Women's Health 2024 | Beyond the Annual Visit

Irritable Bowel Syndrome:
Clarifying the Vagaries and Improving Patient Care in Women

Faculty

Brooks D. Cash, MD, AGAF, FACG, FACP, FASGE, Rome Foundation Fellow

Dan and Lillie Sterling Professor of Medicine
McGovern Medical School
Chief, Division of Gastroenterology, Hepatology, and Nutrition University of Texas Health Science Center
Houston, Texas

Kavita R. Kongara, MD, FACG, FACP

Motility Clinical Chair, United Digestive
Georgia Physician Executive Committee Member, United Digestive
Physician, Atlanta Gastroenterology Associates
Atlanta, Georgia

Disclosure Slide

Brooks D. Cash, MD, AGAF, FACG, FACP, FASGE, Rome Foundation Fellow

Speaker's Bureau: AbbVie, Alnylam, Ardelyx, AstraZeneca, Phathom, Salix

Research support: Napo

Consultant: AbbVie, Ardelyx, AstraZeneca, Phathom

Kavita Kongara, MD, FACG, FACP

Speaker's Bureau: AbbVie, Ardelyx, Phathom, Salix

Consultant: Sitzmarks

Learning Objectives

- Use information from patient history, physical examination, and test results to differentiate between IBS-C and IBS-D
- Demonstrate confidence in your ability to make a diagnosis of IBS
- Make an evidence-based treatment recommendation for a patient diagnosed with IBS-C
- Make an individualized, evidence-based treatment recommendation for a patient diagnosed with IBS-D

Rome IV: Diagnostic Criteria for IBS

Recurrent abdominal pain on average at least 1 day/week in the past 3 months associated with at least 2 of the following criteria*

- Related to defecation
- Associated with a change in frequency of stool
- Associated with a change in form of stool

*Criteria fulfilled for the past 3 months with symptom onset at least 6 months before diagnosis.
Lacy BE, et al. *Gastroenterology*. 2016;150(6):1393-1407.e5.

Epidemiology and Costs of IBS

- Estimated prevalence in the United States: 7% to 16%[1]
  - 35 million Americans impacted[2]
- More prevalent in women and people under 50 years of age[1,3]
- Direct medical costs exceed $1 billion[1]

IBS, Irritable bowel syndrome.

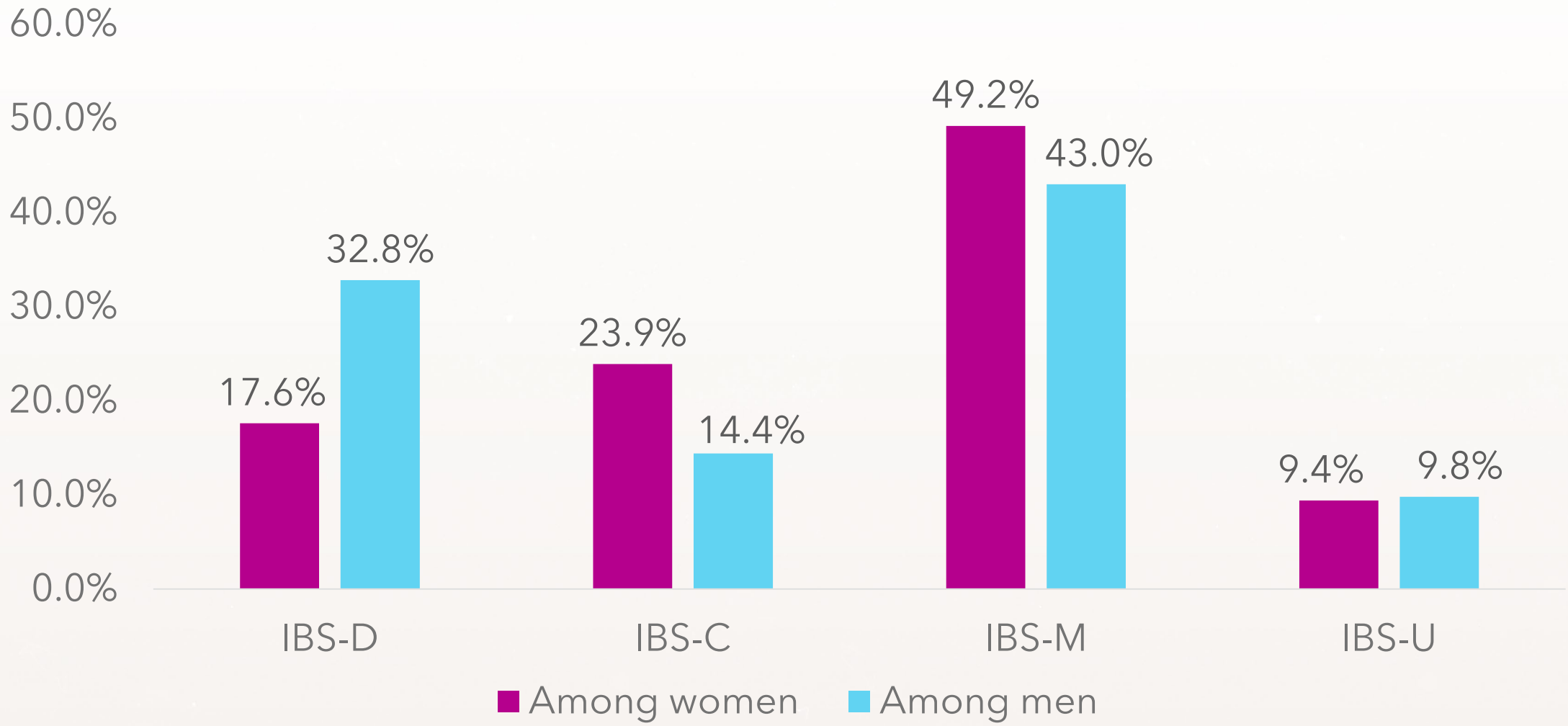
1. Camilleri M. *JAMA*. 2021; 325(9):865-877. 2. American Gastroenterological Association. IBS in America: Survey Summary Findings. 2015. Accessed August 30, 2022. https://www.multivu.com/players/English/7634451-aga-ibs-in-america-survey/docs/survey-findings-pdf-635473172.pdf. 3. Lacy BE, et al. *Gastroenterology*. 2016;150(6):1393-1407.e5.

The Symptom Burden of IBS Is Substantial

- Impaired health status restricts an average of 73 days of activity per year[1]
- Up to 38% of patients report having contemplated suicide as a result of their symptoms[2]
- Average of 1.5 missed days of school/work and 8 days of lost productivity every month[2]

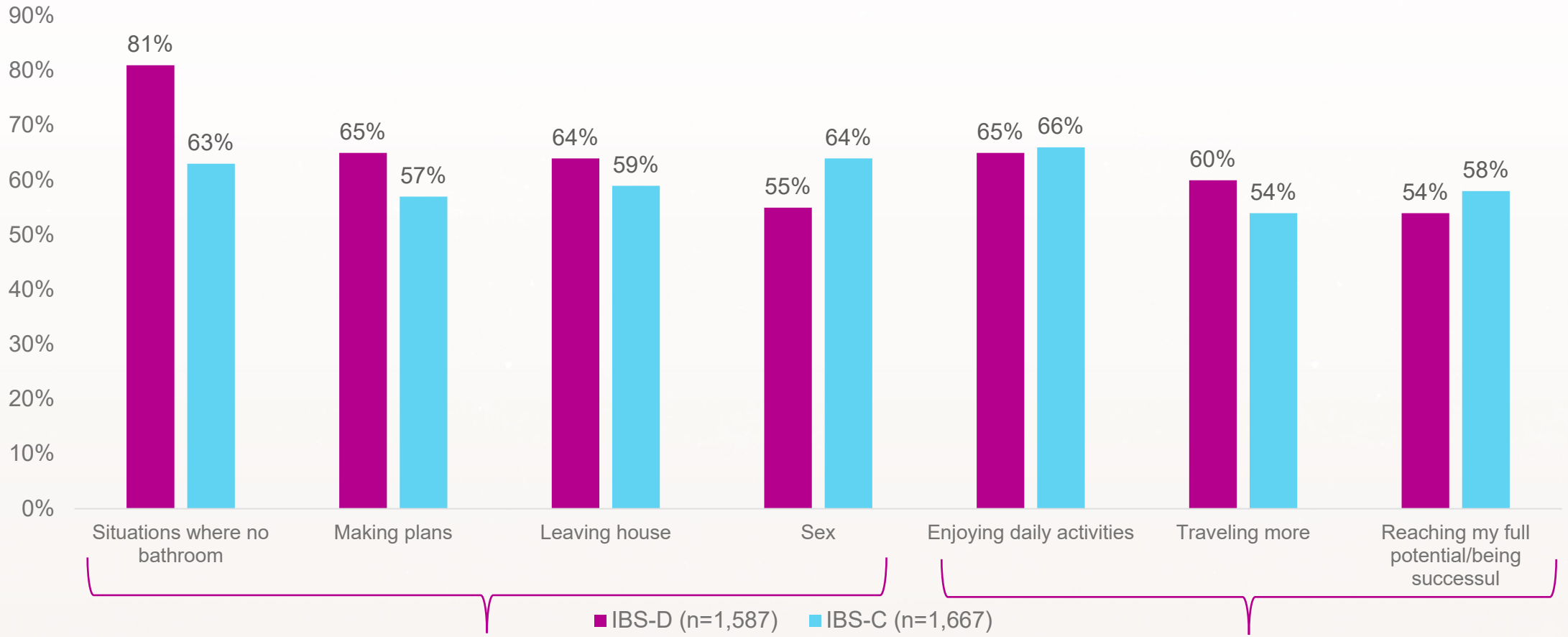
1. Drossman DA, et al. *J Clin Gastroenterol.* 2009;43(6):541-550.
2. Ballou S, et al. *Clin Gastroenterol Hepatol*. 2019;17(12):2471-2478.e3.

IBS Subtype Distribution by Sex



Johansen SG, Ness-Jensen E. *Scand J Gastroenterol*. 2022;4:1-7.

IBS Interferes With Activities and Self-Perception



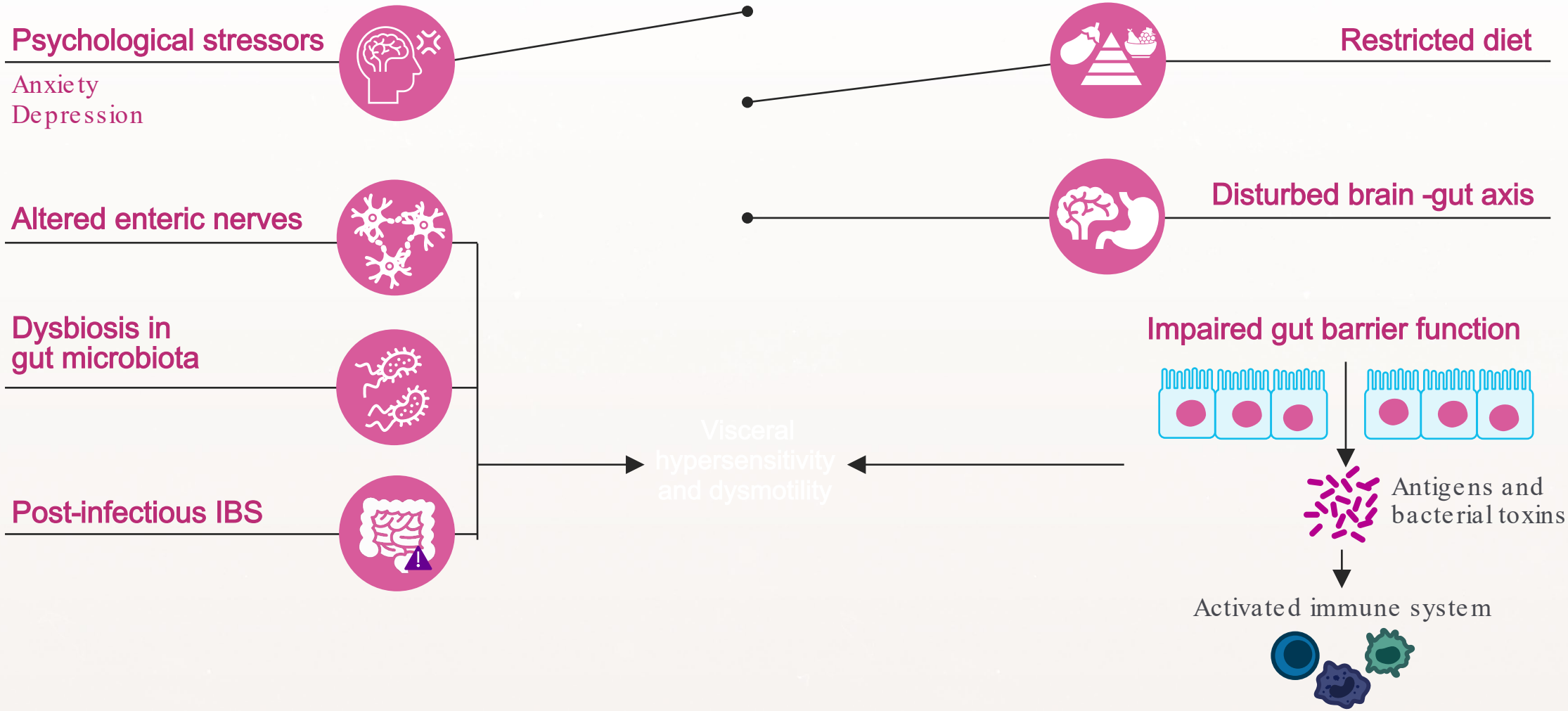
Because of symptoms, I have avoided:

My symptoms prevent me from:

Over 50% said their symptoms make them feel not normal, not like themselves, or self-conscious.

