BMJ Best Practice

Irritable bowel syndrome

Straight to the point of care

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Summary

Irritable bowel syndrome symptoms include recurrent abdominal pain or discomfort that is associated with a change in stool frequency or form. The pain or discomfort may be relieved by defecation.

It is important to determine whether there are any potential precipitating dietary associations such as caffeine, lactose-containing foods, or fructose-containing foods.

Examination of the abdomen is usually unremarkable. There may be mild and poorly localized tenderness in the right lower quadrant and/or left lower quadrant.

The diagnosis is based on the patient's history; there are no specific diagnostic tests. If the patient has worrying symptoms or findings such as anemia, weight loss, or fever, then these require thorough investigation.

Treatment should be individualized and is dependent on the patient's predominant symptoms.

Definition

Irritable bowel syndrome (IBS) is a chronic condition characterized by abdominal pain associated with bowel dysfunction. The pain is often relieved by defecation and is sometimes accompanied by abdominal bloating. There are no structural abnormalities to explain the pain. IBS occurs in about 15% of the adult population. The etiology is probably multifactorial, and evidence suggests motility, inflammatory, genetic, immune, psychological, and dietary components.[1]

Epidemiology

IBS is present in 10% to 15% of adults in the US, and is the most common cause for referral to gastroenterologists, accounting for up to 50% of referred patients.[4] [5] [6] In the UK, it is estimated that the prevalence is between 6.1% and 21.6%, with a higher prevalence in women than men.[7] [8] [9] The prevalence of IBS is similar in Europe and is lower, but increasing, in the Asia-Pacific region.[10] Reports from Africa vary, but prevalence rates as high as 33% have been reported.[10]

In Australia, a postal questionnaire (4500 people ages ≥18 years) showed prevalence of IBS according to Manning, Rome I, and Rome II criteria to be 13.6%, 6.9%, and 4.4%, respectively.[11] Equivalent types of postal surveys conducted in Asia found similarly lower IBS prevalence rates in Singapore (11.0%, 10.4%, and 8.6% according to Manning [>1 criteria], Rome I, and Rome II criteria, respectively) and in China (11.5%, and 5.7% according to Manning and modified Rome II criteria), this last one showing a higher prevalence in women.[12]

One review reported a median incidence of physician-diagnosed IBS of 38.5 per 10,000 patient-years.[13]

Among adults who seek medical help, women outnumber men at a ratio of 2:1.[14] Symptoms of IBS can begin in adolescence or early adulthood, but the onset of symptoms after age 50 years is unusual.[15] [16]

One study conducted in a health maintenance organization population in the US showed the prevalence of IBS symptoms in respondents to be 19.5%.[17]

In one systematic review, the pooled prevalence of IBS in population-based studies that used the Rome III criteria was greater than that in studies employing Rome IV criteria (9.2% vs. 3.8%, respectively).[18] Mixed IBS (IBS-M) was the most common subtype with the Rome III criteria.

Familial aggregation of IBS has been reported; the odds of having IBS increase (odds ratio 2.75) if a first-degree relative has IBS.[19] A history of physical or sexual abuse has been reported in 32% to 44% of patients with IBS.[20] [21] [22] Endometriosis may be a risk factor, with one meta-analysis showing a threefold increased prevalence of IBS in women with endometriosis, compared with women without the condition.[23] IBS symptoms may also develop following enteric infections.[24]

Etiology

IBS is believed to be a disorder of altered gastrointestinal motility. There are no specific endoscopic, biochemical, anatomic, microbiologic, or histologic findings in IBS that make the etiology clear, although most feel that it is an illness with often multiple contributing causes.

Inflammatory or immune system involvement

The fact that IBS can accompany inflammatory bowel disease, or follow a bout of bacterial or parasitic dysentery, has led to the hypothesis that there may be an inflammatory or immune component to IBS. Subtle changes have been reported in some patients with IBS, including alterations of gut-homing T lymphocytes, and an unexplained increase in mast cells in colonic mucosa.[25] [26] However, in patients with IBS alone, mucosal biopsies are generally felt to be normal.

Intestinal microbiota

Intestinal microbiota may play a role in IBS by their actions on certain foods, especially carbohydrates, and also by their effects on epithelial barrier integrity and enteroendocrine signaling. Although an exact microbial signature is uncertain, IBS appears to be associated with dysbiosis and less diversity of the microbiota.[27] [28]

Bacterial overgrowth

Bacterial overgrowth has been demonstrated in some patients with IBS, particularly those with diarrhea predominance.[29]

Bile acid malabsorption

There appears to be a subgroup of patients with IBS and diarrhea who have bile acid malabsorption, despite no history of ileal disease, surgery, or previous cholecystectomy.[30]

Psychological stress or abuse

Stress and emotional tension frequently trigger bouts of IBS, although there are no specific personality profiles or psychiatric diagnoses associated with the condition. A history of physical or sexual abuse has been reported in 32% to 44% of patients.[20] [21] [22] One meta-analysis found that post-traumatic stress disorder (PTSD) is associated with an increased likelihood of IBS (pooled odds ratio 2.80, 95% CI 2.06 to 3.54, P <0.001).[31]

Pathophysiology

Most evidence suggests that there is dysfunction of the motor and sensory aspects of the digestive tract in people with IBS.[32] There is altered gut reactivity (motility and secretion) in response to various stimuli, which may be environmental (personal life stresses or abuse) or luminal (certain foods, bacterial overgrowth or toxins, or gut distension or inflammation). This altered reactivity can lead to pain as well as constipation or diarrhea.

There is evidence that there is gut hypersensitivity with enhanced perception of visceral type pain and sensations.[1] For instance, when a balloon is distended within the lumen of the lower colon or rectum, patients with IBS experience pain at lower pressures compared with people without IBS.[33] People with IBS also have dysregulation of the brain-gut axis. This may be associated with greater stress reactivity and with modulation or perception of afferent signals from the enteric nervous system.[32]

While the histology of the large and small intestinal mucosa is generally felt to be normal, subtle changes, including alterations of gut-homing T lymphocytes and an unexplained increase in mast cells in colonic mucosa, have been reported in patients with IBS.[25] [26] These findings suggest possible immune system involvement.

Classification

Rome IV: subtyping IBS by predominant stool pattern[2][3]

1. IBS with constipation (IBS-C): hard or lumpy stools for ≥25% of bowel movements and loose (mushy) or watery stools for ≤25% of bowel movements.

2. IBS with diarrhea (IBS-D): loose (mushy) or watery stools for ≥25% of bowel movements and hard or lumpy stool for ≤25% of bowel movements.

3. Mixed IBS (IBS-M): hard or lumpy stools for ≤25% of bowel movements and loose (mushy) or watery stools for ≤25% of bowel movements.

4. Unspecified IBS: insufficient abnormality of stool consistency to meet criteria for IBS-C, IBS-D, or IBS-M.

Case history

Case history #1

A 34-year-old mother of three presents to her family physician with a 3-week history of abdominal cramping pain in both lower quadrants. She has been having frequent small, soft stools accompanied by some mucus but no blood. Her symptoms are improved with bowel movement or passage of flatus. She has had these symptoms almost monthly since she was in college, but they have been worse recently. Past history is unremarkable except for three normal pregnancies. Family history is negative for colon cancer. A sister has similar symptoms but has not seen a physician. Personal/social history reveals that she is an accountant working long hours. Her firm is about to merge with another, and she fears her job situation is tenuous. She has not lost any weight or had any other constitutional symptoms. On physical exam, the only finding is some mild tenderness in the right lower quadrant. No mass is felt.

Case history #2

A 40-year-old housewife complains of recurrent constipation. She has had problems since her 20s, but they are worse now. The constipation is accompanied by abdominal bloating and abdominal pain, and the discomfort is only better when she has a bowel movement. On her gynecologist's advice, she has tried more fiber in her diet, including fresh fruits and leafy vegetables, but that has only made the bloating worse. Her past history includes cholecystectomy and hysterectomy. Physical exam is entirely normal. Rectal exam reveals normal consistency stool. Stool samples test negative for occult blood.

Other presentations

Patients can also present with alternating diarrhea and constipation that is associated with abdominal pain.

Approach

IBS is characterized by abdominal pain associated with altered bowel habits. The pain is relieved by defecation or passing flatus. Other common accompanying symptoms include abdominal bloating, passage of mucus with stools, urgency of defecation, and the sensation of incomplete evacuation following a bowel movement.[10]

History

The patient's history may reveal exposure to several risk factors, such as physical or sexual abuse, previous enteric infection, and stress at home or at work.[20] [21] [22][24] [32] Adult patients are twice as likely to be women.[14]

A family history of IBS may be present. Family history of inflammatory bowel disease, colorectal cancer, or celiac disease should increase the index of suspicion for these conditions. A careful dietary history may reveal consumption of foods that exacerbate symptoms (e.g., caffeine, cow's milk, fructose-containing foods, artificial sweeteners, alcohol), irregular or inadequate meals, insufficient fluid intake, or excessive or low (particularly in those with constipation) fiber intake.[10]

Physical exam

The physical exam is usually normal. There may, however, be mild tenderness in the lower quadrants without a mass.

The Carnett test helps distinguish pain of abdominal wall origin from abdominal pain arising from inside the abdomen. In this test, if the pain is increased on tightening the abdomen, it arises from the abdominal wall (positive Carnett test). Intraperitoneal pain is lessened with abdominal wall contraction.[34] A negative Carnett test would be expected in patients with IBS.

Laboratory tests

There is no specific diagnostic test for IBS. The choice of tests for the initial workup will depend upon factors such as symptoms and patient age.[2]

Tests for non-IBS disease, including inflammatory bowel disease and colorectal cancer

Complete blood count (CBC) should be done as part of the initial workup.[35] If the patient is anemic or if the white blood cell count is elevated, then a diagnosis other than IBS should be entertained.

Fecal occult blood testing may be considered. Fecal occult blood testing has a positive predictive value of 97% and a negative predictive value of 43% for distinguishing inflammatory bowel disease from IBS.[36] In the primary care setting, fecal occult blood testing may be used to inform the decision to refer a patient who has unexplained gastrointestinal symptoms, but who is at low risk for colorectal cancer, to a specialist.

Quantitative fecal immunochemical test (FIT) may be ordered when colorectal cancer is suspected. The UK guidelines recommend quantitative FIT to guide referral for suspected colorectal cancer in certain adults with unexplained abdominal pain or in those with a change in bowel habit.[37] [38] If FIT value is ≥10 micrograms hemoglobin/g of feces, urgent referral to secondary care is recommended. Based on FIT results, investigations such as colonoscopy can be avoided in people who are less likely to have colorectal cancer, thus making the resources available to those who need them the most.[37] [38]

A fecal calprotectin test or a stool lactoferrin may be ordered to differentiate IBS from inflammatory bowel disease.[39] [40] [41] [42] [43] American College of Gastroenterology (ACG) guidelines favor calprotectin over lactoferrin because of its higher sensitivity and specificity for inflammatory bowel disease.[39]

C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) can also be used to rule out inflammatory bowel disease.[35] [39] [40] Although both are nonspecific, ACG guidelines advise that CRP is the more useful of the two.[39] A comprehensive meta-analysis evaluated markers in 2145 patients with inflammatory bowel disease, IBS, or healthy controls and found that an elevated ESR or stool lactoferrin could not discriminate between patient groups, while a CRP ≤0.5 mg/dL or fecal calprotectin ≤40 micrograms/g reliably conferred a 1% or lower likelihood of inflammatory bowel disease, essentially excluding it as a diagnosis.[42]

Serologic tests for celiac disease

A tissue transglutaminase antibody test can help exclude celiac disease.[35] [39] [40] [44] [45]

If the patient has diarrhea and/or weight loss, celiac disease should be suspected. The most reliable test is the immunoglobulin (Ig) A human antitissue transglutaminase (anti-tTG) antibody enzyme-linked immunosorbent assay. This test has a reported sensitivity of almost 100% and a specificity of 95% to 97% for celiac disease.[44]

A positive result should be confirmed by duodenal biopsy.[40]

IgA endomysial antibodies (EMAs) may be tested for when anti-tTG is weakly positive or to confirm the diagnosis in children or adults for whom endoscopy is unsuitable.

Patients with IgA deficiency may have a false-negative anti-tTG result. Testing options for these patients include IgG tissue transglutaminase and IgG or IgA deamidated gliadin peptides.[40]

Tests to exclude bile acid malabsorption

Serum fibroblast growth factor 19 and 23-seleno-25-homotaurocholic acid (SeHCAT) tests, if available, are recommended for patients presenting with chronic diarrhea, to exclude bile acid malabsorption.[39] [40] [46]

Forty-eight hour stool collection for total bile acids may also be considered for the same indication.[40]

If other diagnostic tests are unavailable, an empiric trial of bile acid binder may be conducted in patients with chronic diarrhea to exclude bile acid malabsorption.[39] [40]

Hydrogen/methane breath test

In patients with diarrhea or bloating, further investigation with a hydrogen breath test for bacterial overgrowth or lactase deficiency may be warranted. However, this test is not recommended to confirm diagnosis in patients who meet the IBS diagnostic criteria.[35]

Enteric pathogens test

Routine stool testing for enteric pathogens (i.e., fecal leukocytes, ova, and parasites) is not recommended for patients with suspected IBS.[39]

Fecal immunoassay or polymerase chain reaction is indicated for patients with risk factors for giardiasis.[39] [40]

Imaging

Endoscopic assessment

Guidance recommends against routine colonoscopy for patients with IBS younger than 45 years without alarm features, which include:[39]

- hematochezia
- melena
- unintentional weight loss
- older age of onset of symptoms (over 50 years)
- family history of inflammatory bowel disease, colon cancer, or other significant gastrointestinal disease.

