Irritable Bowel Syndrome and Chronic Idiopathic Constipation

A MANAGED CARE GUIDE TO OPTIMIZE PATIENT CARE AND OUTCOMES

Managed Care | LEARNING NETWORK | CME

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Faculty Disclosures

- **Anthony Lembo, MD**: Consultant—Johnson & Johnson, GSK, Takeda Pharmaceuticals, Atmo, Ironwood, Vibrant America, Ardelyx Inc; Data Safety and Monitoring Board—Ironwood Pharmaceuticals; Stock—Johnson & Johnson, BMS
- **Catherine E. Cooke, PharmD, MS, BCPS, PAHM** has disclosed no relevant financial relationship with any ineligible company (commercial interest)

This presentation will discuss the unapproved use of drugs for the treatment of IBS.

IBS = irritable bowel syndrome.

Program Information

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Learning Objectives

- Describe the diagnostic complexity of IBS and CIC and the socioeconomic impact of these conditions due to diagnostic delay, misdiagnosis, and/or suboptimal management
- Assess the safety/efficacy data and mechanisms of action of pharmacologic therapies for the treatment of IBS-C, IBS-D, and CIC
- Implement evidence-based and guideline-directed managed care policies for IBS and CIC that prioritize patient-centered and value-based care

CIC = chronic idiopathic constipation; IBS-C = IBS with predominant constipation; IBS-D = IBS with predominant diarrhea.

Modern Diagnosis and Management Strategies for IBS-C and CIC

Anthony Lembo, MD

Rome IV Criteria for IBS

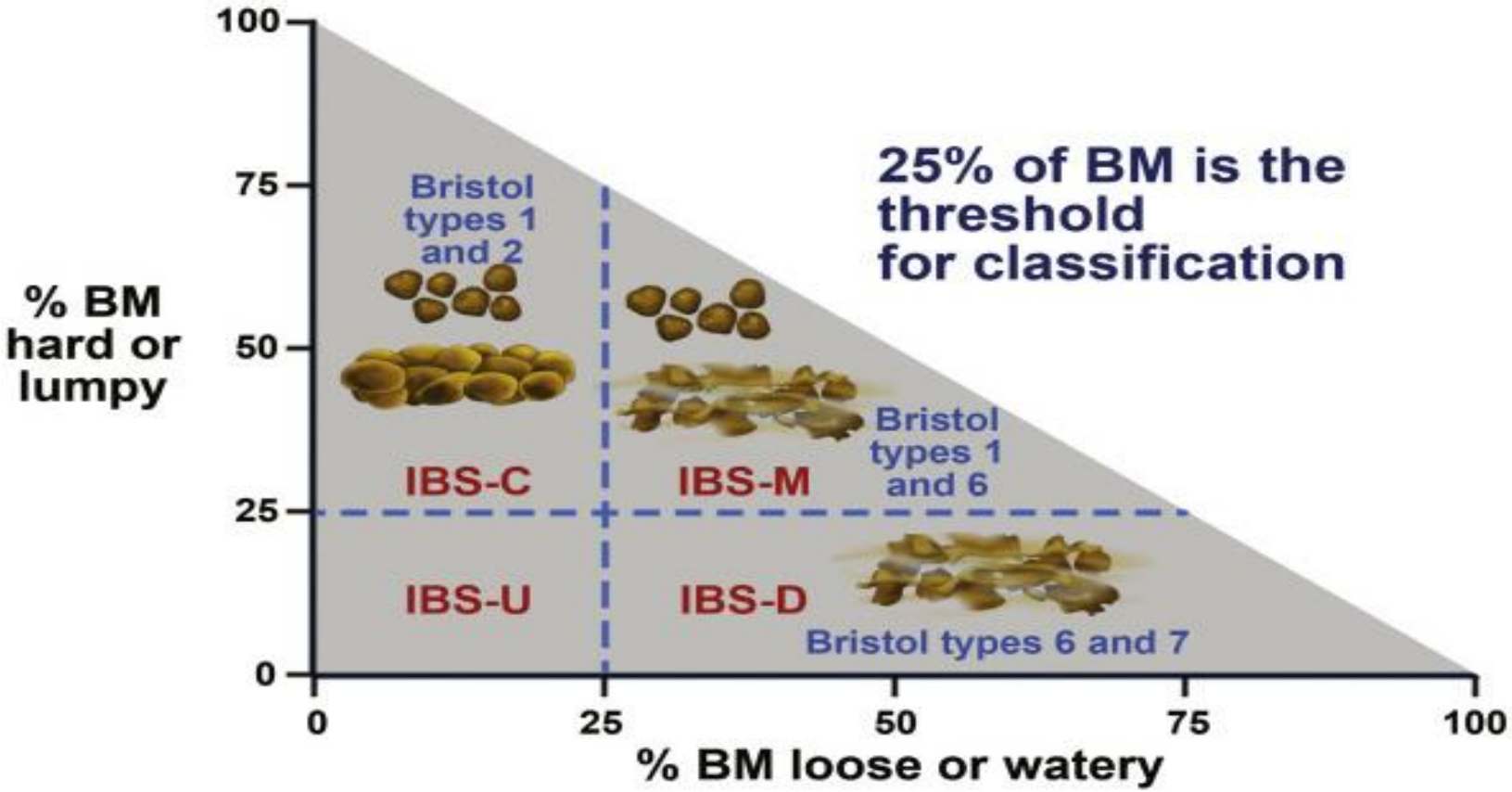
Recurrent abdominal pain
at least 1 day/week in the last 3 months
associated with 2 or more of the following

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

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

Lacy BE, et al. *Gastroenterology*. 2016;150(6):1393-1407. Rome Foundation. Accessed May 9, 2025. https://theromefoundation.org/rome-iv/rome-iv-criteria/.

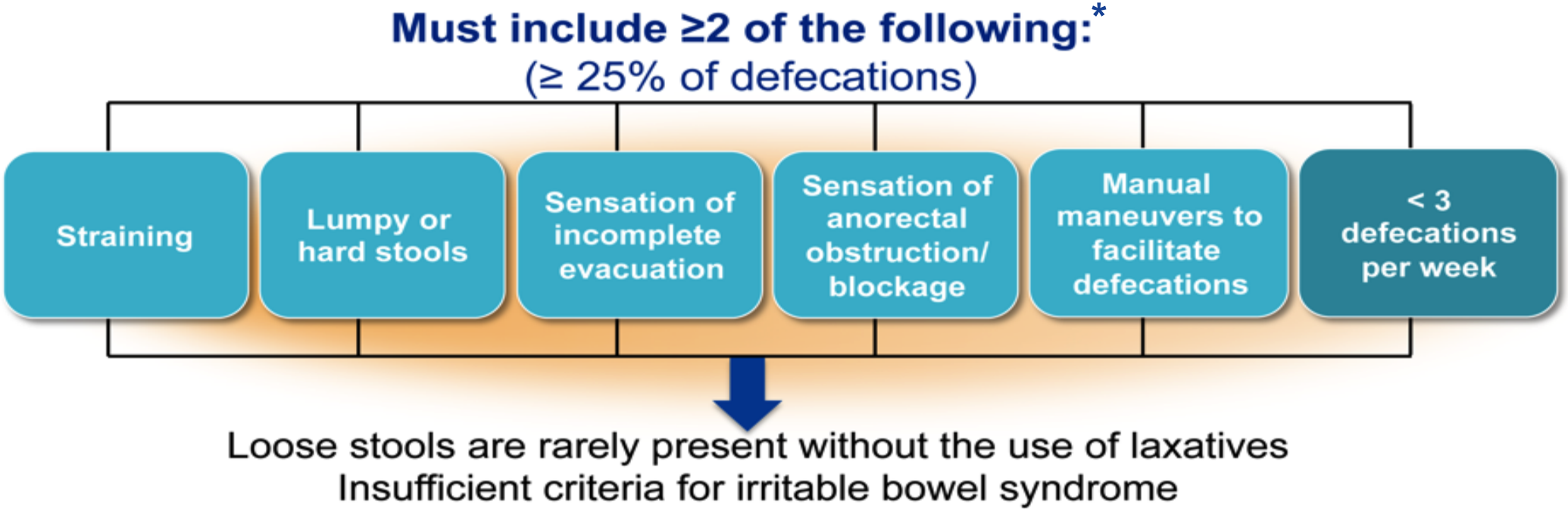
IBS-Subtypes: Stool Form Is the Differentiating Factor



BM = bowel movement.

Menees S, et al. *F100Res*. 2018;7:F1000 Faculty Rev-1029.

