



Practical Updates in Primary Care

Advancing IBS-C and CIC in Primary Care Practice: Evidence-Based Approaches for Diagnosis, Treatment, and Person-Centered Management

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Disclosures

- **Joel J. Heidelbaugh, MD, FAAFP, FACG** has nothing to disclose
- **William D. Chey, MD, MACG, AGAF, FACP, RFF:** Consultant – Ardelyx, Atmo, Bausch/Salix, Biomerica, Gemelli, Phathom, Takeda, Vibrant; research/grant support: Bausch/Salix, Commonwealth Diagnostics International, FDA, NIH; stock options: Coprata, Evinature, FoodMarble, Isothrive, Kiwi BioScience, Modify Health; advisory board – ACG, IFFGD, Rome Foundation; patents – My Nutrition Health, Digital Manometry, Rectal Expulsion Device



Learning Objectives

- Assess guideline-recommended diagnostic criteria for IBS-C and CIC to enable timely, accurate diagnosis and support the implementation of appropriate therapeutic strategies
- Examine the mechanisms of action, efficacy and safety data, and indications of available pharmacologic therapies for adult and pediatric patients with IBS-C and CIC
- Apply person-centered and equitable care plans that consider the needs of individual patients with IBS-C and CIC





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Identifying and Diagnosing IBS-C and CIC

Case #1

- 28-year-old woman presents with a several-year history of intermittent abdominal pain and constipation
- Medical Hx – BMI 32, moderate anxiety, and depression
- Social Hx – works in marketing, admits significant work stress, occasional alcohol and marijuana use, limited exercise, frequent travel for work



Case #1

- What are your first thoughts?
- What questions do you have to use to formulate a differential diagnosis?
- Always find out what OTC medications/supplements the patient is taking
- Be sure to give adequate time to explore the patient's concerns – a challenge in primary care, given there are often many issues to discuss in each clinic visit
- Always validate the patient's symptoms and perform a physical examination



Prevalence and Burden of IBS

- 5-16% of the population using ROME IV criteria
- 2:1 female predominance, which may be related to physician visit data
- Common reason for referral to gastroenterology
- Significant cause of work absenteeism
- Accounts for \$1.5 to \$10 billion annually in direct healthcare costs in the US



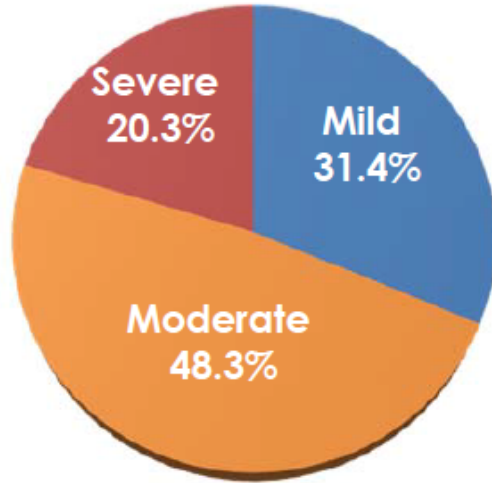
Patient Perceptions of IBS

Common Knowledge	Common Misconceptions	Most Desired Information
Combination of abdominal pain and constipation • And/or diarrhea • And/or bloating	Can develop into • Colitis • Surgical problem • Malnutrition • Cancer	• What foods to avoid? • What causes IBS? • Coping strategies to reduce symptoms?
Triggers include stress at work, relationships, combinations of other (emotional) factors	Will worsen with age	

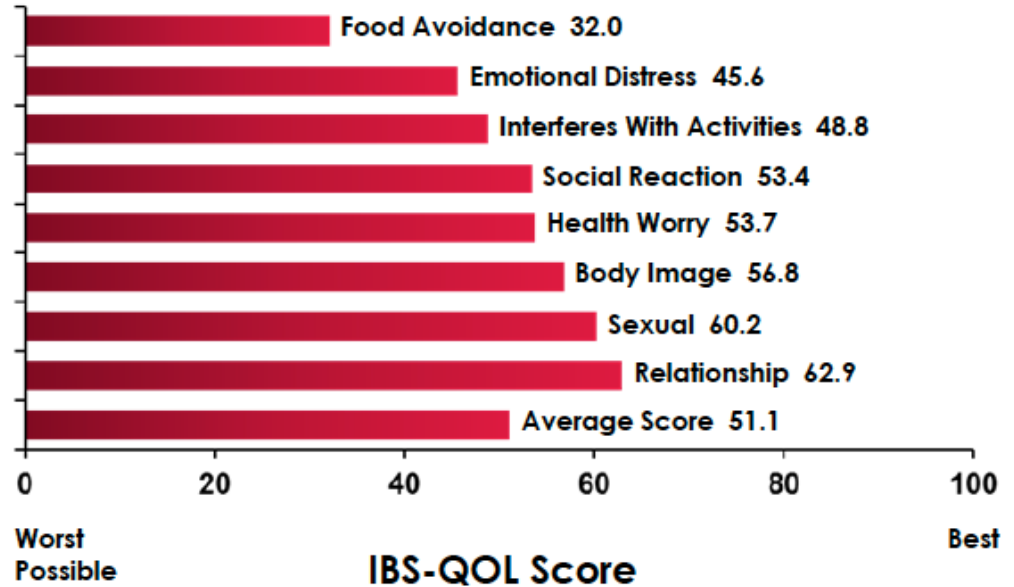


Impact on Quality of Life

IBS Severity



Average QOL Scores in Patients with IBS



QOL = quality of life.

IBS Patients: Their Illness Experience and Unmet Needs. International Foundation for Functional Gastrointestinal Disorders (IFFGD); 2009.



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Perceptions and Practices of PCPs for IBS

- Despite the availability of Rome IV diagnostic criteria, most US and European PCPs still believe that IBS is a diagnosis of exclusion, it is underdiagnosed in primary care practices, and it is difficult to accurately diagnose with confidence
- Patients with suspected IBS are still commonly referred to a gastroenterologist and often a dietitian, yet many are not referred very often to mental health providers
- IBS can be difficult to treat effectively, thus a strong and longitudinal provider-patient relationship is paramount to effectively managing the condition



Perceptions and Practices of PCPs for IBS

Pathophysiology	US PCPs	Europe PCPs	Pathophysiology	US PCPs	Europe PCPs
Dietary factors cause IBS	54%	43%	Existing psychiatric disorders cause IBS	39%	40%
Dietary factors worsen IBS	95%	94%	Existing psychiatric disorders worsen IBS	84%	83%
High FODMAP foods cause IBS	41%	36%	Alterations of gut-brain regulation cause IBS	78%	71%
High FODMAP foods worsen IBS	78%	72%	Alterations of gut-brain regulation worsen IBS	88%	82%
Gluten sensitivity causes IBS	26%	19%	Visceral hypersensitivity causes IBS	66%	59%
Gluten sensitivity worsens IBS	67%	55%	Visceral hypersensitivity worsens IBS	77%	77%
Altered gut microbiome causes IBS	70%	64%	Causes of IBS are poorly understood	92%	90%
Altered gut microbiome worsens IBS	89%	84%			
Stress causes IBS	71%	75%			
Stress worsens IBS	98%	98%			

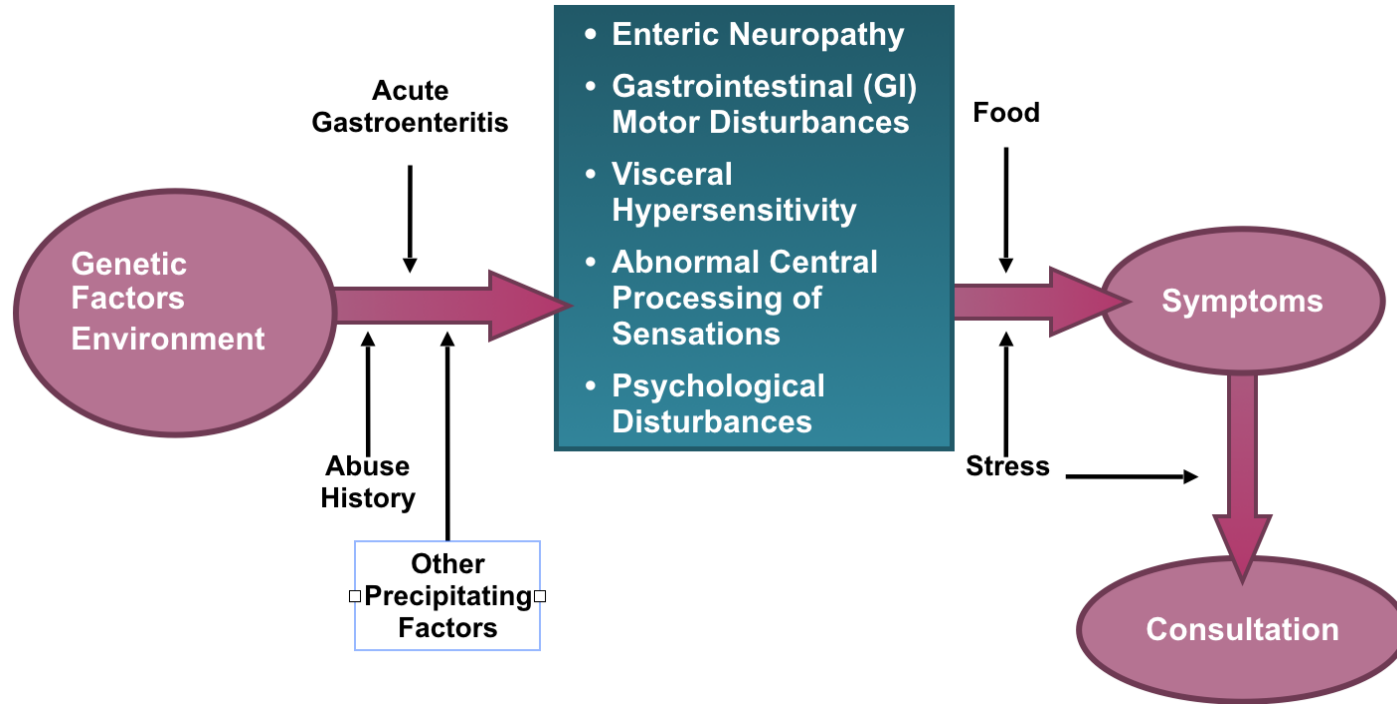


Perceptions and Practices of PCPs for IBS

Diagnosis perceptions and practices	US PCPs	Europe PCPs	Diagnosis perceptions and practices	US PCPs	Europe PCPs
IBS is a diagnosis of exclusion	81%	80%	Criteria needed to make a confident diagnosis		
IBS is under diagnosed in primary care practice	80%	80%	Normal endoscopy	82%	75%
IBS is difficult to diagnose with confidence	78%	80%	Normal serum hematologic and chemistry tests	82%	90%
IBS can be confidently diagnosed always or most of the time	46%	40%	Normal serologic tests for celiac disease	89%	95%
IBS can be diagnosed on symptoms alone	71%	50%	Need for gastroenterology consultation	65%	56%
IBS is stated affirmatively as a diagnosis	63%	87%	Have heard of Rome IV criteria for IBS	84%	85%
			Know Rome IV criteria to make accurate diagnosis of IBS	61%	58%
			Use Rome IV criteria to diagnose IBS	61%	50%
			Diagnostic tests are sufficient with using Rome IV criteria	16%	11%
			Discuss Rome IV criteria with patients upon diagnosis	45%	33%



