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Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis

AUTHOR: Nicholas J Talley, MD, PhD
SECTION EDITOR: J Thomas Lamont, MD
DEPUTY EDITOR: Shilpa Grover, MD, MPH, AGAF

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Literature review current through: **Sep 2023.**
This topic last updated: **Feb 28, 2022.**

INTRODUCTION

Small intestinal bacterial overgrowth (SIBO) is a condition in which the small bowel is colonized by excessive aerobic and anaerobic microbes.

This topic will review the etiology, pathogenesis, clinical manifestations, and diagnosis of SIBO. The management of SIBO is discussed in detail, separately. (See "Small intestinal bacterial overgrowth: Etiology and pathogenesis" and "Small intestinal bacterial overgrowth: Management".)

EPIDEMIOLOGY

The population-based prevalence of SIBO is unclear. The incidence of SIBO increases with age.

ETIOLOGY AND RISK FACTORS

Several disorders predispose to SIBO by altering mucosal defenses (table 1). Intestinal motility disorders and chronic pancreatitis are estimated to account for approximately 90 percent of cases of SIBO [1-3]. Patients may have more than one predisposing cause. As an

example, the high prevalence of SIBO in older adults may be due to small intestinal dysmotility and gastric hypochlorhydria.

- **Motility disorders** – The migrating motor complex (MMC) and in particular, phase III of the MMC clears the small bowel of debris [4]. A lack of interdigestive phase III activity in patients with irritable bowel syndrome, narcotic use, intestinal pseudo-obstruction, and diabetes predisposes them to SIBO. Small bowel motility is also affected in acute or chronic radiation enteritis, amyloidosis, and scleroderma [5-9]. (See "Pathophysiology of irritable bowel syndrome", section on 'Bacterial overgrowth' and "Gastrointestinal manifestations of systemic sclerosis (scleroderma)", section on 'Small intestinal involvement'.)

- **Anatomic disorders** – Adhesions or strictures, small intestinal diverticulosis, blind intestinal loops, and reversed segment can predispose to SIBO due to intestinal stasis [10].

- **Immune disorders** – Immunoglobulins in intestinal secretions are important in maintaining the microbial homeostasis [11]. Patients with common variable immunodeficiency, IgA deficiency, and acquired immunodeficiency (eg, HIV) are therefore at increased risk of SIBO. (See "Gastrointestinal manifestations in primary immunodeficiency".)

- **Gastric hypochlorhydria** – Hypochlorhydria either from long term use of a proton pump inhibitor or autoimmune etiology (chronic atrophic gastritis), is an important co-factor in the development of SIBO when present with other predisposing factors.

- **Metabolic and systemic disorders** – Disorders such as pancreatic insufficiency and cirrhosis can predispose to SIBO by changing the quantity and composition of digestive enzymes or bile. (See "Diabetic autonomic neuropathy of the gastrointestinal tract", section on 'Diabetic diarrhea'.)

PATHOGENESIS

SIBO is usually associated with abnormally high counts of multiple organisms in the small intestine. Data suggests that in traditional SIBO, the most common organisms are *Escherichia coli* and *Klebsiella* [7]. Inflammation is caused by invasive strains of bacteria [11]. Facultative anaerobes can injure the intestinal surface by direct adherence and production of enterotoxins. Aerobic bacteria produce enzymes and metabolic products that can induce epithelial cell injury [12].

- **Intestinal effects** – In its extreme form (usually associated with conditions such as blind loop syndrome) SIBO can cause maldigestion in the intestinal lumen or malabsorption at the level of the intestinal microvillus membrane due to enterocyte damage (eg, tropical sprue). Bacterial overgrowth can also alter small bowel motility [13].

  - **Carbohydrate malabsorption** – Intraluminal degradation of carbohydrates leads to the production of short-chain fatty acids (butyrate, propionate, acetate, lactate) as well as carbon dioxide, hydrogen, hydrogen sulfide, and methane. Enterocyte damage due to bile acids and bacteria results in diarrhea due to reduction in enterocyte disaccharidase activity and transport of monosaccharides [14]. Fermentation of unabsorbed carbohydrates results in bloating, distension, and flatulence.

