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Approach to functional gastrointestinal symptoms in adults with inflammatory bowel disease

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INTRODUCTION

Symptoms such as diarrhea and abdominal pain are common to both active inflammatory bowel disease (IBD) and functional bowel disease. Patients with an established diagnosis of IBD (eg, Crohn disease, ulcerative colitis) may have persistent gastrointestinal (GI) symptoms, despite successful IBD therapy that has resulted in mucosal healing and disease remission. Recognizing functional symptoms in patients with inactive IBD helps to avoid the risk of adverse effects associated with escalating IBD-focused therapies. Functional GI symptoms in patients with IBD are associated with anxiety, depression, lower quality of life, and increased health care utilization [1,2]. Therefore, it is important to identify functional GI symptoms in this setting in order to choose an effective therapeutic approach.

Functional GI symptoms occurring in patients with IBD have been diagnosed as "irritable bowel syndrome" (IBS) but probably should not be referred to as such. If inflammatory mucosal disease is present, the patient's symptoms cannot meet the diagnostic criteria for IBS. Thus, the term "functional GI symptoms" occurring in a patient with IBD is a more accurate description [3].

This topic will discuss recognizing and managing functional GI symptoms in patients with an established diagnosis of IBD. The pathophysiology, clinical manifestations, diagnosis, and management of IBS are discussed separately:

- (See "Pathophysiology of irritable bowel syndrome".)
- (See "Clinical manifestations and diagnosis of irritable bowel syndrome in adults".)
- (See "Treatment of irritable bowel syndrome in adults".)

The clinical manifestations, diagnosis and treatment of Crohn disease are discussed separately:

- (See "Clinical manifestations, diagnosis, and prognosis of Crohn disease in adults".)
- (See "Overview of the medical management of mild (low risk) Crohn disease in adults".)
- (See "Medical management of moderate to severe Crohn disease in adults".)

The clinical manifestations, diagnosis and treatment of ulcerative colitis are also discussed separately:

- (See "Clinical manifestations, diagnosis, and prognosis of ulcerative colitis in adults".)
- (See "Medical management of low-risk adult patients with mild to moderate ulcerative colitis".)
- (See "Management of the hospitalized adult patient with severe ulcerative colitis".)
- (See "Management of moderate to severe ulcerative colitis in adults".)

CLINICAL PRESENTATION

Patients with functional symptoms in the setting of quiescent IBD typically present with nonacute abdominal pain and altered bowel habits (eg, diarrhea, constipation, or alternating diarrhea and constipation). Patients with functional symptoms may also report abdominal bloating and increased gas production in the form of flatulence or belching. Functional symptoms are not limited to the small bowel and colon, but can also include heartburn, nausea, and dyspepsia [4]. The characterization of functional symptoms in patients with inactive IBD is similar to the clinical presentation of IBS, which is discussed separately. (See "Clinical manifestations and diagnosis of irritable bowel syndrome in adults", section on 'Clinical manifestations'.)

EVALUATION

Goals — When a patient with IBD presents with gastrointestinal symptoms (eg, diarrhea, abdominal pain), the goal is to determine whether the symptoms are due to an IBD flare, an IBD-related complication (eg, partial small bowel obstruction), another organic disease process, or functional disease.

Identifying functional symptoms in patients with IBD requires the following:

- Suspect that symptoms are functional based on the patient's clinical presentation, pertinent negative findings (eg, absence of bloody stools), and prior history of IBD in remission (ie, minimally or no active mucosal inflammation demonstrated on endoscopy or by a low fecal calprotectin level (<50 mcg/g) and no systemic inflammation demonstrated by a normal C-reactive protein [CRP]). Because the gastrointestinal tract can express itself in a limited number of ways, functional symptoms highly overlap with those associated with intestinal inflammation. (See 'Clinical presentation' above and 'Initial steps' below.)

- Confirm that IBD has remained in remission (ie, minimally or no active mucosal inflammation and no systemic inflammation, as described above).

- Exclude another organic disease as the etiology if clinical presentation suggests an alternative diagnosis (eg, infectious colitis) (see 'Differential diagnosis' below).

