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Low-FODMAP Diet for Irritable Bowel Syndrome: What We Know and What We Have Yet to Learn

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Abstract

Irritable bowel syndrome (IBS) is the most prevalent of gastrointestinal (GI) conditions, affecting millions of people worldwide. Given that most IBS patients associate their GI symptoms with eating food, specific dietary manipulation has become an attractive treatment strategy. A diet low in FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) has generated the greatest level of scientific and clinical interest. Overall, 52–86% of patients report significant improvement of their IBS symptoms with elimination of dietary FODMAPs. Patients who experience symptom improvement with FODMAP elimination should undergo a structured reintroduction of foods containing individual FODMAPs to determine sensitivities and allow for personalization of the diet plan. This review discusses the literature surrounding the administration of the low-FODMAP diet and its efficacy in the treatment of IBS.

INTRODUCTION

Irritable bowel syndrome (IBS) is the most common gastrointestinal (GI) disorder worldwide, affecting about 15% of the global population (1). Patients with IBS experience abdominal pain and bowel disturbance, leading to significant negative impact on quality of life and productivity. In the United States, IBS has an annual burden of care of 3.1 million healthcare visits and an annual cost of over $20 billion (2, 3). While the majority of IBS patients are women, the female predominance observed in Western countries is not universally seen in Asia (4).

The pathophysiology of IBS, similar to the clinical presentation, is heterogeneous and likely driven by both host and environmental factors. Traditionally, research on the pathogenesis of IBS has focused on host abnormalities in motility, visceral sensation, and brain–gut interactions, but more recently, the roles of environmental influences such as early adverse life events, prior enteric infections, and dietary intolerances have been explored. IBS is the consequence of multiple pathways converging to produce the clinical symptoms of abdominal pain and altered bowel habits. The Rome IV criteria (5) describe the cardinal features of IBS, making this a symptom-based disorder diagnosed in the absence of organic diseases, which are typically excluded by a limited serologic and endoscopic workup (6). IBS patients are subcategorized on the basis of their predominant stool form: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), or IBS with a mixture of constipation and diarrhea (IBS-M) (5). It should be noted that abdominal bloating is not included in the Rome IV criteria despite being a common and bothersome complaint among IBS patients (7).

In most patients, IBS is a chronic relapsing disease in which symptoms, exacerbated by multiple host and environmental factors, may vary over time and sometimes shift between subtypes. One systematic review demonstrated that 2–18% of IBS cases worsened, 30–50% remained unchanged, and 12–38% improved over six months to six years of follow-up (8). Predictors of worse outcomes include previous surgery, longer duration of disease, higher somatic scores, history of trauma/abuse, pain as the predominant complaint, and comorbid anxiety and depression. Recent research has shown that a subgroup of sufferers can trace the onset of their IBS symptoms to an antecedent gastroenteritis. Postinfection IBS appears more likely than other forms of IBS to improve or spontaneously resolve over time (9, 10).

CURRENT TREATMENT STRATEGIES

A respectful patient–physician relationship is the cornerstone of successful IBS treatment, and establishing a secure and confident diagnosis of IBS is crucial to patient acceptance of the diagnosis. Goals of treatment include improving quality of life and reducing stress, in addition to controlling IBS symptoms. The treatment of IBS can be just as varied as the causes of the condition, and strategies can be symptom-based or globally focused. First-line therapies, typically consisting of lifestyle modifications and over-the-counter medications, generally target bowel symptoms (diarrhea or constipation) but offer only a marginal benefit for abdominal symptoms such as pain and bloating. When these strategies fail, prescription medications (6) are often utilized. Furthermore, about half of patients with IBS utilize complementary and alternative approaches either in addition to or instead of conventional medical therapy (11).

Dietary factors are central for patients with IBS, and >80% of IBS patients link their symptoms to eating or to specific foods. In fact, postprandial IBS symptoms are associated with decreased quality of life and increased disease severity (12). This apparent cause-and-effect relationship often prompts patients to attribute their IBS to a food allergy or specific food intolerance (12, 13). There are, however, many potential explanations for postprandial exacerbation of GI symptoms other than a true allergy (14). Given the primary function of the gut, it should come as no surprise

that food ingestion is the most potent stimulus of GI functions, including motility and secretion. Postprandial symptoms in IBS patients can arise as a consequence of triggering exaggerated physiologic responses, such as a hyperactive gastrocolic response, with or without amplified sensory responses to the normal or exaggerated physiology (15). These abnormalities should be viewed within the context of IBS pathophysiology, particularly disordered gut–brain signaling. Part of this reaction to food may be explained by food–microbiota interactions as well, since gut microbes play an important role in the digestion of dietary components, resulting in metabolites that may directly or indirectly contribute to IBS symptoms.