  - **Fat malabsorption** – Fat malabsorption can lead to steatorrhea, weight loss, and deficiencies of fat-soluble vitamins (eg, vitamin A and D). SIBO results in deconjugation of primary bile acids which can further worsen steatorrhea [15,16]. At physiologic pH, bile acids are fully ionized, preventing their absorption in the proximal small intestine and permitting sufficient concentrations for solubilization of dietary fat. However, deconjugated bile salts are reabsorbed by the jejunum, which may lead to fat malabsorption due to depletion of the normal bile acid pool. Bacterial deconjugation also leads to the production of lithocholic acid, which may be toxic to intestinal epithelium, resulting in impaired absorption of fat and other nutrients. Hydroxylated fatty acids (and free bile acids) also stimulate the secretion of water and electrolytes, leading to diarrhea. (See 'Clinical features' below.)

  - **Protein malabsorption** – Protein malabsorption results from damage to the epithelial barrier, resulting in increased intestinal permeability, decreased mucosal uptake of amino acids, and the intraluminal degradation of protein precursors by bacteria [17]. SIBO can also result in a reversible form of protein-losing enteropathy [18]. (See "Protein-losing gastroenteropathy".)

  - **Vitamin deficiency and excess** – Vitamin B12 deficiency in SIBO result from several different mechanisms. Although enteric bacteria synthesize cobalamin, they also successfully compete with the host for its absorption. In patients with severe SIBO, malabsorption of vitamin B12 results from mucosal damage to the ileal binding site. Only anaerobes can utilize vitamin B12 coupled to intrinsic factor. Thiamine and nicotinamide deficiency also result from bacterial utilization.

    In contrast, folate and vitamin K levels are elevated in SIBO due to bacterial synthesis. Increased intestinal permeability also contributes to increased vitamin K levels.

- **Systemic effects** – Production of toxins and increased intestinal permeability in SIBO have been associated with systemic complications. D-lactic acidosis is a rare neurologic syndrome in patients with SIBO associated with short bowel syndrome or a prior jejunoileal bypass. It is characterized by altered mental status ranging from confusion to coma, slurred speech, seizures, and ataxia resulting from bacterial fermentation of unabsorbed carbohydrates [19]. (See "D-lactic acidosis", section on 'Pathogenesis' and 'Clinical features' below.)

  Bacterial overgrowth has also been implicated in the pathogenesis of hepatic encephalopathy, nonalcoholic fatty liver disease, and irritable bowel syndrome. (See "Pathogenesis of nonalcoholic fatty liver disease", section on 'Intestinal microbes' and "Hepatic encephalopathy: Pathogenesis", section on 'Bacterial overgrowth'.)

CLINICAL FEATURES

Clinical presentation — The majority of patients with SIBO present with bloating [20]. Other common symptoms include flatulence, abdominal discomfort, or chronic watery diarrhea. It is important to remember that traditional SIBO was associated with post-surgical anatomy such as blind loop syndrome. However, it is increasingly recognized that SIBO is a potential cause of irritable bowel syndrome (IBS) and, in this case, malabsorption is less common [21].

Steatorrhea with greasy or bulky stools is rare and usually occurs in patients with SIBO and altered anatomy (eg, blind loop syndrome) [22]. Children can present with failure to gain weight [23,24]. In severe cases, patients have weight loss due to diarrhea or poor oral intake.

Patients with severe SIBO in the setting of a jejunoileal bypass surgery or short bowel syndrome (SBS) may have symptoms due to associated vitamin deficiency. Patients with vitamin B12 deficiency can present with weakness, sensory ataxia, and paresthesias. Patients with tetany due to hypocalcemia can present with perioral numbness, paresthesias of the hands and feet, and muscle cramps. Children may also have metabolic bone disease due to vitamin D deficiency. In rare cases, patients with SIBO and SBS present with altered mental status due to D-lactic acidosis after a high carbohydrate meal. Symptoms can range from confusion to coma, slurred speech, seizures, and ataxia [19]. (See "Chronic complications of the short bowel syndrome in adults", section on 'Electrolyte and micronutrient deficiencies' and "D-lactic acidosis".)

Physical examination is usually normal in patients with SIBO. However, in some cases, the abdomen may be distended with an identifiable succussion splash due to fluid-filled loops of

bowel, which may be palpable [25]. Patients with hypoalbuminemia due to malabsorption can have peripheral edema, however, this is rare. (See "Pathophysiology of short bowel syndrome", section on 'The microbiome of SBS and pathophysiology of bacterial overgrowth' and "D-lactic acidosis".)

