Irritable bowel syndrome: Minimize testing, let symptoms guide treatment

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Practice recommendations

- For patients aged <50 years without alarm symptoms, diagnostic testing is unnecessary. Consider celiac sprue testing for patients with diarrhea (C).
- Treatment is indicated when both the patient with irritable bowel syndrome and the physician agree that quality of life has been diminished (C). The goal of therapy is to alleviate global IBS symptoms (abdominal discomfort, bloating, and altered bowel habits that are life-impacting) (C).
- Tegaserod, a 5HT4 receptor agonist, is more effective than placebo at relieving global IBS symptoms in women with constipation (A). Its effectiveness in men is unknown.
- Alosetron, a 5HT3 receptor antagonist, is more effective than placebo at relieving global IBS symptoms in women with diarrhea (A).
- Behavior therapy—relaxation therapy, hypnotherapy, or cognitive therapy—is more effective than placebo at relieving individual symptoms, but no data are available for quality-of-life improvement (B).

An extensive and expensive evaluation for irritable bowel syndrome (IBS) can be avoided if your patient is aged <50 years and is not experiencing alarm symptoms (hematochezia, 10 lbs weight loss, fever, anemia, nocturnal or severe diarrhea), has not recently taken antibiotics, and has no family history of colon cancer. An algorithm (Figure) indicates when work-up is needed and what it should entail.

Newer medications that act on 5HT receptors have proven effective in improving quality of life (global symptom reduction). Evidence supports the use of several traditional medications to reduce individual symptoms of IBS, but not for global symptom reduction.

WHO GETS IRRITABLE BOWEL SYNDROME?

Ten percent to 15% of the North American population has IBS, and twice as many women as men have it. Symptoms usually begin before the age of 35 years, and many patients can trace their symptoms back to childhood. Onset in the elderly is rare. The disorder is responsible for approximately 50% of referrals to gastroenterologists.

The company IBS keeps

Comorbid psychiatric illness is common with IBS, but few patients seek psychiatric care. Depression, anxiety, and somatoform disorders are seen in 94% of patients with IBS. IBS is common in patients with chronic fatigue...
syndrome (51%), fibromyalgia (49%), temporo-mandibular joint syndrome (64%), and chronic pelvic pain (50%). IBS often follows stressful life events, such as a death in the family or divorce. It tends to be chronic, intermittent, and relapsing.

The symptoms of IBS can overlap with those of other illnesses, including thyroid dysfunction (diarrhea or constipation), functional dyspepsia (abdominal pain), Crohn’s disease or ulcerative colitis (diarrhea, abdominal pain), celiac sprue (diarrhea), polyps and cancers (constipation or abdominal pain), and infectious diarrhea.

**Elusive physiologic mechanism**
Several physiologic mechanisms have been proposed for IBS symptoms: altered gut reactivity in response to luminal stimuli, hypersensitive gut with enhanced pain response, and altered brain-gut biochemical axis. Though the symptoms of irritable bowel syndrome appear to have a physiologic basis, there are no structural or biochemical markers for the disease.

**USE SYMPTOM-BASED CRITERIA FOR DIAGNOSIS**
Consider a diagnosis of IBS when a patient complains of abdominal discomfort and altered bowel habits. In the absence of a structural or biochemical marker, IBS must be diagnosed according to symptom-based criteria—such as Manning, Rome I, or Rome II—which have been
Dubious value of diagnostic tests

The literature regarding the value of diagnostic testing for IBS is controversial. Symptom-based criteria have varied in many studies, as have the criteria used to enroll patients and the measured outcomes of treatment (reduction in abdominal pain, in diarrhea, or in constipation, or improvement in quality of life). Because of