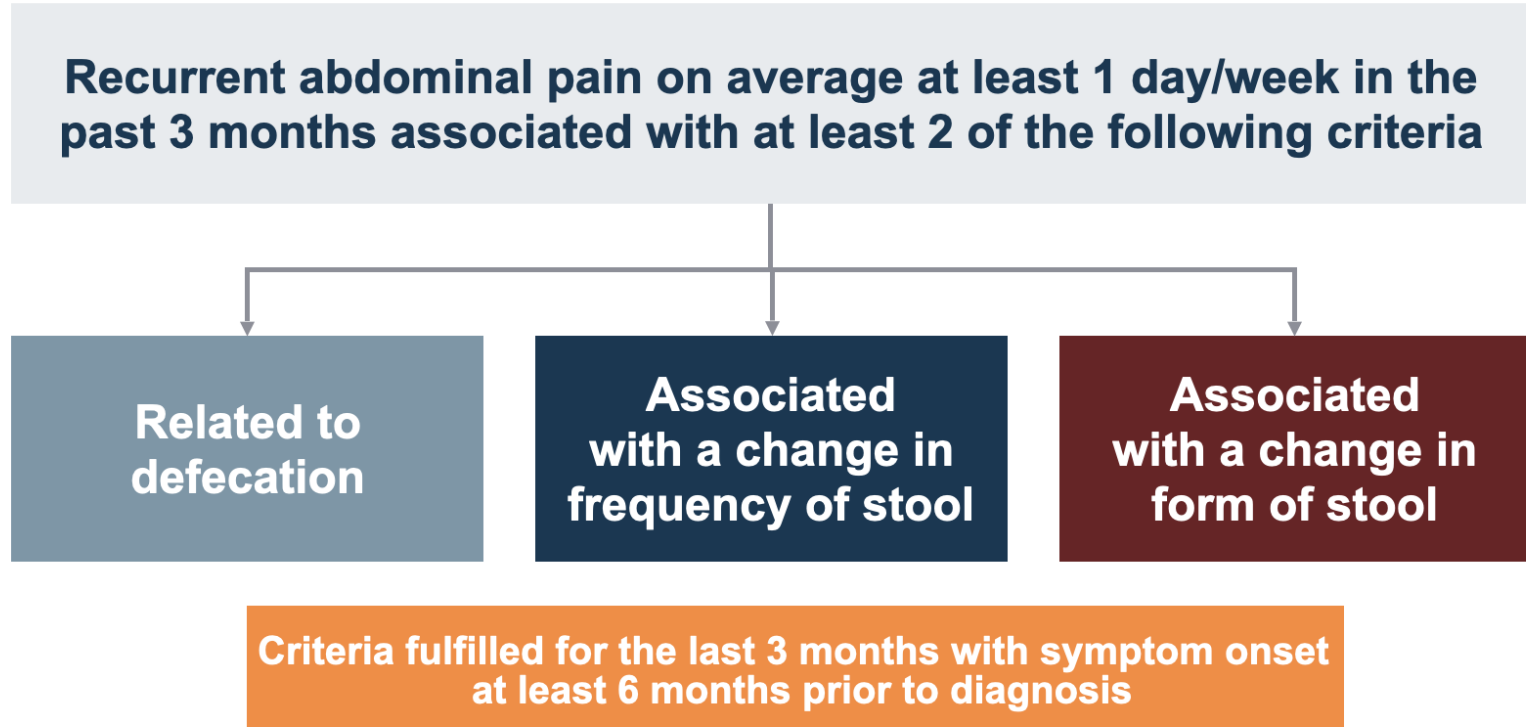
Pathophysiology of IBS



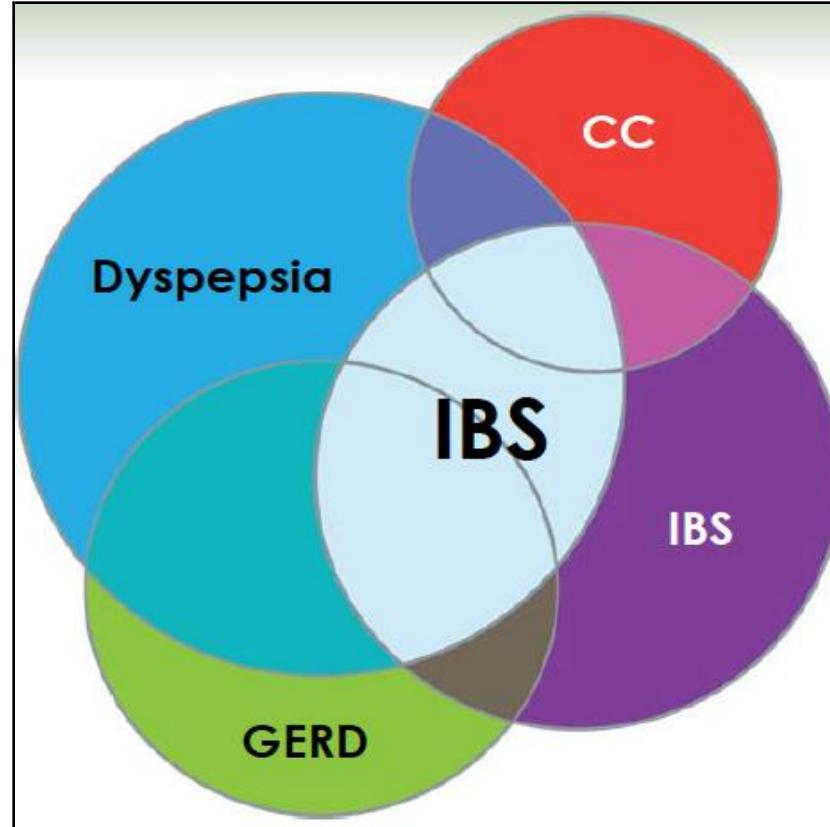
Rome Foundation Functional GI Disorders Specialty Modules.



Rome IV Diagnostic Criteria for IBS



IBS and Symptom Overlap



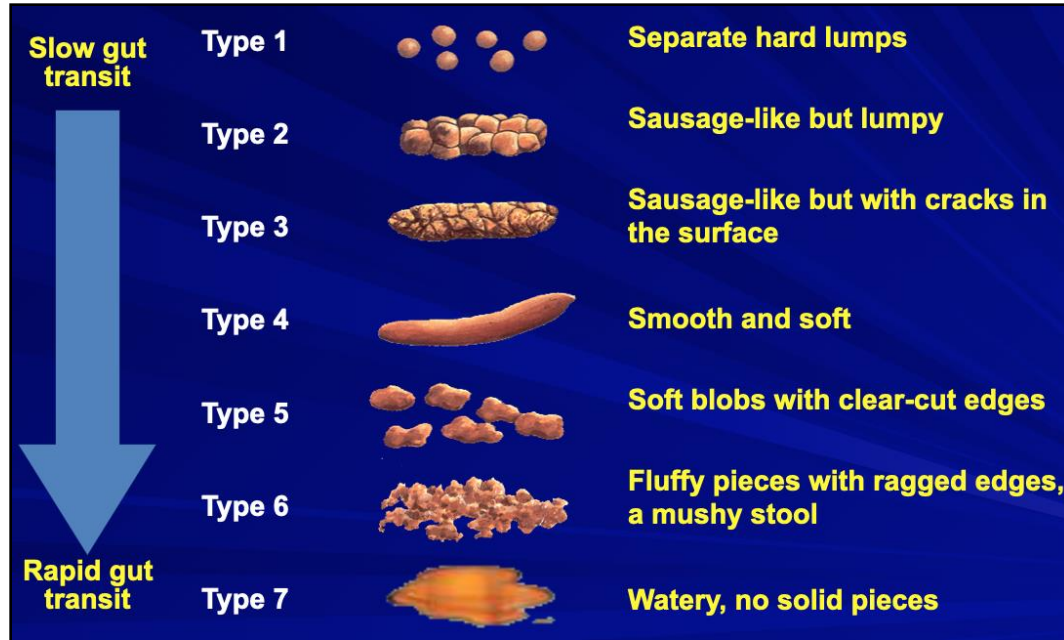
GERD = gastroesophageal reflux disease; CC = chronic constipation.
Frissora CL, Koch KL. *Curr Gastroenterol Rep.* 2005;7(4):264-271.



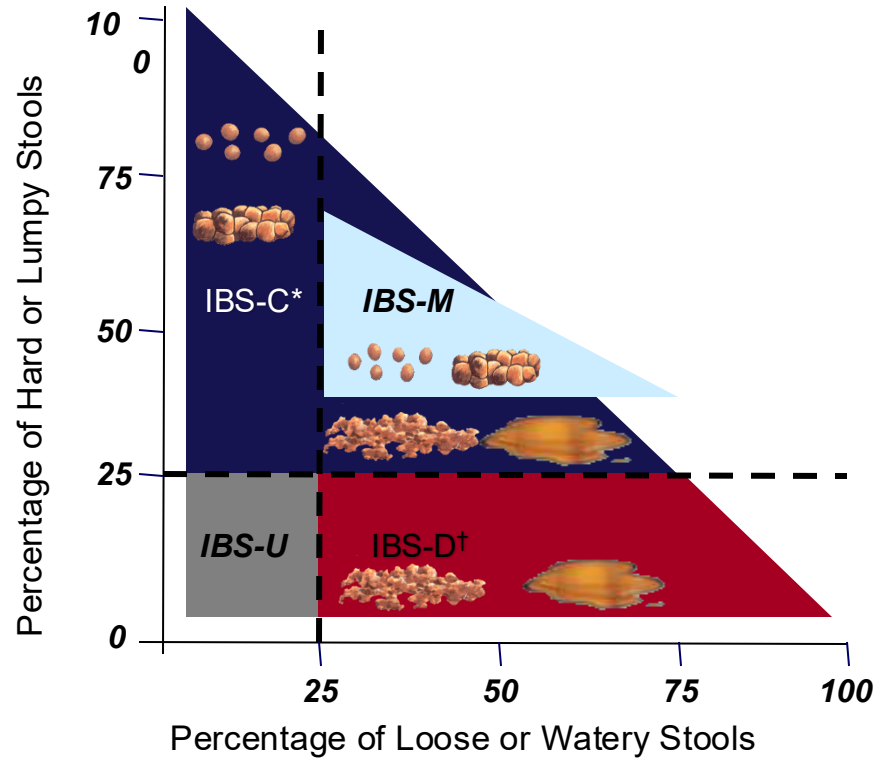
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Stool Consistency, but Not Frequency, Predicts Colon Transit Time

Bristol Stool Form Scale



IBS Subtypes Are Based on Stool Consistency



*Bristol Stool Form Scale 1-2; †Bristol Stool Form Scale 6-7.