Laboratory findings — Laboratory abnormalities are usually associated with severe bacterial overgrowth or when SIBO occurs in association with an underlying anatomic abnormality [20]. Laboratory findings including macrocytic anemia, B12 deficiency, and the presence of fecal fat. Patients may also have low levels of thiamine and niacin and elevated serum folate and vitamin K levels [26]. In rare cases, microcytic anemia results from bleeding due to ulcers in stagnant intestinal loops or associated with ileitis or colitis [27]. Patients with protein losing enteropathy due to SIBO have hypoalbuminemia. (See 'Pathogenesis' above and "Protein-losing gastroenteropathy", section on 'Clinical features'.)

Endoscopy findings — The endoscopic appearance and histopathology of the small intestine and colon is normal in most patients with SIBO. Endoscopic findings of colitis and ileitis associated with severe SIBO include mucosal edema, loss of normal vascular pattern, patchy erythema, friability, and in rare cases, ulceration [25,28]. Non-specific histopathological findings in patients with SIBO include villous blunting, cryptitis, intraepithelial lymphocytosis, and eosinophilia [29].

DIAGNOSIS

Approach to evaluation — The diagnosis of SIBO should be suspected in patients with bloating, flatulence, abdominal discomfort, or chronic diarrhea. The diagnosis is established with a positive carbohydrate breath test or a bacterial concentration of $>10^3$ colony forming units/mL in a jejunal aspirate culture. We perform a carbohydrate breath test to diagnose SIBO and measure hydrogen, methane, and even hydrogen sulfide as it is simple and non-invasive [30]. Due to the limitations of culture (due to contamination and invasive nature of culture), breath testing is the most practical alternative [31].

No additional evaluation is needed to diagnose SIBO. However, we obtain additional tests to diagnose laboratory abnormalities associated with SIBO and to rule out other causes of similar symptoms (eg, celiac disease), which may co-exist with SIBO on a case-by-case basis. In patients with severe diarrhea or iron deficiency anemia, we perform endoscopic evaluation with colonoscopy and, if indicated, an upper endoscopy with small bowel biopsy. The evaluation of patients with chronic diarrhea is discussed in detail, separately. (See "Approach to the adult with chronic diarrhea in resource-abundant settings", section on 'Initial evaluation'.)

Carbohydrate breath test — Breath tests are based on the principle that metabolism of a test dose of carbohydrate substrate (eg, lactulose, glucose) by the bacterial flora leads to the production of an analyte (hydrogen, methane, and hydrogen sulfide), which is absorbed and ultimately excreted in the breath [20].

Lactulose is a nonabsorbable substance that is normally metabolized by gut bacteria in the colon with the production of hydrogen, hydrogen sulfide, and/or methane. In individuals without SIBO, the administration of lactulose results in a single peak in breath hydrogen within two to three hours due to the metabolism of lactulose by colonic flora. In patients with SIBO, administration of lactulose results in an early peak in breath hydrogen levels due to metabolism by small bowel bacteria. Methane and hydrogen sulfide are usually determined by their simply meeting a threshold of detection at any timepoint during testing (10 ppm for methane and 3 ppm for hydrogen sulfide).

Glucose is rapidly absorbed from the proximal small bowel. When used as a substrate in the presence of SIBO, it is metabolized to hydrogen in the small bowel lumen prior to absorption.

- **Patient preparation and test protocol** – There is considerable variability in test methodology and interpretation of carbohydrate breath tests. Our recommendations are consistent with a 2017 North American consensus statement on hydrogen and methane-based breath testing in gastrointestinal disorders [30].
    - Antibiotics should be avoided four weeks prior to testing.
    - Prokinetic drugs and laxatives should be held for one week prior to testing. Faster intestinal transit can lead to earlier delivery of the substrate to the colon and lead to false positive test results.
    - Complex carbohydrates (eg, bread, pasta, fiber) and dairy should be avoided for 12 hours prior to testing. Fermentable foods can cause prolonged hydrogen secretion and elevate basal hydrogen levels.
    - Patients should fast for 8 to 12 hours prior to the breath test.
    - Strenuous exercise and cigarette smoking should be avoided on the day of the breath test. Smoking increases breath hydrogen levels and increases gastric transit time. Hyperventilation associated with strenuous exercise decreases breath hydrogen levels.
    - We sample breath hydrogen, carbon dioxide, and methane at baseline and every 15 minutes following administration of test substrate (glucose 75 grams or lactulose 10

grams) with or followed by one cup of water. Breath testing should be continued for 120 minutes.