Given the heterogeneous factors contributing to the pathophysiology, there currently exists no single universal truth in regard to treatment of IBS. Patients are most likely to experience benefit with tailored, individualized, multifaceted treatment plans, and this has led to a focus on dietary manipulation as a primary strategy to improve symptom severity and quality of life. The optimal dietary strategy for IBS patients would ideally be clinically effective, nutritionally balanced, and safe.

MECHANISMS OF THE LOW-FODMAP DIET

Specifically, a diet low in FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) has been shown to be effective and safe in the IBS population. FODMAPs are a diverse family of osmotically active carbohydrates thought to contribute to GI symptoms, likely via multiple mechanisms (**Figure 1**). These short-chain carbohydrates feature increased concentration of fructose in excess of glucose (apples, pears), lactose (dairy products), fructans (wheat, onions), polyols (artificial sweeteners and sorbitol), and galacto-oligosaccharides (legumes,

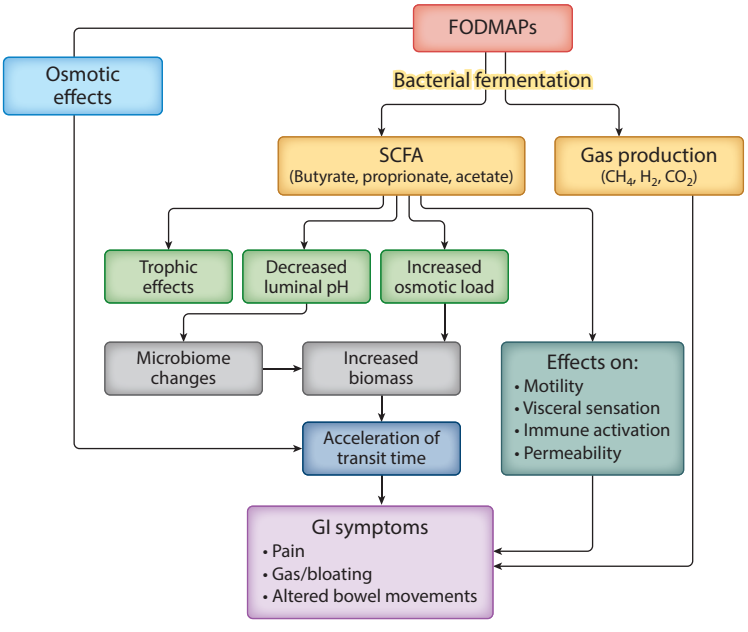

Figure 1

Mechanisms by which FODMAPs cause gastrointestinal symptoms. Abbreviations: FODMAPs, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; GI, gastrointestinal; SCFA, short-chain fatty acid. Adapted from Reference 17 with permission.

Table 1 Examples of low- and high-FODMAP foods[a]

FODMAP[b] content	Grains	Fruits	Vegetables	Dairy/ plant-based alternatives	Proteins	Beverages
High	wheat rye barley	apples/apple juice apricots blackberries cherries dates grapefruits mangos pears watermelons	artichoke asparagus cauliflower garlic leeks mushrooms (button, portabella) onions/shallots sugar snap peas	coconut milk (in the carton) ice cream milk cheese (soft) soy milk yogurt	most beans/legumes processed meats[c]	high-fructose-containing sodas and juices rum teas: chamomile, oolong, fennel, and chai
Low	corn tortillas/ chips grits gluten-free pastas, crackers, and breads oatmeal[c] potatoes popcorn rice sourdough bread quinoa	bananas (unripe) grapes kiwifruits lemons limes mandarin oranges oranges papayas pineapples	bok choy broccoli carrots chives cucumbers eggplants kale lettuce mushrooms (oyster) olives radishes spinach tomatoes	almond milk[c] cheese (most) coconut yogurt hemp milk[c] lactose-free ice cream, milk, yogurt,[c] cottage cheese	edamame lentils canned/rinsed chickpeas beef chicken eggs fish/seafood pork turkey tempeh[c] tofu (firm)	alcohol: wine (most), beer, spirits (most) coffee sucrose-sweetened or diet soft drinks teas (except those listed above) water