IBS-M = IBS-mixed; IBS-U = IBS-unclassified.

Drossman DA. *Gastroenterology*. 2016:S0016-5085(16)00223-7.



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How to Make a Positive Diagnosis of IBS-C

- IBS is NOT a diagnosis of exclusion!
- Difference between
 - Disorders of gut-brain interaction
 - Organic disease
- The diagnosis can be confidently made in primary care practices
- Take a careful history – make it the focus of the visit (many competing issues...)
- Perform a thorough physical examination, including DRE, which provides validation
- Assess for alarm features
- Make appropriate classification of constipation
- IBS-C is constipation with abdominal/visceral pain / CIC does not have chronic pain



Alarm Features of Organic Disorders

- Acute or rapidly progressing symptoms
- Blood in the stool – unexplained rectal bleeding or melena
- Family history of CRC, IBD, celiac disease
- Fever, symptoms of systemic illness
- New symptoms and age >50 (45) years
- Unexplained/uninvestigated anemia
- Unintended weight loss >10% in 3 months
- Symptoms that awaken the patient at night



Appropriate Use of Diagnostic Testing

- IBS-C
 - Celiac testing (10-15% of patients with celiac disease have constipation on presentation)
 - Consider abdominal radiograph to evaluate stool burden
- IBS with diarrhea (IBS-D)
 - Tissue transglutaminase IgA
 - Fecal calprotectin
 - Giardia antigen
 - CRP
- No role for colonoscopy in all patients



Case #1

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28-Year-Old Woman with Chronic Symptoms

- Pain
- Constipation > diarrhea

Additional Symptoms	Pertinent Negatives
• Pain is multifocal • Constipation • Hard stool – No BM but feels urge • Bloating related to eating • Anxiety	• No weight loss • No family history • No rectal bleeding • Labs normal – CBC – TTG IgA – CRP

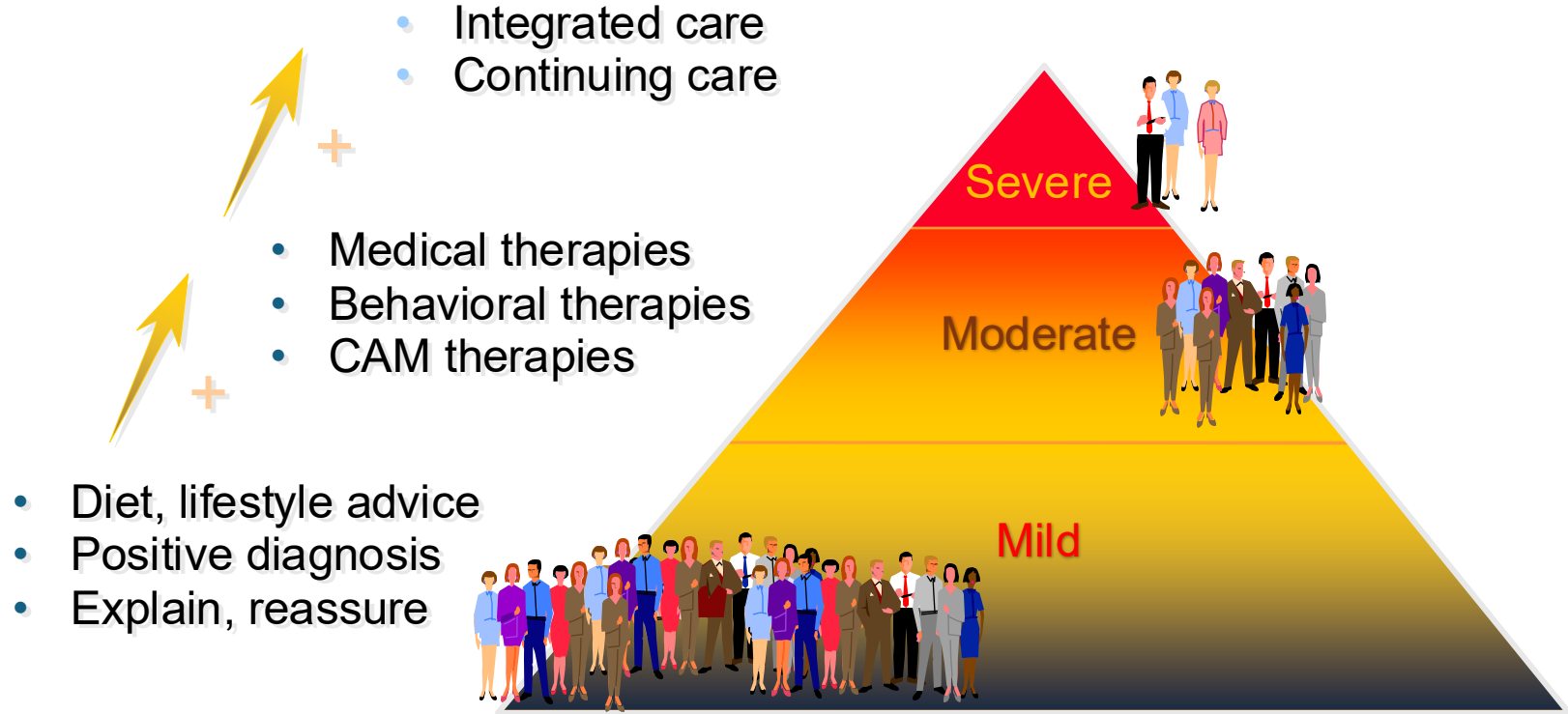




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IBS-C and CIC Treatment Approaches

Graded Integrative Treatment of IBS



CAM = complementary and alternative medicine.

Chang L, et al. *Gastroenterology*. 2022;163(1):118-136. Lembo A, et al. *Gastroenterology*. 2022;163(1):137-151.



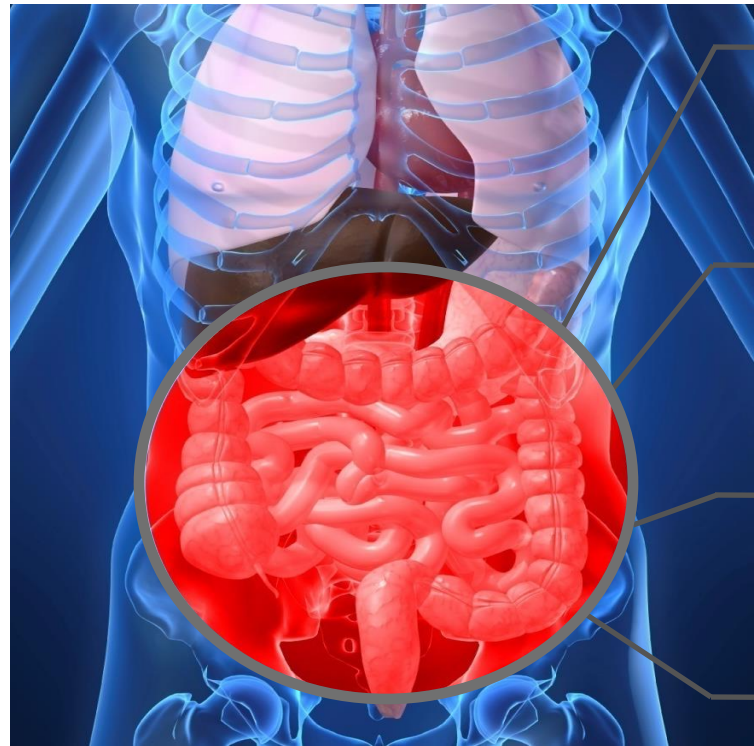
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Dietary & Lifestyle Approaches for Chronic Constipation

- Increased fiber (25-30 g/day)
 - Soluble preferred over insoluble
 - “Start low and go slow”
- Natural laxatives
 - Sorbitol: Prunes, apples, apricots, cherries, peaches, pears
 - Stimulants: Aloe, cascara, rhubarb
 - Other: Kiwi, ripe bananas, mango, papaya, watermelon
- FODMAP restriction
 - Benefits for pain and bloating in IBS-C
- Key point: When **deficient**, supplementing fiber, fluid, and recommending exercise can be helpful. Natural laxatives can be used in place of or along with drug treatments



Pharmacologic Therapy for IBS Is Directed Toward the Dominant Symptoms



Diarrhea

Loperamide*
Ondansetron*
Antibiotics
Eluxadoline
Tricyclic antidepressants (TCAs)

Constipation

Fiber*
Osmotic & stimulants*
Lubiprostone
Linactotide/Plecanatide
Tenapanor

Abdominal pain/
discomfort

Antibiotics
Antispasmodics
Antidepressants*
Lubiprostone
Linaclotide/Plecanatide/Tenapanor