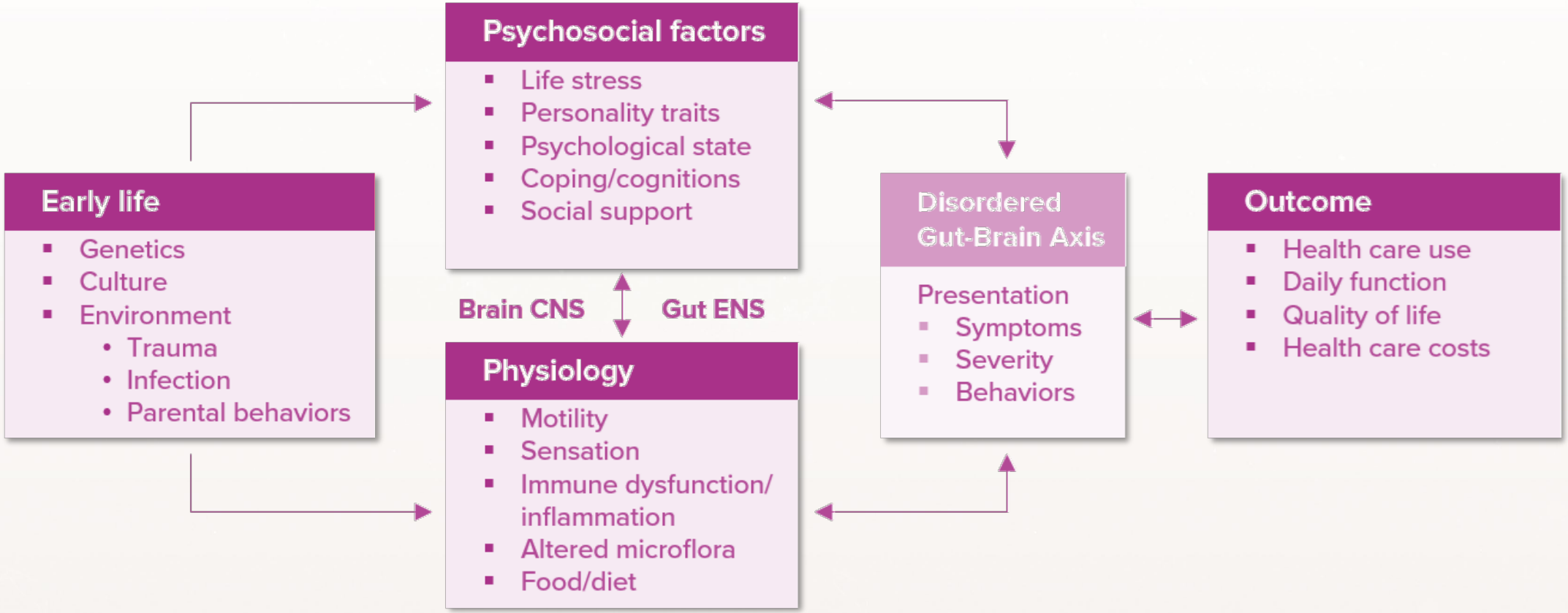
Ballou S, et al. *Clin Gastroenterol Hepatol*. 2019;17(12):2471-2478.e3.

The Complex Pathophysiology of IBS



Spiller R, Major G. *Nat Rev Gastroenterol Hepatol*. 2016;13(10):613-621.

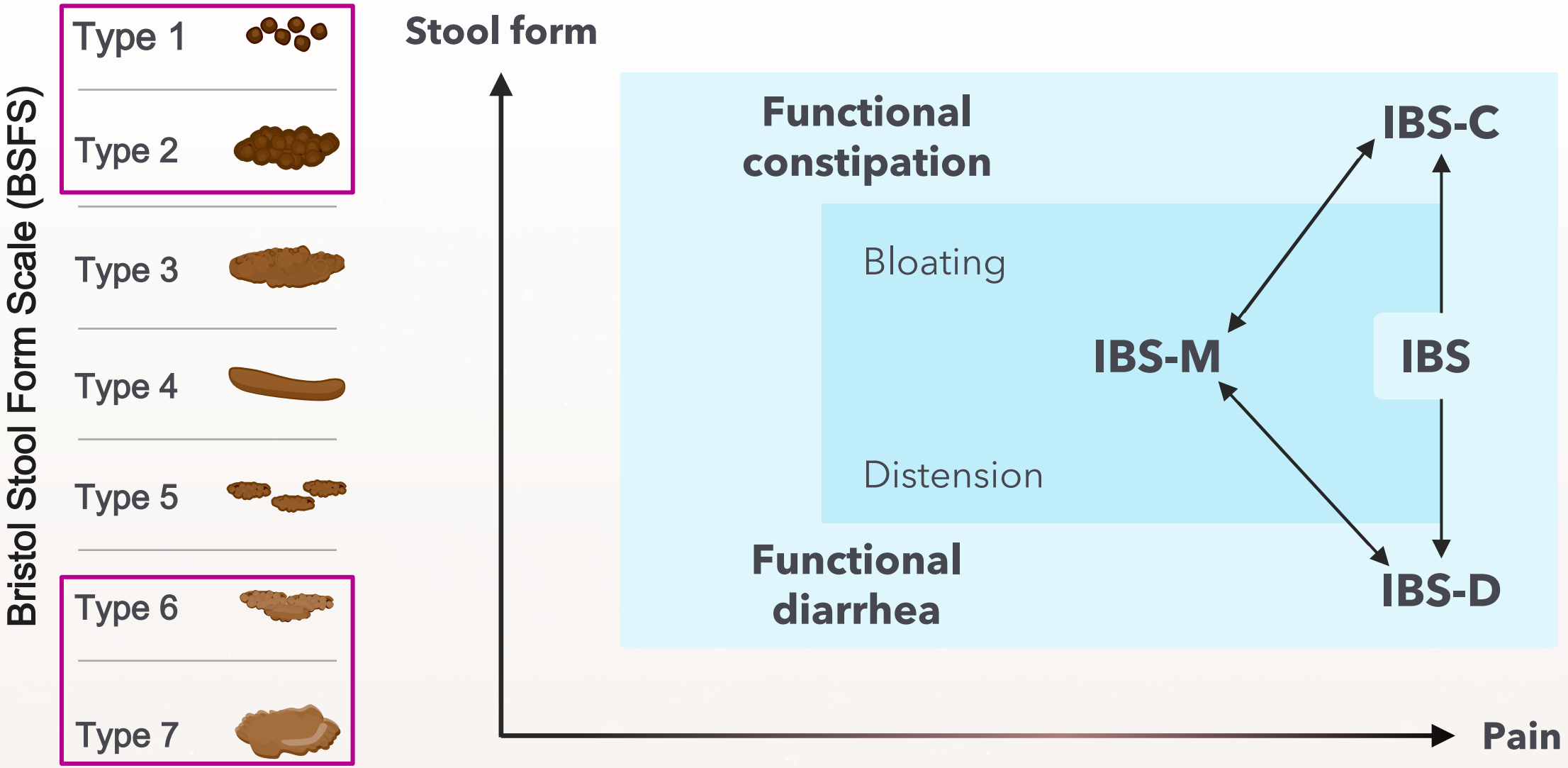
The IBS Journey: A Biopsychosocial Conceptual Model



CNS, central nervous system; ENS, enteric nervous system.

Drossman DA. *Gastroenterology*. 2016;150(6):1262-1279.e2. doi:10.1053/j.gastro.2016.02.032

The Continuum of Functional Bowel Disorders



IBS-D, irritable bowel syndrome with diarrhea; IBS-M, irritable bowel syndrome, mixed bowel pattern.
Lacy BE, et al. *Gastroenterology*. 2016;150(6):1393-1407.e5.

History and Physical Examination for Lower GI Symptoms

History

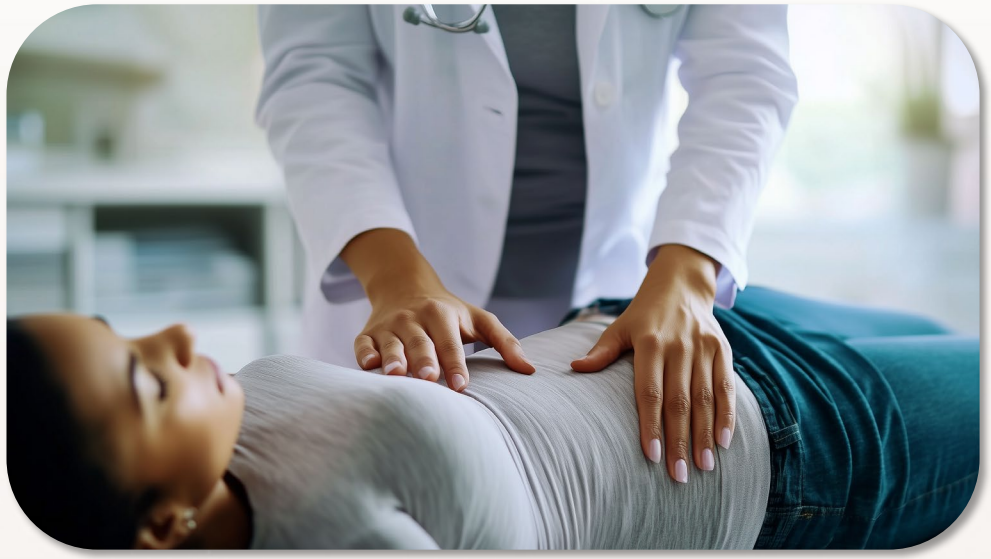
- Presenting symptoms and timeline
- Potential triggers (eg, infection, stress)
- Alarm signs
- Family history of organic GI disorders
- Diet
- Medications

Comorbid conditions

- Fibromyalgia
- Interstitial cystitis
- Migraine headaches
- Chronic pain syndrome

Examination

- Signs of systemic and local diseases that might cause constipation
- Assess the anorectum and pelvic floor muscles
- Other relevant abnormalities



IBS-D, irritable bowel syndrome with diarrhea; IBS-M, irritable bowel syndrome, mixed bowel pattern.

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

Appropriate Diagnostic Tests by IBS Subtype

For All Patients With Suspected IBS: CBC and Age-Appropriate CRC Screening

IBS-M[1]

- **CRP; fecal calprotectin**
- **tTG-IgA ± serum IgA**
- Stool diary
- Consider plain-film radiography to evaluate stool retention

IBS-D[2]

- **CRP; fecal calprotectin**
- **tTG-IgA ± serum IgA**
- *Giardia* antigen assay
- Fecal bile acid testing (total bile acids in stool or FGF19, if available)

IBS-C[1]

- **No special testing**
- If severe or medically refractory, refer to gastroenterology for physiologic testing

CRP, C-reactive protein; FGF19, fibroblast growth factor-19; tTG-IgA, tissue transglutaminase immunoglobin A.

1. Chey WD, et al. *JAMA*. 2015;313(9):949-958. 2. Smalley W, et al. *Gastroenterology*. 2019;157(3):851-854.

Women's Health 2024 | Beyond the Annual Visit

Evidence-Based Management of IBS-C

Case 1: Jessica Let's Review

25-year-old woman with persistent constipation, abdominal pain, and bloating over past 4+ years

Tests performed: CBC, TSH, T4

Diagnosis IBS-C

Current Status

- Tried diet, exercise, fluids, and lifestyle changes
- Used OTC laxatives with little impact (fiber; PEG)
- Still complains of abdominal pain and bloating
- Denies rectal bleeding
- Physical exam WNL
- Digital rectal exam normal

General Principles of IBS Management

Exclude organic GI disease

Make a positive diagnosis

Establish a rapport with the patient; educate and reassure

Categorize IBS subtype based on prevalent stool form (Bristol Stool Form Scale)

First-line treatments: lifestyle and dietary modifications, OTC therapies targeting abnormal stool form and most bothersome symptoms

Escalate to FDA-approved prescription therapies as needed

Consider off-label and/or psychological therapies as needed

OTC, over-the-counter.

