Managing IBS: A Practical Summary for Clinicians

Based on the 2009 American College of Gastroenterology Evidence-Based Position Statement on the Management of Irritable Bowel Syndrome
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Target Audience

- Gastroenterologists
- GI nurse practitioners
- GI physician assistants
- Primary care physicians

Learning Objectives

After participating in this educational activity, participants should be able to:

- Delineate diagnostic criteria used in clinical practice for accurate diagnosis of irritable bowel syndrome (IBS)
- Explain the role of diagnostic testing in patients with IBS
- Discuss the latest data and levels of evidence for current and emerging treatments used in the management of IBS

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Accreditation/Credit Statements

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Darren M. Brenner, MD (Faculty Author)
Nothing to disclose with regard to commercial support

He discusses the non–FDA-approved use of antibiotics, antispasmodics, and antidepressants for IBS management in this monograph.

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Dr Brenner’s research and clinical interests include constipation and anorectal disorders. He is currently the principal gastroenterologist on a National Institutes of Health–National Institute of Diabetes and Digestive and Kidney Diseases–funded, multicenter project investigating the efficacy of minimal-contact cognitive behavioral therapy for IBS. In addition, he has recently authored two research articles on the use of probiotics in IBS management in *The American Journal of Gastroenterology* and *Reviews in Gastroenterological Disorders*. Dr Brenner is the recipient of several honors and awards and is a member of the following professional societies: the American Gastroenterological Association, American College of Gastroenterology, and American Society for Gastrointestinal Endoscopy.

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Dr Heitkemper has been on faculty at the University of Washington since 1981 and has been the recipient of three School of Nursing Excellence in Teaching awards and the University of Washington Distinguished Teaching Award. She also received the Distinguished Nutrition Support Nurse Service Award from the American Society for Parenteral and Enteral Nutrition (ASPEN) in 2002 and the American Gastroenterological Association and Janssen Award for Clinical Research in Gastroenterology in 2003. In addition, she was the first recipient of the Pfizer and Friends of the National Institute for Nursing Research Award for Research in Women’s Health in 2005. In 2006, Dr Heitkemper received the American Academy of Nursing Council for the Advancement of Nursing Science Outstanding Nursing Scientist Award. She was a member of the NIH National Commission on Digestive Diseases in 2007-2008. She is currently the Chair of the Council for the Advancement of Nursing Science organization.
Managing IBS: A Practical Summary for Clinicians

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Introduction

During the past few years, significant discoveries and changes have emerged in the pathogenesis, diagnosis, and treatment of irritable bowel syndrome (IBS). Subsequently, the American College of Gastroenterology (ACG) convened a panel of IBS experts with the goal of updating and revising current IBS guidelines. Through systematic review, this panel methodically reviewed the currently available literature and constructed an updated set of guidelines that were published in January 2009.1

The purpose of this document is to provide primary care and gastroenterology clinicians with a concise summary of the panel’s findings and recommendations. This document is organized into two categories, IBS Diagnosis and IBS Therapeutics, that both summarize the available evidence supporting the ACG panel’s recommendations. The latter section is separated by pharmacologic treatments (both over-the-counter and prescription) and nonpharmacologic treatments.

IBS Diagnosis

The ACG panel recommends that healthcare providers use the Rome criteria to diagnose and categorize IBS and advises against the use of routine testing when patients fit these criteria. However, there are some exceptions when additional testing is needed to rule out other conditions. The rationale for these exceptions and for the Rome criteria are described in more detail below.