Bloating

Antibiotics*
Probiotics*
Lubiprostone
Linaclotide/Plecanatide
Tenapanor

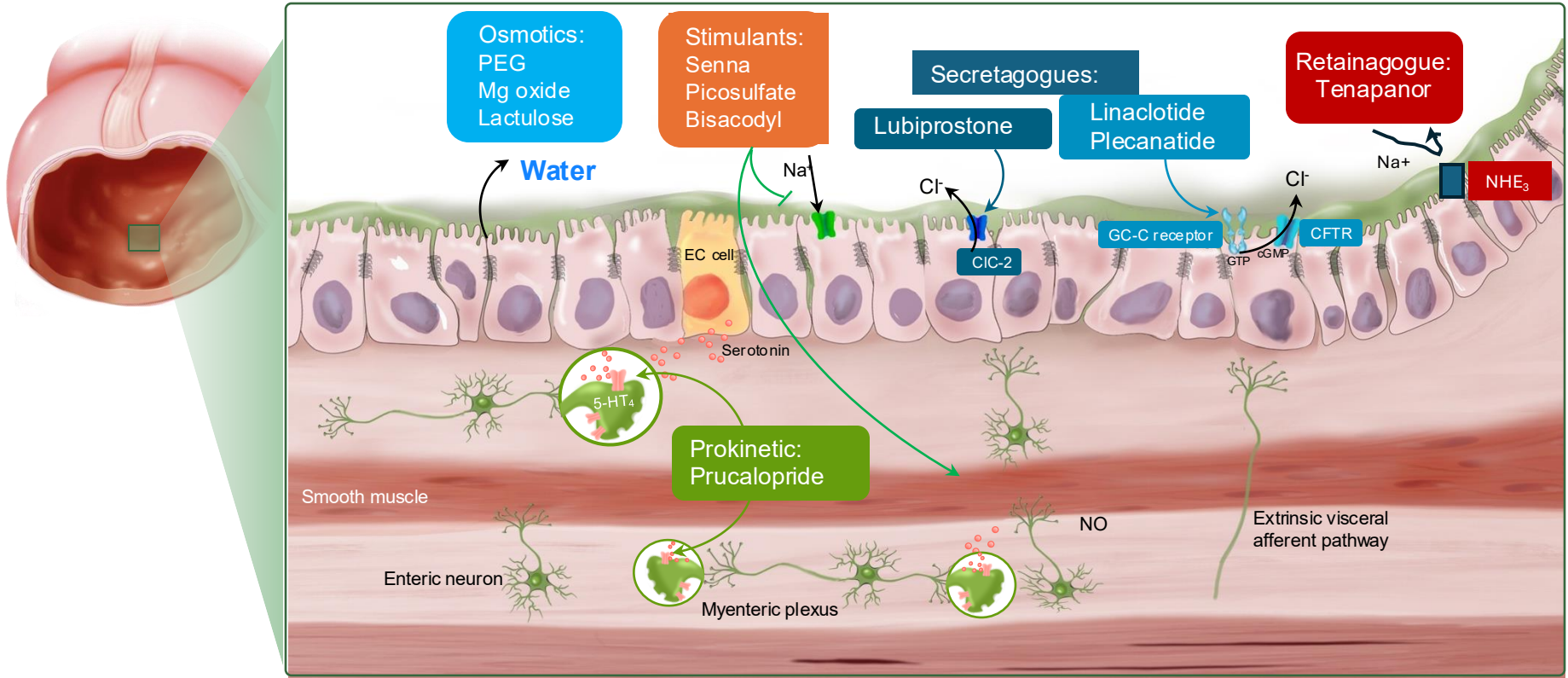
*Not Food and Drug Administration (FDA)-approved for IBS.

Chey WD, et al. *JAMA*. 2015;313(9):949-958. Ford AC, et al. *Am J Gastroenterol*. 2018;113(Suppl 2):1-18.



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MoA of Drug Therapies for IBS-C & CIC



MoA = mechanism of action; EC = enterochromaffin; PEG = polyethylene glycol.
 Chang L, et al. *Gastroenterology*. 2023;164(7):1086-1106.



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Osmotic and Stimulant Laxatives

Osmotic Agents

Contain poorly absorbed ions or molecules that increase water in intestinal lumen

- PEG
- Lactulose
- Magnesium oxide

Recommended for
CIC, based on
varying levels of
evidence

PEG: No evidence for
pain relief in IBS-C

Stimulant Agents

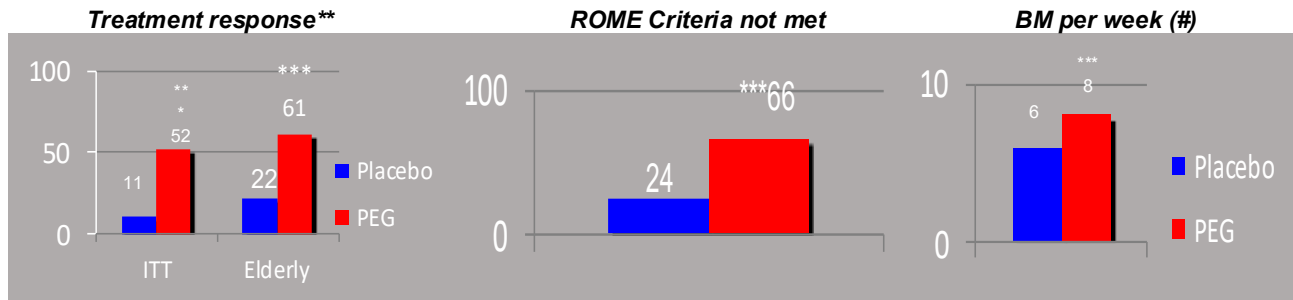
Induce colonic peristalsis and
fluid/electrolyte secretion

- Sodium picosulfate
- Bisacodyl
- Senna
- Cascara
- Rhubarb
- Aloe



PEG 3350 for Chronic Constipation

- US multicenter, double-blind, randomized placebo-controlled trial of PEG vs placebo for 6 months



- Adverse events not different between PEG and placebo

Treatment response = ≥ 3 BMs/week and no more than 1 of the remaining 3 Rome symptoms in the absence of rescue medications = $\geq 50\%$ of the time; * $p < 0.001$ vs placebo.

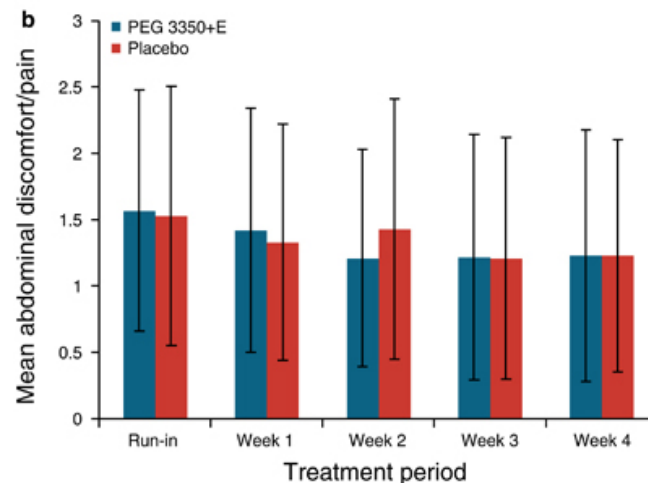
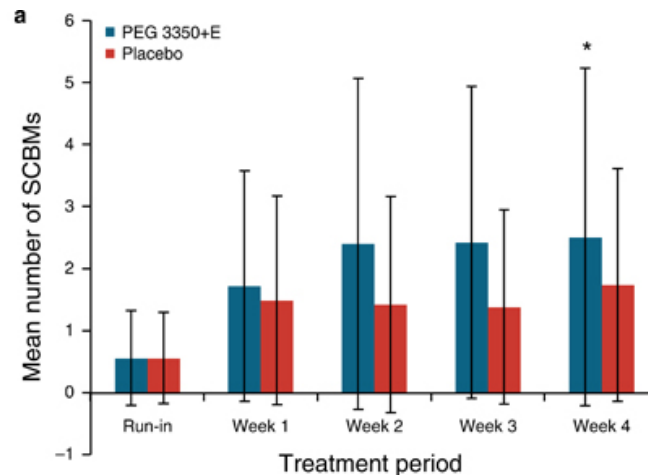
Dipalma JA, et al. *Am J Gastroenterol*. 2007;102(7):1436-1441. Cash BD, et al. *Rev Gastroenterol Disord*. 2007;7(3):116-133



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PEG 3350 for IBS-C

- 139 adult patients with IBS-C
- PEG improved frequency of bowel movements, but not pain



Randomized, Placebo-Controlled Trial of Bisacodyl for Chronic Constipation

- **RCT, 27 centers in UK**

- 368 adults with CC (Rome III), 75% female
- Bisacodyl 10mg/d x 4 wks (n=247) vs placebo (n=121)

	Bisacodyl	Placebo	<i>P</i> value
CSBM/wk (1.1)	5.2 ± 0.3	1.9 ± 0.3	< 0.001
SBM/wk (4)	12-8	unchanged	< 0.001
Global assessment ^a	79.5%	49.6%	< 0.001
QOL			< 0.001

- Bisacodyl superior to placebo for straining, sense of anorectal blockage, and stool form ($p < 0.001$)
- AEs 72% vs 37%, SAEs 6.5% vs 1.7%

^a“Good or “satisfactory”

AE = adverse event; SAE = severe adverse event; CSBM = complete spontaneous bowel movements.
Kamm MA, et al. *Clin Gastroenterol Hepatol*. 2011;9(7):577-583.



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Secretagogues

Drug	Description/Mechanism	FDA Indication(s)	Dosing and Administration
Chloride channel activator			
Lubiprostone	Prostaglandin E1 analogue; activates chloride channel type 2 (CIC-2) on apical surface of intestinal epithelium	IBS-C in women ≥18 years	8 mcg orally twice daily with food and water
		CIC in adults OIC in adults	24 mcg orally twice daily with food and water
Guanylate cyclase-C (GCC) agonists			
	14-amino acid peptide; binds membrane-bound GCC receptor on luminal epithelial cells; may be active throughout the small intestine and colon	IBS-C in adults	290 mcg orally once daily, ≥30 minutes before breakfast
		CIC in adults	145 mcg or 72 mcg orally once daily
		IBS-C / CIC in pediatric patients 7 years and older	145 mcg orally once daily
Plecanatide	16-amino acid peptide; binds to GCC receptor with increased activity in the proximal small intestine	IBS-C in adults	3 mg orally once daily with or without food
		CIC in adults	3 mg orally once daily with or without food

OIC = opioid-induced constipation.

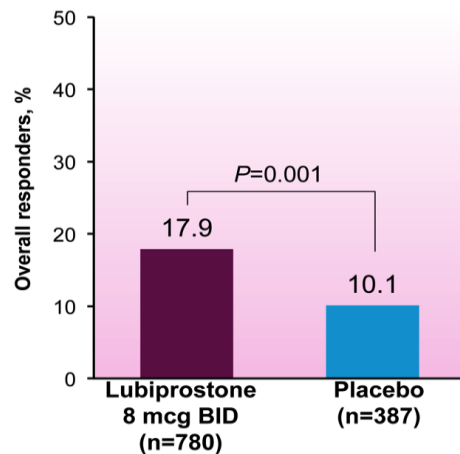
Lacy B, et al. *Am J Gastroenterol*. 2014;109(Suppl 1):S2-26. Thomas RH, Luthin DR. *Pharmacotherapy*. 2015;35:613-630. Shah ED, et al. *Am J Gastroenterol*. 2018;113:329-338. FDA. Accessed April 17, 2026. <https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-1st-drug-children-7-years-and-older-irritable-bowel-syndrome-constipation>.



