

Review of Treatment Options for Irritable Bowel Syndrome with Constipation and Chronic Idiopathic Constipation

Sarah Patel^{1,2}

Bethany Doerfler³

Katerine Boutros⁴

Samson Ng⁴

Machelle Manuel⁵

Elayne DeSimone⁶

¹Department of Gastroenterology and Hepatology, Weill Cornell Medicine, New York, NY, USA; ²Rutgers University, Piscataway, NJ, USA; ³Division of Gastroenterology, Northwestern Medicine, Chicago, IL, USA; ⁴Global Medical Affairs Gastroenterology & Hepatology, AbbVie Inc, Madison, NJ, USA; ⁵Ironwood Pharmaceuticals, Inc, Cambridge, MA, USA; ⁶Community Volunteers in Medicine, West Chester, PA, USA

Abstract: Irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC) are two common disorders of gut–brain interaction. Affected patients often first present to their primary care providers seeking care for symptoms of constipation, abdominal pain, and bloating, which have a significant impact on their health-related quality of life. These patients often require extensive counseling and reassurance, and knowledge of reliable diagnostic criteria and treatment options is imperative to managing their conditions. Family medicine practitioners, including nurse practitioners and physician assistants, are uniquely qualified to provide a diagnosis and safe, effective management of these disorders. This article reviews the latest evidence and provides practical advice related to diagnosis and management of IBS-C and CIC.

Keywords: advanced practice providers, chronic idiopathic constipation, constipation, irritable bowel syndrome, nurse practitioners, physician assistants

Background

Irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC), sometimes referred to as functional constipation, are two symptom-based disorders of gut–brain interaction defined by the Rome diagnostic criteria.^{1–3} Irritable bowel syndrome (IBS) is defined by the presence of recurrent abdominal pain associated with a change in defecation and is subtyped by the predominant stool pattern (ie, constipation for IBS-C). CIC is defined by the frequency of specific bowel symptoms, such as straining and incomplete evacuation, which can be accompanied by abdominal symptoms such as pain or bloating, in patients who do not meet the criteria for IBS. Abdominal pain is considered the hallmark symptom of IBS-C but is not necessarily the predominant symptom in CIC.^{1,2} Nonetheless, symptom overlap does occur between these two disorders, and IBS-C and CIC share symptoms of infrequent bowel movements (BMs), straining during defecation, hard and/or lumpy stools, and the sensation of incomplete evacuation.

Although these two disorders are considered distinct in terms of diagnostic criteria, recent studies have demonstrated that they may exist along a spectrum of severity.^{1,3} One study of patients with CIC with and without abdominal symptoms found that patient-reported disease severity tracked closely with the presence of abdominal symptoms and suggested that abdominal symptoms could provide a measurement of disease severity along a continuum.² Therefore, in clinical

Correspondence: Sarah Patel
Department of Gastroenterology and Hepatology, Weill Cornell Medicine, New York, NY, USA
Tel +1-(908)-642-6979
Email soneil86@gmail.com



practice, there may be little separation between the symptoms of the two disorders, and patients may migrate from one diagnosis to the other over the course of their disorder.^{2,4}

Patients with IBS-C and CIC often seek medical care owing to difficulty with BMs or abdominal pain and bloating⁵ and will often first seek medical care from their primary care providers, who may include nurse practitioners (NPs) and physician assistants (PAs).⁶ NPs and PAs need to be familiar with the latest evidence on the recognition and diagnosis of IBS-C and CIC in order to provide safe and effective healthcare.⁶ In this review, we present current approaches to the differential diagnosis and multifaceted management of both IBS-C and CIC.

The prevalence of constipation in the general population ranges from 2% to 27%, with the variability arising from differing definitions and populations.^{7–9} In the US, the prevalence of IBS-C is 4.3–5.2% of patients with IBS,^{10–12} while the mean prevalence of CIC is 12.0–19.0%.^{1,8,13} IBS most commonly presents between the ages of 25 and 54 years,^{12,14} and the overall prevalence is 67% higher in women internationally.¹⁵ Risk factors for CIC include female sex, reduced caloric intake, and increasing age.¹