Criteria Updates for Making a Diagnosis of IBS: Rome III

- Patients’ symptoms need only be improved, not relieved, with defecation
- IBS subcategorized based on predominant stool pattern

The diagnostic criteria for IBS have undergone multiple revisions; the Rome III criteria are the current standard (Table 1). It is important to recognize that a few significant adjustments were made to the current Rome criteria. Because most IBS patients do not experience complete relief of their pain/discomfort with defecation, the Rome III committee modified the requirement of relief to improvement in pain/discomfort with defecation. Furthermore, the time intervals required to make a diagnosis of IBS were adjusted such that patients now meet criteria if they have experienced symptoms three days a month for the past three months with symptom onset at least six months prior to making the diagnosis. Finally, subtyping of IBS patients has been modified to recognize the importance of a predominant stool pattern with four categories described: IBS with diarrhea (IBS-D), IBS with constipation (IBS-C), IBS mixed subtype (IBS-M), and IBS undefined (IBS-U).2 (Table 2).
The Epidemiology and Utility of Diagnostic Criteria and Testing for IBS

- 7% to 10% of people worldwide have IBS
- Patients fulfilling IBS symptom-based criteria in the absence of alarm signs/symptoms are unlikely to require further diagnostic testing
- Celiac sprue and lactose intolerance may be more prevalent in patients with IBS

Based on a systematic review utilizing only Rome definitions of IBS, the pooled prevalence of IBS is approximately 7% in North America and 7% to 10% worldwide. The prevalence of each of the specific subtypes requires further delineation. Women are 1.5 times more likely to develop IBS than men, and the disorder is more commonly identified in individuals younger than 50 years of age and in lower socioeconomic populations. Despite the perceived benign nature of IBS symptoms, data have also revealed that its health-related quality-of-life impact (HRQOL) parallels other major disorders such as diabetes, hypertension, and chronic kidney disease.

Historically, the need for diagnostic testing has been debated. Many practicing physicians consider IBS to be a diagnosis of exclusion. Thus, they perform many studies before being comfortable with an IBS diagnosis. Recent data have shown that lower abdominal pain has the highest sensitivity (90%) but low specificity (32%) for making a diagnosis of IBS. Conversely, abdominal distention has the highest specificity (77%) but the lowest sensitivity (39%). Furthermore, only a single study has been published evaluating the accuracy of the Rome criteria for diagnosing IBS, with Rome I criteria yielding a sensitivity of 71% and a specificity of 85%. No study to date has validated the Rome II or III criteria.
Despite these limitations, multiple lines of evidence have proven that IBS can be confidently identified without significant diagnostic evaluation. In a prospective study, patients meeting clinical criteria for IBS were subjected to a serologic, radiologic, and endoscopic work-up: 99% had negative evaluations. A subsequent study using Rome I criteria combined with exclusion of alarm symptoms exhibited a positive predictive value and specificity of 100% for IBS. A meta-analysis of six studies revealed that patients meeting symptom-based criteria for IBS have a less than 1% chance of receiving an alternate diagnosis. Two studies have validated the longevity of an IBS diagnosis; a change of diagnosis was exhibited in less than 1% of patients during a follow-up period of three years in one study and more than 20 years in the other study. Based on these data, the ACG IBS Task Force has recommended against the use of routine diagnostic testing in patients who meet the Rome criteria for IBS—with a few exceptions (Table 3).

Table 3: Recommended Diagnostic Testing in Patients With IBS Symptoms

1. Serologic screening for celiac sprue in patients with IBS-D and IBS-M
2. Lactose hydrogen breath testing can be considered if lactose intolerance is suspected
3. Colorectal cancer screening in patients meeting age-appropriate parameters
4. Colonoscopic imaging in patients with alarm features
5. Biopsies for microscopic colitis should be considered when colonoscopy is performed in patients with IBS-D

Emerging evidence suggests that both celiac sprue and lactose intolerance might be more prevalent in patients with IBS. A recent systematic review showed that IBS patients have an approximate four-time increased likelihood of serologic and histopathologic evidence of celiac sprue compared with the general population (OR 4.34; 95% CI, 1.78-10.6). Data from three case-controlled studies also identified an increased prevalence of lactose intolerance in IBS patients compared with controls (38% vs 26%, respectively). The Task Force, however, was quick to caution practicing physicians that these data do not prove causality, but instead suggest that physicians discuss with patients the possibility of symptom exacerbation with lactose consumption.
The Role of Alarm Features in the Diagnosis of IBS