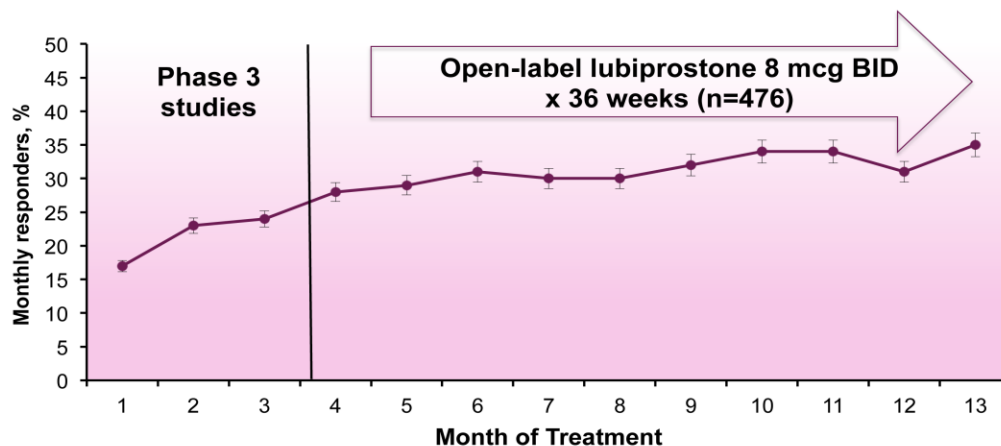
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Lubiprostone for IBS-C

Overall Responders
at 12 Weeks
in Phase 3 Trials^a



Monthly Responder Rates
in Randomized Withdrawal/Extension Studies



FDA Indication: Adult women with IBS-C

^aDefined 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.

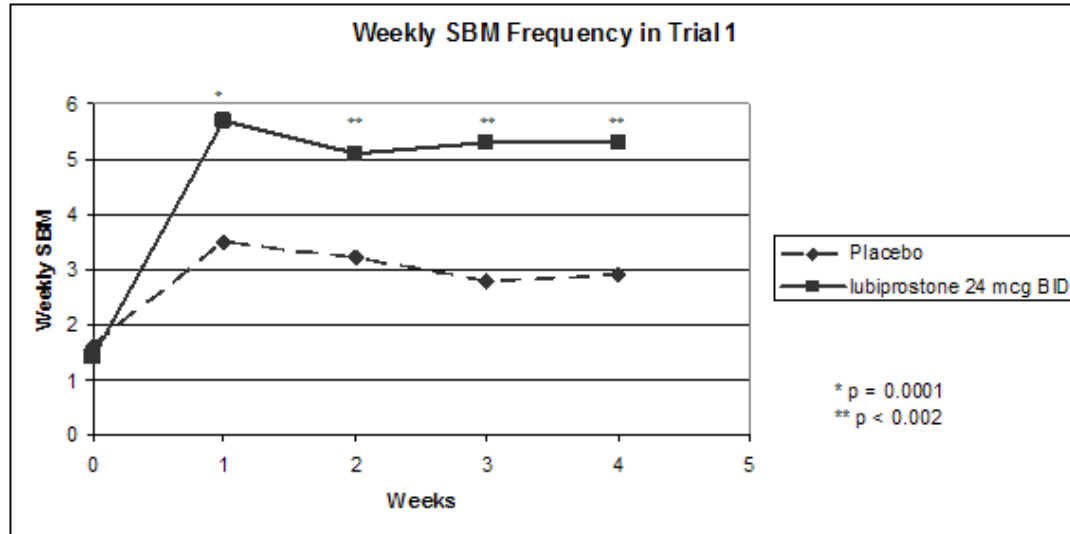
Drossman DA, et al. *Aliment Pharmacol Ther.* 2009;29:329-341. Chey WD, et al. *Aliment Pharmacol Ther.* 2012;35(5):587.



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Lubiprostone for CC: Phase III Data

Lubiprostone 24 mcg BID vs placebo x 4 weeks
242 adults with CC (Modified Rome II)

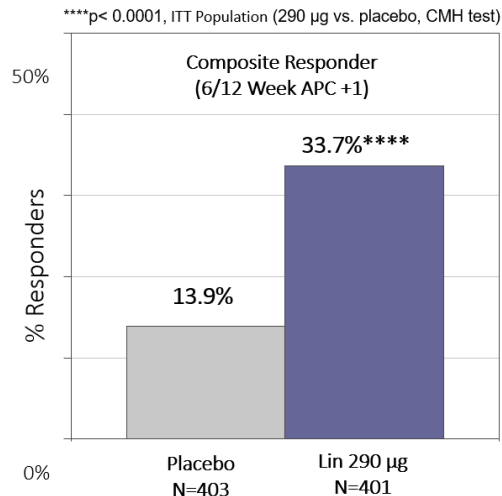


- Most common AE was nausea: Lubiprostone 29%, placebo 3%

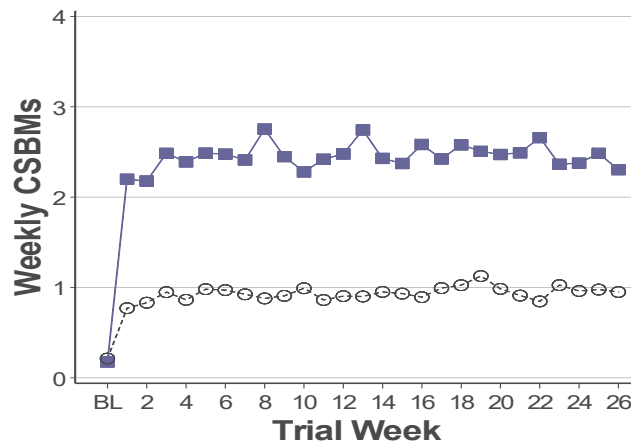
Linaclootide Phase 3 IBS-C Trial

Composite responder, CSBM, and abdominal pain over 26 weeks

Composite

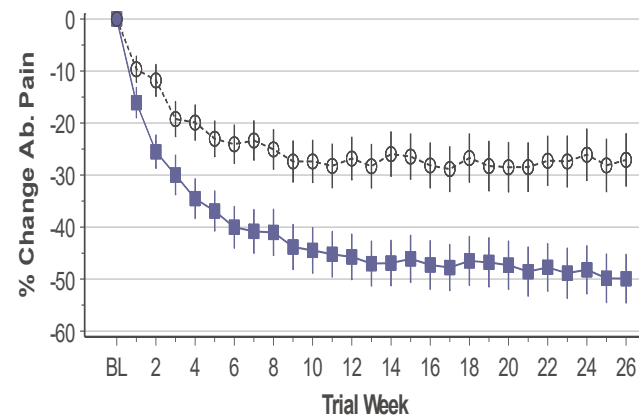


CSBMs



$p < 0.0001$ for each of the 26 Weeks in the Treatment Period for both SBMs and CSBMs

Abd Pain



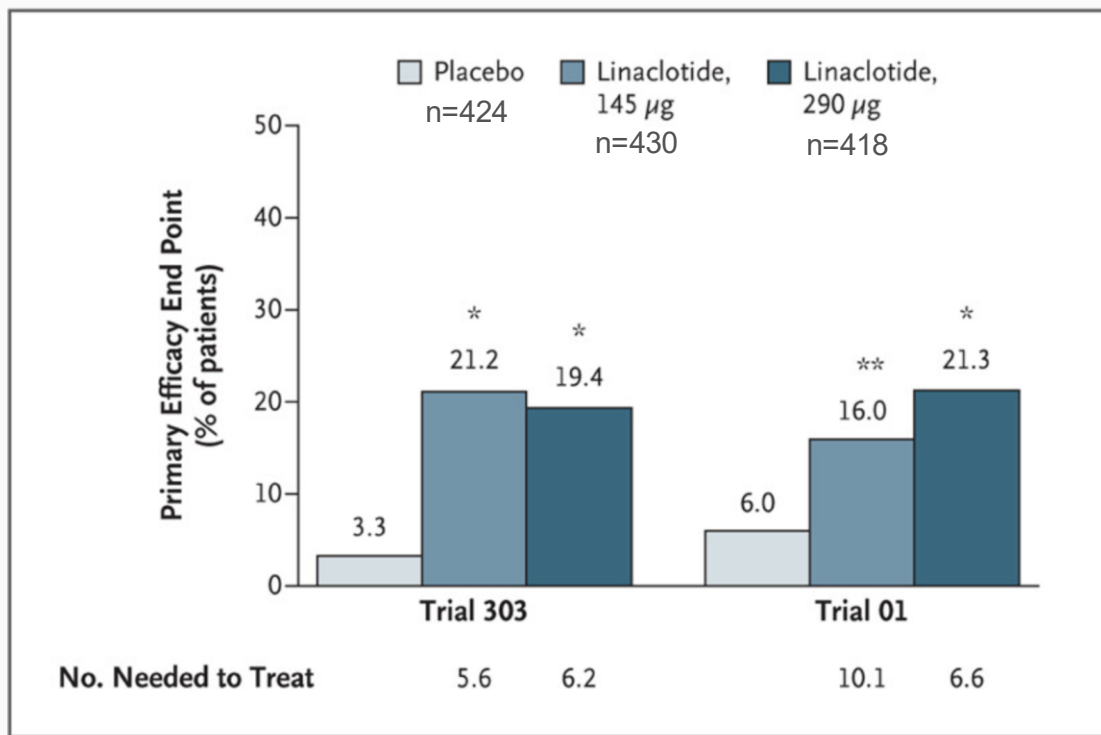
Treatment Groups

■ 290 μ g ○ Placebo



Linaclootide for Chronic Constipation: Primary Results from 2 Phase III Clinical Trials

Responder = ≥ 3 CSBM/wk & increase of ≥ 1 CSBM/wk for $\geq 9/12$ wks



Most common AE: Diarrhea
(14-16% vs 4.7%)
Discontinuation (4% vs. 0.5%)

* $p \leq 0.0012$.