IBS-C Treatment Approaches

Physical activity [1]

Simple recommendation is for patients to take a 20-minute walk (roughly 1 mile) each day

Constipating medications [2]

Whenever possible, medications that impair GI transit should be stopped

Diet and fiber intake [3,4]

Address food sensitivities and improve fiber intake; if using a fiber supplement, psyllium (soluble fiber) is recommended because bran fiber may worsen symptoms

Over-the-counter laxatives/prescription medications [4]

May include osmotic or stimulant laxatives, prosecretory agents, and centrally acting interventions (eg, antidepressants) as appropriate for each individual patient

1. Chey WD, et al. *JAMA*. 2015;313(9):949-958.
2. Lacy BE, et al. *Gastroenterology*. 2016;150(6):1393-1407.e5.
3. Patel A, et al. *Aliment Pharmacol Ther*. 2016;44(3):246-258.
4. Ford AC, et al. *Am J Gastroenterol*. 2018;113(Suppl 2):1-18.

Overview of OTC Treatments for IBS-C

Psyllium Fiber (Soluble)

- Modest benefits for global IBS symptoms
- Strongly recommended by the ACG for overall symptom improvement
- Low cost, lack of significant side effects, and other health benefits make psyllium a reasonable first-line therapy

Osmotic Laxatives

- Example: PEG
- Improves stool frequency and consistency but does not reliably improve abdominal pain or bloating
- ACG gives PEG a weak recommendation ***against*** use for overall symptom improvement in IBS

Stimulant Laxatives

- Examples: senna, cascara sagrada, castor oil, bisacodyl
- ACG makes no recommendations regarding stimulant laxatives
- No randomized controlled trials appear to have been conducted in IBS-C

ACG, American College of Gastroenterology; PEG, polyethylene glycol.

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

FDA-Approved Rx Medications for IBS-C and Chronic Idiopathic Constipation

Agent	Mechanism of Action	Approved Indications	Common AEs
Lubiprostone	Type 2 chloride channel activator	IBS-C, CIC, OIC	Nausea, diarrhea, abdominal pain
Linaclotide	Guanylate cyclase-C receptor agonist	IBS-C, CIC	Diarrhea, abdominal pain, flatulence, abdominal distention
Plecanatide	Guanylate cyclase-C receptor agonist	IBS-C, CIC	Diarrhea
Prucalopride	Highly selective 5-HT_4 receptor agonist	CIC	Abdominal pain, diarrhea, headache, flatulence, fatigue, dizziness, vomiting
Tenapanor	Inhibitor of NHE3	IBS-C	Diarrhea, abdominal distention, flatulence, dizziness

Lubiprostone in IBS-C

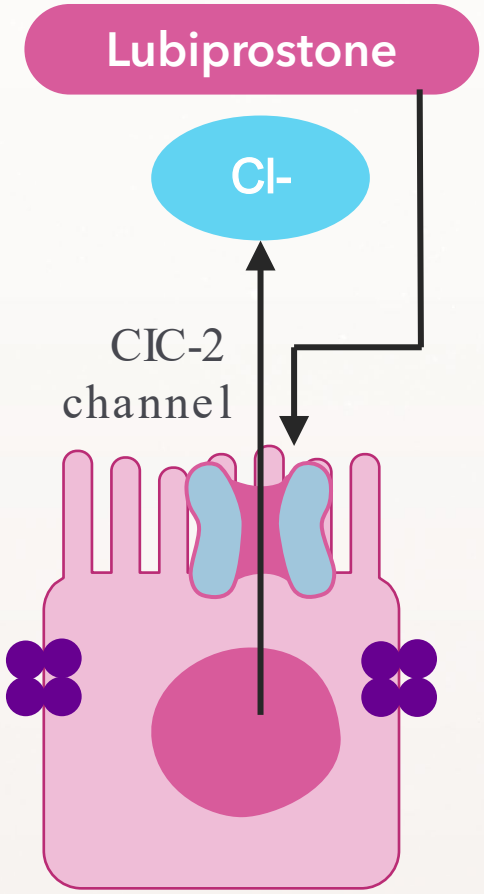
Indications:

- IBS-C: women ≥ 18 years of age
- CIC: adults
- OIC: adults with chronic noncancer pain

Dosing:

- IBS-C: 8 µg twice daily
- CIC and OIC: 24 µg twice daily
- Take with food and water

Mechanism of Action

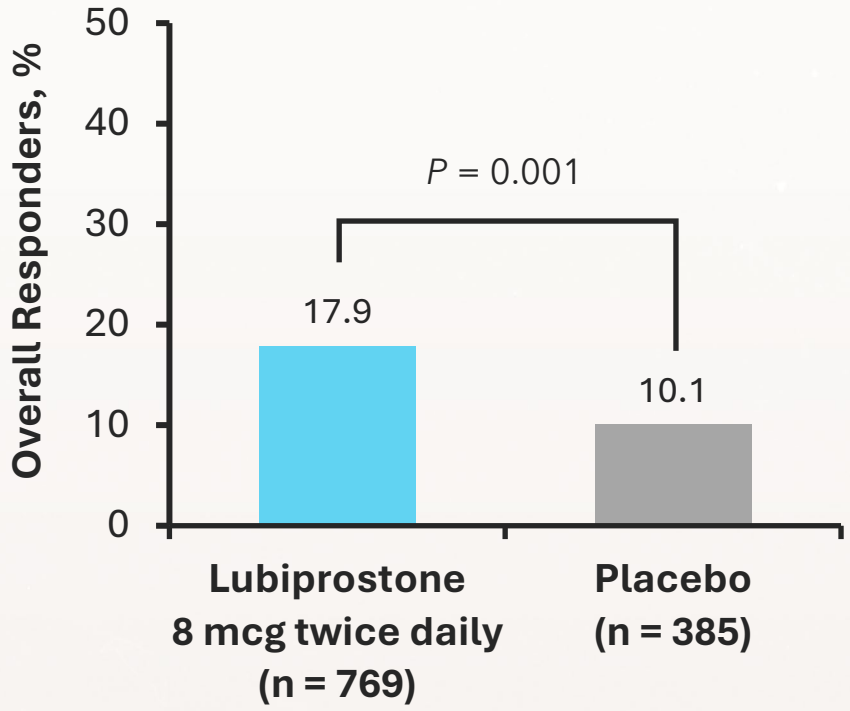


Lubiprostone [PI]. Approved 2006. Revised March 2018.

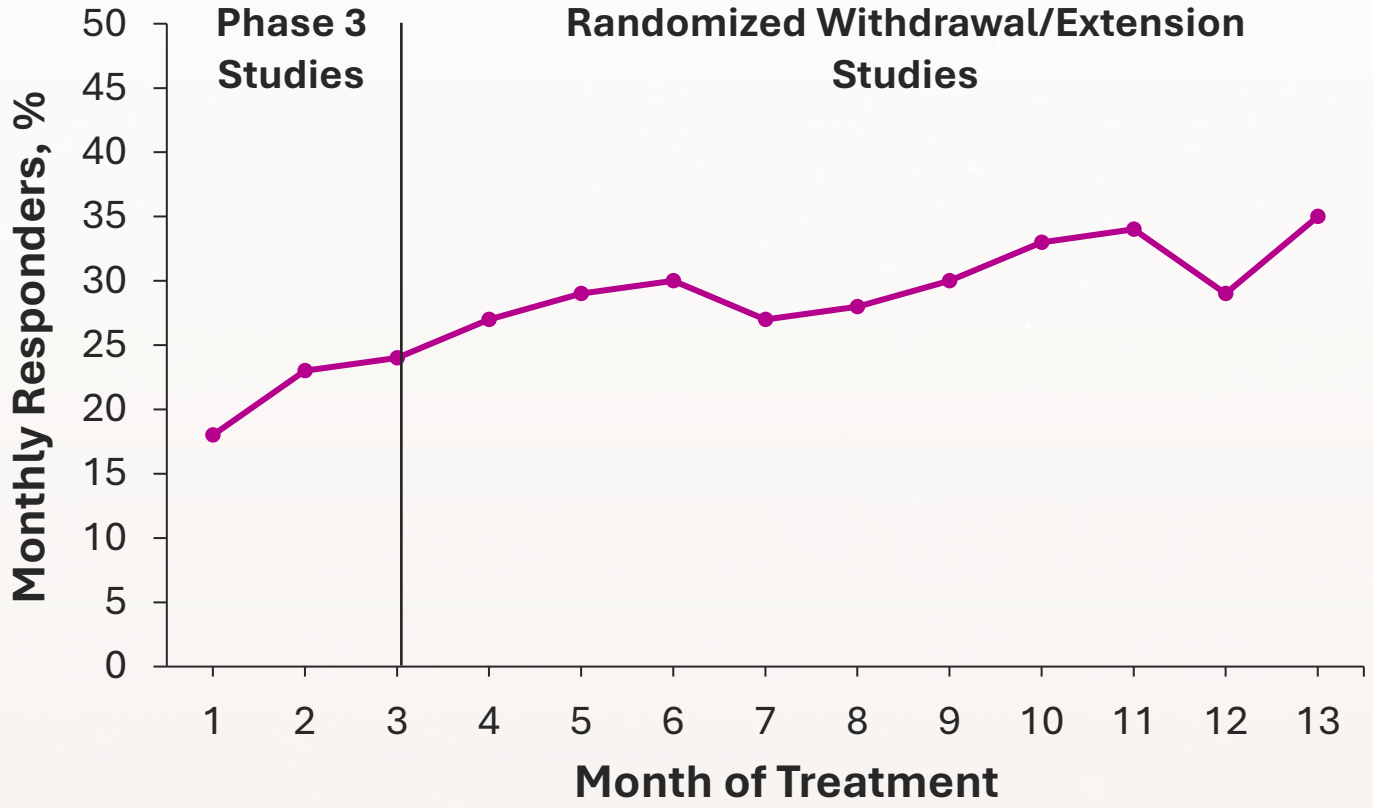
Lubiprostone in IBS-C

Results From Phase 3 Trials and Extension Study

Overall Responders at 12 Weeks in Phase 3 Trials[1,*]



Monthly Responder Rates in Randomized Withdrawal/Extension Studies[2]



Women's Health 2024 | *Beyond the Annual Visit*

***Defined as monthly responder for ≥ 2 of 3 months. Monthly responder defined as having at least moderate relief for 4 of 4 weeks or significant relief for 2 of 4 weeks.**

1. Drossman DA, et al. *Aliment Pharmacol Ther*. 2009;29(3):329-341. 2. Chey WD, et al. *Aliment Pharmacol Ther*. 2012;35(5):587-599. Lubiprostone [PI]. Approved 2006. Revised March 2018.

Lubiprostone in IBS-C

Most Common Reported AEs in IBS-C and CIC Trials*

	IBS-C		CIC	
AE	Placebo (n = 435)	Lubiprostone 8 µg twice daily (n = 1011)	Placebo (n = 316)	Lubiprostone 24 µg twice daily (n = 1113)
Nausea	4	8	3	29
Diarrhea	4	7	1	12
Abdominal pain	5	5	3	8
Abdominal distention	2	3	2	6

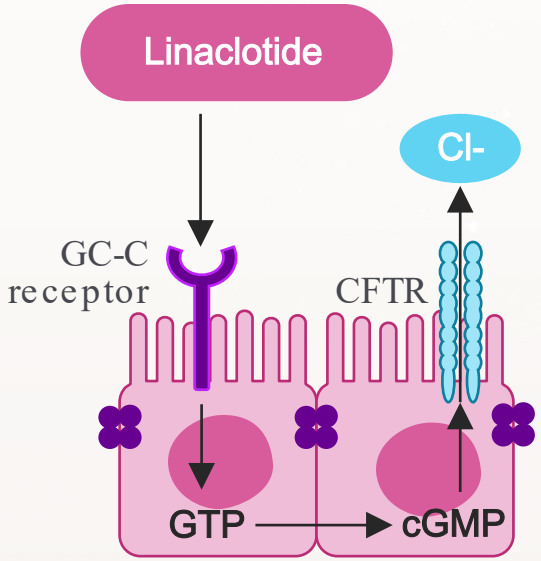
*Includes only those AEs associated with treatment (possibly or probably related, as assessed by investigator). CIC, chronic idiopathic constipation; OIC, opioid-induced constipation. Lubiprostone [PI]. Approved 2006. Revised March 2018.

