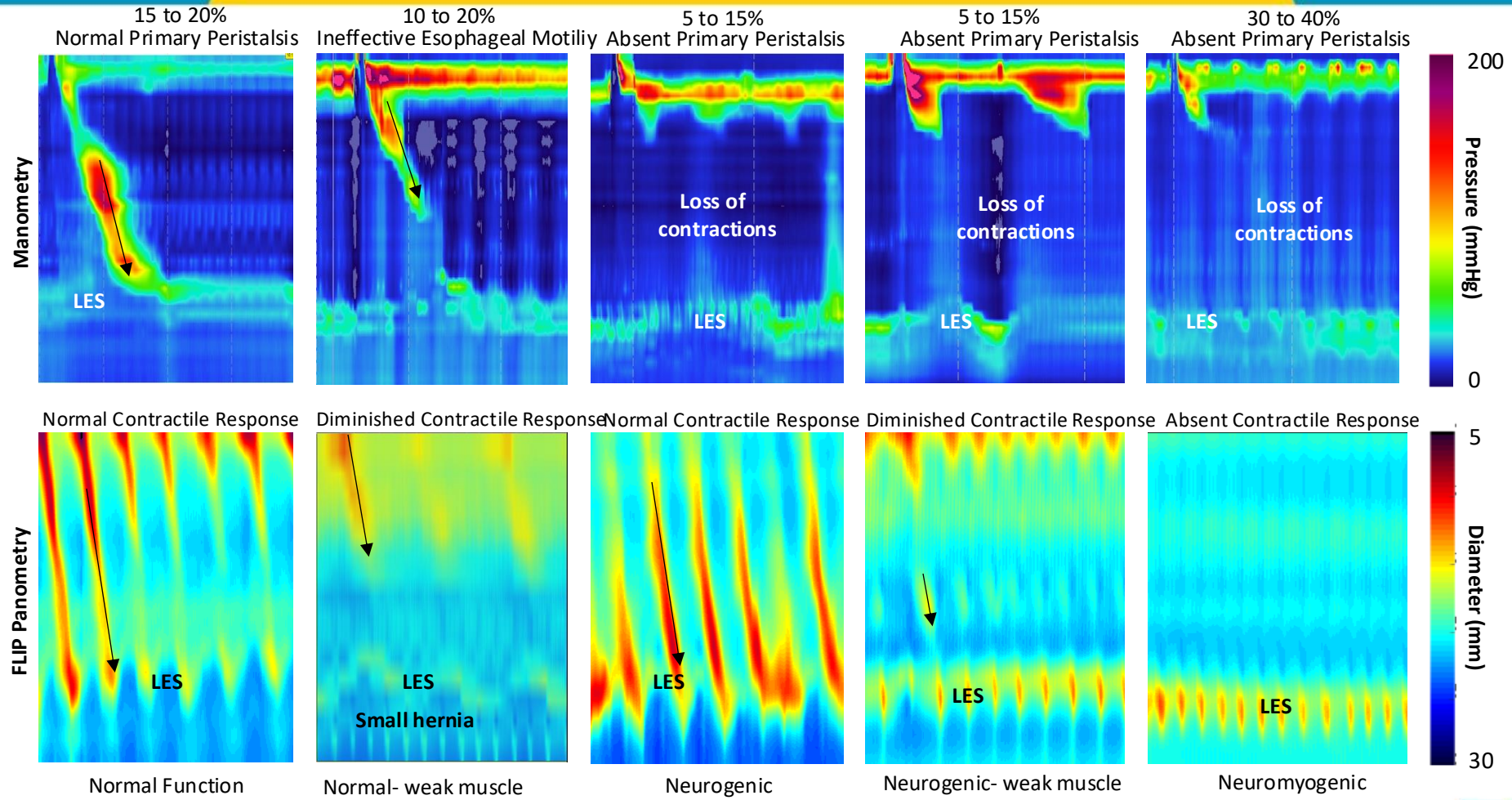
Subtypes of Esophageal Function in SSc Defined by Combined Manometry/FLIP-panometry.



*This model has the capacity to define disease progression along the neurogenic and myogenic pathway in extreme detail to provide a timeline for our translation assessment of molecular targets and biomarkers. Additionally, this assessment may uncover distinct phenotypes beyond the classic progression to aperistalsis and that may have varying levels of neurogenic dysfunction (subtype 3).

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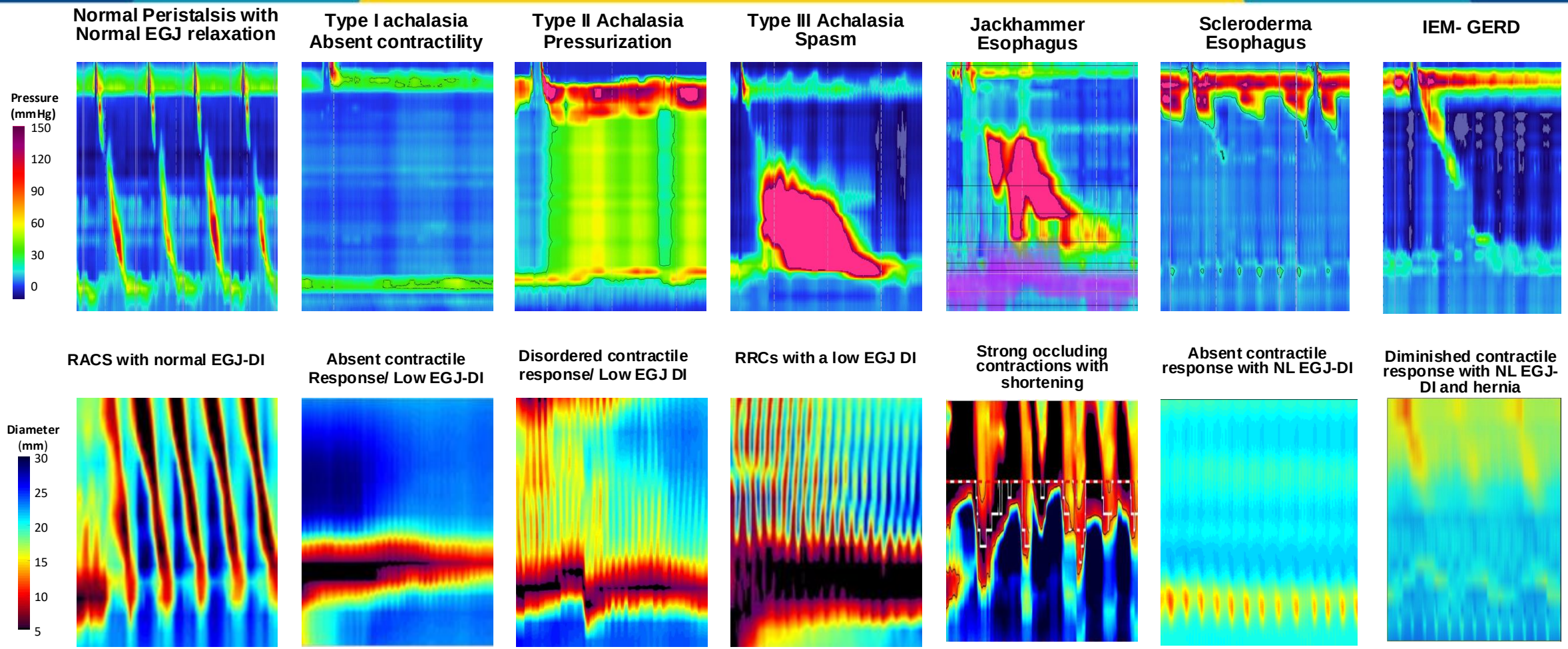
FLIP Panometry: Contractile Patterns - Tempting to Mimic CC



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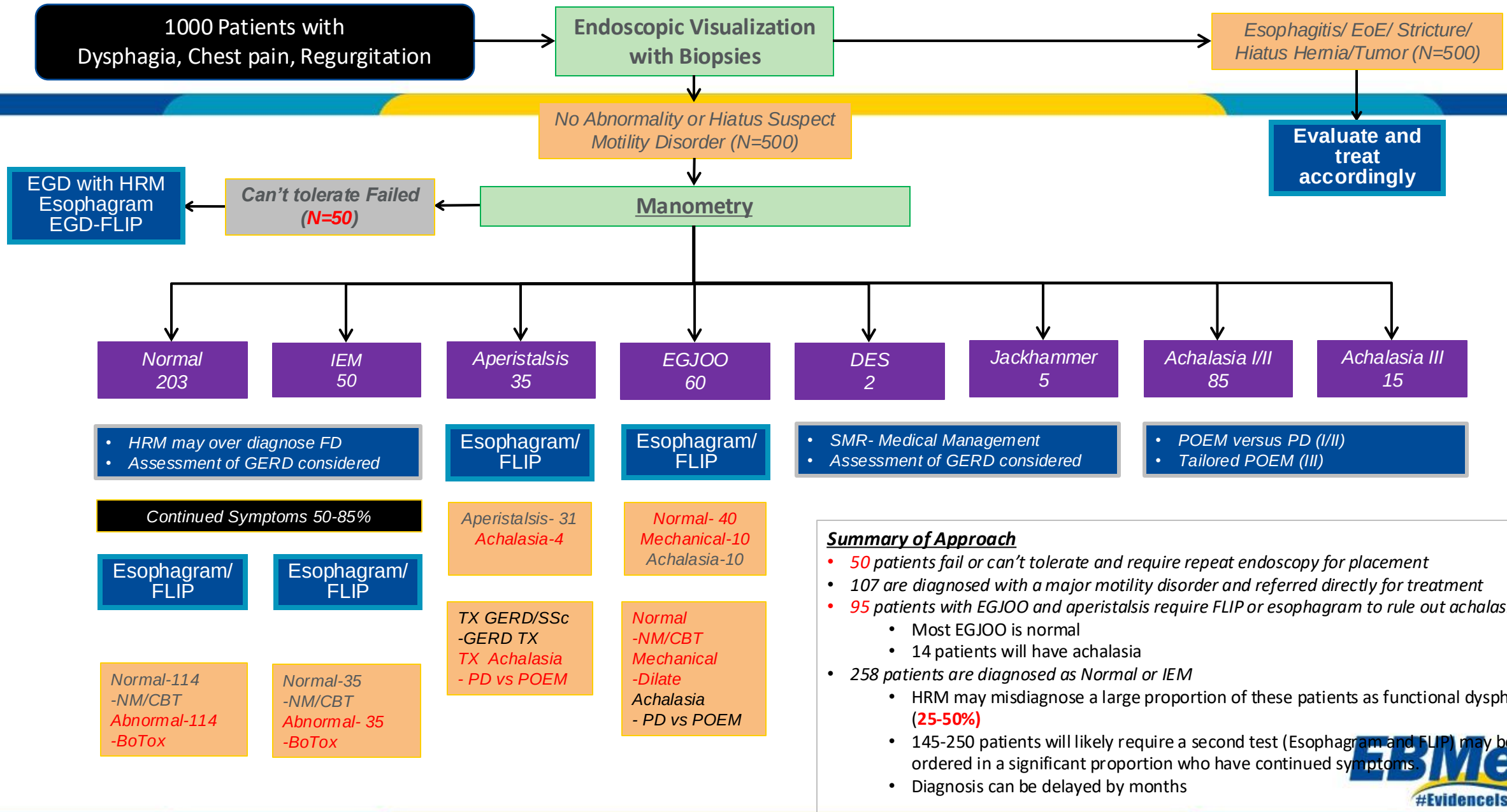
Standard Management for Dysphagia



Summary of Approach

- *50 patients fail or can't tolerate and require repeat endoscopy for placement*
- *107 are diagnosed with a major motility disorder and referred directly for treatment*
- *95 patients with EGJOO and aperistalsis require FLIP or esophagram to rule out achalasia*
  - Most EGJOO is normal
  - 14 patients will have achalasia
- *258 patients are diagnosed as Normal or IEM*
  - HRM may misdiagnose a large proportion of these patients as functional dysphagia- (**25-50%**)
  - 145-250 patients will likely require a second test (Esophagram and FLIP) may be ordered in a significant proportion who have continued symptoms.
  - Diagnosis can be delayed by months

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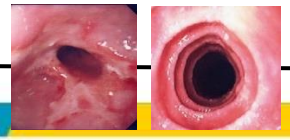
New Management Algorithm

Patient with Esophageal Symptoms
Dysphagia, Regurgitation, Chest Pain- r/o cardiac causes

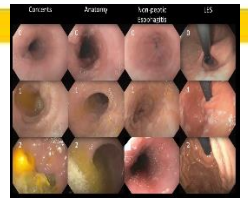
EGD-OFF PPI

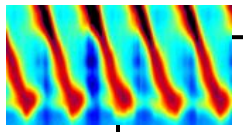
Esophagitis > LA B, LSBE, Hernia > 5cm
Stricture, Overt EoE- EREF > 1
Other esophagitis



Treat accordingly

CARS Score/ FLIP Panometry
Biopsies for Dysphagia and Chest Pain with eating





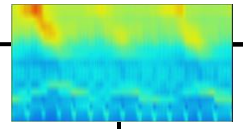
Normal

Bravo

Bravo Positive
Biopsies Negative
DX: GERD
REFLUX TX

Bravo Negative
Biopsies Negative
DX: DGBI
HYP/NMod

Bravo Negative
Biopsies Positive
DX: EoE

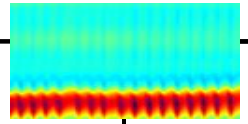


Hypocontractile

Bravo

Bravo Positive
Biopsies Negative
DX: GERD
REFLUX TX

Bravo Negative
Biopsies negative
DX: S-IEM
Lifestyle/Diet
Promotility
HYP/NMod



Possible Obstruction

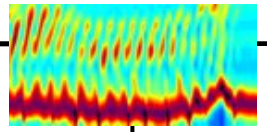
Targeted Dilation
Using MaxD and DP

Disruption:
DX: Stricture
R/O EoE, REFLUX TX

No Response
Biopsies Positive
DX EoE

No Response
Biopsies negative

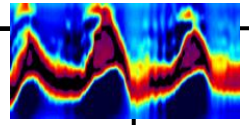
HRM
Probability of MMD based on CARS and Contractile Pattern



Possible Spasm/JH

Rare

HRM
Probability of MMD
CARS ≤ 2- < 50%
CARS > 2- > 75%

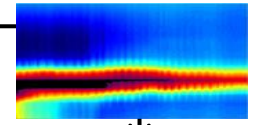


Spastic Obstruction

DX: Achalasia II/III
EGJOO

HRM

Subtype Achalasia
Tailored treatment



Non-Spastic Obstruction

CARS > 4
DX: Achalasia I/II
TX:PD/POEM/LHM

CARS ≤ 4
DX Achalasia,
EGJOO or PDMO

HRM

Subtype Achalasia
Tailored treatment
PDMO- consider BoTox

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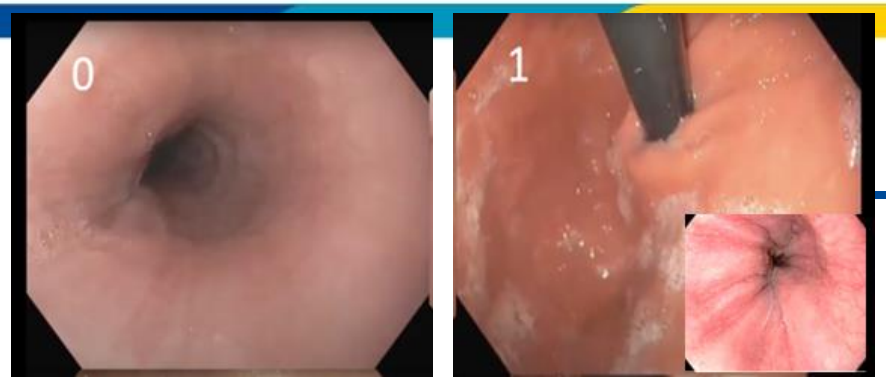
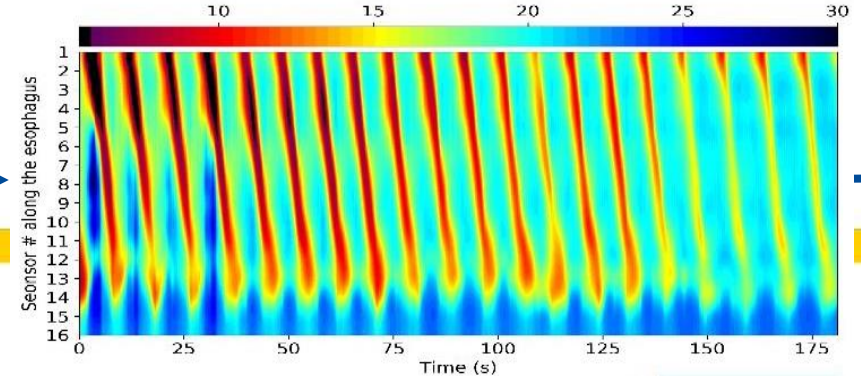
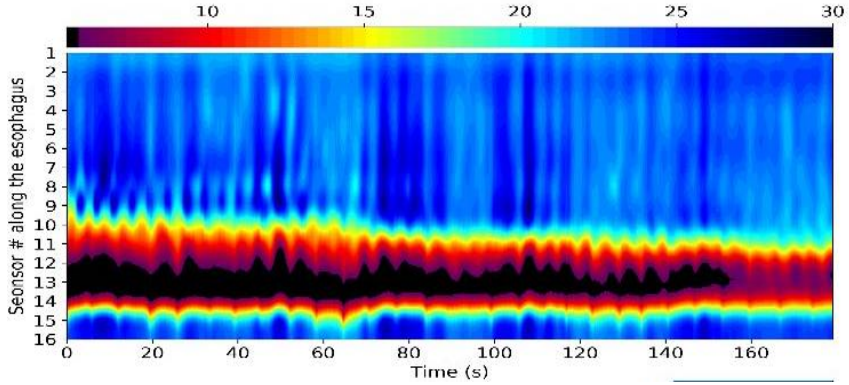
Real Time Assessment

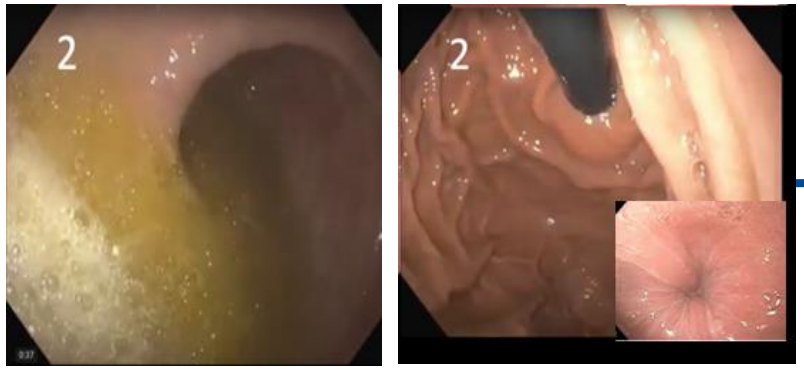


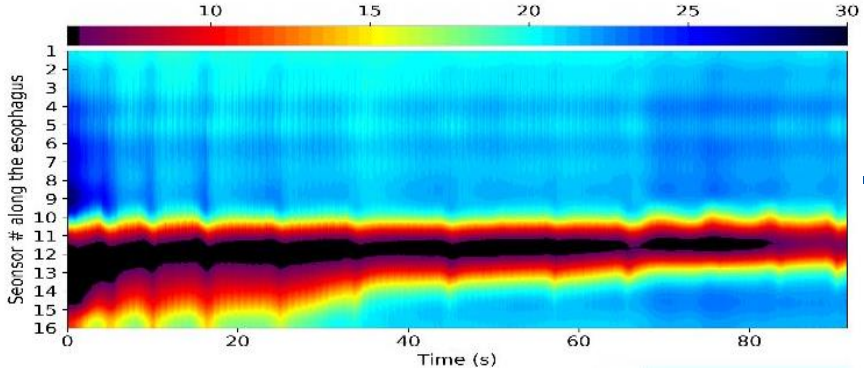


Wireless pH Testing
using Lyon 2.0



Manometry
using CC 4.0





Achalasia I/II
LES Directed therapy

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Helpful features of FLIP Panometry for General Gastroenterology without a Specialty Motility Center

Approach to patient operations and care	▪ Provides esophageal motility evaluation <u>during</u> sedated index endoscopy. ▪ More comfortable for the patient ▪ Placed while the patient is sedated and completed in 4-7 minutes ▪ 10% of patients do not tolerate HRM catheter placement due to discomfort or anatomy ▪ HRM catheter placement is associated with psychological distress ▪ Expedites work up – rapid diagnosis reduces inappropriate testing and medication trials (precision medicine) ▪ Achalasia diagnosis can take 1-4 years after presentation ▪ GERD/Functional heartburn 6-12 months ▪ 50% of endoscopy negative patients will have a diagnosis within 96 hours (GERD, Motility, Functional) ▪ Reduces logistical issues related to operating a motility lab ▪ No requirement for motility technician/nurse ▪ Scheduling is synchronized with endoscopy ▪ No need to maintain manometry system, catheter or lab space for practices without a specialty motility center
Normal FLIP Panometry	▪ Rules out major motility disorder (Achalasia, Spasm, Jackhammer, Absent contractility) ▪ Reduces need for HRM and/or referral to specialty center by 50% ▪ Reduces false positive EGJOO diagnoses ▪ Directs evaluation toward wireless pH to rule out acid reflux as a potential cause of the esophageal symptoms ▪ Provides a confident diagnosis of Functional Disorder in the context of a normal endoscopy/negative wireless pH
Abnormal FLIP Panometry	▪ Identifies the majority of Type I/II achalasia patients that can be directed to definitive therapy without HRM ▪ Non-spastic Obstruction with a CARS score >4 ▪ Prioritizes patients for HRM referral due to a high likelihood of having a treatable motility disorder (CARS ≤ 3): ▪ Non-spastic Obstruction / Spastic obstruction/ Possible Obstruction- <u>Type II/III achalasia or cEGJOO</u> ▪ Spastic Obstruction/ Possible Spasm/ - Spasm and Jackhammer esophagus ▪ Can clarify equivocal/inconclusive manometry and/or esophagram findings (e.g. EGJOO, absent peristalsis versus Type I achalasia, mechanism for retention on TBE)
Post-surgical follow up	▪ Provides important information in patients after esophageal surgery(fundoplication/Pneumatic dilation/myotomy) who have recurrence or new symptoms ▪ Can assess EGJ Opening accurately to rule out obstruction ▪ Can provide an objective measure to guide treatment decisions (before and after dilation)

Eso-Instein vEsophagus™

Input all data into vEsophagus to generate Diagnosis and appropriate treatment

vEsophagus

GutBot

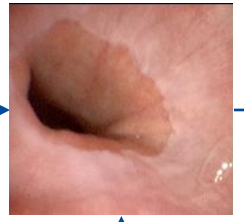
Age, Sex, BMI

APRO, BEDQ, GERDQ

EHAS, NEQOL

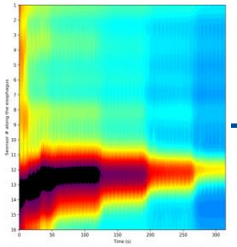
EGD

Esoph-Genius



Probability of:
- Cancer
- Motility DX
- GERD
- EoE

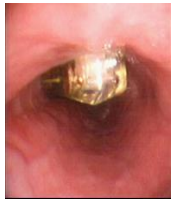
FLIP-Genius



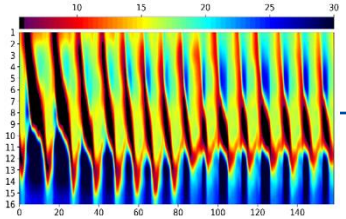
Probability of:
- Cancer
- Motility DX
- GERD
- EoE

Achalasia

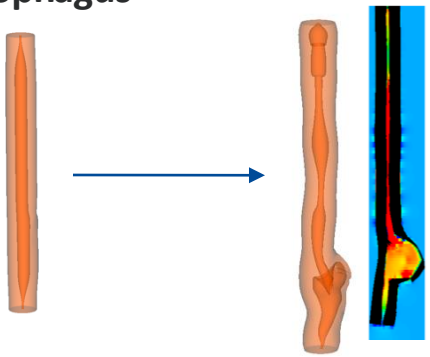
Normal/GERD



EoE



FLIP-Genius-EoE



Prediction

Treatment
Lifestyle- CBT
PPI- dose and timing
Surgery needed- type

Treatment
Dilation, Diet
PPI, Steroids, Dupilumab

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Northwestern Medicine®
Feinberg School of Medicine

Thank You:

Research Team

Dustin Carlson
Walter Kou
Sourav Halder
Peter Kahrilas
Neelesh Patankar
Guy Elisha
Christine Nelson

NIH-NIDDK
Kenneth C. Griffin Esophageal Center
Joe and Nives Rizza

Debate:
Step-Up vs. Top-Down Treatment of Eosinophilic Esophagitis

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Debate: Step-Up Treatment for Eosinophilic Esophagitis (EoE)

March 1, 2025

Joy W. Chang, MD MS

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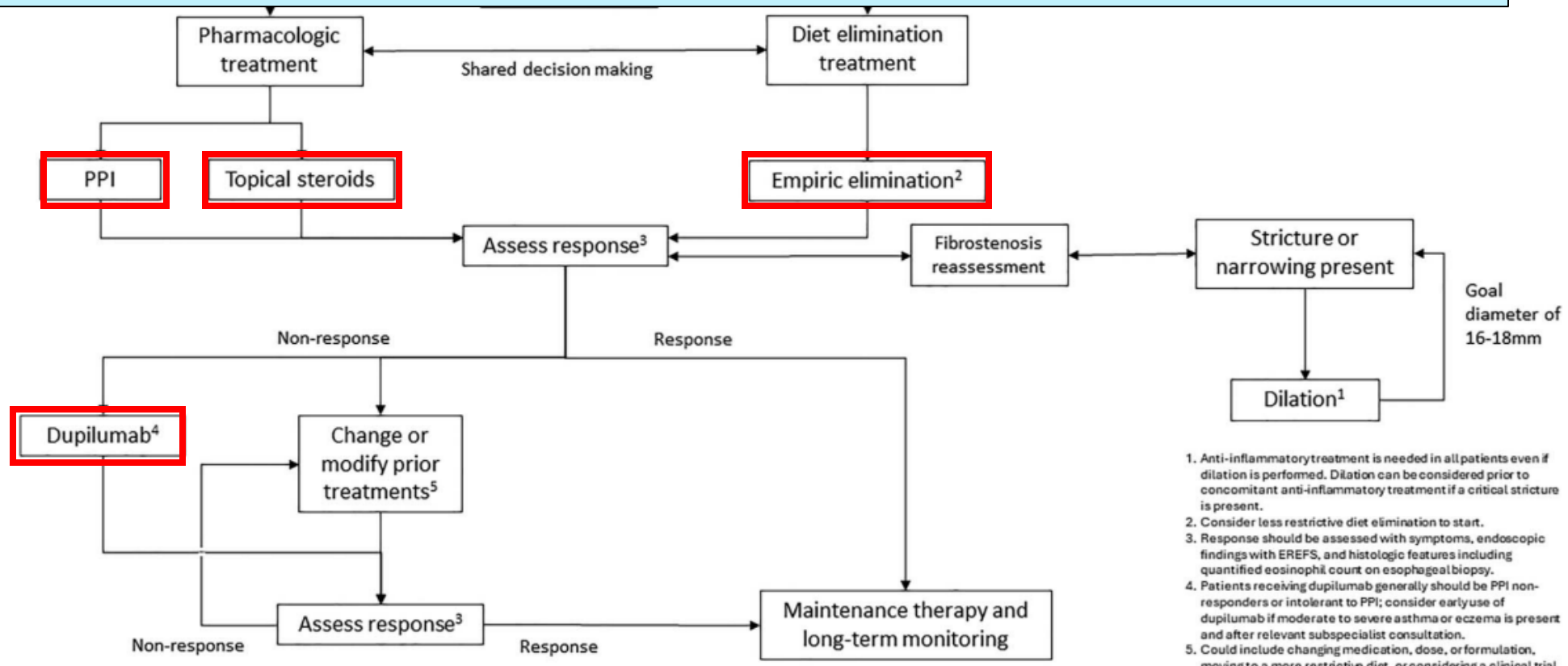
EoE Treatment Algorithm

No studies to date comparing the efficacy of medications versus diet as maintenance therapy

Medications **OR** diet could be potential first-line options to treat EoE inflammation



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

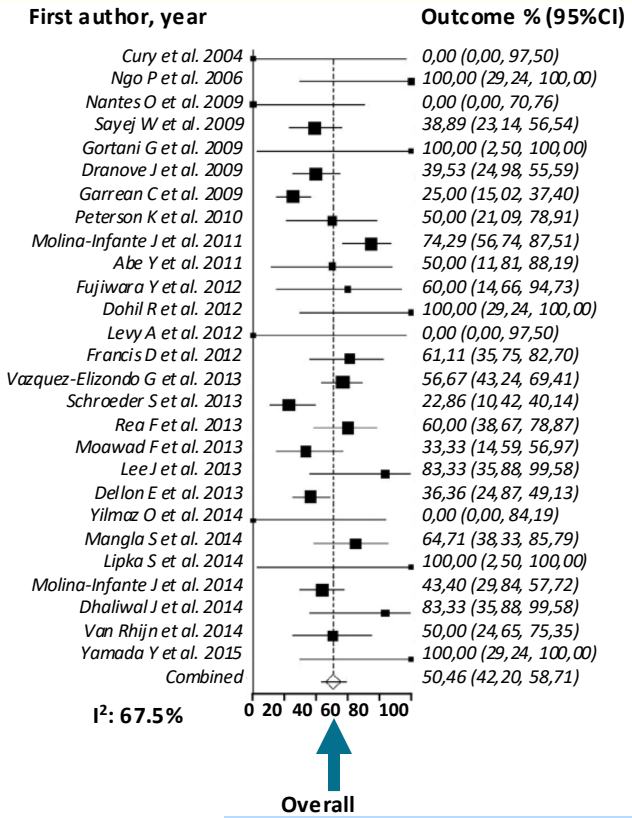
Proton Pump Inhibitors for EoE

Clinical Guidelines	Statement	Level of evidence	Strength of recommendation
European 2017	PPI therapy induces clinical and histological remission in a proportion of pediatric and adult patients with EoE.	Moderate	Strongly in favor
	In PPI responders, long-term PPI therapy is effective in maintaining remission	Low	Strongly in favor
AGA-Joint Task Force 2020	In patients with symptomatic esophageal eosinophilia, the AGA/JTF suggests using proton pump inhibition over no treatment.	Very low quality	Conditional
British Society of Gastro 2022	Proton pump inhibitor therapy is effective in inducing histological and clinical remission in patients with eosinophilic oesophagitis.	Moderate	Strong
	In patients who achieve histological response, proton pump inhibitor therapy appears effective in maintaining remission.	Low	Strong
ACG 2025	We suggest PPIs as a treatment for EoE	Low	Conditional

Lucendo AJ, et al. *United European Gastroenterol J.* 2017;5(3):335-358; Hirano I, et al. *Gastroenterology.* 2020;158(6):1776-1786; Dhar A, et al. *Gut.* 2022;71(8):1459-1487; Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59; Lucendo AJ, et al. *Clin Gastroenterol Hepatol.* 2016;14(1):13-22.e1.

