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Irritable Bowel Syndrome: A review

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Abstract

Irritable Bowel Syndrome (IBS) is a common, chronic gastrointestinal condition defined by disturbances in bowel habits and abdominal pain, in the absence of known organic pathology. IBS reduces patients' quality of life, and exerts a substantial, negative impact on financial resources of patients and society at large. The diagnosis of IBS is made according to a symptom based classification system, the Rome Criteria, with updated guidelines, Rome IV, recently released. Physiological and psychological variables have been identified as playing a role in the etiology and perpetuation of symptomatology, highlighting the cross-talk between the brain and the gut in patients living with IBS. Although research investigations have made gains in understanding the pathophysiology of IBS, therapeutic interventions remain symptom driven, with both pharmacological and non-pharmacological approaches in the treatment arsenal. The purpose of this review is to summarize the epidemiology, pathophysiology, diagnosis, and treatment of IBS, and to discuss implications for clinical nursing practice.

Keywords

Irritable Bowel Syndrome; IBS; Rome Criteria; treatment approaches

Introduction

Irritable bowel syndrome (IBS) is a chronic disorder of the gastrointestinal tract, characterized by abdominal pain and alterations in bowel habits (Canavan, West & Card, 2014). IBS is the disorder most commonly encountered by gastroenterologists (Halmos, Power, Shepherd, Gibson & Muir, 2014), and diagnosis is made according to a symptom-based classification system, the Rome Criteria, with the latest version, Rome IV, recently released (Drossman, 2016). Prevalence rates in North America have been reported as approximately 12%, and symptoms occur more often in patients less than 50 years of age

(Lovell & Ford, 2012). Patients with IBS suffer not only from gastrointestinal distress, but approximately 40–60% experience comorbid psychological disorders, such as depression or anxiety (Dekel, Drossman & Sperber, 2013). In addition, patients with IBS report higher levels of somatization compared to patients without IBS but with gastrointestinal symptoms (Patel et al., 2014). Not surprisingly, IBS has been shown to negatively impact patients' quality of life, as well as to adversely affect society's financial resources.

Despite the substantial cost of IBS to both patients and society, curative, medical interventions have yet to be discovered. The development and persistence of IBS symptoms have been acknowledged as multifactorial in nature, making treatment of the disorder a complicated, clinical endeavor. Approaches are based on the reduction of patient symptomatology, and current pharmacological management often provides suboptimal relief (Grundmann & Yoon, 2014). Evidence of biological dysregulation has been reported in patients with IBS, and efforts are ongoing to advance understanding of the neurohormonal underpinnings of the disorder (Camilleri, 2014). Although gains have been made in understanding the pathophysiology of IBS, exact mechanisms leading to symptom development are not completely understood (Mayer & Tillish, 2011). The prevalence of patients who suffer from IBS, developments in the field of IBS research, and the release of updated diagnostic criteria were the impetus for undertaking this review to summarize the epidemiology, pathophysiology, diagnosis, and treatment of IBS, and to discuss implications for clinical nursing practice.

Epidemiology and Burden of Disease

Incidence rates of IBS are not typically calculated, and prevalence estimates fluctuate internationally, both between and within countries (Canavan, West & Card, 2014). Such discrepancies have been attributed to the heterogeneity of prevalence investigations, including variations in the use of instruments, methods, diagnostic criteria, populations and cultures assessed (Sperber et al., 2016). This recent investigation evaluated 83 community-based studies of IBS prevalence from around the world, confirming the global predominance of females who suffer from IBS, but could not confidently estimate a global prevalence rate due to the heterogeneity amongst investigations. The pooled prevalence rate for North America, Europe, Australia and New Zealand was cited as 8.1% by this investigation (Sperber et al., 2016).

In contrast to the variability of prevalence estimates, the burden or adverse impact of IBS is unfortunately, more consistent. IBS is not associated with increased mortality rates, yet imparts a significant burden to both patients and society as a result of direct medical costs, lost productivity, and reduced health-related quality of life (Inadomi, Fennerty & Bjorkman, 2003). In 2010, the diagnosis of IBS accounted for over 2 million ambulatory visits in the United States, including visits to the office, emergency departments, and hospital outpatient departments (Peery et al., 2015). Fiscal estimates of lost productivity, lost leisure time, and IBS management exceed one billion dollars in the United States (Everhart & Ruhl, 2009).

