Irritable Bowel Syndrome

An evidence-based review of new diagnostic criteria and treatment recommendations.

ABSTRACT: Irritable bowel syndrome (IBS) is a common, chronic gastrointestinal (GI) condition characterized by disturbances in bowel habits and abdominal pain in the absence of known organic pathology. IBS reduces quality of life and is costly to treat. It is diagnosed using the symptom-based Rome criteria for functional GI disorders, which was recently updated and released as Rome IV. Both physiologic and psychological variables play a role in the etiology of IBS and perpetuate symptoms. Although research has shed light on IBS pathophysiology, therapeutic interventions remain symptom driven, employing both pharmacologic and nonpharmacologic approaches. Here, the authors review the epidemiology and pathophysiology of IBS, summarize diagnostic and treatment strategies, and discuss implications for nursing practice.

Keywords: irritable bowel syndrome, Rome criteria, treatment approaches

Irritable bowel syndrome (IBS) is one of the most commonly diagnosed gastrointestinal (GI) disorders. Occurring most often in patients under age 50,[1] this chronic condition is characterized by abdominal pain and bowel dysfunction, presenting as constipation, diarrhea, or alternating periods of both.[2] In addition to its physiologic manifestations, IBS is recognized as having a psychological component. In 40% to 60% of cases, IBS is accompanied by such psychological disorders as depression or anxiety,[3] and patients with IBS have been found to have a greater frequency of somatic symptoms than patients who have GI symptoms in the absence of IBS.[4]

The development and persistence of IBS symptoms are understood to be multifactorial. Consequently, diagnosis and treatment are complicated clinical endeavors. Diagnosis is made according to the symptom-based Rome criteria for functional GI disorders, most recently updated and released as Rome IV.[5] Because curative medical interventions have yet to be discovered, treatment focuses on reducing patient symptoms. Current pharmacologic approaches, however, often provide suboptimal relief.

Evidence of biologic dysregulation has been reported in patients with IBS and efforts to understand the neurohormonal underpinnings of the disorder are ongoing, but the exact mechanisms leading to IBS symptoms are not completely understood.[6,7] This article discusses recent developments in the field of IBS research and the updated diagnostic criteria. It summarizes the epidemiology, pathophysiology, and treatment of IBS, with a focus on nursing practice.

EPIDEMIOLOGY AND BURDEN OF IBS

Incidence rates of IBS are seldom calculated, and prevalence estimates fluctuate both between and within countries.[2] A recent literature review by Sperber and colleagues attributed discrepancies to such factors as differences in the use of instruments, methods, and diagnostic criteria, as well as variations in populations and cultures assessed.[8] This review evaluated 83 community-based studies of IBS prevalence conducted in a total of 41 countries, and confirmed the global predominance of IBS among women, but could not estimate a global prevalence rate owing to the heterogeneity of the studies. The pooled prevalence rate that the investigators cited for North America, Europe, Australia, and New Zealand was 8.1%.

While IBS is not associated with increased mortality rates, it represents a significant burden on affected

patients and society as a result of direct medical costs, lost productivity, and reduced health-related quality of life.[9] In 2010, IBS accounted for more than 2 million diagnoses in U.S. ambulatory care settings, including office, ED, and hospital outpatient visits.[10] In the United States, estimates of IBS costs, both direct (medical management) and indirect (lost productivity and leisure time), exceeded $1 billion in 2004.[11]

A disproportionate amount of health care resources is expended treating patients with IBS and addressing the negative effects it has on patients' quality of life.[12] Despite receiving increased medical attention, however, patients with IBS frequently report problematic visits with health care providers that leave them feeling unsupported, humiliated, insignificant, and abandoned.[13,14] An additional burden of IBS falls on those who live with and care for patients with the disorder. Studies report adverse effects on the quality of life of domestic partners of patients with IBS.[15]