Proton Pump Inhibitors

- Efficacy: ~50%



- Convenience and ease of use

ACG 2025: Initial treatment with “high-dose” PPI (e.g. omeprazole 20mg BID or 40mg daily)

Lucendo AJ, et al. *United European Gastroenterol J.* 2017;5(3):335-358; Hirano I, et al. *Gastroenterology.* 2020;158(6):1776-1786; Dhar A, et al. *Gut.* 2022;71(8):1459-1487; Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59; Lucendo AJ, et al. *Clin Gastroenterol Hepatol.* 2016;14(1):13-22.e1.

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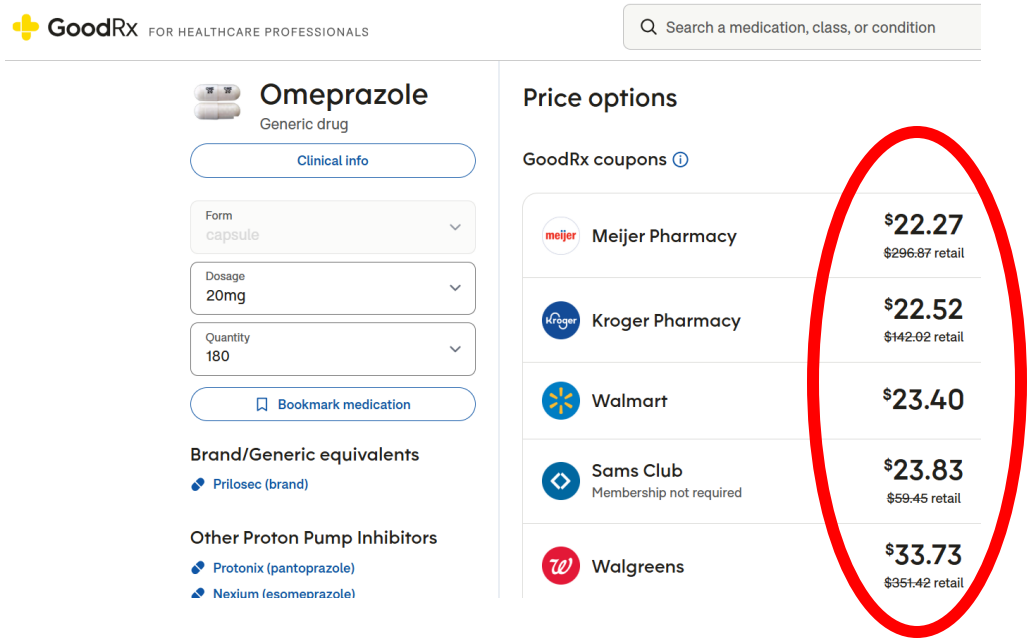
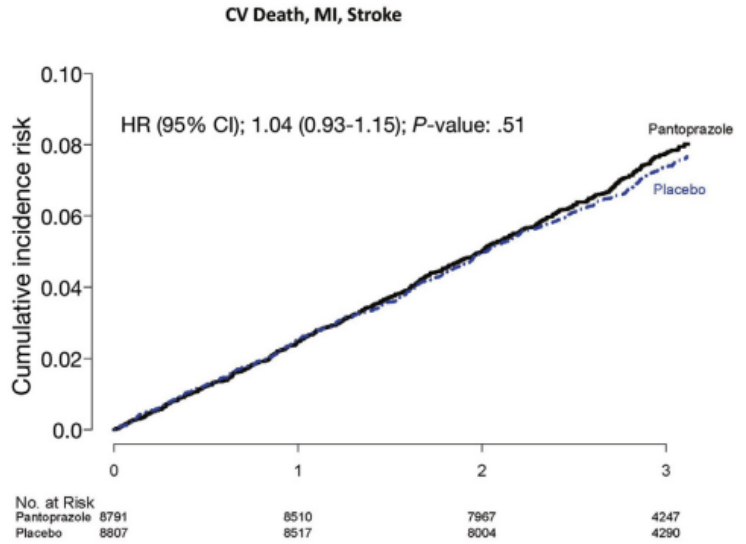
Proton Pump Inhibitors

- Typically low cost



90-day supply!

- Safe
  - No decisive evidence for association with dementia
  - No increased CV risk



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GoodRx. Omeprazole. Available at: https://www.goodrx.com/omeprazole. Accessed Feb 11, 2025; Moayyedi P, et al. *Gastroenterology*. 2019;157(2):403-412.e5.

Next After PPIs?

Topical corticosteroids

- Budesonide oral suspension
  - FDA-approved
- Off-label preparations
  - Swallowed fluticasone
  - Oral viscous budesonide slurry
- Once-twice daily
- Efficacy 53-80%
- Good safety profile
  - Low systemic bioavailability

Empiric elimination diets

- Original 6FED vs less-restrictive diets (1FED or 2FED)
- Treats the “root cause” of EoE
- Potential drug-free remission
- Efficacy 35-90% (*depending on diet)
- Sometimes preferred by patients

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Stepping Up – Topical Steroids

Topical corticosteroids

- Budesonide oral suspension
  - FDA-approved
- Off-label preparations
  - Swallowed fluticasone
  - Oral viscous budesonide slurry
- Once-twice daily
- Efficacy 53-80%
- Good safety profile
  - Low systemic bioavailability

Clinical Guidelines	Statement	Level of evidence	Strength of recommendation
ACG 2013	Topical steroids (i.e., fluticasone or budesonide, swallowed rather than inhaled, for an initial duration of 8 weeks) are a first-line pharmacologic therapy for treatment of EoE.	High	Strong
European 2017	Topical corticosteroids are effective for induction of histological remission in both pediatric and adult EoE patients.	High	Strongly in favor
	In steroids responsive patients, long-term therapy with topical corticosteroids is effective in maintaining remission in a proportion of patients.	Low	Strongly in favor
AGA-Joint Task Force 2020	In patients with EoE, the AGA/JTF recommends topical glucocorticosteroids over no treatment.	Moderate	Strong
British Society of Gastro 2022	Topical steroids are effective for inducing histological and clinical remission in eosinophilic oesophagitis.	High	strong
ACG 2025	We recommend the use of swallowed topical steroids as a treatment for EoE.	Moderate	Strong
	We suggest the use of either fluticasone propionate or budesonide in patients with EoE being treated with topical steroids.	Low	Conditional

Dellon ES, et al. *Am J Gastroenterol.* 2013;108(5):679-693; Lucendo AJ, et al. *United European Gastroenterol J.* 2017;5(3):335-358; Hirano I, et al. *Gastroenterology.* 2020;158(6):1776-1786; Dhar A, et al. *Gut.* 2022;71(8):1459-1487; Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

Dietary Therapy for EoE

Clinical Guidelines	Statement	Level of evidence	Strength of recommendation
ACG 2013	Dietary elimination can be considered as an initial therapy in the treatment of EoE in both children and adults.	Moderate	Strong
European 2017	An **empiric six-food group** elimination diet induces histologic remission in around three quarters of pediatric and adult patients.	Moderate	Weakly in favor
	In adult patients, an **empiric four-food** elimination diet achieves remission in half of the patients, whereas a **two-food elimination diet** (animal milk and gluten-containing cereals) may be still effective in 40% of patients.	Moderate	Weakly in favor
	Prolonged avoidance of triggering foods may lead to drug-free sustained clinical and histological remission of EoE.	Low	Strongly in favor
AGA-Joint Task Force 2020	In patients with EoE, the AGA/JTF suggests using an **empiric, 6-food elimination diet** over no treatment.	Low	Conditional
British Society of Gastro 2022	**Elimination diets are effective** in achieving clinicohistological remission in both adults and paediatric patients with eosinophilic oesophagitis.	Moderate	Strong
	A **six food elimination diet** results in higher histological remission rates than two or four food elimination diets, but is associated with lower compliance and an increased number of endoscopies.	Low	Strong
ACG 2025	We suggest an **empiric food elimination diet** as a treatment for EoE.	Low	Conditional

Empiric elimination diets

- Original 6FED vs less-restrictive diets (1FED or 2FED)
- Treats the “root cause” of EoE
- Potential drug-free remission
- Efficacy 35-90% (*depending on diet)
- Sometimes preferred by patients

Dellon ES, et al. *Am J Gastroenterol.* 2013;108(5):679-693; Lucendo AJ, et al. *United European Gastroenterol J.* 2017;5(3):335-358; Hirano I, et al. *Gastroenterology.* 2020;158(6):1776-1786; Dhar A, et al. *Gut.* 2022;71(8):1459-1487; Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

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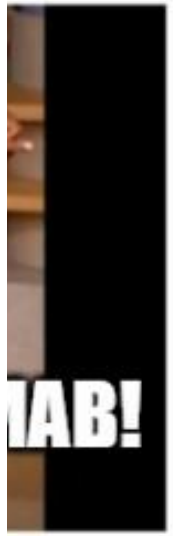
“Since it’s the first FDA-approved treatment, should I use dupilumab for all EoE?”



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Top-Down(sides): Dupilumab

- Cost and coverage
  - Costs = $80,000/year
  - Some insurance may require failure of other treatments first
- Patient preferences
  - Fear of injections
  - Maintenance use?
- Unknown long-term safety of immune modulation in EoE

ACG 2025: Advise use of dupilumab as step-up therapy in difficult-to-treat patients, and consider using it in patients with EoE and multiple atopic conditions that would also meet requirements for dupilumab use.

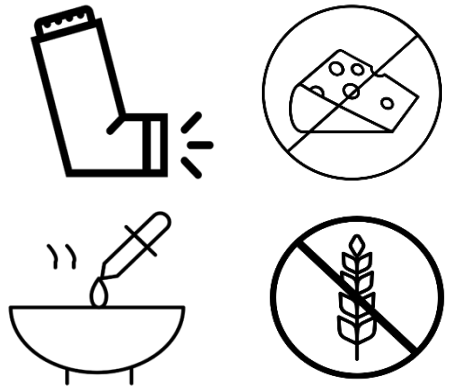
Dellon ES, et al. *Am J Gastroenterol.* 2025;120(1):31-59.

Summary:

Step-Up Treatment = Good Treatment Stewardship

Finally… save biologics

- Backup plan
- Severe disease



Next… topical steroids or diet

- Effective
- Long-term data available
- FDA-approved (BOS)
- Less restrictive diets are ok
- Patient preferences

Try PPIs first

- Effective
- Easy, convenient, and low cost
- Safe

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Is Top-Down Treatment Preferred in PPI Resistant Eosinophilic Esophagitis?

Rena Yadlapati MD MSHS
Professor of Clinical Medicine
Director, Center for Esophageal Diseases
Medical Director, GI Motility Lab
University of California San Diego

EoE Mafia

"Don't ever take sides with anyone against the family again. Ever."

Michael Corleone

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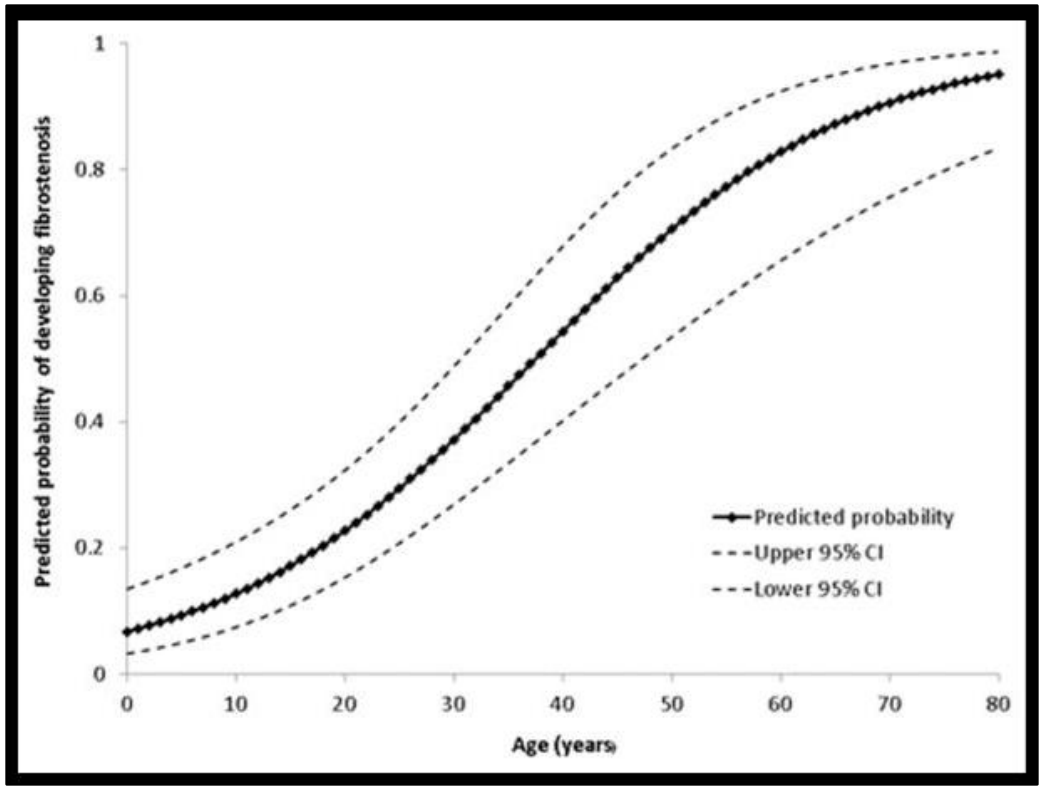
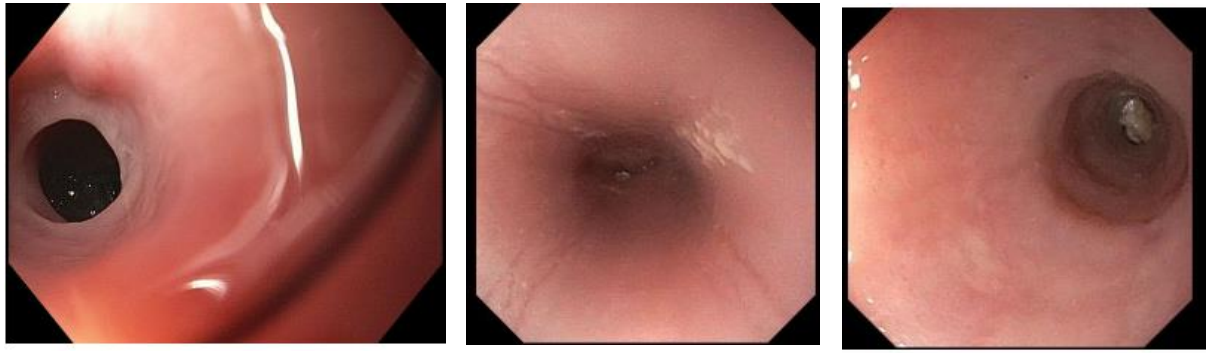
Primary Goal in EoE:

Prevent Fibrostenotic Disease!





Dellon E, et al. *Gastrointest Endosc.* 2014;79(4):577-585.e4.

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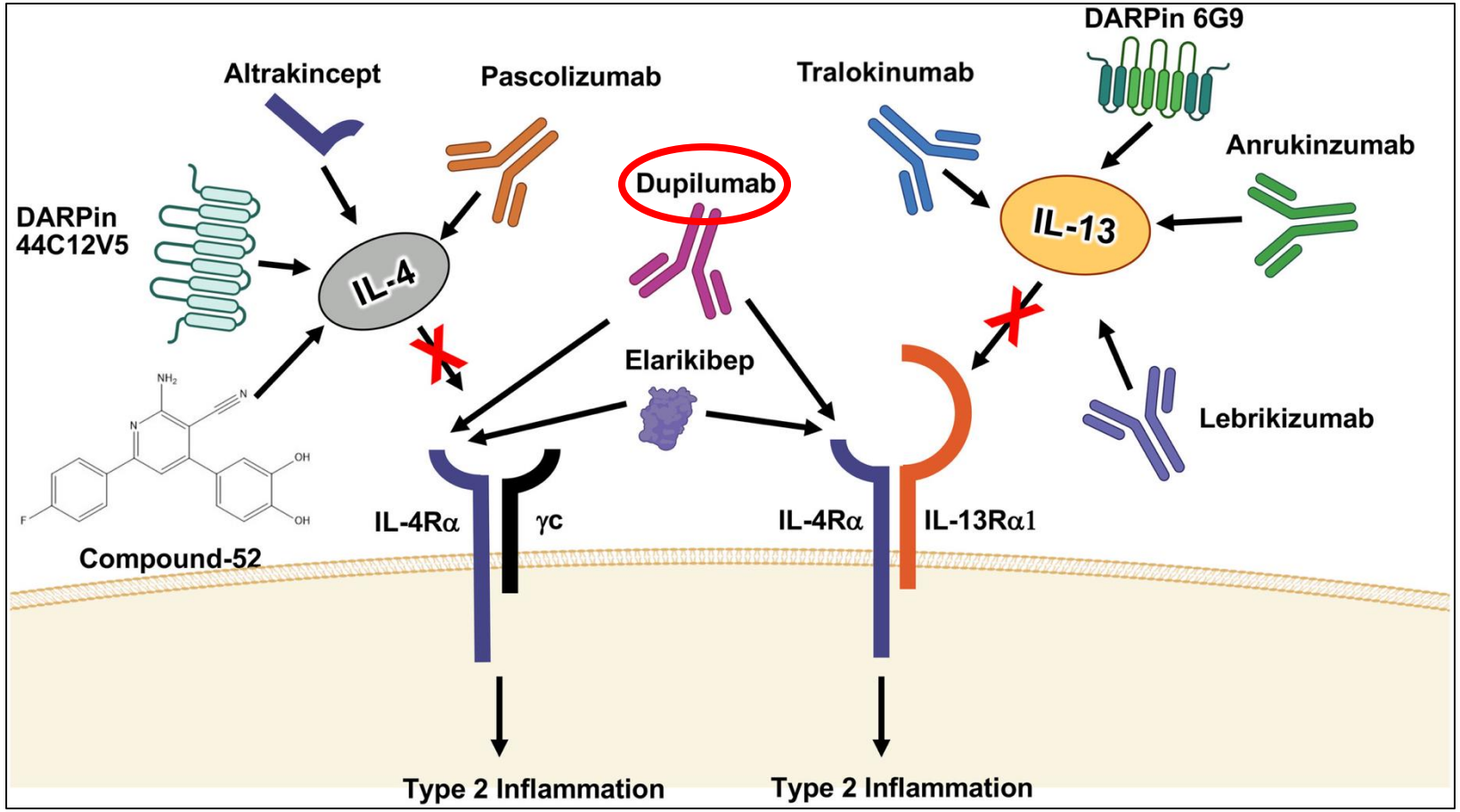
Precision Medicine in EoE



Bernstein ZJ, et al. *Immunol Rev*. 2023;320(1):29-57.

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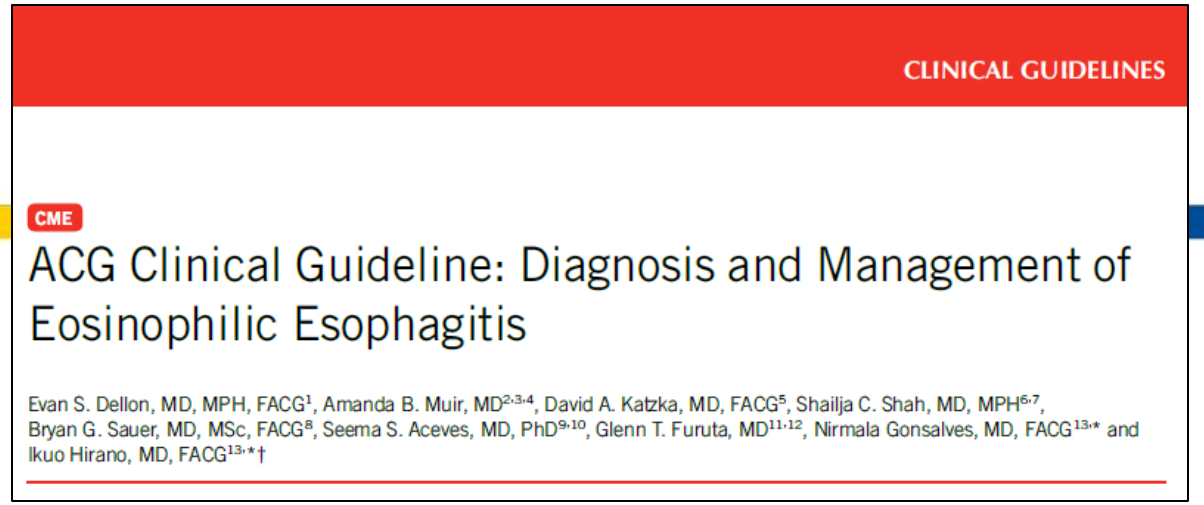
Topical Corticosteroids

Eczematous diseases	Seborrheic dermatitis
	Atopic dermatitis
	Contact dermatitis
Papulosquamous diseases	Lichen planus
	Psoriasis
	Erythroderma
Bullous diseases	Pemphigus foliaceus
	Bullous and cicatricial pemphigoid
Connective tissue diseases	Morphea
	Discoid lupus erythematosus
Pigmentary disorders	Vitiligo
	Melasma (Kligman's formula)
Mucous membrane diseases	Aphthous stomatitis
Neutrophilic diseases	Behcet's syndrome
	Sweet's syndrome
Cutaneous malignancies	Cutaneous T-cell lymphoma
	Lymphocytoma cutis
	Lymphomatoid papulosis
Miscellaneous	Papular urticaria
	Alopecia areata
	Lichen sclerosus et atrophicus



"concept was to coat the esophagus with an anti-inflammatory medication, analogous to how a steroid cream might be applied to the skin in atopic dermatitis"

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

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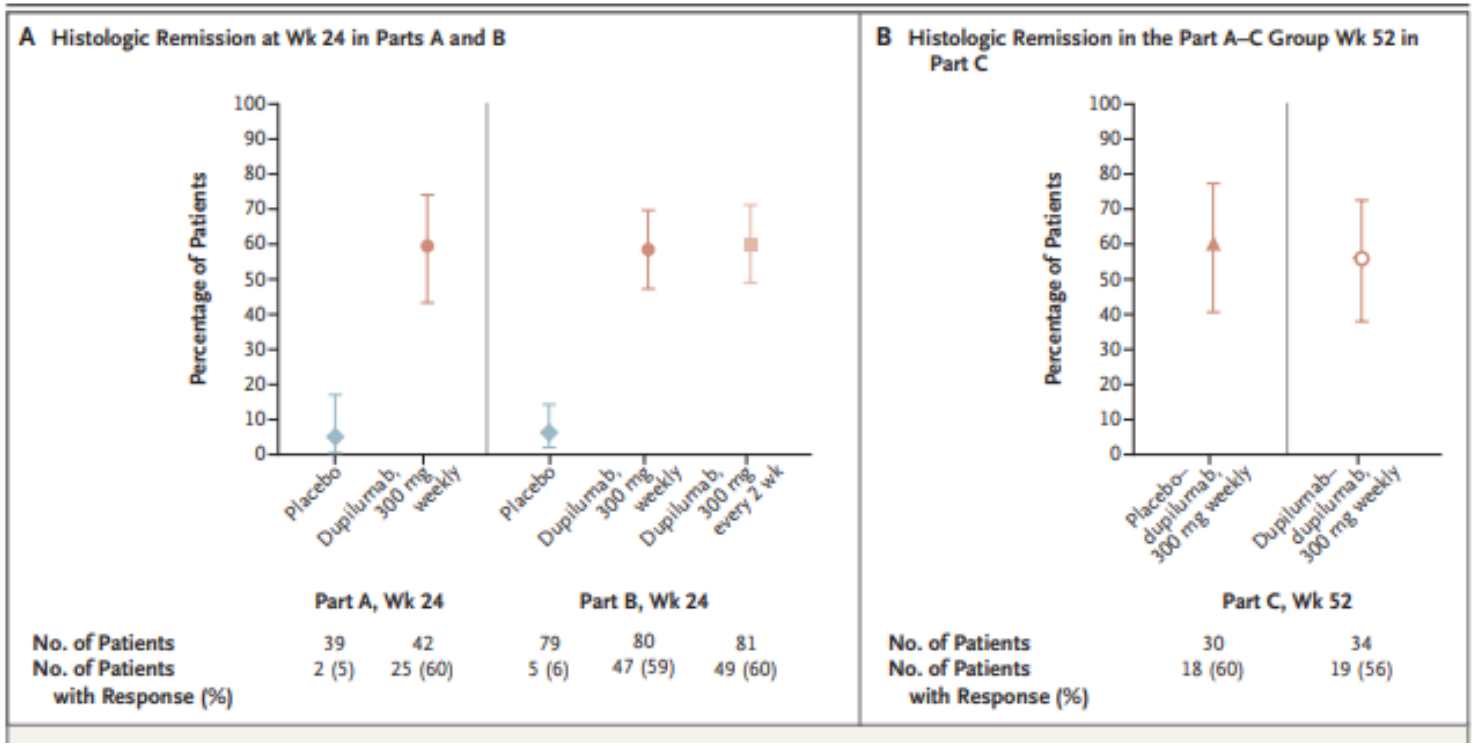
Efficacy of Dupilumab in PPI-resistant EoE?

ORIGINAL ARTICLE

Dupilumab in Adults and Adolescents with Eosinophilic Esophagitis

E.S. Dellon, M.E. Rothenberg, M.H. Collins, I. Hirano, M. Chehade, A.J. Br
A.J. Lucendo, J.M. Spergel, S. Aceves, X. Sun, M.P. Kosloski, M.A. I
J.D. Hamilton, B. Beazley, E. McCann, K. Patel, L.P. Mannent, E. Laws, E
N. Amin, W.K. Lim, M.F. Wipperman, M. Ruddy, N. Patel, D.R. Wei
G.D. Yancopoulos, B. Shumel, J. Maloney, A. Giannelou, and A. Sh

ABSTRACT



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

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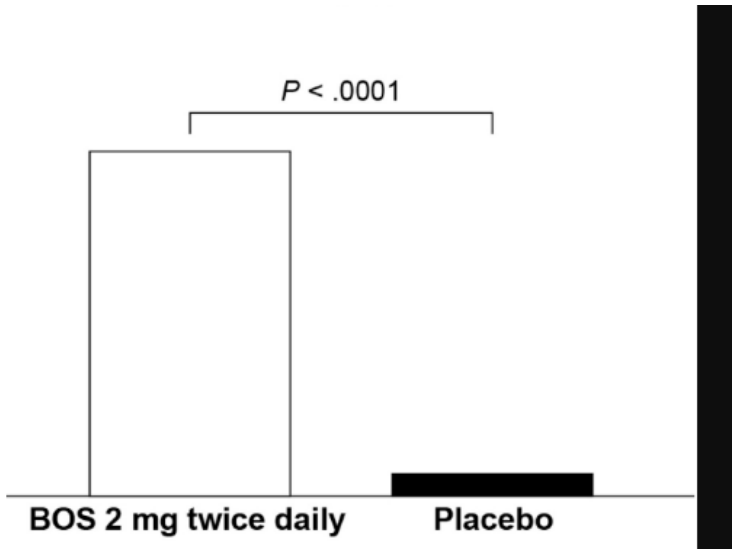
Efficacy of TCS in PPI-resistant EoE?