- **Alarm features necessitate further diagnostic evaluation**
- **Nocturnal symptoms and rectal bleeding are minimally valuable when discriminating between organic diseases and IBS**

Alarm features have always been considered a reason for further diagnostic evaluation; however, a specific set of alarm features has not previously been standardized. Based on a high specificity for organic disease, the ACG IBS panel established a specific set of warning signs/symptoms that mandate further evaluation (Table 4).

Interestingly, nocturnal pain and rectal bleeding do not appear to offer any diagnostic advantage for differentiating organic diseases from IBS. Thus, physicians should not consider these subjective/objective findings as impetus for further diagnostic testing.

### Table 4: Alarm Features Necessitating Further Diagnostic Evaluation

<table>
<thead>
<tr>
<th>1. Anemia</th>
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</thead>
<tbody>
<tr>
<td>2. Weight loss</td>
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<tr>
<td>3. Family history of colorectal cancer</td>
</tr>
<tr>
<td>4. Family history of inflammatory bowel disease</td>
</tr>
<tr>
<td>5. Family history of celiac sprue</td>
</tr>
</tbody>
</table>

**IBS Therapeutics**

Various pharmacologic and nonpharmacologic treatment options are available for IBS management. Historically, therapies have targeted a specific IBS symptom; however, there has been a paradigm shift toward developing treatments beneficial for global IBS symptoms. For the current ACG guidelines, systematic reviews were performed for each IBS treatment and, based on the available data, a combined numeric and alphabetic grade assessing the quality of evidence and strength of recommendation was assigned to each intervention. The strength of the committee’s recommendations was defined on a two-point scale with 1 and 2 representing strong and weak recommendations, respectively. The quality of evidence supporting the committee’s recommendations was delineated by an alphabetic score with high-, moderate-, and low-quality evidence represented by letter scores of A, B, and C, respectively. A summary of the evidence used to evaluate IBS therapies and assign their grades follows. The therapeutics in each section are listed from the strongest to weakest recommendations (Table 5).

**Pharmacologic Treatment: Prescription and Over-the-Counter Options**

**Serotonin (5-HT)\textsubscript{3} Receptor Modulators**

Multiple serotonin (5-hydroxytryptamine; 5-HT) receptor mediators have shown efficacy for treating global IBS symptoms. Approximately 95% of the body’s 5-HT receptors are located throughout the GI tract with the 5HT\textsubscript{3} and 5HT\textsubscript{4} receptors playing a pivotal role in GI motility, secretion, and sensation.
5-HT\textsubscript{4} Agonists (1A–Women with IBS-C; 1B–IBS-M)

- Tegaserod is more effective than placebo in alleviating global IBS symptoms in women with IBS-C and in IBS-M patients
- Tegaserod was removed from the market because of a small but significantly increased risk of cardiovascular events

Tegaserod was the only 5-HT\textsubscript{4} agonist approved for treating IBS in the United States. Multiple studies have evaluated the efficacy of tegaserod in IBS-C and IBS-M patients, and in the meta-analysis performed for the ACG position statement, 6 mg of tegaserod twice daily resulted in significant improvement in global IBS symptoms compared with placebo (RR of IBS not improving=0.85; 95% CI, 0.80-0.90).\textsuperscript{13} The studies incorporated into the analysis were well designed; however, significant heterogeneity was apparent in the results. In individual studies, 5% to 19% of patients taking tegaserod experienced improvements in global IBS symptoms compared with placebo, and significant improvements were also identified in sub-syndrome symptoms including abdominal discomfort, bloating, and overall satisfaction with bowel habits. All of the tegaserod trials recruited primarily women; thus, it was approved for women with IBS-C. Common side effects include abdominal pain, nausea, headaches, and diarrhea. Tegaserod was withdrawn from the market in March 2007 after postmarketing analyses revealed a small but significant increase in cardiovascular events (0.11%) in patients taking this medication. Tegaserod is still available through an investigational drug program.