Rome IV Diagnostic Criteria for Functional Constipation

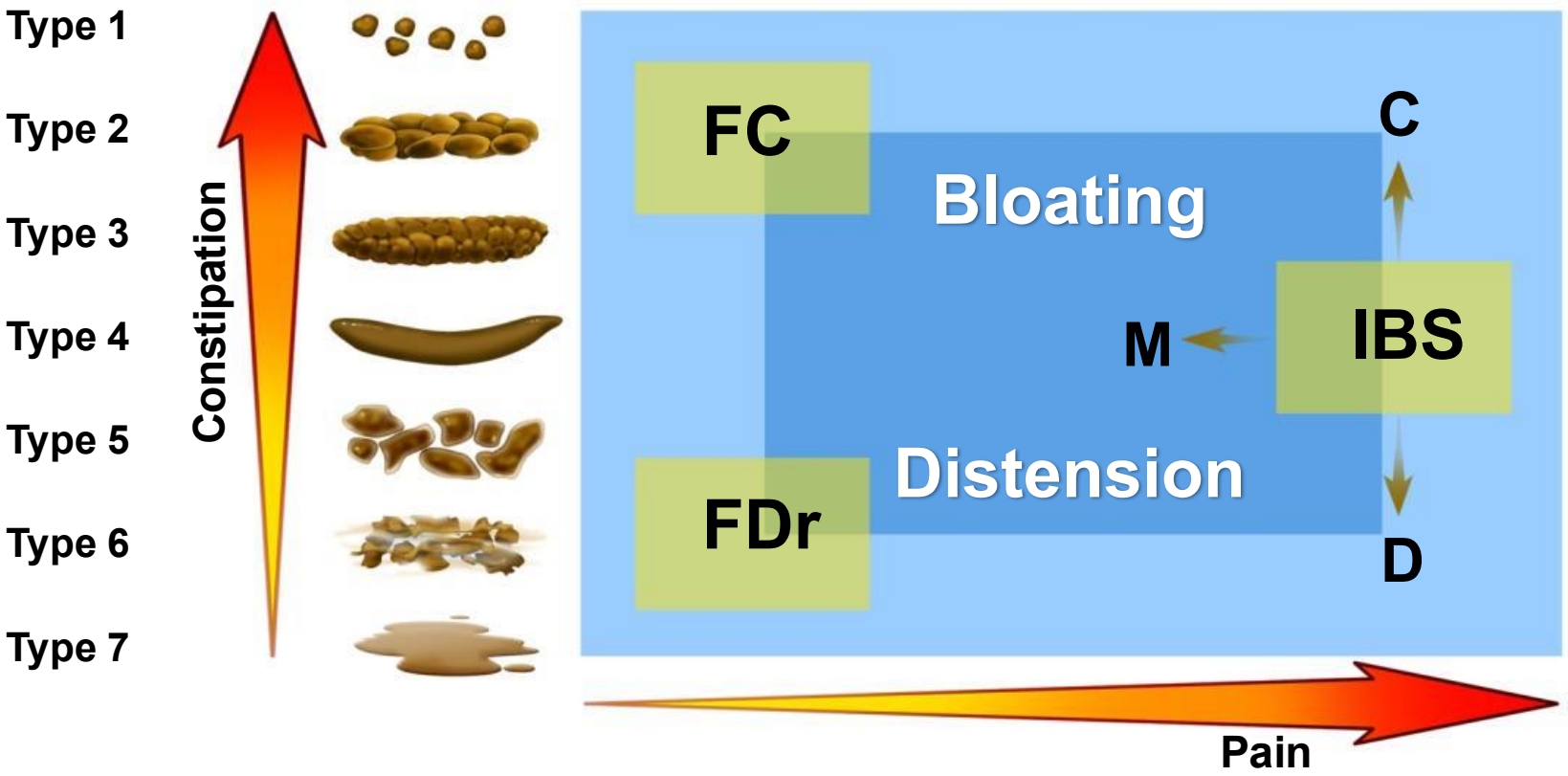


Abdominal pain is the major differentiating feature from IBS

***Criteria fulfilled for the last 3 months with symptom onset ≥6 months prior to diagnosis.**

Mearin F, et al. *Gastroenterology*. 2016:S0016-5085(16)00222-5.

Overlap in Bowel Disorders (Rome IV)



FC = functional constipation; FDr = functional diarrhea; C = constipation; D = diarrhea; M = mixed.

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

Worldwide Prevalence of Functional Constipation

Table 2. Prevalence Rates (% and 95% CI) for 5 Selected Major Functional Gastrointestinal Diagnoses (Rome IV)– for Any FGID (26 Countries) and Rome III IBS (14 Countries) in the Internet Survey and for All 9 Countries in the Household Survey

	N	Any FGID	Functional Dyspepsia	IBS (Rome IV)	IBS (Rome III) (N=14)	Functional Constipation	Functional Diarrhea	Functional bloating/distention
INTERNET								
Argentina	2057	43.9 (41.8–46.1)	6.9 (5.8–8.0)	3.5 (2.7–4.3)	N/A	12.2 (10.7–13.6)	.3 (5.2–7.3)	5.2 (4.2–6.1)
Australia	2036	37.6 (35.5–39.7)	7.2 (6.0–8.3)	3.5 (2.7–4.3)	N/A	7.7 (6.6–8.9)	.1 (4.1–6.0)	4.2 (3.3–5.0)
Belgium	2021	35.6 (33.5–37.7)	5.0 (4.0–5.9)	3.3 (2.5–4.0)	7.5 (6.4–8.7)	11.0 (9.7–12.4)	.0 (3.2–4.9)	2.4 (1.7–3.0)
Brazil	2004	43.6 (41.4–45.8)	10.6 (9.2–11.9)	4.7 (3.8–5.6)	8.3 (7.1–9.5)	11.9 (10.5–13.3)	.8 (3.9–5.7)	2.7 (2.0–3.5)
Canada	2029	41.3 (39.1–43.4)	7.8 (6.7–9.0)	4.2 (3.3–5.1)	10.12 (8.8–11.4)	9.3 (8.0–10.5)	.6 (6.4–8.7)	3.3 (2.5–4.1)
China	2914	34.4 (32.7–36.1)	5.9 (5.0–6.7)	2.3 (1.8–2.9)	7.4 (6.5–8.4)	10.6 (9.5–11.7)	.6 (4.8–6.5)	0.7 (0.4–1.0)
Colombia	2007	42.5 (40.3–44.7)	7.2 (6.0–8.3)	4.3 (3.4–5.2)	N/A	12.8 (11.3–14.2)	.1 (3.2–5.0)	4.5 (3.6–5.4)
Egypt	2020	47.7 (45.5–49.9)	12.3 (10.8–13.7)	7.6 (6.4–8.7)	14.0 (12.4–15.59)	14.1 (12.6–15.6)	.2 (1.6–2.9)	3.2 (2.4–3.9)
France	2019	47.3 (45.1–49.5)	8.5 (7.3–9.7)	4.2 (3.3–5.0)	9.8 (8.5–11.1)	14.5 (12.6–16.1)	.1 (5.1–7.2)	6.0 (5.0–7.0)
Germany	2020	36.5 (34.4–38.6)	6.9 (5.8–8.0)	3.7 (2.8–4.5)	11.1 (9.8–12.5)	9.8 (7.9–10.5)	.4 (4.4–6.4)	2.8 (2.1–3.5)
Holland	2008	30.6 (28.6–32.6)	4.1 (3.2–5.0)	3.8 (2.9–4.6)	9.7 (8.4–11.0)	9.2 (7.9–10.5)	.2 (2.5–4.0)	1.5 (1.0–2.0)
Israel	2012	36.4 (34.3–38.5)	3.6 (2.8–4.4)	3.2 (2.5–4.0)	12.8 (11.4–14.3)	13.1 (11.6–14.6)	.4 (1.8–3.1)	2.1 (1.5–2.7)
Italy	2063	47.2 (45.1–49.4)	9.1 (7.8–10.3)	5.0 (4.1–5.9)	N/A	14.4 (12.7–15.8)	.2 (2.5–4.0)	8.2 (7.1–9.4)
Japan	2504	39.4 (37.5–41.3)	2.4 (1.8–3.0)	2.2 (1.6–2.7)	9.3 (8.2–10.4)	16.6 (15.1–18.0)	.2 (4.3–6.0)	1.2 (0.8–1.6)
South Korea	2022	39.3 (37.2–41.4)	4.9 (4.0–5.9)	4.7 (3.8–5.6)	N/A	12.5 (11.0–13.9)	.8 (4.8–6.8)	2.1 (1.5–2.8)
Mexico	2001	40.2 (38.0–42.3)	6.6 (5.5–7.7)	4.0 (3.2–4.9)	12.6 (11.1–14.0)	11.5 10.1–12.9)	.4 (3.5–5.3)	3.4 (2.6–4.2)
Poland	2057	46.0 (43.9–48.2)	8.3 (7.1–9.5)	4.4 (3.5–5.3)	N/A	14.2 (12.7–15.8)	.5 (3.6–5.4)	5.3 (4.3–6.3)
Romania	2049	40.1 (38.1–42.2)	7.4 (6.3–8.6)	3.5 (2.7–4.3)	N/A	11.7 (10.3–13.1)	.6 (1.9–3.3)	6.7 (5.6–7.8)
Russia	2000	44.6 (42.4–46.8)	10.3 (9.0–11.6)	5.9 (4.8–6.9)	16.5 (14.9–18.1)	11.6 (10.1–13.0)	.1 (6.0–8.2)	2.6 (1.9–3.2)
Singapore	2047	31.1 (29.1–33.1)	5.9 (4.9–6.9)	1.3 (0.8–1.8)	4.3 (3.4–5.1)	9.5 (8.2–10.7)	.3 (3.4–5.1)	3.6 (2.8–4.4)
South Africa	2021	45.2 (43.0–47.3)	11.0 (9.7–12.4)	5.9 (4.9–7.0)	N/A	11.1 (9.7–12.5)	.1 (4.2–6.1)	4.2 (3.3–5.1)