Gastroenterology 2017;152:776–786

Budesonide Oral Suspension Improves Symptomatic, Endoscopic, and Histologic Parameters Compared With Placebo in Patients With Eosinophilic Esophagitis

Evan S. Dellon,[1] David A. Katzka,[2] Margaret H. Collins,[3] Mohamed Hamdani,[4] Sandeep K. Gupta,[5] and Ikuo Hirano,[6] on behalf of the MP-101-06 Investigators

Beware of y-axis!



Dellon ES, et al. *Gastroenterology*. 2017;152(4):776-786.e5.

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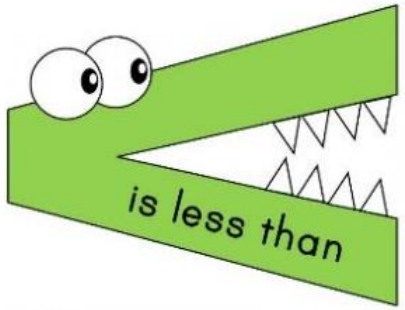
What is the Relationship?

40% 

60%

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Efficacy of Diet Elimination?

Table 5. Dietary elimination therapy options

Diet	Details[a]	Efficacy range
1FED	Dairy elimination alone; also referred to as animal milk elimination[b]	35%–45%
2FED	Dairy and wheat elimination	40%–45%
4FED	Dairy, wheat, egg, and soy elimination	40%–50%
6FED	Dairy, wheat, egg, soy, nuts, and seafood elimination	40%–70%
Elemental formula	Amino acid–based hypoallergenic formula	>90% (if adherent)
Allergy test-directed	Not recommended[c]	—

"Despite efficacy of 6FED, significant challenges remain, including the restrictive nature of this diet and the need for multiple endoscopies to identify food triggers"

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

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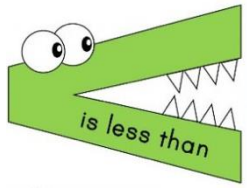
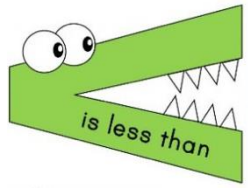
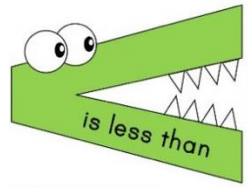
What is the Relationship?

35% 

40% 

45% 

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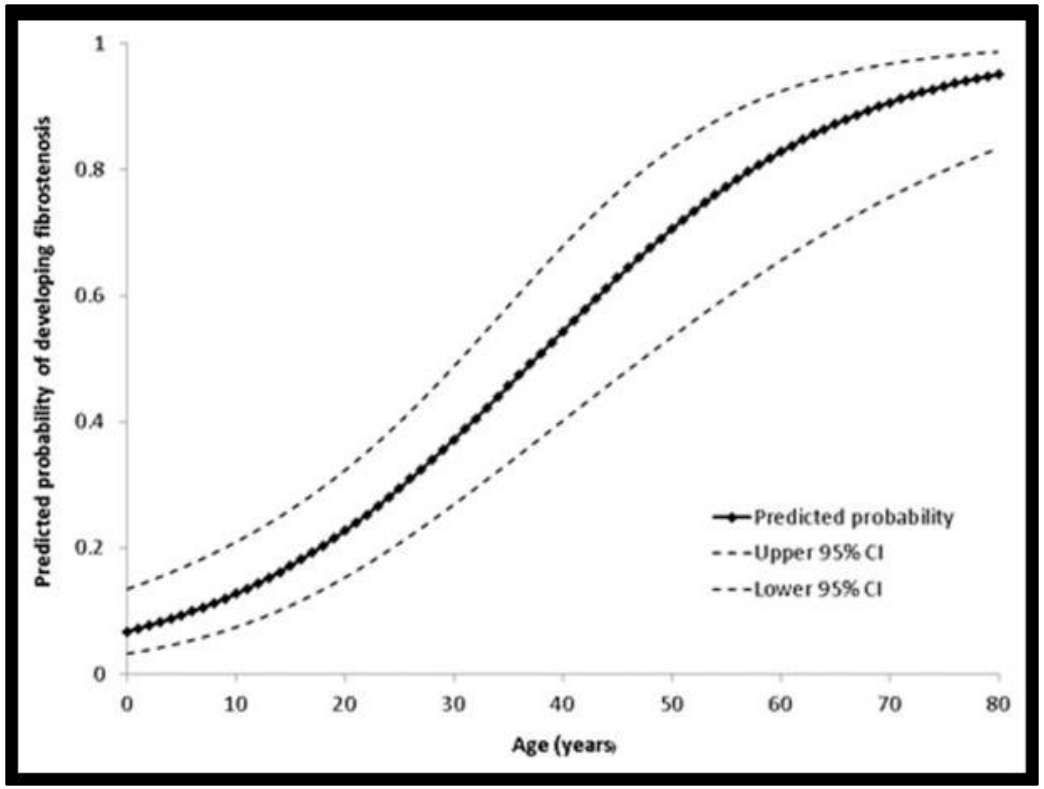
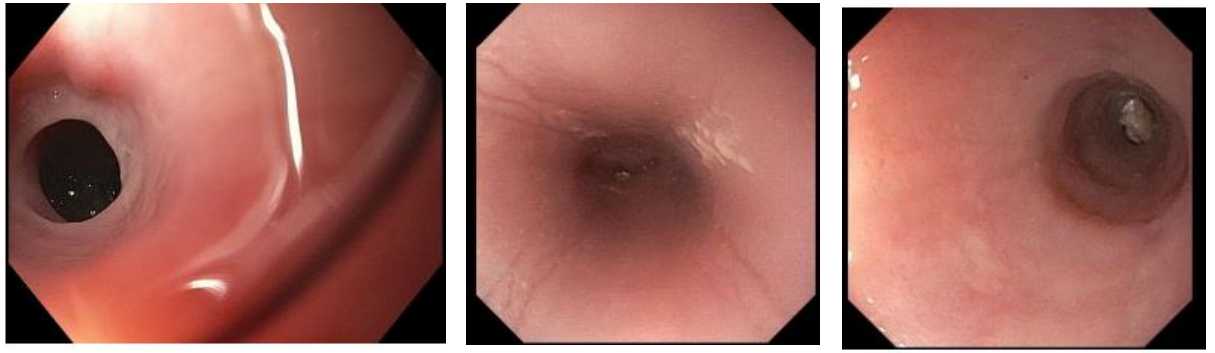
Goal is to Reduce Fibrostenotic Progression!





Dellon E, et al. *Gastrointest Endosc.* 2014;79(4):577-585.e4.

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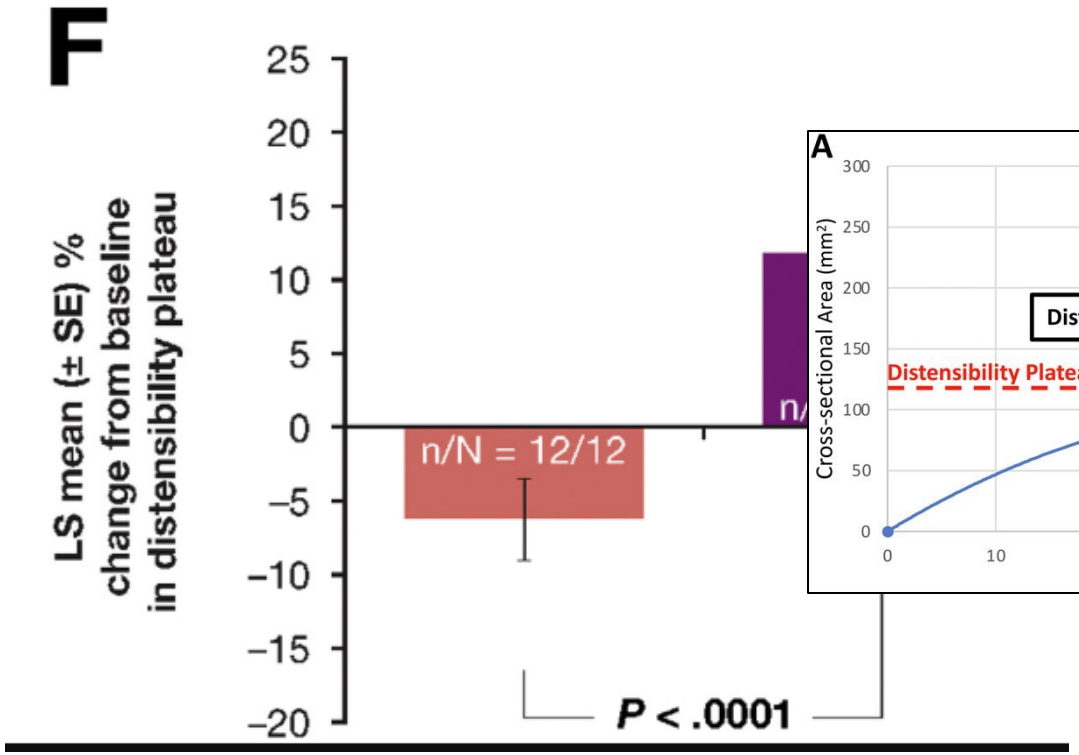
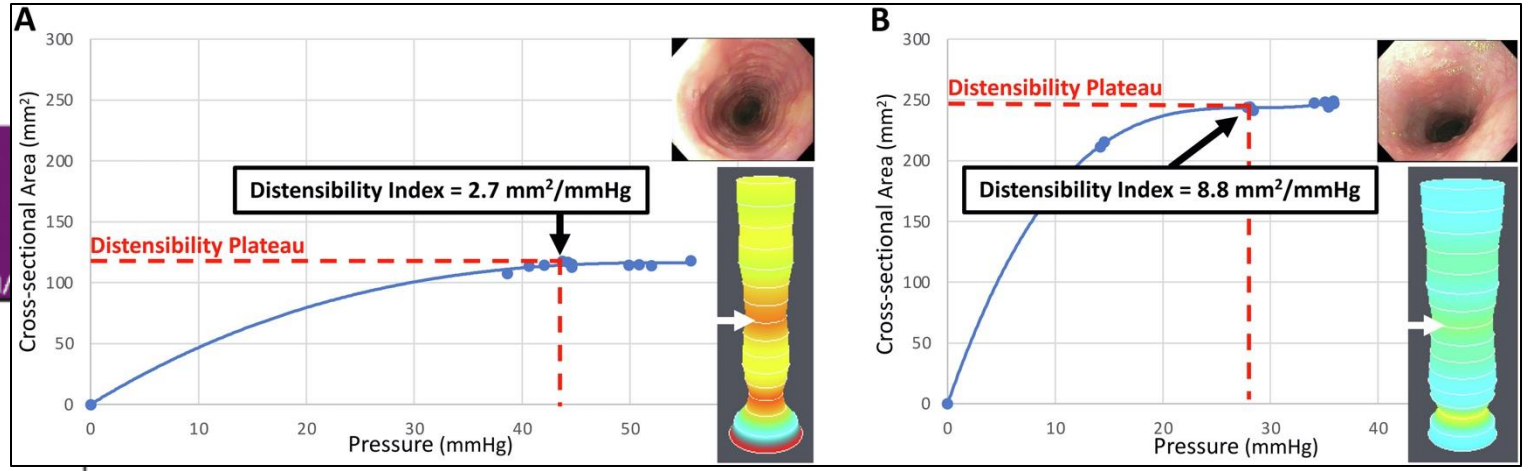
Dupilumab Improves Esophageal Distensibility



Hirano I, et al. *Gastroenterology*. 2020;158(1):111-122.e10



Hoffmann NV, et al. *Clin Gastroenterol Hepatol*. 2023;21(5):1188-1197.e4.

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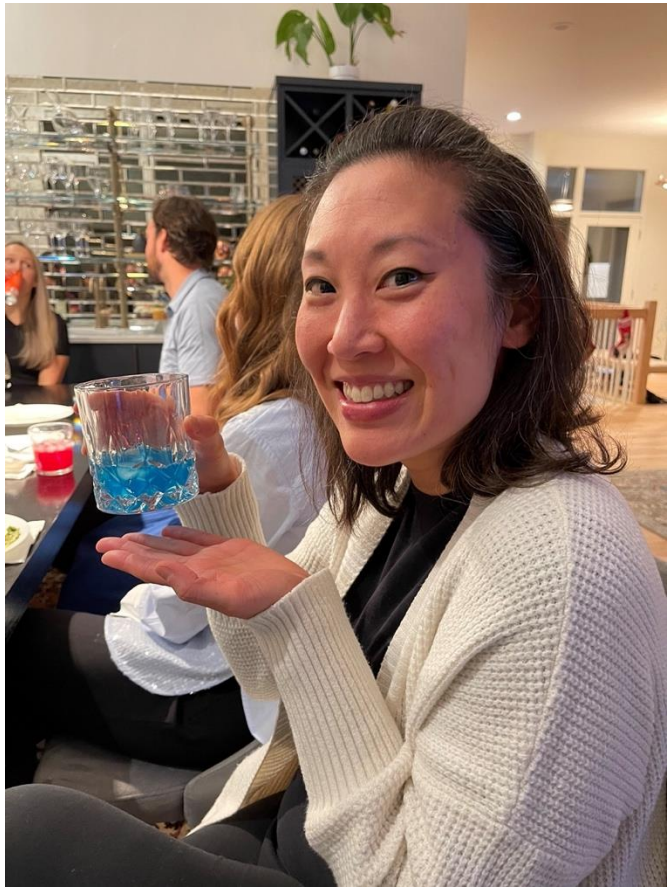
Drinking the Kool-Aid



Dr. Joy Chang

"It's not personal, it's strictly business."
Michael Corleone

Dr. Joy Chang's adorable baby

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Top Down Approach?

Role of Dupilumab in Clinical Practice?

- Severe EoE Phenotypes
- Fibrostenotic complications
- Patients affected by multiple Th2/atopic diseases
- Patient preference
- Failure of or intolerance to other treatment options

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Parting Thoughts

- Thank you to my accomplices
- Much respect to Dr. Joy Chang
- CEGIR has been transformative

“Leave the gun, take the cannoli.” ***Peter Clemenza***

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Help Me to Help You: Building Your Mentoring Network

Jennifer Christie, MD, MASGE, AGAF
Immediate Past-President, American Society for Gastrointestinal Endoscopy
Professor of Medicine
Division Director for Gastroenterology and Hepatology
University of Colorado School of Medicine

Great GI Debates March 2025

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WISE AND SUCCESSFUL PEOPLE ARE ALWAYS IN A POSITION TO MAXIMIZE RESOURCES, BECAUSE THEY NEVER STOP CULTIVATING RELATIONSHIPS.

“RELATIONSHIPS MATTER”

-Sent by Mr. Sylvester
Emory University Hospital Concierge

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Our Objectives for this talk:

Understand why networking and mentorship is important to career success.

Identify ways to build your mentorship network.

Review best practices for sustaining effective mentor/mentees relationships.

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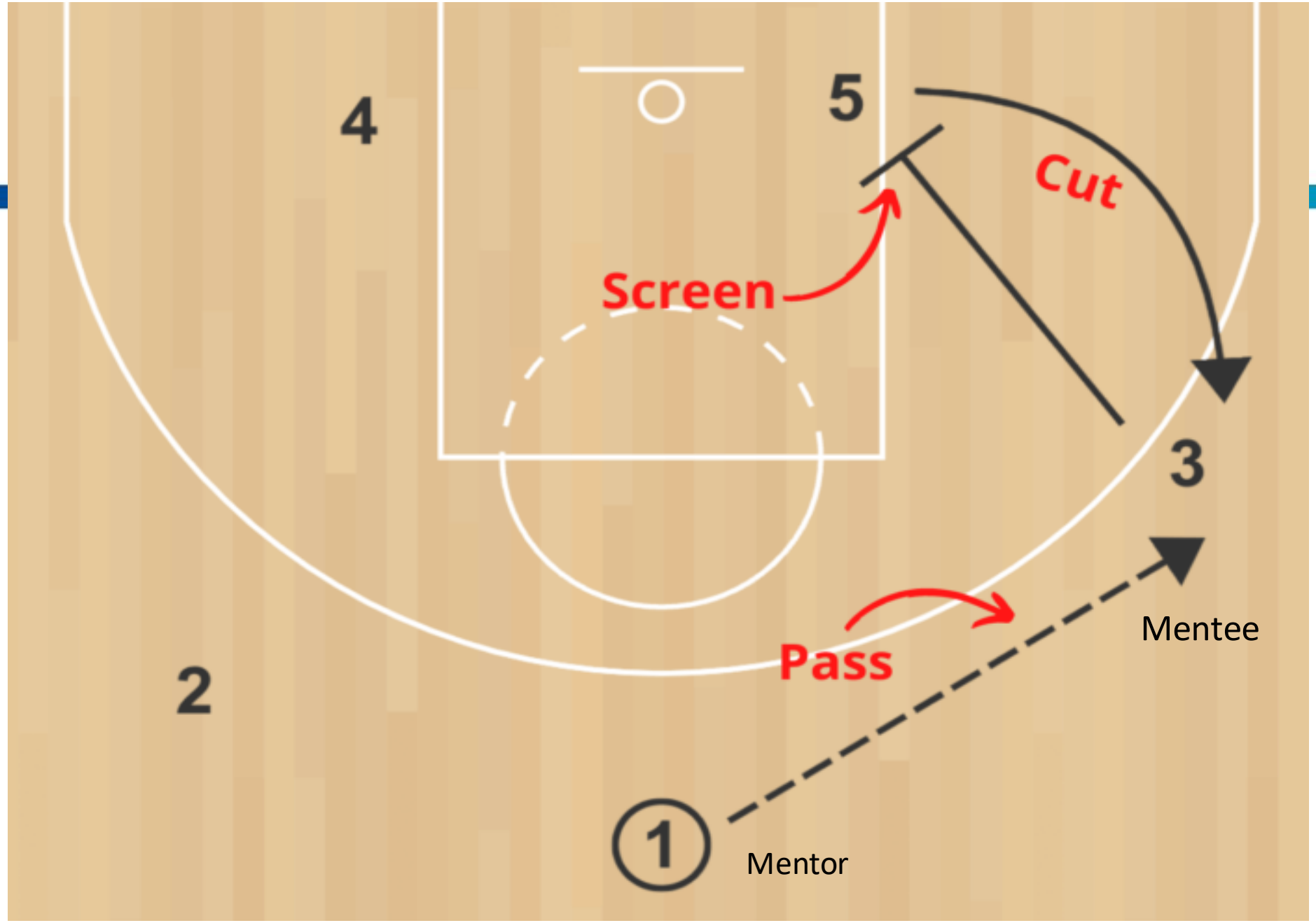

There are Multiple Mentoring Relationships

Traditional
- Research
- Clinical Expertise

Advisor

Coach

Sponsor

Goal Focuser

Confidant

Mentor

Clinics in Dermatology 2015:33;257-250

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Why Mentoring is Important

Mentor

In Academic Medicine correlated with:

- Career choice
- Skill Building
- Career satisfaction, longevity
- Networking
- Career advancement
- ↑ productivity (publications, funding, flourishing clinical practice)

Mentee

Sambunjak, et al. JAMA 2006

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Why Network? It's Everything!

- Direct correlation with career satisfaction as well as salary growth rate
- More beneficial for career success than single mentor relationship alone
- Impact of mentor relationship and mentee success is mediated by networking behaviors
- Exchange ideas and create opportunities
- Growth in self confidence

[1] *Wolff H. Moser K. Appl Psycholol 2009;94:196-206 Bianca Miller Cole*
[2] *Blickle et al. J Vocat Behav 2009;74:181-9.*
[3] *Forbeswoman.com March 2019*

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Why the Minoritized and Women Individuals May Find Networking More Difficult

1. Traditionally left out of the powerful networking circle
2. Likes Attract
3. Separate spheres dynamic
4. Fear of “Using People”
5. Limited Time

www.forbes.com April 2016 by
https://www.ellevatenetwork.com by Solange Lopes

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Networking Venues Are Everywhere

- School of Medicine, Departmental, and Hospital Committees
- Grand rounds

Institutional

Regional Meetings/ Conferences

- Attend Small Group Discussions
- Opening receptions
- Attend monthly local meetings

National Meetings (ANMS, DDW, ACG, AASLD)

- Seminars
- Focused Receptions
- Luncheons

Professional GI Societies

- Specific committee request
- Attend business meeting
- Volunteer to serve on abstract review committee

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Digital Connections

- Social Media (SoMe)
  - Online communities with professional societies
  - Easily Accessible
  - Informal Communication
  - Knowledge quickly distributed
  - Tags: @GITwitter, #NeuroGI, @ANMSociety, #motility, @scrubsandheels

doximity

twitter

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Networking Ugh!
"I'm an Introvert"

- Ask and listen
- Do some research in advance
- Plan what you might say
- Have an Exit Strategy: "Stick and Move"
- Preserve your energy

The Introvert's Edge to Networking: HarperCollins Leadership. M. Poland 2021.

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Strategic Mentoring

Mentor

Be thoughtful about your role/style
Suggest not instruct
Follow-up/Accountability
Awareness of implicit bias

Mentee

Choosing the “Right” Mentor
Prepare for the ask
Be specific about your ask
Follow-up/Accountability

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Effective Mentor-Mentee Relationship

- **Align Expectations**
  - Shared understanding of what each person expects from the relationship
  - Create Time-lines and Set Goals
- **Active communication**
  - Active listening
  - Reflective listening
  - Summarizing
  - Open-ended questions
  - Probing
  - Confrontation

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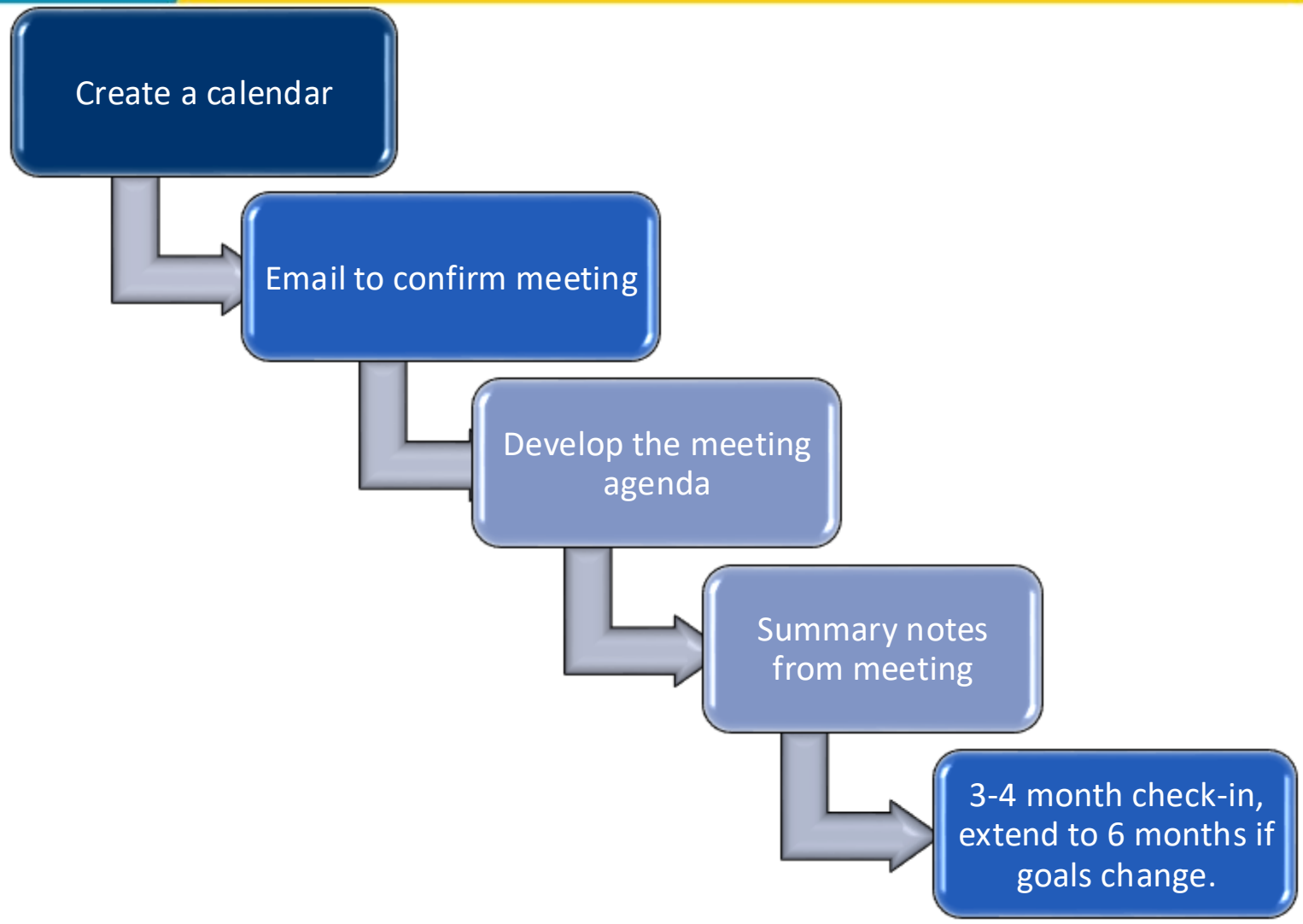
Mentees: Managing your mentor



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Effective Communication Builds Trust

- Honest and Effective Feedback
- Respect each other's boundaries

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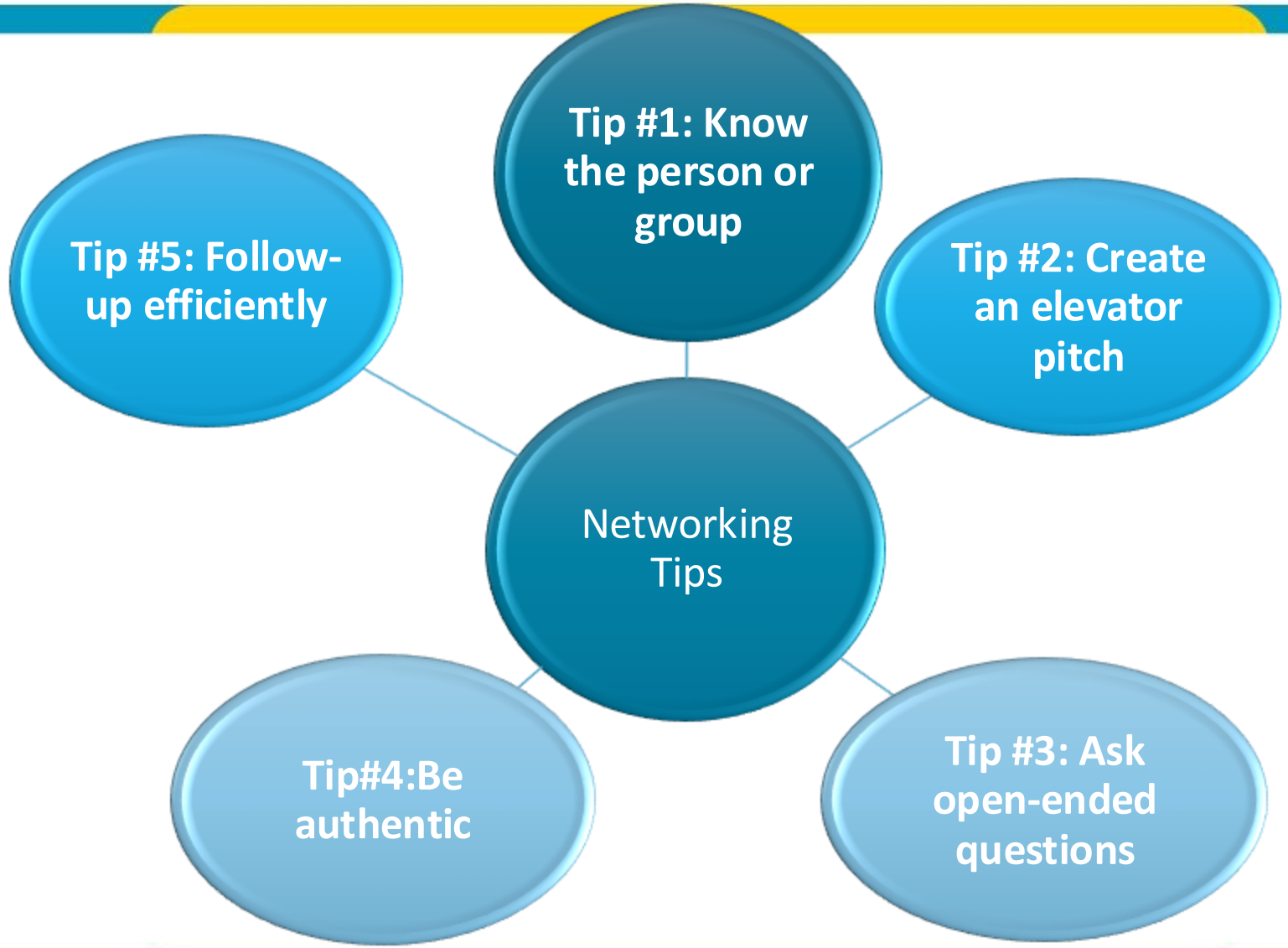
Pitfalls and Opportunities