IBS-C and CIC are both associated with recurrent, bothersome symptoms that profoundly reduce patients' quality of life (QoL)^{16,17} and productivity, and increase the number of missed days of work or school.^{2,18} IBS-C and CIC also pose a significant financial burden to patients and healthcare systems. In the US, the reported mean annual all-cause healthcare cost associated with IBS-C in 2010 was \$11,182 per patient, with over half (53.7%) of costs attributable to outpatient services, including physician office visits and other outpatient services (13.1% and 40.6%, respectively).¹⁰ In 2002, the direct cost per patient ranged from \$1600 to \$7500 per year for IBS and from \$1900 to \$7500 per year for CIC.¹⁶

Making a Diagnosis

Role of NPs and PAs in Recognizing IBS-C and CIC

Many patients with IBS-C or CIC suffer for years before discussing their symptoms with a healthcare practitioner.¹⁹ Patients may feel embarrassed about their disorder; therefore, establishing effective communication is important.^{19,20} Patient-centered interviewing focused on identifying how the patient experiences the disorder in

their everyday life encourages patients to lead the discussion, and may ultimately increase patient satisfaction and adherence.²¹

Most often, NPs and PAs are the first healthcare providers to encounter patients with IBS-C or CIC, often diagnosing and managing them in the primary care setting. Owing to the time required, NPs and PAs are well positioned to care for patients with IBS-C or CIC, particularly those who require extensive counseling, education, and/or reassurance (ie, frequent office visits or phone calls). In addition, patients may speak first to an NP or PA regarding constipation or abdominal symptoms prior to seeing a gastroenterologist. Therefore, it is important for NPs and PAs to recognize these disorders and make confident diagnoses in the primary care setting in order to prevent unnecessary referrals.

Differential Diagnosis of IBS-C and CIC

The Rome IV diagnostic criteria distinguish disorders of gut–brain interaction based on clinical symptoms, but there is some overlap between the disorders (Figure 1). While abdominal pain is the hallmark symptom of all IBS subtypes, patients with CIC primarily experience constipation, but may also secondarily experience abdominal pain as well as abdominal bloating and distension.

A detailed patient assessment is critical to determine a diagnosis and the appropriate treatment for each patient, depending on where their condition falls along the spectrum (Figure 2). A thorough clinical history and physical examination are useful to reassure the patient and exclude organic

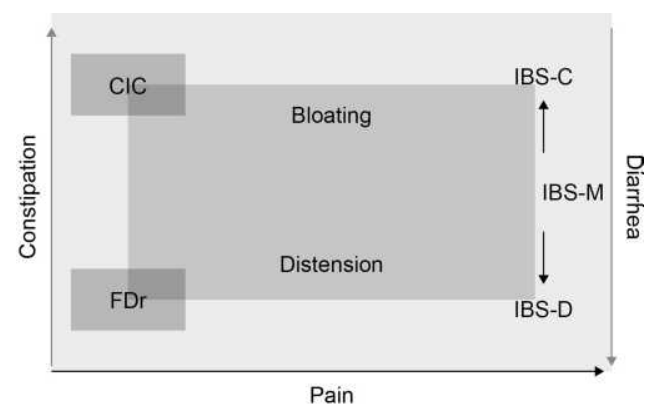


Figure 1 Disorders of gut–brain interaction exist on a continuum.

Note: © 2016 Rome Foundation, Inc. All Rights Reserved. Modified from Rome Foundation's Rome IV Functional Gastrointestinal Disorders, Disorders of the Gut-Brain Interaction – Volume II – Page 970.⁵⁶

Abbreviations: CIC, chronic idiopathic constipation; FDr, functional diarrhea; IBS-C, irritable bowel syndrome with constipation; IBS-D, irritable bowel syndrome with diarrhea; IBS-M, irritable bowel syndrome with mixed bowel habits.