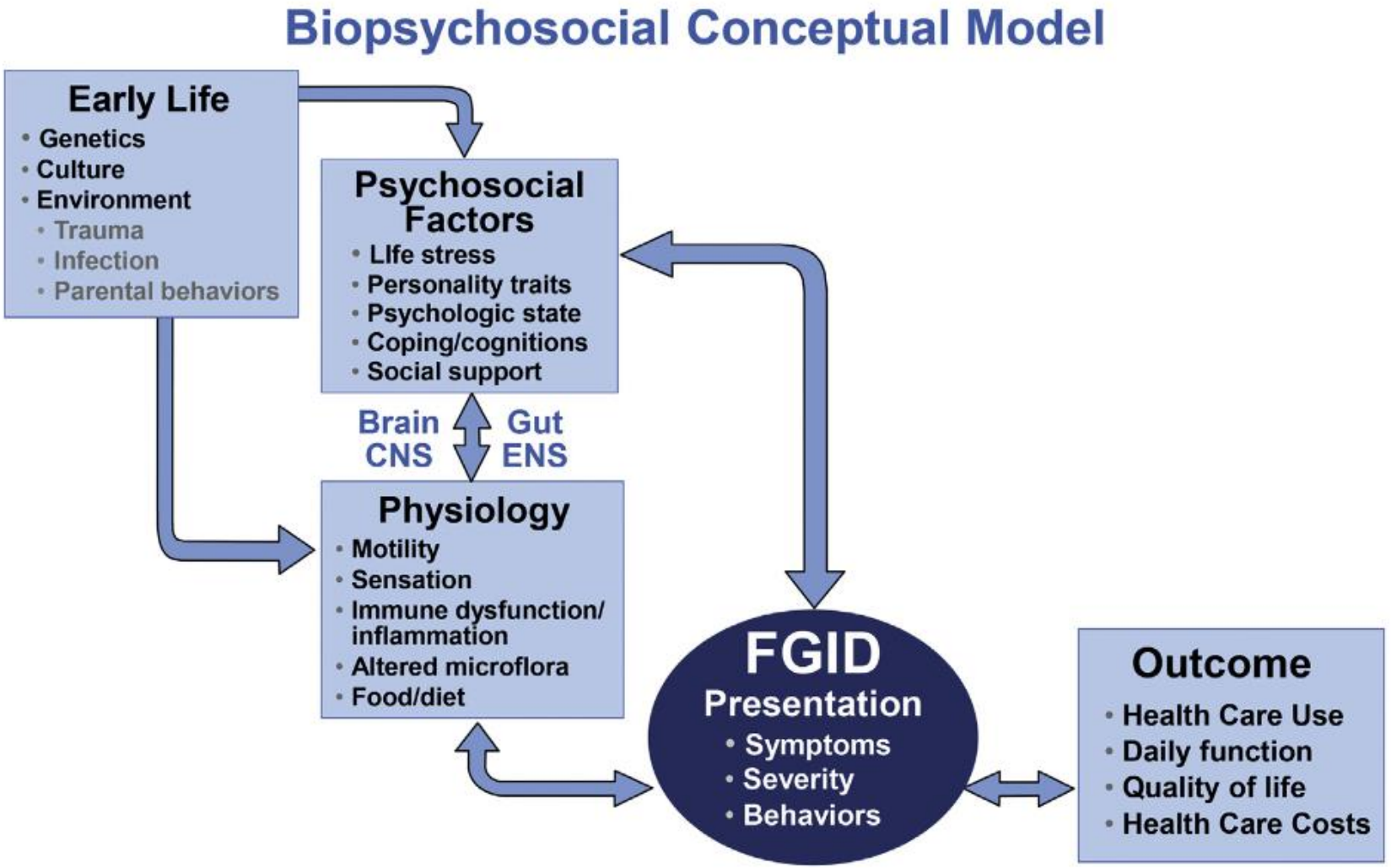
Functional Constipation

IBS

CI = confidence interval; FGID = functional gastrointestinal disorder.

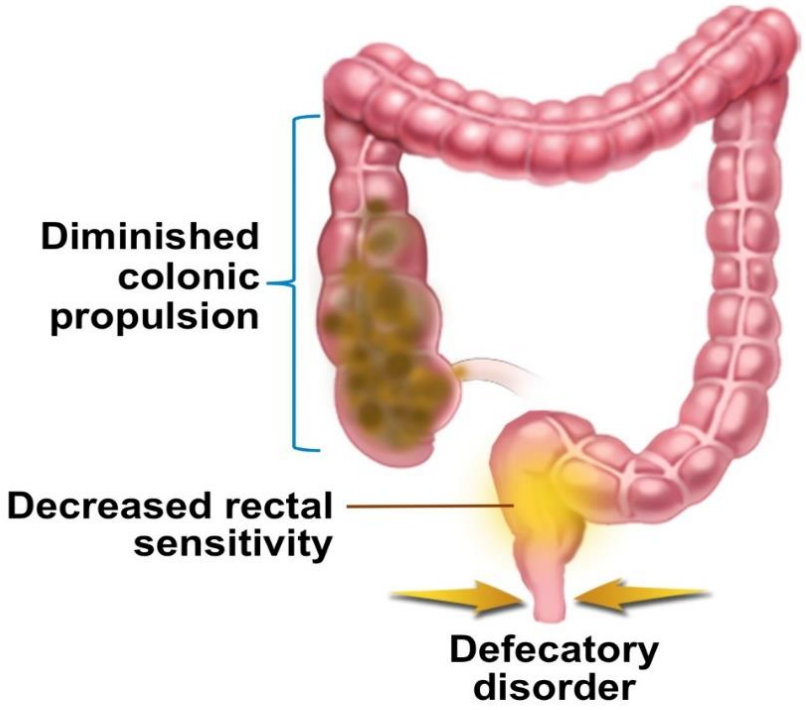
Sperber AD, et al. *Gastroenterology*. 2021;160(1):99-114.e3. Camilleri M, et al. *Nat Rev Dis Primers.* 2017;3:17095.

Pathophysiology of IBS

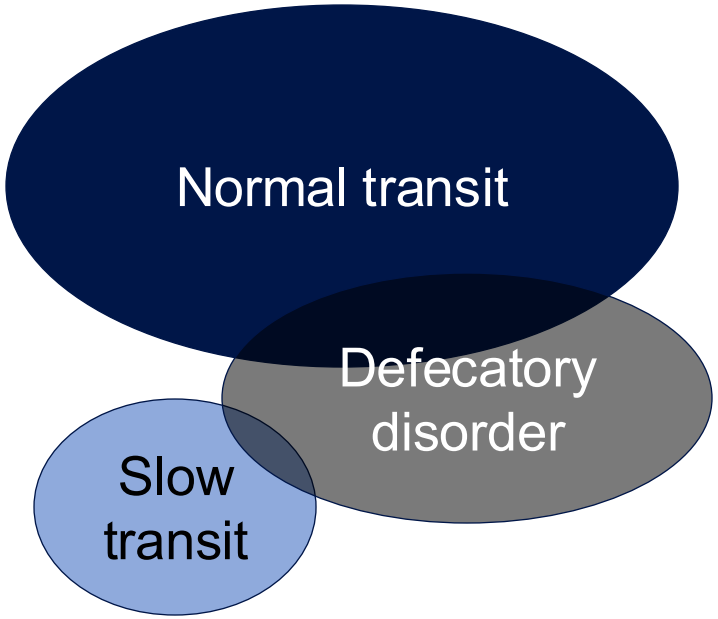


CNS = central nervous system; ENS = enteric nervous system.
Drossman DA. *Gastroenterology*. 2016:S0016-5085(16)00223-7.