Linaclotide in IBS-C

Indications and Dosing:

- Adults ≥ 18 years of age
  - IBS-C: 290 mcg/day
  - CIC: 145 mcg or 72 mcg/day
- Ages 6-17: 72 mcg/day for functional constipation
- Take on empty stomach at least 30 minutes before first meal of day
- Contraindicated in patients aged under 2 years

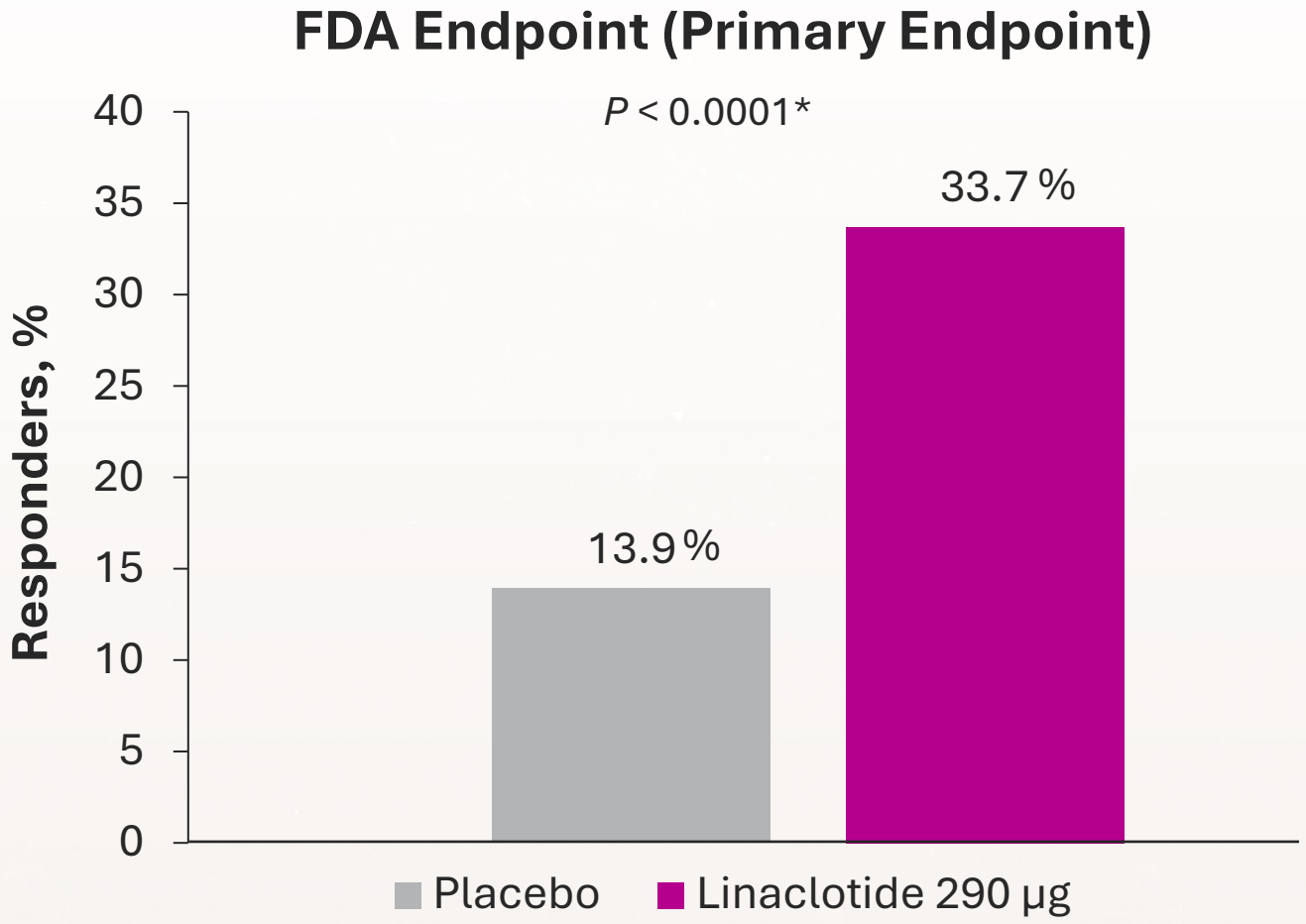
Mechanism of Action



Linaclotide [PI]. Approved 2012. Revised August 2021.

Linaclotide in IBS-C

Phase 3 Trial



- Efficacy in IBS-C established in 2 phase 3 RCTs
  - N = 1,604

FDA Primary Endpoint:

- ≥ 30% reduction in WAP and increase ≥ 1 CSBM, both for ≥ 6 of 12 weeks

CSBM, complete spontaneous bowel movement; WAP, worst abdominal pain.
*$P < 0.0001$ for all analyses of linaclotide vs placebo groups, using Cochran-Mantel-Haenszel test.
Chey WD, et al. *Am J Gastroenterol*. 2012;107(11):1702-1712. Linaclotide [PI]. Approved 2012. Revised August 2021.

Linaclotide in IBS-C

Common GI AEs in Adult IBS-C and CIC Trials*

	IBS-C		CIC	
AE	Placebo, % (n = 798)	Linaclotide 290 µg, % (n = 807)	Placebo, % (n = 423)	Linaclotide 145 µg, % (n = 430)
Diarrhea	3	20	5	16
Abdominal pain†	5	7	6	7
Flatulence	2	4	5	6
Abdominal distention	1	2	2	3

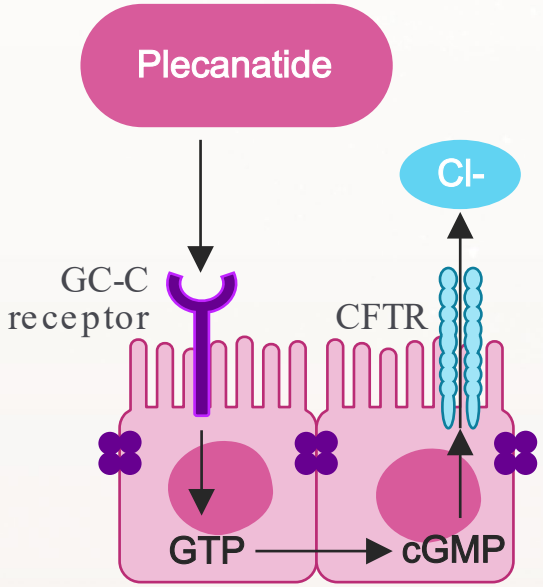
*Occurring in ≥ 2% of patients treated with linaclotide and at an incidence greater than placebo.
†Includes abdominal pain, upper abdominal pain, and lower abdominal pain.
Linaclotide [PI]. Approved 2012. Revised August 2021.

Plecanatide

Indications and Dosing:

- IBS-C and CIC in adults aged ≥ 18 years of age
- 3 mg once daily
- Contraindicated in pediatric patients under 6 years of age
- Avoid use in children aged 6 through 17 years
- Take with or without food
- Is an analog of uroguanylin and works in a pH-dependent release

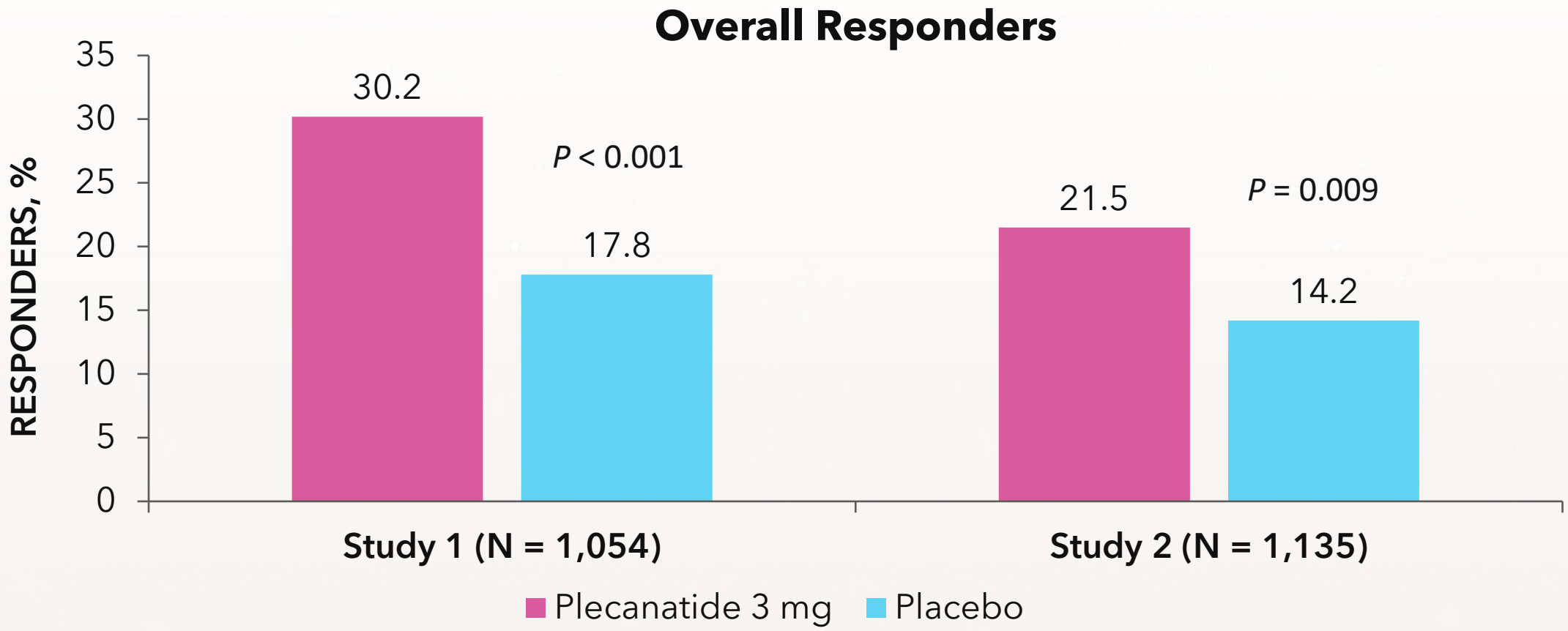
Mechanism of Action



Plecanatide [PI]. Approved 2017. Revised February 2021.

Plecanatide in IBS-C

Phase 3 Trial Results



*Overall responder defined as ≥ 30% reduction in abdominal pain plus an increase of ≥ 1 CSBM from baseline same week 6 of 12 weeks.

Brenner DM, et al. *Am J Gastroenterol*. 2018;113(5):735-745.
Plecanatide [PI]. Approved 2017. Revised February 2021.

Plecanatide in IBS-C

Most Common AEs in IBS-C Trials*

AE	Placebo, % (n = 726)	Plecanatide 3 mg, % (n = 723)
Diarrhea	1.0	4.3

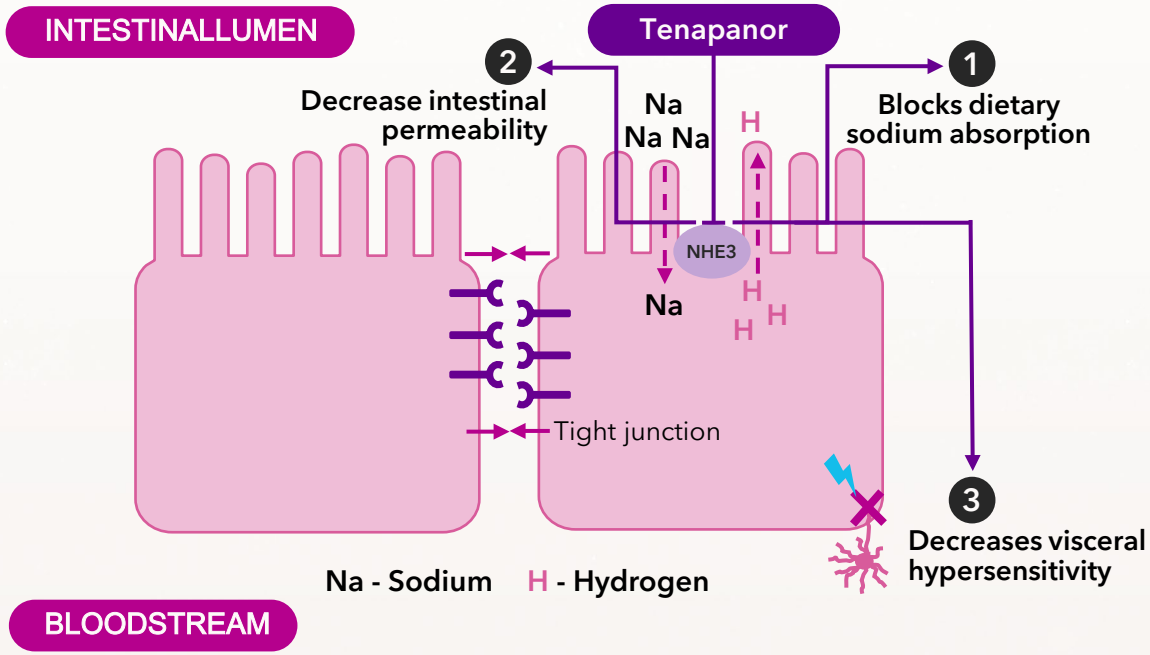
*Occurring in ≥ 2% of plecanatide-treated patients and at an incidence greater than placebo. Plecanatide [PI]. Approved 2017. Revised February 2021.