Colonoscopy should be considered for patients with alarm features.[39]

In patients with suspected IBS with diarrhea who are at high risk of microscopic colitis, i.e., older age (over 60 years), female sex, and more intense diarrhea, there is some evidence to support the use of colonoscopy.[39] Microscopic colitis should also be suspected if the patient does not have any abdominal pain.

Flexible sigmoidoscopy can detect abnormal mucosa, which could indicate inflammatory bowel disease and polyps or carcinoma; however, guidelines do not support its use to confirm diagnosis of IBS.[35]

Plain abdominal radiographs may be useful in the evaluation of patients with bloating.[47]

History and exam

Key diagnostic factors

abdominal pain (common)

- Generally cramping in nature and in the lower and/or mid-abdomen. Can be mild or severe.

alteration of bowel habits associated with pain (common)

- There may be diarrhea or more frequent soft stool, constipation, or alternating diarrhea and constipation. The passage of stool relieves the abdominal pain.

abdominal bloating or distension (common)

- This increases during the day and is not associated with nausea and vomiting. It is improved with defecation or passage of flatus.

normal exam of abdomen (common)

- There are no significant findings. Mild tenderness may be found in the right lower quadrant or left lower quadrant.

Other diagnostic factors

passage of mucus with stool (uncommon)

- Occurs when the patient is symptomatic and is not accompanied by blood.

urgency of defecation (uncommon)

- This symptom is more prevalent in Asian populations.[10]

Risk factors

Strong

physical and sexual abuse

- Several studies have shown that a history of physical and/or sexual abuse is more common in patients with IBS than in patients with other gastrointestinal disorders. Abuse has been reported in 32% to 44% of patients with IBS.[20] [21] [22]

posttraumatic stress disorder (PTSD)

- One meta-analysis found that PTSD is associated with an increased likelihood of IBS (pooled odds ratio 2.80, 95% CI 2.06 to 3.54, P <0.001).[31]

age <50 years

- Symptoms of IBS can begin in adolescence or early adulthood. The onset of IBS in patients aged >50 years is unusual, and patients in this group need to be evaluated carefully for other etiologies of their symptoms.[15] [16]

female sex

- There is a 2:1 female/male ratio among adults who seek help for symptoms of IBS.[14]

previous enteric infection

- Symptoms of IBS may occur in up to 30% of patients following acute bacterial gastroenteritis.[24] [32]

family history

- The odds of having IBS increase (odds ratio 2.75) if a first-degree relative has IBS.[19]

Weak

family and job stress

- Stressful life events sometimes correlate with symptom exacerbation, but the nature of this link is unclear.[2]

Tests

1st test to order

Test	Result
CBC • CBC should be done as part of the initial workup.[35] If the patient is anemic or if the WBC count is elevated, then a diagnosis other than IBS should be entertained.	**normal; anemia or raised WBC count suggests non-IBS disease**

Other tests to consider

Test	Result
fecal occult blood test • May be ordered when inflammatory bowel disease or colorectal cancer is suspected.[35] Fecal occult blood testing has a positive predictive value of 97% and a negative predictive value of 43% for distinguishing inflammatory bowel disease from IBS.[36] • In the primary care setting, fecal occult blood testing may be used to inform the decision to refer a patient who has unexplained gastrointestinal symptoms, but who is at low risk for colorectal cancer, to a specialist.	**normal; may be positive in inflammatory bowel disease or colorectal cancer**
quantitative fecal immunochemical test (FIT) • May be ordered when colorectal cancer is suspected. The UK guidelines recommend quantitative FIT to guide referral for suspected colorectal cancer in certain adults with unexplained abdominal pain or in those with a change in bowel habit.[37] [38] If FIT value is ≥10 micrograms hemoglobin/g of feces, urgent referral to secondary care is recommended. Based on FIT results, investigations such as colonoscopy can be avoided in people who are less likely to have colorectal cancer, thus making the resources available to those who need them the most.[37] [38]	**FIT value of ≥10 micrograms of hemoglobin/g of feces indicates possible colorectal cancer**
serologic tests for celiac disease • A tissue transglutaminase antibody test can help exclude celiac disease.[35] [39] [40] [44] [45] • If the patient has diarrhea and/or weight loss, celiac disease should be suspected. The most reliable test is the immunoglobulin (Ig) A human antitissue transglutaminase (anti-tTG) antibody enzyme-linked immunosorbent assay. This test has a reported sensitivity of almost 100% and a specificity of 95% to 97% for celiac disease.[44] • A positive result should be confirmed by duodenal biopsy.[40] • IgA endomysial antibodies (EMAs) may be tested for when anti-tTG is weakly positive or to confirm the diagnosis in children or adults for whom endoscopy is unsuitable. • Patients with IgA deficiency may have a false-negative anti-tTG result. Testing options for these patients include IgG tissue transglutaminase and IgG or IgA deamidated gliadin peptides.[40]	**negative**
fecal calprotectin • This may be ordered to differentiate IBS from inflammatory bowel disease (IBD).[35] [39] [40] [41] [42] [43] It has greater clinical utility for this purpose than fecal lactoferrin. A comprehensive meta-analysis evaluated markers in 2145 patients with IBD, IBS, or healthy controls and found that an elevated stool lactoferrin could not reliably discriminate between patient groups, while a fecal calprotectin ≤40 micrograms/g conferred a 1% or lower likelihood of IBD, essentially excluding it as a diagnosis.[42]	**<50 micrograms/g makes IBD unlikely (and IBS more likely)**
fecal lactoferrin • This test may be ordered to differentiate IBS from inflammatory bowel disease (IBD).[39] [40] It has inferior clinical utility for this purpose than fecal lactoferrin. A comprehensive meta-analysis evaluated markers in 2145 patients with IBD, IBS, or healthy controls and found that an elevated stool lactoferrin could not reliably discriminate between patient groups, while a fecal calprotectin ≤40 micrograms/g	**<7.25 micrograms/g makes IBD unlikely**

Test	Result
conferred a 1% or lower likelihood of IBD, essentially excluding it as a diagnosis.[42]	
serum C-reactive protein (CRP) • If testing for fecal lactoferrin or calprotectin are not available, serum CRP is a reasonable option to screen for inflammatory bowel disease (IBD).[35] [39] [40] • Serum CRP above 5-6 mg/L has a sensitivity of 0.73 (95% CI 0.64 to 0.80) and specificity of 0.78 (95% CI 0.58 to 0.91) for identifying IBD in patients with diarrhea.[40] A comprehensive meta-analysis evaluated serologic markers in 2145 patients with IBD, IBS, or healthy controls and found that a CRP ≤0.5 mg/dL reliably conferred a 1% or lower likelihood of IBD, essentially excluding it as a diagnosis.[42]	**normal**
erythrocyte sedimentation rate (ESR) • Erythrocyte sedimentation can be used to help rule out inflammatory bowel disease (IBD).[35] [39] [40] However, a comprehensive meta-analysis evaluated serologic markers in 2145 patients with IBD, IBS, or healthy controls and found that an elevated ESR could not reliably discriminate between patient groups. C-reactive protein is therefore preferred.[42]	**normal**
serum fibroblast growth factor 19 • Recommended for patients presenting with chronic diarrhea, if available, to exclude bile acid malabsorption.[39] [40] [46]	**normal; reduced level suggests bile acid malabsorption**
23-seleno-25-homotaurocholic acid (SeHCAT) test • Recommended for patients presenting with chronic diarrhea, if available, to exclude bile acid malabsorption.[39] [40] • The patient ingests a synthetic bile acid labeled with a radionuclide tracer atom (SeHCAT). Two whole-body scans using a gamma camera are conducted, 1 week apart, and the proportion of retained bile acid can be calculated.[35] The test is not available in North America.	**normal; <15% SeHCAT retention after 1 week indicates bile acid malabsorption**
48-hour stool collection for total bile acids • May be considered for patients presenting with chronic diarrhea to exclude bile acid malabsorption.[40]	**normal; increased fecal bile acids suggests bile acid malabsorption**
empiric trial of bile acid binder • May be conducted in patients with chronic diarrhea to exclude bile acid malabsorption if other diagnostic tests are unavailable.[39] [40]	**no improvement in diarrhea symptoms**
hydrogen/methane breath test • This may be ordered if the patient has diarrhea and/or bloating. However, this test is not recommended to confirm diagnosis in patients who meet the IBS diagnostic criteria.[35]	**normal; abnormal if bacterial overgrowth or lactase deficiency**
stool tests for Giardia lamblia • Routine stool testing for enteric pathogens (i.e., fecal leukocytes, ova, and parasites) is not recommended for patients with suspected IBS, but these tests are commonly ordered by primary care physicians.[39] • Fecal immunoassay or polymerase chain reaction is indicated for patients with risk factors for giardiasis.[39] [40]	**normal; WBCs in stool or presence of parasites suggests non-IBS disease**

Test	Result
plain abdominal radiograph • This test may be useful in the evaluation of a patient who has bloating.[47]	**normal; abnormal bowel pattern suggests obstruction**
colonoscopy • Guidance recommends against routine colonoscopy for patients with IBS younger than 45 years without alarm features, which include: hematochezia; melena; unintentional weight loss; older age of onset of symptoms (over 50 years); or family history of inflammatory bowel disease, colon cancer, and other significant gastrointestinal disease.[39] • For patients with alarm features a colonoscopy should be considered.[39] • In patients with suspected IBS with diarrhea who are at high risk of microscopic colitis, i.e., older age (over 60 years), female sex, and more intense diarrhea, there is some evidence to support the use of colonoscopy.[39] Microscopic colitis should also be suspected if the patient does not have any abdominal pain.	**normal; mucosal inflammation or ulceration suggests inflammatory bowel disease**
flexible sigmoidoscopy • Flexible sigmoidoscopy can detect abnormal mucosa, which could indicate inflammatory bowel disease, polyps, or carcinoma; however, guidelines do not support its use to confirm diagnosis of IBS.[35]	**normal; abnormal mucosa suggests inflammatory bowel disease**

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Crohn disease	• May present with fatigue, diarrhea, abdominal pain, weight loss, fever and rectal bleeding. • Other signs may include oral ulcers, perianal skin tags, fistulae, abscesses and sinus tracts; abdominal exam may reveal a palpable mass in the ileocecal area; no mass present on digital rectal examination.	• Stool culture, microscopy and antigen testing: negative. • Fecal occult blood: positive. • Upper gastrointestinal and small bowel series: edema and ulceration of the mucosa with luminal narrowing and strictures. • CT/MRI abdomen: skip lesions, bowel wall thickening, surrounding inflammation, abscess, fistulae. • Colonoscopy: aphthous ulcers, hyperemia, edema, cobblestoning, skip lesions.
Ulcerative colitis	• May present with bloody diarrhea, history of lower abdominal pain, fecal urgency, presence of extraintestinal manifestations (e.g., erythema nodosum, acute arthropathy), history of primary sclerosing cholangitis. No mass present on digital rectal exam.	• Stool culture, microscopy and antigen testing: negative. • Histology: continuous distal disease, mucin depletion, basal plasmacytosis, diffuse mucosal atrophy, absence of granulomata and anal sparing. • Colonoscopy: rectal involvement, continuous uniform involvement, loss of vascular marking, diffuse erythema, mucosal granularity, normal terminal ileum (or mild "backwash" ileitis in pancolitis).
Microscopic colitis	• Chronic watery, non-bloody diarrhea. • Other common symptoms include fecal urgency, fecal incontinence, and nocturnal stools. • More common in patients >50 years and female.	• Ileocolonoscopy with biopsies from the right and left colon: confirms diagnosis.[48] Colonic mucosa has a normal or near-normal gross appearance. • Biopsy: demonstrates collagenous colitis (i.e., thickened subepithelial collagenous band of ≥10 micrometer (normal <5 micrometer) or lymphocytic colitis (i.e., increased number of intraepithelial lymphocytes of ≥20 per

Condition	Differentiating signs / symptoms	Differentiating tests
		100 surface epithelial cells (normal <5 micrometer). Both types show an increased inflammatory infiltrate in the lamina propria.[48]
Celiac disease	• Patients with celiac disease usually have weight loss. The physical exam is usually normal. Some patients with celiac disease will have early osteoporosis.	• Basic laboratory tests: may show iron-deficiency anemia, hypocalcemia, or a prolonged prothrombin time, although many patients with celiac disease will have no routine laboratory abnormalities. • Anti-tissue transglutaminase antibodies may be detected in celiac disease.[44] Small bowel biopsy will be abnormal with partial villous atrophy in celiac disease.
Colon cancer	• Colon cancer can sometimes cause a change in bowel habits with either constipation or more frequent, smaller caliber stools. Some, but not all, colon cancer patients will have blood in their stool, and a rectal cancer may be palpable on rectal exam.	• CBC: iron-deficiency anemia may be present. • Fecal occult blood: may be positive. • Quantitative fecal immunochemical test (FIT): The UK guidelines recommend urgent referral to secondary care for FIT value of ≥10 micrograms of hemoglobin/g of feces.[37] [38] • Endoscopy: will demonstrate malignant growth; colon cancer can be diagnosed by colonoscopy, whereas cancers of the rectum, sigmoid, and lower descending colon can be seen with flexible sigmoidoscopy. • Barium enema: although less sensitive than endoscopy, many colon cancers can be seen on air-contrast barium enema. • CT colonography is an option for screening for colorectal cancer.
Bowel infections	• Most bacterial and viral infections in immunocompetent patients are acute. The parasite	• Stool exam positive for ova and parasites or stool antigen detection positive for *G lamblia* can be used

Condition	Differentiating signs / symptoms	Differentiating tests
	Giardia can be associated with diarrhea, nausea, and bloating. Giardiasis may also cause steatorrhea.	for screening. Multiple stools should be examined.
Nonceliac gluten sensitivity	• Patients will have bloating, abdominal cramping, and diarrhea similar to IBS.	• Studies will be negative, including tissue transglutaminase antibody. • There is no biomarker. • Patient's symptoms improve on gluten-free diet, especially without wheat.[49]
Bile acid malabsorption	• Patients have persistent diarrhea. May be clinically indistinguishable from diarrhea-predominant IBS (IBS-D). More than 25% of patients who meet the diagnostic criteria for IBS-D have bile acid malabsorption.[30]	• Test result indicating bile acid malabsorption: elevated fecal bile acids on 48-hour stool collection; reduced serum fibroblast growth factor 19; <15% retained 23-seleno-25-homotaurocholic acid (SeHCAT) 1 week after ingestion. • Symptoms improve with an empiric trial of bile acid binder.
Small bowel bacterial overgrowth	• Patients present with abdominal bloating, diarrhea, and abdominal cramps. History may show conditions that alter intestinal anatomy, motility, and gastric acid secretion (e.g., use of proton pump inhibitors or anatomical disturbances in the bowel, including fistulae, diverticula, and blind loops created after surgery).[50]	• Hydrogen breath testing indicates bacterial overgrowth.