Pathophysiology of Functional Constipation

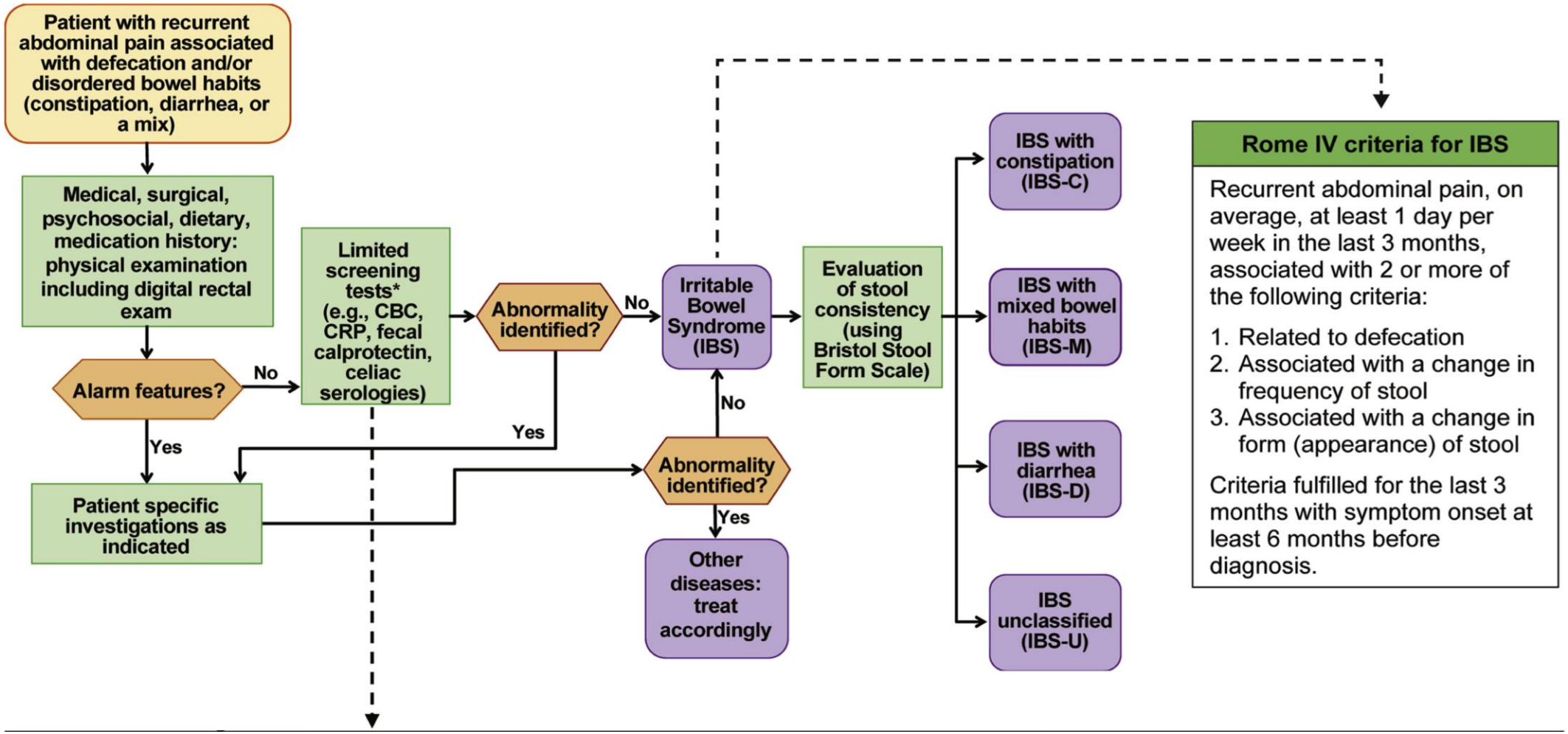


Subtypes of Constipation



Schiller LR. *Aliment Pharmacol Ther.* 2001;15(6):749-763. Mertz H, et al. *Am J Gastroenterol*. 1999;94(3):609-615.

Diagnostic Algorithm for IBS



***Limited screening tests.**

Chang L. *Gastroenterology*. 2021;161(4):1092-1098.

Diagnostic Testing for Patients with Symptoms Suggestive of IBS

Tests Recommended

- CBC, TSH
- CRP or fecal calprotectin
- IBS-D
  - IgA TtG ± quantitative IgA
  - When colonoscopy performed, obtain random biopsies
  - Fecal bile acids or serum 7αC4 where available
  - Giardia antigen
- IBS-C
  - Consider KUB r/o fecal loading (IBS-M)
  - Anorectal physiology testing if symptoms suggest pelvic floor dysfunction (IBS-C)

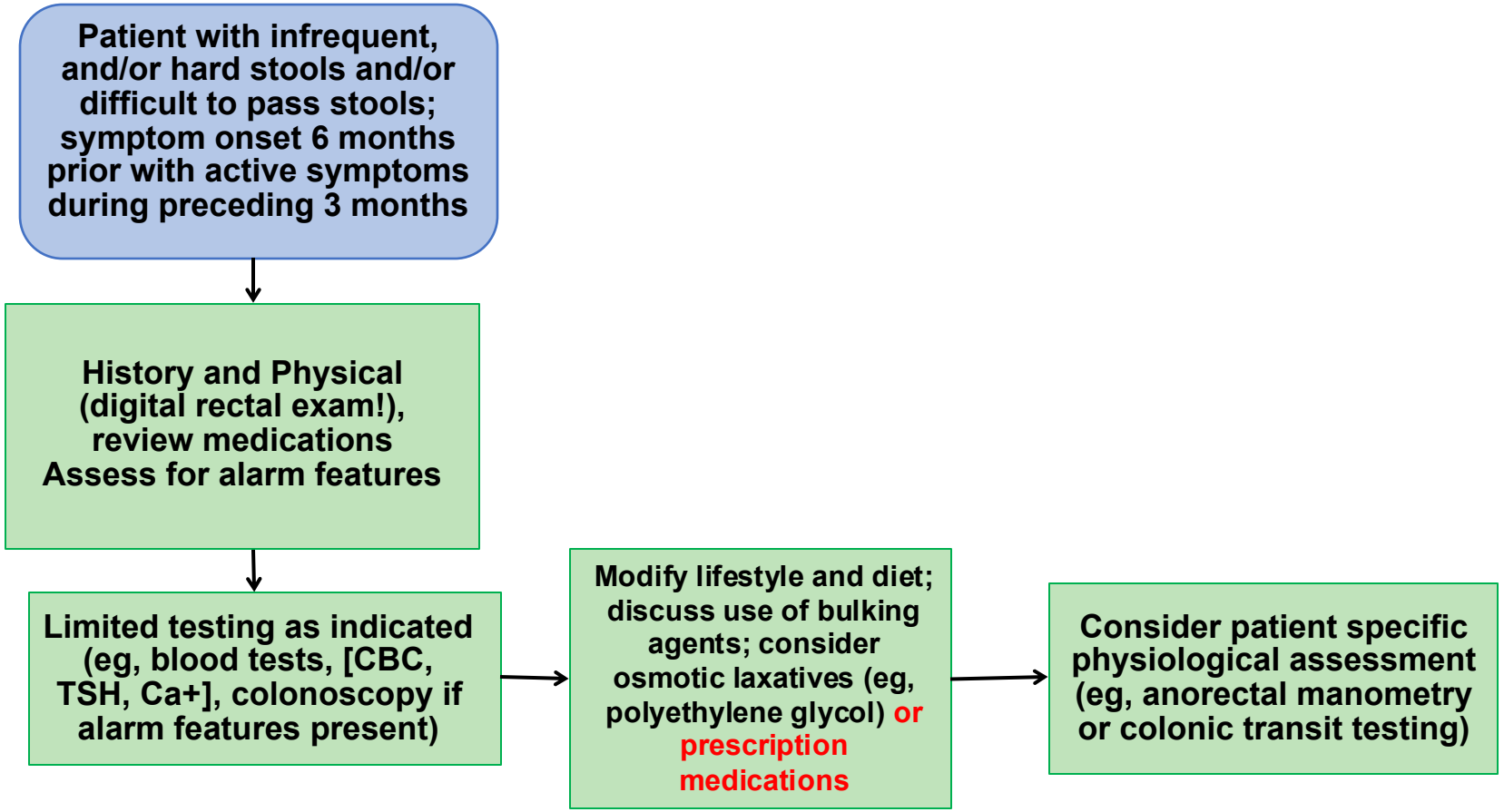
Tests Not Recommended Routinely

- Stool testing including O&P (other than giardia)
  - With no travel to high-risk areas
- Colonoscopy <45 years of age
- Food allergy or sensitivity testing
- Lactulose or glucose breath testing
- Imaging: X-ray, ultrasound, CT, MRI

CRP = C-reactive protein; Ttg = tissue transglutaminase; IgA = immunoglobulin A; KUB = kidney, ureter, bladder; r/o = rule out; O&P = ova and parasite; CT = computed tomography; MRI = magnetic resonance imaging.

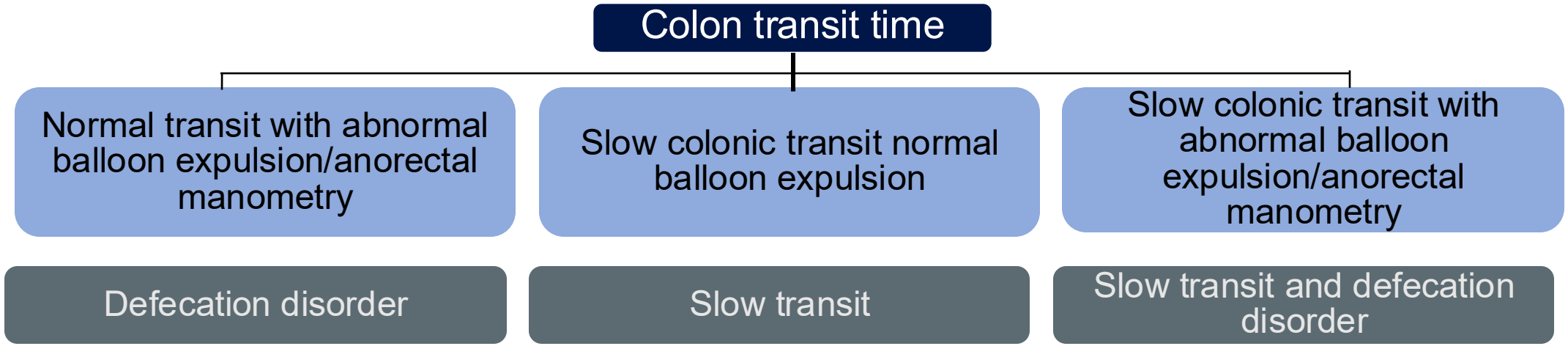
Chey WD, et al. *JAMA*. 2015;313(9):949-958. Smalley W, et al. *Gastroenterology*. 2019;157(3):851-854. Lacy BE, et al. *Am J Gastroenterol*. 2021;116(1):17-44. Moayyedi P, et al. *J Can Assoc Gastroenterol*. 2019;2(1):6-29. Vasant DH, et al. *Gut*. 2021;70(7):1214-1240.