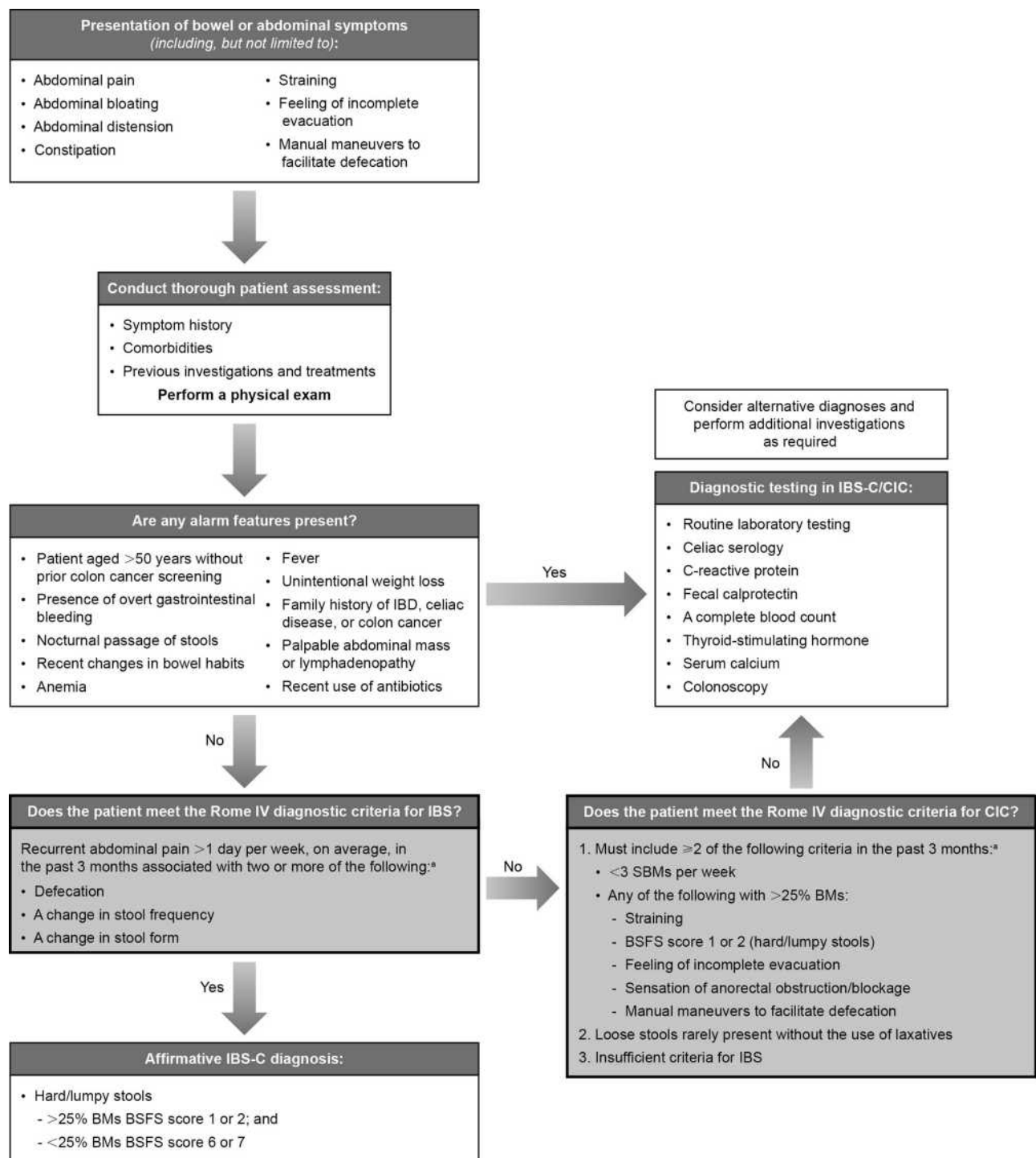


Figure 2 Diagnosing IBS-C and CIC.

Note: ^aCriteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.

Abbreviations: BM, bowel movement; BSFS, Bristol Stool Form Scale; CIC, chronic idiopathic constipation; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; IBS-C, irritable bowel syndrome with constipation; SBM, spontaneous bowel movement.

etiologies via the identification of any alarm features.¹ Alarm features indicating further testing may be required include patients >50 years of age without prior colon cancer screening, presence of overt gastrointestinal bleeding, nocturnal passage of stools, unintentional weight loss, a family history

of inflammatory bowel disease or colorectal cancer, recent changes in bowel habits, and the presence of a palpable abdominal mass or lymphadenopathy. Additional features prompting further evaluation include anemia, fever, a family history of celiac disease, or recent use of antibiotics.