Initial steps — The initial evaluation for patients with IBD who present with GI symptoms (eg, diarrhea, abdominal pain, and/or constipation) includes performing a history and physical examination, and obtaining initial diagnostic studies (eg, C-reactive protein, fecal calprotectin). The medical history serves to identify potential organic causes for the symptoms. In general, patients whose symptoms are functional in nature do not present acutely and do not have any of the following alarm features: bloody stools, fever, unintentional weight loss, nocturnal bowel movements, fecal incontinence, large volume diarrhea (ie, ≥6 watery stools daily), abdominal distension, or abdominal mass. These features suggest active IBD (or another organic etiology) and require further investigation. (See "Clinical manifestations and diagnosis of irritable bowel syndrome in adults", section on 'Additional evaluation based on the presence of alarm features'.)

Physical examination is usually normal in patients with functional symptoms. However, patients may have mild abdominal tenderness but without abdominal distension. For patients with constipation-predominant symptoms, digital rectal examination may be useful in identifying dyssynergic defecation, particularly if the patient complains of a sense of incomplete evacuation or is requiring digital maneuvers to empty the rectum. (See "Clinical manifestations and diagnosis of irritable bowel syndrome in adults", section on 'History and physical examination' and "Etiology and evaluation of chronic constipation in adults", section on 'Physical examination'.)

Initial diagnostic testing includes the following:

- **Serum markers** – We assess for systemic inflammation by testing for an acute phase reactant such as CRP; erythrocyte sedimentation rate (ESR) is an alternative. Elevated CRP or ESR in the absence of other causes (eg, rheumatoid arthritis, infection) typically represents active intestinal inflammation in patients with IBD. However, normal values do not always confirm inactive disease because not all patients have elevated acute phase reactants despite active inflammation. In addition, the results of CRP and ESR determinations may be discrepant due to factors related to the inflammatory process (eg, differences in specific cytokines), and these issues are discussed separately. (See "Acute phase reactants", section on 'Clinical use'.)

- **Stool markers of inflammation** – We obtain the stool marker fecal calprotectin to assess for intestinal inflammation [5-7]. A fecal calprotectin value within the reference range (generally <50 mcg/g) indicates that the mucosal disease likely remains in remission [8-10]. If the fecal calprotectin value is above the reference range, we evaluate the mucosa for active inflammation with ileocolonoscopy and/or small bowel imaging. (See 'Assessment of IBD activity' below.)

  The diagnostic accuracy of fecal calprotectin for distinguishing functional bowel disease from IBD is discussed separately. (See "Clinical manifestations and diagnosis of irritable bowel syndrome in adults", section on 'Laboratory testing'.)

  Fecal lactoferrin is an alternative stool marker to calprotectin, but lactoferrin is less commonly used [5].

- **Other stool studies** – For patients with chronic diarrhea, we limit stool testing to evaluating for chronic infectious pathogens (eg, *Giardia duodenalis*); however, the approach is individualized depending on the patient's risk factors for infectious diarrhea and whether symptom exacerbation is present. For patients at risk for amebiasis (eg, travel to an endemic area), we obtain serology or antigen testing together with identification of the parasite in the stool. Intestinal amebiasis is discussed separately. (See "Intestinal Entamoeba histolytica amebiasis".)

  The approach to evaluating patients with acute or chronic diarrhea is discussed in more detail separately. (See "Approach to the adult with acute diarrhea in resource-abundant settings" and "Approach to the adult with chronic diarrhea in resource-abundant settings".)

Assessment of IBD activity — For patients with symptoms or diagnostic studies suggestive of active IBD (eg, bloody diarrhea, unintentional weight loss, elevated CRP or fecal calprotectin), we assess the degree intestinal inflammation with the following tests (see 'Initial steps' above):

- **Endoscopy** – We perform ileocolonoscopy with biopsies because endoscopic and histologic evaluation determines the degree and extent of ileocolonic disease activity. Mucosal biopsies may demonstrate active inflammation or may confirm that histologic remission of IBD has been achieved, which supports the concept that symptoms are functional [11]. Flexible sigmoidoscopy may be an alternative to colonoscopy for patients with history of distal colitis.