Criteria

Rome IV criteria[2][3]

Recurrent abdominal pain, on average at least 1 day per week in the last 3 months and associated with two or more of the following criteria:

- Related to defecation
- Associated with a change in frequency of stool
- Associated with a change in form (appearance) of stool.

Manning criteria[51]

Recurrent abdominal pain and at least two of the following:

- Relief of pain with defecation
- More frequent stools at the onset of pain
- Looser stools at the onset of pain
- Visible abdominal distension
- Passage of mucus per rectum
- A sensation of incomplete evacuation.

Approach

The main goal of treatment is to decrease the severity of symptoms and improve quality of life.

Pharmacologic therapy is frequently used, in addition to lifestyle and dietary modifications. Placebo effect may be robust; one meta-analysis found that more than one quarter of patients with IBS experienced significant improvement in global symptoms with placebo treatment alone.[54]

Lifestyle and dietary modifications

It is important to establish an effective therapeutic relationship with each patient, and to provide education and reassurance.

Initial treatments should be conservative, including discussion of lifestyle changes that may lessen stress. Possible precipitating substances, such as caffeine, lactose, or fructose, may need to be eliminated from the diet. Symptom monitoring with a diary can be helpful to identify precipitating substances and factors. UK guidelines recommend that all patients should be advised of the potential benefits of regular exercise, citing evidence from randomized controlled trials (RCTs) that this can be beneficial, particularly for constipation.[53] However, US guidelines do not recommend exercise as a treatment.[39] One Cochrane review reported that physical activity may improve symptoms, but not quality of life or abdominal pain, in people with IBS, although the certainty of evidence was very low.[55]

Dietary advice should be given to all patients who can associate triggering or worsening of their IBS symptoms with eating food (this encompasses over 80% of patients with IBS) and who are motivated to make the necessary changes.[56] Referral to a registered dietitian nutritionist (RDN) should be made for patients who are willing to engage and patients who are not able to implement recommended dietary changes on their own.[56]

Low FODMAP diet

A trial of a low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) diet is recommended.[35] [39] [53] The low FODMAP diet is the most evidence-based diet for treating IBS.

FODMAPs are poorly absorbed short-chain carbohydrates that are prone to cause symptoms in patients with IBS. The low FODMAP diet induces favorable changes in the intestinal microbiota and significantly diminishes histamine, which may play a provocative role in some patients.[57] [58]

A diet low in FODMAPs has been shown to improve multiple symptoms, including diarrhea, flatus, bloating, and pain.[59] [60] [61] [62] [63] However, RCTs have typically been of short duration and at risk of bias.[64] [65] One meta-analysis showed significant superiority of a low FODMAP diet over British Dietetic Association dietary advice in reducing abdominal pain, bloating, and distension.[66] One European randomized trial found that in patients with IBS in primary care, a smartphone FODMAP-lowering diet application was superior to an antispasmodic agent in improving IBS symptoms. The authors concluded that a low FODMAP diet should be considered the first-line treatment for IBS in primary care.[67] However, it is uncertain which patients respond to specific FODMAP restrictions and adherence can be an issue.

Clinicians should consider an individualized approach to the low FODMAP diet, such as dietary restriction relevant to the patients' ethnicity, symptom profile, and usual dietary intake.[68]

Before recommending a restrictive diet of this nature, it is important to exclude disordered eating behaviors and eating disorders through careful history taking, as these are common in patients with gastrointestinal disorders.[56] Screening for malnutrition using a validated tool should also be considered. If the results indicate malnutrition, the patient is not suitable for dietary restrictions and should be referred to an RDN for a comprehensive nutritional assessment.[56]

A low FODMAP diet consists of three phases: restriction of FODMAP foods (lasting no more than 4-6 weeks); reintroduction of FODMAP foods; and personalization of ongoing diet based on the outcome of reintroduction. These diet interventions should be attempted for a predetermined time period, and ideally supervised by a registered dietitian.[56] Studies have demonstrated that 4-6 weeks of a low FODMAP diet is sufficient to determine whether a patient is going to respond.[56]

It remains unclear whether a gluten-free diet is of similar benefit to patients with IBS, with mixed results from RCTs.[56] [69] [70] Currently, a gluten-free diet is not recommended for the treatment of IBS.[53]

Probiotics

Probiotics can help reduce abdominal bloating and flatulence, alleviate pain, and improve quality of life in patients with IBS.[71] Response to probiotics varies between studies and individuals.[72] [73] They are not routinely recommended due to the heterogeneity in trials regarding outcome, design, magnitude of benefit, and uncertainty regarding the most effective strain.[39] [74]

Systematic review and meta-analyses indicate that composite probiotics containing *Bifidobacterium infantis* may be more effective than single strain probiotic therapy.[72] [75]

If a patient chooses to try probiotics, one UK guideline recommends taking them for up to 12 weeks at the dose recommended by the manufacturer, and discontinuing treatment if there is no improvement in symptoms.[56]

Constipation-predominant IBS (IBS-C)

Soluble fiber

If the patient has constipation or alternating constipation and diarrhea, then soluble fiber (found in psyllium, oat bran, barley, and beans) is often recommended. People with IBS should avoid insoluble fiber.[35] [39][53] [56] One UK guideline advises starting soluble fiber at a low dose (3-4 g/day) and building up gradually to avoid bloating.[53]

Effectiveness has not been consistently demonstrated, but the lack of significant adverse effects makes soluble fiber a reasonable first-line therapy for patients with IBS with symptoms.[7][39] [76] [77] [78]

Osmotic laxatives

The American Gastroenterological Association (AGA) suggests that polyethylene glycol (PEG) may be used for specific symptom relief, or as adjunctive therapy for the treatment of IBS with constipation (IBS-C).[79] American College of Gastroenterology (ACG) guidelines contradict this, however, citing a lack of evidence that PEG alleviates abdominal pain, and thus global symptoms, in patients with IBS-C.[39] They therefore recommend against the use of PEG alone for the treatment of global IBS-C symptoms, although they recognize that clinicians may use PEG as first-line treatment of constipation in IBS, given its low cost and availability.[39]

Secretagogues

Lubiprostone, linaclotide, plecanatide, or tenapanor are recommended for patients with persistent constipation despite treatment with initial laxatives.[39][53] [79] One systematic review and network meta-analysis examining the relative efficacy of these secretagogues across 15 RCTs found that they were all superior to placebo.[80] Linaclotide was the most efficacious agent for relieving constipation; plecanatide had the best safety profile.[80] Analyses utilized data extracted at a 12-week timepoint; longer-term effects are unknown.

Linaclotide and plecanatide are minimally absorbed 14-amino acid peptides that bind and activate the guanylate cyclase C receptor on the luminal surface of the enterocyte. This results in increased levels of cyclic guanosine monophosphate (cGMP), a second messenger that increases secretion of intestinal fluid.[81] Plecanatide and linaclotide are comparably effective, safe, and well tolerated.[39] [82] Diarrhea is a common side effect of both medications.[53]

Treatment with lubiprostone, a chloride-channel 2 (CIC2) activator, is an alternative in patients with constipation-predominant IBS who do not tolerate laxatives or stool softeners, or in whom these are ineffective.[39] [83] [84] Lubiprostone is approved by the Food and Drug Administration (FDA) for the treatment of IBS with constipation only in women ages ≥18 years old. Diarrhea is a less common adverse effect with lubiprostone than with other secretagogues; however, patients should be warned that nausea is a frequent side effect.[53]

Tenapanor, an inhibitor of the sodium-proton exchanger NHE3, is another alternative. It is effective for constipation and other global symptoms of IBS like bloating. As with linaclotide and plecanatide, diarrhea is a side effect.[53]

Tegaserod

Tegaserod, a serotonin-4 (5HT-4) receptor partial agonist, was previously recommended in some countries for the treatment of IBS with constipation in women aged under 65 years with ≤1 cardiovascular risk factor who did not adequately respond to secretagogues.[39] Tegaserod was originally withdrawn from the US market in 2007 following concerns about an increased risk of cardiovascular events. In 2019, based on a safety review, the FDA approved the reintroduction of tegaserod in the US. The drug has never been approved by the European Medicines Agency.[85] [86] According to a 2022 announcement, tegaserod has been withdrawn once again from the US market in June 2022; the withdrawal is reported to be because of commercial reasons and not because of product safety and efficacy or imposed recall.[87] The manufacturer has stated that the drug will be available in the US market until the depletion of existing supplies.

Diarrhea-predominant IBS

Antidiarrheals

Loperamide and opioid agonists/antagonists (e.g., eluxadoline) are variously recommended for patients with diarrhea-predominant IBS.[35] [39] [88]

Loperamide is a synthetic peripheral opioid agonist. It inhibits peristalsis and antisecretory activity and prolongs intestinal transit time with limited penetrance of the blood-brain barrier.[88]

The ACG and AGA both note that loperamide improves diarrhea but not global IBS symptoms.[39] [88]

Eluxadoline is a minimally absorbed mixed opioid receptor agonist and antagonist that was developed to reduce abdominal pain and diarrhea in patients who have IBS with predominant diarrhea (IBS-D), without constipating side effects.[89] In studies it has demonstrated significant improvements in stool consistency and urgency, but less effect on abdominal pain. It may therefore be more useful in patients with IBS-D with predominant and troublesome diarrhea than in those with predominant or more severe abdominal pain.[88] Eluxadoline is contraindicated in patients without a gallbladder or in patients who drink more than 3 alcoholic beverages per day because of increased risk of pancreatitis resulting in hospitalization or death.[90]

Cholestyramine

Cholestyramine may be more effective than loperamide in patients who have had a cholecystectomy. If bile acid-related diarrhea is suspected, a trial of cholestyramine may be warranted, either empirically or following testing if available.[40]

Alosetron

Alosetron is a 5-HT3 antagonist; these have been shown to significantly improve symptoms in patients with IBS-D.[91] [92]

Availability of alosetron may be restricted due to safety concerns. It was originally approved by the FDA in 2000 for the treatment of IBS-D in women; however, it was voluntarily withdrawn due to serious adverse events, particularly ischemic colitis and serious complications of constipation.[88] [92] [93] It was reintroduced in 2002, but with use restricted to the treatment of severe IBS-D in women under a risk management program. Though safety risks with alosetron still exist, the FDA has discontinued the risk management program. Counseling patients on the signs and symptoms of serious complications of constipation and ischemic colitis is recommended. Immediate discontinuation of treatment is recommended in patients with signs or symptoms of ischemic colitis.

Alosetron is only recommended for women with severe, diarrhea-predominant IBS who have had symptoms for 6 months or longer, do not have physical or biochemical abnormalities of the gastrointestinal tract, and have not responded adequately to conventional treatment.[39] [88] Severe symptoms are defined as 1 or more of the following: frequent and severe abdominal pain/discomfort, frequent bowel urgency or fecal incontinence, and/or disability or restriction of daily activities due to IBS.[88]

Rifaximin

Rifaximin, a minimally absorbed broad-spectrum oral antibiotic, has been shown to reduce global symptoms, bloating, abdominal pain, and loose watery stools in patients with IBS without constipation.[73] [88][94] [95] [96] Rifaximin may be used as an initial or recurrent treatment.[88] It has been approved by the FDA as a 14-day course for the treatment of diarrhea-predominant IBS. For recurrent symptoms, up to three courses are approved.