If these warning signs are absent, a further patient history should be obtained to quantify the frequency of symptoms and determine whether the patient meets any of the Rome IV diagnostic criteria for disorders of gut–brain interaction.^{1,3} The Bristol Stool Form Scale (BSFS) is a useful tool for evaluating stool consistency in line with Rome criteria.^{1,22} Diagnostic testing for IBS-C and CIC can include limited laboratory tests including specialized testing for alternative etiologies (eg, celiac serology, C-reactive protein, fecal calprotectin), especially if not previously performed. A complete blood count should also be taken, as well as thyroid-stimulating hormone and serum calcium levels assessed where clinically indicated when diagnosing CIC.¹

IBS-C

Diagnosis of IBS is made based on clinical history, physical examination, minimal laboratory tests, and other appropriate tests (eg, colonoscopy) as indicated. Diagnosis of IBS requires prior symptom onset of ≥ 6 months, recurrent abdominal pain occurring >1 day per week, on average, over the past 3 months, associated with two or more of defecation, change in stool frequency, or change in stool form. Absence of abdominal pain precludes diagnosis of IBS. IBS-C is defined as $>25\%$ of BMs with BSFS scores of 1 or 2 (hard/lumpy stool) and $<25\%$ of BMs with BSFS scores of 6 or 7 (diarrhea/watery stool). Although not required for a diagnosis of IBS, the majority of IBS patients experience abdominal bloating, and abdominal distention may also be reported.¹ In a study of over 300 patients with IBS-C, abdominal discomfort and bloating were reported as “very or extremely bothersome” by 58% and 56% of patients, respectively,² demonstrating the negative impact of these IBS symptoms on patients’ lives.

CIC

Diagnosis of CIC is made based on clinical history, physical examination, minimal laboratory tests as clinically indicated, and specific tests of constipation pathophysiology as required, including anorectal manometry and electromyography; however, these tests are not clinically indicated in all patients.¹ These tests may be required to identify dyssynergic defecation, which can often overlap with CIC in the same patient. Diagnostic evaluation should only be performed in patients who do not respond to empiric therapy and should be performed while the patient is not taking laxatives. Diagnosis of CIC requires symptom onset ≥ 6 months before diagnosis and presentation of

symptoms during the last 3 months. Abdominal pain, bloating, and distension may be present, but they are not necessarily the predominant symptoms; therefore, individuals with CIC do not fulfill the criteria for IBS.¹ Diagnostic criteria must include two or more of the following: straining, BMs with BSFS scores 1 or 2, sensation of incomplete evacuation, sensation of anorectal obstruction, a requirement for manual maneuvers for facilitation of defecation for $>25\%$ of BMs, <3 spontaneous BMs per week, loose stools rarely present without the use of laxatives, and insufficient criteria for IBS.

Management of IBS-C and CIC

Role of NPs and PAs

Once a diagnosis is established, the overall aim should be to help patients manage their symptoms and improve their health-related QoL (HRQoL). NPs and PAs are uniquely qualified to establish a positive, communicative, and therapeutic relationship with patients with IBS-C or CIC.²³ A careful and thorough assessment should be performed, including an evaluation of current symptoms, patient history (including lifestyle, daily habits, activity and exercise levels, food intake and aversions, fluid intake, and sleep habits), and any prior medications and treatment interventions, along with the patient’s response to those treatments.^{1,23}

Lifestyle and/or Diet Modifications

Exercise, stress reduction, adequate daily fluid intake, and improved sleep can all help to improve the symptoms of IBS.¹ Patients with IBS-C or CIC should be educated about eliminating medications that cause or worsen constipation where possible, including opiates, diuretics, and iron or calcium supplements (Table 1).^{1,9,24} A thorough evaluation of patient diet and consultation on maintenance of a routine bathroom schedule should also be discussed.^{1,25}

A diet low in fermentable oligo-saccharides, disaccharides, and mono-saccharides and polyols (FODMAPs) may be useful for overall symptom improvement in IBS,²⁶ although it is only weakly suggested by current guidelines to treat IBS-C, and is not recommended for treatment of CIC.^{26,27} While evidence suggests that a low FODMAP diet is useful for treating abdominal symptoms in the short term, additional long-term studies are needed. Patients should also be referred to a registered dietitian to assist in nutritional assessment and to provide guidance on dietary modifications.^{28,29}