[a]Not a complete list of foods. Portion size matters; several foods have a specific serving size in which they would be high versus low in FODMAPs.
[b]Abbreviation: FODMAPs, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.
[c]Read labels of packaged foods to ensure they do not have added high-FODMAP ingredients (e.g., high-fructose corn syrup, wheat, onion, garlic).

cabbage), all of which are poorly absorbed from the GI lumen (**Table 1**) (16). By reducing consumption of these short-chain carbohydrates, symptoms of abdominal pain, bloating, and flatus production, in particular, may be alleviated. More recently, improvement in disease-specific quality of life has also been demonstrated, improving the acceptance of the low-FODMAP diet in the treatment of IBS (18).

Conventional thinking has focused on the fact that FODMAPs are poorly absorbed or nonabsorbed in the small intestine. Some FODMAPs exert direct osmotic effects that draw water into the intestinal and/or colonic lumen. FODMAPs that reach the distal ileum and colon undergo fermentation to short-chain fatty acids and gases (hydrogen, methane, carbon dioxide), which can trigger symptoms, particularly in patients who have underlying abnormalities in gut motility and visceral sensation (19, 20).

Previous studies reporting alterations in the gut microbiota and fermentation patterns suggest that physiological responses to FODMAPs, such as luminal water secretion or gas production, might differ between IBS patients and healthy volunteers (21, 22). However, recent work from the United Kingdom argues otherwise and suggests that different FODMAPs exert different effects along the GI tract. Using functional magnetic resonance imaging (fMRI), a recent study showed differential effects of fructose and fructans in the small intestine and colon in healthy volunteers

and IBS patients (23, 24). After fructose or inulin (a fructan) challenges, healthy controls reported significantly lower symptom scores than patients with IBS, despite similar fMRI parameters and breath hydrogen responses. Fructose led to increased small-bowel water content in both IBS patients and controls (potentially accelerating small-bowel transit and peristalsis as well), whereas inulin increased colonic volume and gas via fermentation by resident bacteria. Thus, the physiologic responses to FODMAP intake do not seem to differ between patients with IBS and healthy controls, suggesting that visceral hypersensitivity, rather than alterations in fermentation patterns and gas production, may be the primary driver of FODMAP-related symptoms in IBS patients.

Aside from osmotic and fermentation effects, FODMAPs may also generate symptoms via immune activation. McIntosh et al. (25) compared urinary metabolomic profiles of 40 IBS patients after 21 days of a low- or high-FODMAP diet. Following dietary intervention, there was a significant separation in urinary metabolomic profiles of patients with IBS in the two diet groups. In the low-FODMAP diet group, the urinary histamine level of a single postintervention sample showed a marginal decrease ($p < 0.05$) compared to the high-FODMAP group. Another study reported a decrease in inflammatory cytokines interleukin (IL)-6 and IL-8 in IBS patients on a low-FODMAP diet (26). Regarding gut microbiota, a low-FODMAP diet does lead to measurable changes in the fecal microbiota composition (and metabolome composition), including a decrease in gut microbes generally associated with health, such as *Bifidobacteria*, which may seem counterintuitive (25–27). However, the relevance of such changes in the gut luminal microenvironment and changes in symptoms remain unclear.

EFFICACY OF THE LOW-FODMAP DIET

Since its efficacy was first hypothesized in the early 2000s (28), numerous randomized controlled trials (RCTs) and observational studies have reported that the majority of IBS patients (ranging from 52% to 86% of patients) experience significant improvement in their GI symptoms with the low-FODMAP diet (29–31). In the seminal feeding trial, Halmos et al. (32) compared the low-FODMAP diet to a general Australian diet in a single-blind, crossover RCT. Thirty IBS patients were randomized into the low-FODMAP diet group or a general Australian diet group for 21 days. The primary endpoint was overall GI symptoms measured by the 100-mm Visual Analog Scale with secondary endpoints of abdominal pain, bloating, and flatus. The study found that overall GI symptom scores were lower on the low-FODMAP diet than a general diet (22.8 versus 44.9, $p < 0.001$) and that individual symptoms of bloating, flatus, and abdominal pain also significantly improved. While this study sparked much interest in the low-FODMAP diet, the small sample size and highly homogeneous study population were limitations. Furthermore, the provision of all of the subjects' food, which contributed to the scientific rigor of the study, opened the door to questions about the practical application of the low-FODMAP diet in real-world clinical practice.