Pain or bloating

There are many options for treatment of pain, including lifestyle and dietary modifications.[97]

Antispasmodics

Antispasmodics may be considered for patients experiencing pain or bloating.[35] [88] They act by relaxing smooth muscle, thereby reducing gut motility. One Cochrane review found that patients taking antispasmodics experienced significantly greater improvement in both abdominal pain and global IBS symptoms.[77] The effect of individual antispasmodics was difficult to interpret, however, because of the inclusion of 12 different drugs and the small number of studies evaluated for each drug. There was also considerable variation between the studies concerning diagnostic and inclusion criteria, dosing schedule, and study end points.[88]

Because of the lack of high-quality evidence available, ACG guidelines recommend against the use of antispasmodics currently available in the US to treat global IBS symptoms (dicyclomine and hyoscyamine). They concede that there are more robust data supporting the use of alternative antispasmodics available internationally.[39] The AGA differs in its guidance and does recommend hyoscyamine and dicyclomine.[79] [88]

Peppermint oil has antispasmodic properties, and is recommended by both the ACG and AGA for the relief of global IBS symptoms.[39] [79][88] It is available as drops or enteric-coated sustained-release tablets. Evidence is mixed. One meta-analysis found that peppermint oil reduced abdominal pain and overall IBS symptoms compared with placebo.[98] However, a subsequent RCT (that employed end points recommended by regulatory authorities) concluded that peppermint oil does not significantly reduce abdominal pain or improve overall symptom relief.[99]

Antidepressants

If pain persists despite antispasmodics, a tricyclic antidepressant (TCA), used as a gut-brain neuromodulator, may be beneficial.[39] [79][88] [100] TCAs are thought to improve visceral and central pain by acting on norepinephrine and dopaminergic receptors. They may also improve abdominal pain because of their anticholinergic effects. At higher doses they can slow gastrointestinal transit, which can be useful in patients with urgency and diarrhea, but potentially problematic in patients with constipation. Secondary amine TCAs (e.g., desipramine and nortriptyline) may be better tolerated in patients with constipation-predominant IBS due to their lower anticholinergic effects.[79] [88]

Notable adverse events include dry mouth and eyes, urinary retention, cardiac arrhythmias, sedation, and constipation, so careful patient selection is needed.[39] [88] The beneficial effects of TCAs on IBS symptoms appear to be independent of effects on depression and may take several weeks.[88]

Selective serotonin-reuptake inhibitors (SSRIs) are not recommended in US guidelines because of a lack of high quality evidence that they significantly improve global symptoms or abdominal pain in patients with IBS.[39] [88]

In one meta-analysis, subgroup analysis by antidepressant class found no significant benefit from SSRIs in patients with IBS and abdominal pain; the beneficial effect on abdominal pain appeared to be limited to TCAs.[101] AGA guidelines note that in some patients, however, SSRIs may improve the perception of overall IBS symptoms and well-being by improving gastrointestinal symptoms, mood, and extraintestinal symptoms.[88] UK guidelines differ from US guidelines, recommending that SSRIs can be used as an alternative to TCAs for treating global symptoms of IBS.[53]

Psychological therapies

Patients who do not respond to pharmacologic treatment may need referral for more intensive psychological treatments and support.[35] One meta-analysis of RCTs of psychological therapies for IBS

demonstrated that several types of therapy were more efficacious than control interventions. However, the most compelling evidence, based on the number of trials and long-term outcomes, was for IBS-specific cognitive behavioral therapy (CBT) and gut-directed hypnotherapy.[102] Both are recommended in US and UK guidelines; UK National Institute for Health and Care Excellence (NICE) guidelines specify a role for them when symptoms have not improved after 12 months of pharmacologic treatment, whereas ACG guidelines recommend their use in conjunction with other IBS therapies for patients who are emotionally stable but exhibit cognitive-affective drivers of IBS.[35] [39]

Patients with predominantly pain-related symptoms may need referral to a pain specialist or clinic.

IBS occurring after enteric infection

There are no specific treatments for IBS occurring after enteric infection. It should be managed according to the predominant symptom, which is usually diarrhea or a mixed stool pattern.[103]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Ongoing (summary)

constipation-predominant		
pain or bloating not predominant	1st	lifestyle and dietary modifications
	adjunct	laxative
	2nd	lifestyle and dietary modifications
	plus	secretagogue
	3rd	lifestyle and dietary modifications
with pain or bloating predominant	1st	lifestyle and dietary modifications
	adjunct	laxative
	plus	antispasmodic
	2nd	lifestyle and dietary modifications
	plus	antidepressant
	plus	secretagogue
	adjunct	psychological therapy
	3rd	lifestyle and dietary modifications
	plus	antidepressant
	adjunct	psychological therapies
diarrhea-predominant		
pain or bloating not predominant	1st	lifestyle and dietary modifications
	plus	antidiarrheal
pain or bloating predominant	1st	lifestyle and dietary modifications
	plus	antidiarrheal
	plus	antispasmodic
	2nd	lifestyle and dietary modifications
	plus	antidepressant
	adjunct	psychological therapy

Ongoing (summary)

alternating constipation and diarrhea		
pain or bloating not predominant	**1st**	**lifestyle and dietary modifications**
	adjunct	**laxative**
	adjunct	**loperamide**
pain or bloating predominant	**1st**	**lifestyle and dietary modifications**
	plus	**antispasmodic**
	adjunct	**laxative**
	adjunct	**loperamide**
	2nd	**lifestyle and dietary modifications**
	plus	**antidepressant**
	adjunct	**psychological therapy**

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Ongoing

constipation-predominant

pain or bloating not predominant

1st

lifestyle and dietary modifications

» In all patients, an effective therapeutic relationship should be established, followed by education and reassurance.

» Initial treatments should be conservative, including discussion of lifestyle changes that may lessen stress.

» Possible precipitating substances such as caffeine, lactose, or fructose may need to be eliminated from the diet. UK guidelines recommend that all patients should be advised of the potential benefits of regular exercise, citing evidence from randomized controlled trials (RCTs) that this can be beneficial, particularly for constipation.[53] However, US guidelines do not recommend exercise as a treatment.[39] One Cochrane review reported that physical activity may improve symptoms, but not quality of life or abdominal pain, in people with IBS.[55]

» Dietary advice should be given to all patients who can associate triggering or worsening of their IBS symptoms with eating food (this encompasses over 80% of patients with IBS) and who are motivated to make the necessary changes.[56] Referral to a registered dietitian nutritionist (RDN) should be made for patients who are willing to engage and patients who are not able to implement recommended dietary changes on their own.[56]

» A trial of a low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) diet is recommended.[35] [39] [53] The low FODMAP diet is currently the most evidence-based diet for treating IBS.

» FODMAPs are poorly absorbed short-chain carbohydrates that are prone to cause symptoms in patients with IBS. The low FODMAP diet induces favorable changes in the intestinal microbiota and significantly diminishes histamine, which may play a provocative role in some patients.[57] [58]

Ongoing

» A diet low in FODMAPs has been shown to improve multiple symptoms, including diarrhea, flatus, bloating, and pain.[59] [60] [61] [62] [63] However, RCTs have typically been of short duration and at risk of bias.[64] [65]

» One meta-analysis showed significant superiority of a low FODMAP diet over British Dietetic Association dietary advice in reducing abdominal pain, bloating, and distension.[66] One European randomized trial found that in patients with IBS in primary care, a smartphone FODMAP-lowering diet application was superior to an antispasmodic agent in improving IBS symptoms. The authors concluded that a low FODMAP diet should be considered the first-line treatment for IBS in primary care.[67] However, it is uncertain which patients respond to specific FODMAP restrictions and adherence can be an issue. Clinicians should consider an individualized approach to the low FODMAP diet, such as dietary restriction relevant to the patients' ethnicity, symptom profile, and usual dietary intake.[68]

» Before recommending a restrictive diet of this nature, it is important to exclude disordered eating behaviors and eating disorders through careful history taking, as these are common in patients with gastrointestinal disorders.[56] Screening for malnutrition using a validated screening tool should also be considered. If the results indicate malnutrition, the patient is not suitable for dietary restrictions and should be referred to an RDN for a comprehensive nutritional assessment.[56]

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» It remains unclear whether a gluten-free diet is of similar benefit to patients with IBS, with mixed results from RCTs.[56] [69] [70] Currently, a gluten-free diet is not recommended for the treatment of IBS.[53]

Ongoing

» If the patient has constipation or alternating constipation and diarrhea, then soluble fiber (found in psyllium, oat bran, barley, and beans) is often recommended. People with IBS should avoid insoluble fiber.[35] [39] [56] One UK guideline advises starting soluble fiber at a low dose (3-4 g/day) and building up gradually to avoid bloating.[53]

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» Probiotics may also be considered. Probiotics can help reduce flatulence and improve quality of life.[71] Response to probiotics varies between studies and individuals.[72] [73] They are not routinely recommended due to the heterogeneity in trials regarding outcome, design, magnitude of benefit, and uncertainty regarding the most effective strain.[39] [74]

» Systematic review and meta-analyses indicate that composite probiotics containing *Bifidobacterium infantis* may be more effective than single strain probiotic therapy.[72] [75]

» If a patient chooses to try probiotics, one UK guideline recommends taking them for up to 12 weeks at the dose recommended by the manufacturer, and discontinuing treatment if there is no improvement in symptoms.[56]

adjunct **laxative**

Treatment recommended for SOME patients in selected patient group

» The American Gastroenterological Association suggests that polyethylene glycol (PEG) may be used for specific symptom relief, or as adjunctive therapy for the treatment of IBS with constipation (IBS-C).[79] American College of Gastroenterology guidelines contradict this, however, citing a lack of evidence that PEG alleviates abdominal pain, and thus global symptoms, in patients with IBS-C.[39] They therefore recommend against the use of PEG alone for the treatment of global IBS-C symptoms, although they recognize that clinicians may use PEG as first-line treatment of constipation in IBS, given its low cost and availability.[39]

2nd **lifestyle and dietary modifications**

Ongoing

» In all patients, an effective therapeutic relationship should be established, followed by education and reassurance.

» Initial treatments should be conservative, including discussion of lifestyle changes that may lessen stress.

» Possible precipitating substances such as caffeine, lactose, or fructose may need to be eliminated from the diet. UK guidelines recommend that all patients should be advised of the potential benefits of regular exercise, citing evidence from randomized controlled trials (RCTs) that this can be beneficial, particularly for constipation.[53] However, US guidelines do not recommend exercise as a treatment.[39] One Cochrane review reported that physical activity may improve symptoms, but not quality of life or abdominal pain, in people with IBS.[55]

» Dietary advice should be given to all patients who can associate triggering or worsening of their IBS symptoms with eating food (this encompasses over 80% of patients with IBS) and who are motivated to make the necessary changes.[56] Referral to a registered dietitian nutritionist (RDN) should be made for patients who are willing to engage and patients who are not able to implement recommended dietary changes on their own.[56]

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FODMAP-lowering diet application was superior to an antispasmodic agent in improving IBS symptoms. The authors concluded that a low FODMAP diet should be considered the first-line treatment for IBS in primary care.[67] However, it is uncertain which patients respond to specific FODMAP restrictions and adherence can be an issue. Clinicians should consider an individualized approach to the low FODMAP diet, such as dietary restriction relevant to the patients' ethnicity, symptom profile, and usual dietary intake.[68]

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plus **secretagogue**

Treatment recommended for ALL patients in selected patient group

Primary options

» lubiprostone: women: 8 micrograms orally twice daily

OR

» linaclotide: 290 micrograms orally once daily

OR

» plecanatide: 3 mg orally once daily

OR

» tenapanor: 50 mg orally twice daily

» Lubiprostone, linaclotide, plecanatide, or tenapanor are secretagogues that are recommended for patients with persistent constipation despite treatment with initial laxatives.[39][53] [79]

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3rd **lifestyle and dietary modifications**

» In all patients, an effective therapeutic relationship should be established, followed by education and reassurance.

