



A Practical Approach to Managing IBS: Understanding and Applying the Evidence for Optimal Care

This activity is supported by independent educational grants from Allergan, Ironwood Pharmaceuticals and Salix.



CLINICAL PEARLS

Irritable bowel syndrome (IBS) is a relatively common condition that affects 10%-15% of the adults in the United States. Although many patients will seek treatment from their primary care physician, IBS presents several challenges in both its diagnosis and management. This CME-certified activity, *A Practical Approach to Managing IBS: Understanding and Applying the Evidence for Optimal Care*, is intended to help health care providers recognize IBS and arrive at a timely, accurate diagnosis, and develop patient-oriented treatment plans that address patients' most troubling symptoms.

IBS can be diagnosed based on the presence of characteristic symptoms

- The key feature of IBS in the Rome IV criteria is the presence of recurrent abdominal pain on average at least 1 day/week in the past 3 months
- Abdominal pain must also be associated with at least 2 of the following: defecation, a change in the frequency of stool, or a change in the form or appearance of stool

Additional diagnostic testing is not indicated if the patient meets the Rome IV diagnostic criteria in the absence of alarm features

- Colonoscopy or additional diagnostic testing is needed to exclude organic disease in patients over age 50, those with severe or progressively worsening symptoms, unexplained weight loss or iron-deficiency anemia, nocturnal diarrhea, rectal bleeding or melena, or a family history of colon cancer, celiac disease, or inflammatory bowel disease
- Nocturnal pain, unlike nocturnal diarrhea, is not indicative of organic disease
- Routine screening for celiac disease in patients with diarrhea-predominant IBS (IBS-D) can be cost-effective and avoids the risk of long-term consequences from missing this diagnosis

- A colonoscopy to investigate constipation-predominant IBS (IBS-C) is usually not indicated in the absence of alarm features
- Patients with IBS-C who do not respond to initial treatment should be tested for signs of dyssynergic defecation

A post-infectious etiology for patients' symptoms suggests a different clinical course and prognosis

- Between 3%-36% of patients relate the onset of their symptoms to a gastrointestinal infection, usually bacterial gastroenteritis
- Establishing a post-infectious etiology can be reassuring—two-thirds of these patients will have improvement and resolution of symptoms within 6-8 years

Initial treatment for patients with mild symptoms includes education, dietary and lifestyle modification, and over-the-counter medications

- Pain is minimal or mild in these patients, and their overall quality of life and daily activities are minimally affected
- A review of medications may identify possible pharmacologic contributors to the patients' symptoms
- Loperamide, taken preventatively or before situations that provoke symptoms, can be used to reduce stool frequency and improve stool consistency in patients with IBS-D; however, loperamide will not address abdominal pain, discomfort, or other IBS symptoms
- The loperamide dose should be adjusted until diarrhea symptoms improve; too high a dose can cause constipation, and some patients may find it easier to optimize the dose using a pediatric liquid formulation
- Only soluble sources of fiber (found in psyllium and oat bran, for example) have been shown to improve constipation, whereas insoluble fiber may not only be



A Practical Approach to Managing IBS: Understanding and Applying the Evidence for Optimal Care

ineffective but could cause abdominal discomfort and bloating

- Polyethylene glycol (PEG) can improve stool frequency and consistency in patients with IBS-C who have not improved after increasing their intake of soluble fiber, but PEG can also worsen abdominal pain and bloating
- Dietary modifications include avoiding gas-producing foods, fermentable oligo-, di-, and mono-saccharides and polyols (FODMAPs), fat, insoluble fiber, and caffeine
- Approach dietary modifications as a 3-step process: FODMAPs are initially eliminated, and if symptoms improve, individual foods can be reintroduced in the second step; once a patient's food sensitivities are identified, a personalized maintenance diet can be developed as the final step
- If possible, consider a referral to gastroenterology for patients who do not respond to over-the-counter treatments

Antispasmodics or peppermint oil can provide symptomatic relief for patients with abdominal pain

- Peppermint oil may reduce cramping and reduce pain sensitivity
- Antispasmodics taken as needed or preventatively can reduce pain, but their use may be limited by anticholinergic effects

Antidepressants, bile acid sequestrants, eluxadoline, and rifaximin are second-line options for patients with IBS-D

- No comparative clinical trials of the available treatments have been conducted
- Sub-psychoactive doses of a tricyclic antidepressant can improve pain and overall IBS symptoms, and increase transit time
- An empirical trial of a bile acid sequestrant may relieve symptoms in patients with bile acid malabsorption, but this class is also associated with bloating, flatulence,

abdominal discomfort, and constipation

- In phase 3 trials, eluxadoline improved abdominal pain and stool consistency within 4 weeks of starting treatment in patients previously treated with loperamide
- In randomized trials, rifaximin improved diarrhea, bloating, and other IBS symptoms; a 2-week trial of rifaximin can determine if this treatment will improve a patient's symptoms

Alosetron is approved for women with severe IBS-D symptoms that have not responded to other conventional therapies

- In clinical trials, 10% of patients discontinued alosetron because of constipation, although there was not an increased risk of serious adverse events related to constipation
- Ischemic colitis during alosetron treatment has an incidence of 0.15%, but is usually transient and without long-term sequelae
- The majority of adverse events during alosetron treatment have an onset within 30 days of treatment initiation

Prosecretory agents are second-line options for patients with IBS-C

- No comparative clinical trials of the available treatments have been conducted
- Lubiprostone is approved for women with IBS-C; in phase 3 trials, lubiprostone improved constipation and other symptoms
- The response rate to lubiprostone improved from 16% after 1 month of treatment to 37%-44% after 10-13 weeks of treatment
- Nausea can be reduced if lubiprostone is taken at mealtimes
- In placebo-controlled trials, linaclotide improved the number of bowel movements and other abdominal symptoms



A Practical Approach to Managing IBS: Understanding and Applying the Evidence for Optimal Care

- Patients may need 8-12 weeks of treatment with linaclotide to experience an improvement in abdominal pain and bloating
- Diarrhea is a possible side effect, but can be reduced if linaclotide is taken 30-60 minutes before breakfast
- Plecanatide improved abdominal pain and increased spontaneous bowel movements in 2 phase 3 trials

This program reviewed the diagnostic criteria and alarm features that indicate the need for additional diagnostic testing. It also addressed the initial management steps and reviewed the prescription options for patients who do not respond to dietary and lifestyle modification, and over-the-counter treatments.