### Symptom-based criteria for irritable bowel syndrome

<table>
<thead>
<tr>
<th>Symptom-based criteria</th>
<th>Symptoms</th>
<th>Sn</th>
<th>Sp</th>
<th>PV+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manning⁴,¹⁰,¹³,¹⁴</td>
<td>• Abdominal pain&lt;br&gt;• Pain relief with bowel movement&lt;br&gt;• More frequent stools with pain&lt;br&gt;• Looser stools with pain&lt;br&gt;• Mucus in stools&lt;br&gt;• Feeling of incomplete evacuation</td>
<td>42%–90%</td>
<td>70%–100%</td>
<td>74%</td>
</tr>
<tr>
<td>Rome I⁴,¹⁰,¹³</td>
<td>• &gt;3 months of continuous or recurrent abdominal pain relieved with defecation or associated with change in stool consistency&lt;br&gt;• plus: &gt;2 of the following on 25% of days&lt;br&gt;  – altered stool frequency&lt;br&gt;  – altered stool form&lt;br&gt;  – altered stool passage&lt;br&gt;  – passage of mucus&lt;br&gt;  – bloating or abdominal distention</td>
<td>65%–84%</td>
<td>100%</td>
<td>69%–100%</td>
</tr>
<tr>
<td>Rome II¹¹–¹³</td>
<td>• Abdominal discomfort or pain for at least 12 weeks (not necessarily consecutive) in the preceding 12 months, and having 2 of the 3 following features:&lt;br&gt;  – relieved with defecation&lt;br&gt;  – onset associated with a change in frequency of stool&lt;br&gt;  – onset associated with a change in form (appearance) of stool&lt;br&gt; Supportive symptoms&lt;br&gt; Fewer than 3 bowel movements per week&lt;br&gt;More than 3 bowel movements per day&lt;br&gt;Hard or lumpy stools</td>
<td>49%–65%*</td>
<td>100%*</td>
<td>69%–100%*</td>
</tr>
</tbody>
</table>

*Found to have similar sensitivity and specificity to Rome I.⁴
Sn, sensitivity; Sp, specificity; PV+, positive predictive value

Subtypes of IBS have been described (diarrhea-predominant IBS or constipation-predominant IBS), but they are not diagnostically useful, since the treatment goal is improved quality of life.
these discrepancies, it is difficult to apply the literature clinically. Of the 6 landmark studies that considered the value of diagnostic testing for IBS patients,15–20 only 2 compared IBS patients with groups of healthy controls.17,19

Test results yield little. Most research in this area has compared the prevalence of specific illnesses in the general population with the yield of positive test results for these illnesses among persons meeting the symptom-based diagnostic criteria for IBS.

Two studies15,16 determined the incidence of abnormal test results in patients who met the Manning or Rome I criteria for IBS. In these studies, most diagnostic tests yielded positive results in 2% (range, 0%–8.2%) of patients or less, except for thyroid and lactose intolerance testing. That is equivalent to the incidence in the general population. The prevalence of thyroid disorders and lactose malabsorption was higher in IBS patients (6% and 22%–26%, respectively), but prevalence in the general population is similarly higher (5%–9% and 25%). Based on these results, testing for thyroid disease or lactose malabsorption is indicated only for patients exhibiting symptoms of these disorders (fatigue/weight change or diarrhea related to dietary intake of dairy products, respectively).

An exception. Some clinicians propose that diagnostic testing for patients with IBS symptoms should be driven by the pretest probability of organic disease (prevalence) compared with the general population. Cash21 found the pretest probability of inflammatory bowel disease, colorectal cancer, and infectious diarrhea is less than 1% among IBS patients without alarm symptoms (Table 2). He demonstrated that patients with IBS had a 5% pretest probability of celiac sprue compared with healthy patients (<1% prevalence). Therefore, testing for celiac sprue (eg, complete blood count, antiendomysial antibody, and antigliadin antibody) may be considered for patients with diarrhea.6,21,22 Sigmoidoscopy,15,17 rectal biopsy,17 and abdominal ultrasound24 have low positive yield in patients meeting the diagnostic criteria for IBS.