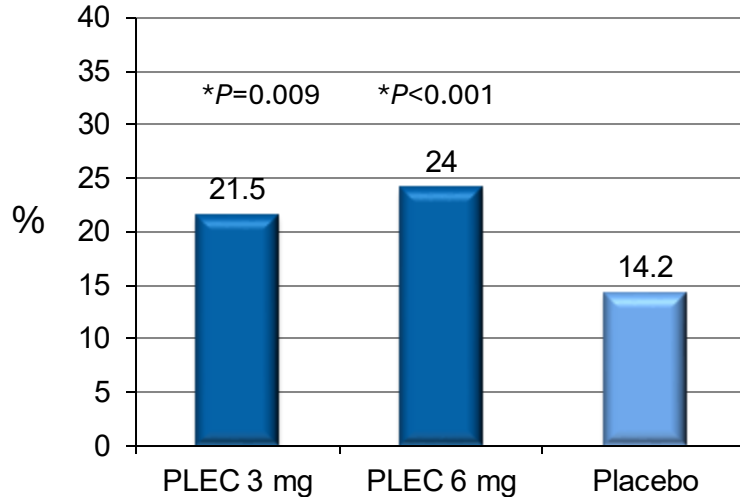
Lembo AJ, et al. *N Engl J Med*. 2011;365(6):527-536.



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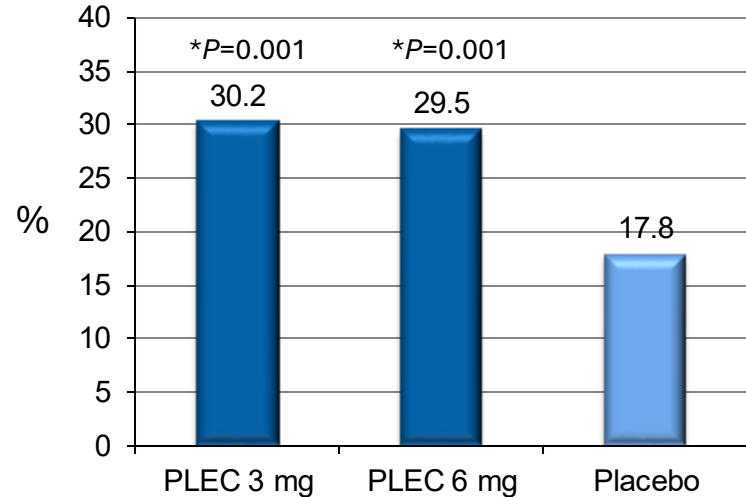
Plecanatide Improved Overall Responder Rate vs Placebo in IBS-C Phase 3 RCTs

Study 1 (12 weeks, n=1135)



Diarrhea: 3.2% (3 mg), 3.7% (6 mg), 1.3% (Placebo)

Study 2 (12 weeks, n=1054)

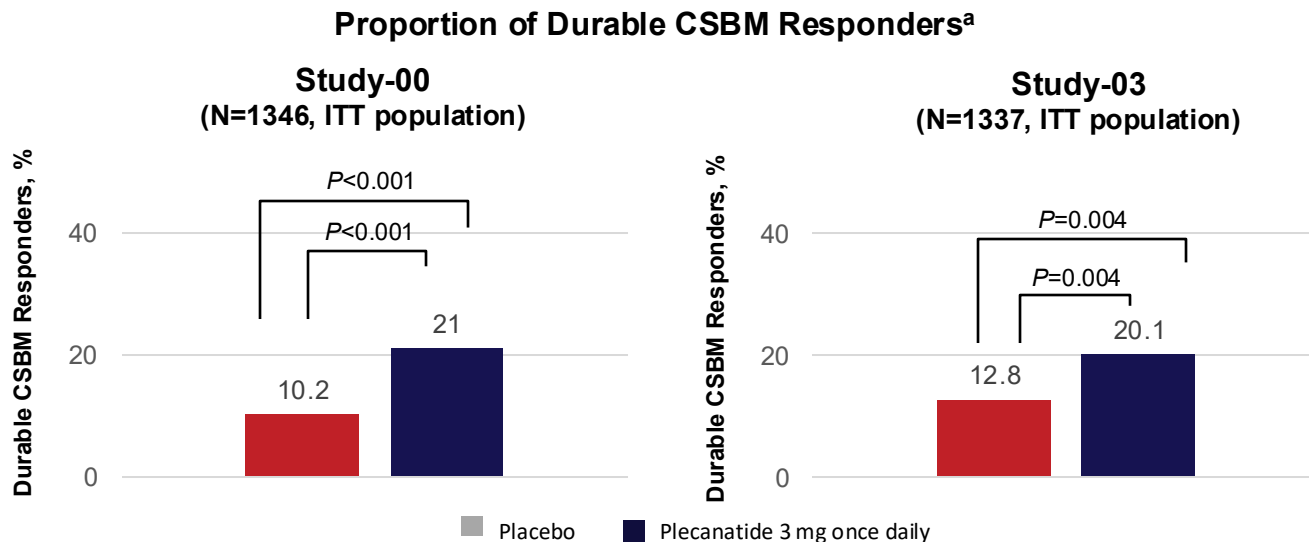


Diarrhea: 5.4% (3 mg), 4.3% (6 mg), 0.6% (Placebo)

- **FDA endpoint:** $\geq 30\%$ abdominal pain reduction + increase ≥ 1 CSBM from baseline; in the same week for ≥ 6 of 12 treatment weeks
- **FDA indication:** Adults with IBS-C



Plecanatide for CIC



Diarrhea: Plecanatide 5%, placebo 1%; ^aDefined as weekly responders for at least 9 of 12 treatment weeks, for at least 3 of the last 4 weeks. Weekly responders had ≥ 3 CSBMs and an increase of ≥ 1 CSBM from baseline.

ITT = intention to treat.

Miner PB Jr, et al. *Am J Gastroenterol*. 2017;112(4):613-621. Miner PB, et al. Presented: at Digestive Disease Week (DDW) 2016; May 21-24, 2016; San Diego, CA. Su1214.



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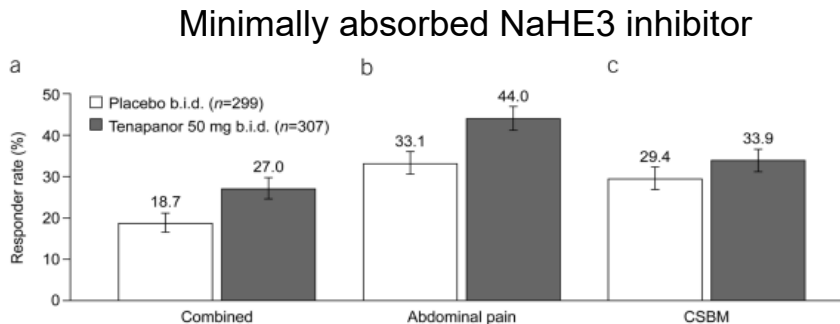
Retainagogue

Drug	Description/Mechanism	FDA Indication(s)	Dosing and Administration
			Sodium Uptake inhibitor
Tenapanor	Inhibitor of the sodium/hydrogen exchanger isoform 3 (NHE3), an antiporter located on the apical surface of enterocytes in the small intestine and colon.	IBS-C in adults	50 mg orally immediately before the morning and evening meals.



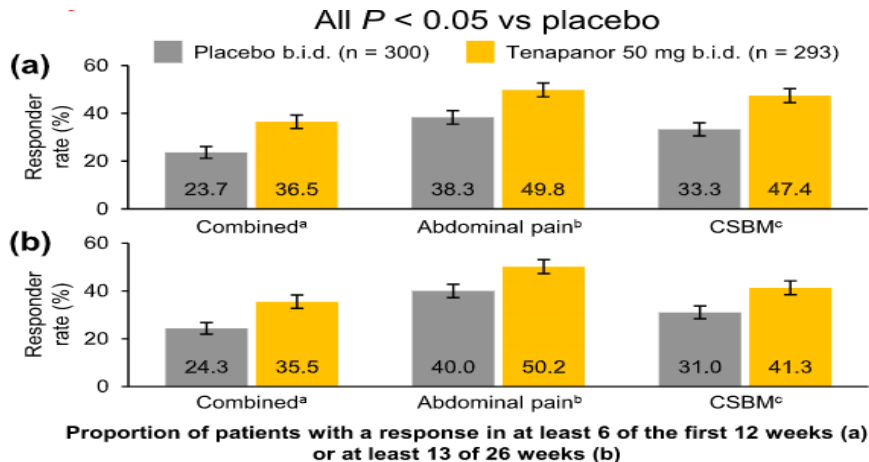
Tenapanor for IBS-C

T3MPO-1 Responder Rates



FDA indication: Adults with IBS-C

T3MPO-2 Responder Rates



Prokinetic Agent



Drug	Description/Mechanism	FDA Indication(s)	Dosing and Administration
Selective serotonin-4 (5-HT ₄) receptor agonist			
Prucalopride	Dihydrobenzofurancarboxamide compound with high affinity for 5-HT ₄ receptors; stimulates GI motility	CIC in adults	2 mg orally once daily, with or without food (1 mg daily in patients with severe renal impairment)

5-HT = 5-hydroxytryptamine.

Camilleri M, et al. *Dig Dis Sci*. 2016;61:2357-2372. De Maeyer JH, et al. *Neurogastroenterol Motil*. 2008;20:99-112. Layer P, et al. *Ther Clin Risk Manag*. 2007;3:107-118.