- Misinterpret the mentee's potential.
- Be mindful of individual differences (sex, gender, race/ethnicity, religion, sexual orientation) and attempt to learn about each other's experiences.
- Inappropriate praise or criticism.
- Disregard for the mentee's opinions, other types of unethical and, rarely, immoral behavior.
- Impose your career goals on your mentee.
- Transitioning to another mentor who is more appropriate for the stage of your career.
- Explore Peer Mentoring

Mentoring Making the Transition From Mentee to Mentor, David R. Holmes, Jr, MD; Patricia K. Hodgson, BA; Robert D. Simari, MD; Rick A. Nishimura, MD *Circulation.* 2010;121:336-340, American Heart Association

5 Tips for Networking and Building Lasting Relationships



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Case Studies in GI Motility Disorders

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Case Studies in GI Motility Disorders

Jill K Deutsch, MD, MA
Assistant Professor, Section of Digestive Diseases
Director, Yale Functional Gastrointestinal Disorders Program
Medical Director, GI Motility Laboratory
Yale School of Medicine - Yale New Haven Health

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Bloating 101: The Low FODMAP Diet vs Rifaximin

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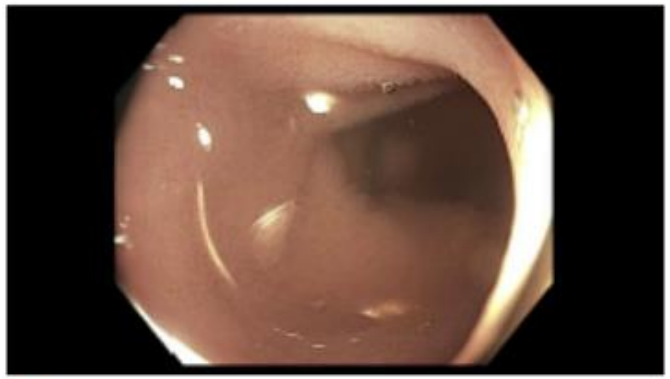
Case

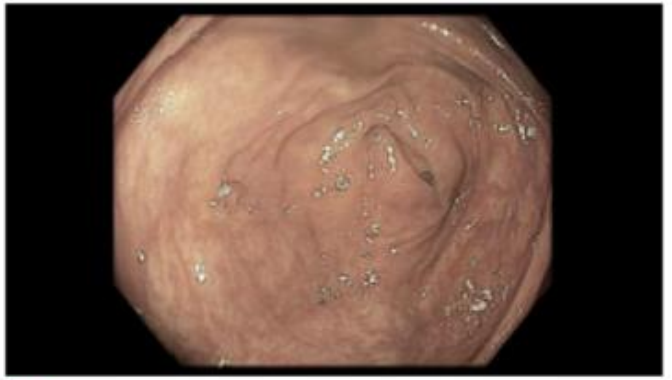
- 37 year old endoscopy nurse who was diagnosed with IBS in college presents with abdominal bloating and diarrhea with fecal urgency
- Bloating is accompanied by lower abdominal cramping which then results in urgent, loose/watery BMs up to 4-5 times (BSFS 6-7) within 20 minutes before feeling empty
  - After completion of BMs, abdominal pain is nearly entirely resolved
- Reports scant blood on the TP when wiping, but no hematochezia
  - Had a hemorrhoid when pregnant in the past

Case

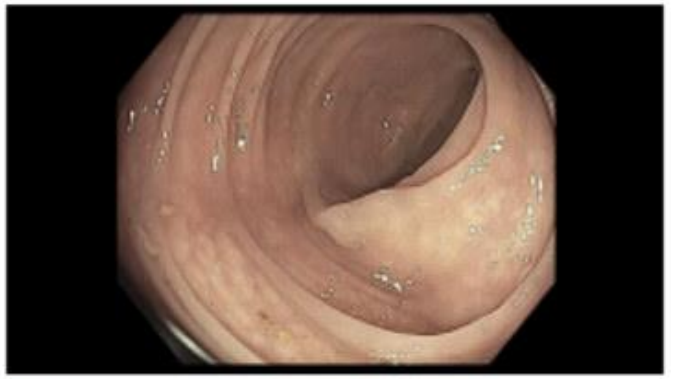
- Patient reports no other alarm features, noting stable weight
- Labs including CBC, celiac serologies, and CRP were within normal ranges
- No prior EGD or colonoscopy



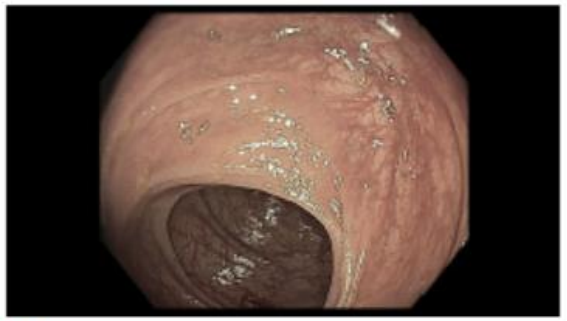
6 Terminal ileum



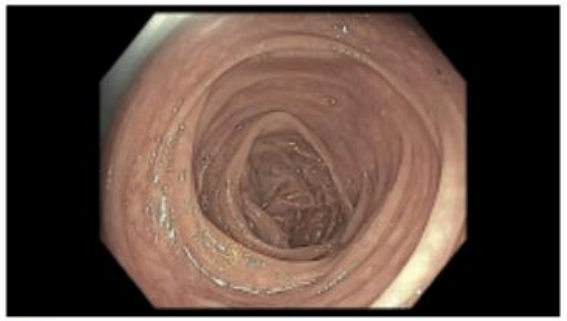
2 Cecum



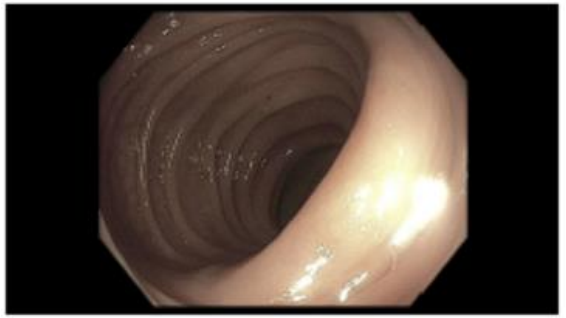
11 Descending Colon



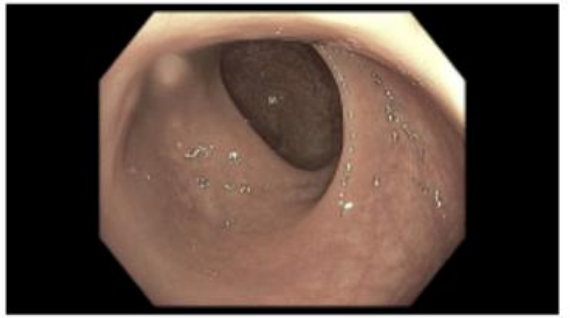
8 Ascending Colon



9 Transverse Colon



12 Sigmoid Colon



13 Rectum

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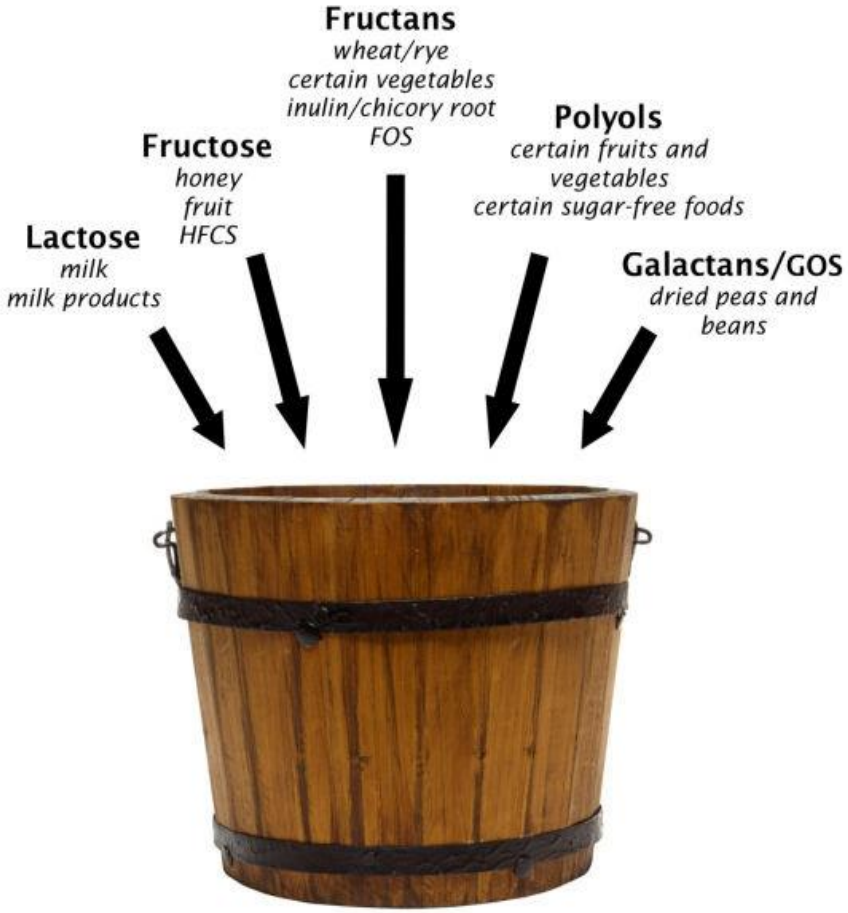
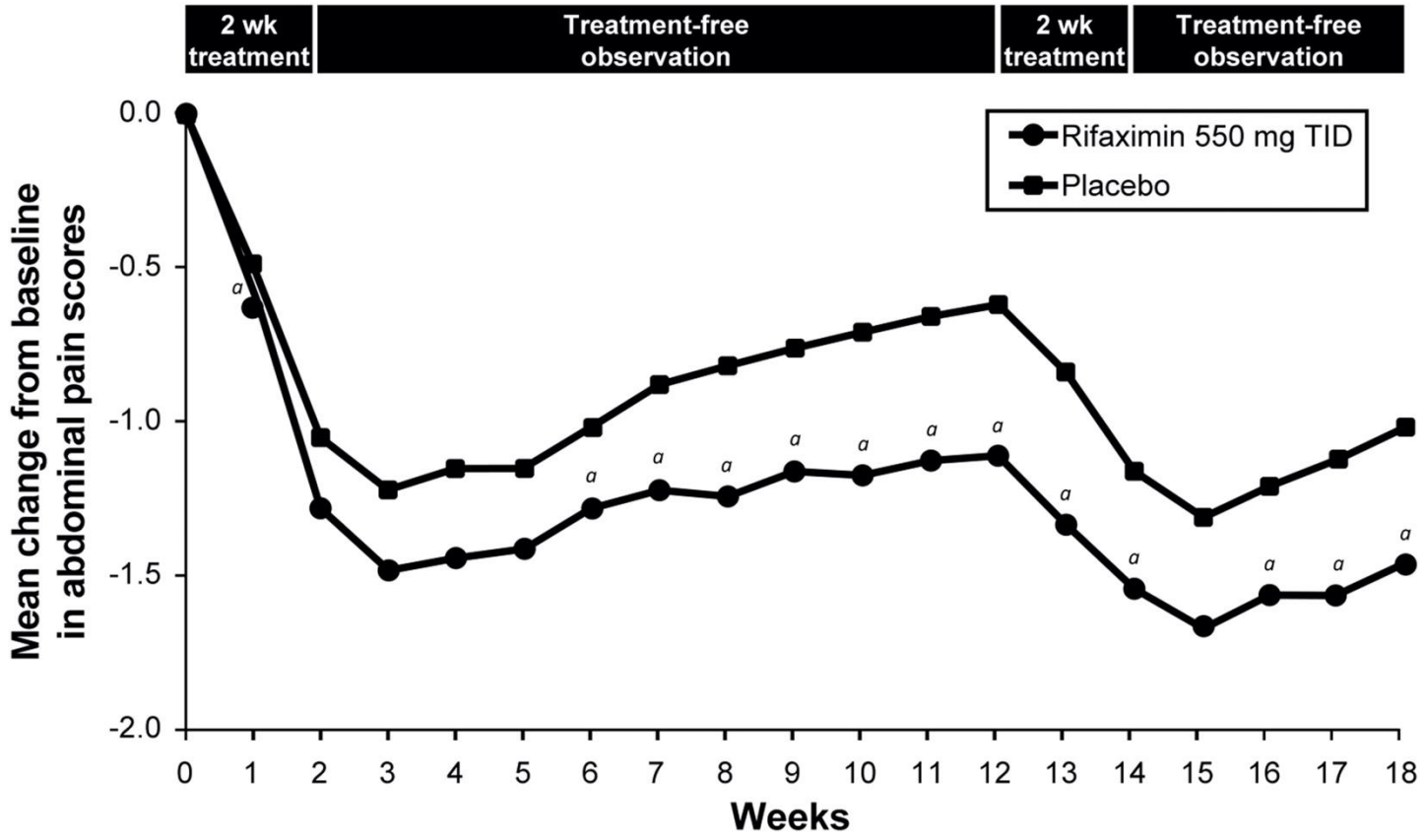
- Patient adheres to a vegetarian diet and has tried to cut back on dairy without improvement in symptoms
- She does note frequent snacking on cookies, candies, pizza, etc when available at work
  - Drinks at least one energy drink daily at work

Choose Low FODMAP vs Rifaximin?





Lembo A, et al. *Gastroenterology*. 2016;151:1113-1121.

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“My Belly Hurts:” Optimizing Abdominal Pain Relief in IBS

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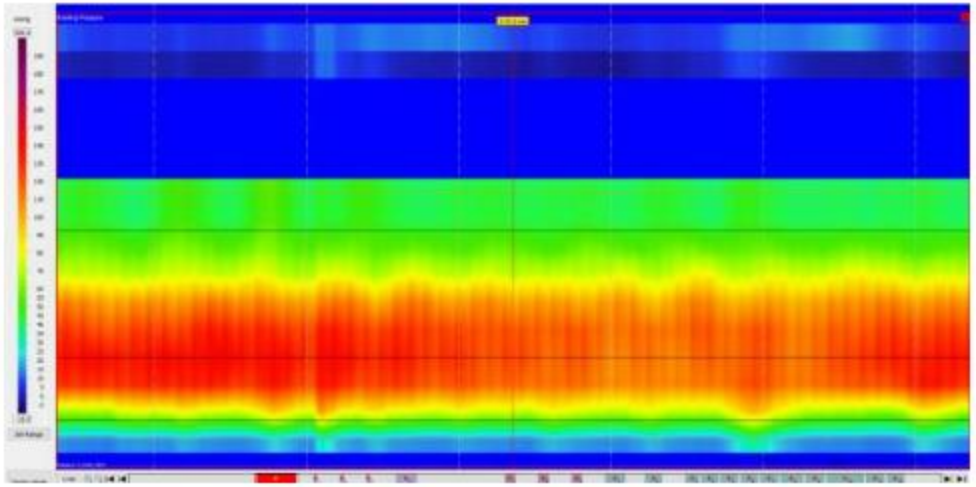
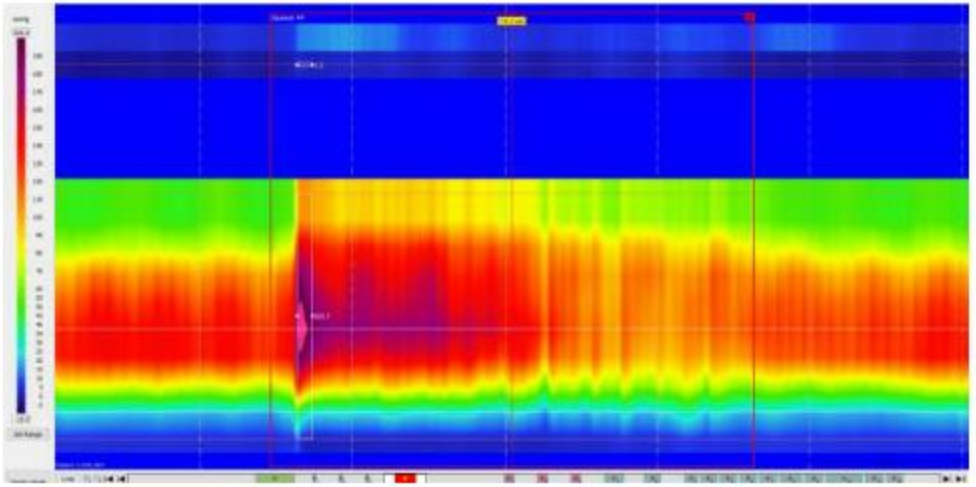
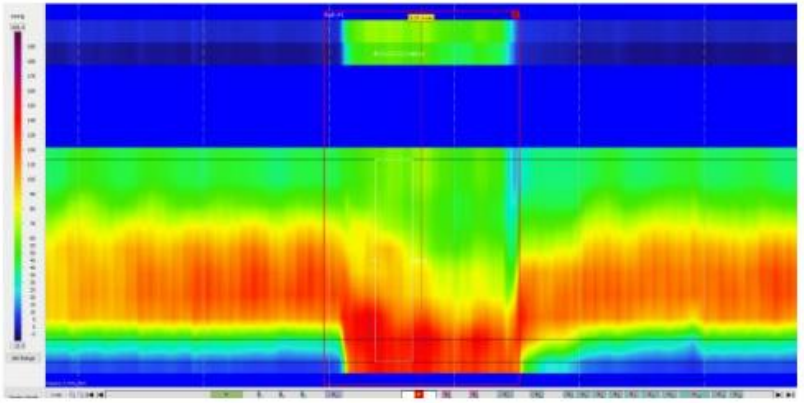
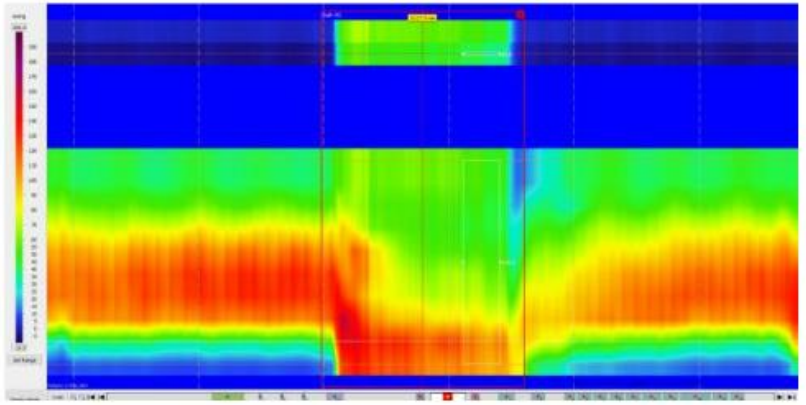
Case

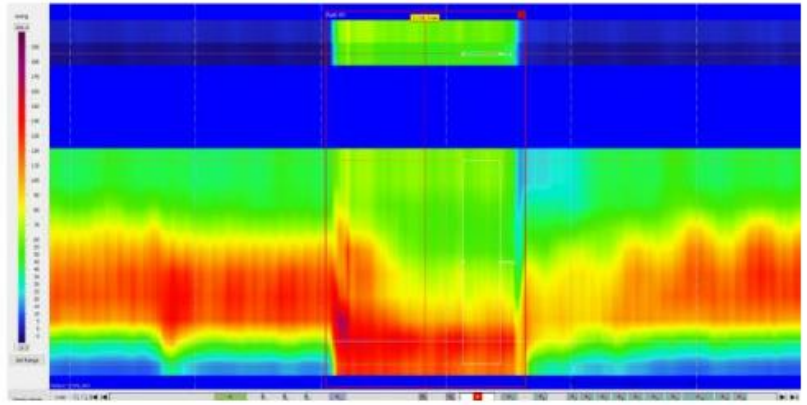
- 54 year old school teacher presents after evaluation with colorectal surgery for constipation and fecal urgency
- Patient completed ARM and engaged with pelvic floor physical therapy prior to consultation
  - Experienced minimal relief in constipation
- Has a BM after using a glycerin suppository after her workday is over (when time allows), but always reports a sensation of incomplete evacuation











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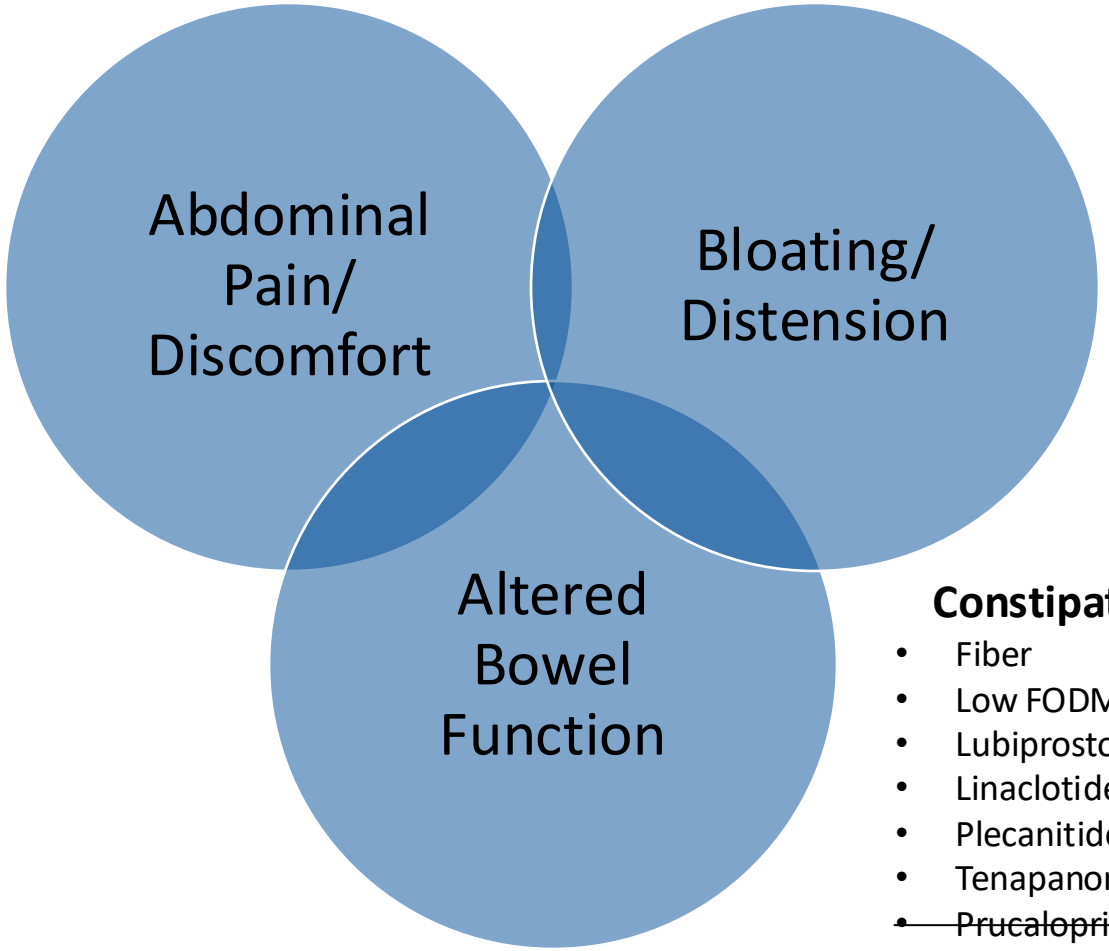
- She also has significant daily bloating and “all consuming” LLQ and suprapubic cramping pain that worsens throughout the day until she can get home and use the bathroom
  - Of note, weekends and school holidays tend to be less burdened with pain symptoms

- There are no reports of blood in the stool, unintentional weight loss, or other alarm features
- Recent colonoscopy for CRC screening was normal
- Labs including CBC, celiac serologies, and CRP were within normal ranges

How would you treat her pain/bloating?

Abdominal Pain/Discomfort:

- Fiber
- Peppermint oil
- **Antidepressants**
- Lubiprostone
- Linaclotide
- Plecanitide
- Tenapanor
- **Gut directed psychotherapy**



Bloating:

- Rifaximin
- Lubiprostone
- Linaclotide
- Plecanitide
- Tenapanor

Constipation:

- Fiber
- Low FODMAP diet
- Lubiprostone
- Linaclotide
- Plecanitide
- Tenapanor
- ~~Prucalopride~~

Lacy BE, et al. *Gastroenterology*. 2016;150:1393-1407.e5; Lacy BE, et al. *Am J Gastroenterol*. 2021;116:17-44.