- **Imaging** – We obtain small bowel imaging for patients with a history of Crohn disease when active small bowel inflammation is suspected (eg, chronic diarrhea, elevated CRP) but when ileocolonoscopy with biopsies does not demonstrate inflammation. Several imaging modalities are available including computed tomography (CT) enterography, magnetic resonance (MR) enterography, capsule endoscopy, or gastrointestinal ultrasound [12]. We prefer MR enterography over CT enterography (although both have high sensitivities) for detecting active small bowel inflammation because MR enterography lacks radiation exposure and provides a detailed characterization of stenotic lesions [13]. In centers where expertise is available, transabdominal ultrasound is also preferred over CT enterography because it is noninvasive, well-accepted by patients, and requires no preparation [12]. (See "Transabdominal ultrasonography of the small and large intestine", section on 'Crohn disease'.)

The endoscopic and imaging evaluation for patients who are suspected of having active IBD is discussed in more detail separately. (See "Clinical manifestations, diagnosis, and prognosis of Crohn disease in adults", section on 'Diagnostic evaluation' and "Clinical manifestations, diagnosis, and prognosis of ulcerative colitis in adults", section on 'Evaluation'.)

Additional studies — If active IBD or an IBD-related complication is not suspected as the cause of symptoms based upon clinical presentation and initial diagnostic evaluation, we may obtain the following tests to exclude other conditions:

- **Serology for celiac disease** – Serology for celiac disease (eg, anti-tissue transglutaminase antibody) is obtained if it was not performed during the patient's initial diagnostic work-up for IBD and if the patient is not following a gluten-restricted diet (see "Diagnosis of celiac disease in adults", section on 'Serologic evaluation').

- **Stool testing for fecal elastase** – Stool testing for fecal elastase is performed in patients with symptoms suggestive of pancreatic exocrine insufficiency (ie, chronic diarrhea that may be accompanied by steatorrhea, abdominal pain, or unintentional weight loss). (See "Exocrine pancreatic insufficiency".)

- **Tests for patients with constipation-predominant symptoms** – For patients with constipation-predominant symptoms, we typically obtain a plain abdominal x-ray or gastrointestinal ultrasound (if expertise in this technique is available) to assess the stool burden, particularly for patients with ulcerative colitis [14]. If symptoms are suggestive of pelvic floor dyssynergia (eg, a sense of incomplete evacuation, need for digital maneuvers), we perform a digital rectal examination and anorectal manometry. (See "Etiology and evaluation of chronic constipation in adults".)

- **Screening for psychologic distress** – Psychologic factors such as anxiety, depression, or coping strategies may influence the expression of both IBD-related and functional symptoms [15]. Assessment of the patient's psychologic status may be facilitated by the use of screening questionnaires, and this is discussed separately [16]. (See "Medical management of low-risk adult patients with mild to moderate ulcerative colitis" and "Screening for depression in adults".)

- **Tests of uncertain value** – Breath testing for specific carbohydrate malabsorption has limited utility in guiding dietary therapy, with the exception of lactose breath testing. Demonstrating normal lactose absorption may help avoid the unnecessary restriction of calcium-rich foods. The diagnosis and management of lactose intolerance are discussed separately. (See "Lactose intolerance and malabsorption: Clinical manifestations, diagnosis, and management".)

  Assessing fructose, sorbitol, or mannitol absorption has little utility in designing dietary approaches because functional symptoms do not correlate well with malabsorption demonstrated on breath testing [17,18].

DIFFERENTIAL DIAGNOSIS

When patients with IBD present with an exacerbation of their symptoms and active disease has been excluded, the differential diagnosis remains broad. Subsequent evaluation often depends on whether the predominant bowel-related symptom is diarrhea or constipation. Other organic disorders that result in diarrhea include the following (see 'Additional studies' above):

- **Celiac disease** – Patients with celiac disease often report nonbloody diarrhea, while signs of malabsorption (eg, iron deficiency anemia) may also be present. (See "Diagnosis of celiac disease in adults" and "Approach to the adult patient with suspected malabsorption".)