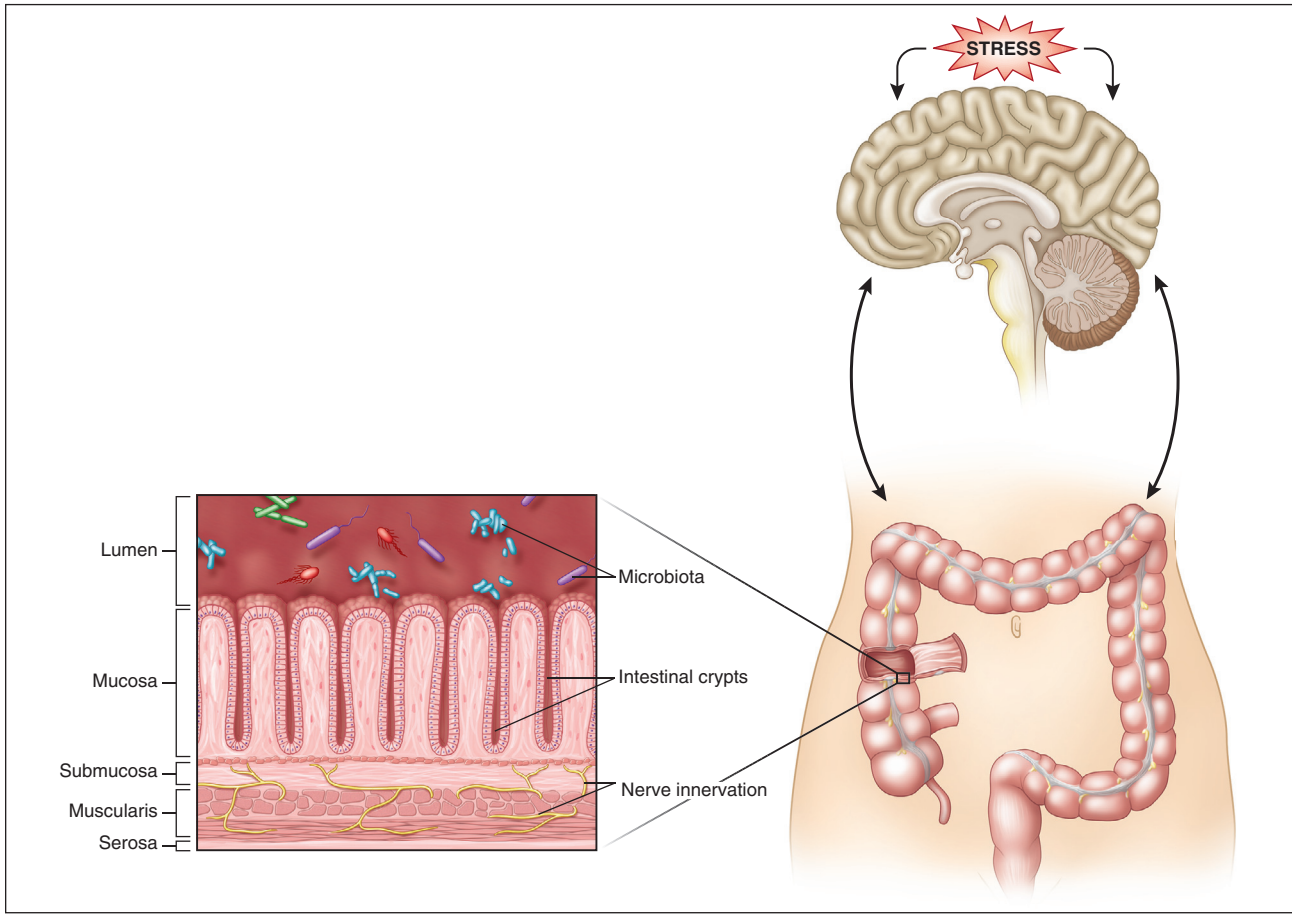
IBS ETIOLOGY AND PATHOPHYSIOLOGY

The following physiologic and psychological variables have been proposed as potential factors in the etiology and pathophysiology of IBS[16]:

- GI dysmotility
- inflammation
- visceral hypersensitivity
- altered intestinal microbiota
- diet
- genetic predisposition
- stress exposure (including early life events)

IBS and stress. Stress has been identified as a mechanism in the development of IBS, and the major

Figure 1. The Brain–Gut Axis



The mechanisms that disrupt "cross talk" between the brain and the gut along endocrine, neural, and neuroimmune pathways are not fully understood, but this disruption appears to play a role in producing the symptoms of irritable bowel syndrome. Shown here are layers of the colon wall along with some of the structures that may be affected. Illustration by Sara Jarret.