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EoE Treat to Target — Symptoms Improved, But HistologicallyUnchanged

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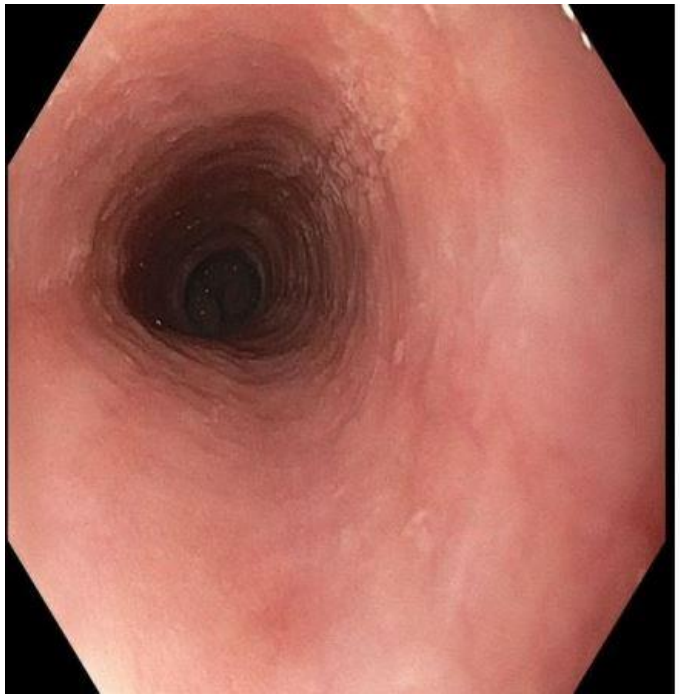
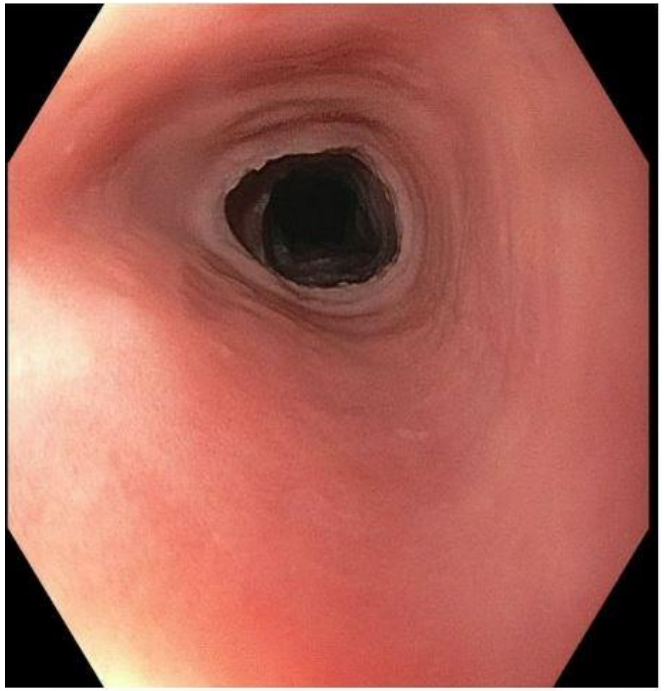
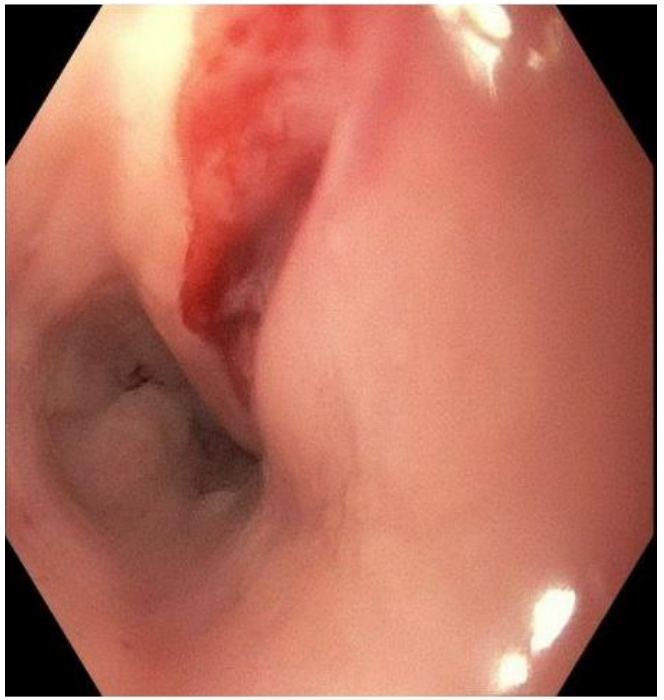
History of Present Illness

- 47 year-old female with EoE and seasonal allergies
  - Dysphagia started at 16 y/o, no heartburn/regurgitation
  - Diagnosed with EoE at 41 y/o after food impaction (one food impaction prior)
  - Has required 4 dilations (last 2019 - dilated to 51 French, no path results)
  - Previously failed 6 food elimination diet
  - Not on therapy
- Family History – EoE in son (who also has Crohn's disease) and paternal GF
- Surgical History – Hysterectomy for cervical caner
- Medical History – As above

EGD Off Therapy







- E1R1Ex1F1S1
- Stricture at GEJ – dilated from 8mm to 10mm
- Proximally up to 30 eos/hpf, distally up to 65 eos/hpf

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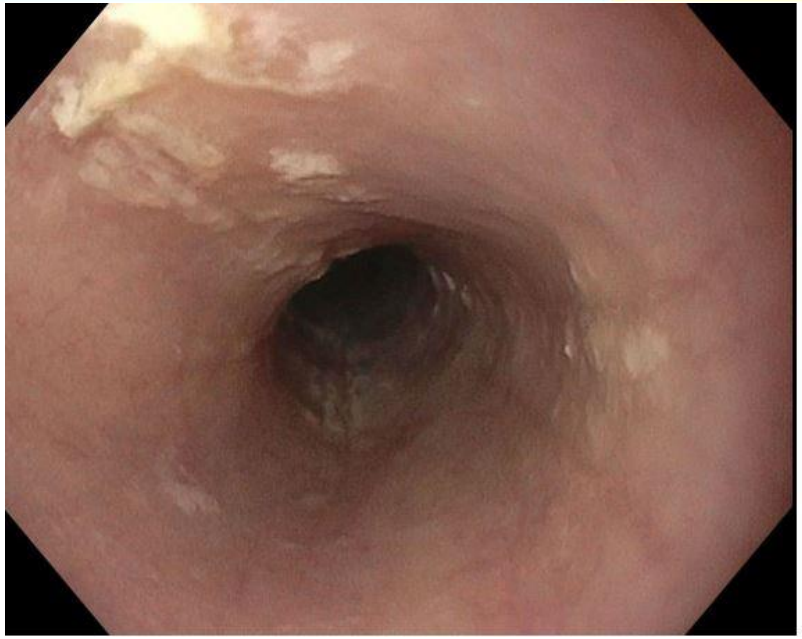
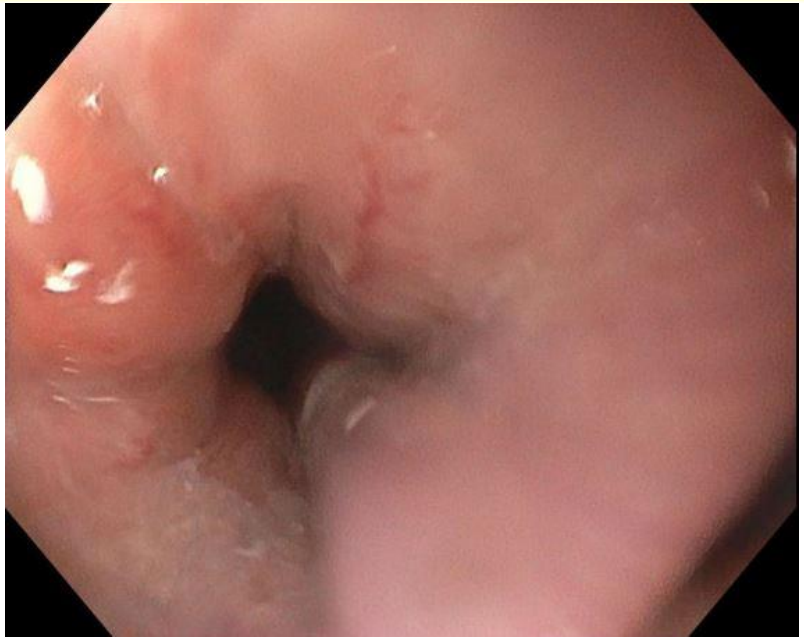
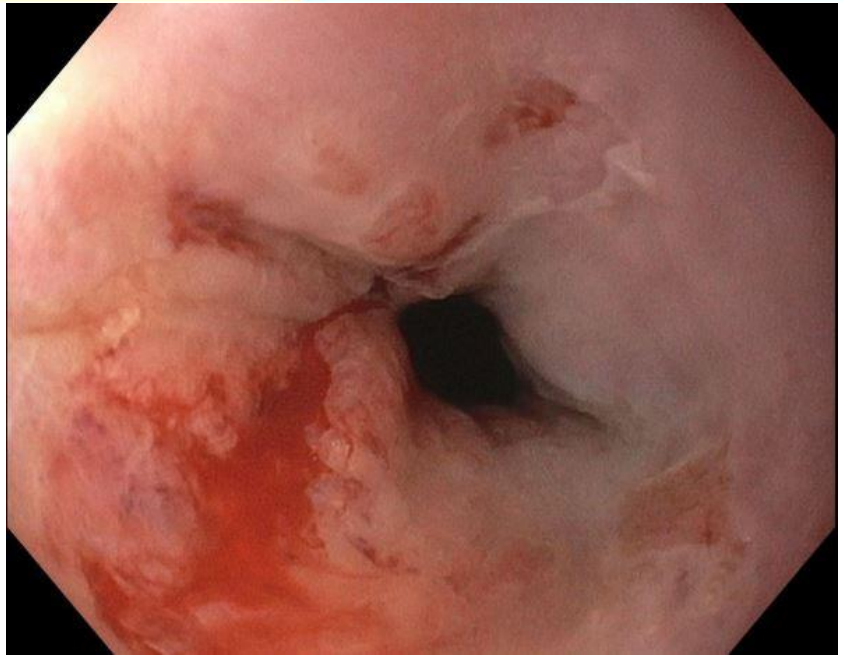
3 Months Later EGD on Omeprazole 20mg BID

- Symptoms fully resolved
- E1R1Ex1F1S1
- CRE dilation from 10mm to 13.5mm
- Proximally up to 4 eos/hpf, distally up to 80 eos/hpf

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Panel Questions

- What do the panelists make of the improved proximal eos and worsening distal eos on double dose PPI?
- How do you define a response to therapy?
- Do you always require <15 eos/hpf to be considered responsive to a therapy?
- Would this be considered a partial response or non-response?
- Would you continue PPI or transition to another therapy?
- If you would transition therapy, which therapy?
- How soon would you repeat the next EGD?

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Case Outcomes

- Patient started on Dupixent 300mg weekly
- Has follow-up clinic appointment scheduled and instructed to repeat EGD in 3 months

Debate:
Step-Up vs Top-Down Treatment of IBS-C

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Don’t Let Her Pretty Face Fool You: The 10+ Reality Commandments Validating **FOOD AND EXERCISE!!** As The Holy Grail of 1st line Treatment for IBS-C

(Seriously Folks Do We Really Have To Waste The Next 10 Minutes Validating This Argument)?

Darren M. Brenner, MD, AGAF, FACG, RFF
Professor of Medicine and Surgery
Director—Northwestern Neurogastromotility Northwestern University Feinberg School of Medicine

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Disclosures and Concessions:

- Disclosures:
  - Last year I argued FDA Rx should be 1st line agents
    - Work better than OTCs for abdominal symptoms
    - Validated in rigorous high-quality trials
    - Guidelines (ACG) strongly recommend them
    - Patient survey found them more effective than diet (IN 2015)!!!! Data Now 2022-2025

- Concessions:
  - OTCs should not be used to treat IBS
  - FDA approved therapies & neuromodulators DO improve global IBS symptoms
  - FDA trials more rigorous

Realism: What feels real or Baha's own approach to realty; What you want to believe

Aka: Expensive meds with lots of side-effects 1st-line

Reality: The state of being real or the true nature of things

Aka: Food and exercise 1st

So, Let's Deal In Reality

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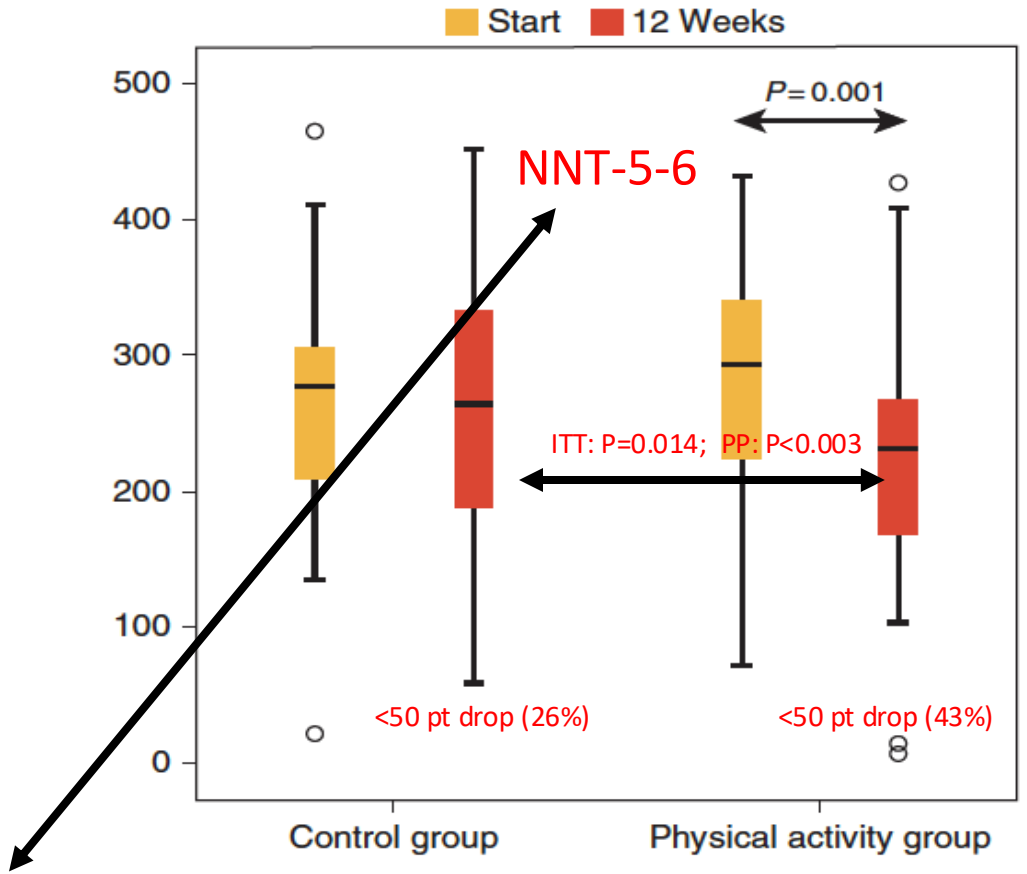
Realty #1: Exercise Works With NNT ½ Of That OF Prescription Meds

- Rome II IBS (N=102)
- Physical activity (20-60 min cardio 3-5 days/week) vs. control (maintain lifestyle)
- Results as per ITT & PP analyses for GLOBAL SYMPTOMS



NNT Pharmaceuticals: 8-12

Johannesson E et al. AJG 2011;106:915-922

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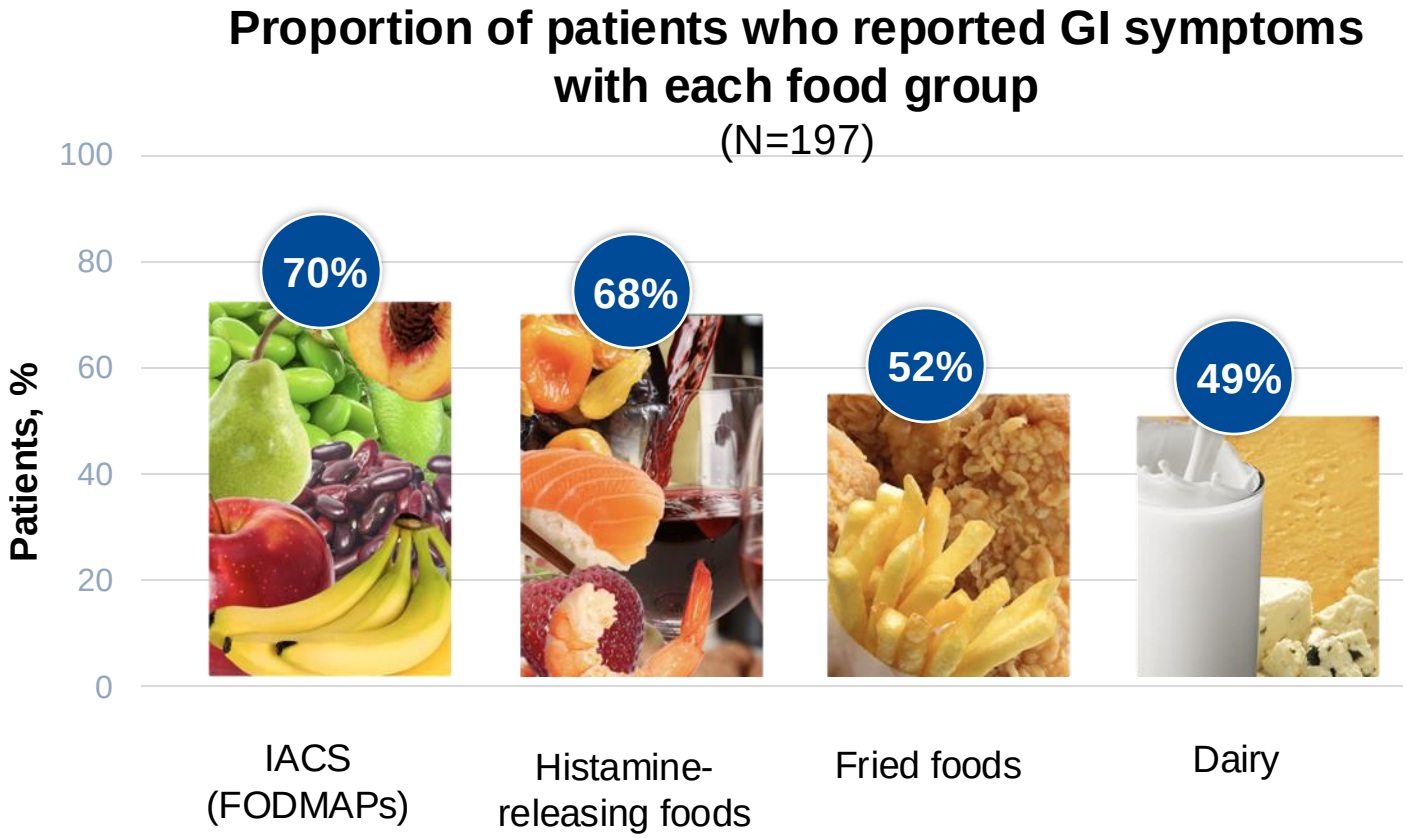
Reality #2: Food Really Causes Symptoms in IBS:

If We Have Identified A Specific Cause We Should Treat It



84% of patients with IBS **endorsed food-induced GI symptoms**

THP: Almost all IBS patients identify foods as triggers & **avoid them**

Bohn L et al. Am J Gastroenterol. 2013;108:634-641.

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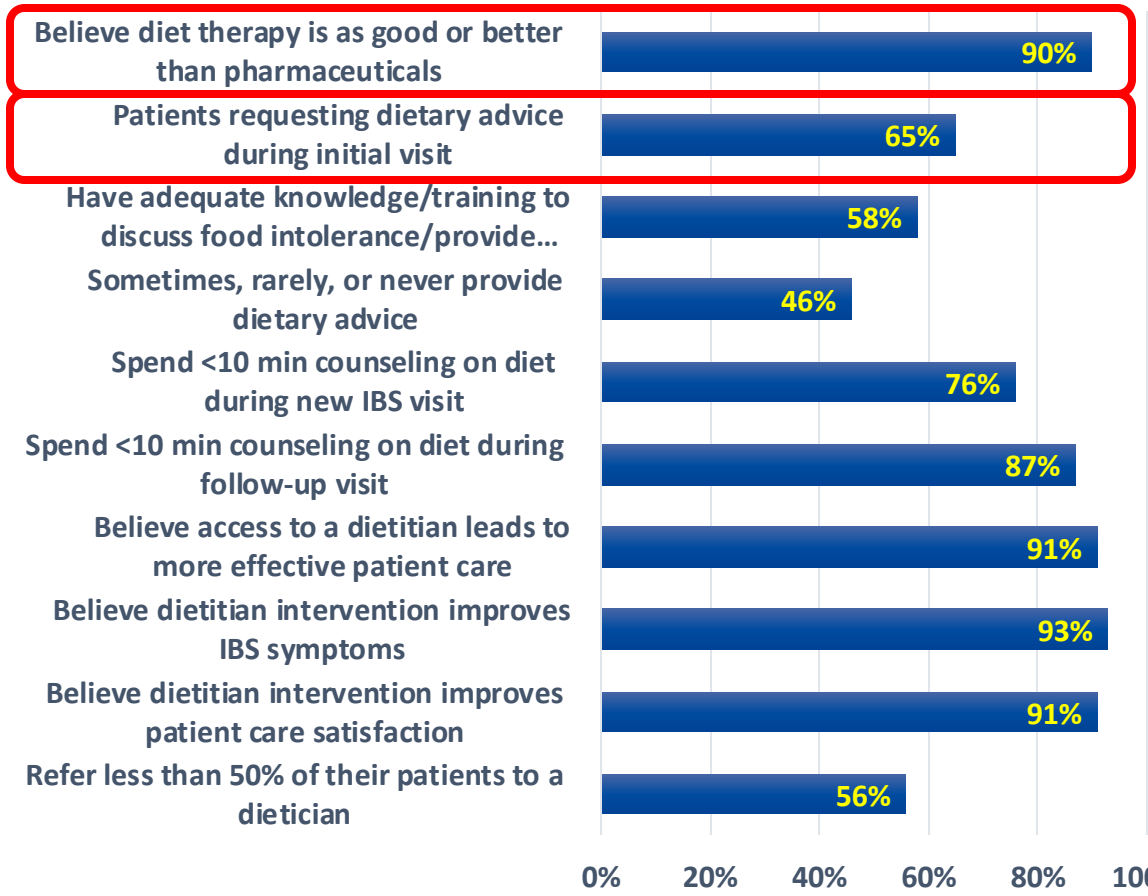
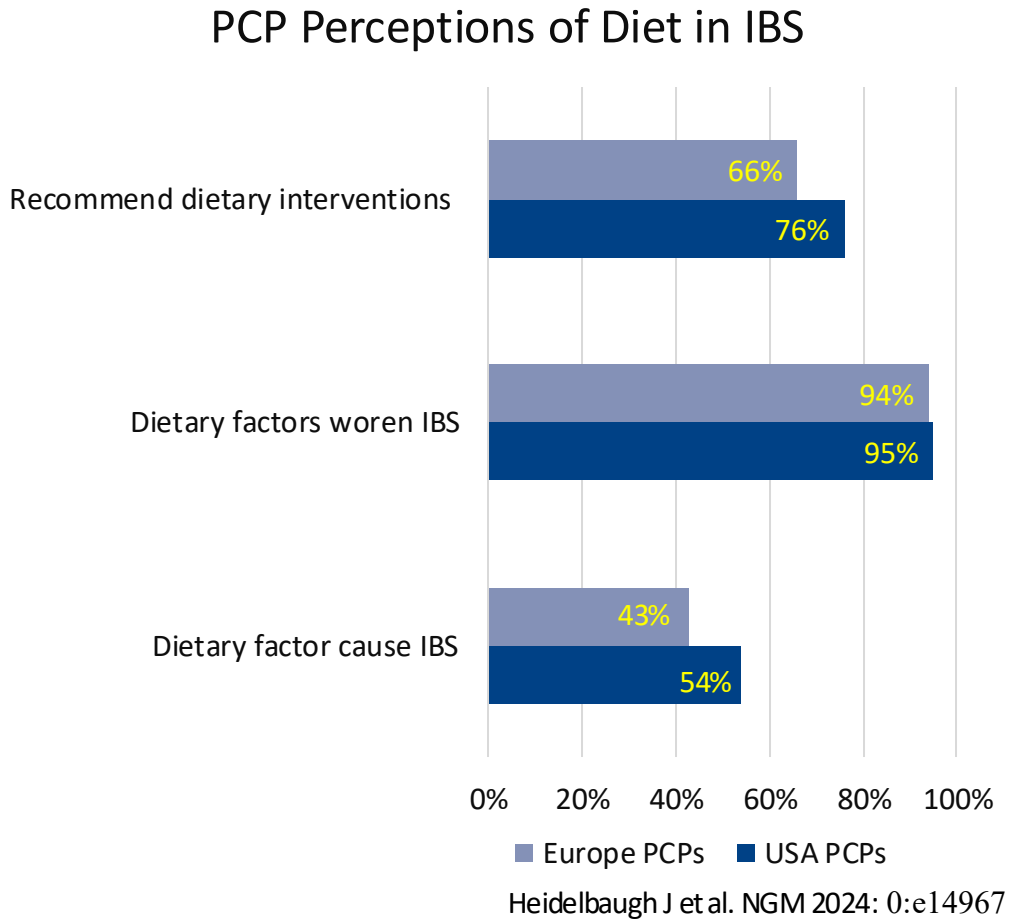
Reality #3: PCPs & Gastroenterologists Believe Food Causes and Improves IBS Symptoms



Scarlata K et al. AJG 2022;117:923-926.



Heidelbaugh J et al. NGM 2024: 0:e14967

THP: Patients Want Diet Advice 1st Line and We Believe It Works As Good Or Better Than Pharma

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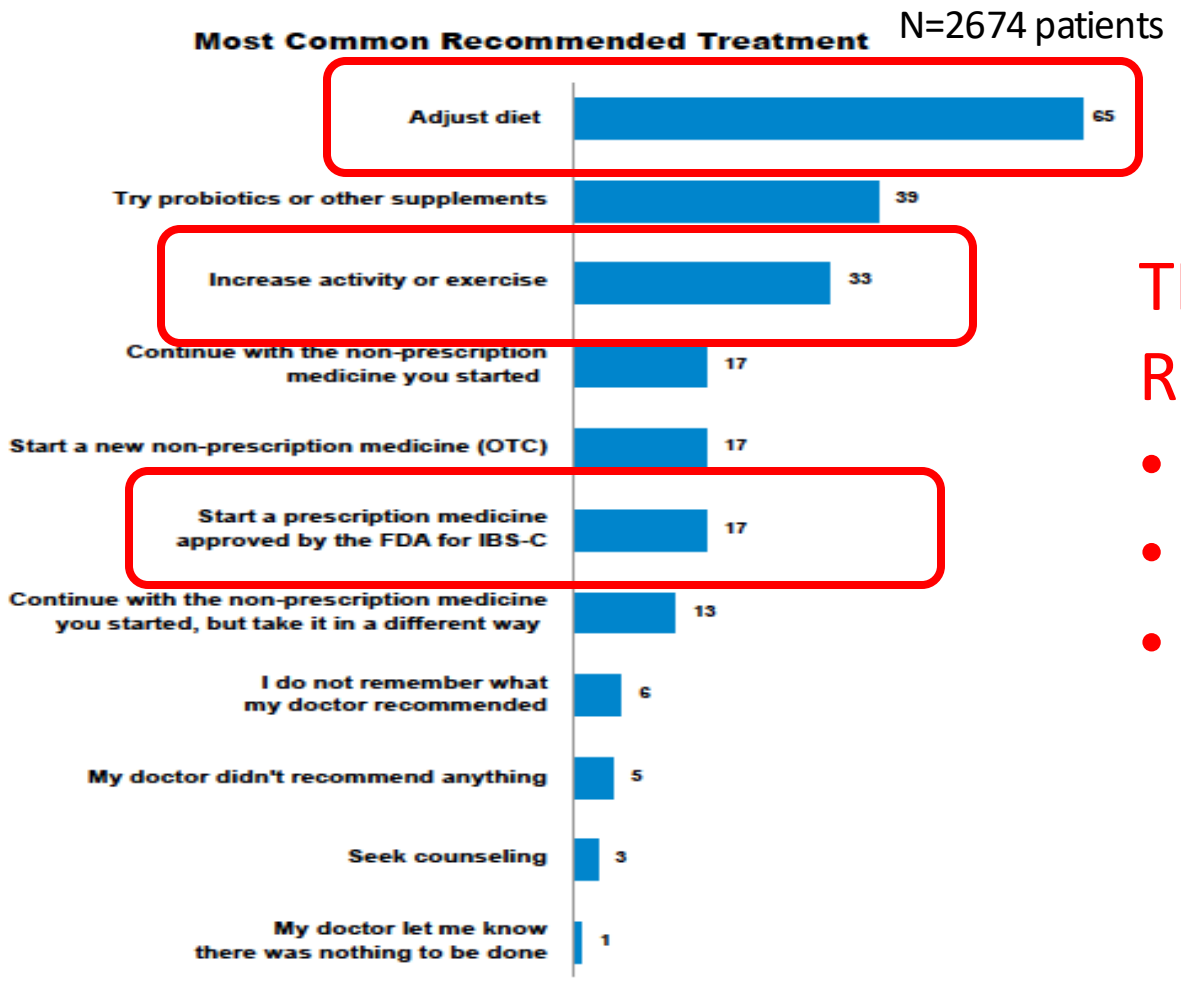
Reality #4: We Practice What We Preach Because We Believe!!!



THP: Most Common Treatment Recommendations:

- 66% diet
- 33% Exercise
- 17% FDA approved IBS therapies

Shin A and Lembo A. AGA IBS in America Survey 2015: 1-45.