Tenapanor in IBS-C

Indications and Dosing:

- IBS-C in adults aged ≥ 18 years
- 50 mg orally twice daily
- Contraindicated in pediatric patients aged under 6 years
- Avoid use in children aged 6 through 11 years
- Take immediately prior to first meal of the day and dinner

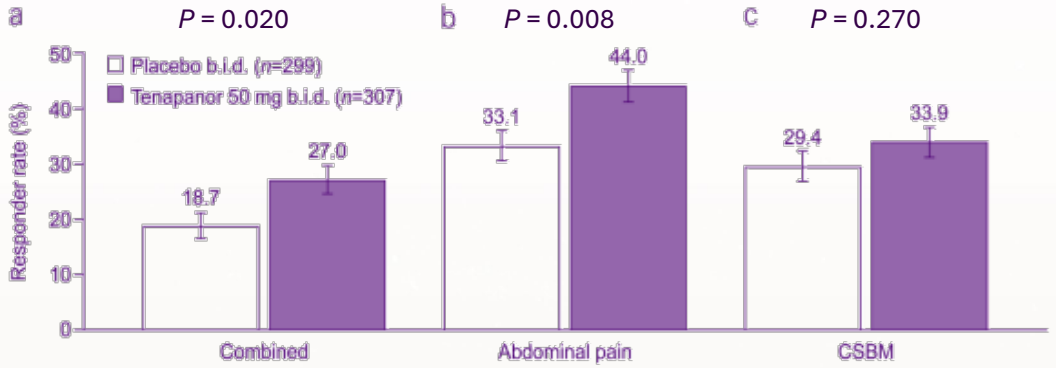
Mechanism of Action



Tenapanor in IBS-C

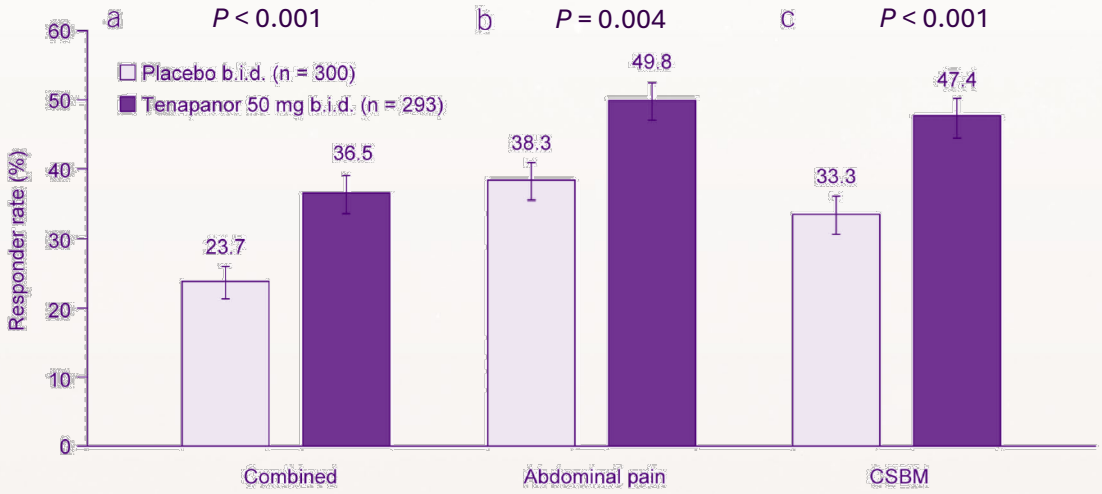
- Small molecule inhibitor of NHE3[1,2]
- FDA approved in 2019 for IBS-C in adults aged ≥ 18 years[1]
- Approval based on data from the 16-week T3MPO-1 and the 26-week T3MPO-2 clinical trials[2,3]
- T3MPO-3, an open-label safety study, found tenapanor to be safe and well tolerated when taken for up to 52 consecutive weeks[4]

T3MPO-1 Responder Rates[2]



Proportion of Patients With Response in At Least 6 of the First 12 Weeks

T3MPO-2 Responder Rates[3]



Proportion of Patients With Response in at Least 6 of the First 12 Weeks

Response defined as ≥ 30% reduction in worse pain and ≥ 1 complete spontaneous bowel movement.

b.i.d., twice daily.

1. Tenapanor [PI]. Approved 2019. Revised April 2022.
2. Chey WD, et al. *Am J Gastroenterol*. 2020;115(2):281-293.
3. Chey WD, et al. *Am J Gastroenterol*. 2021;116(6):1294-1303.
4. Lembo AJ, et al. *Am J Gastroenterol*. 2018;113(suppl):S252.

Tenapanor in IBS-C

Indications and Dosing:

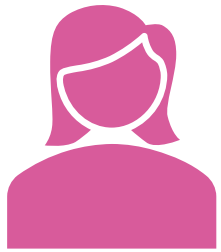
- IBS-C in adults aged ≥ 18 years
- 50 mg orally twice daily
- Contraindicated in pediatric patients aged under 6 years
- Avoid use in children aged 6 through 11 years
- Take immediately prior to first meal of the day and dinner

Most Common AEs in IBS-C Trial 1 (26 weeks)*

AE	Placebo, % (n = 300)	Tenapanor 50 mg BID, % (n = 293)
Diarrhea	4	16
Abdominal Distention	< 1	3
Flatulence	1	3
Dizziness	< 1	2

*Occurring in ≥ 2% of tenapanor-treated patients and at an incidence greater than placebo.
Tenapanor [PI]. Approved 2019. Revised April 2022.

Case 1: Jessica
Case Conclusion



25-year-old woman with persistent constipation, abdominal pain, and bloating over past 4+ years

Diagnosis IBS-C

Women's Health 2024 | Beyond the Annual Visit

Evidence-Based Management of IBS-D

Case 2: Roberta Let's Review

45-year-old woman diagnosed with IBS-D

Medical Background

- Overweight (BMI: 27)
- IBS-D diagnosed by her PCP 2 years ago (did not follow up)
- 10 years of abdominal pain and diarrhea
- No gastrointestinal disease
- No prior surgeries
- No alarm features (ie, hematochezia)

Social Background

- Does not drink

Current Status

- Typically has 3 to 4 loose stools per day
  - 40% to 50% BSFS 6 to 7
- Denies nocturnal diarrhea
- Denies recent travel; fever, chills
- Rare instances of urge incontinence
- Failed probiotic and anti-spasmodic therapy
- Self-medicates with loperamide
- Takes lorazepam to help with sleep

PCP, primary care provider.

Categories of IBS-D Therapies by MOA

Modulation of Gut Flora

- Rifaximin*
- Probiotics
- Low-FODMAP diet

Bile Acid Binding Agents

- Cholestyramine/ Colestid/Colesevelam

Antispasmodics

- Peppermint oil
- Dicyclomine/ hyoscyamine

5-HT_3 Antagonists

- Alosetron†
- Ondansetron

Opioid Receptor Modulators

- Diphenoxylate
- Eluxadoline*
- Loperamide

Neuromodulation

- Antidepressants
- Gut-directed behavioral therapy

*FDA approved for IBS-D.
†FDA approved for women with severe IBS-D who do not respond to conventional therapies.
MOA, mechanism of action.

FODMAPs in IBS

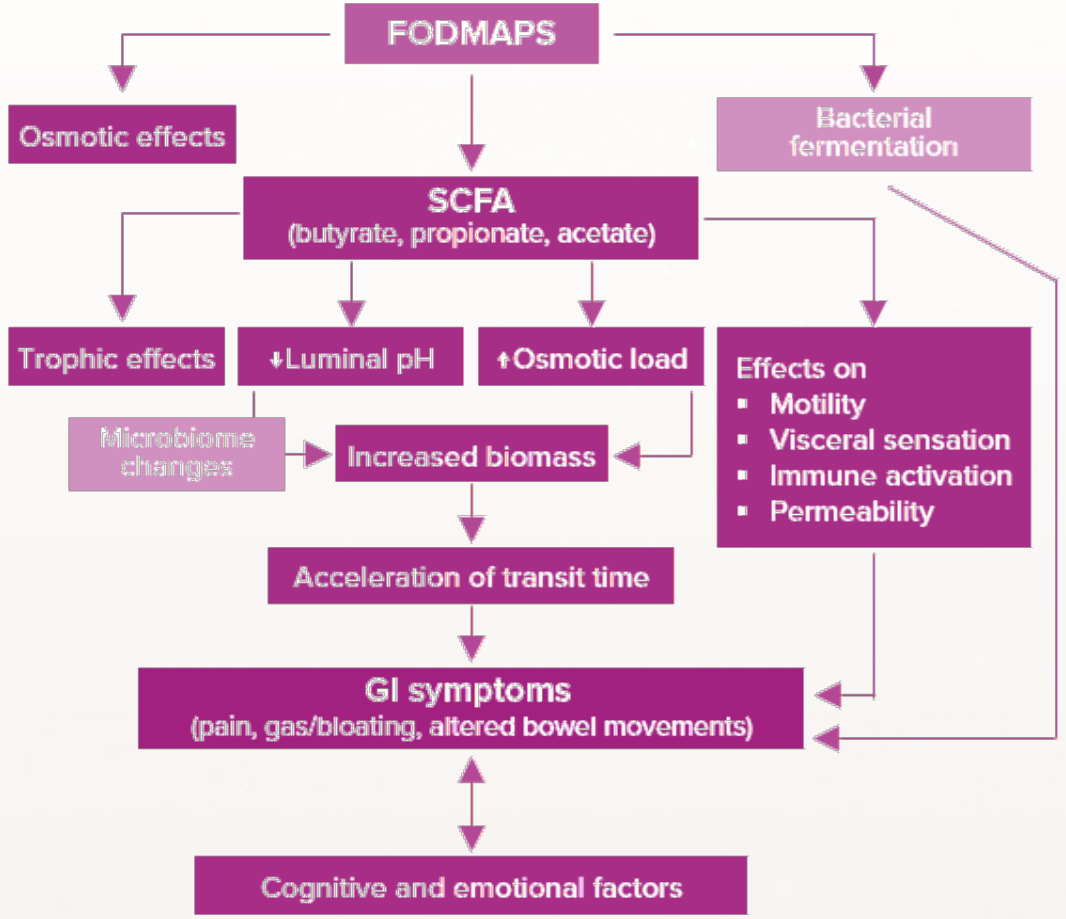
(Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols)

Excess fructose
Honey, apples, pears, peaches, mangos, fruit juice, dried fruit

Raffinose
Lentils, cabbage, brussels sprouts, asparagus, green beans, legumes

Fructans
Wheat (large amounts)
Rye (large amounts)
Onions, leeks, zucchini

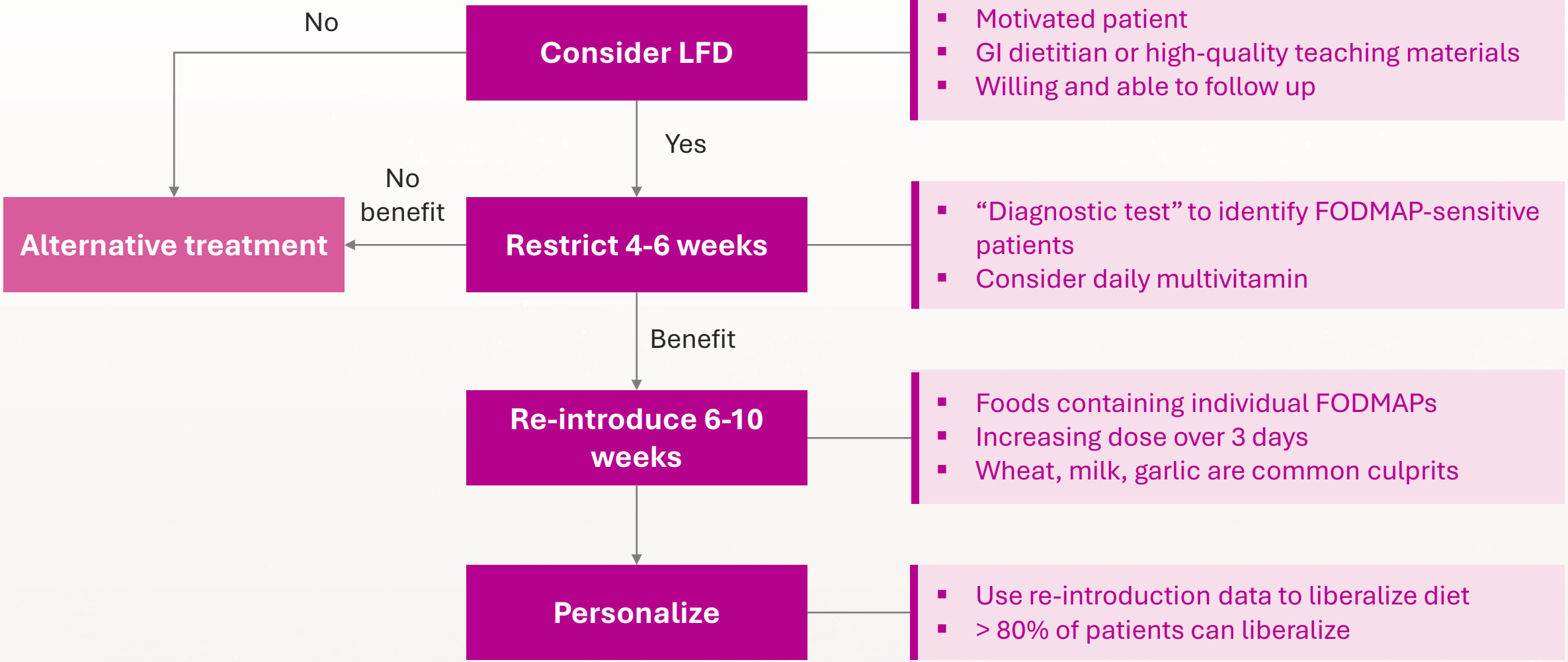
Sorbitol
Apricots, peaches, artificial sweeteners, artificially sweetened gums



SCFA, short-chain fatty acids.