components of the stress response system—the autonomic nervous system and the hypothalamic–pituitary–adrenal axis—have been the subject of numerous IBS studies. An analysis of medical data collected from active-duty U.S. service members between 2001 and 2009 found the risk of developing IBS was significantly increased in those with a greater number of life stressors, a positive screen for panic syndrome or other anxiety syndromes on the Patient Health Questionnaire, and previous infectious gastroenteritis.[17] Posttraumatic stress disorder (PTSD) and depression were also associated with elevated risk, though in this study the increased risk was not found to be significant. Since both depression and PTSD have been significantly associated with IBS in previous studies of military veterans, the investigators attribute their finding to study design. These findings illustrate the interdependence or "cross talk" between the brain and the gut in IBS, a connection commonly known as the brain–gut axis.

The brain–gut axis refers to endocrine, neural, and neuroimmune pathways that facilitate bidirectional communication between the gut, the central nervous system, the enteric nervous system, the autonomic nervous system, and the hypothalamic–pituitary–adrenal axis.[18, 19] Disturbances in the brain–gut axis, including disruption of central and autonomic functions, peripheral hormones, amines, and peptides, have been documented in patients with IBS.[6] Clinical reviews of neuroimaging studies have also shown that, compared with healthy control participants, patients with IBS demonstrate differences in the central processing mechanisms of the brain–gut axis, such as changes in connectivity and functional responsiveness.[20] Although disruptions in the brain–gut axis may play a significant role in producing many clinical manifestations of IBS, the underlying mechanisms are not fully understood.[21] For the most part, patient diagnosis remains one of exclusion, with treatment being symptom driven.

DIAGNOSING IBS

The Rome III criteria for functional GI disorders served as the symptom-based diagnostic criteria for IBS since its release in 2006 until early 2016, when the Rome Foundation updated the criteria with the release of Rome IV (see Table 1[22, 23]).[5] Like Rome III, the Rome IV criteria maintains that an IBS diagnosis requires symptoms to be chronic (having persisted for at least six months), active (having occurred within the previous three months), and like all functional bowel disorders, to occur in the absence of an anatomic or physiologic abnormality.[23] Requisite symptom frequency, however, has been increased from at least three days per month in Rome III to at least one day per week in Rome IV. Furthermore, in contrast to Rome III, Rome IV specifically calls for abdominal pain (rather than *pain or discomfort*) to be related to (versus *improved with*) defecation, and clarifies that it is the abdominal pain (rather than the pain's *onset*) that must be associated with changes in stool frequency or form.[22, 23] In Rome IV, subtyping by predominant stool pattern—as IBS-C (with constipation), IBS-D (with diarrhea), IBS-M (with a mixed stool pattern), and IBS-U (unclassified because of an insufficient consistency of stool abnormality)—is now based on

Table 1. Comparison of Rome III and Rome IV Criteria[22, 23]

Characteristic	Rome III	Rome IV
Diagnostic time frame	• Symptom onset at least six months prior • Symptom activity during the last three months • Symptom frequency at least three days per month	• Symptom onset at least six months prior • Symptom activity during the last three months • Symptom frequency at least one day per week
Symptom description	Abdominal discomfort or pain	Abdominal pain
Symptom association (2 or more)	• Improvement with defecation • Onset associated with change in the form of stool • Onset associated with a change in the frequency of stool	• Related to defecation • Associated with a change in the form of stool • Associated with a change in the frequency of stool
Predominant stool pattern of IBS subtype (IBS-C, IBS-D, IBS-M, IBS-U)	Stool type based on bowel movements on all days	Stool type based on days with abnormal bowel movements
Tool to categorize bowel habit	Bristol Stool Form Scale	Bristol Stool Form Scale

IBS = irritable bowel syndrome; IBS-C = IBS with constipation; IBS-D = IBS with diarrhea; IBS-M = IBS with a mixed stool pattern; IBS-U = IBS unclassified.

stool form on the days in which at least one bowel movement is abnormal, as opposed to stool form on all days since onset.[23] Rome IV retains the Bristol Stool Form Scale[24] as a means of categorizing abnormal stool form, using 25% of stools as the threshold for subtyping the stool pattern.[23]

The differential diagnosis of IBS should include celiac disease, microscopic colitis, inflammatory bowel disease, bile acid malabsorption, colorectal cancer, and dyssynergic defecation.[25] However, using the Rome IV criteria, clinicians can diagnose IBS based on the following data[23]:

- patient history, including diet as well as symptoms
- physical examination, including an anorectal examination
- complete blood count
- C-reactive protein or fecal calprotectin level
- celiac serology, if clinical suspicion is high
- a colonoscopy or upper endoscopy, if recommended by guidelines because of patient age, alarm signs, or family history

Symptom overlap. In clinical practice, GI diagnoses commonly share symptoms. For instance, a systematic review and meta-analysis of IBS symptoms in patients with inflammatory bowel disease (IBD) found that IBS symptoms were significantly higher in both patients with active IBD and patients whose IBD was in remission than in control participants without IBD.[26] The pooled prevalence of IBS symptoms in the two IBD groups was 39%, 35% among patients believed to be in remission and 44% among those with active IBD. Clinical trials are needed to develop evidence-based approaches for treating patients with IBD who have IBS-type symptoms.[27] It's been suggested that fecal calprotectin, which is a very sensitive measure of disease activity in IBD, should be measured in the initial evaluation of such patients.[27]

A recent systematic review and meta-analysis demonstrated that IBS symptoms also overlap with those of microscopic colitis, though therapeutic interventions are very different.[28] This review reported the pooled prevalence of IBS symptoms in patients with microscopic colitis to be 33.4%, similar to that seen in patients with other diarrhea etiologies. Symptom overlap between IBS and other GI disorders has prompted the use of invasive medical procedures and spurred efforts to develop biomarkers to aid in IBS diagnosis.

Biomarkers. Over the years, it's been suggested that various biomarkers could aid in diagnosing IBS. In 2009, Lembo and colleagues proposed a serum panel consisting of 10 biomarkers that included two cytokines, two antibodies, a chemokine, a nerve growth factor, a tissue-repair enzyme, an autoantibody, a metalloproteinase inhibitor, and a lipocalin protein.[29] A few years later, Jones and colleagues extended the panel, incorporating an additional 24 biomarkers, including serologic markers for gene expression, and incorporating four psychological measures.[30]

Biomarker initiatives have included studies of

- colonic transit and fecal bile acids to distinguish patients with IBS from healthy participants or to discriminate among IBS subgroups.[31]
- anticytolethal distending toxin B and antivinculin antibodies to distinguish IBS-D from other diagnostic possibilities.[32]
- intestinal microbiota to identify and characterize fecal dysbiosis in patients with IBS or IBD.[33]

Although the diagnostic value of these tests is encouraging, biomarkers have yet to become the gold standard for diagnosing IBS in clinical practice.

Pharmacologic management of IBS focuses on the predominant bowel symptom (diarrhea or constipation) and abdominal pain. Patient education, suggestions for lifestyle modifications, and reassurance should be provided with all IBS treatments.

PHARMACOLOGIC INTERVENTIONS

IBS is a multifactorial disorder. For this reason, pharmacologic management focuses on the predominant bowel symptom (diarrhea or constipation) and abdominal pain (see Table 2[23]). Patients with IBS-M may require treatments for both diarrhea and constipation.[34] Patient education, suggestions for lifestyle modifications, and reassurance should be provided with all IBS treatments.

The American Gastroenterological Association (AGA) guidelines on the pharmacologic management of IBS characterizes the strength of its recommendations as conditional (weak) or strong and grades the quality of the supporting evidence as very low, low, moderate, or high.[35] Although these guidelines discuss nine pharmaceutical agents or classes used in the treatment of IBS—linaclotide, lubiprostone, polyethylene glycol laxatives, rifaximin, alosetron, loperamide, tricyclic antidepressants, selective

Table 2. Pharmacologic Interventions for IBS[23]

Abdominal Pain	Bowel Subtype: IBS-C	Bowel Subtype: IBS-D
Antispasmodics	Chloride channel activators	Opioid agonists
Peppermint oil	Polyethylene glycol	Antibiotics
Selective serotonin reuptake inhibitors	Psyllium	Bile acid sequestrants
Tricyclic antidepressants	Guanylate cyclase-C agonists	Probiotics
		Mixed opioid receptor modulators
		Serotonin-3 antagonists

IBS = irritable bowel syndrome; IBS-C = IBS with constipation; IBS-D = IBS with diarrhea.