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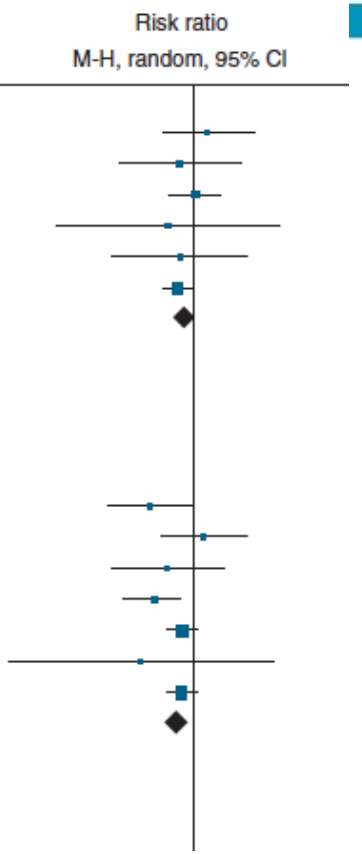
Realty #5: Add In The Good Food Because It Works

Lower Cholesterol In The Process

- Confusing to many practitioners
  - Soluble (psyllium, oat bran, barley, beans
  - Insoluble (wheat bran, whole grains)
  - Combination (Kiwi, Prunes)

Study or subgroup	Fiber Events	Fiber Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio M-H, random, 95% CI	Year
Bran							
Soltoft, 1976	17	32	12	27	2.4%	1.20 (0.70, 2.04)	1976
Manning, 1977	7	14	7	12	1.3%	0.86 (0.42, 1.74)	1977
Kruis, 1986	29	40	28	40	8.6%	1.04 (0.78, 1.37)	1986
Lucey, 1987	3	14	4	14	0.4%	0.75 (0.20, 2.75)	1987
Rees, 2005	6	14	7	14	1.0%	0.86 (0.39, 1.91)	2005
Bijkerk, 2009	66	97	75	93	23.5%	0.84 (0.71, 1.00)	2009
Subtotal (95% CI)		211		200	37.2%	0.90 (0.79, 1.03)	
Total events	128		133				
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 2.76$, d.f. = 5 ($P = 0.74$); $I^2 = 0\%$							
Test for overall effect: $Z = 1.47$ ($P = 0.14$)							
Ispaghula → soluble, viscous, poorly fermentable							
Ritchie, 1979	7	12	12	12	2.9%	0.60 (0.37, 0.97)	1979
Longstreth, 1981	17	37	16	40	2.5%	1.15 (0.69, 1.92)	1981
Arthurs, 1983	11	40	14	38	1.6%	0.75 (0.39, 1.43)	1983
Nigam, 1984	13	21	21	21	5.9%	0.63 (0.45, 0.88)	1984
Prior, 1987	33	40	37	40	23.8%	0.89 (0.75, 1.05)	1987
Jalihal, 1990	2	11	3	9	0.3%	0.55 (0.11, 2.59)	1990
Bijkerk, 2009	60	85	75	93	23.3%	0.88 (0.74, 1.04)	2009
Subtotal (95% CI)		246		253	60.2%	0.83 (0.73, 0.94)	
Total events	143		178				
Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 7.32$, d.f. = 6 ($P = 0.29$); $I^2 = 18\%$							
Test for overall effect: $Z = 2.80$ ($P = 0.005$)							



2021 ACG IBS Guideline: Suggest soluble but not insoluble fiber be used to treat global IBS symptoms--Strong Recommendation

2022 AGA Clinical Practice Update: Soluble fiber is effective in treating global IBS symptoms

THP: Soluble Fiber Good!!! IT'S Subtype Agnostic: Goal 8-12 g supplemental/day

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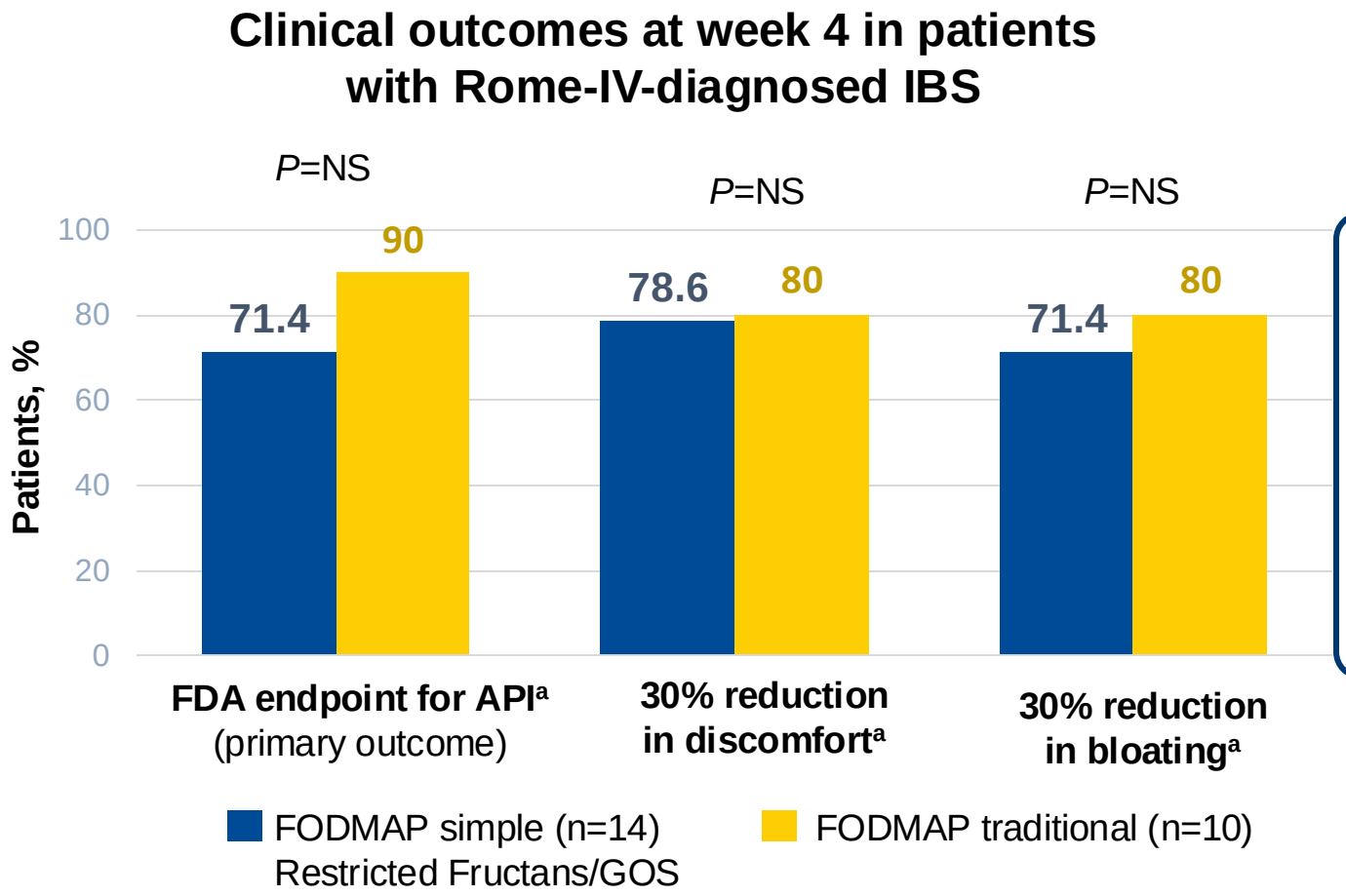
Moayyedi P et al. AJG 2014;109:1367-1374. ; Ford AC et al. AJG 2018;113:1-18. ; Lacy BE et al. AJG 2021;116:17-44.; Chey WD et al. Gastro 2022;162:1737-1745

Reality #6: Forget The Highly Restrictive Low FODMAP Diet. It's Muerto



THP: YOU DON'T HAVE TO STARVE!!

- **A step-up approach to the low FODMAP diet (initial restriction of only fructans & GOS) may be feasible in IBS-D.**
- **Response rates: 70-80%**
- **Subtype agnostic**

Singh P et al. *CGH 2025*;23(2):362-364

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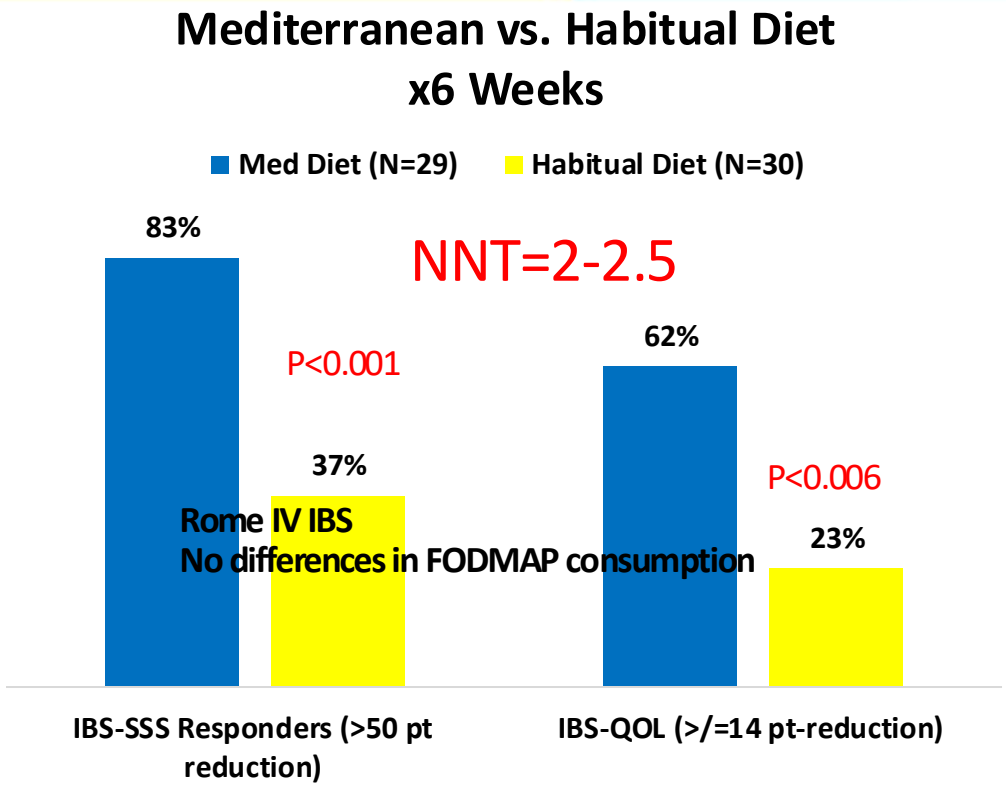
Reality #7: Mediterranean Diet Also Effective



THP: Mediterranean diet feasible and clinically significantly improves biopsychological symptoms in 60-80% of IBS patients & is subtype agnostic

Staudacher HM et al. APT 2024;59(4):492-503.

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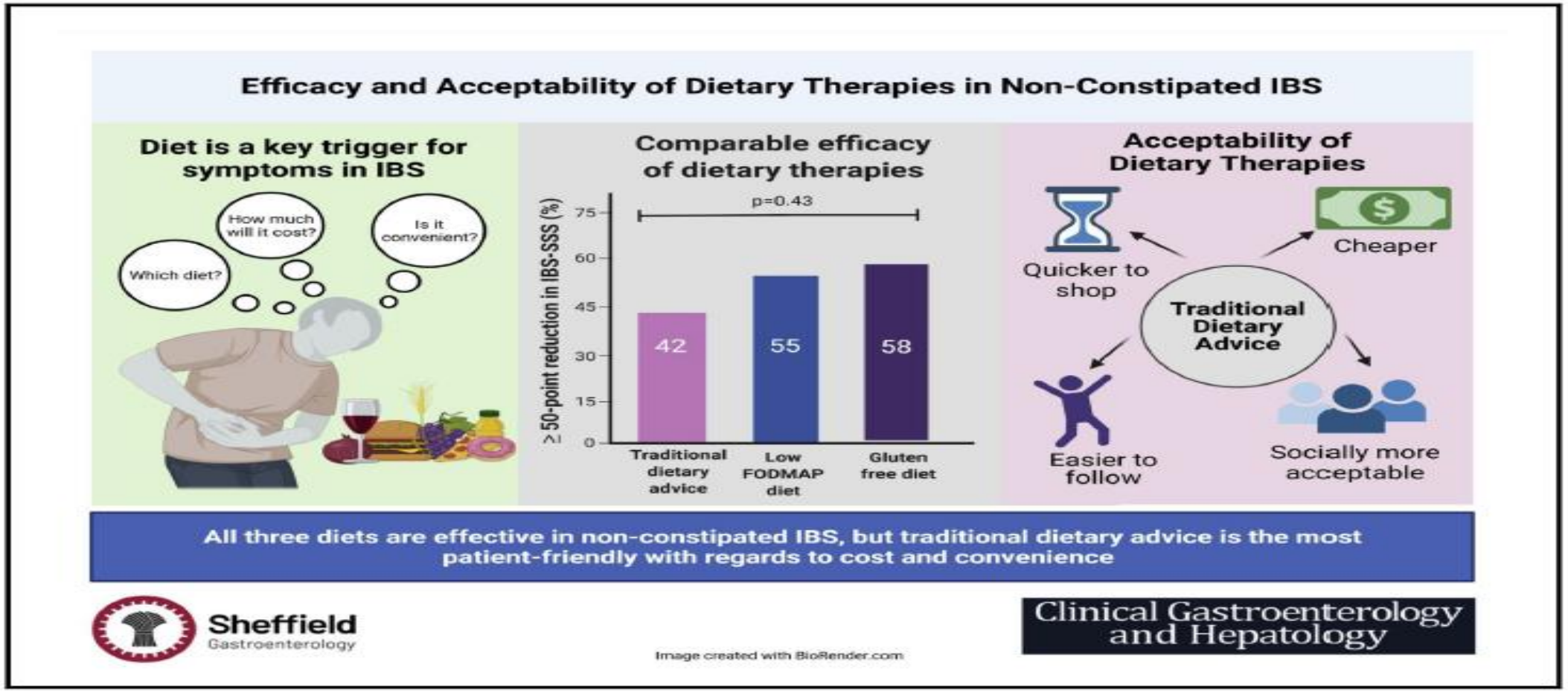
Reality #8: You Hate Strict Diets? That's Ok Modifying Diet Works Too



THP: Eating slower, more frequently, reducing fat, insoluble fiber, caffeine improves symptoms, saves time & $$ and allows you to be more human

Rej et al. CGH 2022;S15142-3565

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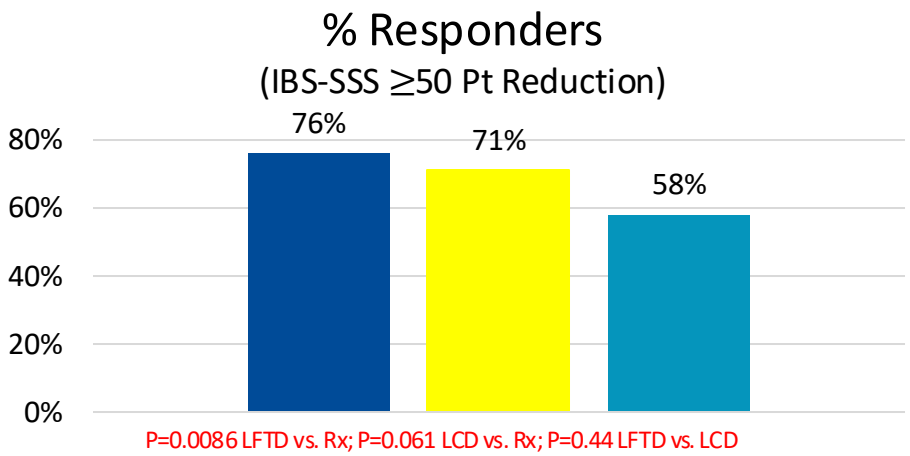
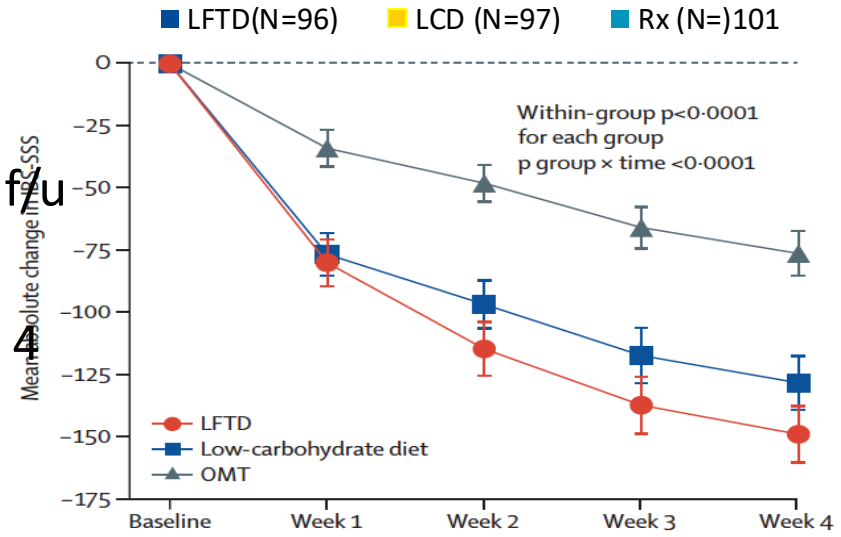
Reality #9: Diets Work Better Than Medications CARBIS Trial
Low FODMAP + TDA (LFTD) vs. Low Carb (LCD) vs. Rx

Study Design:

- Single center, single-blind (to diet), randomized trial
- Pts Rome IV IBS ALL SUBTYPES
- Meds at practitioner discretion
- 4 weeks with 6-month follow-up (diet)
  - Personalization occurred during 6 mo f/u
- 1^0 endpoint: ≥50 pt reduction IBS-SSS @ 4 weeks



P=0.0086 LFTD vs. Rx; P=0.061 LCD vs. Rx; P=0.44 LFTD vs. LCD



Δ from baseline @ 4 weeks: LFTD -149; LCD -128; Rx -76

P=<0.0001 LFTD vs. Rx; P=0.004 LCD vs. Rx; LFTD vs. LCD P=NS

Nybacka S et al. Lancet Gastroenterol Hepatol 2024;9:507-20.

Take Home Points:

- Both diets more successful than Rx for global symptoms
- Both diets more successful for Rx for QoL (Diets > Rx; P=0.0029)
- Both diets more successful for improving non-GI somatic symptoms (Diets > Rx; P=0.0003)
- Diet response maintained @ 6 months further supporting use of dietary management as 1^{st} line interventions

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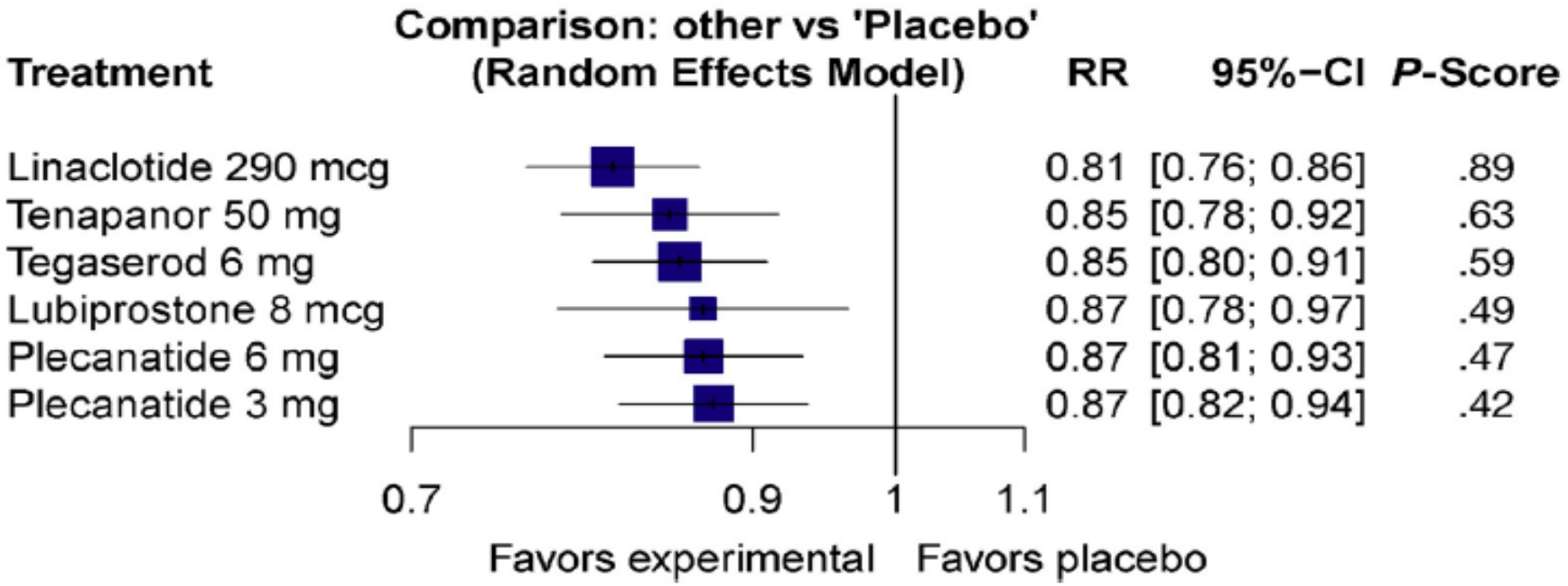
Reality #10: No Clue Which Rx Therapy Should Be 1st Line IBS-C? Network Meta-Analysis RCTs For IBS-C (N=14)

Overall FDA Responder



THP: None better none worse & all with NNT=8-12: How Do You Choose?

Black CJ et al. CGH 2020;1238-1239

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Bonus Reality # 11: Good Luck Getting An Assist From Guidelines: AGA & ACG Cannot Agree On Pharma Treatment Recommendations

Therapeutic	American College of Gastroenterology (ACG)	American Gastroenterological Association (AGA)
Linaclotide	**Strong recommendation for use IBS-C**	**Strong recommendation for use IBS-C**
Plecanatide	Strong recommendation for use IBS-C	Conditional suggestion for use IBS-C
Lubiprostone	Strong recommendation for use IBS-C	Conditional suggestion for use IBS-C
Tenapanor	Not reviewed	Conditional suggestion for use IBS-C
PEG laxatives	Conditional suggestion **against** use IBS-C	Conditional suggestion **for** use IBS-C
TCAs	Strong recommendation for use	Conditional suggestion for use

THPs: Same data reviewed with discordant recommendations so thanks for the help!!

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Lacy BE, Pimentel M, Brenner DM, et al. AJG 2021;116:17-44.; Chang L et al. Gastroenterology 2022;163:118-136. Lembo A et al. Gastroenterology 2022;163:137-151.

The Reality Of All Realities:

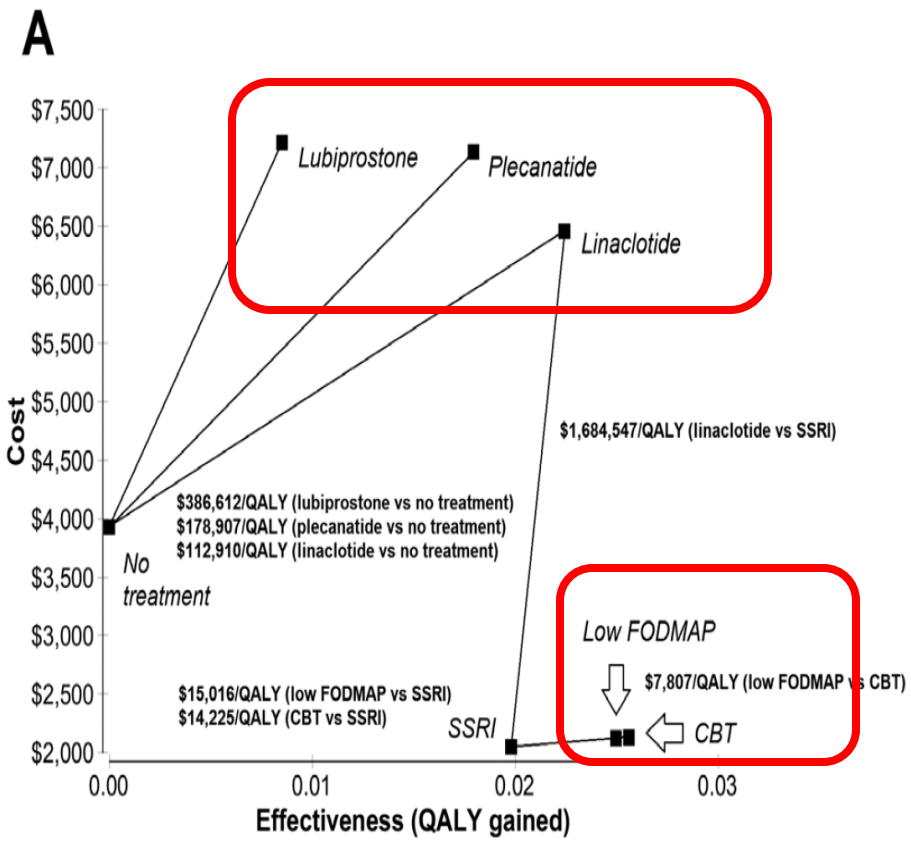
Can you afford these meds anymore?
Should you afford these meds anymore?

- Direct patient quotes IBS-Rx from 1 day my chart:

"The medicine is $365. I will not be able to afford that. If there is nothing, I can be put on that costs under $100 I will just have to go back to the PEG 3350 and stool softeners

"Hi. My insurance is telling me that even though they have covered my linaclotide in the past, until I meet my deductible even with the manufacturer coupon, they are charging $350 per 30 days to get it filled? This is obscenely expensive

"You gave me a refill and I don't know if it's the new year, but it is saying I owe $544.72, I cannot afford that. Is there something else I can be put on that is cheaper? Until then I will be doing PEG 3350 daily and Fleet's as needed."



low FODMAP, and CBT were cost-saving to a payer compared to "no treatment" for IBS-C, with cost savings of approximately $1800 to $1900 per year for patients receiving one of these interventions. In contrast, payers would spend an additional $2531.26 to $3288.63 per-patient annually for patients receiving lubiprostone, plecantide, or linaclotide at their current drug prices compared to "no treatment" for IBS-C.

THP: Patients cannot afford these meds, and they are NOT cost effective

Shah et al. MDM Policy and Practice 2021;6(1):1-14

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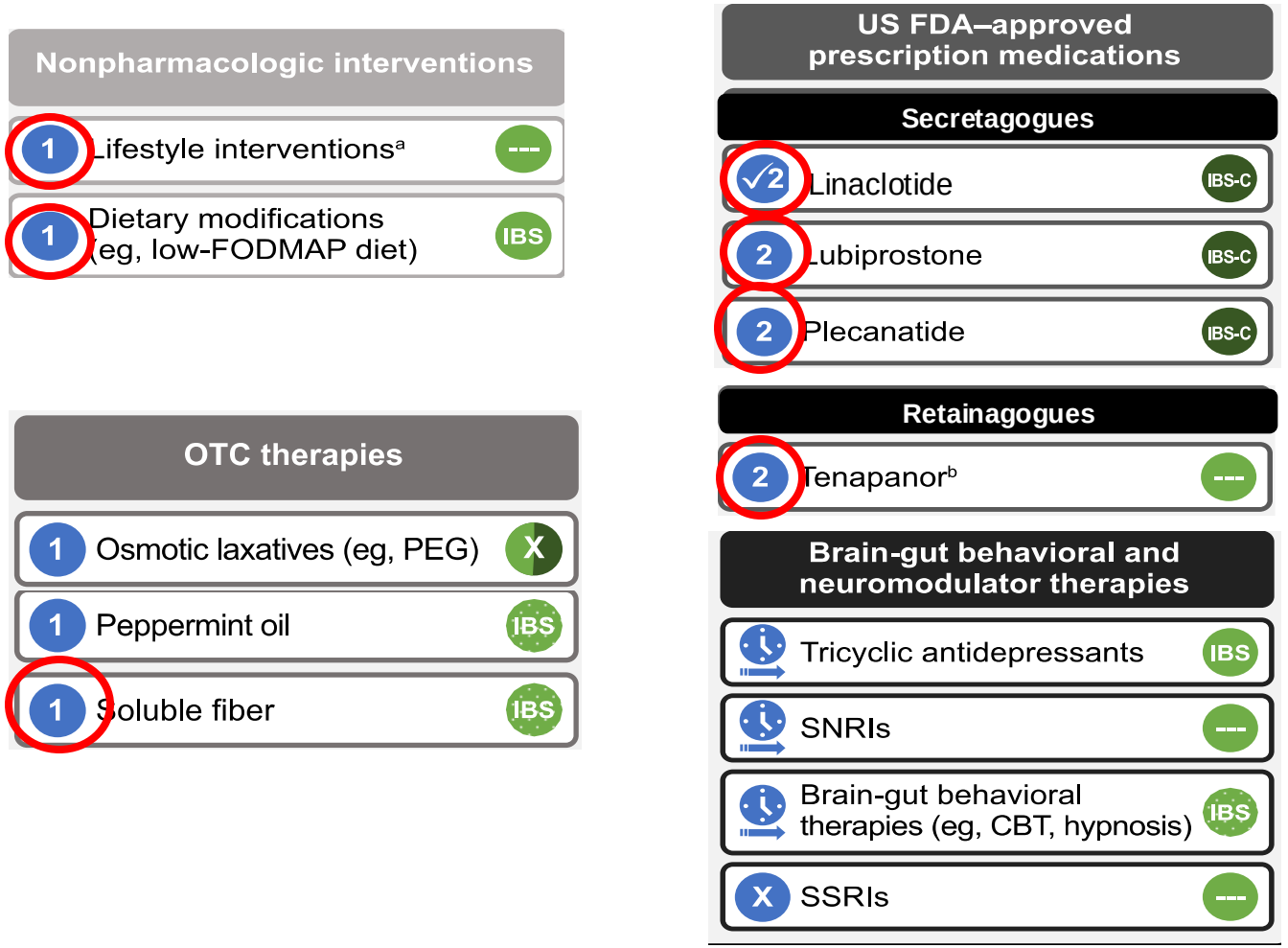
Finally Baha Agrees: Treatments Recommendations From ACG/AGA Guidelines for IBS-C (From 2024)!!!!



THP: Baha's summary of the guidelines reveals her reality:

(1) Indicates 1st line agents

(2) Indicates 2nd line agents

Where are the 1's???

- Sendzischew Shane MA, et al; Moshiree B. Clin Exp Gastroenterol. 2024;17:227-253.