REFERENCES

- Lacy BE, Patel NK. Rome criteria and a diagnostic approach to irritable bowel syndrome. *J Clin Med*. 2017;6(11).
- Chey WD, Kurlander J, Eswaran S. Irritable bowel syndrome: a clinical review. *JAMA*. 2015;313(9):949-958.
- Ford AC, Moayyedi P, Lacy BE, et al. American College of Gastroenterology monograph on the management of irritable bowel syndrome and chronic idiopathic constipation. *Am J Gastroenterol*. 2014;109 Suppl 1:S2-26; quiz S27.
- American College of Gastroenterology Task Force on Irritable Bowel Syndrome. An evidence-based position statement on the management of irritable bowel syndrome. *Am J Gastroenterol*. 2009;104 Suppl 1:S1-35.
- Bharucha AE, Pemberton JH, Locke GR, 3rd. American Gastroenterological Association technical review on constipation. *Gastroenterology*. 2013;144(1):218-238.
- Schuster BG, Kosar L, Kamrul R. Constipation in older adults: stepwise approach to keep things moving. *Can Fam Physician*. 2015;61(2):152-158.
- Spiller R, Garsed K. Postinfectious irritable bowel syndrome. *Gastroenterology*. 2009;136(6):1979-1988.
- Lacy BE, Chey WD, Cash BD, Lembo AJ, Dove LS, Covington PS. Eluxadoline efficacy in IBS-D patients who report prior loperamide use. *Am J Gastroenterol*. 2017;112(6):924-932.
- Lembo AJ, Lacy BE, Zuckerman MJ, et al. Eluxadoline for irritable bowel syndrome with diarrhea. *N Engl J Med*. 2016;374(3):242-253.
- Menees SB, Maneerattannaporn M, Kim HM, Chey WD. The efficacy and safety of rifaximin for the irritable bowel syndrome: a systematic review and meta-analysis. *Am J Gastroenterol*. 2012;107(1):28-35; quiz 36.
- Pimentel M, Cash BD, Lembo A, Wolf RA, Israel RJ, Schoenfeld P. Repeat rifaximin for irritable bowel syndrome: no clinically significant changes in stool microbial antibiotic sensitivity. *Dig Dis Sci*. 2017;62(9):2455-2463.
- Khanna R, MacDonald JK, Levesque BG. Peppermint oil for the treatment of irritable bowel syndrome: a systematic review and meta-analysis. *J Clin Gastroenterol*. 2014;48(6):505-512.
- Chang L, Chey WD, Harris L, Olden K, Surawicz C, Schoenfeld P. Incidence of ischemic colitis and serious complications of constipation among patients using alosetron: systematic review of clinical trials and post-marketing surveillance data. *Am J Gastroenterol*. 2006;101(5):1069-1079.
- Moayyedi P, Quigley EM, Lacy BE, et al. The effect of fiber supplementation on irritable bowel syndrome: a systematic review and meta-analysis. *Am J Gastroenterol*. 2014;109(9):1367-1374.
- Eswaran S, Muir J, Chey WD. Fiber and functional gastrointestinal disorders. *Am J Gastroenterol*. 2013;108(5):718-727.
- Drossman DA, Chey WD, Johanson JF, et al. Clinical trial: lubiprostone in patients with constipation-associated irritable bowel syndrome—results of two randomized, placebo-controlled studies. *Aliment Pharmacol Ther*. 2009;29(3):329-341.
- Chey WD, Drossman DA, Johanson JF, Scott C, Panas RM, Ueno R. Safety and patient outcomes with lubiprostone for up to 52 weeks in patients with irritable bowel syndrome with constipation. *Aliment Pharmacol Ther*. 2012;35(5):587-599.



A Practical Approach to Managing IBS: Understanding and Applying the Evidence for Optimal Care

Castro J, Harrington AM, Hughes PA, et al. Linaclotide inhibits colonic nociceptors and relieves abdominal pain via guanylate cyclase-C and extracellular cyclic guanosine 3',5'-monophosphate. *Gastroenterology*. 2013;145(6):1334-1346 e1331-1311.

Chey WD, Lembo AJ, Lavins BJ, et al. Linaclotide for irritable bowel syndrome with constipation: a 26-week, randomized, double-blind, placebo-controlled trial to evaluate efficacy and safety. *Am J Gastroenterol*. 2012;107(11):1702-1712.

Synergy Pharmaceuticals Announces FDA Approval of Trulance® (Plecanatide) for the Treatment of Irritable Bowel Syndrome with Constipation (IBS-C) in Adults [press release]. 2018.

ADDITIONAL SOURCES OF INFORMATION

Chey WD, Eswaran S, Kurlander J. JAMA patient page. Irritable bowel syndrome. *JAMA*. 2015;313(9):982.

Francis CY, Morris J, Whorwell PJ. The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. *Aliment Pharmacol Ther*. 1997;11(2):395-402.



ANNENBERG CENTER FOR HEALTH SCIENCES
AT EISENHOWER
Imparting knowledge. Improving patient care.