- **Infectious diarrhea** – Patients who travel to endemic areas are at higher risk for chronic infectious diarrhea such as giardiasis, whereas patients with recent antibiotic exposure are at risk for *Clostridiodes* [formerly *Clostridium*] *difficile* infection. (See "Giardiasis: Epidemiology, clinical manifestations, and diagnosis" and "*Clostridioides difficile* infection in adults: Clinical manifestations and diagnosis".)

- **Lactose malabsorption** – Some types of carbohydrate malabsorption (eg, lactose) may be more common in patients with IBD. In a study of 91 patients with Crohn disease, 56 patients with ulcerative colitis and 71 healthy controls, the rates of lactose malabsorption detected by breath hydrogen testing were higher in patients with Crohn disease or ulcerative colitis compared with healthy controls (42 or 40 percent, respectively, versus 18 percent) [19]. (See "Lactose intolerance and malabsorption: Clinical manifestations, diagnosis, and management".)

- **Small intestinal bacterial overgrowth** – Patients with Crohn disease who have strictures, fistula, or history of surgical resection may be at increased risk for small intestinal bacterial overgrowth (SIBO). Intestinal hypomotility in the setting of quiescent Crohn disease and a history of prior bowel surgery may be a risk factors for SIBO [20,21]. (See "Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis".)

- **Bile acid diarrhea** – Patients with ileal Crohn disease or ileal resection are at risk for bile acid diarrhea. Ileal disease or resection reduces small bowel absorption of bile acids and results in excessive bile acids in the colon, leading to diarrhea. In addition, diarrhea following cholecystectomy is often due to bile acid diarrhea which is discussed separately. (See "Approach to the adult with chronic diarrhea in resource-abundant settings", section on 'Post-cholecystectomy diarrhea'.)

- **Pancreatic exocrine insufficiency** – Patients with IBD may be at increased risk for pancreatic exocrine insufficiency, and they can present with chronic diarrhea with or without steatorrhea and abdominal pain. In a cross-sectional study including 200 patients with IBD and 100 healthy controls, patients with IBD were more likely to have pancreatic insufficiency based on screening with a fecal elastase test (≤200 mcg/g) compared with healthy controls (odds ratio 10.5, 95% CI 2.5-44.8) [22]. However, fecal elastase values may be falsely low in patients with chronic diarrhea, if this is not corrected for stool water by the laboratory. (See "Chronic pancreatitis: Clinical manifestations and diagnosis in adults".)

Constipation-predominant symptoms may be due to pelvic floor dyssynergia; however, pelvic floor disorders may also lead to fecal urgency and overflow diarrhea [23,24]. The evaluation and management of pelvic floor dyssynergia is discussed separately. (See "Etiology and evaluation

of chronic constipation in adults", section on 'Dyssynergic defecation' and "Management of chronic constipation in adults", section on 'Biofeedback'.)

MANAGEMENT

Goals and sequence of therapies — Because the most effective treatment for functional symptoms in patients with inactive IBD is not well defined and often depends on the specific symptom(s), our treatment approach is based on the following principles (see 'Initial measures' below):

- The goal of therapy is to provide relief of symptom(s).

- Our preference for therapies is based on limited data and clinical experience, and selection among them depends on the specific symptom(s), severity of symptoms, response to prior therapy, risk of adverse effects, and patient preferences.

- Managing functional symptoms in patients with inactive IBD is similar to the management of IBS or functional dyspepsia (if upper GI symptoms are present). However, much of the supporting evidence is indirect and is extrapolated from studies in patients with functional GI disorders but without coexisting IBD.

Initial measures — Establishing a clinician-patient relationship is an important aspect of management of patients with IBD and functional GI symptoms. We initially use dietary and lifestyle modification for patients with symptoms that do not impair quality of life rather than begin specific pharmacologic agents. For patients who fail to respond to initial management and for patients with severe symptoms that affect quality of life, we proceed with symptom-based therapy. (See 'Subsequent symptom-based therapy' below.)