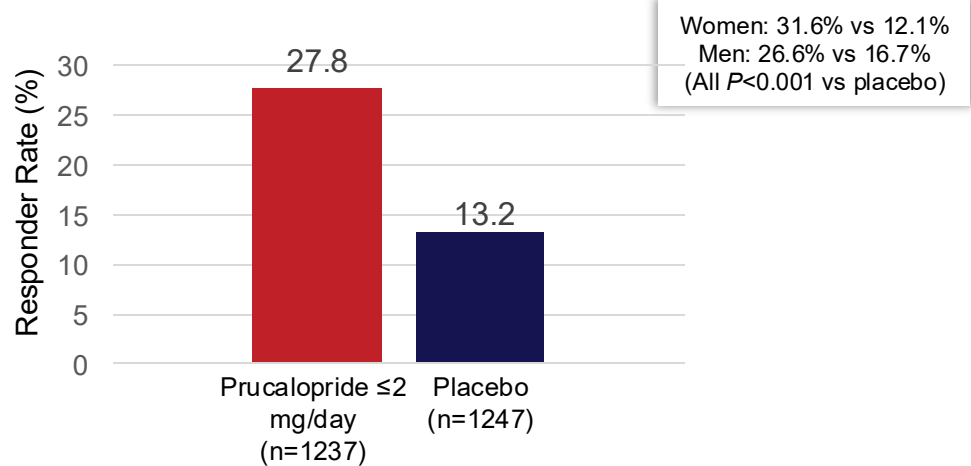


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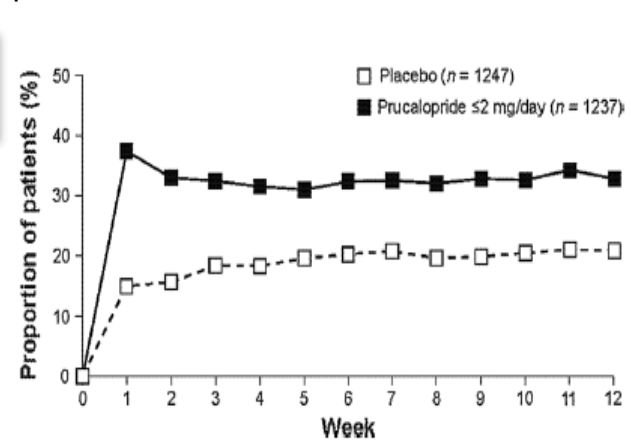
Prucalopride for Chronic Constipation

- Integrated analysis of 6 randomized, placebo-controlled phase 3 and 4 clinical trials
 - A total of 2484 adult patients with ≤ 2 SBMs per week for ≥ 6 months

Overall Response: Patients with Mean Frequency ≥ 3 SCBMs/Week Over 12 Weeks



Proportion of Patients with ≥ 3 SCBMs Each Week



Most common AEs: Headache, abdominal pain, nausea, diarrhea



Key Learning Points

- Secretagogues include lubiprostone, linaclotide, and plecanatide
 - Linaclotide and plecanatide are FDA-approved for treatment of both IBS-C and CIC in adults; linaclotide was recently FDA-approved for treatment of IBS-C and CIC in pediatric patients 7 years and older
- Retainagogue tenapanor is FDA-approved for IBS-C in adults
- The selective serotonin-4 (5-HT₄) receptor agonist prucalopride is FDA-approved for CIC in adults
- Osmotic and stimulant laxatives are recommended for CIC with varying levels of evidence





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Non-Pharmacological Treatments

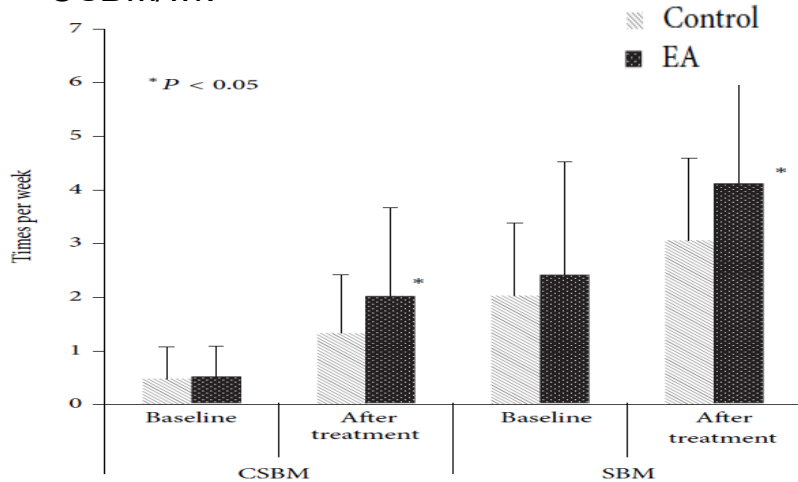
Biofeedback for Dyssynergic Defecation

- Biofeedback: A process in which a person learns to reliably influence body responses through the use of feedback cues, ultimately leading to the correction of maladaptive behaviors
- Types of biofeedback
 - Pressure (perineometry)
 - Electromyography (EMG)
 - Sensory (rectal balloon retraining)
 - Pelvic floor muscle contraction indicator devices
 - Real time ultrasound

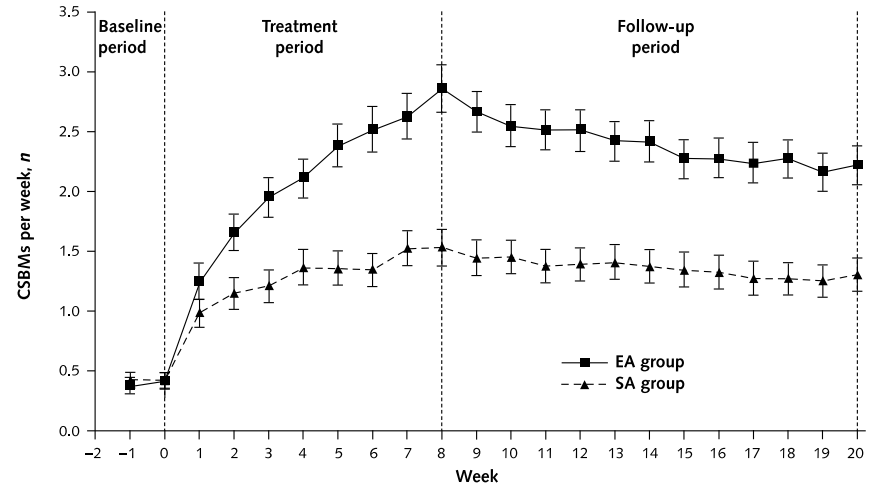


Acupuncture for Functional Constipation

- 67 patients with functional constipation received 28 deep or shallow electro-acupuncture treatments over 8 wks
- Primary outcome responder definition: Rate of CSBM/wk
- 1057 patients with functional constipation received 28 true or sham electro-acupuncture treatments over 8 wks at 15 Chinese centers
- Primary outcome responder definition: Rate of CSBM/wk



BSS & PAC-QOL improved from baseline but not between groups; no SAEs



Minimal AEs

PAC-QOL = Patient Assessment of Constipation Quality of Life; BSS = Bristol Stool Scale.

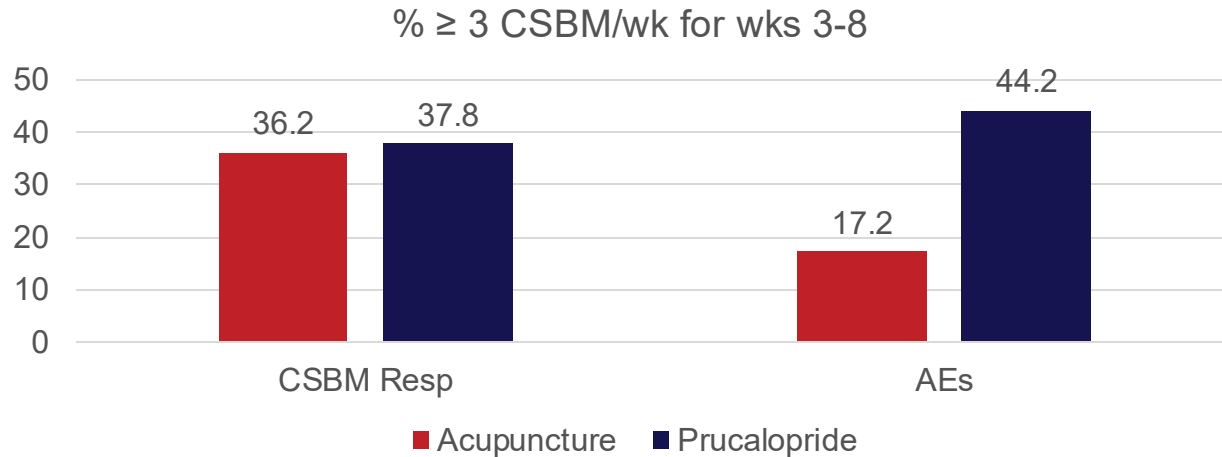
Da N, et al. *Evid Based Complement Alternat Med*. 2015;2015:670963. Liu Z, et al. *Ann Int Med*. 2016;165(11):761.



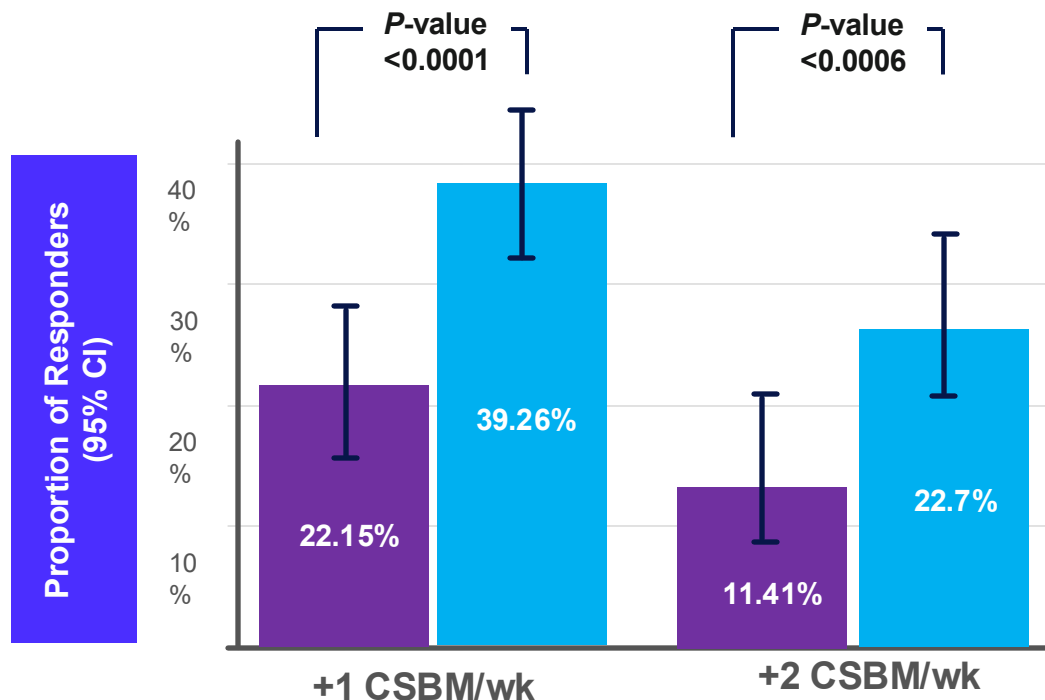
Practical Updates
in Primary Care

Electroacupuncture vs Prucalopride: RCT in Patients with Severe Chronic Constipation

- 560 pts with SCC (<2 CSBM/wk) randomized to 28 sessions of EA over 8 weeks vs prucalopride 2 mg qd x 32 wks
- Primary outcome: Proportion with ≥ 3 CSBM/wk for wks 3-8