- **Test interpretation**
  - An absolute increase in hydrogen by ≥20 ppm above baseline within 90 minutes on the lactulose/glucose breath test is diagnostic of SIBO [20,30].
  - A methane level ≥10 ppm at any point during the test is diagnostic of intestinal methanogen overgrowth (IMO) [20]. While this was previously considered to be diagnostic of SIBO, the term IMO has been introduced to more accurately describe this condition as methanogens are not bacteria and may also overgrow in the colon and not just the small intestine. *Methanobrevibacter smithii* appears to be the key methanogen responsible for breath methane production. For hydrogen sulfide, the recommended cutoff is ≥3 ppm at any point during the test.
  - Other patterns of elevation may be in seen in subgroups of patients.
    - High baseline hydrogen ≥20 ppm may be due to lack of adherence to the test protocol for dietary restriction or fasting, or may represent of a variant of SIBO.
    - Low fixed hydrogen and no methane production may be due to hydrogen sulfide producing bacteria. However, further studies are needed to clarify the significance.
    - Constipation is associated with elevated levels of breath methane.
- **Test performance** – Rapid delivery of the test substrate to the colon (eg, in patients with short bowel syndrome) may lead to false-positive results [32]. False-negative results may occur in 30 to 40 percent of patients due to low anaerobic organism counts [33]. In a systematic review that included 11 studies and patients with evidence of SIBO on jejunal aspirate cultures, the glucose breath test had a sensitivity of 20 to 93 percent and specificity of 45 to 86 percent [34]. The lactulose breath test had a sensitivity of 17 to 68 percent and specificity of 44 to 86 percent [32,35-37]. However, these studies had several limitations including heterogeneity in patient populations, small sample sizes, and variable cutoffs to define a positive test [34-40]. Elevation in methane on the breath test may be due to associated constipation. Although some studies have suggested that the lactulose breath test has a slightly higher sensitivity for diagnosing SIBO as compared with the glucose breath test, others have failed to demonstrate significant differences in test performance [34-37,41]. (See "Pathophysiology of short bowel syndrome", section on 'Small intestine length'.)

Jejunal aspirate culture — A bacterial concentration of >10^3 colony forming units/mL of jejunal aspirate is diagnostic of SIBO [6,20,34]. Patients may have multiple organisms in varying concentrations. The most common species include *Bacteroides*, *Enterococcus*, and *Lactobacillus* [42].

Jejunal aspirate is obtained during upper gastrointestinal endoscopy by placing a sterile catheter through a sterile overtube in the suction port of an endoscope or by fluoroscopy. Aspirates should be transferred to an anaerobic transport vial immediately, and contents should be cultured for the growth of aerobic and anaerobic organisms [43].

Although jejunal aspirate cultures, have been considered the reference standard for the diagnosis of SIBO, the process of obtaining jejunal aspirate is invasive and the results are poorly reproducible [44]. Culture of anaerobic organisms requires careful microbiologic technique, despite which only approximately 40 percent of the total gut flora can be identified using conventional culture methods [22]. Bacterial overgrowth may be patchy, confined to the distal small intestine (eg, early SIBO), or located in relatively inaccessible sites (eg, blind loop) leading to false negative results [45]. False positive cultures can result from contamination with oropharyngeal flora during specimen collection.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of diarrhea due to SIBO includes other causes of chronic diarrhea. This is discussed in detail, separately. (See "Approach to the adult with chronic diarrhea in resource-abundant settings", section on 'Initial evaluation'.)

- **Celiac disease** – Patients with celiac disease and SIBO may have similar symptoms, elevation in fecal fat, and villous blunting on small bowel biopsy. However, patients with celiac disease have a negative breath test for SIBO and positive celiac serologies. (See "Diagnosis of celiac disease in adults", section on 'Serologic evaluation'.)

- **Crohn disease** – Patchy ileitis or colitis in patients with severe SIBO can mimic Crohn disease. Characteristic features of Crohn disease including the presence of perianal disease (fissures, fistulas), chronic transmural inflammation and granulomas on biopsy are absent in SIBO. (See "Clinical manifestations, diagnosis, and prognosis of ulcerative colitis in adults", section on 'Differential diagnosis'.)