Initial measures include the following:

- **Low FODMAP diet** – For the initial treatment of functional symptoms (eg, diarrhea, abdominal pain, bloating) in patients with IBD in remission, we begin a diet low in slowly absorbed and indigestible short-chain carbohydrates (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols [FODMAPs]) (table 1). These short-chain carbohydrates are osmotically active in the small intestine and are rapidly fermented in the colon, resulting in symptoms of abdominal pain and bloating. Low FODMAP diet is discussed in more detail separately. (See "Treatment of irritable bowel syndrome in adults", section on 'Low FODMAP diet'.)

Implementation of a low FODMAP diet should be performed by a dietitian with training in gastrointestinal disorders who can assess the patient for disordered eating patterns and nutritional risk of a restrictive diet, so that the diet is individualized and food over-restriction is avoided [25,26]. Low FODMAP education consists of initially eliminating FODMAPs from the diet for two to six weeks and then, following symptom resolution, gradual reintroduction of foods high in fermentable carbohydrates to determine individual tolerance to specific fermentable carbohydrates [27].

Data suggested that a low FODMAP diet reduced persistent GI symptoms in patients with quiescent IBD [28-32]. In a meta-analysis of six studies including 319 patients with IBD in remission, a low FODMAP diet resulted in improvement in multiple symptoms: diarrhea (odds ratio [OR] 0.24, 95% CI 0.11-0.52); bloating (OR 0.17, 95% CI 0.06-0.16); and abdominal pain (OR 0.24, 95% CI 0.16-0.35) [29]. In a blinded rechallenge study including 29 patients with quiescent IBD, patients ingesting fructans had lower rates of pain relief compared with those ingesting glucose (62 versus 90 percent), suggesting that FODMAPs were the likely inducer of symptoms [30].

- **Other diet options** – The use of other dietary approaches depends on the patient's predominant symptom, the underlying disease process, and clinician preference. For example, for patients with constipation-predominant symptoms, we advise an increase in dietary fiber if baseline intake is low (eg, less than 14 grams per 1000 calories). (See "Nutrition and dietary management for adults with inflammatory bowel disease", section on 'Fiber' and "Healthy diet in adults", section on 'Fiber'.)

  For patients with symptoms that are related to ingesting moderate amounts of lactose-containing foods (eg, bloating, abdominal pain), we advise lactose restriction (if the patient declines a trial of a low FODMAP diet). Both of these dietary approaches are reasonable, while data to support them are limited. (See "Lactose intolerance and malabsorption: Clinical manifestations, diagnosis, and management".)

  Other restrictive diets, (eg, gluten-restricted diet, specific carbohydrate diet), may help relieve functional symptoms, but these have not been studied in randomized controlled trials in adults with IBD [33].

  In addition, restriction of fat, alcohol, and caffeine is often advised; however the effect of these dietary restrictions on intestinal inflammation is unknown.

  The role of hypersensitivity reactions to food proteins in patients with functional gastrointestinal disorders is unclear, although studies on restricting certain dietary antigens (eg, wheat, dairy) followed by rechallenge in patients with mucosal inflammation

are promising [34]. Methods for evaluating food allergies (eg, serum immunoglobulins, elimination of responsible food, skin prick testing) are discussed separately. (See "Diagnostic evaluation of IgE-mediated food allergy".)

- **Physical activity** – Mild to moderate intensity exercise is safe and improves well-being in patients with IBD, but there is no conclusive data suggesting an anti-inflammatory effect [35]. Hence, exercise may have a positive effect on functional GI symptoms, but this aspect has not been directly studied [36]. (See "Exercise prescription and guidance for adults".)

Subsequent symptom-based therapy — Pharmacologic or behavioral therapies directed at specific symptoms are used for patients who do not have adequate relief of symptoms with initial interventions or for patients with severe symptoms that impair quality of life. (See 'Initial measures' above.)

 Patients with diarrhea — Symptomatic treatment with antidiarrheal medications such as loperamide is an option for patients who have diarrhea in the absence of active mucosal inflammation. We do not use loperamide for patients with active inflammatory disease or for those who are hospitalized. The use of loperamide for patients with Crohn disease or ulcerative colitis is discussed separately. (See "Overview of the medical management of mild (low risk) Crohn disease in adults", section on 'Antidiarrheal medications' and "Medical management of low-risk adult patients with mild to moderate ulcerative colitis", section on 'Other therapies'.)