Barrett JS, et al. *Ther Adv Gastroenterol*. 2012;5(4):261-268. Spencer M, et al. *Curr Treat Options Gastroenterol*. 2014;12(4):424-440.

Putting the Low-FODMAP Diet Into Practice

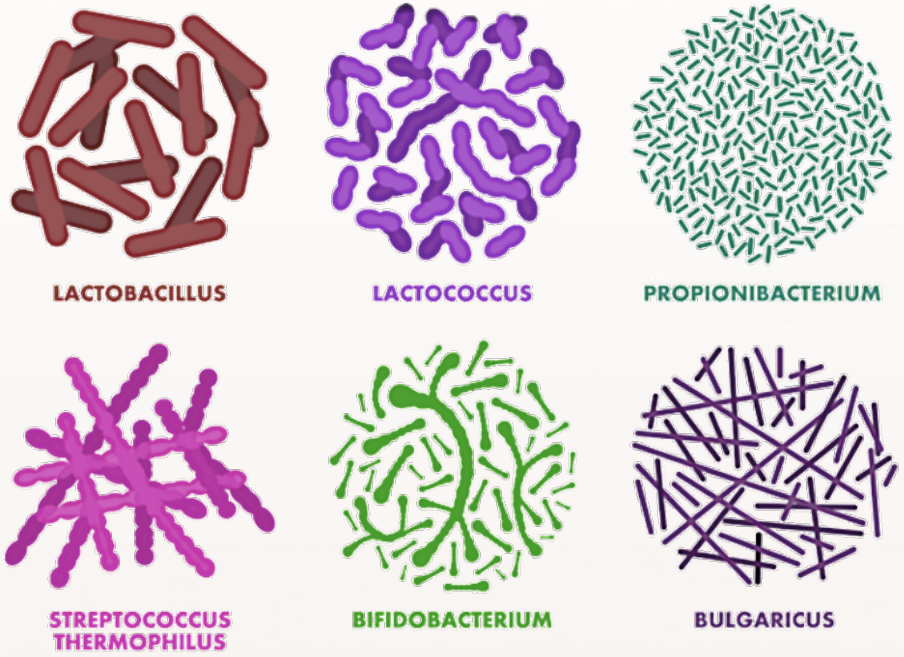


LFD, low-FODMAP diet.

Chey WD, et al. *Gastroenterology*. 2022;162(6):1737-1745.e5.

Probiotics in IBS: Yay, Nay, or Unsure?

Probiotics



AGA recommends using probiotics only in the setting of clinical trials [1]

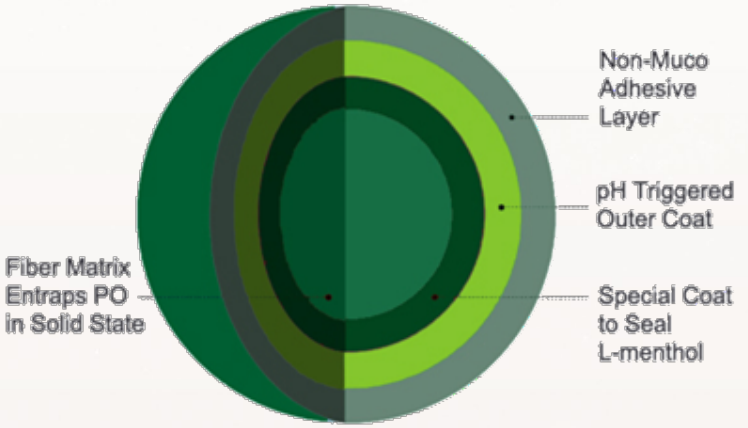
The ACG recommends against the use of probiotics [2]

ACG, American College of Gastroenterology; AGA, American Gastroenterological Association.

1. Su GL, et al. *Gastroenterology*. 2020;159(2):697-705.
2. Lacy BE, et al. *Am J Gastroenterol*. 2021;116(1):17-44.

Peppermint Oil

- Primary active component: L-menthol
- Antispasmodic, anti-inflammatory, antibacterial, anesthetic properties
- Meta-analyses of 12 RCTs involving 835 IBS patients[1]
  - Reduced global IBS symptoms and abdominal pain
  - NNT = 3 for global symptoms, 4 for abdominal pain
  - AEs similar to placebo
- RCT of triple-coated peppermint oil (microspheres)[2]
  - 40% improvement in TISS from baseline
  - Reduced frequency and intensity of symptoms
  - Improvements in abdominal pain, bloating or distention, pain at evacuation

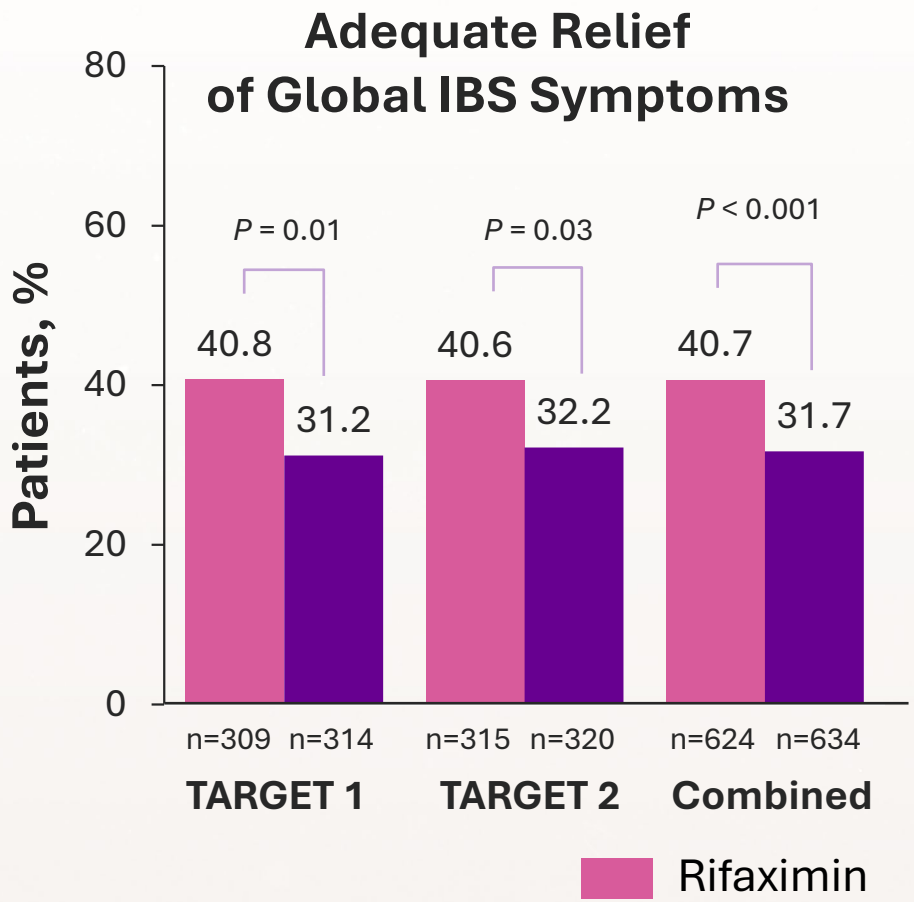


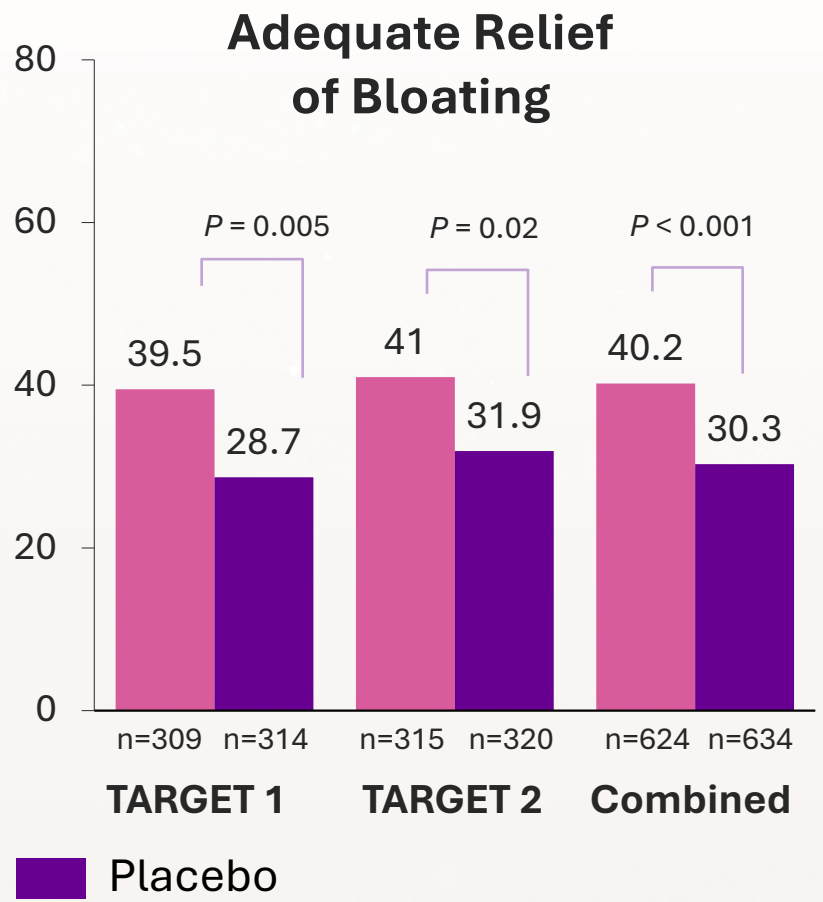
NNT, number needed to treat; PO, peppermint oil; TISS, Total IBS Symptom Score.

1. Alammar N, et al. *BMC Complement Altern Med*. 2019;19(1):21.
2. Cash BD, et al. *Dig Dis Sci*. 2016;61(2):560-571.

Rifaximin in IBS-D
TARGET 1 and TARGET 2 Trials

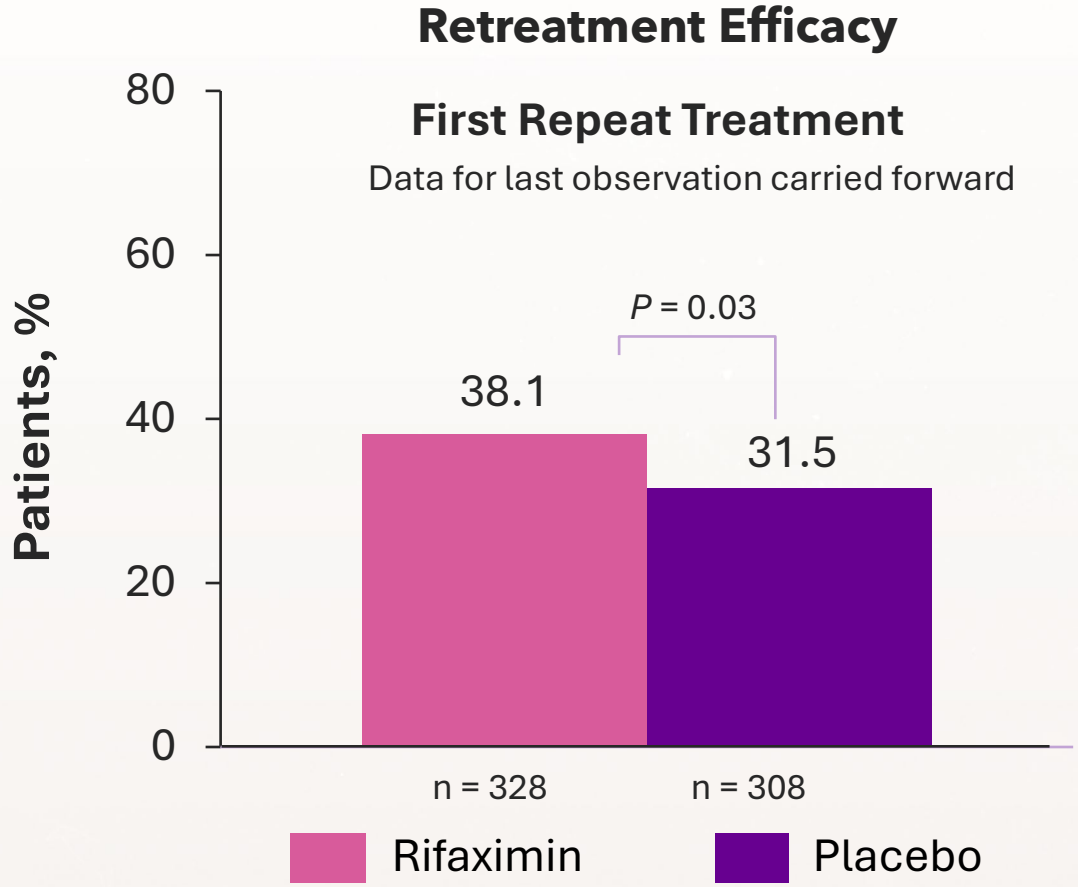
- Poorly absorbed antibiotic; inhibits bacterial protein synthesis
- Indicated for the treatment of IBS-D in adults
- 3 RCTs; 3,837 patients
- AEs similar to placebo





Rifaximin [PI]. Approved 2004. Revised October 2020.
Pimentel M, et al. *N Engl J Med*. 2011;364(1):22-32.