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Ongoing

with pain or bloating predominant — **1st** — **lifestyle and dietary modifications**

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» FODMAPs are poorly absorbed short-chain carbohydrates that are prone to cause symptoms in patients with IBS. The low FODMAP diet induces favorable changes in the intestinal microbiota and significantly diminishes histamine, which may play a provocative role in some patients.[57] [58]

» A diet low in FODMAPs has been shown to improve multiple symptoms, including diarrhea, flatus, bloating, and pain.[59] [60] [61] [62] [63] However, RCTs have typically been of short duration and at risk of bias.[64] [65]

» One meta-analysis showed significant superiority of a low FODMAP diet over British Dietetic Association dietary advice in reducing abdominal pain, bloating, and distension.[66]

Ongoing

One European randomized trial found that in patients with IBS in primary care, a smartphone FODMAP-lowering diet application was superior to an antispasmodic agent in improving IBS symptoms. The authors concluded that a low FODMAP diet should be considered the first-line treatment for IBS in primary care.[67] However, it is uncertain which patients respond to specific FODMAP restrictions and adherence can be an issue. Clinicians should consider an individualized approach to the low FODMAP diet, such as dietary restriction relevant to the patients' ethnicity, symptom profile, and usual dietary intake.[68]

» Before recommending a restrictive diet of this nature, it is important to exclude disordered eating behaviors and eating disorders through careful history taking, as these are common in patients with gastrointestinal disorders.[56] Screening for malnutrition using a validated screening tool should also be considered. If the results indicate malnutrition, the patient is not suitable for dietary restrictions and should be referred to an RDN for a comprehensive nutritional assessment.[56]

» A low FODMAP diet consists of three phases: restriction of FODMAP foods (lasting no more than 4-6 weeks); reintroduction of FODMAP foods; and personalization of ongoing diet based on the outcome of reintroduction. These diet interventions should be attempted for a predetermined time period, and ideally supervised by a registered dietitian, although in some cases this may not be practical or affordable.[56] Studies have demonstrated that 4-6 weeks of a low FODMAP diet is sufficient to determine whether a patient is going to respond.[56]

» It remains unclear whether a gluten-free diet is of similar benefit to patients with IBS, with mixed results from RCTs.[56] [69] [70] Currently, a gluten-free diet is not recommended for the treatment of IBS.[53]

» If the patient has constipation or alternating constipation and diarrhea, then soluble fiber (found in psyllium, oat bran, barley, and beans) is often recommended. People with IBS should avoid insoluble fiber.[35] [39] [56] One UK guideline advises starting soluble fiber at a low dose (3-4 g/day) and building up gradually to avoid bloating.[53]

» Effectiveness has not been consistently demonstrated, but the lack of significant adverse

Ongoing

effects makes soluble fiber a reasonable first-line therapy for patients with IBS with symptoms.[7] [39] [76] [77] [78]

» Probiotics may also be considered. Probiotics can help reduce abdominal bloating and flatulence, alleviate pain, and improve quality of life.[71] Response to probiotics varies between studies and individuals.[72] [73] They are not routinely recommended due to the heterogeneity in trials regarding outcome, design, magnitude of benefit, and uncertainty regarding the most effective strain.[39] [74]

» Systematic review and meta-analyses indicate that composite probiotics containing *Bifidobacterium infantis* may be more effective than single strain probiotic therapy.[72] [75]

» If a patient chooses to try probiotics, one UK guideline recommends taking them for up to 12 weeks at the dose recommended by the manufacturer, and discontinuing treatment if there is no improvement in symptoms.[56]

adjunct **laxative**

Treatment recommended for SOME patients in selected patient group

» The American Gastroenterological Association suggests that polyethylene glycol (PEG) may be used for specific symptom relief, or as adjunctive therapy for the treatment of symptoms of IBS with constipation (IBS-C).[79] American College of Gastroenterology (ACG) guidelines contradict this, however, citing a lack of evidence that PEG alleviates abdominal pain, and thus global symptoms, in patients with IBS-C.[39] They therefore recommend against the use of PEG alone for the treatment of global IBS-C symptoms, although they recognize that clinicians may use PEG as first-line treatment of constipation in IBS, given its low cost and availability.[39]

plus **antispasmodic**

Treatment recommended for ALL patients in selected patient group

Primary options

» dicyclomine: 10-20 mg orally four times daily when required

OR

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» hyoscyamine: 0.125 to 0.25 mg orally/ sublingually three to four times daily when required, maximum 1.5 mg/day

OR

» peppermint oil (Mentha x piperita): consult product literature for guidance on dose

» Antispasmodics may be considered for patients experiencing pain or bloating.[35] [88] They act by relaxing smooth muscle, thereby reducing gut motility. One Cochrane review found that patients taking antispasmodics experienced significantly greater improvement in both abdominal pain and global IBS symptoms.[77] The effect of individual antispasmodics was difficult to interpret, however, because of the inclusion of 12 different drugs and the small number of studies evaluated for each drug. There was also considerable variation between the studies concerning diagnostic and inclusion criteria, dosing schedule, and study end points.[88]

» Because of the lack of high-quality evidence available, American College of Gastroenterology (ACG) guidelines recommend against the use of antispasmodics currently available in the US to treat global IBS symptoms (dicyclomine and hyoscyamine). They concede that there are more robust data supporting the use of alternative antispasmodics available internationally.[39] The American Gastroenterological Association (AGA) differs in its guidance and does recommend hyoscyamine and dicyclomine.[79] [88]

» Peppermint oil has antispasmodic properties, and is recommended by both the ACG and AGA for the relief of global IBS symptoms.[39] [79] [88] It is available as drops or enteric-coated sustained-release tablets. Evidence is mixed. One meta-analysis found that peppermint oil reduced abdominal pain and overall IBS symptoms compared with placebo.[98] However, a subsequent randomized controlled trial (that employed end points recommended by regulatory authorities) concluded that peppermint oil does not significantly reduce abdominal pain or improve overall symptom relief.[99]

2nd **lifestyle and dietary modifications**

» In all patients, an effective therapeutic relationship should be established, followed by education and reassurance.

Ongoing

» Initial treatments should be conservative, including discussion of lifestyle changes that may lessen stress.

» Possible precipitating substances such as caffeine, lactose, or fructose may need to be eliminated from the diet. UK guidelines recommend that all patients should be advised of the potential benefits of regular exercise, citing evidence from randomized controlled trials (RCTs) that this can be beneficial, particularly for constipation.[53] However, US guidelines do not recommend exercise as a treatment.[39] One Cochrane review reported that physical activity may improve symptoms, but not quality of life or abdominal pain, in people with IBS.[55]

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» If a patient chooses to try probiotics, one UK guideline recommends taking them for up to 12 weeks at the dose recommended by the manufacturer, and discontinuing treatment if there is no improvement in symptoms.[56]

plus **antidepressant**

Treatment recommended for ALL patients in selected patient group

Primary options

» amitriptyline: 10 mg orally once daily initially, increase dose gradually according to response, maximum 100 mg/day

OR

» nortriptyline: 10-25 mg orally once daily initially, increase dose gradually according to response, maximum 75 mg/day

OR

» desipramine: 10 mg orally once daily initially, increase dose gradually according to response, maximum 100 mg/day

Secondary options

» paroxetine: 20-40 mg orally once daily

OR

» citalopram: 20-40 mg orally once daily

» If pain persists despite antispasmodics, a tricyclic antidepressant (TCA) such as amitriptyline, nortriptyline, or desipramine, used as a gut-brain neuromodulator, may be beneficial.[39][79] [88] [100] TCAs are thought to improve visceral and central pain by acting on norepinephrine and dopaminergic receptors. They may also improve abdominal

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pain because of their anticholinergic effects. At higher doses they can slow gastrointestinal transit, which can be useful in patients with urgency and diarrhea, but potentially problematic in patients with constipation. Secondary amine TCAs (e.g., desipramine and nortriptyline) may be better tolerated in patients with constipation-predominant IBS due to their lower anticholinergic effects.[79] [88] Notable adverse events include dry mouth and eyes, urinary retention, cardiac arrhythmias, sedation, and constipation, so careful patient selection is needed.[39] [88] The beneficial effects of TCAs on IBS symptoms appear to be independent of effects on depression and may take several weeks.[88]

» Selective serotonin-reuptake inhibitors (SSRIs) are not recommended in US guidelines because of a lack of high-quality evidence that they significantly improve global symptoms or abdominal pain in patients with IBS.[39] [88] In one meta-analysis, subgroup analysis by antidepressant class found no significant benefit from SSRIs in patients with IBS and abdominal pain; the beneficial effect on abdominal pain appeared to be limited to TCAs.[101] American Gastroenterological Association guidelines note that in some patients, however, SSRIs may improve the perception of overall IBS symptoms and well-being by improving gastrointestinal symptoms, mood, and extraintestinal symptoms.[88] UK guidelines differ from US guidelines, recommending that SSRIs can be used as an alternative to TCAs for treating global symptoms of IBS.[53]

» Treatment should be started at low doses and titrated gradually according to response and tolerability.

plus **secretagogue**

Treatment recommended for ALL patients in selected patient group

Primary options

» lubiprostone: women: 8 micrograms orally twice daily

OR

» linaclotide: 290 micrograms orally once daily

OR

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» plecanatide: 3 mg orally once daily

OR

» tenapanor: 50 mg orally twice daily

» Lubiprostone, linaclotide, plecanatide, or tenapanor are secretagogues that are recommended for patients with persistent constipation despite treatment with initial laxatives.[39][53] [79]

» One systematic review and network meta-analysis examining the relative efficacy of these secretagogues across 18 randomized controlled trials found that they were all superior to placebo.[80] Linaclotide was the most efficacious agent for relieving constipation; plecanatide had the best safety profile.[80] Analyses utilized data extracted at a 12-week timepoint; longer-term effects are unknown.

» Linaclotide and plecanatide are minimally absorbed 14-amino acid peptides that bind and activate the guanylate cyclase C receptor on the luminal surface of the enterocyte. This results in increased levels of cyclic guanosine monophosphate (cGMP), a second messenger that increases secretion of intestinal fluid.[81] Plecanatide and linaclotide are comparably effective, safe, and well tolerated.[39] [82] Diarrhea is a common side effect of both these medications.[53]

» Treatment with lubiprostone, a chloride-channel 2 (CIC2) activator, is an alternative in patients with constipation-predominant IBS who do not tolerate laxatives or stool softeners, or in whom these are ineffective.[39] [83] [84] Lubiprostone is approved by the Food and Drug Administration (FDA) for the treatment of IBS with constipation only in women ages ≥18 years. Diarrhea is a less common adverse effect with lubiprostone than with other secretagogues; however, patients should be warned that nausea is a frequent side effect.[53]

» Tenapanor, an inhibitor of the sodium-proton exchanger NHE3, is another alternative. It is effective for constipation and other global symptoms of IBS like bloating. As with linaclotide and plecanatide, diarrhea is a side effect.[53]

adjunct **psychological therapy**

Treatment recommended for SOME patients in selected patient group

Ongoing

» Patients who do not respond to pharmacologic treatment may need referral for more intensive psychological treatments and support.[35] One meta-analysis of randomized controlled trials of psychological therapies for IBS demonstrated that several types of therapy were more efficacious than control interventions. However, the most compelling evidence, based on the number of trials and long-term outcomes, was for IBS-specific cognitive behavioral therapy (CBT) and gut-directed hypnotherapy.[102] Both are recommended in US and UK guidelines; UK National Institute for Health and Care Excellence guidelines specify a role for them when symptoms have not improved after 12 months of pharmacologic treatment, whereas American College of Gastroenterology guidelines recommend their use in conjunction with other IBS therapies for patients who are emotionally stable but exhibit cognitive-affective drivers of IBS.[35] [39]

» Patients with predominantly pain-related symptoms may need referral to a pain specialist or clinic.

3rd **lifestyle and dietary modifications**

» In all patients, an effective therapeutic relationship should be established, followed by education and reassurance.

» Initial treatments should be conservative, including discussion of lifestyle changes that may lessen stress.

» Possible precipitating substances such as caffeine, lactose, or fructose may need to be eliminated from the diet. UK guidelines recommend that all patients should be advised of the potential benefits of regular exercise, citing evidence from randomized controlled trials (RCTs) that this can be beneficial, particularly for constipation.[53] However, US guidelines do not recommend exercise as a treatment.[39] One Cochrane review reported that physical activity may improve symptoms, but not quality of life or abdominal pain, in people with IBS.[55]

» Dietary advice should be given to all patients who can associate triggering or worsening of their IBS symptoms with eating food (this encompasses over 80% of patients with IBS) and who are motivated to make the necessary changes.[56] Referral to a registered dietitian nutritionist (RDN) should be made for patients who are willing to engage and patients who are

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» Before recommending a restrictive diet of this nature, it is important to exclude disordered eating behaviors and eating disorders through careful history taking, as these are common in patients with gastrointestinal disorders.[56] Screening for malnutrition using a validated screening tool should also be considered. If the results indicate malnutrition, the patient is not suitable for dietary restrictions and should be referred to an RDN for a comprehensive nutritional assessment.[56]

» A low FODMAP diet consists of three phases: restriction of FODMAP foods (lasting no more than 4-6 weeks); reintroduction of FODMAP foods; and personalization of ongoing diet

Ongoing

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» If a patient chooses to try probiotics, one UK guideline recommends taking them for up to 12 weeks at the dose recommended by the manufacturer, and discontinuing treatment if there is no improvement in symptoms.[56]

plus **antidepressant**

Treatment recommended for ALL patients in selected patient group

Primary options

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» amitriptyline: 10 mg orally once daily initially, increase dose gradually according to response, maximum 100 mg/day

OR

» nortriptyline: 10-25 mg orally once daily initially, increase dose gradually according to response, maximum 75 mg/day

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Secondary options

» paroxetine: 20-40 mg orally once daily

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» Patients with predominantly pain-related symptoms may need referral to a pain specialist or clinic.

diarrhea-predominant

pain or bloating not predominant

1st **lifestyle and dietary modifications**

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Ongoing

» Initial treatments should be conservative, including discussion of lifestyle changes that may lessen stress.