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The 10 Commandments of Reality (Not Realism)

1. Exercise improves everything (duh)
2. Patients know/endorse food causes IBS symptoms
3. Practitioners feel diet as good if not better than Rx & recommend 1st line
4. Multiple Diets Available, Feasible, & Effective
   - Increased Fiber
   - FODMAP Lite
   - Mediterranean
   - Just modification of eating habits
5. Diet works better than meds in head-head clinical trials
6. Diets are IBS subtype agnostic
7. NNT lower & NNH higher with diets than meds
8. Diets reduce costs and improve QoL
9. Meds increase costs and people cannot afford them
10. Baha believes diet should be first line

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Top-Down Treatment for IBS-C

Baha Moshiree MD, Msc
Professor of Medicine, Wake Forest Univ.
Director of Motility
Atrium Health
baha.moshiree@atriumhealth.org

Advocate Health Care · Atrium Health · Aurora Health Care · Wake Forest University School of Medicine

Now part of ADVOCATEHEALTH

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Goals of Step-Down Therapy for IBS-C

Intensive therapy first for moderate to severe IBS patients tailored to predominant symptoms

Gradually introduce dietary modifications with low FODMAP diet and adding exercise, or stress reduction once symptom control is achieved

Ultimate Goal is to improve patients QOL and for a positive person-centered care to management

- Educate
- Reassure
- Involve --patients in the decision-making process
- Cost-Effectiveness over time

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IBS in America Survey 2024

45% feel out of control with their financial situation as a result of missed work days.[2]

In one study, patients with IBS said they would be willing to sacrifice 25% of their remaining life, averaging to about 15 years, and 14% of patients would risk a 1/1000 chance of death associated with the treatment, provided it would relieve them of their IBS symptoms![1]

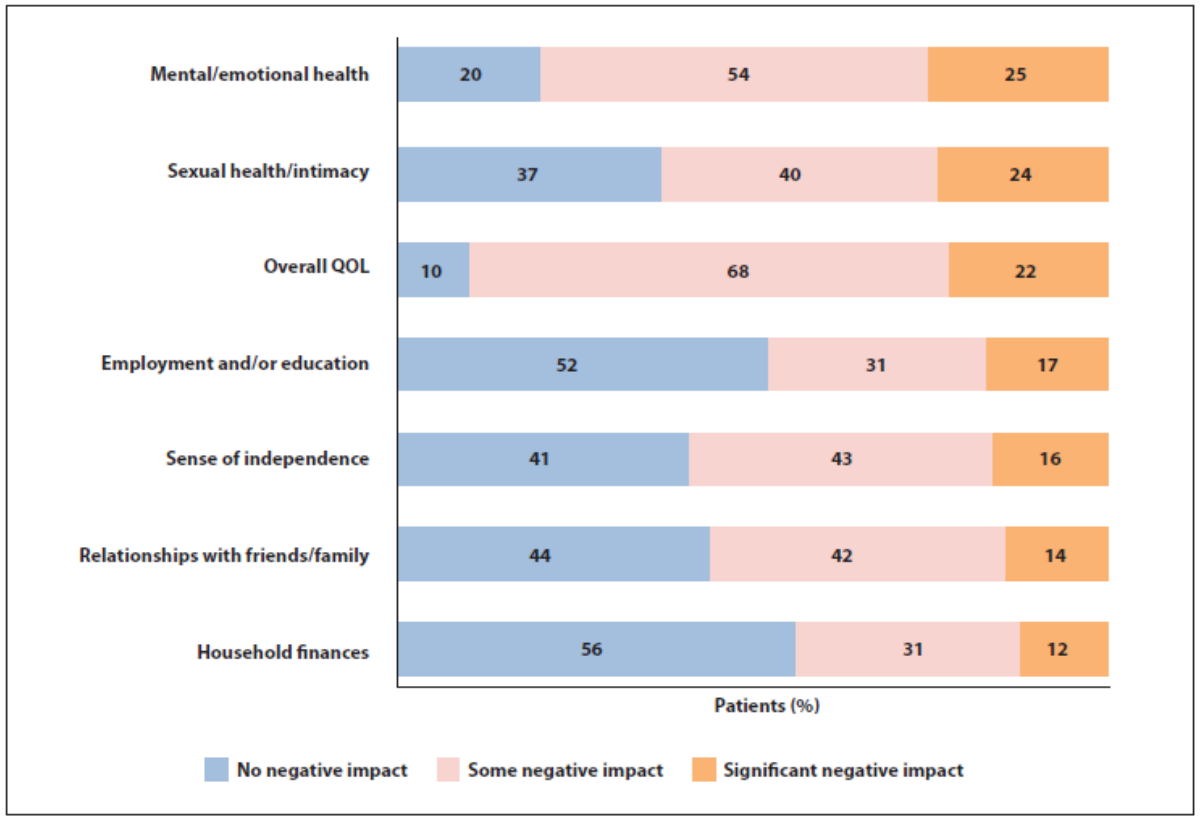

Figure 1. Impact of irritable bowel syndrome with constipation on the QOL of patient respondents in the IBS in America 2024 Real-World Survey. QOL, quality of life. Adapted from Shah E, et al. Abstract P0641. Presented at: American College of Gastroenterology 2024 Annual Scientific Meeting; October 25-30, 2024; Philadelphia, Pennsylvania.[1]

1. Drossman DA, et al. *J Clin Gastroenterol.* 2009;43(6):541–550. 2. Shah E, et al; Moshiree B. Presented at: American College of Gastroenterology 2024 Annual Scientific Meeting; October 25-30, 2024; Philadelphia, PA. Abstract P0641.

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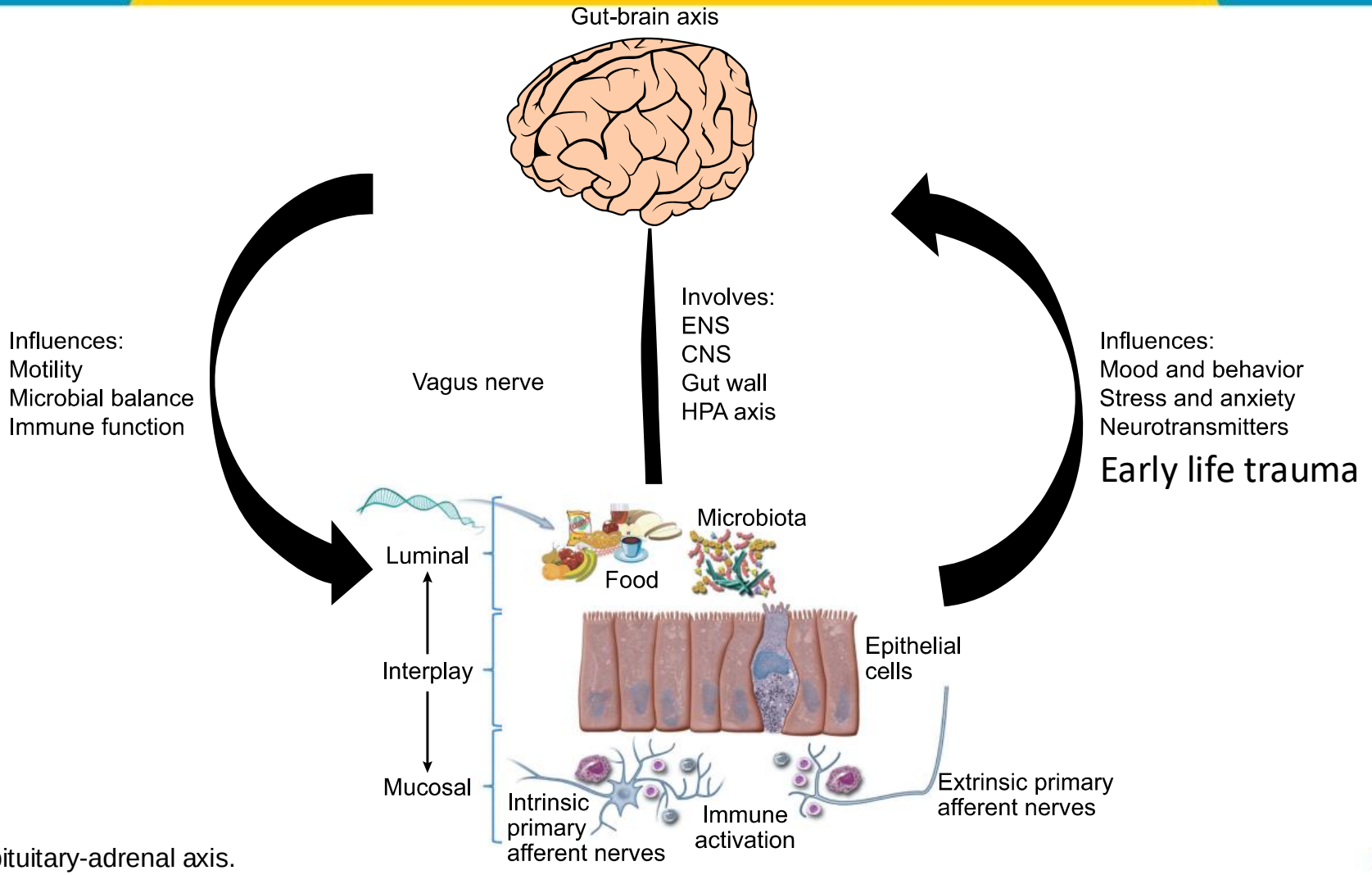
IBS-C Pathophysiology



HPA = hypothalamic-pituitary-adrenal axis.

Sendzischew Shane MA, et al; Moshiree B. *Clin Exp Gastroenterol.* 2024;17:227-253.

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ORIGINAL ARTICLE

Neurogastroenterology & Motility NGM WILEY

Burden of illness and treatment attitudes among participants meeting Rome IV criteria for irritable bowel syndrome: A nationwide survey in the United States

Brian E. Lacy[1] | Yanqing Xu[2] | Douglas C. A. Taylor[3] | Katherine J. Kosch[2] | Rachel Dobrescu[4] | Amy Morlock[4] | Robert Morlock[5] | Ceciel Rooker[6]

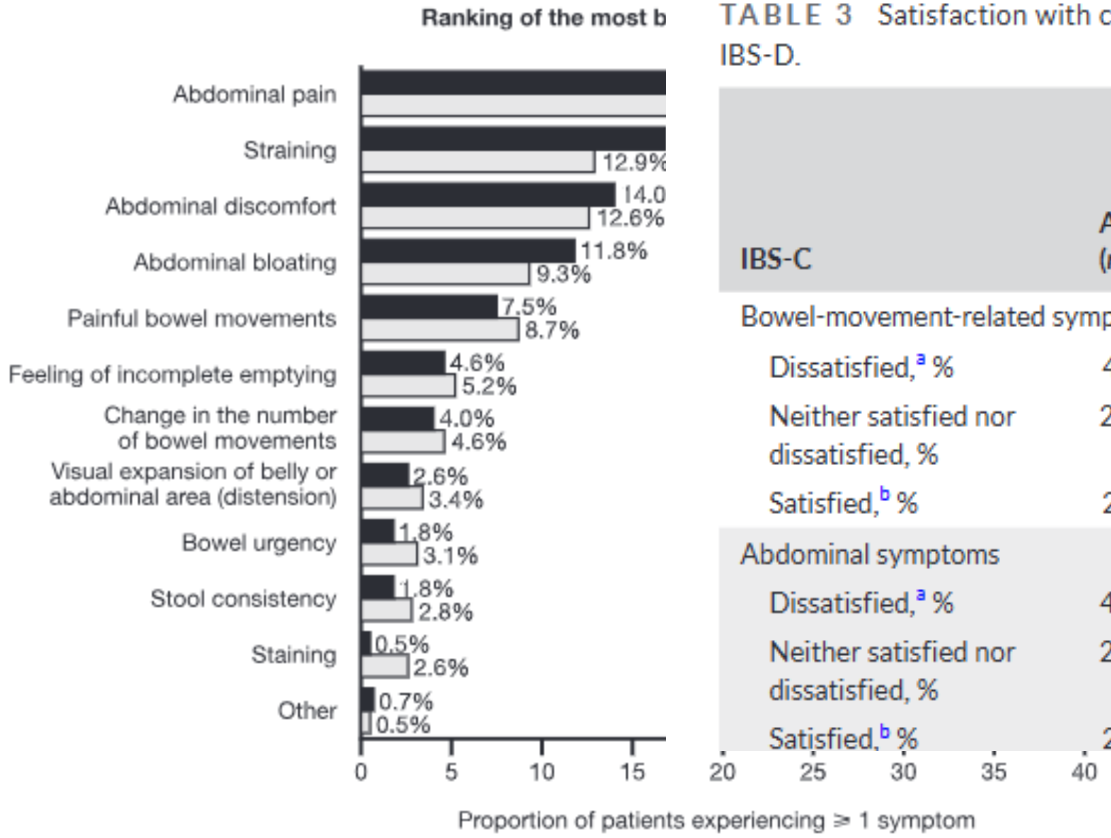

TABLE 3 Satisfaction with control of symptoms, HCP management of symptoms, and treatment to manage symptoms of IBS-C and IBS-D.

IBS-C	All respondents ($n=910$)	HCP management ($n=841$)	By type of current medication (all respondents): Prescription, with or without current OTC use ($n=249$)	By type of current medication (all respondents): OTC medication only ($n=426$)	p Value (prescription vs. OTC)
Bowel-movement-related symptoms					
Dissatisfied,[a] %	47.4	27.2	36.5	53.3	<0.001
Neither satisfied nor dissatisfied, %	25.4	27.2	20.9	24.2	
Satisfied,[b] %	27.3	42.0	42.6	22.5	
Abdominal symptoms					
Dissatisfied,[a] %	45.9	25.6	32.9	52.3	<0.001
Neither satisfied nor dissatisfied, %	26.3	29.1	20.5	26.8	
Satisfied,[b] %	27.8	40.9	46.6	20.9	

N=910 respondents with IBS-C

Lacy BE, et al. *Neurogastroenterol Motil*. 2024;36:e14903.

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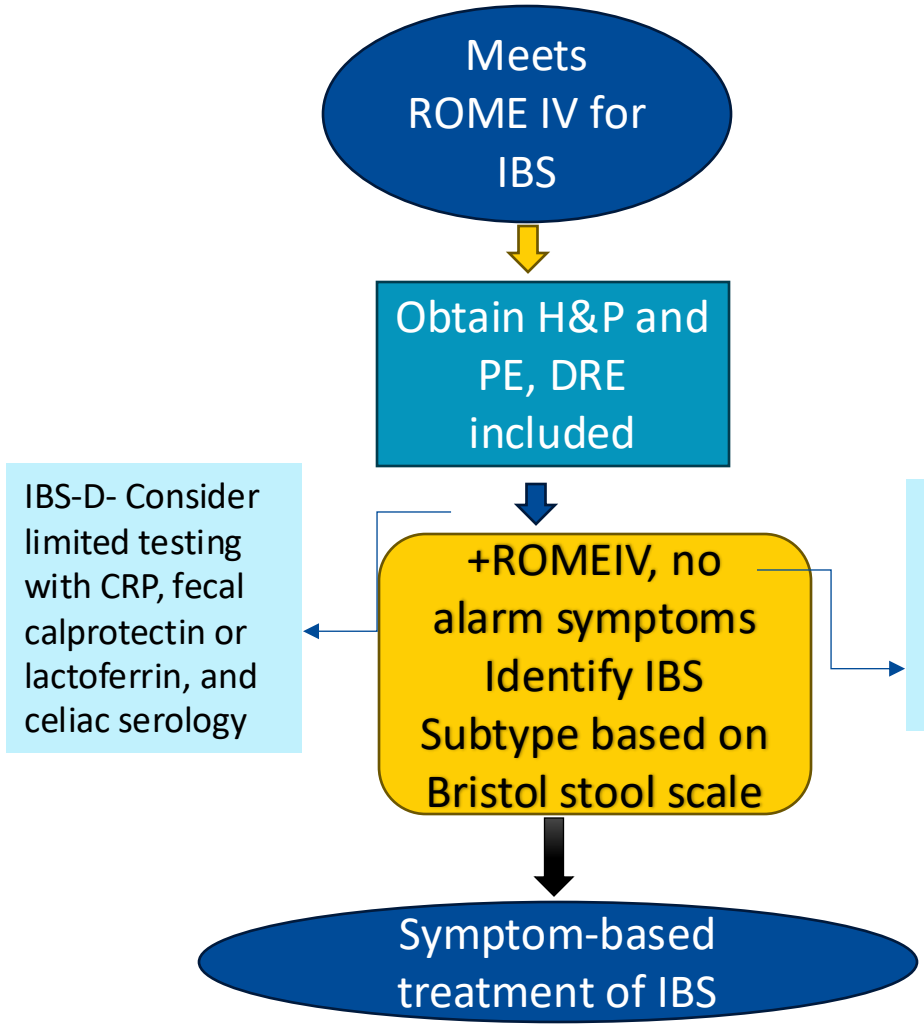
Top-Down Approach to IBS: A Treatment Sequence Based On Predominant Symptoms



Symptom	First Step treatments	Second Step– More effective
Abdominal pain	Antispasmodic, peppermint oil Gut directed therapies Yoga/exercise: NNT=6-7	Pregabalin, SNRI, TCA- NNT 4 Psychologic therapy- CBT NNT=3, hypnotherapy NNT=4
Bloating	Adjust diet: Low FODMAP NNT=4-5 Treat constipation & r/o PFD	Linaclotide, lubiprostone, plecanatide, tenapanor (if constipated) Rifaximin SNRIs, TCAs
Constipation	Fiber supplement (e.g., ispaghula-NNT=7), Polyethylene glycol NNT: 1-2	Linaclotide, lubiprostone, plecanatide, tenapanor

Pathipati M, Moshiree B, Talley NJ. Irritable bowel syndrome. In: Qayed E, Shahnavaz N, eds. Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management. 12th ed. Philadelphia, PA: Elsevier Health Sciences; 2025; Lacy BE, et al.Am J Gastroenterol. 2021;116:17-44.

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OTCs Fail to Treat the Cardinal IBS Symptoms, Says Brenner!

Therapeutic Class (OTC)	Improve Bowel Symptoms	Improve Abdominal Symptoms
Osmotic Laxatives	YES	NO
Stimulant Laxatives	YES	NO
Soluble Fiber	**YES**	**YES**
Saline (Mg) Laxatives	YES	NO
Stool Softeners	??	No
Therapeutic Class (Prescription)		
Secretagogues (plecanatide, linaclotide, lubiprostone)	**YES**	**YES**
Retainagogues (tenapanor)	**YES**	**YES**

OTC=Over the counter.

Rao SSC, Brenner DM. *Am J Gastroenterol*. 2021;116:1156-1181; Sayuk GS, et al. *Am J Gastroenterol*. 2022;117:S6-S13.

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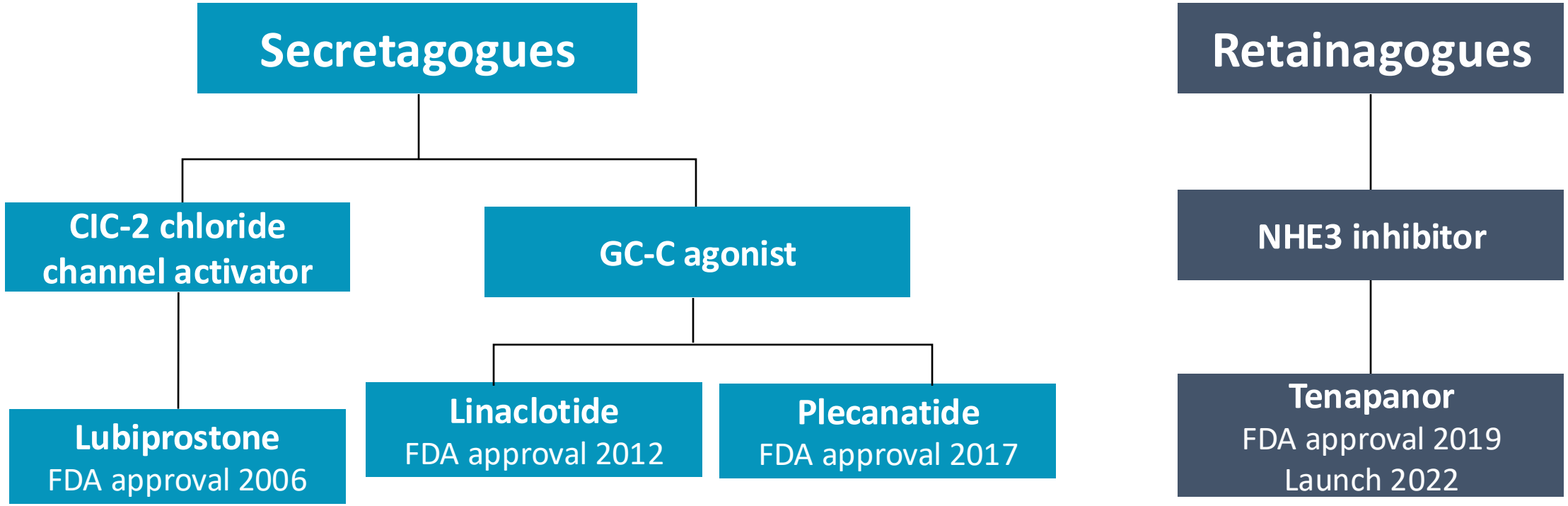
The Goal Is to "Improve Pain and Discomfort" Says Dr. Brenner While Coining the Word "Retainagogues"!



**These RCTS followed rigorous FDA Endpoints of both CSBM and abdominal pain improvement

GC=gunylate cyclase C.

Brenner DM. *Gastroenterol Hepatol (N Y)*. 2023;19:749-756.

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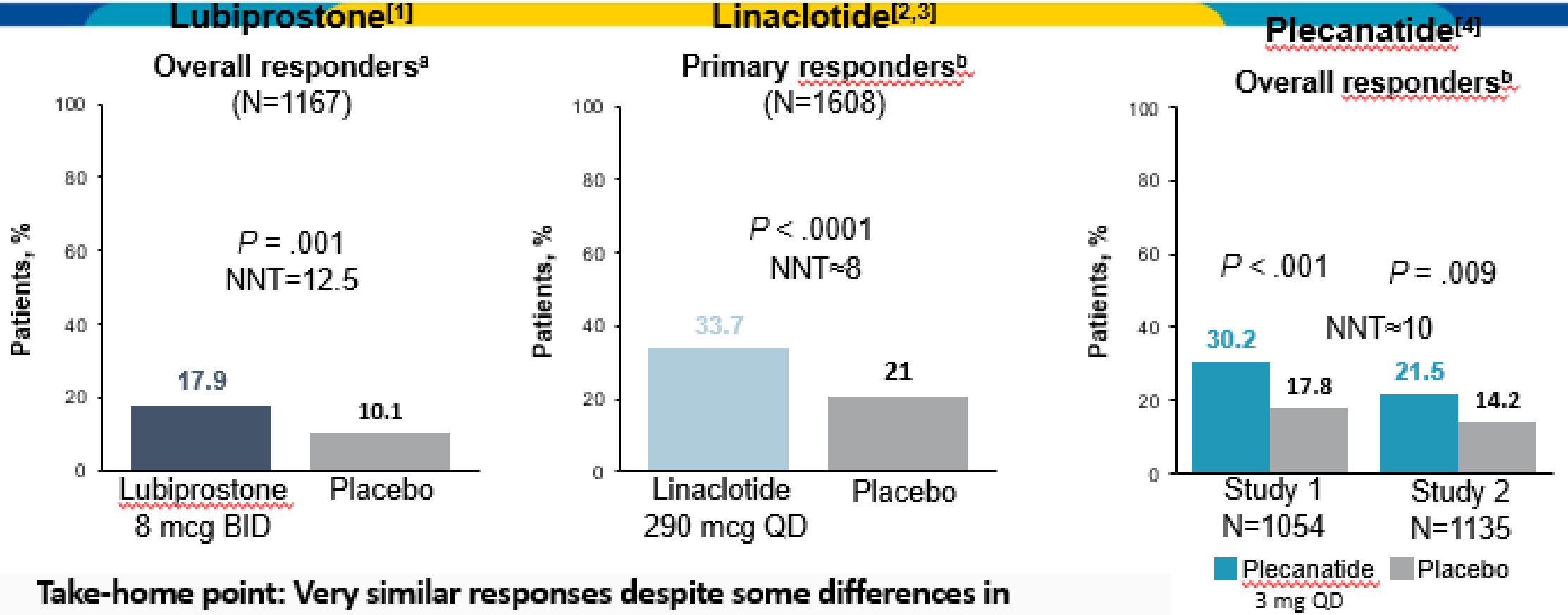
ACG Guideline for IBS Agrees on the Pain Postulate

Therapeutic	American College of Gastroenterology (ACG)
Linaclotide	Strong recommendation for use IBS-C
Plecanatide	Strong recommendation for use IBS-C
Lubiprostone	Strong recommendation for use IBS-C
Tenapanor	Not reviewed
PEG laxatives	Conditional suggestion **against** use IBS-C
TCAs	Strong recommendation for use
Peppermint Oil	Conditional suggestion for use
Antispasmodics	Conditional recommendation **against** use of those available in the USA to treat global symptoms

IBS-C=irritable bowel syndrome with constipation; PEG=polyethylene glycol; TCA=tricyclic antidepressant.

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

Secretagogues for IBS-C



Take-home point: Very similar responses despite some differences in endpoints but effective for global IBS symptoms

[a]Defined as monthly responder for ≥ 2 of 3 months. Monthly responder defined as having ≥ moderate relief for 4 of 4 weeks or significant relief for 2 of 4 weeks.

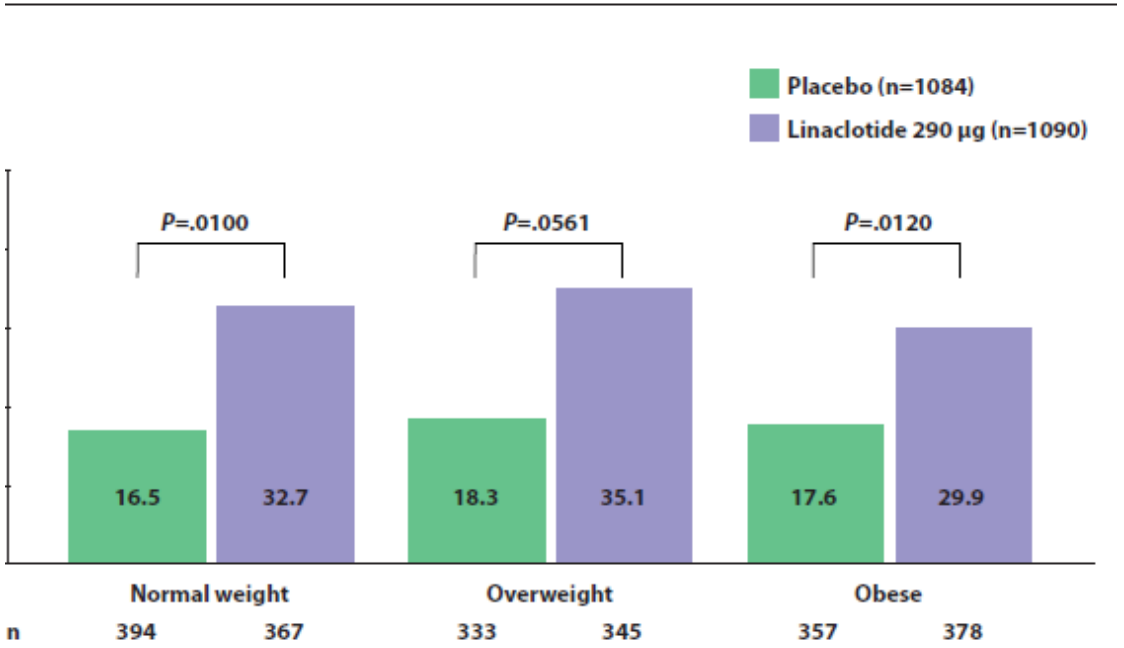
[b]Defined as ≥ 30% reduction in abdominal pain plus an increase of ≥ 1 CSBM from baseline in the same week 6 of 12 weeks.

1. Drossman DA, et al. *Aliment Pharmacol Ther*. 2009;29:329-341; 2. Chey WD, et al. *Am J Gastroenterol*. 2012;107:1702-1712; 3. Rao SSC, et al. *Am J Gastroenterol*. 2012;107:1714-1724; 4. Brenner DM, et al. *Am J Gastroenterol*. 2018;113:735-745.

Shorter Time to Respond to Linaclotide Than Placebo Across All BMIs

- Response times to CSBM across all BMIs is 1-2 weeks with Linaclotide versus with placebo where it was 4-5 weeks

- Similar abdominal pain improvement was seen across all BMIs



ions of APC+1 responders for patients with irritable bowel syndrome with constipation treated with lina
y mass index category. APC+1, abdominal pain and constipation +1. Adapted from Moshiree B, et al. A
at: American College of Gastroenterology 2024 Annual Scientific Meeting; October 25-30, 2024; Phila

Moshiree B, et al. ACG. 2024.