Rifaximin for IBS-D
TARGET 3 Trial



Responder defined as

- Responding to IBS-related abdominal pain and stool consistency for at least 2 of 4 weeks

Recurrence defined as

- Loss of response for at least 3 of 4 weeks

Urgency and bloating improved significantly with both repeat treatments

Abdominal pain and stool consistency improved significantly with first retreatment

Lembo A, et al. *Gastroenterology*. 2016;151(6):1113-1121.
Rifaximin [PI]. Approved 2004. Revised October 2020.

Rifaximin in IBS-D

Dosage for IBS-D[1]

- 550 mg 3 times daily for 14 days
- For recurrence, up to 2 retreatments with the same regimen
- Pooled safety analysis demonstrated no difference between rifaximin and placebo for any AE[2]

Most Common Reported AEs (≥ 2%)[2,*]

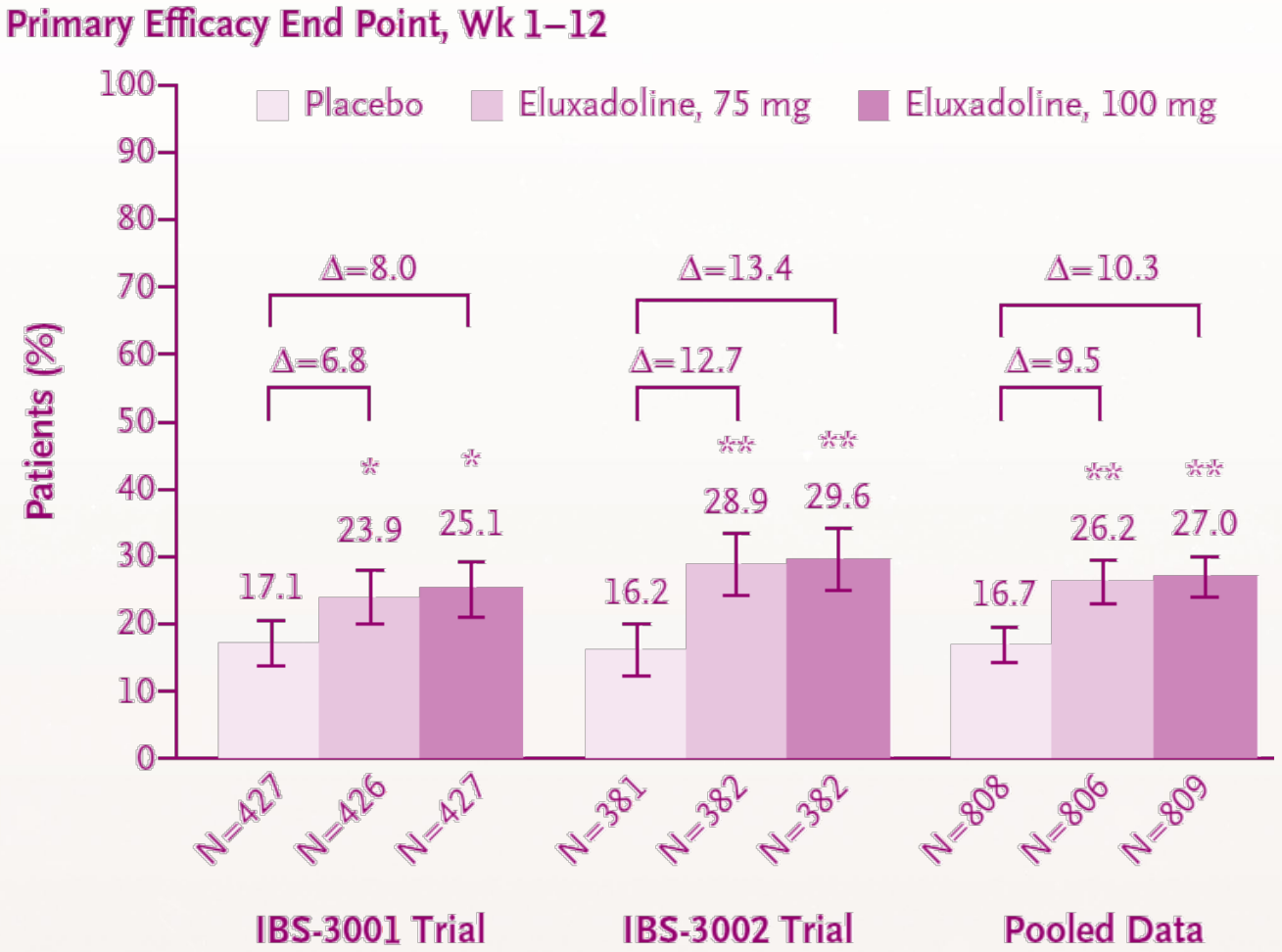
AEs, n (%)	Rifaximin 550 mg (n = 1008)	Placebo (n = 829)
Headache	55 (5.5)	51 (6.2)
URT infection	45 (4.5)	47 (5.7)
Nausea	41 (4.1)	31 (3.7)
Abdominal pain	40 (4.0)	39 (4.7)
Diarrhea	35 (3.5)	26 (3.1)
Urinary tract infection	32 (3.2)	18 (2.2)

*Pooled analysis of phase 2b and phase 3 trials of rifaximin in non-IBS-C.

1. Rifaximin [PI]. Approved 2004. Revised October 2020. 2. Schoenfeld P, et al. *Aliment Pharmacol Ther*. 2014;39(10):1161-1168.

Eluxadoline in IBS-D

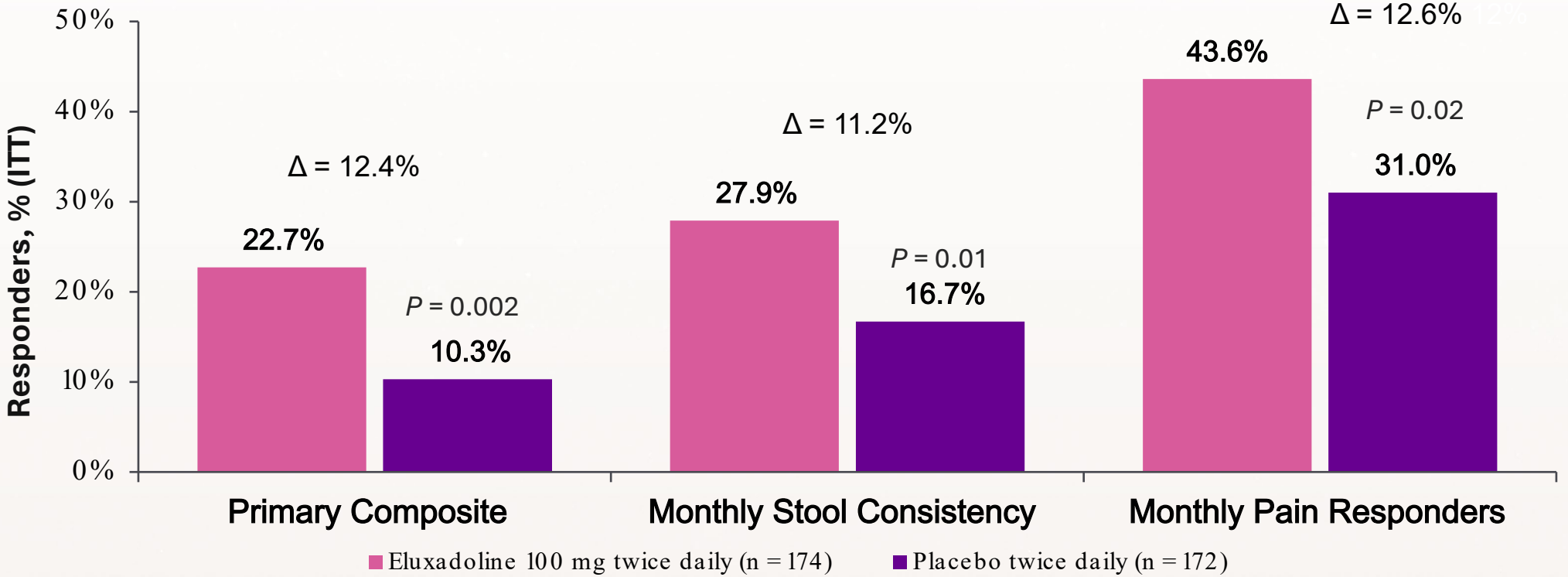
- Mixed opioid receptor modulator
  - μ/κ-opioid receptor agonist/δ-opioid receptor antagonist
- 2 RCTs; 2,426 patients
- AEs: constipation, abdominal pain, SO spasm, pancreatitis
  - Contraindicated if no gall bladder or h/o pancreatitis, heavy ETOH users



*$P < 0.05$ vs placebo; **$P < 0.001$ vs placebo.
ETOH, ethyl alcohol; SO, sphincter of Oddi.
Eluxadoline [PI]. Approved 2015. Revised June 2020.
Lembo AJ, et al. *N Engl J Med*. 2016;374(3):242-253.

Eluxadoline in Patients Who Failed Loperamide: RELIEF Trial

Phase 4, multicenter, double-blind RCT evaluating eluxadoline in patients subjectively reporting failure of loperamide to adequately control IBS-D symptoms in prior 12 months



Primary composite: ≥ 40% improvement in WAP compared with baseline and Bristol Stool Score of < 5 or absence of a bowel movement if accompanied by ≥ 40% improvement in WAP.

WAP, worst abdominal pain.

Brenner DM, et al. *Am J Gastroenterol*. 2019;114(9):1502-1511.
Eluxadoline [PI]. Approved 2015. Revised June 2020.