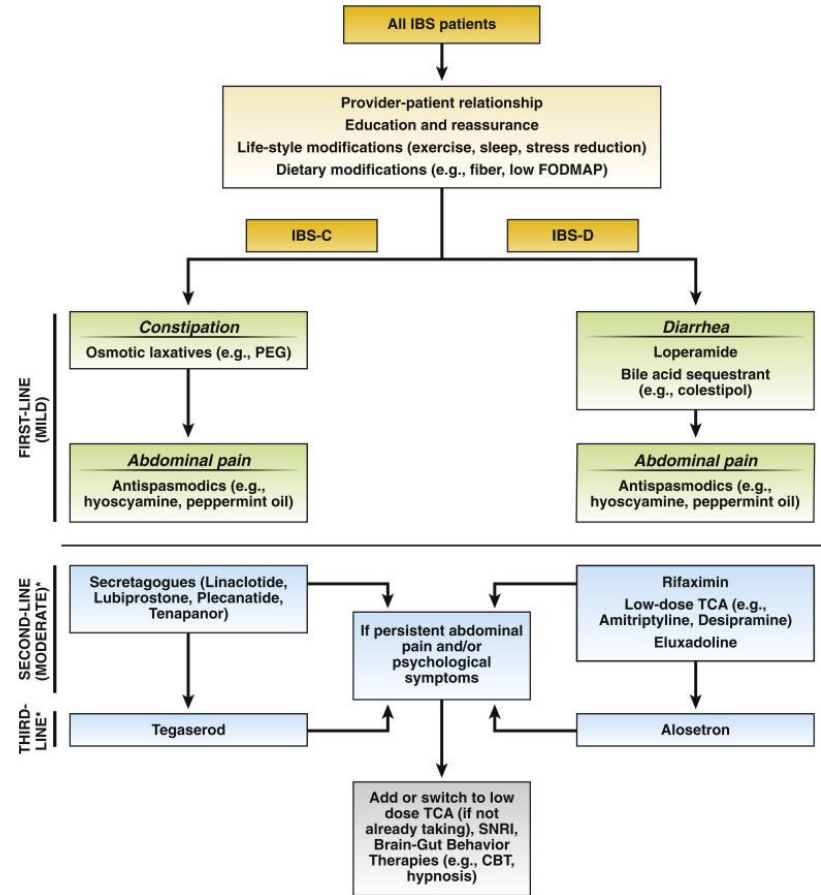
Vibrating Capsule for CIC



- Key point: VC led to significant improvements in stool frequency & other constipation symptoms vs sham capsule



Clinical Decision Support Tool: IBS Treatment



*Selection of the medication should be based on the clinical features and needs of the patient.

CBT = cognitive behavioral therapy; SNRI = serotonin-norepinephrine reuptake inhibitor.

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

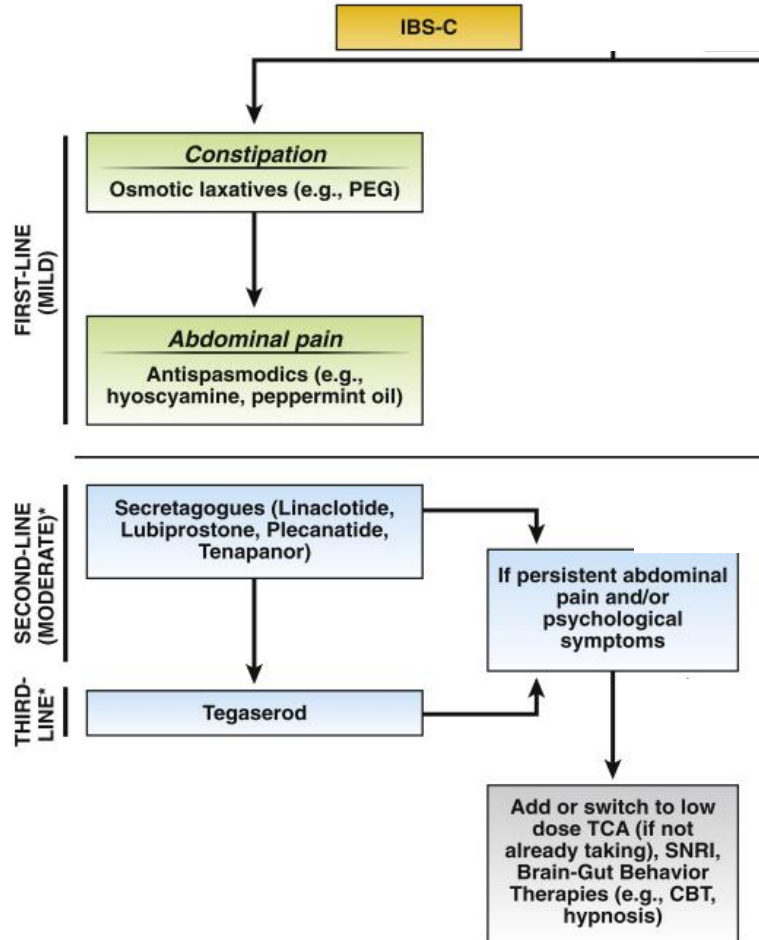


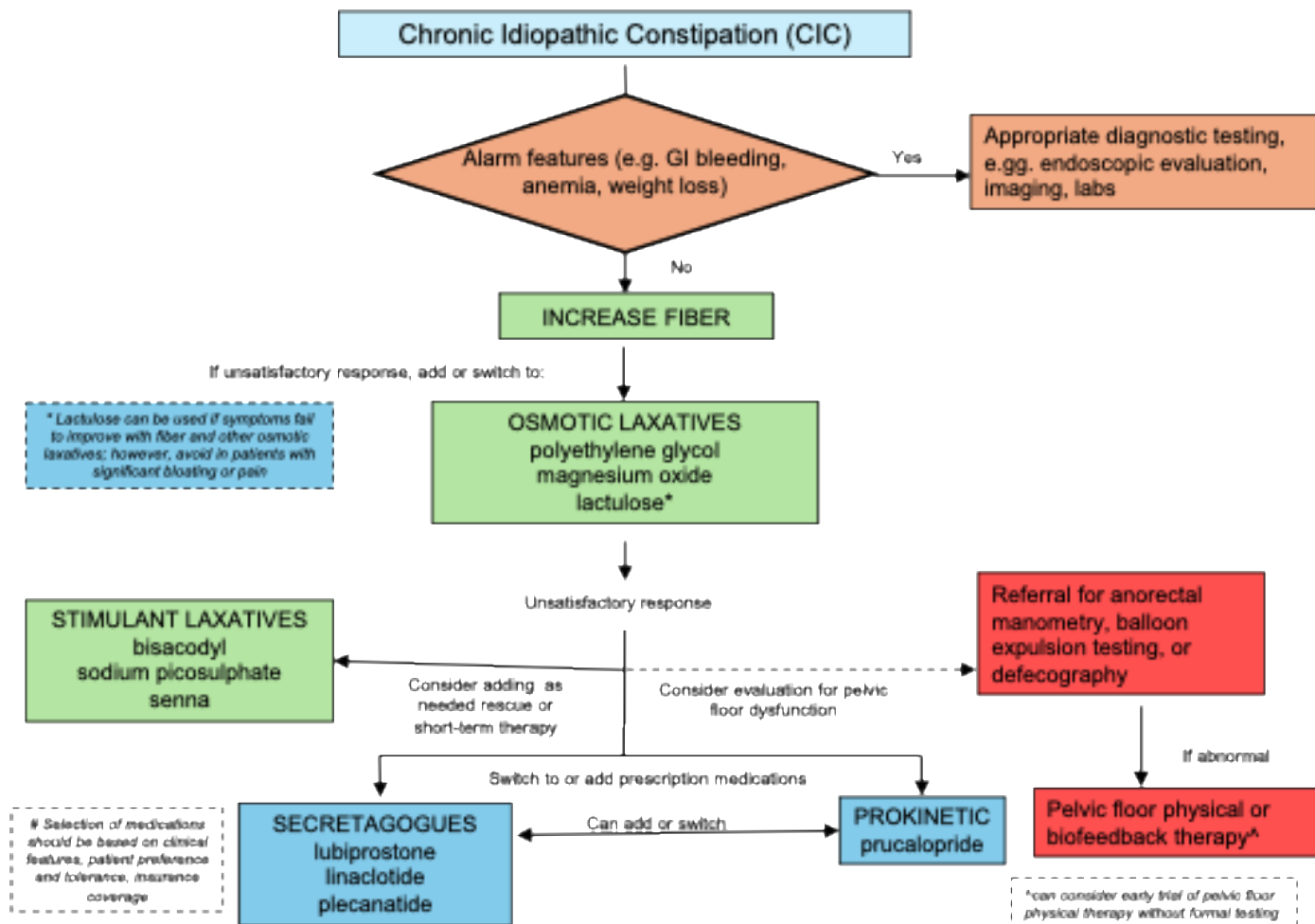
Practical Updates
in Primary Care

First-line
(mild)

Second-line
(moderate)

Third-line
(severe)







Practical Updates
in Primary Care

Patient-Centered Care in IBS-C and CIC

Overcoming Barriers to Equitable Access and Care

- Consider trauma-informed history when delivering appropriate care for patients with IBS-C and CIC
- Keep the conversation positive; you can make a positive diagnosis and rule out significant organic disease, and there are many treatment options to improve symptoms and function
- Recognize complex interactions between abdominal symptoms, mental health, and function
- Understand cultural cues and differences
- Validate patients' symptoms and the impact on their lives - - -> goal is to improve quality of life



Incorporating Patient Preferences in Treatment Decision Making

- Understand patient understanding of and preferences for treatments and medications: Both OTC and prescription
- Always review ALL medications patients are taking
- Take a detailed dietary history, offer resources
- Offer frequent follow up visits, portal messages
- Consider a multi-disciplinary approach to care



Multi-Disciplinary Care in IBS-C and CIC

- Primary care
- Gastroenterology
- Psychology/gastropsychology
- Nutrition
- Social work
- Pharmacy



Key Learning Points

- IBS-C and CIC are prevalent conditions that can be accurately diagnosed in primary care practices
 - IBS-C is distinguished from CIC by recurrent abdominal pain (Rome IV criteria)
- Patients with these conditions deserve appropriate consideration and time during visits, with appropriate follow-up and coordination of care
- Diagnostic testing should be limited when evaluating patients for IBS-C and CIC
- Primary care clinicians can institute initial therapies for treatment of IBS-C and CIC, and offer appropriate dietary guidance