Diagnostic Algorithm for Chronic Constipation



Tests for Chronic Constipation

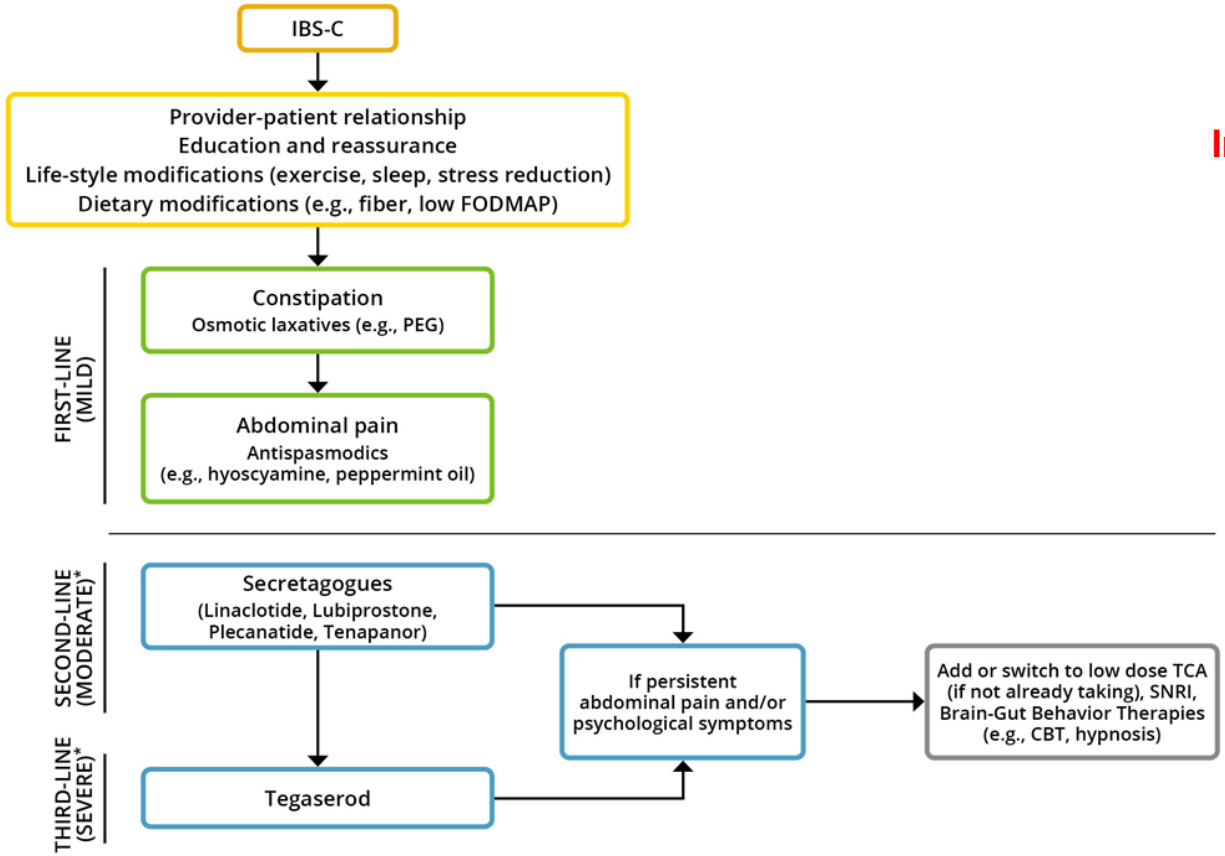
- Digital Rectal Exam!!!
- Limited laboratory testing: CBC, TSH, calcium when appropriate
- Colonoscopy not recommended for routine patients with constipation without alarm features
- GI motility testing
  - GI transit (colon marker or wireless pH-motility capsule testing)
  - ARM with balloon expulsion
  - Defecography



GI = gastrointestinal; ARM = anorectal manometry.

Lacy BE, et al. *MedGenMed*. 2005;7(2):19. Cash BD, et al. *Rev Gastroenterol Disord*. 2007;7(3):116-133.

Clinical Decision Support Tool for IBS Treatment

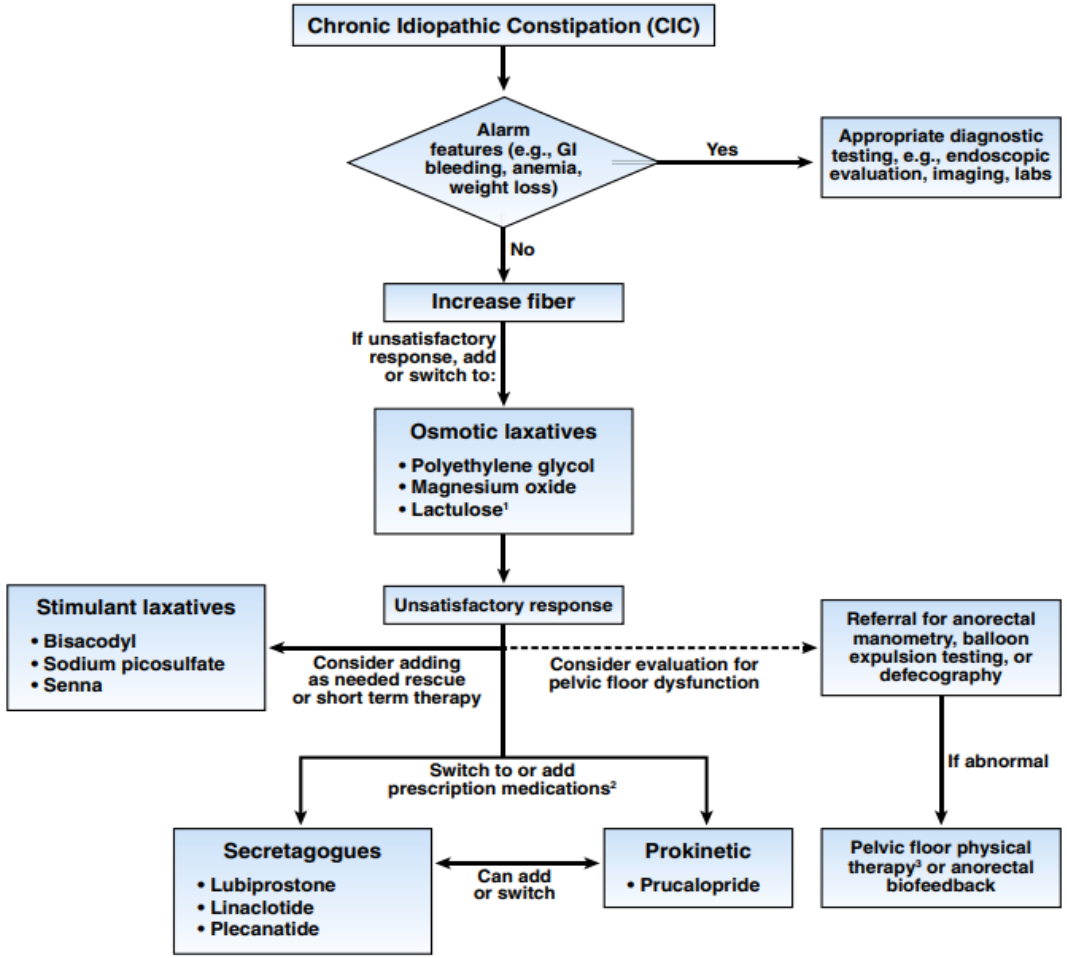


In patients with IBS-C, the AGA

Recommends using	**Linaclotide****
	Tenapanor
	Plecanatide
Suggests using	**Tegaserod**
	Lubiprostone
	PEG laxatives

***Selection of the medication should be based on the clinical features and needs of the patient; **Strong recommendation.**
TCA = tricyclic antidepressant; SNRI = serotonin-norepinephrine reuptake inhibitor; PEG = polyethylene glycol; CBT = cognitive behavioral therapy; AGA = American Gastroenterological Association.
Cheng L, et al. *Gastroenterology*. 2022;163(1):118-136. Clinical Decision Support Tool: IBS Treatment. *Gastroenterology.* 2022;163(1):152.