Numerous investigations have established the disproportionate utilization of health care resources by patients with IBS, as well as the negative impact of IBS on patients' quality of

life (Agarwal & Spiegel, 2011). Despite the increase in medical attention that patients with IBS receive, many patients experience difficulties and problems with their healthcare encounters (Ringstrom, Sjøvall, Simren & Ung, 2013). Patients with IBS have reported unsupportive encounters with their healthcare providers, shaped by experiences of humiliation, insignificance, and abandonment (Hakanson, Sahlberg-Blom & Ternstedt, 2010). An additional burden of IBS falls on those who live with or care for people with the disorder; studies report adverse effects on the quality of life of partners of IBS patients (Canavan, West & Card, 2014). In summary, IBS is a common gastrointestinal condition that has high comorbidity rates, reduces the quality of life of patients, and exerts a substantial, negative impact on the monetary resources of both patients and society.

Pathophysiology

IBS is recognized as a multifactorial disorder, with the following among the proposed mechanisms contributing to symptomatology: gastrointestinal dysmotility, inflammation, visceral hypersensitivity, and altered intestinal microbiota (Lee & Park, 2014). Diet and stress exposure (including early life events) have been proposed as contributing factors to this heterogeneous disorder (Heitkemper, Jarrett & Jun, 2013). Because stress has been identified as a mechanism in the development of IBS, the major components of the stress response system, the autonomic nervous system (ANS) and the hypothalamic-pituitary-adrenal (HPA) axis, have been the subject of numerous investigations of IBS (Fichna & Storr, 2012). Lastly, genetic predisposition and environmental interactions, such as familial susceptibility and psychosocial stressors, have been implicated in the multifactorial pathogenesis of IBS (Fukudo & Kanazawa, 2011).

Physiological and psychological variables have jointly been identified as playing a role in the etiology and perpetuation of IBS symptomatology. In an investigation of risk factors for military personnel developing IBS, Riddle et al. (2016) found the risk of developing IBS to be increased after cases of infectious gastroenteritis, and also to be increased in subjects with post-traumatic stress disorder (PTSD), increased number of life stressors, and self-reported anxiety and depression. 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 or (BGA).

The BGA refers to pathways among physiological systems, including the central nervous system (CNS), the enteric nervous system (ENS), and the autonomic nervous system (ANS) (Ohman & Simren, 2007). Endocrine, neural, and neuroimmune pathways facilitate bi-directional communication between the CNS and the gut (Fichna & Storr, 2012). Patients with IBS have been noted to exhibit disturbances in the BGA, including central and autonomic functions, peripheral factors, peptides, and hormones (Camilleri, 2014). Differences in central processing mechanisms of the BGA have also been demonstrated in IBS patients compared to healthy controls, through the use neuroimaging techniques (Stasi, Rosselli, Bellini, Laffi & Milani, 2012). Such investigations illustrate that patients with IBS exhibit differences in brain structure, connectivity, and functional responsiveness in comparison to healthy controls (Weaver, Sherwin, Walitt, Melkus & Henderson, 2016). It is proposed that the clinical presentation of IBS patients with pain, psychological comorbidities, and altered gut motility may be explained through changes in the BGA,

although mechanisms are not fully understood (Coss-Adame & Rao, 2014). Despite great progress in understanding the pathophysiology of IBS, such discoveries have not been fully translated to the clinical arena; patient diagnosis remains one primarily of exclusion, and treatment interventions remain symptom driven.

Diagnosis

IBS is the gastrointestinal disorder that is most commonly diagnosed; the diagnosis is made from the presence of certain symptoms in the absence of organic disease (Chey, Kurlander & Eswaran, 2015). IBS has been categorized as a functional bowel disorder, defined by symptom onset greater than six months and recurrence at least three days per month during the last three months (Longstreth et al., 2006). Diagnostic criteria require abdominal discomfort or pain to be associated with two or more of the following: improvement with defecation, onset associated with change in the form of stool, or onset associated with a change in the frequency of stool (Longstreth et al., 2006). This diagnostic criteria, known as Rome III classification, also subtypes IBS patients based on their predominant stool pattern: constipation (IBS-C), diarrhea (IBS-D), mixed (IBS-M) or unsubtyped (IBS-U) (Longstreth et al., 2006). Rome III has served as the symptom-based, diagnostic criteria for IBS since its release in 2006; in early 2016 the Rome Foundation released Rome IV, an updated classification system for conceptualizing and diagnosing functional gastrointestinal disorders (Drossman, 2016) (see Table 1).