The efficacy of other 5-HT\textsubscript{4} agonists has been poor. Both cisapride and renzapride have been tested in patients with IBS. In a meta-analysis of four IBS-C trials, cisapride did not yield benefits compared with placebo. Similar results were identified in three renzapride trials. Cisapride was withdrawn from the market in July 2000 because of its propensity to induce severe cardiac arrhythmias, and further development of renzapride has been halted.

Antidepressants (1B)*

- TCAs are more effective than placebo in alleviating global IBS symptoms
- SSRIs are more effective than placebo in alleviating global IBS symptoms

Antidepressants have long been used to treat the pain component of IBS. Multiple trials using tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) have been completed. Thirteen randomized controlled trials (RCTs) were incorporated into the ACG systematic review.\textsuperscript{14} When the data from both TCA and SSRI trials were combined, IBS patients receiving antidepressants experienced significant improvements in global IBS symptoms compared with placebo with a relative risk of IBS symptoms not improving equal to 0.66 (95% CI, 0.57-0.78). In individual pooled analyses of nine TCA trials and five SSRI studies, the data further suggested that both classes of medications were superior to placebo with relative risks of not improving of 0.68 (95% CI, 0.56-0.83; number needed to treat [NNT]=4) and 0.62 (95% CI, 0.45-0.97; NNT=3.5), respectively. Studies assessing the efficacy of these medications for each specific IBS subgroup are lacking; however, inherent properties of these medications and anecdotal experience suggest that the anticholinergic TCAs may be more useful in patients with IBS-D, whereas the prokinetic SSRIs may work better in patients with IBS-C. Safety data were reported in six of the studies and suggested an increased risk of adverse events, which did not reach statistical significance. No TCA/SSRI comparison trials have been published.

*Not approved by the FDA for IBS treatment
Antibiotics (1B)*

- Neomycin improved global IBS symptoms in a single small RCT
- Rifaximin repeatedly demonstrates improvement in global IBS symptoms and bloating
- Rifaximin is most likely to be beneficial in patients with IBS-D

Two antibiotics have been tested in RCTs: neomycin and rifaximin. Neomycin was the first tested, and in a single RCT of 111 patients, a significantly higher percentage of neomycin-treated patients experienced a greater than 50% improvement in global IBS symptoms compared with placebo (43% vs 23%, \(P<0.05\)).\(^\text{15}\)

Rifaximin, a nonabsorbable antibiotic, has also proven efficacious. In three RCTs, subjects taking rifaximin experienced 8% to 23% improvements in abdominal bloating, global IBS symptoms, or both. In the largest of these trials, 388 patients with IBS-D received rifaximin 550 mg twice daily or placebo; patients receiving rifaximin experienced significantly greater symptom responses (52.4% vs 44.2%, \(P=0.03\)).\(^\text{16}\)

In a second well-designed trial, 80 patients were randomized to receive rifaximin 400 mg three times daily or placebo for 10 days. Participants were defined as responders if they experienced a 50% improvement in their global IBS symptoms from baseline to 1 week after completing the course of antibiotics. A significantly higher percentage of patients receiving rifaximin responded (37.2% vs 15.9%, \(P<0.05\), and symptom improvement persisted in a higher proportion of rifaximin-treated patients for 10 weeks after discontinuation of the antibiotics (36.4% vs 21%, \(P=0.02\)).\(^\text{17}\) The final RCT studied 103 patients whose chief complaint was bloating; however, 70 of these patients met Rome II criteria for IBS. At trial completion, a significantly greater proportion of IBS patients treated with rifaximin reported symptom improvement (41% vs 18%), but the effect waned after 10 days in both the rifaximin and placebo groups (27% vs 9%).\(^\text{18}\)