Clinical Decision Support Tool for CIC



The AGA and ACG **recommends**

- Polyethylene glycol#
- Bisacodyl# – short term/rescue
- Linaclotide*#
- Plecanatide*#
- Prucalopride*#

The AGA and ACG **suggests**

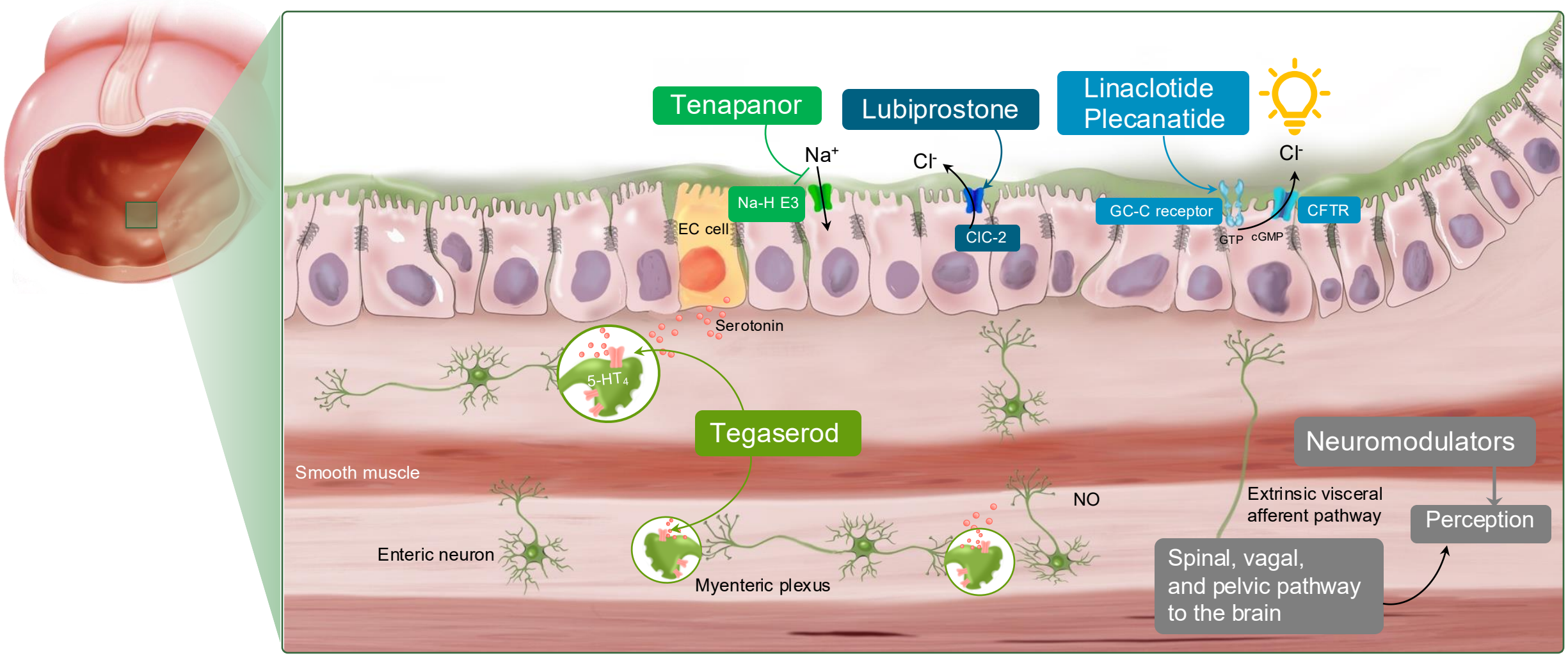
- Fiber
- Magnesium
- Senna
- Lubiprostone*
- Lactulose*

[1]Lactulose can be used if symptoms fail to improve with fiber or other osmotic laxatives, however, avoid in patients with significant bloating or abdominal pain; [2]Selection of medications should be based on clinical features, patient preference and tolerance, insurance coverage; [3]Can consider early trial or pelvic floor physical therapy without formal testing. Consider pelvic floor evaluation if unsatisfactory response or refractory symptoms after prescription therapies, if not previously done; *Patients who do not respond to OTC agents; #Strong recommendation.

ACG = American College of Gastroenterology.

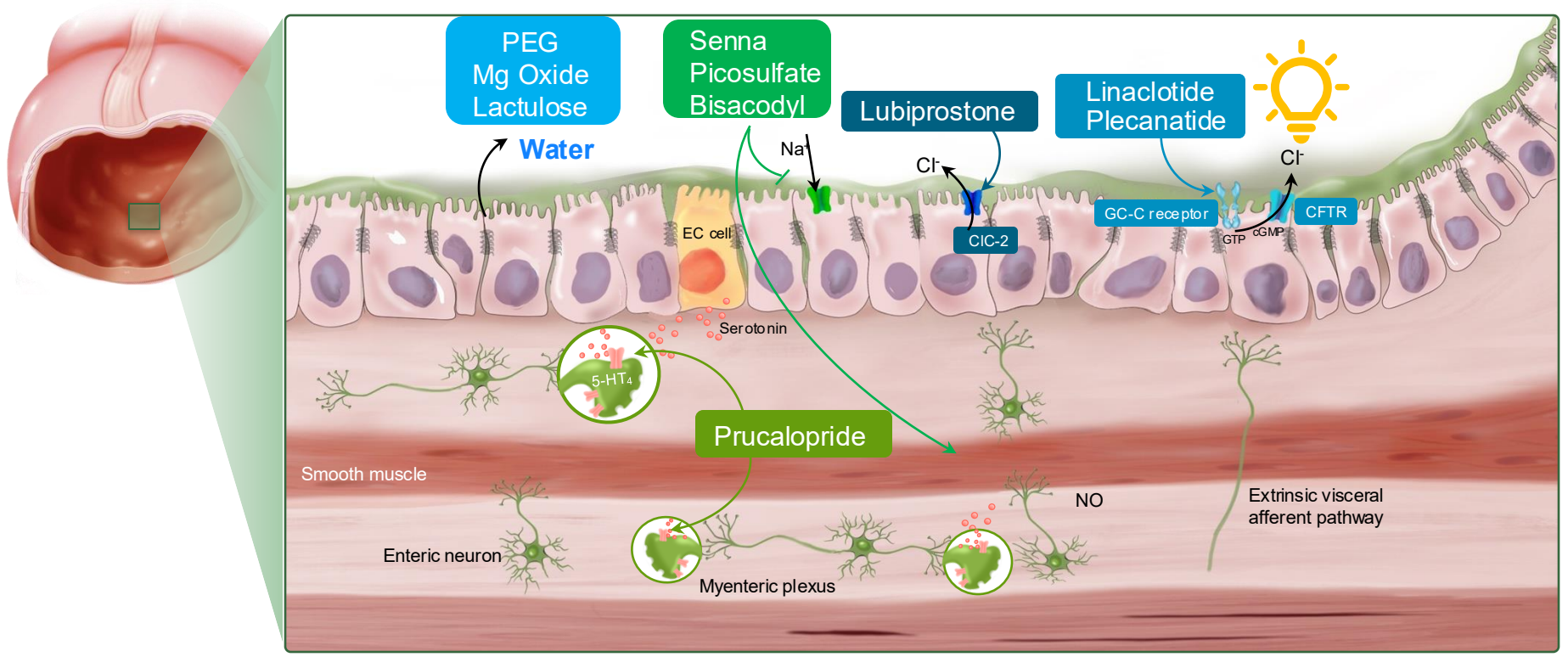
AGA Guideline. *Gastroenterology*. 2023;164:1107.

Mechanism of Action of IBS-C Treatments



EC = enterochromaffin; GC-C = guanylate cyclase C; CFTR = cystic fibrosis transmembrane conductance regulator.
Chang L, et al. *Gastroenterology*. 2022;163(1):153.

Mechanism of Action of CIC Treatments



Chang L, et al. *Gastroenterology*. 2023;164(7):1086-1106. Chang L, et al. *Am J Gastroenterol*. 2023;118(6):936-954.