Antispasmodics (eg, dicyclomine, hyoscyamine) or tricyclic antidepressants (eg, imipramine or amitriptyline) at a low dose (25 mg or less at bedtime) are subsequent options for patients with diarrhea-predominant symptoms that may be accompanied by abdominal pain. The use of antispasmodics and tricyclic antidepressants for patients with functional GI symptoms are discussed in more detail separately. (See "Treatment of irritable bowel syndrome in adults", section on 'Antispasmodic agents' and "Treatment of irritable bowel syndrome in adults", section on 'Antidepressants'.)

For patients with Crohn disease in remission who have chronic diarrhea, bile acid diarrhea should be suspected. Consensus clinical practice guidelines suggest performing testing to confirm bile acid malabsorption [37]. (See "Approach to the adult with chronic diarrhea in resource-abundant settings", section on 'Post-cholecystectomy diarrhea'.).

The principles of using bile acid-sequestering agents are that there is no optimal dose but that these agents should be initiated at low doses. The dose may be increased at weekly intervals if symptoms do not improve or reduced if constipation develops. For cholestyramine, the initial dose is 4 g daily (which represents one sachet of powder daily). If symptoms persist, the dose is titrated to a maximum of 12 g daily, taken in three divided doses [38,39]. If cholestyramine is

poorly tolerated because of side effects (eg, constipation, nausea), an alternative bile acid-sequestering agent, such as coleserelam, can be used. Colesevelam is usually available in capsule form with each capsule containing 625 mg. Initial therapy is three capsules, taken once or twice a day (3.75 g) [38-40]. Published evidence that informs the maximum colesevelam dose is limited but suggests a maximum dose of six capsules daily.

For patients with Crohn disease and extensive ileal involvement or resection resulting in short bowel syndrome, use of bile acid sequestering agents should be avoided. (See "Management of short bowel syndrome in adults", section on 'Other interventions with unclear role'.)

Patients with abdominal pain — Chronic abdominal pain in the absence of active mucosal inflammation or an IBD-related complication can present a management challenge. There are few studies that can guide choosing a specific medication for abdominal pain in this setting, and our approach is similar to the management of patients with irritable bowel syndrome. We use antispasmodic medications (eg, dicyclomine, hyoscyamine) as needed for patients with abdominal pain but without constipation, and for patients with abdominal pain and constipation if the pain persists after successful treatment of constipation [41]. (See 'Patients with constipation' below.)

The use and adverse effects of antispasmodics for patients with functional bowel disorders is discussed separately. (See "Treatment of irritable bowel syndrome in adults", section on 'Antispasmodic agents'.)

For patients who cannot tolerate or do not improve with an antispasmodic agent, a low-dose tricyclic antidepressant (eg, amitriptyline) or a selective serotonin reuptake inhibitor may result in symptomatic improvement, similar to therapy in patients with IBS. (See "Treatment of irritable bowel syndrome in adults", section on 'Antidepressants' and "Tricyclic and tetracyclic drugs: Pharmacology, administration, and side effects".)

Drug therapy directed toward neuropathic pain, such as gabapentin, is an alternative to antidepressants for chronic abdominal pain, but there are few published data to guide with this. (See "Pharmacologic management of chronic non-cancer pain in adults", section on 'Antiseizure medications'.)

Patients with constipation — Our approach for patients with IBD and constipation-predominant functional symptoms includes adequate intake of fluids and fiber along with at least three mealtimes per day. If dietary intervention is not helpful, polyethylene glycol (PEG) solution is a subsequent option.

Low dietary fiber intake can be addressed by dietary counseling or by initiating a fiber supplement. Psyllium, a slowly fermentable fiber, is a good choice. However, if such a fiber supplement is not well tolerated, a non-fermentable fiber such as sterculia or methylcellulose can be tried, but published data to support this approach is lacking. Wheat bran should be avoided due to its fructan content [42]. Because some patients may experience increased bloating and gas with increasing fiber intake, we initiate fiber supplements at a low dose (eg, one teaspoon daily), and then increase the dose every three days (if tolerated) to a target dose of two heaped teaspoons twice daily. Fiber supplementation for functional disorders is discussed separately. (See "Treatment of irritable bowel syndrome in adults", section on 'Fiber' and "Nutrition and dietary management for adults with inflammatory bowel disease", section on 'Fiber'.)