Low-FODMAP Diet Compared to Other Active Diet Interventions

Given the difficulties with blinding and implementing a true placebo in dietary studies, most larger-scale trials have compared the low-FODMAP diet to another active diet intervention rather than placebo. Standard dietary advice for IBS, which includes the National Institute for Health and Care Excellence (NICE) guidelines and advice from the British Dietetic Association, recommends patients eat regular, small meals; avoid caffeine and alcohol; and limit their fiber intake. Studies comparing the low-FODMAP diet to this standard dietary advice have demonstrated mixed results. In a retrospective study by Staudacher et al. (29), a greater number of patients reported

improvement in a GI composite symptoms score (which assessed bloating, diarrhea, abdominal pain, and flatulence) with the low-FODMAP diet compared to the NICE guidelines (86% versus 49%, $p < 0.001$). Patients were also more satisfied with the results of the low-FODMAP diet than standard dietary advice (76% versus 54%, $p = 0.038$). Similarly, a single-blind trial from Iran concluded that there was a significantly greater decrease in the Irritable Bowel Syndrome Severity Scoring System (IBS-SSS) scores ($n = 110$, score 108 versus 149.75, $p < 0.001$), abdominal pain, and abdominal distention for those with IBS-D on a low-FODMAP diet as opposed to standard advice, although both interventions resulted in symptom improvement from baseline (33).

A multicenter, single-blind RCT in Sweden compared a dietitian-led low-FODMAP diet versus standard dietary advice over four weeks in 75 IBS patients. Investigators found no difference in the number of patients reporting symptom reduction between the two diets for the primary endpoint of a reduction in IBS-SSS score of ≥ 50 ($p = 0.62$) (34). An American single-center RCT in 84 IBS-D patients found no statistically significant difference in primary outcome of adequate relief of GI symptoms between four weeks of a dietitian-led low-FODMAP diet or a diet based upon modified NICE guidelines (foods containing FODMAPs were not excluded in the modified NICE guideline group). Interestingly, the low-FODMAP diet did achieve a therapeutic gain over the modified NICE diet of 11% (52% for low-FODMAP diet and 41% for modified NICE, $p = 0.31$), raising questions about whether this study was adequately powered for the primary endpoint (30). In this study, the low-FODMAP diet led to significant improvements in abdominal pain, bloating, and stool frequency scores compared to the modified NICE diet. In a secondary analysis from this study, the low-FODMAP diet was more than twice as likely as the modified NICE diet to achieve a clinically meaningful improvement in disease-specific quality of life (52% versus 21%, $p < 0.001$) (18).

Low-FODMAP Diet Compared to Placebo/Sham Diet

Given the powerful placebo response already present in functional GI disease, controlling for the nocebo response in dietary trials is particularly important to minimize patient bias, as the clinical outcome to a dietary change is invariably influenced by patient expectations (both positive and negative). The development of a true sham diet of comparable feasibility and complexity, however, can be challenging (36). The only true placebo-controlled trial was performed in the United Kingdom and utilized a bespoke sham diet of similar complexity, intensity, and fiber/energy content as a low-FODMAP diet (37). Although the percentage of participants reporting adequate symptom relief in the intention-to-treat analysis did not reach statistical significance (57% in the low-FODMAP group versus 38% in the sham diet group, $p = 0.051$), the difference was significant in the per-protocol analysis (61% versus 39%, $p = 0.042$). In addition, the IBS-SSS score for the low-FODMAP group was also significantly lower than for the sham group (173 in the low-FODMAP group versus 224 in the sham diet group, $p = 0.001$). The totality of clinical outcomes pointed toward the clinical efficacy of the low-FODMAP diet over a true placebo, and was the first to do so using dietary advice, making it directly relevant to clinical practice.

Comparative Effectiveness of the Low-FODMAP Diet and Nondietary Interventions

In addition to other diets, comparative studies between the low-FODMAP diet and other forms of nonpharmacologic treatments have been conducted. A 2016 Australian study compared the low-FODMAP diet, gut hypnotherapy, and the combination of the two in 74 patients (38). Improvement from baseline was observed in all three groups (71%, 72%, and 73% of patients, respectively)

at both six weeks and six months. However, there was no statistically significant difference between the groups at six weeks ($p = 0.67$), suggesting individual benefits for the low-FODMAP diet and hypnotherapy, but no additive benefit.