How to proceed
Those under 50 years of age who have no alarm symptoms can forgo further testing. Testing for celiac sprue and lactose malabsorption might be considered for patients with diarrhea that improves or worsens with change in diet (strength of recommendation [SOR]: C).

Threshold for treatment
Treatment for IBS is indicated when both patient and physician believe global symptoms (abdominal discomfort, bloating, altered bowel habits) have diminished the quality of life (SOR: C). The goal of treatment is to alleviate all IBS symptoms (SOR: C). Treating altered bowel habits (constipation, diarrhea, and fecal urgency) without addressing other IBS symptoms (eg, abdominal pain) is inferior treatment.23,24

Treatment options for IBS
Treatments for IBS include medications, behavior therapy, and complimentary and alternative therapies. Medications traditionally prescribed include bulking agents, anticholinergics/antispasmodics, antidiarrheals, and antidepressants. A 5HT₃ receptor antagonist and a 5HT₄ receptor partial agonist are now available. Table 3 summarizes the traditional treatments in terms of efficacy, strength of recommendations, and outcomes measured. Alternative and complimentary therapies appear in Table 4.

As Brandt24 has noted, the evidence for treatment effectiveness is difficult to review and summarize, because the quality of studies has been poor. Most studies did not use healthy control groups, and the numbers of participants were small. Many studies did not use blinded placebo groups. Outcomes measured varied among the studies, with most of them measuring reductions of individual bowel symptoms
IRRITABLE BOWEL SYNDROME

Table 2

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pretest probability–IBS patients (%)</th>
<th>Prevalence–general population (%)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colitis/inflammatory inflammatory bowel disease</td>
<td>0.51–0.98</td>
<td>0.3–1.2</td>
<td>Structural colon lesions were detected with barium enema, colonoscopy, sigmoidoscopy</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>0–0.51</td>
<td>4–6</td>
<td>Structural colon lesions were detected with barium enema, colonoscopy, sigmoidoscopy</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>4.67</td>
<td>0.25–0.5</td>
<td>Note: celiac disease prevalence higher than in general population.</td>
</tr>
<tr>
<td>Gastrointestinal infection</td>
<td>0–1.7</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Thyroid dysfunction</td>
<td>6</td>
<td>5–9</td>
<td>Prevalence high in both groups</td>
</tr>
<tr>
<td>Lactose malabsorption</td>
<td>22–26</td>
<td>25</td>
<td>Prevalence high in both groups</td>
</tr>
</tbody>
</table>


(eg, diarrhea or constipation). Quality-of-life tools were used in other studies to measure reduction in global IBS symptoms (eg, IBS Quality of Life25). Because of these discrepancies, there is no sound evidence for traditional therapies.

**Medications**

**Strength of recommendation: A.** The recently approved 5HT4 receptor agonist tegaserod (Zelnorm) is more effective than placebo at relieving global symptoms in women with constipation (number needed to treat [NNT]=3.9–17).26–30 Diarrhea can be a serious side effect.

The 5HT3 receptor antagonist alosetron (Lotronex) is more effective than placebo at relieving global IBS symptoms in women with diarrhea (NNT=2.5–8.3).31–35 Severe constipation can be an adverse effect. The prescribing of alosetron is currently restricted to physicians who participate in the manufacturer’s risk management program.

In addition to these serotoninergic agents, others in this class are being developed and undergoing clinical trials. The knowledge being gained about 5HT receptors may revolutionize the care of patients with IBS.