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» If a patient chooses to try probiotics, one UK guideline recommends taking them for up to 12 weeks at the dose recommended by the manufacturer, and discontinuing treatment if there is no improvement in symptoms.[56]

plus **antidiarrheal**

Treatment recommended for ALL patients in selected patient group

Primary options

» loperamide: 2-4 mg orally initially, followed by 2 mg after each loose stool when required, maximum 16 mg/day

OR

» cholestyramine: 2-4 g orally two to four times daily

OR

» eluxadoline: 75-100 mg orally twice daily

Secondary options

» alosetron: 0.5 to 1 mg orally twice daily

OR

» rifaximin: 550 mg orally three times daily for 14 days; course may be repeated twice if recurrent symptoms

» Loperamide and opioid agonists/antagonists (e.g., eluxadoline) are variously recommended for patients with diarrhea-predominant IBS (IBS-D).[35] [39] [88]

» Loperamide is a synthetic peripheral opioid agonist. It inhibits peristalsis and antisecretory activity and prolongs intestinal transit time with limited penetrance of the blood-brain barrier.[88] The American College

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of Gastroenterology (ACG) and American Gastroenterological Association (AGA) both note that loperamide improves diarrhea but not global IBS symptoms.[39] [88]

» Eluxadoline is a minimally absorbed mixed opioid receptor agonist and antagonist that was developed to reduce abdominal pain and diarrhea in patients who have IBS-D, without constipating side effects.[89] In studies it has demonstrated significant improvements in stool consistency and urgency, but less effect on abdominal pain. It may therefore be more useful in patients with IBS-D with predominant and troublesome diarrhea than in those with predominant or more severe abdominal pain.[88] Eluxadoline is contraindicated in patients without a gallbladder or in patients who drink more than 3 alcoholic beverages per day because of increased risk of pancreatitis resulting in hospitalization or death.[90]

» Cholestyramine may be more effective than loperamide in patients who have had a cholecystectomy. If bile acid-related diarrhea is suspected, a trial of cholestyramine may be warranted, either empirically or following testing if available.[40]

» Alosetron and rifaximin are recommended for the management of IBS-D in patients whose symptoms persist despite treatment with loperamide or an opioid agonist/antagonist.[39] [88]

» Alosetron is a 5-HT3 antagonist; these have been shown to significantly improve symptoms in patients with IBS-D.[91] [92]

» Availability of alosetron may be restricted due to safety concerns. It was originally approved by the Food and Drug Administration (FDA) in 2000 for the treatment of IBS-D in women; however, it was voluntarily withdrawn due to serious adverse events, particularly ischemic colitis and serious complications of constipation.[88] [92] [93] It was reintroduced in 2002, but with use restricted to the treatment of severe IBS-D in women under a risk management program. Though safety risks with alosetron still exist, the FDA has discontinued the risk management program. Counseling patients on the signs and symptoms of serious complications of constipation and ischemic colitis is recommended. Immediate discontinuation of treatment is recommended in patients with signs or symptoms of ischemic colitis. Alosetron is only recommended for women with severe, diarrhea-predominant

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IBS who have had symptoms for 6 months or longer, do not have physical or biochemical abnormalities of the gastrointestinal tract, and have not responded adequately to conventional treatment.[39] [88] Severe symptoms are defined as 1 or more of the following: frequent and severe abdominal pain/discomfort, frequent bowel urgency or fecal incontinence, and/or disability or restriction of daily activities due to IBS.[88]

» Rifaximin, a minimally absorbed broad-spectrum oral antibiotic, has been shown to reduce global symptoms, bloating, abdominal pain, and loose watery stools in patients with IBS without constipation.[73] [88][94] [95] [96] Rifaximin has been approved by the FDA as a 14-day course for the treatment of diarrhea-predominant IBS. For recurrent symptoms, up to three courses are approved.

pain or bloating predominant — **1st** — **lifestyle and dietary modifications**

» In all patients, an effective therapeutic relationship should be established, followed by education and reassurance.

» Initial treatments should be conservative, including discussion of lifestyle changes that may lessen stress.

» Possible precipitating substances such as caffeine, lactose, or fructose may need to be eliminated from the diet. UK guidelines recommend that all patients should be advised of the potential benefits of regular exercise, citing evidence from randomized controlled trials (RCTs) that this can be beneficial, particularly for constipation.[53] However, US guidelines do not recommend exercise as a treatment.[39] One Cochrane review reported that physical activity may improve symptoms, but not quality of life or abdominal pain, in people with IBS.[55]

» Dietary advice should be given to all patients who can associate triggering or worsening of their IBS symptoms with eating food (this encompasses over 80% of patients with IBS) and who are motivated to make the necessary changes.[56] Referral to a registered dietitian nutritionist (RDN) should be made for patients who are willing to engage and patients who are not able to implement recommended dietary changes on their own.[56]

» A trial of a low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) diet is recommended.[35] [39] [53]

Ongoing

The low FODMAP diet is currently the most evidence-based diet for treating IBS.

» FODMAPs are poorly absorbed short-chain carbohydrates that are prone to cause symptoms in patients with IBS. The low FODMAP diet induces favorable changes in the intestinal microbiota and significantly diminishes histamine, which may play a provocative role in some patients.[57] [58]

» A diet low in FODMAPs has been shown to improve multiple symptoms, including diarrhea, flatus, bloating, and pain.[59] [60] [61] [62] [63] However, RCTs have typically been of short duration and at risk of bias.[64] [65]

» One meta-analysis showed significant superiority of a low FODMAP diet over British Dietetic Association dietary advice in reducing abdominal pain, bloating, and distension.[66] One European randomized trial found that in patients with IBS in primary care, a smartphone FODMAP-lowering diet application was superior to an antispasmodic agent in improving IBS symptoms. The authors concluded that a low FODMAP diet should be considered the first-line treatment for IBS in primary care.[67] However, it is uncertain which patients respond to specific FODMAP restrictions and adherence can be an issue. Clinicians should consider an individualized approach to the low FODMAP diet, such as dietary restriction relevant to the patients' ethnicity, symptom profile, and usual dietary intake.[68]

» Before recommending a restrictive diet of this nature, it is important to exclude disordered eating behaviors and eating disorders through careful history taking, as these are common in patients with gastrointestinal disorders.[56] Screening for malnutrition using a validated screening tool should also be considered. If the results indicate malnutrition, the patient is not suitable for dietary restrictions and should be referred to an RDN for a comprehensive nutritional assessment.[56]

» A low FODMAP diet consists of three phases: restriction of FODMAP foods (lasting no more than 4-6 weeks); reintroduction of FODMAP foods; and personalization of ongoing diet based on the outcome of reintroduction. These diet interventions should be attempted for a predetermined time period, and ideally supervised by a registered dietitian, although in some cases this may not be practical or affordable.[56] Studies have demonstrated that

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4-6 weeks of a low FODMAP diet is sufficient to determine whether a patient is going to respond.[56]

» It remains unclear whether a gluten-free diet is of similar benefit to patients with IBS, with mixed results from RCTs.[56] [69] [70] Currently, a gluten-free diet is not recommended for the treatment of IBS.[53]

» If the patient has constipation or alternating constipation and diarrhea, then soluble fiber (found in psyllium, oat bran, barley, and beans) is often recommended. People with IBS should avoid insoluble fiber.[35] [39] [56] One UK guideline advises starting soluble fiber at a low dose (3-4 g/day) and building up gradually to avoid bloating.[53]

» Effectiveness has not been consistently demonstrated, but the lack of significant adverse effects makes soluble fiber a reasonable first-line therapy for patients with IBS with symptoms.[7] [39] [76] [77] [78]

» Probiotics may also be considered. Probiotics can help reduce abdominal bloating and flatulence, alleviate pain, and improve quality of life.[71] Response to probiotics varies between studies and individuals.[72] [73] They are not routinely recommended due to the heterogeneity in trials regarding outcome, design, magnitude of benefit, and uncertainty regarding the most effective strain.[39] [74]

» Systematic review and meta-analyses indicate that composite probiotics containing *Bifidobacterium infantis* may be more effective than single strain probiotic therapy.[72] [75]

» If a patient chooses to try probiotics, one UK guideline recommends taking them for up to 12 weeks at the dose recommended by the manufacturer, and discontinuing treatment if there is no improvement in symptoms.[56]

plus **antidiarrheal**

Treatment recommended for ALL patients in selected patient group

Primary options

» loperamide: 2-4 mg orally initially, followed by 2 mg after each loose stool when required, maximum 16 mg/day

OR

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» cholestyramine: 2-4 g orally two to four times daily

OR

» eluxadoline: 75-100 mg orally twice daily

Secondary options

» alosetron: 0.5 to 1 mg orally twice daily

OR

» rifaximin: 550 mg orally three times daily for 14 days; course may be repeated twice if recurrent symptoms

» Loperamide and opioid agonists/antagonists (e.g., eluxadoline) are variously recommended for patients with diarrhea-predominant IBS (IBS-D).[35] [39] [88]

» Loperamide is a synthetic peripheral opioid agonist. It inhibits peristalsis and antisecretory activity and prolongs intestinal transit time with limited penetrance of the blood-brain barrier.[88] The American College of Gastroenterology (ACG) and American Gastroenterological Association (AGA) both note that loperamide improves diarrhea but not global IBS symptoms.[39] [88]

» Eluxadoline is a minimally absorbed mixed opioid receptor agonist and antagonist that was developed to reduce abdominal pain and diarrhea in patients who have IBS-D, without constipating side effects.[89] In studies it has demonstrated significant improvements in stool consistency and urgency, but less effect on abdominal pain. It may therefore be more useful in patients with IBS-D with predominant and troublesome diarrhea than in those with predominant or more severe abdominal pain.[88] Eluxadoline is contraindicated in patients without a gallbladder or in patients who drink more than 3 alcoholic beverages per day because of increased risk of pancreatitis resulting in hospitalization or death.[90]

» Cholestyramine may be more effective than loperamide in patients who have had a cholecystectomy. If bile acid-related diarrhea is suspected, a trial of cholestyramine may be warranted, either empirically or following testing if available.[40]

Ongoing

» Alosetron and rifaximin are recommended for the management of IBS-D in patients whose symptoms persist despite treatment with loperamide or an opioid agonist/antagonist.[39] [88]

» Alosetron is a 5-HT3 antagonist; these have been shown to significantly improve symptoms in patients with IBS-D.[91] [92]

» Availability of alosetron may be restricted due to safety concerns. It was originally approved by the Food and Drug Administration (FDA) in 2000 for the treatment of IBS-D in women; however, it was voluntarily withdrawn due to serious adverse events, particularly ischemic colitis and serious complications of constipation.[88] [92] [93] It was reintroduced in 2002, but with use restricted to the treatment of severe IBS-D in women under a risk management program. Though safety risks with alosetron still exist, the FDA has discontinued the risk management program. Counseling patients on the signs and symptoms of serious complications of constipation and ischemic colitis is recommended. Immediate discontinuation of treatment is recommended in patients with signs or symptoms of ischemic colitis. Alosetron is only recommended for women with severe, diarrhea-predominant IBS who have had symptoms for 6 months or longer, do not have physical or biochemical abnormalities of the gastrointestinal tract, and have not responded adequately to conventional treatment.[39] [88] Severe symptoms are defined as 1 or more of the following: frequent and severe abdominal pain/discomfort, frequent bowel urgency or fecal incontinence, and/or disability or restriction of daily activities due to IBS.[88]

» Rifaximin, a minimally absorbed broad-spectrum oral antibiotic, has been shown to reduce global symptoms, bloating, abdominal pain, and loose watery stools in patients with IBS without constipation.[73] [88][94] [95] [96] Rifaximin has been approved by the FDA as a 14-day course for the treatment of diarrhea-predominant IBS. For recurrent symptoms, up to three courses are approved.

plus **antispasmodic**

Treatment recommended for ALL patients in selected patient group

Primary options

» dicyclomine: 10-20 mg orally four times daily when required

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OR

» hyoscyamine: 0.125 to 0.25 mg orally/ sublingually three to four times daily when required, maximum 1.5 mg/day

OR

» peppermint oil (Mentha x piperita): consult product literature for guidance on dose

» Antispasmodics may be considered for patients experiencing pain or bloating.[35] [88] They act by relaxing smooth muscle, thereby reducing gut motility. One Cochrane review found that patients taking antispasmodics experienced significantly greater improvement in both abdominal pain and global IBS symptoms.[77] The effect of individual antispasmodics was difficult to interpret, however, because of the inclusion of 12 different drugs and the small number of studies evaluated for each drug. There was also considerable variation between the studies concerning diagnostic and inclusion criteria, dosing schedule, and study end points.[88]

» Because of the lack of high-quality evidence available, American College of Gastroenterology (ACG) guidelines recommend against the use of antispasmodics currently available in the US to treat global IBS symptoms (dicyclomine and hyoscyamine). They concede that there are more robust data supporting the use of alternative antispasmodics available internationally.[39] The American Gastroenterological Association (AGA) differs in its guidance and does recommend hyoscyamine and dicyclomine.[79] [88]

» Peppermint oil has antispasmodic properties, and is recommended by both the ACG and AGA for the relief of global IBS symptoms.[39] [79] [88] It is available as drops or enteric-coated sustained-release tablets. Evidence is mixed. One meta-analysis found that peppermint oil reduced abdominal pain and overall IBS symptoms compared with placebo.[98] However, a subsequent randomized controlled trial (that employed end points recommended by regulatory authorities) concluded that peppermint oil does not significantly reduce abdominal pain or improve overall symptom relief.[99]

2nd **lifestyle and dietary modifications**

Ongoing

» In all patients, an effective therapeutic relationship should be established, followed by education and reassurance.

» Initial treatments should be conservative, including discussion of lifestyle changes that may lessen stress.

» Possible precipitating substances such as caffeine, lactose, or fructose may need to be eliminated from the diet. UK guidelines recommend that all patients should be advised of the potential benefits of regular exercise, citing evidence from randomized controlled trials (RCTs) that this can be beneficial, particularly for constipation.[53] However, US guidelines do not recommend exercise as a treatment.[39] One Cochrane review reported that physical activity may improve symptoms, but not quality of life or abdominal pain, in people with IBS.[55]

» Dietary advice should be given to all patients who can associate triggering or worsening of their IBS symptoms with eating food (this encompasses over 80% of patients with IBS) and who are motivated to make the necessary changes.[56] Referral to a registered dietitian nutritionist (RDN) should be made for patients who are willing to engage and patients who are not able to implement recommended dietary changes on their own.[56]

» A trial of a low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) diet is recommended.[35] [39] [53] The low FODMAP diet is currently the most evidence-based diet for treating IBS.