Another mind–body practice, yoga, has also been compared to the low-FODMAP diet. A single-blind study in 59 IBS patients compared twice-weekly yoga sessions to the low-FODMAP diet over 12 weeks. Both groups demonstrated improvement in IBS-SSS from baseline, with no difference found between groups at 12 weeks [$\Delta = 31.80$; 95% confidence interval (CI) $= -11.90$, 75.50; $p = 0.151$] (39). Combination therapy was not assessed in this study.

These preliminary studies punctuate the growing trend toward nonpharmacologic, multimodal treatment of IBS. Though they are quite promising, further studies are needed to explore this approach to IBS therapy.

Limitations of the Low-FODMAP Diet

Despite the widespread adoption of the low-FODMAP diet for IBS patients in clinical practice, several concerns have been raised regarding potential effects of prolonged FODMAP elimination on nutritional status and the gut microbiome. A decrease in calcium intake with a low-FODMAP diet has been demonstrated (37); however, a similar study found that this decrease was no longer significant after correcting for calorie-adjusted nutrient intake (40). Furthermore, a modified low-FODMAP diet (after reintroduction to determine sensitivities) is likely nutritionally adequate as assessed by a longer-term study of dietary intake utilizing postal questionnaires (41). Fiber intake may also decrease during the elimination phase of the low-FODMAP diet. Like calcium intake, this issue can be addressed during FODMAP reintroduction (42). Additional research to more fully understand the effects of the low-FODMAP diet on nutrition and energy status is clearly needed, particularly in patients already susceptible to nutritional deficiencies such as those with inflammatory bowel disease.

Diet is perhaps the most important influence on the human gut microbiome (43, 44). Thus, it should come as no surprise that restricting dietary FODMAPs exerts measurable effects on the gut microbiome. Several investigators have reported a relative decrease in total bacterial abundance (45) and bacteria thought to be beneficial to the GI tract (18, 21, 22). For example, some studies have found reduced *Bifidobacterium* species (25, 26, 37) and increases in potentially harmful species such as *Porphyromonadaceae* (25). Whether these changes are associated with long-term effects—bad, good, or indifferent—remains to be determined. Some of these changes may be reversible with the reintroduction of FODMAPs (26) and/or with probiotic use (37).

Additionally, questions have been raised about the generalizability of the available data from clinical research to real-world practice. Almost all of the current research has assessed the efficacy or effectiveness of the elimination phase of the low-FODMAP diet plan. There are almost no data regarding the other two phases of the diet plan: reintroduction of foods containing individual FODMAPs and personalization of the diet for more long-term use. Given that IBS is a chronic condition, the short-term duration of most of the research studies raises questions about the durability of the clinical benefits of the low-FODMAP diet. Most RCTs only followed patients for several weeks, with the longest duration being six months. Retrospective trials have had longer follow-up times, up to 16 months (31, 46). Finally, initial reactions from patients and providers are that the low-FODMAP diet is prohibitively restrictive and confusing. Ultimately, however, studies have not supported this impression and have demonstrated that patients generally have good comprehension and adherence when treatment is administered under the guidance of a dietitian (31, 32, 47).

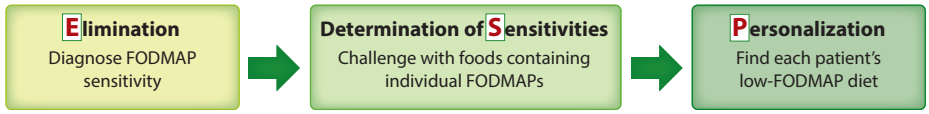

Figure 2

Three phases of the low-FODMAP diet: elimination, determination of sensitivities, and personalization. Elimination is the beginning, not the end! Abbreviation: FODMAPs, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.

DELIVERY OF THE LOW-FODMAP DIET

The low-FODMAP diet is composed of three distinct phases for which we have created the acronym ESP: *elimination*; reintroduction of foods containing individual FODMAPs to determine a person's *sensitivities*; and *personalization* (**Figure 2**) (48, 49). The elimination phase, which typically lasts about 2–6 weeks, should be viewed as a diagnostic test to determine if a patient is sensitive to FODMAPs. If there is no response, the diet should be discontinued. If a therapeutic response is achieved, patients should undergo the reintroduction phase to determine their sensitivities and tolerances. This information can then be used to create a personalized version of the low-FODMAP diet for long-term use.