Table 1 Medications Commonly Associated with Constipation

<ul style="list-style-type: none"> • Adrenergic drugs
<ul style="list-style-type: none"> • Analgesics <ul style="list-style-type: none"> • NSAIDs • Opiates • Tramadol
<ul style="list-style-type: none"> • Anticholinergics
<ul style="list-style-type: none"> • Anticonvulsants
<ul style="list-style-type: none"> • Antihypertensives <ul style="list-style-type: none"> • Antiarrhythmic agents • Calcium channel blockers • Diuretics <ul style="list-style-type: none"> • Furosemide • Hydrochlorothiazide
<ul style="list-style-type: none"> • Antiparkinsonian drugs <ul style="list-style-type: none"> • Dopaminergic agents
<ul style="list-style-type: none"> • Antipsychotics <ul style="list-style-type: none"> • Phenothiazine derivatives
<ul style="list-style-type: none"> • Bile salt chelators/bile acid binders
<ul style="list-style-type: none"> • Bisphosphonates
<ul style="list-style-type: none"> • Drugs containing cations <ul style="list-style-type: none"> • Aluminum- or calcium-containing antacids • Bismuth • Calcium supplements • Iron supplements • Lithium • Sucralfate
<ul style="list-style-type: none"> • Spasmolytics
<ul style="list-style-type: none"> • Tricyclic antidepressants

Abbreviation: NSAID, nonsteroidal anti-inflammatory drug.

Over-the-Counter Agents

The majority of patients with IBS-C and CIC have tried an over-the-counter medication before consulting a healthcare practitioner.¹⁹ Empiric treatment for IBS-C and CIC should begin with a fiber supplement, followed by osmotic and stimulant laxatives.¹ In addition, antispasmodics such as peppermint oil are used to treat abdominal pain or cramps, discomfort, and/or bloating associated with IBS, but typically do not improve transit time or stool quality.^{1,26}

Fiber

Soluble fibers such as psyllium or ispaghula husk may provide some symptom relief and improve stool viscosity and frequency in IBS and CIC and remain an evidence-based treatment for IBS. In addition, the low cost and lack of

significant side effects make soluble fiber a reasonable first-line therapy.²⁶ In patients with CIC, 7 g of psyllium fiber daily was 3.4 times more effective at increasing stool output and water content than bran cereal alone.³⁰ Prunes and prune fiber have also demonstrated efficacy in alleviating constipation, with one meta-analysis demonstrating increased stool frequency and greater improvement in stool consistency compared with the administration of psyllium fiber in patients with constipation or IBS-C.³¹ For CIC, insoluble, nonfermentable fibers increase stool biomass and stool water content and may accelerate transit due to increased stimulation of secretion and motility. Importantly, insoluble fibers such as bran-containing cereals should be limited in IBS as they can exacerbate symptoms such as pain and bloating, and there is no evidence demonstrating efficacy in alleviating symptoms.^{1,26} Total fiber intake of 20–30 g/day is recommended.¹

Laxatives

Osmotic laxatives such as polyethylene glycol and lactulose have demonstrated effectiveness for the treatment of CIC and have improved stool consistency in IBS-C, but have demonstrated little effect on global IBS symptoms, including abdominal pain, compared with placebo (Table 2).^{1,26,32} Stimulant laxatives have demonstrated clinical benefits for stool frequency and other constipation-associated symptoms; however, they are not indicated for chronic use³³ and can induce or worsen abdominal pain symptoms as abdominal pain and cramping are common adverse effects.^{1,20}

US Food and Drug Administration-Approved Therapies

Patients whose symptoms are not adequately controlled by lifestyle changes or over-the-counter agents may require further pharmaceutical intervention. Medication selection is dependent on the patient's most bothersome symptom (constipation, abdominal pain, etc.), response to any prior therapies, as well as patient and provider preference. Prescription medication options include linaclotide, lubiprostone, and plecanatide for both IBS-C and CIC. Tegaserod and tenapanor are approved for the treatment of IBS-C while prucalopride is approved for use in CIC (Table 2).¹

Non-Approved Medications

Although not approved by the US Food and Drug Administration, certain prescription medications such as