- **Irritable bowel syndrome** – Patients with SIBO and irritable bowel syndrome (IBS) may both have diarrhea and constipation [30,46]. IBS is a functional syndrome that is predominantly characterized by recurrent chronic abdominal pain. The abdominal pain in

IBS, unlike SIBO, is related to defecation and is associated with a change in frequency or form (appearance) of stool. However, it appears that a proportion of IBS subjects have SIBO [30,47]. (See "Pathophysiology of irritable bowel syndrome", section on 'Bacterial overgrowth'.)

EVALUATION TO DETERMINE THE ETIOLOGY

Most patients with established SIBO have a known underlying condition (table 1). In patients without risk factors for SIBO, we perform an upper endoscopy and colonoscopy to rule out predisposing conditions (eg, atrophic gastritis and Crohn disease). If endoscopic evaluation is unrevealing, we perform imaging of the small bowel to evaluate for partial obstruction, dilation, inflammation, diverticula, or a fistula. We perform a MR enterography as it has the advantage of avoiding radiation exposure and has a high sensitivity for detecting small bowel strictures but is expensive. (See "Clinical manifestations, diagnosis, and prognosis of Crohn disease in adults", section on 'Imaging'.)

SIBO, again in extreme cases, may also be associated with a small intestinal motility disorder, cirrhosis, end-stage kidney disease, chronic pancreatitis, and immunodeficiency states. Additional testing for these conditions should be performed in patients with a history or physical examination findings suggestive of these disorders [4]. (See "Chronic intestinal pseudo-obstruction: Etiology, clinical manifestations, and diagnosis" and "Cirrhosis in adults: Etiologies, clinical manifestations, and diagnosis", section on 'Clinical manifestations' and "Clinical manifestations, epidemiology, and diagnosis of common variable immunodeficiency in adults".)

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: Small intestinal bacterial overgrowth".)

SUMMARY AND RECOMMENDATIONS

- SIBO is a condition in which the small bowel is colonized by excessive aerobic and anaerobic microbes that are normally present in the colon. The incidence of SIBO increases with age. Several disorders predispose to SIBO by altering mucosal defenses (table 1). In many cases, patients have more than one predisposing cause. (See 'Epidemiology' above.)

- SIBO can cause maldigestion in the intestinal lumen or malabsorption at the level of the intestinal microvillus membrane due to enterocyte damage. Bacterial overgrowth can also alter small bowel motility. (See 'Pathogenesis' above.)

- The majority of patients with SIBO present with bloating, flatulence, abdominal discomfort, or watery diarrhea. Steatorrhea with greasy or bulky stools is rare and usually occurs in patients with altered anatomy (eg, blind loop syndrome). Children can present with failure to gain weight. In severe cases, patients have weight loss due to diarrhea or poor oral intake. (See 'Clinical features' above.)

- Laboratory abnormalities are usually seen in patients with SIBO that is severe or that occurs in association with an anatomic abnormality. Laboratory findings including macrocytic anemia, B12 deficiency, and the presence of fecal fat. Patients may also have low levels of thiamine and niacin, and elevated serum folate and vitamin K levels. In rare cases, patients have microcytic anemia or hypoalbuminemia. (See 'Laboratory findings' above.)

- The endoscopic appearance and histopathology of the small intestine and colon is normal in most patients with SIBO. Endoscopic findings of colitis and ileitis associated with severe SIBO are nonspecific and include mucosal edema, loss of normal vascular pattern, patchy erythema, friability and ulceration. Histopathological findings associated with SIBO include villous blunting, cryptitis, intraepithelial lymphocytosis, and eosinophilia. (See 'Endoscopy findings' above.)

- The diagnosis of SIBO should be suspected in patients with bloating, flatulence, abdominal discomfort, or diarrhea, and is established with a positive carbohydrate breath test or jejunal aspirate culture. We perform a carbohydrate breath test to diagnose SIBO as it is simple, non-invasive, and widely available. (See 'Diagnosis' above.)

- A bacterial concentration of $>10^3$ colony forming units/mL of jejunal aspirate is diagnostic of SIBO. However, the test requires an upper endoscopy to obtain an aspirate and the results are poorly reproducible. (See 'Jejunal aspirate culture' above.)