**Strength of recommendation: B.** Tricyclic antidepressants are no more effective than placebo at relieving global IBS symptoms, but they do decrease abdominal pain (NNT=3.2–5).36–39 Loperamide is no more effective than placebo at treating IBS global symptoms, but it may be used to treat diarrhea (NNT=2.3–5).31,40–42
## TABLE 3
### Treatments for irritable bowel syndrome

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Efficacy (NNT)</th>
<th>SOR (studies)</th>
<th>Outcomes measured</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>5HT₄ receptor agonist</strong> *(tegaserod)*²²,²⁴,²⁶–³⁰</td>
<td>More effective than placebo at relieving global IBS symptoms in women with constipation (3.9–17)</td>
<td>A (4)</td>
<td>Global IBS symptoms, individual IBS symptoms</td>
<td>83%–100% of study participants were women with IBS and constipation. Rome I and II criteria for entry. May cause diarrhea</td>
</tr>
<tr>
<td><strong>5HT₄ receptor agonist</strong> *(alosetron)*²²,²⁴,²⁶–³⁰</td>
<td>More effective than placebo at relieving global IBS symptoms in women with diarrhea (2.5–8.3)</td>
<td>A (4)</td>
<td>Global IBS symptoms, individual IBS symptoms, adverse events</td>
<td>82%–93% of study participants were women. Rome I and II criteria for entry. May cause severe constipation; restricted use</td>
</tr>
<tr>
<td><strong>Tricyclic antidepressants</strong> *(trimipramine, desipramine)*²²,²⁴,²⁸–³²</td>
<td>Reduces abdominal pain. No more effective than placebo at relieving global IBS symptoms (3.2–5)</td>
<td>B (6)</td>
<td>GI symptoms</td>
<td>May cause constipation; no studies done with SSRI's</td>
</tr>
<tr>
<td><strong>Loperamide</strong>²²,²⁴,²⁸–³²</td>
<td>Relieves diarrhea. No more effective than placebo at relieving global IBS symptoms (3.2–5)</td>
<td>B (3)</td>
<td>Global IBS symptoms, diarrhea</td>
<td>Constipation or paralytic ileus can occur</td>
</tr>
<tr>
<td><strong>Bulking agents</strong> *(corn fiber, wheat bran, psyllium, ispaghula husks, calcium poly-cabophil)*²²,²⁴,²⁷,³¹,⁴⁰–⁴²</td>
<td>Improves constipation. No more effective than placebo in studies considering global symptom improvement (2.2–8.6)</td>
<td>B (13)</td>
<td>GI symptoms, global IBS symptoms</td>
<td>May increase bloating. All studies small numbers of patients</td>
</tr>
<tr>
<td><strong>Anti-spasmodics</strong> *(hyoscymine, dicyclomine)*²²,²⁴,²⁶–³⁰</td>
<td>No evidence on improvement of global IBS symptoms (5.9)</td>
<td>B (3)</td>
<td>Individual IBS and global symptoms</td>
<td>Studies were short, small numbers, inconsistent effectiveness. Could worsen constipation; 15 additional studies done on drugs not available in the US</td>
</tr>
<tr>
<td><strong>Behavioral therapies</strong> *(hypnotherapy, relaxation therapy, psychotherapy, biofeedback)*²²,²⁴,³⁴,³⁵,⁴⁴,⁵²–⁵⁷</td>
<td>More effective than placebo at relieving individuals IBS symptoms (1.4–1.9)</td>
<td>B (16)</td>
<td>GI symptoms, psychological symptoms</td>
<td>None measures global IBS symptom improvement. Small numbers of patients</td>
</tr>
<tr>
<td><strong>SSRI antidepressants</strong> *(paroxetine, fluoxetine)*²²,²⁴,⁵⁰–⁵¹</td>
<td>Improved quality of life, decreased abdominal pain</td>
<td>B (16)</td>
<td>Abdominal</td>
<td>One study severe IBS, other study only 10 participants quality of life</td>
</tr>
</tbody>
</table>

SOR: strength of recommendation; IBS, irritable bowel syndrome; GI, gastrointestinal; SSRI, selective serotonin reuptake inhibitor. For an explanation of SORs, see page 954.
Complementary and alternative treatments for irritable bowel syndrome