serotonin reuptake inhibitors, and antispasmodics—only the use of linaclotide for IBS-C was given a strong recommendation, based on high-quality evidence.[35] Linaclotide (Linzess), a guanylate cyclase-C agonist, stimulates the secretion of chloride and bicarbonate into the intestine, thereby increasing intestinal fluid and accelerating GI transit.[36]

The American College of Gastroenterology (ACG) performed a systematic review to determine the efficacy of 11 IBS therapies, both pharmacologic and nonpharmacologic, compared with placebo or no treatment.[37] The nonpharmacologic interventions included dietary manipulation, fiber, probiotics, prebiotics, peppermint oil, and psychological therapies, including hypnotherapy. As with the AGA guidelines, the ACG graded the quality of the evidence on which its recommendations were based (very low, low, moderate, or high) and characterized the strength of its recommendations as strong or weak. Only two therapies overall received strong recommendations for use and were supported, respectively, by evidence of high and moderate quality: linaclotide and lubiprostone for the treatment of IBS-C. Lubiprostone (Amitiza), a chloride channel activator, increases intestinal fluid secretion, thereby increasing intestinal motility and stool passage.[38]

NONPHARMACOLOGIC INTERVENTIONS

Nonpharmacologic interventions, such as diet modification, exercise, mind–body therapies, and other complementary approaches, are often used to provide relief of IBS symptoms. A Cochrane review of the efficacy of psychological interventions found that cognitive behavioral therapy and interpersonal psychotherapy may benefit patients with IBS, though issues regarding study heterogeneity, validity, and sample size were noted.[39] A systematic review and meta-analysis by Ford and colleagues, which included 30 studies on the effect of psychological therapies on patients with IBS, found some beneficial effects of cognitive behavioral therapy, multicomponent psychological therapy, dynamic psychotherapy, and hypnotherapy.[40]

Dietary modifications to alleviate IBS symptoms have garnered increasing interest in recent years.[41] Food ingestion can stimulate chemoreceptors, mechanoreceptors, osmotic actions, altered secretion, activation of motor reflexes, and colonic fermentation, which may contribute to IBS symptoms.[42] Patients with IBS are more likely than the general population to report adverse reactions to food, with dietary intolerance often attributed to gluten (wheat and related grain species); lactose; fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs); and fructose malabsorption.[43] Patients with IBS have used diets excluding suspected IBS triggers with conflicting results.[44]

In a recent prospective study of 41 patients with IBS-D, a six-week gluten-free diet significantly improved symptom severity scores in 29 (71%), and there was significant overall improvement in anxiety, depression, fatigue, and quality of life.[45] The low-FODMAP diet has also been found to improve abdominal and bowel symptoms in some patients with IBS, although guidance from a nutritionist is generally recommended.[34] A systematic review and meta-analysis of 14 randomized controlled trials, which included 96 patients with various IBS subtypes, found that soluble fiber supplementation had beneficial effects on global IBS symptoms.[46]

Intestinal microbiota play a major role in GI processes and overall health.[47] Numerous studies have investigated the value of probiotics in manipulating the intestinal microbiota and improving IBS symptoms. A meta-analysis of 10 randomized controlled trials that compared the efficacy of probiotics with placebo in treating IBS symptoms found that probiotics containing *Bifidobacterium breve*, *Bifidobacterium longum*, or *Lactobacillus acidophilus* significantly reduced IBS pain.[48] Abdominal distension was significantly reduced by probiotics containing *B. breve*, *Bifidobacterium infantis*, *Lactobacillus casei*, or *Lactobacillus plantarum*. The researchers noted, however, that further research into such variables as

probiotic dose, species, combinations, treatment duration, IBS subtypes, and specific symptoms was needed, and emphasized that clinicians should always consider comorbid conditions when prescribing probiotics to patients.[48] A systematic review and meta-analysis of 43 randomized controlled trials similarly concluded that probiotics can be effective in treating global IBS symptoms, flatulence, abdominal pain, and bloating, though investigators could draw no conclusions about individual strains or species.[49]

Fecal microbiota transplantation (FMT). Whereas probiotics aim to alter the native gut microbiota, FMT introduces a community of gut microorganisms to replace or repair the native gut microbiota.[50] Although it has been suggested that FMT may improve IBS symptoms, the procedure has been performed on a limited number of patients.[51] Randomized controlled trials are needed to confirm the safety and efficacy of FMT, and the U.S. Food and Drug Administration requires an investigational drug application to perform FMT for any condition other than *Clostridium difficile* infection that is not responsive to standard therapy.[51]

use of needles or pressure.[54] Whereas acupuncture is the insertion of needles into these acupoints, moxibustion is the application of heat (by ignited moxa).