The Rome IV definition of IBS maintains symptom chronicity (greater than six months) and current activity (present within the prior three months); however, symptom frequency has been changed to at least one day per week (from at least three days per month), specifically requires abdominal pain (discomfort has been eliminated) to be related to (versus improved with) defecation, and the “onset” of abdominal pain has been eliminated from the association of pain with changes in stool (Lacy et al., 2016). Rome IV also updates the subtyping of IBS patients (IBS-C, IBS-D, IBS-M and IBS-U), in that stool type is based on days with abnormal bowel movements, as opposed to bowel movements on all days (Lacy et al., 2016). In addition, Rome IV retains the Bristol Stool Form Scale (Lewis & Heaton, 1997) as a useful tool to categorize bowel habit (Lacy et al., 2016).

In order to make an accurate diagnosis of IBS, it is recommended to incorporate Rome IV Criteria along with the following: patient history (including dietary questions), physical examination (including anorectal examination), limited laboratory tests (such as complete blood count, C-reactive protein or fecal calprotectin, possible celiac disease serology), and when indicated (either due to recommended guidelines for patient age, alarm signs, family history, etc.), a colonoscopy and/or upper gastrointestinal endoscopy as well as other tests (Lacy et al., 2016). Alternative diagnoses that should be considered when patients present with IBS symptomatology include celiac disease, microscopic colitis (MC), inflammatory bowel disease (including Crohn’s disease and ulcerative colitis), bile acid malabsorption, colorectal cancer, and dyssynergic defecation (Chey, Kurlander & Eswaran, 2015).

The symptoms of IBS and other gastrointestinal diagnoses commonly overlap in clinical practice, therefore, investigations have examined the prevalence of such associations. For

instance, Halpin & Ford (2012) conducted a systematic review and meta-analysis on IBS symptoms in patients with inflammatory bowel disease (IBD). These authors report that IBS symptoms were significantly higher in IBD patients with active disease and in remission (overall prevalence approximately 40%), than in comparison to non-IBD controls. In order to guide therapy for such patients (IBD with IBS-type symptoms), it has been suggested to measure fecal calprotectin as an initial evaluation, and that clinical trials are needed to foster evidence-based approaches (Quigley, 2016). Symptoms also overlap between IBS and another diagnosis, MC, although therapeutic interventions are quite different (Kamp, Kane & Ford, 2016). This recent systematic review and meta-analysis reported the pooled prevalence of IBS to be approximately 33% in patients with MC, although these odds were not higher than in other patients with diarrhea. Such overlap of symptoms between patients with IBS and other gastrointestinal disorders, has prompted the use of invasive medical procedures in efforts to obtain a diagnosis. This situation has fostered the efforts of biomarker development to aid in the assessment and diagnosis of patients with IBS.

Over the years, various biomarkers have been proposed to differentiate patients with IBS from healthy controls. For instance, Lembo et al. (2009) proposed a ten biomarker blood-based panel which included a cytokine, nerve growth factor, autoantibody, antibodies, etc. A few years later, Jones et al. (2014) built on these original ten parameters and compiled an extensive panel (34 markers) that incorporated serological markers, gene expression, and psychological measures. Biomarker initiatives have also investigated colonic transit and fecal bile acids (Camilleri et al., 2014), anti-cytolethal distending toxin B, and anti-vinculin antibodies for distinguishing patients with IBS-D (Pimentel et al., 2015) as well as tests of fecal dysbiosis to characterize patients with IBS (Casen et al., 2015). Although these tests are encouraging in their diagnostic ability and highlight the biological underpinnings of IBS, biomarkers have yet to become the gold standard in clinical practice for diagnosing patients with IBS.