» FODMAPs are poorly absorbed short-chain carbohydrates that are prone to cause symptoms in patients with IBS. The low FODMAP diet induces favorable changes in the intestinal microbiota and significantly diminishes histamine, which may play a provocative role in some patients.[57] [58]

» A diet low in FODMAPs has been shown to improve multiple symptoms, including diarrhea, flatus, bloating, and pain.[59] [60] [61] [62] [63] However, RCTs have typically been of short duration and at risk of bias.[64] [65]

» One meta-analysis showed significant superiority of a low FODMAP diet over British Dietetic Association dietary advice in reducing abdominal pain, bloating, and distension.[66] One European randomized trial found that in patients with IBS in primary care, a smartphone

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FODMAP-lowering diet application was superior to an antispasmodic agent in improving IBS symptoms. The authors concluded that a low FODMAP diet should be considered the first-line treatment for IBS in primary care.[67] However, it is uncertain which patients respond to specific FODMAP restrictions and adherence can be an issue. Clinicians should consider an individualized approach to the low FODMAP diet, such as dietary restriction relevant to the patients' ethnicity, symptom profile, and usual dietary intake.[68]

» Before recommending a restrictive diet of this nature, it is important to exclude disordered eating behaviors and eating disorders through careful history taking, as these are common in patients with gastrointestinal disorders.[56] Screening for malnutrition using a validated screening tool should also be considered. If the results indicate malnutrition, the patient is not suitable for dietary restrictions and should be referred to an RDN for a comprehensive nutritional assessment.[56]

» A low FODMAP diet consists of three phases: restriction of FODMAP foods (lasting no more than 4-6 weeks); reintroduction of FODMAP foods; and personalization of ongoing diet based on the outcome of reintroduction. These diet interventions should be attempted for a predetermined time period, and ideally supervised by a registered dietitian, although in some cases this may not be practical or affordable.[56] Studies have demonstrated that 4-6 weeks of a low FODMAP diet is sufficient to determine whether a patient is going to respond.[56]

» It remains unclear whether a gluten-free diet is of similar benefit to patients with IBS, with mixed results from RCTs.[56] [69] [70] Currently, a gluten-free diet is not recommended for the treatment of IBS.[53]

» If the patient has constipation or alternating constipation and diarrhea, then soluble fiber (found in psyllium, oat bran, barley, and beans) is often recommended. People with IBS should avoid insoluble fiber.[35] [39] [56] One UK guideline advises starting soluble fiber at a low dose (3-4 g/day) and building up gradually to avoid bloating.[53]

» Effectiveness has not been consistently demonstrated, but the lack of significant adverse effects makes soluble fiber a reasonable first-line

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therapy for patients with IBS with symptoms.[7] [39] [76] [77] [78]

» Probiotics may also be considered. Probiotics can help reduce abdominal bloating and flatulence, alleviate pain, and improve quality of life.[71] Response to probiotics varies between studies and individuals.[72] [73] They are not routinely recommended due to the heterogeneity in trials regarding outcome, design, magnitude of benefit, and uncertainty regarding the most effective strain.[39] [74]

» Systematic review and meta-analyses indicate that composite probiotics containing *Bifidobacterium infantis* may be more effective than single strain probiotic therapy.[72] [75]

» If a patient chooses to try probiotics, one UK guideline recommends taking them for up to 12 weeks at the dose recommended by the manufacturer, and discontinuing treatment if there is no improvement in symptoms.[56]

plus **antidepressant**

Treatment recommended for ALL patients in selected patient group

Primary options

» amitriptyline: 10 mg orally once daily initially, increase dose gradually according to response, maximum 100 mg/day

OR

» nortriptyline: 10-25 mg orally once daily initially, increase dose gradually according to response, maximum 75 mg/day

OR

» desipramine: 10 mg orally once daily initially, increase dose gradually according to response, maximum 100 mg/day

Secondary options

» paroxetine: 20-40 mg orally once daily

OR

» citalopram: 20-40 mg orally once daily

» If pain persists despite antispasmodics, a tricyclic antidepressant (TCA) such as amitriptyline, nortriptyline, or desipramine,

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used as a gut-brain neuromodulator, may be beneficial.[39] [79][88] [100] TCAs are thought to improve visceral and central pain by acting on norepinephrine and dopaminergic receptors. They may also improve abdominal pain because of their anticholinergic effects. At higher doses they can slow gastrointestinal transit, which can be useful in patients with urgency and diarrhea, but potentially problematic in patients with constipation. Secondary amine TCAs (e.g., desipramine and nortriptyline) may be better tolerated in patients with constipation-predominant IBS due to their lower anticholinergic effects.[79] [88] Notable adverse events include dry mouth and eyes, urinary retention, cardiac arrhythmias, sedation, and constipation, so careful patient selection is needed.[39] [88] The beneficial effects of TCAs on IBS symptoms appear to be independent of effects on depression and may take several weeks.[88]

» Selective serotonin-reuptake inhibitors (SSRIs) are not recommended in US guidelines because of a lack of high-quality evidence that they significantly improve global symptoms or abdominal pain in patients with IBS.[39] [88] In one meta-analysis, subgroup analysis by antidepressant class found no significant benefit from SSRIs in patients with IBS and abdominal pain; the beneficial effect on abdominal pain appeared to be limited to TCAs.[101] American Gastroenterological Association guidelines note that in some patients, however, SSRIs may improve the perception of overall IBS symptoms and well-being by improving gastrointestinal symptoms, mood, and extraintestinal symptoms.[88] UK guidelines differ from US guidelines, recommending that SSRIs can be used as an alternative to TCAs for treating global symptoms of IBS.[53]

» Treatment should be started at low doses and titrated gradually according to response and tolerability.

adjunct **psychological therapy**

Treatment recommended for SOME patients in selected patient group

» Patients who do not respond to pharmacologic treatment may need referral for more intensive psychological treatments and support.[35] One meta-analysis of randomized controlled trials of psychological therapies for IBS demonstrated that several types of therapy were more efficacious than control interventions. However, the most compelling evidence,

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based on the number of trials and long-term outcomes, was for IBS-specific cognitive behavioral therapy (CBT) and gut-directed hypnotherapy.[102] Both are recommended in US and UK guidelines; UK National Institute for Health and Care Excellence guidelines specify a role for them when symptoms have not improved after 12 months of pharmacologic treatment, whereas American College of Gastroenterology guidelines recommend their use in conjunction with other IBS therapies for patients who are emotionally stable but exhibit cognitive-affective drivers of IBS.[35] [39]

» Patients with predominantly pain-related symptoms may need referral to a pain specialist or clinic.

alternating constipation and diarrhea

pain or bloating not predominant

1st

lifestyle and dietary modifications

» In all patients, an effective therapeutic relationship should be established, followed by education and reassurance.

» Initial treatments should be conservative, including discussion of lifestyle changes that may lessen stress.

» Possible precipitating substances such as caffeine, lactose, or fructose may need to be eliminated from the diet. UK guidelines recommend that all patients should be advised of the potential benefits of regular exercise, citing evidence from randomized controlled trials (RCTs) that this can be beneficial, particularly for constipation.[53] However, US guidelines do not recommend exercise as a treatment.[39] One Cochrane review reported that physical activity may improve symptoms, but not quality of life or abdominal pain, in people with IBS.[55]

» Dietary advice should be given to all patients who can associate triggering or worsening of their IBS symptoms with eating food (this encompasses over 80% of patients with IBS) and who are motivated to make the necessary changes.[56] Referral to a registered dietitian nutritionist (RDN) should be made for patients who are willing to engage and patients who are not able to implement recommended dietary changes on their own.[56]

» A trial of a low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols

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(FODMAPs) diet is recommended.[35] [39] [53] The low FODMAP diet is currently the most evidence-based diet for treating IBS.

» FODMAPs are poorly absorbed short-chain carbohydrates that are prone to cause symptoms in patients with IBS. The low FODMAP diet induces favorable changes in the intestinal microbiota and significantly diminishes histamine, which may play a provocative role in some patients.[57] [58]

» A diet low in FODMAPs has been shown to improve multiple symptoms, including diarrhea, flatus, bloating, and pain.[59] [60] [61] [62] [63] However, RCTs have typically been of short duration and at risk of bias.[64] [65]

» One meta-analysis showed significant superiority of a low FODMAP diet over British Dietetic Association dietary advice in reducing abdominal pain, bloating, and distension.[66] One European randomized trial found that in patients with IBS in primary care, a smartphone FODMAP-lowering diet application was superior to an antispasmodic agent in improving IBS symptoms. The authors concluded that a low FODMAP diet should be considered the first-line treatment for IBS in primary care.[67] However, it is uncertain which patients respond to specific FODMAP restrictions and adherence can be an issue. Clinicians should consider an individualized approach to the low FODMAP diet, such as dietary restriction relevant to the patients' ethnicity, symptom profile, and usual dietary intake.[68]

» Before recommending a restrictive diet of this nature, it is important to exclude disordered eating behaviors and eating disorders through careful history taking, as these are common in patients with gastrointestinal disorders.[56] Screening for malnutrition using a validated screening tool should also be considered. If the results indicate malnutrition, the patient is not suitable for dietary restrictions and should be referred to an RDN for a comprehensive nutritional assessment.[56]

» A low FODMAP diet consists of three phases: restriction of FODMAP foods (lasting no more than 4-6 weeks); reintroduction of FODMAP foods; and personalization of ongoing diet based on the outcome of reintroduction. These diet interventions should be attempted for a predetermined time period, and ideally supervised by a registered dietitian, although in some cases this may not be practical or

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affordable.[56] Studies have demonstrated that 4-6 weeks of a low FODMAP diet is sufficient to determine whether a patient is going to respond.[56]

» It remains unclear whether a gluten-free diet is of similar benefit to patients with IBS, with mixed results from RCTs.[56] [69] [70] Currently, a gluten-free diet is not recommended for the treatment of IBS.[53]

» If the patient has constipation or alternating constipation and diarrhea, then soluble fiber (found in psyllium, oat bran, barley, and beans) is often recommended. People with IBS should avoid insoluble fiber.[35] [39] [56] One UK guideline advises starting soluble fiber at a low dose (3-4 g/day) and building up gradually to avoid bloating.[53]

» Effectiveness has not been consistently demonstrated, but the lack of significant adverse effects makes soluble fiber a reasonable first-line therapy for patients with IBS with symptoms.[7] [39] [76] [77] [78]

» Probiotics may also be considered. Probiotics can help reduce flatulence and improve quality of life.[71] Response to probiotics varies between studies and individuals.[72] [73] They are not routinely recommended due to the heterogeneity in trials regarding outcome, design, magnitude of benefit, and uncertainty regarding the most effective strain.[39] [74]

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» If a patient chooses to try probiotics, one UK guideline recommends taking them for up to 12 weeks at the dose recommended by the manufacturer, and discontinuing treatment if there is no improvement in symptoms.[56]

adjunct **laxative**

Treatment recommended for SOME patients in selected patient group

» The American Gastroenterological Association suggests that polyethylene glycol (PEG) may be used for specific symptom relief, or as adjunctive therapy for the treatment of IBS with constipation (IBS-C).[79] American College of Gastroenterology guidelines contradict this, however, citing a lack of evidence that PEG alleviates abdominal pain, and thus

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global symptoms, in patients with IBS-C.[39] They therefore recommend against the use of PEG alone for the treatment of global IBS-C symptoms, although they recognize that clinicians may use PEG as first-line treatment of constipation in IBS, given its low cost and availability.[39]

adjunct **loperamide**

Treatment recommended for SOME patients in selected patient group

Primary options

» loperamide: 2-4 mg orally initially, followed by 2 mg after each loose stool as needed, maximum 16 mg/day

» Loperamide should be used when needed in a diarrheal phase.

» Long-term use of antidiarrheals should be monitored.

pain or bloating predominant

1st **lifestyle and dietary modifications**

» In all patients, an effective therapeutic relationship should be established, followed by education and reassurance.

» Initial treatments should be conservative, including discussion of lifestyle changes that may lessen stress.

» Possible precipitating substances such as caffeine, lactose, or fructose may need to be eliminated from the diet. UK guidelines recommend that all patients should be advised of the potential benefits of regular exercise, citing evidence from randomized controlled trials (RCTs) that this can be beneficial, particularly for constipation.[53] However, US guidelines do not recommend exercise as a treatment.[39] One Cochrane review reported that physical activity may improve symptoms, but not quality of life or abdominal pain, in people with IBS.[55]

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» If a patient chooses to try probiotics, one UK guideline recommends taking them for up to 12 weeks at the dose recommended by the manufacturer, and discontinuing treatment if there is no improvement in symptoms.[56]

plus **antispasmodic**

Treatment recommended for ALL patients in selected patient group

Primary options

» dicyclomine: 10-20 mg orally four times daily as needed

OR

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» hyoscyamine: 0.125 to 0.25 mg orally/sublingually three to four times daily as needed, maximum 1.5 mg/day

OR

» peppermint oil (Mentha x piperita): consult product literature for guidance on dose

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adjunct **laxative**

Treatment recommended for SOME patients in selected patient group

MANAGEMENT

Ongoing

» The American Gastroenterological Association suggests that polyethylene glycol (PEG) may be used for specific symptom relief, or as adjunctive therapy for the treatment of IBS with constipation (IBS-C).[79] American College of Gastroenterology guidelines contradict this, however, citing a lack of evidence that PEG alleviates abdominal pain, and thus global symptoms, in patients with IBS-C.[39] They therefore recommend against the use of PEG alone for the treatment of global IBS-C symptoms, although they recognize that clinicians may use PEG as first-line treatment of constipation in IBS, given its low cost and availability.[39]

adjunct **loperamide**

Treatment recommended for SOME patients in selected patient group

Primary options

» loperamide: 2-4 mg orally initially, followed by 2 mg after each loose stool as needed, maximum 16 mg/day

» Loperamide should be used when needed in a diarrheal phase.