Given the complexity of low-FODMAP meal planning and education, counseling is best provided by a properly trained dietitian. It is worth pointing out that nearly all of the RCTs assessing the low-FODMAP diet have utilized one-on-one instruction with a registered dietitian. However, there is evidence that group education may achieve similar outcomes to individual counseling. A UK study that looked at the clinical effectiveness and cost of group versus one-on-one counseling demonstrated no difference in IBS symptom reduction between study arms (54% for group versus 60% for individual, $p = 0.271$), but cost savings significantly favored the group-education arm of the study (50). Internet- or app-based instructions may be a useful adjunct, but research currently supports having a dietitian lead the education in either a group or individual setting. The reality, however, is that many patients receive little or no formal instruction on the low-FODMAP diet and may find a plethora of anecdotes, testimonials, and inaccurate information online. A list of trustworthy sources about IBS and FODMAPs for patients and providers is included in **Table 2**.

FUTURE DIRECTIONS AND CONCLUDING REMARKS

The low-FODMAP diet has become a key component in the management of IBS and reinvigorated discussions around the role of diet in the pathophysiology and treatment of IBS patients. It has also laid bare the inadequacies of the "medicine first" strategy that dominated the treatment of IBS for decades. The low-FODMAP diet has helped to usher in a new age of IBS management which recognizes that outcomes are maximized when providers and patients embrace an integrative, holistic clinical care model—one that considers diet, behavior/lifestyle, and exercise, along with medications. One size does not fit all when it comes to IBS.

That same logic should be more generally applied to the emerging role of diet therapies for IBS. The low-FODMAP diet has validated the importance of food to the pathogenesis and treatment of IBS. However, just as the elimination phase should be viewed as the beginning, not the end, of the low-FODMAP diet plan, the low-FODMAP diet should be viewed as the beginning, not the end, of our quest for effective diet interventions for IBS patients. Future research should focus on the identification of biomarkers to assist providers to identify IBS patients who are more likely to benefit from the low-FODMAP diet. Preliminary research suggests that "precision nutrition"

Table 2 Best easy-to-use resources to implement the low-FODMAP diet

Resource	Details
My Nutrition Health **http://myginutrition.com**	A comprehensive website for both patients and providers explaining the low-FODMAP diet, complete with videos, recipes, and frequently asked questions
University of Michigan gastrointestinal Pinterest Page **http://www.pinterest.com/UMGIdietitians**	Pinterest account from University of Michigan dietitians with up-to-date low-FODMAP products that are suitable for the low-FODMAP diet elimination phase as well as low-FODMAP recipes. Great for visual learners and for making grocery shopping easier
Monash University website and phone app **http://www.monashfodmap.com**	Researchers at Monash University developed the low-FODMAP diet and a corresponding smartphone app to assist patients and providers in implementing the diet. Additionally, they maintain an informative and up-to-date low-FODMAP blog
Kate Scarlata website and books **http://www.katescarlata.com**	Kate Scarlata, registered dietitian, is a low-FODMAP diet expert who has low-FODMAP diet resources, recipes, and blog articles available on her website. Her book *The Low-FODMAP Diet: Step by Step* is a great resource for patients and providers (57)
Patsy Catsos website and books **http://www.ibsfree.net**	Patsy Catsos, registered dietitian, is a low-FODMAP diet expert who has low-FODMAP diet resources, recipes, and blog articles available on her website. Her book *The IBS Elimination Diet and Cookbook* is a great resource for patients and providers (58)
FODMAP Everyday **http://www.fodmapeveryday.com**	Website with low-FODMAP recipes, products, and diet guidance as well as resources and support

might be possible by leveraging characteristics of the gut microbiome (51, 52), metabolome (25, 53), or genetics (54). We should also remember that not all IBS patients with symptoms related to eating respond to the low-FODMAP diet. This likely reflects the heterogeneity that is inherent to the pathophysiology of IBS and should motivate researchers and clinicians alike to remain curious and open to the possibility of other effective diet interventions for our IBS patients. We should also broaden our focus beyond dietary exclusion; supplementation rather than restriction may provide an as yet largely untapped treatment approach (55, 56). Through education and practical advice based upon sound science, our collective goal should be to transition IBS patients from viewing food as a source of pain and misery to something closer to how the rest of us view food—a source of sustenance, nutrition, and joy.

DISCLOSURE STATEMENT

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