Treatment

Pharmacological Interventions

IBS is a multifactorial disorder, and approaches to treatment are similarly diverse. Patient education and reassurance by the provider, however, should be included in all treatments (Halland & Saito, 2015). Pharmacological management is mainly geared towards the predominant bowel symptom of the patient (diarrhea or constipation), and in patients with IBS-M, a combination of treatments may be needed (Lacy, Chey & Lembo, 2015). Therapeutic options for relieving abdominal pain in IBS patients include antispasmodics, peppermint oil, selective serotonin reuptake inhibitors (SSRIs), and tricyclic antidepressants; interventions for bowel disturbances (IBS-D) include opioid agonists, antibiotics, bile salt sequestrants, probiotics, mixed opioid agonists/antagonists, and 5-HT₃ antagonists, IBS-C is treated with chloride channel activators, polyethylene glycol (PEG), psyllium, and guanylate cyclase C agonists (Lacy et al., 2016) (see Table 2).

The American Gastroenterological Association (AGA) released guidelines on the pharmacological management of IBS, with interventions based on patient subgroups of IBS-C and IBS-D (Weinberg, Smalley, Heidelbaugh & Sultan, 2014). These guidelines vary in

the level of recommendation from conditional (weak) to strong, and are based on the quality level of the evidence (very low, low, moderate, and high). Included in these guidelines are recommendations for nine pharmaceutical agents in the treatment of IBS: linaclotide, lubiprostone, PEG laxatives, rifaximin, alosetron, loperamide, tricyclic antidepressants, SSRIs and antispasmodics. Overall, the only strong pharmacotherapy recommendation, with high-quality evidence, is the use of linaclotide, a guanylate cyclase C agonist, for patients with IBS-C.

The American College of Gastroenterology (ACG) performed a recent systematic review on the efficacy of eleven therapies (both pharmacological and non-pharmacological) for treating IBS (Ford et al., 2014). Therapies were evaluated in comparison to placebo or no treatment. In addition, treatments were evaluated in relation to predominant stool pattern and adverse events of treatment. Similar to the AGA guidelines, the ACG recommendations include not only strength of the recommendations (weak versus strong), but also the quality of the evidence upon which the recommendations were based (very low, low, moderate, and high). Non-pharmacological therapies evaluated by the ACG included dietary manipulation, fiber/psyllium, probiotics/prebiotics, peppermint oil, and psychological therapies including hypnotherapy. Overall, the two therapies that received strong recommendations for use, supported by high and moderate quality of evidence, respectively, were the prosecretory agents, linaclotide and lubiprostone, for the treatment of IBS-C.

Non-pharmacological Interventions

The goal of treatment interventions is to provide IBS patients with symptomatic relief; often this is attempted through the use of non-pharmacological interventions such as mind-body therapies, diet modification, exercise, and other complementary and alternative approaches (Saha, 2014). Conclusions from a Cochrane Review on the efficacy of psychological interventions in IBS patients, were that cognitive behavioral therapy and interpersonal psychotherapy may be beneficial in patients with IBS, although issues were noted regarding study heterogeneity, validity and sample size (Zijdenbos et al., 2009). More recently, Ford et al. (2014) carried out a systematic review and meta-analysis of 30 studies on the effect of psychological therapies in patients with IBS. The authors found beneficial treatment effects of cognitive behavioral therapy, multicomponent psychological therapy, dynamic psychotherapy, and hypnotherapy.

A growing focus of clinical research has been to improve IBS symptomatology through dietary modifications (Chey, 2016). Food ingestion can contribute to the generation of symptoms through stimulation of chemoreceptors, mechanoreceptors, by osmotic actions, altered secretion, activation of motor reflexes, and colonic fermentation (Eswaran, Tack & Chey, 2011). Patients with IBS are more likely than the general population to report adverse reactions to food; dietary intolerance of IBS patients has been attributed to gluten, wheat, lactose, fermentable oligosaccharides, disaccharides, monosaccharides and polyols (or FODMAPs) as well as fructose malabsorption (Mullin et al., 2014). Exclusion diets have been used in patients with IBS, for instance with wheat and dairy, although conflicting results have been reported (Halland & Saito 2015). A recent investigation of patients with IBS-D, found a six-week gluten-free diet significantly improved scores of symptom severity,

anxiety, depression, fatigue, and quality of life (Aziz et al., 2016). The low-FODMAP diet has also been examined in patients with IBS and found to result in improved abdominal and bowel symptoms in some patients, although guidance from a nutritionist is generally recommended (Lacy, Chey & Lembo, 2015). Another dietary manipulation, the use of soluble fiber supplementation, was found to have beneficial effects on global symptomatology in patients with IBS, according to a systematic review and meta-analysis of 14 investigations (Moayyedi et al., 2014).