Eluxadoline

Dosage for IBS-D[1]

- 100 mg twice daily taken with food
- 75 mg twice daily with food in patients who:
  - Are unable to tolerate the 100-mg dose
  - Are receiving concomitant OATP1B1 inhibitors
  - Have mild or moderate hepatic impairment
  - Have end-stage renal disease and are not yet on dialysis

Contraindications[2]

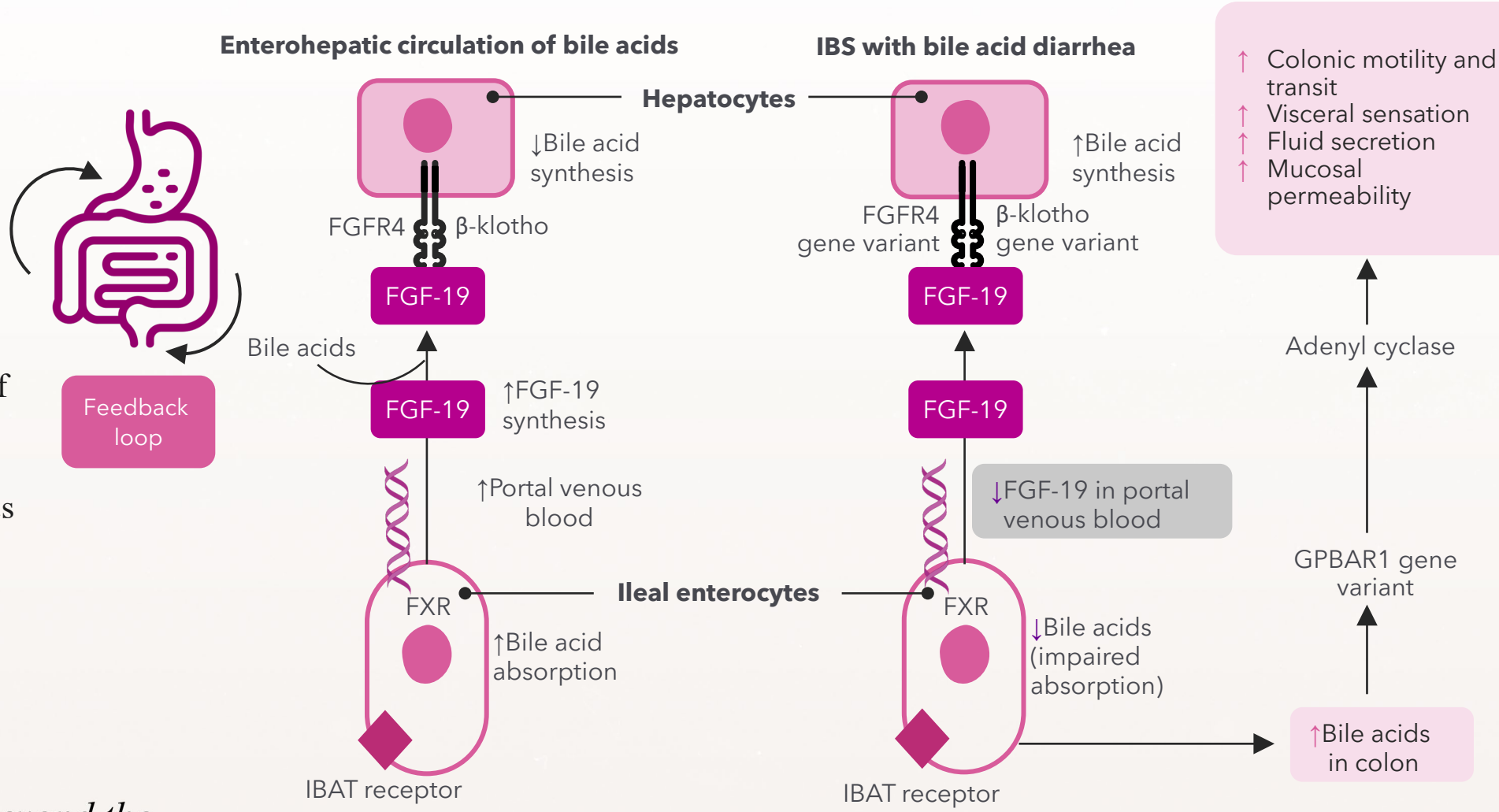
- Cholecystectomy
- Bile duct obstruction
- Sphincter of Oddi disease or dysfunction
- Pancreatitis
- Severe liver impairment (Child-Pugh class C)
- Severe constipation
- Patients who consume > 3 alcoholic drinks per day

1. Eluxadoline [PI]. Approved 2015. Revised June 2020.
2. Lembo AJ, et al. *N Engl J Med*. 2016;374(3):242-253.

Bile Acid Sequestrants

25% to 50% of patients with IBS-D may have bile acid malabsorption (unproven)

- Excess bile acids in the colon stimulate colonic motility and increase visceral sensation and fluid secretion
- Testing for bile acid diarrhea can be challenging
- Uncontrolled studies of bile acid sequestrants suggest benefit in subset of IBS-D patients
- Little supporting evidence of benefit



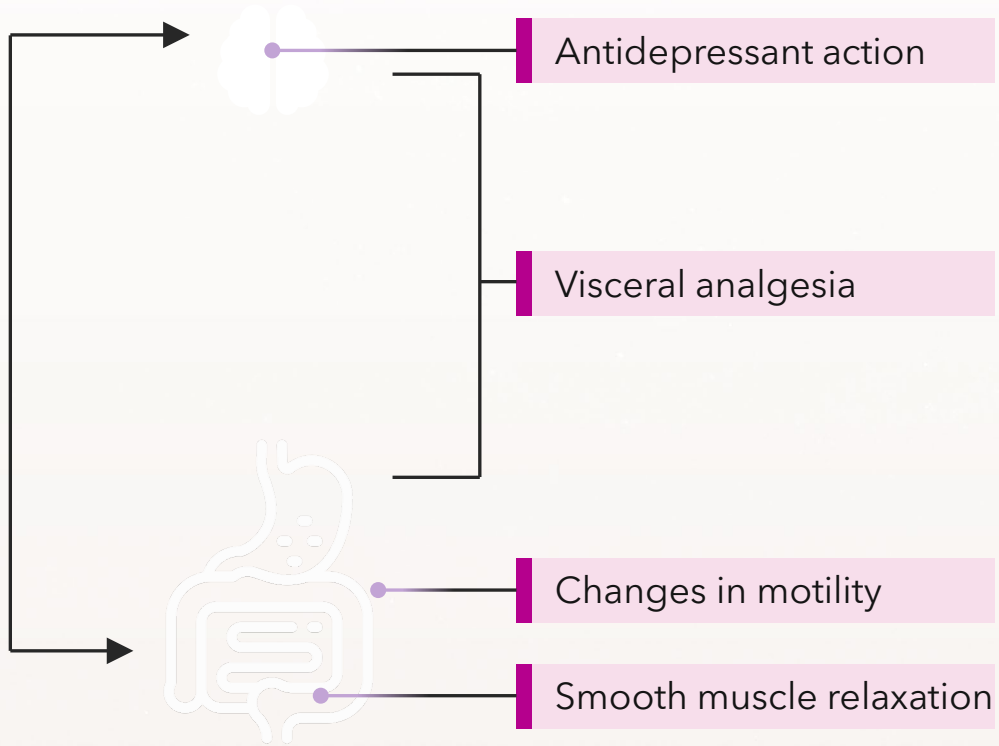
IBAT, ileal bile acid transporter.

Camilleri M. *Gut Liver*. 2015;9(3):332-339.

Do Antidepressants Work in IBS?

- Meta-analysis: tricyclics and SSRIs are effective in reducing IBS symptoms[1]
  - Significant heterogeneity between SSRI studies[1]
- Tricyclics most rigorously studied in IBS[2,3]
  - Reduce pain sensitivity in chronic neuropathic animal models more effectively than SSRIs[2]
- SSRIs may be preferred in IBS-C[3]
- SNRIs not yet studied in large RCTs[3]

Potential Antidepressant Actions in IBS[3]

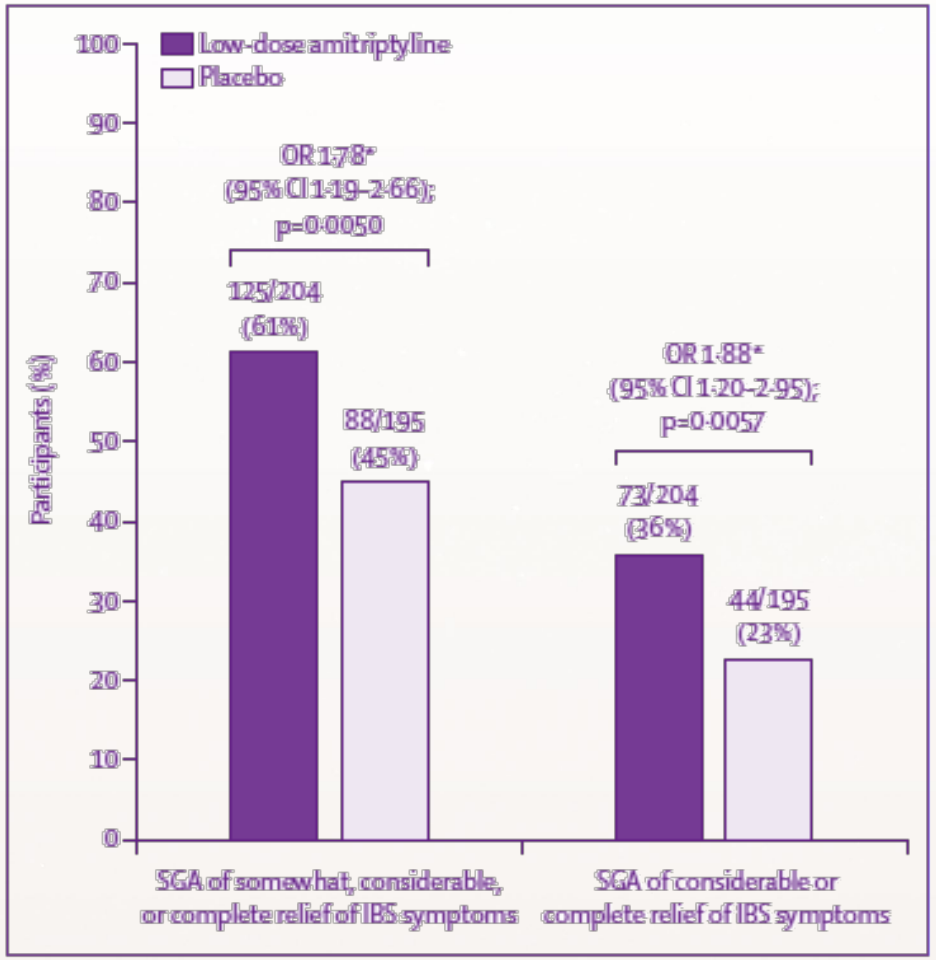


SNRI, serotonin noradrenaline reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

1. Ford AC, et al. *Am J Gastroenterol*. 2014;109(9):1350-1365. 2. Grover M, Drossman DA. *Gastroenterol Clin N Am*. 2011;40(1):183-206. 3. Chey WD, et al. *Gut Liver*. 2011;5(3):253-266.

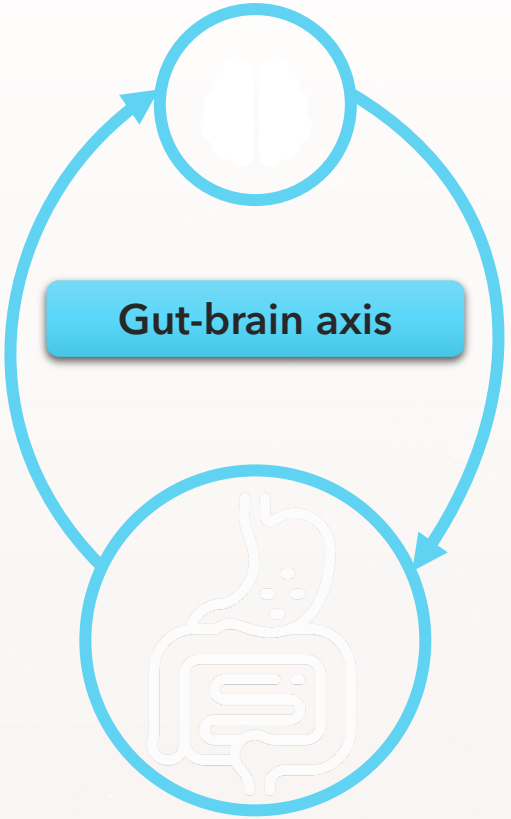
TCA for IBS in Primary Care: ATLANTIS Trial

- 338 (73%) of all participants completed 6 months' treatment; 173 (75%) in the amitriptyline group and 165 (71%) in the placebo group
- Primary outcome: Low-dose amitriptyline significantly better than placebo
    - IBS-SSS score between groups at 6 months –27.0; *P* = 0.0079
    - 46 (20%) participants discontinued low-dose amitriptyline; 13% due to adverse events
    - 59 (26%) discontinued placebo; 9% due to adverse events
    - 5 serious adverse reactions (2 in the amitriptyline group and 3 in the placebo group), and 5 serious adverse events unrelated to trial medication
- No effect of low-dose amitriptyline on somatoform symptom-reporting scores, or anxiety or depression scores, during 6-month follow-up, nor was there any impact on work and social activities



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

The Gut-Brain Axis: The Mechanistic Basis for Behavioral Therapies in IBS



- Gut-directed hypnotherapy
- Cognitive behavior therapy
  (With or without IE)
- Mindfulness-based stress reduction
- Relaxation training
  (All BGPs)

Case 2: Roberta
Case Conclusion

45-year-old woman diagnosed with IBS-D

Medical Background

- Overweight (BMI: 27)
- IBS-D diagnosed by her PCP 2 years ago (did not follow up)

Diagnosis IBS-D

PCP, primary care provider.

Conclusions

- IBS is a common, chronic disorder of gut-brain interaction
  - Syndrome of symptoms with diverse etiologies
- Diagnose IBS using a positive strategy incorporating the Rome criteria, thorough history and physical exam, and limited testing
- Treatments for IBS include diet and lifestyle modifications, OTC and prescription medications, and psychological therapy
- Appropriate to initiate therapy in primary care; refer to specialty care for severe and/or refractory symptoms