» Long-term use of antidiarrheals should be monitored.

2nd **lifestyle and dietary modifications**

» In all patients, an effective therapeutic relationship should be established, followed by education and reassurance.

» Initial treatments should be conservative, including discussion of lifestyle changes that may lessen stress.

» Possible precipitating substances such as caffeine, lactose, or fructose may need to be eliminated from the diet. UK guidelines recommend that all patients should be advised of the potential benefits of regular exercise, citing evidence from randomized controlled trials (RCTs) that this can be beneficial, particularly for constipation.[53] However, US guidelines do not recommend exercise as a treatment.[39] One Cochrane review reported that physical activity may improve symptoms, but not quality of life or abdominal pain, in people with IBS.[55]

» Dietary advice should be given to all patients who can associate triggering or worsening of their IBS symptoms with eating food (this encompasses over 80% of patients with IBS)

Ongoing

and who are motivated to make the necessary changes.[56] Referral to a registered dietitian nutritionist (RDN) should be made for patients who are willing to engage and patients who are not able to implement recommended dietary changes on their own.[56]

» A trial of a low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) diet is recommended.[35] [39] [53] The low FODMAP diet is currently the most evidence-based diet for treating IBS.

» FODMAPs are poorly absorbed short-chain carbohydrates that are prone to cause symptoms in patients with IBS. The low FODMAP diet induces favorable changes in the intestinal microbiota and significantly diminishes histamine, which may play a provocative role in some patients.[57] [58]

» A diet low in FODMAPs has been shown to improve multiple symptoms, including diarrhea, flatus, bloating, and pain.[59] [60] [61] [62] [63] However, RCTs have typically been of short duration and at risk of bias.[64] [65]

» One meta-analysis showed significant superiority of a low FODMAP diet over British Dietetic Association dietary advice in reducing abdominal pain, bloating, and distension.[66] One European randomized trial found that in patients with IBS in primary care, a smartphone FODMAP-lowering diet application was superior to an antispasmodic agent in improving IBS symptoms. The authors concluded that a low FODMAP diet should be considered the first-line treatment for IBS in primary care.[67] However, it is uncertain which patients respond to specific FODMAP restrictions and adherence can be an issue. Clinicians should consider an individualized approach to the low FODMAP diet, such as dietary restriction relevant to the patients' ethnicity, symptom profile, and usual dietary intake.[68]

» Before recommending a restrictive diet of this nature, it is important to exclude disordered eating behaviors and eating disorders through careful history taking, as these are common in patients with gastrointestinal disorders.[56] Screening for malnutrition using a validated screening tool should also be considered. If the results indicate malnutrition, the patient is not suitable for dietary restrictions and should be referred to an RDN for a comprehensive nutritional assessment.[56]

Ongoing

» A low FODMAP diet consists of three phases: restriction of FODMAP foods (lasting no more than 4-6 weeks); reintroduction of FODMAP foods; and personalization of ongoing diet based on the outcome of reintroduction. These diet interventions should be attempted for a predetermined time period, and ideally supervised by a registered dietitian, although in some cases this may not be practical or affordable.[56] Studies have demonstrated that 4-6 weeks of a low FODMAP diet is sufficient to determine whether a patient is going to respond.[56]

» It remains unclear whether a gluten-free diet is of similar benefit to patients with IBS, with mixed results from RCTs.[56] [69] [70] Currently, a gluten-free diet is not recommended for the treatment of IBS.[53]

» If the patient has constipation or alternating constipation and diarrhea, then soluble fiber (found in psyllium, oat bran, barley, and beans) is often recommended. People with IBS should avoid insoluble fiber.[35] [39] [56] One UK guideline advises starting soluble fiber at a low dose (3-4 g/day) and building up gradually to avoid bloating.[53]

» Effectiveness has not been consistently demonstrated, but the lack of significant adverse effects makes soluble fiber a reasonable first-line therapy for patients with IBS with symptoms.[7] [39] [76] [77] [78]

» Probiotics may also be considered. Probiotics can help reduce abdominal bloating and flatulence, alleviate pain, and improve quality of life.[71] Response to probiotics varies between studies and individuals.[72] [73] They are not routinely recommended due to the heterogeneity in trials regarding outcome, design, magnitude of benefit, and uncertainty regarding the most effective strain.[39] [74]

» Systematic review and meta-analyses indicate that composite probiotics containing *Bifidobacterium infantis* may be more effective than single strain probiotic therapy.[72] [75]

» If a patient chooses to try probiotics, one UK guideline recommends taking them for up to 12 weeks at the dose recommended by the manufacturer, and discontinuing treatment if there is no improvement in symptoms.[56]

plus **antidepressant**

Ongoing

Treatment recommended for ALL patients in selected patient group

Primary options

» amitriptyline: 10 mg orally once daily initially, increase dose gradually according to response, maximum 100 mg/day

OR

» nortriptyline: 10-25 mg orally once daily initially, increase dose gradually according to response, maximum 75 mg/day

OR

» desipramine: 10 mg orally once daily initially, increase dose gradually according to response, maximum 100 mg/day

Secondary options

» paroxetine: 20-40 mg orally once daily

OR

» citalopram: 20-40 mg orally once daily

» If pain persists despite antispasmodics, a tricyclic antidepressant (TCA) such as amitriptyline, nortriptyline, or desipramine, used as a gut-brain neuromodulator, may be beneficial.[39] [79][88] [100] TCAs are thought to improve visceral and central pain by acting on norepinephrine and dopaminergic receptors. They may also improve abdominal pain because of their anticholinergic effects. At higher doses they can slow gastrointestinal transit, which can be useful in patients with urgency and diarrhea, but potentially problematic in patients with constipation. Secondary amine TCAs (e.g., desipramine and nortriptyline) may be better tolerated in patients with constipation-predominant IBS due to their lower anticholinergic effects.[79] [88] Notable adverse events include dry mouth and eyes, urinary retention, cardiac arrhythmias, sedation, and constipation, so careful patient selection is needed.[39] [88] The beneficial effects of TCAs on IBS symptoms appear to be independent of effects on depression and may take several weeks.[88]

» Selective serotonin-reuptake inhibitors (SSRIs) are not recommended in US guidelines because of a lack of high-quality evidence that they

Ongoing

significantly improve global symptoms or abdominal pain in patients with IBS.[39] [88] In one meta-analysis, subgroup analysis by antidepressant class found no significant benefit from SSRIs in patients with IBS and abdominal pain; the beneficial effect on abdominal pain appeared to be limited to TCAs.[101] American Gastroenterological Association guidelines note that in some patients, however, SSRIs may improve the perception of overall IBS symptoms and well-being by improving gastrointestinal symptoms, mood, and extraintestinal symptoms.[88] UK guidelines differ from US guidelines, recommending that SSRIs can be used as an alternative to TCAs for treating global symptoms of IBS.[53]

» Treatment should be started at low doses and titrated gradually according to response and tolerability.

adjunct **psychological therapy**

Treatment recommended for SOME patients in selected patient group

» Patients who do not respond to pharmacologic treatment may need referral for more intensive psychological treatments and support.[35] One meta-analysis of randomized controlled trials of psychological therapies for IBS demonstrated that several types of therapy were more efficacious than control interventions. However, the most compelling evidence, based on the number of trials and long-term outcomes, was for IBS-specific cognitive behavioral therapy (CBT) and gut-directed hypnotherapy.[102] Both are recommended in US and UK guidelines; UK National Institute for Health and Care Excellence guidelines specify a role for them when symptoms have not improved after 12 months of pharmacologic treatment, whereas American College of Gastroenterology guidelines recommend their use in conjunction with other IBS therapies for patients who are emotionally stable but exhibit cognitive-affective drivers of IBS.[35] [39]

» Patients with predominantly pain-related symptoms may need referral to a pain specialist or clinic.

Emerging

Microbiota-directed therapies

Patients with IBS have significant differences in their microbiota compared with people without IBS, but it is unclear whether this represents cause or effect.[104] [105] [106] Some randomized placebo-controlled trials report an improvement in IBS symptoms in patients receiving fecal microbiota transplantation (FMT), while other studies report no difference in symptom control between the FMT and placebo groups.[107] [108] [109] [110] FMT can be successfully accomplished with colonoscopy, use of nasojejunal tubes, or pills.

Ramosetron

Ramosetron, a 5HT-3 receptor antagonist, has been shown to be effective in both men and women for reducing diarrhea and abdominal pain in diarrhea-predominant IBS.[111] [112] Constipation is a side effect in around 10% of patients.[113] It is approved for the treatment of IBS with diarrhea in several countries, including Japan and India, but not in the US or Europe.

Ondansetron

Ondansetron, a 5HT-3 receptor antagonist, has long been used as an antiemetic. One large prospective study demonstrated that it was modestly effective versus placebo for improving diarrhea and well-being in patients with diarrhea-predominant IBS.[114]

Patient discussions

Patients should be helped to feel more in control and able to manage their symptoms. A support group may be an effective way to achieve this. Patients should be advised to limit, or completely eliminate possible precipitating substances such as caffeine, lactose, or fructose. Symptom monitoring with a diary can be helpful to identify these substances. Patients should also be asked to consider taking a daily probiotic and fiber supplement, and to ensure adequate fluid intake.

Monitoring

Monitoring

No long-term monitoring is necessary. Patients with IBS should follow the standard recommendations for screening for colorectal, gynecologic, and genitourinary malignancies.

Complications

Complications	Timeframe	Likelihood
damage to family and work relationships	**variable**	**low**
The recurrent nature of IBS can lead to disruptions in daily life that can alter family and work relationships.		
diverticulosis	**variable**	**low**
There is some evidence that patients with diarrhea-predominant IBS are at increased risk for diverticulosis, but not diverticulitis.[115]		
depression	**variable**	**low**
Compared with healthy controls, patients with IBS have more severe and more frequent symptoms of depression. Female sex and younger age are associated with more severe symptoms.[116]		
sleep disorders	**variable**	**low**
One meta-analysis found that over 37% of patients with IBS have a concomitant sleep disorder.[117]		
lower urinary tract symptoms	**variable**	**low**
Male and female patients with IBS are more likely to have lower urinary tract symptoms, compared with the general population.[118]		

Prognosis

Patients with IBS have a normal life expectancy, and there are no long-term complications of their disease. However, the symptoms of the disease tend to recur for much of adulthood, particularly at times of stress, emotional difficulty, or dietary indiscretions.

IBS following a viral enteric infection is more likely to improve or remit over time.[103]

Diagnostic guidelines

International

American Society for Gastrointestinal Endoscopy guideline on informed consent for GI endoscopic procedures (https://www.giejournal.org/article/S0016-5107(21)01759-4/fulltext) [52]

Published by: American Society for Gastrointestinal Endoscopy **Last published:** 2022

ACG clinical guideline: management of irritable bowel syndrome (https://gi.org/guidelines) [39]

Published by: American College of Gastroenterology **Last published:** 2021

AGA clinical practice guidelines on the laboratory evaluation of functional diarrhea and diarrhea-predominant irritable bowel syndrome in adults (IBS-D) (https://gastro.org/guidelines) [40]

Published by: American Gastroenterological Association **Last published:** 2019

Irritable bowel syndrome: a global perspective (https://www.worldgastroenterology.org/guidelines/global-guidelines) [10]

Published by: World Gastroenterology Organisation **Last published:** 2015

British Society of Gastroenterology guidelines on the management of irritable bowel syndrome (https://www.bsg.org.uk/resource-type/guidelines) [53]

Published by: British Society of Gastroenterology **Last published:** 2021

Irritable bowel syndrome in adults: diagnosis and management (https://www.nice.org.uk/guidance/CG61) [35]

Published by: National Institute for Health and Care Excellence **Last published:** 2017

Treatment guidelines

International

AGA clinical practice guideline on the pharmacological management of irritable bowel syndrome with diarrhea (https://gastro.org/guidelines) [88]

Published by: American Gastroenterological Association **Last published:** 2022

AGA clinical practice guideline on the pharmacological management of irritable bowel syndrome with constipation (https://gastro.org/guidelines) [79]

Published by: American Gastroenterological Association **Last published:** 2022

AGA clinical practice update on the role of diet in irritable bowel syndrome: expert review (https://gastro.org/guidelines) [56]

Published by: American Gastroenterological Association **Last published:** 2022

ACG clinical guideline: management of irritable bowel syndrome (https://gi.org/guidelines) [39]

Published by: American College of Gastroenterology **Last published:** 2021

Probiotics and prebiotics (https://www.worldgastroenterology.org/guidelines/probiotics-and-prebiotics/probiotics-and-prebiotics-english)

Published by: World Gastroenterology Organisation **Last published:** 2023

Irritable bowel syndrome: a global perspective (https://www.worldgastroenterology.org/guidelines/global-guidelines) [10]

Published by: World Gastroenterology Organisation **Last published:** 2015

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Published by: British Society of Gastroenterology **Last published:** 2021

Irritable bowel syndrome in adults: diagnosis and management (https://www.nice.org.uk/guidance/CG61) [35]

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This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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