A systematic review and meta-analysis evaluating the efficacy of acupuncture in treating IBS found no differences between actual and sham acupuncture on either IBS symptoms or quality of life.[55] Other investigations have used functional magnetic resonance imaging (fMRI) to evaluate the effects of acupuncture on brain activation in patients with IBS-D during rectal distension. Chu and colleagues reported significant fMRI differences between actual and sham acupuncture groups: true electroacupuncture significantly heightened activation at the right insula, the pulvinar, and the medial nucleus of the thalamus, compared with sham treatment.[56] Another fMRI study of patients with IBS-D and rectal distension found that patients who received actual moxibustion treatment experienced a significant reduction in IBS symptoms compared with those who received sham moxibustion treatment.[57]

A nurse-delivered intervention of cognitive-behavioral strategies, diet, relaxation, and education resulted in significantly improved GI symptoms and quality of life and greater reductions in daily depression and anxiety scores in patients with IBS.

Increased physical activity. In a randomized controlled trial of 102 patients, Johannesson and colleagues found that a 12-week intervention of moderately increased physical activity significantly reduced IBS symptom severity and improved quality of life.[52] In addition, this study found that the proportion of worsening IBS symptoms was significantly greater in the physically inactive control group than in the physically active intervention group.

Yoga. A recent systematic review of six randomized controlled trials found that yoga may have significant beneficial effects on IBS severity, anxiety, and quality of life.[53] Investigators, however, could not make recommendations regarding yoga practice for IBS because of methodologic flaws in the studies reviewed.

Traditional Chinese medicine modalities, such as acupuncture and moxibustion, have been explored as potential IBS treatments. In traditional Chinese medicine, the natural life force, or qi, flows through conduits or meridians, with disease resulting when there is circulatory interference. Stimulating acupoints restores the flow of qi, and may be accomplished through the

Comprehensive self-management. Jarrett and colleagues evaluated the effect on patients with IBS of a nine-session, nurse-delivered, comprehensive self-management intervention that incorporated cognitive–behavioral strategies, diet, relaxation, and education. These investigators found that patients who underwent the intervention experienced significantly improved GI symptoms and quality of life compared with patients who received usual care.[58] A secondary data analysis of that study revealed long-term, beneficial effects of the intervention, reflected by significantly lower daily levels of patient-reported stress at three-, six-, and 12-month follow-up.[59] Patients with IBS who received the comprehensive self-management intervention were also found to have significantly greater reductions in daily depression and anxiety scores across three-, six-, and 12-month follow-up, compared with patients who received usual care.[60] A recent follow-up evaluation of this program found that 94% of the participants who received the intervention still incorporate comprehensive self-management strategies into their lives, one year after their last session.[61] These investigations highlight the potential for

nurse-led initiatives to impart long-lasting, positive health effects to patients with IBS.

IMPLICATIONS FOR NURSING PRACTICE

Nurses can promote early consideration of IBS as a potential diagnosis and improve patient education, support, and communication in the following ways:

- Become familiar with IBS prevalence rates, as well as IBS sex and age predominance.
- Learn about the disorders that can mimic IBS signs and symptoms.
- Review the Rome IV guidelines, noting which tests and invasive procedures may be avoided.
- Remain aware of the advances in research into IBS etiology and perpetuation of symptoms.
- Understand the high frequency of comorbid psychological disorders and possible life stressors in patients with IBS.
- As part of patient assessment, inquire about dietary and medication changes, life stressors, and support networks.

Although IBS is a common, multifactorial, GI disorder that exacts a significant toll on both patients and society, significant advances have been made in the field, and therapeutic options show promise. Ongoing efforts to understand the many components of IBS will foster a comprehensive, personalized approach to patient care that recognizes the individuality of each affected patient. Nursing professionals play a vital role in the collaborative process of patient care and can aid in the development of diagnostic and therapeutic approaches, in both the clinical and the research domains. Such innovation, when attuned to the diverse needs of patients with IBS, can produce therapeutic gains and bring symptomatic relief to this deserving patient population. ▼

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