These studies reveal inconsistencies in the longevity of treatment effect; however, one retrospective, open-labeled study revealed that patients with recurrent symptoms responded to repeated courses of rifaximin.\(^\text{19}\)

Overall, neomycin demonstrated efficacy in a single small cohort of IBS patients. Rifaximin consistently demonstrated improvement in bloating and global IBS symptoms in doses of 1100 to 1200 mg daily for 10 to 14 days. Most patients had IBS-D; thus, rifaximin is most likely to be efficacious in this population or in a cohort of patients with severe bloating as their predominant symptom. None of the studies reported overall adverse events, but all stated that the antibiotics were well tolerated and no serious adverse events occurred. It is important to note that neither antibiotic is FDA approved for treating IBS, and the Task Force stressed that it could not make recommendations regarding continuous or intermittent use given the risks of drug-induced side effects and bacterial resistance.

Chloride C-2 Channel Activators (1B–Women with IBS-C)

- In women with IBS-C, lubiprostone is more effective than placebo in alleviating global IBS symptoms

Lubiprostone is the only C-2 selective chloride channel (CIC-2) activator currently available. It functions primarily in the small intestine where topical activation of luminal CIC-2 receptors results in the net secretion of chloride (Cl) ions into the intestinal lumen. As a result of this negative ion gradient, positively charged sodium ions enter the lumen and water follows passively.

*Not approved by the FDA for IBS treatment
Lubiprostone initially showed effectiveness in reducing abdominal discomfort in early dose-ranging studies. It was subsequently tested in 1171 patients with IBS-C in two 12-week phase III RCTs. In both, patients (primarily women) with IBS consumed 8 mcg twice daily and experienced significant improvements in global symptoms compared with controls (18% vs 10%, respectively; \( P < 0.001 \) for both trials). The responder and placebo rates in these trials were significantly lower than those recognized in most other IBS studies; however, this was attributed to the rigorous definitions of responder set forth in each of the individual phase III trials. Side effects most commonly identified included nausea (8%), diarrhea (6%), and abdominal pain (5%).

Two extension studies from the original phase III trials have also been completed. In the first, a 36-week, open-labeled, extension trial, patients who continued to receive lubiprostone and those who had initially received placebo but subsequently switched to lubiprostone during the open-labeled period experienced increased response rates (22% and 23%, respectively) after 36 weeks. In the second, patients who received lubiprostone during the initial trial were randomized to either continue the medication or receive placebo, and both groups were followed for an additional four weeks. No differences in global or individual symptoms were identified between the groups, suggesting that at least in the short-term, withdrawal of lubiprostone does not lead to a rebound effect and that clinical benefits may extend beyond drug cessation. Given these findings, the FDA subsequently approved lubiprostone at a dose of 8 mcg twice daily for the treatment of IBS-C in women.

5-HT\textsubscript{3} Antagonists (2A–Women with IBS-D; 2B–Men with IBS-D)

- *In men and women with IBS-D, alosetron is more effective than placebo in alleviating global IBS symptoms*
- *The quality of evidence is high*
- *The use of alosetron is limited by severe side effects—constipation and ischemic colitis*
- *Risk/benefit analyses suggest that alosetron is best used by women with IBS-D who have failed conventional therapies*

Antagonists to the 5-HT\textsubscript{3} receptor delay GI transit, decrease colonic tone, and reduce visceral sensitivity, thus making them attractive candidates for treating IBS-D. The only currently available agent in this class is alosetron. Eight placebo-controlled studies were incorporated into the systematic review assessing the efficacy of alosetron in patients with IBS-D. Using the predefined endpoint “adequate relief” of abdominal pain/discomfort or urgency, the relative risk of patients continuing to experience these symptoms after taking alosetron was 0.79 (95% CI, 0.69-0.90; NNT=8). In individual studies, alosetron has repeatedly improved global and individual IBS-D symptoms in women, and a single RCT in 662 patients also illustrated its efficacy in men.