Parallel to the focus on dietary modifications are efforts to manipulate or alter the intestinal microbiota. Undigested food is used by intestinal microbes (GI microbiota) upon entering the intestine, and microbiota play a major role in gastrointestinal processes and overall health (Barbara et al., 2016). Therefore, numerous studies have investigated the utility of probiotics in IBS, in efforts to manipulate the intestinal microbiota and improve symptomatology. For instance, a meta-analysis found a positive effect of probiotics in treating IBS pain, abdominal distension and flatulence, but noted further research was needed on variables such as probiotic dose, species, and duration (Ortiz-Lucas et al., 2013). Another systematic review and meta-analysis reported similar findings, concluding that probiotics are effective in treating IBS in terms of global symptoms, flatulence, abdominal pain and bloating, although conclusions could not be drawn regarding individual strains or species. (Ford et al., 2014). Further manipulation of the intestinal microbiota includes initiatives on fecal microbiota transplantation (FMT). Whereas probiotics aim to alter the native gut microbiota, FMT introduces a community of gut micro-organisms to replace or repair the native gut microbiota (Borody & Khoruts, 2012). Although it is suggested that restoring intestinal homeostasis via FMT might improve symptoms in patients with IBS, this has been performed on a limited number of cases; RCTs are needed to confirm safety and efficacy of the treatment, and the Federal Drug Administration requires an investigational drug application for use (Pinn, Aroniadis & Brandt, 2015).

Additional types of non-pharmacological interventions have been investigated in IBS patients. For instance, Johannesson et al. (2011) in a randomized control trial of 102 patients, found a 12-week intervention of moderately increased physical activity to decrease symptom severity of IBS and to improve some aspects of quality of life (related to physical role and physical functioning). In addition, this study found that the proportion of IBS symptoms worsening during the study was greater in the physically inactive group than in the physically active one. In a follow-up study (median time 5.2 years), 39 of the prior participants were found to report a positive, long-term effect of moderately increased physical activity on IBS symptomatology, quality of life, depression, anxiety, and fatigue (Johannesson et al., 2015). Yoga is another mind-body intervention that has been explored in the IBS patient population. A recent systematic review, surveying six randomized controlled trials, reports benefits of yoga on gastrointestinal symptoms, anxiety, and quality of life in patients with IBS (Schumann et al., 2016). This investigation could not make recommendations regarding yoga practice for IBS, however, because of the methodological heterogeneity that existed between reviewed studies.

Treatment modalities explored in the IBS patient population have also come from traditional Chinese medicine; these include acupuncture, electroacupuncture (EA) and moxibustion.

Acupuncture involves the insertion of needles to target acupoints, whereas moxibustion is the application of heat (by ignited moxa) to the acupuncture points (Ma et al., 2014). In an investigation of acupuncture in IBS, Chu et al. (2012) used functional magnetic resonance imaging (fMRI) to evaluate brain activation in patients with IBS-D. These researchers used actual EA and sham EA to evaluate central processing in response to rectal distension, and report significant fMRI differences between acupuncture groups. These authors postulate that acupuncture's therapeutic mechanism may potentially be modulated via the medial and pulvinar nucleus of the thalamus, as well as the right insula. Another fMRI study of patients with IBS-D undergoing rectal distension, evaluated brain imaging changes before and after, sham and actual, moxibustion treatment (Zhu et al., 2014). These researchers report the group who received actual moxibustion experienced decreased IBS symptoms, improved quality of life, and decreased rectal sensitivity; brain regions implicated in these changes include the prefrontal cortex and anterior cingulate cortex. A systematic review and meta-analysis on the efficacy of acupuncture in treating IBS, found patients who received acupuncture to report greater improvement than those receiving pharmacological therapies, although no differences were found between actual and sham acupuncture on IBS symptoms or quality of life (Manheimer et al., 2012).