Table 2 Overview of Medications Commonly Used in the Management of IBS-C or CIC

	MoA	Indication	Dose and Administration	Efficacy and Safety	Other Considerations	ACG Recommendation ^{26,27a}
OTC medications						
Peppermint oil	Smooth muscle relaxant	IBS-C	1–2 capsules TID orally, 15–30 min before food for 1 month ³⁷	<ul style="list-style-type: none"> Improves abdominal pain, discomfort, and bloating³⁸ Impact on motility is more limited³⁸ Most common AE is heartburn 	<ul style="list-style-type: none"> Formulations using novel coating have been developed in an attempt to overcome AEs³⁸ 	<ul style="list-style-type: none"> Weak recommendation for overall symptom improvement in IBS based on low-quality evidence
Polyethylene glycol	Osmotic laxative	IBS-C CIC	17 g/day, dissolved in 8 oz of water ^{23,39}	<ul style="list-style-type: none"> Improves stool consistency and frequency in IBS-C^{26,38} No evidence of improvement in abdominal pain or global symptoms compared with PBO^{26,32,38} Common AEs include abdominal pain and headache¹¹ 	<ul style="list-style-type: none"> Not approved for chronic use 	<ul style="list-style-type: none"> Weak recommendation for overall symptom improvement in IBS based on low-quality evidence Strongly recommended for improving CIC symptoms based on high-quality evidence
FDA-approved medications						
Linacotide	GC-C agonist	IBS-C CIC	IBS-C: 290 µg QD CIC: 72 or 145 µg QD <ul style="list-style-type: none"> To be taken on an empty stomach at least 30 minutes prior to the first meal of the day⁴⁰ 	<ul style="list-style-type: none"> In IBS-C, significantly more pts receiving linacotide met the primary efficacy endpoints: ≥30% improvement in WAP and an increase of ≥1 CSBM from baseline within the same wk (≥6/12 wks of treatment FDA endpoint); or ≥3 CSBMs/wk with an increase of ≥1 CSBM from baseline (and component responses) for ≥9/12 wks vs PBO^{41,42} In CIC, significantly more pts receiving either dose of linacotide achieved the primary endpoint compared with PBO (≥3 CSBMs/wk and increase of ≥1 CSBM from baseline for ≥9/12 wks)⁴³ The most common AEs (reported in ≥2% of pts with IBS-C or CIC) are diarrhea, abdominal pain, flatulence, and abdominal distension⁴⁰ 	<ul style="list-style-type: none"> Contraindicated in pts <6 years of age and pts with known or suspected mechanical GI obstruction Recommended to avoid linacotide in pts 6 to <18 years of age⁴⁰ 	<ul style="list-style-type: none"> Strongly recommended for overall symptom improvement in IBS-C based on high-quality evidence Strongly recommended for treatment of CIC based on high-quality evidence

(Continued)

Table 2 (Continued).

	MoA	Indication	Dose and Administration	Efficacy and Safety	Other Considerations	ACG Recommendation ^{26,27a}
Lubiprostone	Chloride channel activator	IBS-C (females), CIC	IBS-C: 8 µg BID CIC: 24 µg BID <ul style="list-style-type: none"> To be taken with food and water⁴⁴ 	<ul style="list-style-type: none"> Significantly more pts receiving lubiprostone were considered overall responders (reported moderate relief 4 wks/month or significant relief ≥2 wks/month [with no reports of moderate or severely worse relief] for ≥2/3 months) compared with PBO in pts with IBS-C⁴⁵ Studies in pts with CIC demonstrated higher frequency of SBMs across 4 wks of treatment in lubiprostone-treated pts compared with PBO-treated pts⁴⁴ The most common AEs (reported in >4% of pts): nausea, diarrhea and abdominal pain for IBS-C pts and nausea, headache, abdominal pain, abdominal distension and flatulence for CIC pts⁴⁴ 	<ul style="list-style-type: none"> Contraindicated in pts with known or suspected mechanical GI obstruction Approved for use in female adult pts with IBS-C; not determined if men with IBS-C respond differently⁴⁴ 	<ul style="list-style-type: none"> Strongly recommended for overall symptom improvement in IBS-C pts based on moderate-quality evidence Strongly recommended for treatment of CIC based on high-quality evidence
Plecanatide	GC-C agonist	IBS-C CIC	3 mg QD <ul style="list-style-type: none"> To be taken with or without food⁴⁶ 	<ul style="list-style-type: none"> In IBS-C, a significantly greater proportion of pts receiving plecanatide were overall responders compared with pts receiving PBO (≥30% improvement in WAP and increase in ≥1 CSBM/wk from baseline for ≥6/12 wks)⁴⁷ A significantly greater percentage of durable overall CSBM responders was observed with plecanatide vs PBO in pts with CIC (≥3 CSBMs/wk with an increase of ≥1 CSBM/wk from baseline for ≥9/12 wks including ≥3 of the last 4 wks)^{48,49} Diarrhea is the most common AE (occurring in ≥2% of pts)⁴⁶⁻⁴⁹ 	<ul style="list-style-type: none"> Contraindicated in pts <6 years of age and pts with known or suspected mechanical GI obstruction Recommended to avoid plecanatide in pts 6 to <18 years of age⁴⁶ 	<ul style="list-style-type: none"> Recommended for overall symptom improvement in IBS-C based on moderate-quality evidence^b