Alosetron was approved by the FDA for the treatment of women with IBS-D in February 2000. Subsequently, it was linked to the development of constipation and ischemic colitis in a small but significant number of patients and was voluntarily withdrawn from the US market in November 2000. In June 2002, the FDA reapproved the use of alosetron for the treatment of women with severe IBS-D.
who fail to respond to other conventional treatments, but its use is regulated by an FDA prescribing program. In a recent systematic review, patients consuming alosetron reported significantly more adverse events than those taking placebo (RR=1.18; 95% CI, 1.08-1.29; NNH=10). The risk of developing constipation appeared to be dose dependent (0.5 mg twice daily=11%; 1 mg twice daily=29%) whereas the risk of ischemic colitis was independent. A second systematic review reported incidences of severe constipation and ischemic colitis in 0.66 and 1.1 patients per 1000 patient-years, respectively. Based on supporting data, the currently recommended starting dose of alosetron is 0.5 mg twice daily. If this dose is ineffective after four weeks, the dose can be increased to 1 mg twice daily. If this dose is ineffectual after four weeks or the patient develops signs/symptoms of severe constipation/ischemic colitis, the drug should be discontinued immediately.

Peppermint Oil (2B)

- Limited data suggest that peppermint oil may improve IBS symptoms compared with placebo

Data regarding the efficacy of this intervention are limited but suggest that peppermint oil has the propensity to relax smooth muscle. Only four studies were identified for the systematic review, and there was significant heterogeneity in study design. Despite these limitations, the relative risk of symptoms persisting after utilization of peppermint oil was 0.43 (95% CI, 0.32-0.59; NNT=2.5) compared with placebo. Minimal adverse event data were reported.

Fiber, Bulking Agents, Laxatives (2C)

- Psyllium (ispaghula husk) has received a conditional recommendation

Twelve studies assessing the efficacy of fiber/bulking agents were identified and incorporated into this systematic review. Most of these studies were small, had suboptimal design, and used a variety of agents. Wheat bran and psyllium (ispaghula husk) were the most commonly tested. In aggregate, treatment with wheat bran did not result in improvement in IBS symptoms compared with placebo. Psyllium, however, resulted in global symptom improvement in four of six studies with a relative risk of IBS symptoms not improving of 0.78 (95% CI, 0.63-0.96; NNT=6). Safety and adverse events were not formally evaluated in any of these studies, and recurrent reports of increased bloating, flatulence, and abdominal distention have limited their tolerability. Laxatives have not been studied in placebo-controlled trials in patients with IBS. In a single sequential study in adolescents with IBS-C, polyethylene glycol laxative was shown to increase stool frequency without improving pain outcomes.

Antispasmodic Agents (2C)*

- Most trials of antispasmodics have been small and of poor methodologic quality
- Current efficacy data most strongly support the use of hyoscine

Twenty-two studies were incorporated into the ACG review with data suggesting that, as a class, antispasmodics appear efficacious for treating IBS symptoms. However, 18 of the studies evaluated drugs not currently available in the United States. Most of the trials were performed prior to 2000 and

*Not approved by the FDA for IBS treatment
were of poor quality. Three studies assessing the efficacy of hyoscine were performed, but the formulation of hyoscine used in the trials differed from the ones currently available in practice. However, for individual drugs, the strongest efficacy data exist for hyoscine with a NNT of 4. In total, 1778 patients were enrolled in the 22 trials, and, in meta-analysis, the relative risk of symptom persistence after taking antispasmodics as a class compared with placebo was 0.68 (95% CI, 0.57-0.81; NNT=5). Unfortunately, the data do not allow for identification of baseline factors indicative of a response to these agents. The most common class-related side effects were dry mouth, dizziness, and blurred vision.