- Carbohydrate breath tests are easy to perform, noninvasive, and inexpensive. The lactulose/glucose breath test is diagnostic of SIBO if any one of the following:

  - An absolute increase in hydrogen by ≥20 ppm above baseline within 90 minutes.

  - A methane level ≥10 ppm, regardless of the time during the breath test, can identify intestinal methanogen overgrowth (associated with a constipation phenotype).

- Some patients with established SIBO have a known underlying condition (table 1). However, additional tests should be performed if the underlying etiology is unknown and the patient is refractory to treatment. An upper endoscopy and colonoscopy should also be performed to rule out predisposing conditions (eg, atrophic gastritis and Crohn disease). In patients without a clear underlying predisposing cause, imaging of the small intestine (eg, small bowel follow-through, computed tomography/magnetic resonance enterography) should be performed to rule out an underlying anatomic cause of SIBO. (See 'Evaluation to determine the etiology' above.)

ACKNOWLEDGMENT

The editorial staff at UpToDate would like to acknowledge Jon Vanderhoof, MD, Rosemary Pauley-Hunter, NP-C, and Mark Pimentel, MD, FRCP(C), who contributed to earlier versions of this topic review.

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GRAPHICS

Disorders associated with bacterial overgrowth

Small intestinal stasis
Anatomic abnormalities
Small intestinal diverticulosis
Surgically created blind loops (end-to-side anastomosis)
Strictures (Crohn disease, radiation, surgery)
Abnormal small intestinal motility
Diabetes mellitus
Scleroderma
Idiopathic intestinal pseudo-obstruction
Radiation enteritis
Crohn disease
Abnormal communication between the proximal and distal gastrointestinal tract
Gastrocolic or jejunocolic fistula
Resection of the ileocecal valve
Associations usually with multifactorial causes
Hypochlorhydria due to atrophic gastritis or medications. These are usually not clinically significant unless they coexist with concomitant motility disturbances of the small bowel.
Immunodeficiency states (common variable immunodeficiency, AIDS, severe malnutrition)
Chronic pancreatitis
Cirrhosis
Alcoholism
End-stage kidney disease
Advanced age
Total parenteral nutrition (TPN) in children

Graphic 81285 Version 6.0

Contributor Disclosures

Nicholas J Talley, MD, PhD Patent Holder: Australian Provisional Patent [Diagnostic marker for functional gastrointestinal disorders]; Biomarkers of irritable bowel syndrome [Irritable bowel syndrome]; Mayo Clinic [Dysphagia questionnaire]; Mayo Clinic [Bowel Disease questionnaire]; Nepean Dyspepsia Index [Dyspepsia]; Nestec [Irritable bowel syndrome]; Singapore Provisional Patent [BDNF Tissue Repair Pathway]. Grant/Research/Clinical Trial Support: Alimetry [Gastric mapping device research collaboration]; Allakos [Gastric eosinophilic disease]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; Intrinsic Medicine [Bowel syndrome with constipation]; NHMRC Centre for Research Excellence in Digestive Health [NHMRC Investigator grant]. Consultant/Advisory Boards: Adelphi Values [Functional dyspepsia]; Allakos [Gastric eosinophilic disease, AK002]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; AusEE [Eosinophilic gut diseases]; Bayer [Inflammatory bowel syndrome]; BluMaiden [Microbiome Ad Board]; Comvita Mānuka Honey [Digestive health]; Dr Falk Pharma [Eosinophilia]; GlaxoSmithKline Australia [Educational speaker eosinophilic gut disease]; Glutagen [Celiac disease]; International Foundation for Functional Gastrointestinal Disorders [Advisory board, functional GI disorders]; Intrinsic Medicine [Human milk oligosaccharide]; IsoThrive [Esophageal microbiome]; Planet Innovation [Gas capsule, inflammatory bowel syndrome]; Progenity Inc [Intestinal capsule]; Rose Pharma [IBS]; Viscera Labs [Inflammatory bowel syndrome, diarrhea]. Other Financial Interest: Elsevier textbook royalties [Medical education]. All of the relevant financial relationships listed have been mitigated. **J Thomas Lamont, MD** Equity Ownership/Stock Options: Allurion [Weight loss]. Consultant/Advisory Boards: Teledoc [Gastrointestinal diseases]. All of the relevant financial relationships listed have been mitigated. **Shilpa Grover, MD, MPH, AGAF** No relevant financial relationship(s) with ineligible companies to disclose.

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Conflict of interest policy

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