(Continued)

Table 2 (Continued).

	MoA	Indication	Dose and Administration	Efficacy and Safety	Other Considerations	ACG Recommendation ^{26,27a}
Prucalopride	5-HT ₄ receptor agonist	CIC	2 mg QD 1 mg QD for pts with severe renal impairment ⁵⁰	<ul style="list-style-type: none"> A significantly greater proportion of pts receiving prucalopride were responders vs pts receiving PBO (responder defined as ≥ 3 CSBMs/wk over 12 wks)^{51,52} The most common AEs (occurring in $\geq 2\%$ of pts): headache, abdominal pain, nausea, diarrhea, abdominal distension, dizziness, vomiting, flatulence, and fatigue⁵⁰ 	<ul style="list-style-type: none"> Contraindicated in pts with hypersensitivity to prucalopride or in pts with intestinal perforation or obstruction Pts should be monitored for suicidal ideation and behavior as suicides, suicide attempts, and suicidal ideation have been reported⁵⁰ 	<ul style="list-style-type: none"> Strongly recommended and determined to be more effective than PBO in improving symptoms of CIC based on moderate-quality evidence^c
Tegaserod	5-HT ₄ receptor agonist	IBS-C, female pts aged <65 years ^d	6 mg BID ≥ 30 min before meals ⁵³	<ul style="list-style-type: none"> Significantly greater proportions of pts receiving tegaserod were responders vs pts receiving PBO (responders defined as pts reporting considerable or complete relief of IBS symptoms 2/4 wks or somewhat relieved 4/4 wks)⁵³ Headache, abdominal pain, nausea, flatulence, dyspepsia, and dizziness are the most common AEs (occurring in $\geq 2\%$ of pts) 	<ul style="list-style-type: none"> Contraindicated in pts with a history of MI, stroke, intestinal ischemia, severe renal impairment, moderate or severe hepatic impairment, bowel obstruction, symptomatic gallbladder disease, suspected SOD, abdominal adhesions, or hypersensitivity to tegaserod⁵³ Pts should be monitored for clinical worsening of depression and emergence of suicidal thoughts and behaviors⁵³ 	–
Tenapanor ^e	NHE3 inhibitor	IBS-C	50 mg, BID <ul style="list-style-type: none"> To be taken immediately prior to the first and last meals of the day⁵⁴ 	<ul style="list-style-type: none"> A significantly greater proportion of pts receiving tenapanor were primary responders (defined as simultaneous $\geq 30\%$ improvement in WAP and increase of ≥ 1 CSBM/wk from baseline for 6/12 wks)⁵⁴ The most common AEs (occurring in $\geq 2\%$ of pts) are diarrhea, abdominal distension, flatulence, and dizziness⁵⁴ 	<ul style="list-style-type: none"> Tenapanor is contraindicated in pts <6 years of age and pts with known or suspected mechanical GI obstruction Recommended to avoid tenapanor in pts 6 to <12 years of age⁵⁴ 	–
Non-FDA-approved prescription medications						
Antispasmodics	Smooth muscle relaxant	Not approved for use in IBS or CIC	Hyoscyamine, up to 15 mg/day Dicyclomine 20–40 mg QD ³⁷	<ul style="list-style-type: none"> Can provide short-term symptom relief Effective as a category in IBS, although evidence supporting individual agents is limited²⁶ Blurred vision, dizziness, and dry mouth are common AEs 	–	<ul style="list-style-type: none"> Weak recommendation for certain antispasmodics (otilonium, pinaverium, hyoscine, cimetropium, drotaverine, and dicyclomine) for overall symptom improvement in IBS based on low-quality evidence

(Continued)

Table 2 (Continued).