Investigations have also been performed on non-pharmacological, self-management interventions to diminish IBS symptomatology. Jarrett et al. (2009) evaluated the efficacy of a 9-session, nurse-delivered, comprehensive self-management (CSM) intervention that incorporated cognitive-behavioral strategies, diet, relaxation, and education. This study found significant improvement in GI symptoms and quality of life measures in patients with IBS who underwent CSM intervention in comparison to patients who received usual care (UC). Further analysis of the CSM patients revealed long term, beneficial effects of the intervention, reflected by lower daily levels of patient-reported stress (Deechakawan et al., 2013). Patients with IBS who received the CSM intervention were also found to have significantly greater reductions in daily depression and anxiety scores across three, six and twelve months follow-up, compared with patients with IBS who received UC (Deechakawan et al., 2014). A recent evaluation of this program, found 94% of CSM participants still incorporating intervention strategies, one year after their last session (Zia et al., 2016). These investigations highlight the potential for nursing-led initiatives to impart long-lasting, positive health effects on patients with IBS. Nurses are in a prime position, as members of the healthcare team, to facilitate improved outcomes for patients living with IBS.

Implications for Clinical Nursing Practice

Nurses can positively affect the clinical outcomes of patients with IBS in countless ways. Familiarity with prevalence rates of IBS, as well as gender and age predominance, will promote early consideration of IBS as a potential diagnosis. Recognizing disorders that could mimic the signs and symptoms of IBS, as well as understanding Rome IV guidelines, will enable nurses to facilitate an early diagnosis, possibly reducing unnecessary tests or invasive procedures. Once the diagnosis of IBS is made, nursing interventions can truly aid in the well-being of this patient population. Awareness of the advances in the field of IBS research, will enable greater appreciation of the multifactorial nature of the disorder in terms of etiology and perpetuation of symptomatology. Knowledge pertaining to the high rates of

comorbid psychological disorders, and possible life stressors in this patient population, will allow nurses to tailor communication and patient interaction, accordingly.

Perhaps the mechanism whereby nurses can have the greatest, positive impact upon patients with IBS is through education and support. Nurses who are familiar with pharmacological options for treating the global symptoms of IBS, as well as symptoms by IBS subtype, can actively engage patients regarding medication types and mechanisms of action. By remaining up-to-date on evidence-based reviews of non-pharmacological options, nurses can help patients navigate treatment alternatives to select appropriate interventions. Given the numerous influences upon generation and perpetuation of IBS symptoms, it is important for nurses to question patients about dietary and medication changes, life stressors and support networks, as part of their ongoing assessment. Lastly, nurses should provide reassurance throughout the treatment process, thereby maintaining a therapeutic relationship as efforts are made towards diminishing IBS symptoms, and improving patients' quality of life.

Although IBS is a common, multifactorial, gastrointestinal disorder that exacts a significant toll on both patients and society, significant advances have been made in the field, and therapeutic options show promise. Efforts to understand the many components of IBS, and to recognize the individuality of each IBS patient, are leading the way towards a comprehensive, personalized approach to patient care. Nursing professionals are key players in the collaborative process of patient care, and can aid in the development of diagnostic and therapeutic approaches, both in the clinical and research domain. Such innovation, while remaining attuned to IBS patients' diverse needs, will potentiate therapeutic gains and bring about symptomatic relief, to this deserving patient population.

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Table 1

Rome Criteria

	Rome III (Longstreth et al., 2006)	Rome IV (Lacy et al., 2016)
Diagnostic timeframe	Symptom onset greater than 6 months. Symptom activity during the last 3 months. Symptom frequency at least 3 days per month.	Symptom onset greater than 6 months. Symptom activity during the last 3 months. Symptom frequency at least 1 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

Table 2

Pharmacological Interventions for IBS (Lacy et al., 2016)

Abdominal Pain	Bowel Subtype: IBS-C (abnormal bowel movements – usually constipation)	Bowel Subtype: IBS-D (abnormal bowel movements – usually diarrhea)
Antispasmodics	Chloride channel activators	Opioid agonists
Peppermint oil	Polyethylene glycol (PEG)	Antibiotics (Rifaximin)
Selective serotonin reuptake inhibitors (SSRIs)	Psyllium	Bile salt sequestrants
Tricyclic antidepressants	Guanylate cyclase C agonists	Probiotics
		Mixed opioid agonists/antagonists
		5-HT ₃ antagonists