The goal for daily fluid intake varies depending on a number of factors including the patient's activity level and stool output, and this is discussed separately. (See "Maintenance and replacement fluid therapy in adults", section on 'Water balance'.)

For patients with constipation-predominant symptoms that do not improve with dietary intervention, we begin PEG because it is inexpensive, widely available, and has fewer side effects compared with other osmotic laxatives (eg, magnesium hydroxide). The use of osmotic and other laxatives for patients with functional disorders are discussed separately. (See "Treatment of irritable bowel syndrome in adults", section on 'Osmotic laxatives'.)

Patients with mood disorders — Patients with quiescent IBD and persistent gastrointestinal symptoms that are associated with mood disorders (eg, depression, anxiety) may benefit from behavioral modification in conjunction with antidepressants, similar to the approach to patients with IBS, which is discussed separately. (See "Treatment of irritable bowel syndrome in adults", section on 'Behavior modification'.)

For patients with functional bowel disease, data show that psychotherapeutic techniques (eg, cognitive behavior therapy, gut-directed hypnotherapy, mindfulness therapy) have a positive impact on gastrointestinal symptoms and quality of life, based on superiority over either standard treatment or wait-listing [43], or based on noninferiority compared with a low FODMAP diet [44,45]. However, similar studies in patients with IBD have mostly addressed effects on coping skills, anxiety, and depression, rather than on symptoms or inflammatory activity [46]. Psychological stress can affect the degree of intestinal inflammation, and this also supports the use of psychological strategies for treating persistent symptoms in patients with quiescent IBD [47].

Therapies of uncertain benefit — The therapeutic benefit of the following interventions is uncertain in patients with inactive IBD and functional GI symptoms:

- **Complementary and alternative medicine** – Complementary and alternative medicine (CAM) remedies (eg, herbal preparations, cannabis) may help relieve IBD-related symptoms such as abdominal pain [35]. In a study including 38 patients with Crohn disease in remission, osteopathic treatment was associated with greater improvement in IBS-related symptoms and in fatigue compared with no osteopathic therapy [48]. However, most CAM studies have not specifically addressed functional GI symptoms in patients with IBD. More data are needed before CAM remedies are routinely used in this setting. (See "Overview of herbal medicine and dietary supplements".)

- **Therapies that modify intestinal microbiota** – Therapies that modify the intestinal microbiota (eg, antibiotics, probiotics, prebiotics, fecal microbiota transplantation) have mainly been studied in patients with either IBS or active IBD. Probiotics have been assessed for their effect on inflammation in patients with IBD, while they have been more widely studied for functional symptoms. The degree of benefit from probiotics and the most effective species are unclear, and the use of probiotics is discussed separately. (See "Probiotics for gastrointestinal diseases".)

  Antibiotics, such as rifaximin, may improve gastrointestinal symptoms in patients with IBD and functional symptoms, presumably by treating underlying small intestinal bacterial overgrowth [21]. However, no data are available to guide antibiotic therapy in this setting. (See "Small intestinal bacterial overgrowth: Management".)

  Treatment with prebiotics or fecal microbiota transplantation has been directed toward mucosal inflammation in patients with IBD, but their effect on functional GI symptoms in this setting is generally unknown. However, in a trial including 103 patients with Crohn disease, patients given supplemental fructo-oligosaccharides had more severe functional symptoms (eg, abdominal pain, flatulence) compared with patients taking placebo [49]. (See "Treatment of irritable bowel syndrome in adults", section on 'Other therapies'.)

Therapies to avoid — Opioids should be avoided for patients with IBD and functional GI symptoms because of the potential adverse effects and risks (opioid-induced constipation, narcotic bowel syndrome, opioid-induced hyperalgesia, and opioid dependence) [50]. (See "Use of opioids in the management of chronic non-cancer pain".)