Antidiarrheals (2C)

- Loperamide decreases stool frequency and improves consistency but is not more effective in reducing IBS symptoms compared with placebo
- Other antidiarrheals have not been tested in RCTs

There have been only two randomized studies assessing the efficacy of antidiarrheals for the treatment of IBS-D, in 60 and 21 patients, respectively, both were poorly designed. Loperamide was used in both studies, and no significant differences in global symptom improvement were identified. Loperamide improved stool consistency in each of the individual trials compared with placebo ($P=0.006$), and pooled analysis also suggested an improvement in stool frequency (RR of not improving 0.2; 95% CI, 0.05-0.9). Side effects were minimal, but poorly reported.

Nonpharmacologic Treatments

Psychological Therapies (1C)

- Cognitive behavioral therapy, hypnotherapy, and dynamic psychotherapy are more effective than standard therapy in relieving global IBS symptoms

Psychological therapies include cognitive behavioral therapy (CBT), hypnotherapy, relaxation therapy, and psychotherapy. In the systematic review compiled for the ACG position statement, 20 RCTs were incorporated and revealed an overall class benefit for psychological therapy with a relative risk of IBS not improving of 0.67 (95% CI, 0.57-0.79; NNT=4). However, pooling of the data resulted in significant heterogeneity, and overall study quality was deemed poor. When each of the therapies was evaluated independently, CBT (seven studies), hypnotherapy (two studies), dynamic psychotherapy (two studies), and multicomponent therapy (three studies) were all beneficial in improving global IBS symptoms. Relaxation therapy offered no significant benefit compared with standard therapy. None of the trials reported any adverse events.

Probiotics (2C)

- Bifidobacteria and certain combinations of probiotics demonstrate some efficacy for improving IBS symptoms

Nineteen studies were incorporated into this systematic review. In aggregate, probiotics were shown to significantly decrease IBS symptoms with a relative risk of symptom persistence after probiotic consumption equal to 0.71 (95% CI, 0.57-0.88; NNT=4). However, there was significant heterogeneity
between studies because the species (individual or combination), dosages of probiotics used, and outcomes of each of the individual studies were highly variable. Furthermore, most agents were assessed in small individual studies. Based on the available data, the panel concluded that *Bifidobacteria* may act as the active ingredient in probiotic combinations. A subsequent systematic review also determined that *Bifidobacterium infantis* 35624 demonstrated efficacy in the treatment of IBS. Safety and tolerability data have been inconsistently reported.

**Dietary Modification (2C)**

- **Symptom exacerbations after eating are common**
- **There is little supportive evidence for dietary modification**

Many patients experience symptom exacerbations after eating, and surveys have shown that 60% to 70% of patients believe their symptoms are precipitated by food allergies. However, studies assessing patients’ subjective intolerances to isolated foods have not identified a correlation, and currently, a gold standard diagnostic test is not available. A recent RCT in 150 patients evaluated the efficacy of a food elimination diet based on IgG testing for 29 common food antigens. Each of the IBS patients enrolled in the trial had at least one food allergy, and the patients were randomized to receive an exclusion or sham diet. In intention-to-treat analysis, no differences in symptom responses were identified ($P=0.19$). Therefore, there is little evidence to support modification of a patient’s diet unless there is concern for possible gluten and/or lactose intolerance. Then, specific testing as outlined in Table 3 should be considered.

**Herbal Therapies/Acupuncture (No grade, insufficient data)**

- There are insufficient data to comment on the efficacy of these alternative therapies

Randomized trials have primarily tested Chinese herbal mixtures. Although these studies have shown benefits, the data are limited, and concerns regarding toxicity limit their use. The efficacy of acupuncture has been previously reviewed by the Cochrane Collaboration. The Collaboration identified six poor-quality studies with heterogeneous outcomes. Thus, the IBS Task Force feels that more rigorous studies are necessary before recommendations regarding either therapy can be made.