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Efficacy</th>
<th>SOR</th>
<th>Outcomes measured</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neomycin&lt;sup&gt;40&lt;/sup&gt;</td>
<td>Treatment for 1 week improved symptoms of</td>
<td>A</td>
<td>Abdominal pain, diarrhea, or</td>
<td>Studies measuring global symptom improvement lacking</td>
</tr>
<tr>
<td></td>
<td>abdominal pain, diarrhea, and constipation</td>
<td></td>
<td>constipation</td>
<td></td>
</tr>
<tr>
<td>Peppermint oil&lt;sup&gt;31,48–49&lt;/sup&gt;</td>
<td>Some demonstrated improvement in abdominal pain</td>
<td>B</td>
<td>Individual IBS symptoms</td>
<td>Studies measuring global symptom improvement lacking</td>
</tr>
<tr>
<td>Guar gum&lt;sup&gt;44&lt;/sup&gt;</td>
<td>Improved abdominal pain and bowel alterations</td>
<td>B</td>
<td>Study compared fiber to guar gum—</td>
<td>No placebo-controlled trials</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>equal affect on abdominal pain.</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Gum was better tolerated</td>
<td></td>
</tr>
<tr>
<td>Probiotics&lt;sup&gt;48&lt;/sup&gt; (lactobacillus)</td>
<td>Improvement of abdominal pain and flatulence</td>
<td>C</td>
<td>Abdominal pain, flatulence</td>
<td>Two studies with small numbers</td>
</tr>
<tr>
<td>Elimination diets&lt;sup&gt;48&lt;/sup&gt;</td>
<td>Improvement of diarrhea</td>
<td>C</td>
<td>Diarrhea</td>
<td>Milk, wheat, eggs eliminated; 15%–71% improvement of diarrhea</td>
</tr>
<tr>
<td>Lactose and fructose avoidance&lt;sup&gt;48&lt;/sup&gt;</td>
<td>Conflicting evidence results</td>
<td>D</td>
<td></td>
<td>No controlled studies available</td>
</tr>
<tr>
<td>Pancreatic enzymes&lt;sup&gt;48&lt;/sup&gt;</td>
<td>No evidence</td>
<td>D</td>
<td></td>
<td>Evidence lacking</td>
</tr>
<tr>
<td>Ginger&lt;sup&gt;48&lt;/sup&gt;</td>
<td>No evidence</td>
<td>D</td>
<td></td>
<td>No studies</td>
</tr>
</tbody>
</table>

Bulking agents (such as calcium poly-carbophil or psyllium) are no more effective than placebo at relieving IBS global symptoms, but they may decrease constipation (NNT=2.2–8.6).<sup>31,30,43–47</sup>

Peppermint oil may be helpful for abdominal pain, but global symptom reduction has not been demonstrated.<sup>31,48–49</sup> Only a few studies have looked at the use of antispasmodic agents for IBS. They are of poor quality and used small numbers with no placebo controls.<sup>23,31,30,43</sup>

**Strength of recommendation:** C. There are limited studies evaluating the selective serotonin reuptake inhibitors (SSRIs) fluoxetine and paroxetine. Paroxetine was shown in 1 study to improve quality of life.<sup>40</sup> Fluoxetine reduced abdominal pain, but did not improve quality of life.<sup>51</sup>

**Behavioral and complementary/alternative therapies**
Relaxation therapy, hypnotherapy, and cognitive therapy are effective at relieving individual IBS symptoms, but have not been shown to reduce global IBS symptoms (SOR: B).<sup>52–57</sup> Other alternative therapies (eg, guar gum<sup>44</sup> [SOR: B], ginger<sup>48</sup> [SOR: B], and pancreatic enzymes<sup>48</sup> [SOR: C]) have been studied, but high-quality
studies considering global improvement have not been published.

**PROMOTE SELF-AWARENESS**

Quality-of-life assessment should be done routinely in the care of IBS patients. Provide support, empathy, and basic behavior modification tools. Educate patients and their families on the theoretical biochemical basis of this illness, and help them connect symptoms with stressors, to facilitate lifestyle modification.

**REFERENCES**

26. Jones BW, Moore DJ, Robinson SM, Song F. A systematic