Patients with chronic abdominal pain that is not improving with dietary and symptom-based therapy may benefit from consultation with a pain management specialist.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Irritable bowel syndrome" and "Society guideline links: Ulcerative colitis in adults" and "Society guideline links: Crohn disease in adults".)

SUMMARY AND RECOMMENDATIONS

- **Background** – For some patients with inflammatory bowel disease (IBD), symptoms such as diarrhea and abdominal pain may persist despite healing of intestinal inflammation. Recognizing functional symptoms in patients with inactive IBD helps to avoid the risk of adverse effects associated with escalating IBD-focused therapies. (See 'Introduction' above.)

- **Evaluation** – Identifying functional gastrointestinal (GI) symptoms in patients with IBD requires the following steps (see 'Goals' above):

  - Suspect that symptoms may be functional based on the patient's clinical presentation, pertinent negative findings (eg, absence of bloody stools or fever), and prior history of IBD in remission (minimally or no active mucosal inflammation).

  - Assess for active intestinal inflammation (ie, IBD flare) or an IBD-related complication as the etiology of symptoms.

  - Evaluate for other organic diseases if clinical presentation suggests an alternative diagnosis (eg, infectious colitis).

  For patients with IBD and suspected functional GI symptoms, the initial assessment includes history, physical examination, and diagnostic testing to evaluate for an IBD flare or other organic disease. We obtain C-reactive protein (CRP) and fecal calprotectin. (See 'Initial steps' above.)

  For patients with IBD and symptoms and/or diagnostic studies suggestive of active disease (eg, bloody diarrhea, elevated CRP, or fecal calprotectin), we assess for active mucosal inflammation with ileocolonoscopy with biopsies. For patients with a history of Crohn disease and minimal or no inflammation on ileocolonoscopy with biopsies, we obtain small bowel imaging (eg, magnetic resonance enterography or transabdominal ultrasound, if expertise is available). (See 'Assessment of IBD activity' above.)

- **Differential diagnosis** – For patients with persistent gastrointestinal symptoms despite inactive IBD, the differential diagnosis remains broad. For example, other possible causes of nonacute diarrhea include celiac disease, lactose malabsorption, or small intestinal bacterial overgrowth. (See 'Differential diagnosis' above.)

- **Management** – For patients with IBD in remission and functional GI symptoms that do not impair quality of life, we suggest a diet that is low in slowly absorbed and indigestible short-chain carbohydrates (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols [FODMAPs]) (**Grade 2B**). Low FODMAP dietary education is provided by a trained dietician to avoid unnecessary dietary restriction and to maintain a nutritionally replete diet. (See 'Initial measures' above and "Treatment of irritable bowel syndrome in adults", section on 'Low FODMAP diet'.)

  Pharmacologic or behavioral therapies directed at specific functional GI symptoms are used for patients who do not have adequate relief of symptoms with initial measures or for patients with severe symptoms that impair quality of life. (See 'Subsequent symptom-based therapy' above and "Treatment of irritable bowel syndrome in adults", section on 'Adjunctive pharmacologic therapy'.)

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GRAPHICS

Characteristics and sources of common FODMAPs

	Word that corresponds to letter in acronym	Compounds in this category	Foods that contain these compounds
F	**F**ermentable		
O	**O**ligosaccharides	Fructans, galacto-oligosaccharides	Wheat, barley, rye, onion, leek, white part of spring onion, garlic, shallots, artichokes, beetroot, fennel, peas, chicory, pistachio, cashews, legumes, lentils, and chickpeas
D	**D**isaccharides	Lactose	Milk, custard, ice cream, and yogurt
M	**M**onosaccharides	"Free fructose" (fructose in excess of glucose)	Apples, pears, mangoes, cherries, watermelon, asparagus, sugar snap peas, honey, high-fructose corn syrup
A	**A**nd		
P	**P**olyols	Sorbitol, mannitol, maltitol, and xylitol	Apples, pears, apricots, cherries, nectarines, peaches, plums, watermelon, mushrooms, cauliflower, artificially sweetened chewing gum and confectionery

FODMAPs: fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.

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