**Emerging IBS Therapies**

- **Multiple phase I to III studies are currently underway to evaluate new therapies for treating IBS-C, IBS-D, and IBS-M**

Many peripheral and centrally acting therapies are currently undergoing testing for treating IBS. Multiple phase II and III studies have recently been completed, with the results still pending. Further discussion regarding these medications is beyond the scope of this review.
Conclusions

IBS Diagnosis Summary

The ACG IBS Task Force has recommended against the use of routine diagnostic testing in patients who meet the Rome criteria for IBS. Exceptions, such as alarm features, exist in which additional diagnostic testing is needed. A guide summarizing the ACG panel’s recommendations regarding IBS diagnosis is presented below.

Evaluate Patient Symptoms

- Frequency and duration of symptoms?
- Improvement with defecation?
- Changes in stool consistency?

Identify Predominant Stool Pattern to Make Diagnosis of IBS Subtype

- IBS with diarrhea (IBS-D)
- IBS with constipation (IBS-C)
- Mixed IBS (IBS-M)
- Undefined IBS (IBS-U)

Considerations for Additional Diagnostic Testing

- Celiac sprue testing in patients with IBS-D or IBS-M
- Lactose intolerance is suspected
- Patient meets age-appropriate guidelines for colorectal cancer screening
- Alarm features are present
  - Anemia
  - Weight loss
  - Family history of
    - Colorectal cancer
    - Inflammatory bowel disease
    - Celiac sprue
**IBS Treatment Summary**

Several treatment strategies are available to help manage IBS, but each has received a different grade from the ACG panel. These grades were assigned to help guide healthcare providers’ recommendations. A two-point scale was used in which 1 is a strong recommendation and 2 is a weak recommendation. The quality of evidence was given an alphabetic score in which high-quality evidence is A, moderate-quality evidence is B, and low-quality evidence is C. The strongest to weakest overall recommendations are listed in Table 5.

<table>
<thead>
<tr>
<th>IBS Treatment</th>
<th>ACG Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tegaserod(^\dagger) (5-HT(_4) Agonist)</td>
<td>1A–Women with IBS-C, 1B–IBS-M</td>
</tr>
<tr>
<td>TCAs/SSRIs* (Antidepressants)</td>
<td>1B</td>
</tr>
<tr>
<td>Antibiotics*</td>
<td>1B</td>
</tr>
<tr>
<td>Lubiprostone (CIC-2 channel activator)</td>
<td>1B–Women with IBS-C</td>
</tr>
<tr>
<td>CBT, hypnotherapy, and dynamic psychotherapy</td>
<td>1C</td>
</tr>
<tr>
<td>Alosetron(^\dagger) (5-HT(_3) Antagonist)</td>
<td>2A–Women with IBS-D, 2B–Men with IBS-D*</td>
</tr>
<tr>
<td>Peppermint Oil</td>
<td>2B</td>
</tr>
<tr>
<td>Probiotics</td>
<td>2C</td>
</tr>
<tr>
<td>Fiber, bulking agents, and laxatives</td>
<td>2C</td>
</tr>
<tr>
<td>Antidiarrheals</td>
<td>2C</td>
</tr>
<tr>
<td>Antispasmodics*</td>
<td>2C</td>
</tr>
<tr>
<td>Dietary modification</td>
<td>2C</td>
</tr>
<tr>
<td>Herbals/Acupuncture</td>
<td>Data too limited to grade</td>
</tr>
</tbody>
</table>

\(^\dagger\) Tegaserod: withdrawn from the US market in March 2007; available through an investigational drug program

*Not approved by the FDA for IBS treatment

\(^\dagger\) Alosetron: withdrawn from the US market in November 2000; reapproved in June 2002 by the FDA for use in women with severe IBS-D who do not respond to conventional treatment; regulated by FDA prescribing program
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