Key Learning Points

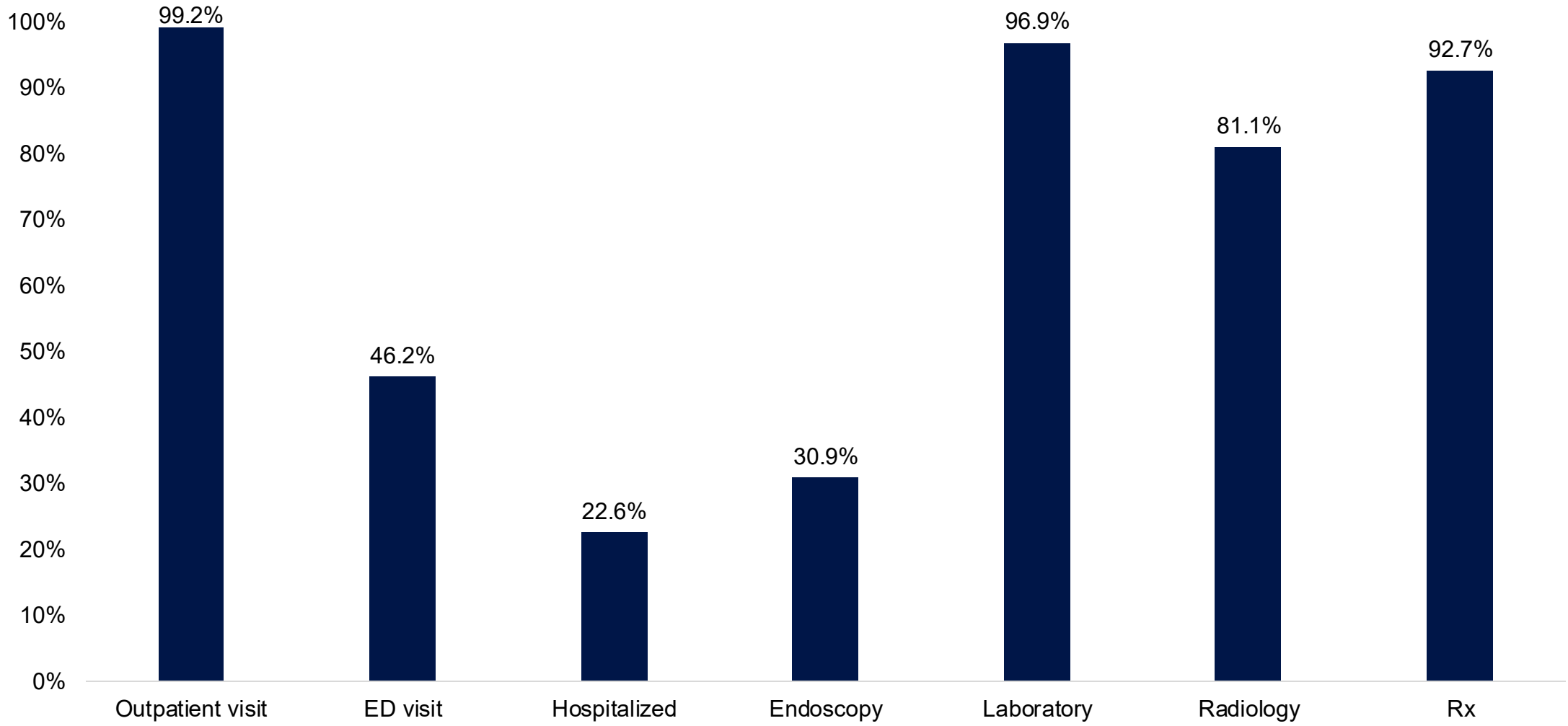
- IBS and CIC are common DGBIs
- Diet, lifestyle modifications, OTC (loperamide, PEG, fiber) therapies are first line
- Best clinical trial evidence for IBS
  - IBS-C: Secretogogues (**linaclotide**, plecanatide, lubiprostone, tenapanor)
  - Pain: Peppermint oil (for all subtypes); TCAs, SNRIs —allow 4 weeks minimum; antispasmodics
  - Psychological: CBT, hypnosis
- Best clinical trial evidence for CIC
  - Fiber (1st line treatment)
  - Secretogogues (plecanatide, **linaclotide**)
  - Prokinetics (prucalopride)
  - Osmotic (PEG) and stimulant laxatives (bisacodyl – short term)
  - Pelvic floor therapy when dyssynergia is present

DGBIs = disorders of the gut-brain interaction; OTC = over-the-counter.

Managed Care Considerations

Catherine E. Cooke, PharmD, MS, BCPS, PAHM

Healthcare Resource Use in IBS-C

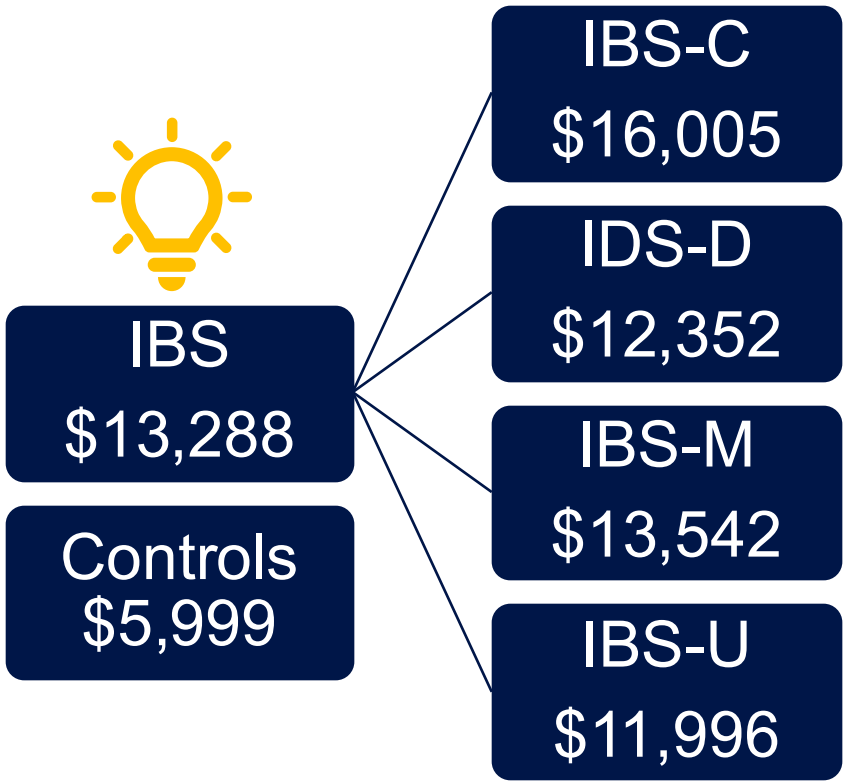


ED = emergency department; Rx = prescription.

Shin A, et al. *Am J Gastroenterol*. 2024;119(8):1571-1579.

IBS Associated with Substantially Higher Healthcare Costs

Annual total per patient for all-cause healthcare spend (median)

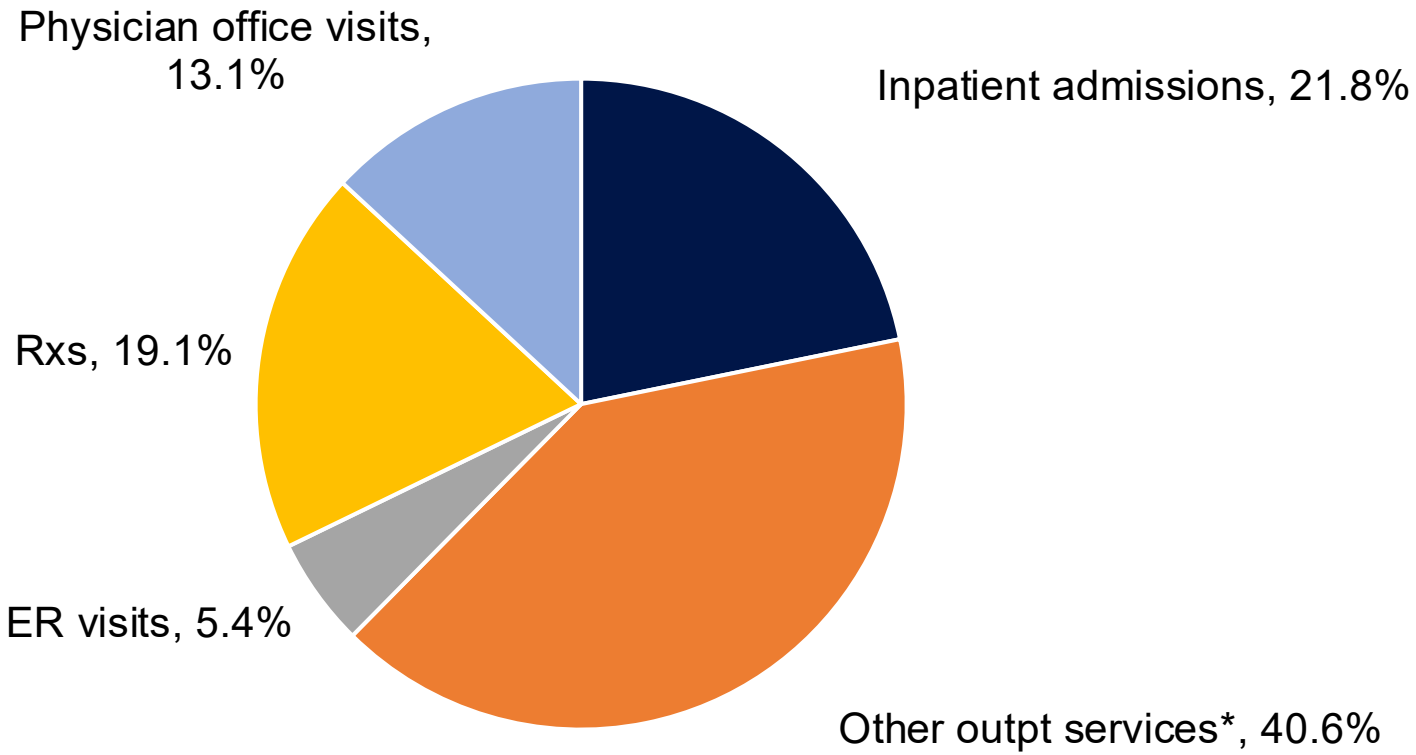


- ~$7,000 additional healthcare spend on IBS each year
- IBS-C subtype associated with highest annual costs

Shin A, et al. *Am J Gastroenterol*. 2024;119(8):1571-1579.

Cost Drivers in IBS-C

Distribution of Annual (mean) All-Cause Health Care Costs for IBS-C



***Other outpatient services: diagnostic tests, outpatient procedures (eg, endoscopies), laboratory tests, radiology services, and nonpharmacological therapies.**

Doshi JA, et al. *J Manag Care Spec Pharm*. 2014;20(4):382-390.