	MoA	Indication	Dose and Administration	Efficacy and Safety	Other Considerations	ACG Recommendation ^{26,27a}
SSRIs: fluoxetine, paroxetine, citalopram	Serotonin reuptake inhibitor	Not approved for use in IBS or CIC	Fluoxetine: 20 mg QD Paroxetine: 10–50 mg QD Citalopram: 20–40 mg QD ³⁷	<ul style="list-style-type: none"> Effective in providing global symptom relief and improving pain^{26,55} Nausea, insomnia, diarrhea or constipation, decreased libido, ejaculatory dysfunction, and weight gain are common AEs³⁷ Use may be limited by AEs and healthcare provider acceptance²⁷ 	<ul style="list-style-type: none"> Cost of SSRIs may be a concern for some pts²⁷ 	<ul style="list-style-type: none"> Weak recommendation for overall symptom improvement in IBS based on low-quality evidence

Notes: ^aIBS-C recommendations based on the 2018 monograph and CIC recommendations based on the 2014 monograph; ^bplecanatide was approved for treatment of CIC subsequent to the publication of the 2014 monograph for CIC; ^cprucalopride was not available in the US at the time of the 2014 ACG monograph for CIC, but was available in Canada and the European Union; ^dtegaserod was withdrawn from the US market in 2007 owing to concerns about cardiovascular AEs and was approved for this specific patient population in March 2019, subsequent to publication of the monograph; ^etenapanor was approved for treatment of IBS-C in September 2019.

Abbreviations: 5-HT₄, serotonin-4; ACG, American College of Gastroenterology; AE, adverse event; BID, twice daily; CIC, chronic idiopathic constipation; CSBM, complete spontaneous bowel movement; FDA, US Food and Drug Administration; GC-C, guanylate cyclase-C; GI, gastrointestinal; IBS, irritable bowel syndrome; IBS-C, irritable bowel syndrome with constipation; MI, myocardial infarction; mo, month; MoA, mechanism of action; NHE3, sodium/hydrogen exchanger 3; OTC, over-the-counter; PBO, placebo; pts, patients; QD, once daily; SBM, spontaneous bowel movement; SOD, sphincter of Oddi dysfunction; SSRI, selective serotonin reuptake inhibitor; TID, three times daily; VAP, worst abdominal pain; wk, week.

selective serotonin reuptake inhibitors (SSRIs) and antispasmodics are often used off label (Table 2). SSRIs have demonstrated efficacy in relieving pain and overall symptoms in IBS; however, they are not recommended by the American College of Gastroenterology as the overall evidence is weak.^{1,26} Antispasmodics are sometimes used to treat abdominal cramping, but they should be used with caution as constipation is a common side effect (Table 2).²⁶

Patients may also seek complementary or alternative medicines, such as herbs, acupuncture, and homeopathy,^{34,35} to treat or supplement the treatment of their condition; however, their efficacy in treating symptoms remains inconclusive and controversial,^{34,36} and these treatments are outside the scope of this review.

Conclusions

IBS-C and CIC are two disorders of gut–brain interaction, each characterized by a spectrum of bowel and abdominal symptoms, with predominant abdominal pain defining IBS-C, and bowel symptoms including straining and feelings of incomplete evacuation defining CIC. These disorders are thought to exist on a continuum of disease severity, and although distinct diagnostic criteria are available for each disorder, it is important to consider each patient's experience over the course of the disorder, as symptom overlap is quite high. Owing to their impact on patient HRQoL and the burden on the healthcare system, reliable diagnosis and

effective treatment are critical to the management of these disorders. Management often includes a thorough explanation of the disorder, patient reassurance, and extensive patient counseling. NPs and PAs therefore should feel confident in making a diagnosis of IBS-C or CIC as well as developing individualized management plans for patients based on symptoms. Diet and lifestyle interventions, such as scheduled meals, adequate fluids, increased soluble fiber intake, and exercise, all demonstrate benefit to patients and improvement of symptoms. Some patients may require both lifestyle modifications and pharmaceutical interventions to optimize management of their symptoms.

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