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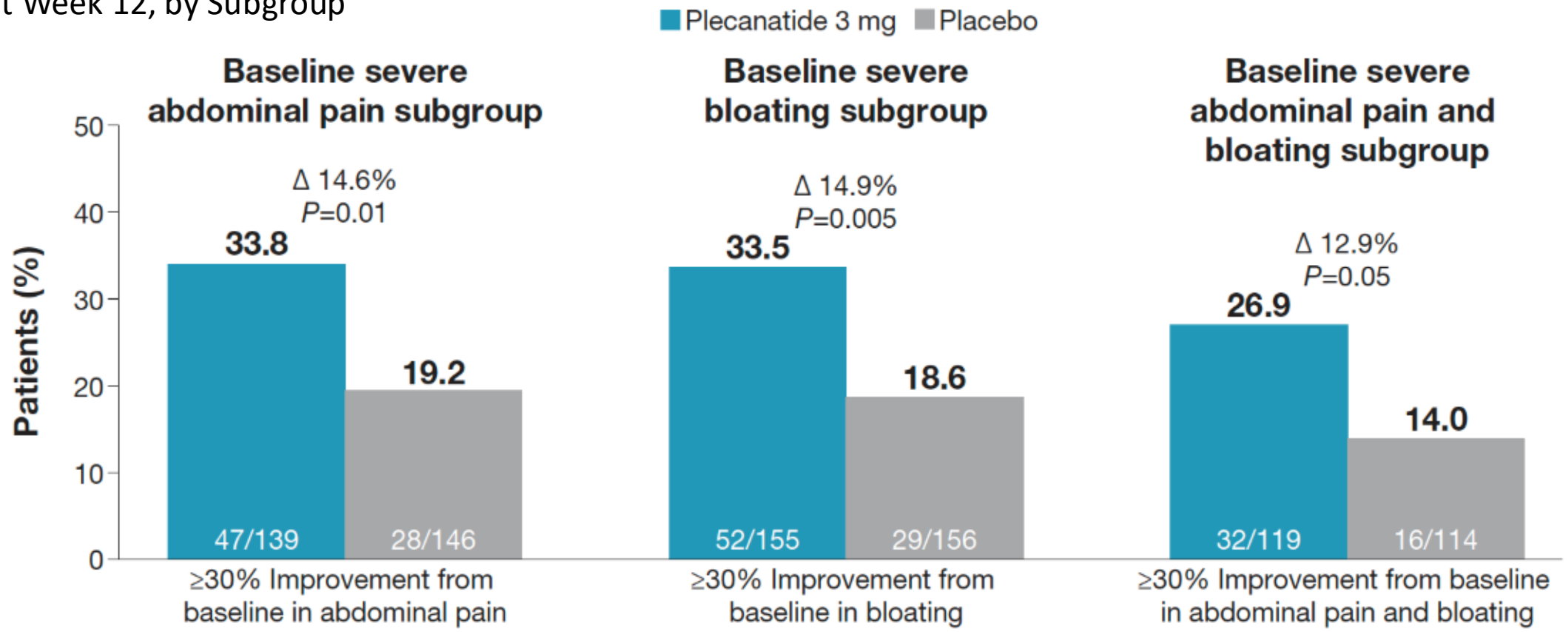
Plecanatide Effect on Severe Abdominal Pain and Severe Bloating in Individuals With IBS-C: A Pooled Analysis of 2 Phase 3 Trials

Percentage of Patients With ≥ 30% Improvement From Baseline in Severe Abdominal Pain, Bloating, or Both at Week 12, by Subgroup

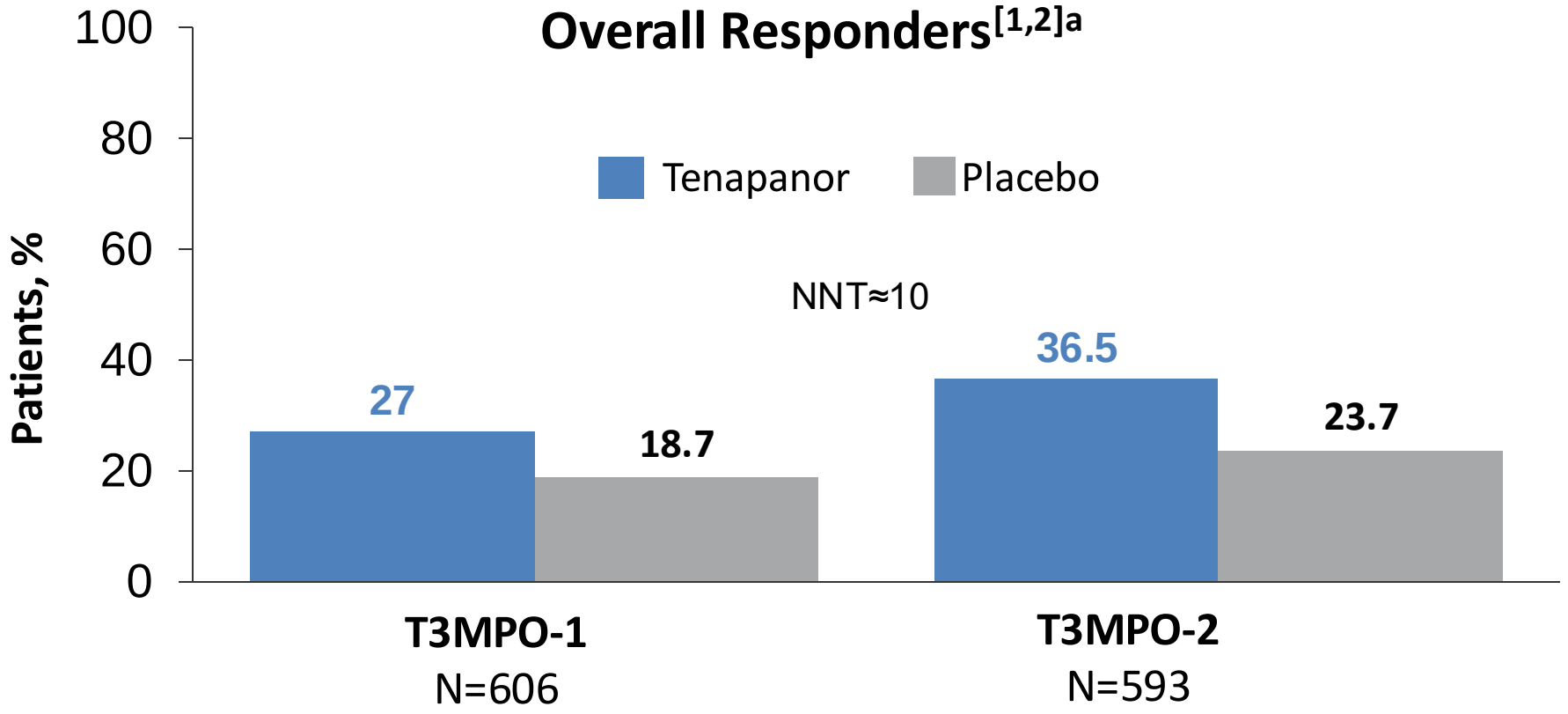


Plecanatide reduces severe abdominal symptoms in IBS-C

EBMed #EvidenceIsPower

Sayuk G, et al. ACG 2022. B0261.

Tenapanor for IBS-C Global Response

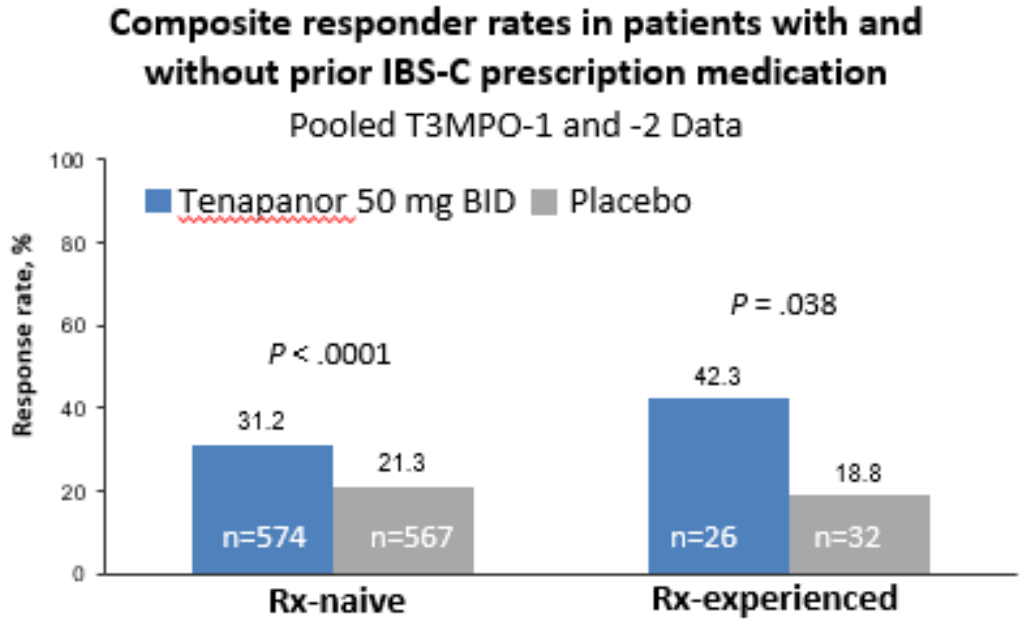


Tenapanor is effective for global IBS-C symptoms

a. Defined as ≥ 30% reduction in abdominal pain plus an increase of ≥ 1 CSBM from baseline in the same week 6/12 weeks.

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

Tenapanor Effect De Novo or After Secretagogue Failure for IBS-C (DDW 2024)



A clinically meaningful response to treatment with tenapanor among adults with IBS-C was observed regardless of prior IBS-C prescription medication use.

Reduction ≥30% in average weekly worst abdominal pain and an increase of ≥1 weekly CSBM from baseline, both in the same week, for ≥6 of the first 12 treatment weeks (6/12-week combined responder).

Reduction ≥30% in average weekly worst abdominal pain and an increase of ≥1 weekly CSBM from baseline, both in the same week, for ≥6 of the first 12 treatment weeks (6/12-week combined responder).

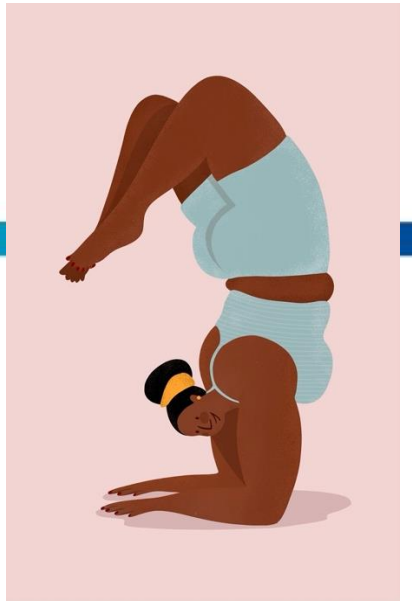
Shah E, et al. Digestive Disease Week 2024. Tu1658.

These Drugs Are Safe!

Drug	AEs in Clinical Trials
Linaclotide	▪ Diarrhea most common AE: linaclotide (16.3%) vs placebo (2.3%) ▪ Diarrhea led to discontinuations in 3.4% patients receiving linaclotide vs 0.2% receiving placebo ▪ No SAEs due to diarrhea ▪ No deaths were reported in any of the trials
Lubiprostone	▪ Similar number of patient with AEs leading to discontinuation: lubiprostone (12.8%) vs placebo (12.3%) ▪ GI-related AEs: lubiprostone (19%) vs placebo (14%)
Plecanatide	▪ Diarrhea most common AE: plecanatide (4.3%) vs placebo (1%) ▪ Diarrhea led to disconinuation in 1.2% patients receiving plecanatide (3 mg) vs 0% receiving placebo ▪ Incidence of SAEs was 0.8%, which was similar for plecanatide and placebo ▪ No SAEs due to diarrhea
Tenapanor	▪ Diarrhea most common AE: tenapanor (14.8%) vs placebo (2.3%) ▪ Diarrhea led to discontinuation in 6.6% patients receiving tenapanor vs 1.0% receiving placebo ▪ SAEs: 11 patient receiving tenapanor vs 7 patients receiving placebo ▪ No deaths occurred in the trials

Chang L et al. *Gastroenterology*. 2022 Jul;163:118-136.

Yoga and IBS: Quality of Studies Poor



Systemic review of 12 yoga studies generally showed symptom reduction and safety for patients with IBS, UC, chronic pancreatitis, and GI cancer

Studies for IBS demonstrated that yoga improved IBS symptom severity, mood-related symptoms (anxiety and/or depression), and QoL vs controls

The exact mechanisms of action of yoga in GI conditions is unknown

- Studies of light to moderate exercise, diaphragmatic breathing, and meditation have shown benefit for various GI conditions

Reduction in stress, positively altering the microbiota-brain-gut-axis and autonomic nervous system

- Biogravitational explanation

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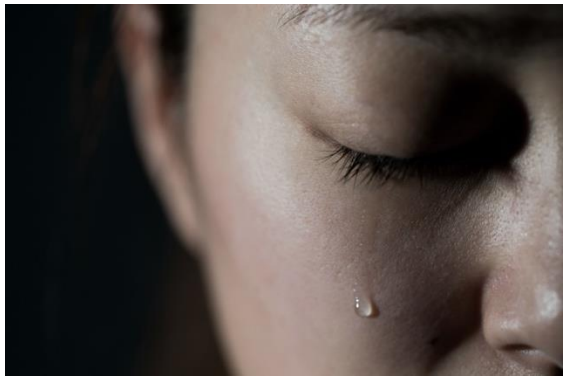
Thakur ER, et al. *Neurogastroenterol Motil*. 2024:e14915.

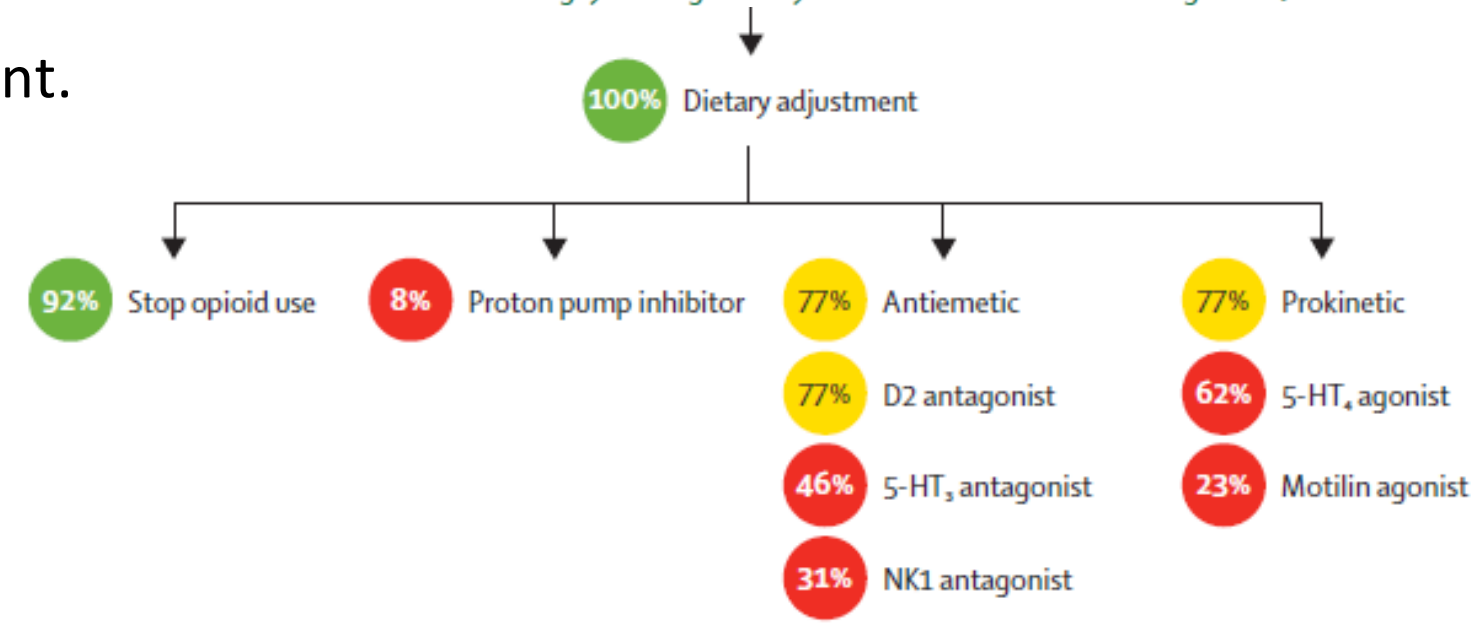
IBS-Don’t Be Like Gastroparesis Guidelines

Rome Foundation and international neurogastroenterology and motility societies’ consensus on idiopathic gastroparesis

Jolien Schol, I-Hsuan Huang, Florencia Carbone, Luis Maria Bustos Fernandez, Guillaume Gourcerol, Vincent Ho, Geoffrey Kohn, Brian E Lacy, Aurelio Lopez Colombo, Hiroto Miwa, Baha Moshiree, Linda Nguyen, Greg O’Grady, Kewin T H Siah, Vincenzo Stanghellini, Jan Tack

Only diet gets agreement.
Nothing else!





Schol J, et al; Moshiree B. *Lancet Gastroenterol Hepatol*. 2025;10:68-81.

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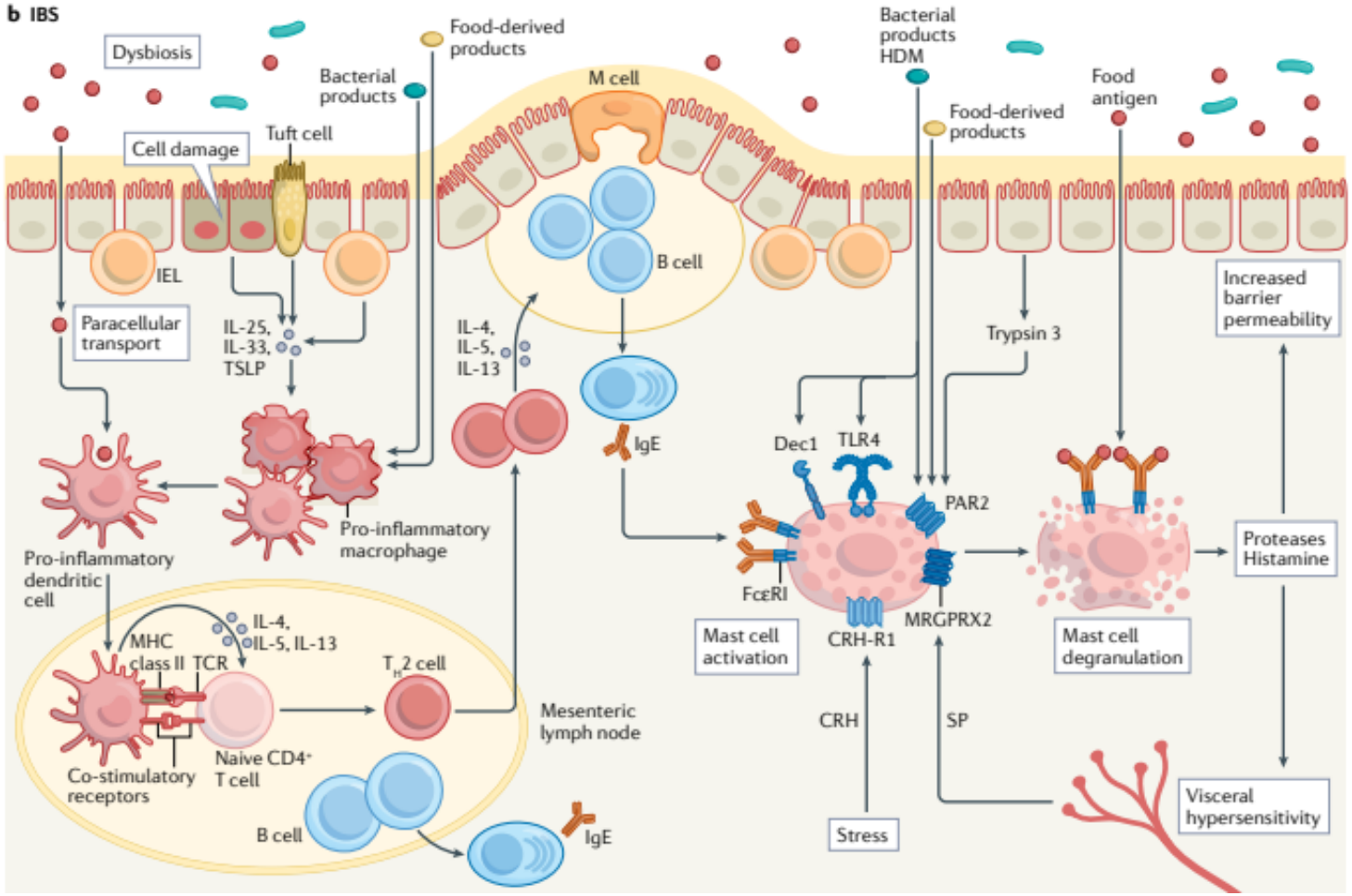
Immune Activation in IBS is Similar to IBD

Be like IBD

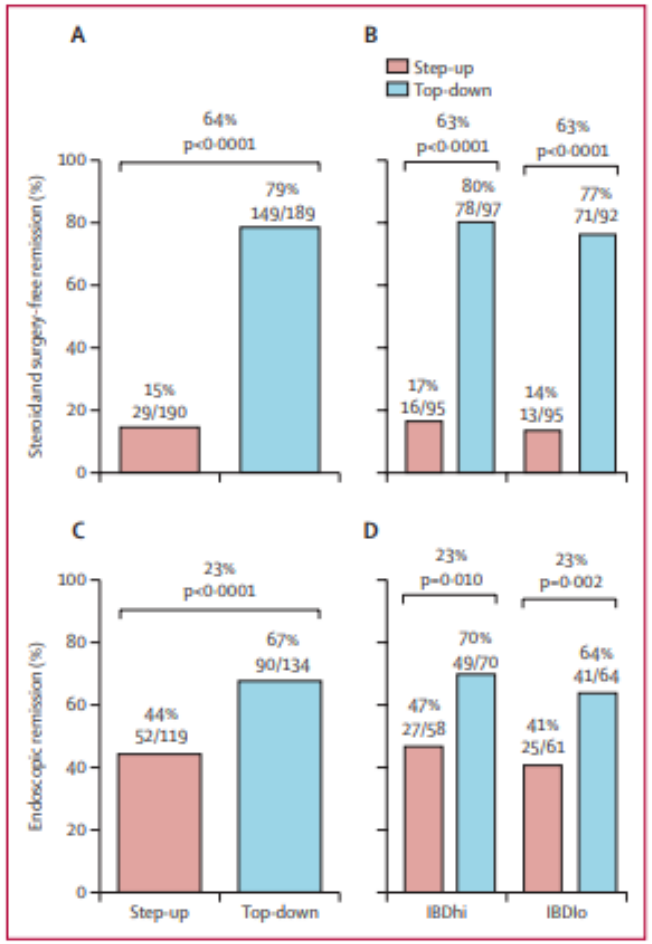


Aguilera-Lizarraga J, et al. *Nat Rev Immunol*. 2022;22:674-686.

Profile Trial: Top-Down Treatment Works Better for CD

Trial visit	Accelerated step-up	Top-down
Week -2 (screening)	Start steroid induction for active Crohn's disease	Start steroid induction for active Crohn's disease
Week 0 (randomisation)	Following randomisation, continue steroid taper	Following randomisation, start infliximab and immunomodulator, and continue steroid taper
Week 4, 16, 32, 48 (after randomisation)	If in remission, continue on current step of treatment If flare 1, start steroids and immunomodulator If flare 2, start infliximab alongside immunomodulator	If in remission, continue infliximab and immunomodulator If flare 1, additional course of steroid medication If flare 2, consider non-response and trial withdrawal

- Top-down treatment with **combination infliximab and immunomodulator** was significantly better than accelerated step-up (conventional) treatment for both maintaining steroid-free and surgery-free remission (48 weeks follow-up).
- Top-down treatment showed **greater efficacy** in achieving endoscopic remission, improved QOL, and reduced number of flares requiring treatment escalation.
- Top-down treatment **was safer** than accelerated step-up treatment, with fewer adverse and serious adverse events, no increased rate of infection, and reduced need for urgent abdominal surgery.
- There was no biomarker treatment interaction effect noted.



Steroid-Free remission

Endoscopic remission

Noor NM, et al. *Lancet Gastroenterol Hepatol*. 2024;9:415-427.

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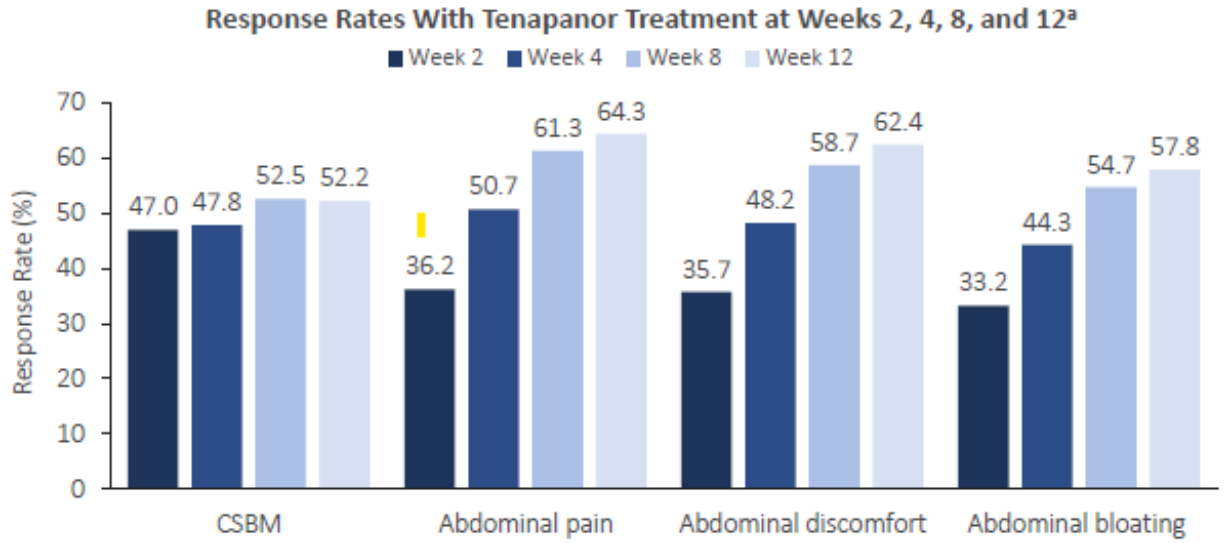
Stick With the Treatment: Treatment Success of IBS-C Symptoms Increases With Duration of Therapy

- Pooled data of 3 studies within first 12 weeks of therapy analyzed.
- Aim: Time to first CSBM response (increase ≥1 from BL in average weekly CSBMs
- Time to first abdominal pain, bloating and discomfort improvement (decrease of ≥30% from baseline in average weekly score of abdominal symptom)
- Findings: Weekly response rates increase with longer treatment duration: 52.2% of patients have CSBM response and 57.8-64. achieve abdominal symptom response at 1 weeks.
- Calculated median time to first response
  - 2 weeks for CSBM response
  - 4 weeks for abdominal pain response, discomfort and bloating

Weekly Rate for Complete Spontaneous Bowel Movement Response and Abdominal Pain, Bloating, and Discomfort Response



ctober 20-25, Vancouver, Canada

ªCSBM response was defined as achieving an increase of ≥1 in average weekly CSBMs from baseline and abdominal pain, bloating, and discomfort response was defined as achieving a decrease of 30% or more in average weekly abdominal score from baseline.
CSBM, complete spontaneous bowel movement.

Lacy B, et al. ACG 2023.

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Payer Versus Patient Perspective

- All treatments were cost-saving compared to leaving IBS-C untreated.
- Linaclotide was the most cost-saving IBS-C intervention to a patient at $2982 over 1 year, compared to no treatment.
- SSRI, low FODMAP, or CBT were less cost saving to patients overall ($2529.21 to $2794.70/year) than linaclotide therapy, but were more cost-saving than plecanatide ($2193.99/year) or lubiprostone ($1208.96/year), referenced against no treatment for IBS-C.

Cost

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lth

Health Gain →

Health Gain improved

Shah ED, et al. *MDM Policy Pract*. 2021;6:2381468320978417.

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Conclusion and EBM Why Fruits and Fiber Are Not Always the Answer

- We presented evidence here!!
- Pharmacologic agents target the pathophysiology of IBS
- A top-down approach works better and achieves symptom response faster across all symptoms of IBS!
- Its also less costly and patient and practitioner-centered

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COI Again: Brenner Owns a N
Supplement Kitchen!

FOLLOW THE $$$$

Directions to the Brenner FIT Kitchen

Address:

William G. White Jr. Family YMCA
775 West End Blvd., Winston-Salem

Kitchen is located inside the YMCA.

Parking:

Park right outside the kitchen if spaces are available. The parking lot is accessed from *N. Sunset Drive*, on the Hanes Park side of the YMCA.

Questions & Answers

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EBMed's Great GI Debates: Thank You!

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