Disparities in IBS Care

	Asian	Black	Hispanic
	Percentage points vs White		
IBS-related primary care visits	1.7*	1.7*	.7
Patients with GI consults	-44.8*	-30.6*	-30.5*
Patients who received GI procedures	17.4*	27.2*	22.4*
Patients who received colonoscopy	8*	14.3*	9*
Patients who received esophagogastroduodenoscopy	3.6	14.8*	21.8*

***Significant differences vs White patients.**

Silvernale C, et al. *Neurogastroenterol Motil*. 2021;33(5):e14039.

Management Strategies for IBS

OTC = over-the-counter.

Management Strategies for IBS

3 steps in SDM

1. Introducing choice
2. Describing options
3. Helping patients explore preferences and make decisions

- An informed, patient-centered discussion to assist with choosing IBS management
- Requires bidirectional communication
- Decision aids may support SDM
- Several factors to consider when determining IBS treatment approach
  - Patient's personal beliefs
  - Efficacy/effectiveness/tolerability/safety
  - Duration of therapy
  - Convenience
  - Cost

SDM = shared decision making.

Perspectives and Preferences for IBS-C and CIC Treatments

Patient perspective
On-label prescription drug therapy

Payer perspective

Global IBS treatments

- FODMAP diet
- Cognitive behavioral therapy (CBT)
- Neuromodulators

Prescription therapies

- Linaclotide
- Plecanatide
- Lubiprostone

FODMAP = fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.

Shah ED, et al. *MDM Policy Pract*. 2021;6(1):2381468320978417. Shah ED, et al. *Am J Gastroenterol*. 2021;116(4):748-757.

Coverage Restrictions Are Cost-Effective from Payer Perspective

- Microsimulation tracking costs/outcomes of hypothetical IBS patients over 1 year
- Population: patients with moderate to severe IBS
- Routinely using global IBS treatments (central neuromodulator; low fermentable oligo-, di-, and mono-saccharides and polyols; and cognitive behavioral therapy) before FDA-approved drug therapies
  - Result: per-patient cost savings of $2,972.83 for IBS-C over 1 year to insurers, compared with patients starting with on-label drug therapy

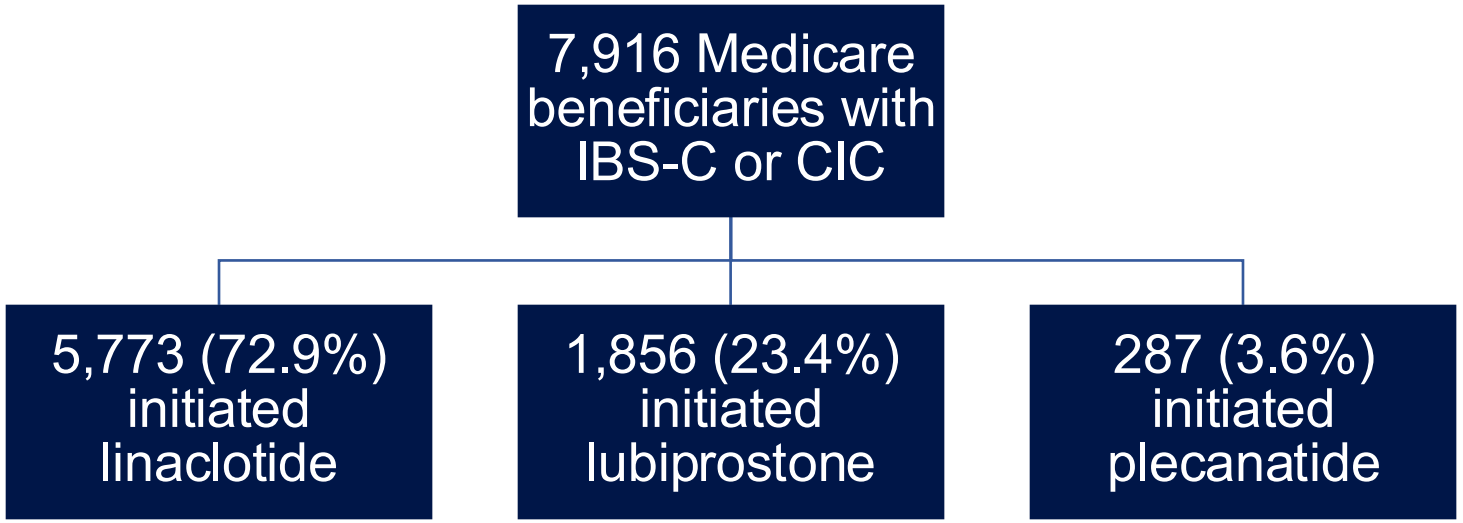
- Health outcomes similar, regardless of treatment sequence
- The most cost-saving and cost-effective IBS-C algorithm was linaclotide, compared to plecanatide or lubiprostone

Shah ED, et al. *Am J Gastroenterol*. 2021;116(4):748-757.

Prior Authorization of IBS-C or CIC Treatments

- Commonly used criteria include
  - Diagnosis of IBS-C or CIC
  - Duration of ≥3 months
  - Trial and failure ≥2 formulary laxatives
    - Lack of effectiveness
    - Safety/tolerability concern
    - Contraindications

HCRU and Costs after Initiating Oral Therapies for IBS-C or CIC



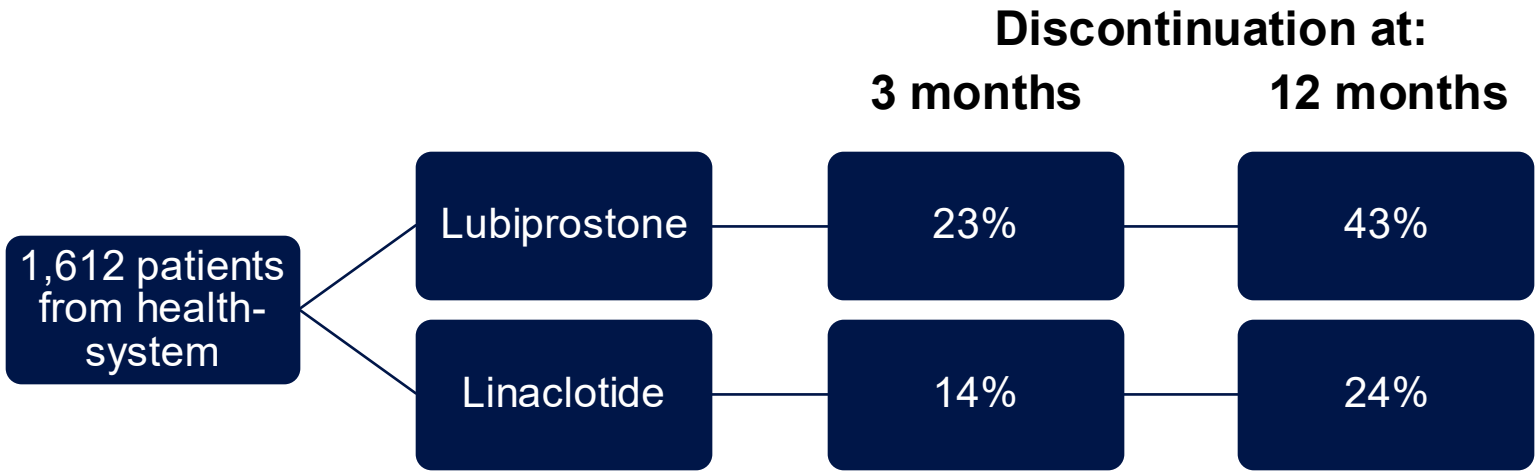
Findings

- Lubiprostone vs linaclotide: higher HCRU and greater all-cause costs
- Plecanatide vs linaclotide: no significant differences in HCRU but greater all-cause costs

HCRU = healthcare resource utilization.

Shah E, et al. *Adv Ther*. 2025;42(5):2500-2512.

Adherence to IBS-C Treatments



- >50% of discontinuations due to intolerance occurred in first 3 months for both drugs
- Linaclotide users more likely to discontinue due to intolerance (but less likely to discontinue due to insufficient efficacy of therapy)
- Loss of prescription drug coverage remained a common reason for discontinuation over the first year of therapy

Shah ED, et al. *Am J Gastroenterol*. 2020;115(4):596-602.

Strategies for Optimizing IBS Care

Facilitate early diagnosis

Enhance patient-provider communication

Address the patient's concerns

Employ shared decision-making for treatment decisions

Address both the physical and mental health aspects of the patient

Monitor outcomes to ensure the patient's goals of therapy are met

Ensure medication access, monitor for treatment effectiveness, tolerability and safety

Key Learning Points

- Management of IBS in the United States costs, on average, tens of thousands of dollars per patient per year
- Early diagnosis and management can minimize costs
  - Eg, initiating linaclotide treatment associated with lower total healthcare costs compared to lubiprostone and plecanatide
- Patient preferences should be considered when selecting evidence-based treatments
- Monitoring the effectiveness and tolerability of treatment can identify appropriate adjustments and may improve medication adherence and reduce the need for emergency interventions

Thank You!