

Fiber and Functional Gastrointestinal Disorders

Shanti Eswaran, MD¹, Jane Muir, PhD² and William D. Chey, MD, AGAF, FACG, FACP¹

Despite years of advising patients to alter their dietary and supplementary fiber intake, the evidence surrounding the use of fiber for functional bowel disease is limited. This paper outlines the organization of fiber types and highlights the importance of assessing the fermentation characteristics of each fiber type when choosing a suitable strategy for patients. Fiber undergoes partial or total fermentation in the distal small bowel and colon leading to the production of short-chain fatty acids and gas, thereby affecting gastrointestinal function and sensation. When fiber is recommended for functional bowel disease, use of a soluble supplement such as ispaghula/psyllium is best supported by the available evidence. Even when used judiciously, fiber can exacerbate abdominal distension, flatulence, constipation, and diarrhea.

Am J Gastroenterol 2013; 108:718–727; doi:10.1038/ajg.2013.63; published online 2 April 2013

INTRODUCTION

Fiber has long been used for the treatment of various gastrointestinal and non-gastrointestinal conditions including constipation (1–4), diarrhea (5–12), ulcerative colitis (13–15), obesity in children and adolescents (16,17), hypercholesterolemia (18–23), and diabetes mellitus (22,24,25). The National Academy of Sciences Institute of Medicine recommends that adults consume 20–35 g of dietary fiber per day, but the average American's daily intake of dietary fiber is only 12–18 g (26). Although a universally accepted definition for dietary fiber does not exist, it is generally agreed that this term includes carbohydrates that are not hydrolyzed or absorbed in the upper part of the gastrointestinal tract. For the purpose of communicating nutrition information to the consumer, the term dietary fiber is of great value because it clearly distinguishes between this non-digestible class of carbohydrates and digestible, glycemic carbohydrates such as sugars and starches. Despite the confusing terminology surrounding the different fiber types, the term dietary fiber has been useful in nutrition education and product development. In nutritional labeling, fiber is typically listed as a single category and not broken down into soluble or insoluble subtypes.

Fiber metabolism

Dietary fiber has a major role in the gastrointestinal tract (**Figure 1**). Any undigested carbohydrate that reaches the colon will be fermented (partly or totally) by the gut bacteria to produce short-chain fatty acids (SCFAs) and a number of gases, including carbon dioxide, hydrogen, and methane (27,28). SCFAs (mainly acetate, propionate, and butyrate) in turn create an osmotic load, are absorbed, and are further metabolized by colonocytes, hepatocytes, or the peripheral tissues (29–31). The fermentation of fiber

also influences fecal bulking in an indirect manner as fermentation by colonic microflora stimulates growth and results in increased microbial biomass (32). Thus, the type of fiber consumed leads to adaptation of, and changes to, the microbiome. Dietary fiber can also influence bulking directly via water retention (3,33,34). The unwanted side-effect of fiber ingestion and subsequent fermentation, however, is the production of gas. This gas is often malodorous and may in turn cause undesirable discomfort, bloating, and flatus in many individuals. This characteristic of many fiber types may be particularly relevant for those with functional gastrointestinal disorders.

Types of fiber

The fermentability and solubility of different “fiber” types relates closely to their chemical composition (e.g., presence of cellulose, hemicellulose, gums, resistant starch, lignins, pectins). For the purpose of this review, fiber will be broadly divided into short chain- and long- chain carbohydrates or fiber-types, based on their solubility and fermentation characteristics (**Table 1** (35–38)). Short chain carbohydrates or fiber includes the oligosaccharides: fructo-oligosaccharides and galacto-oligosaccharides (e.g., raffinose and stachyose). Owing to their size and solubility, both fructo-oligosaccharides and galacto-oligosaccharide fibers are highly fermentable. The long-chain carbohydrates include four major groups: (1) soluble, highly fermentable non-starch polysaccharide fiber (e.g., resistant starch, pectin, inulin, guar gum); (2) intermediate soluble and fermentable fiber (psyllium/ispaghula) and oats; (3) insoluble, slowly fermentable fiber (wheat bran, lignin (flax), and fruits and vegetables); and finally (4) insoluble, non-fermentable fiber (cellulose, sterculia, and methylcellulose).

¹Division of Gastroenterology, University of Michigan Health System, Ann Arbor, Michigan, USA; ²Monash University, Melbourne, Victoria, Australia.

Correspondence: William D. Chey, MD, AGAF, FACG, FACP, Division of Gastroenterology, University of Michigan Health System, 3912 Taubman Center, SPC 5362, Ann Arbor, Michigan 48109-5362, USA. E-mail: wchey@umich.edu

Received 17 December 2012; accepted 11 February 2013

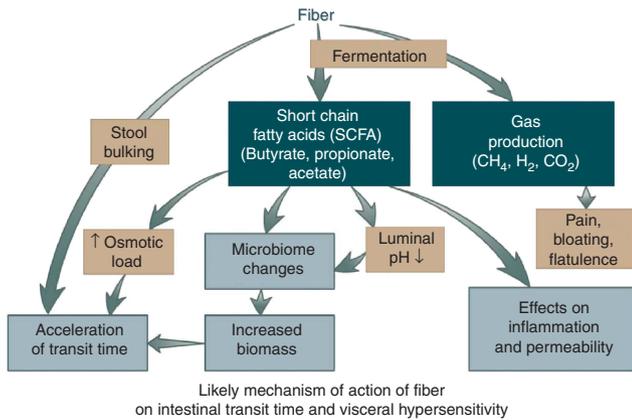


Figure 1. Likely mechanism of action of fiber on intestinal transit time and visceral hypersensitivity.

The physiological characteristics (and potential health benefits) of each different fiber type, in turn, depends on its proportion of soluble- and insoluble carbohydrate components. For example, fiber types that are high in soluble, viscous fiber may slow rates of glucose and lipid absorption from the small intestine, likely by sequestering bile acids and monoglycerides during passage through the intestinal lumen (39). Soluble fiber (pectin, beta-glucan (from oats and barley), ispaghula/psyllium) is believed to be beneficial in lowering blood cholesterol and plaque-forming low-density lipoprotein levels by interrupting the enterohepatic circulation of bile salts, thereby increasing hepatic conversion of cholesterol into newly synthesized bile acids and decreasing serum LDL (18–20). Dietary fiber can contribute to net metabolizable energy, depending on how readily it is fermented. For example, fermentable fiber contributes 8 kJ/g (resistant starch (8.8 kJ/g), fructo-oligosaccharides (8.4 kJ/g), and inulin (8.8 kJ/g)) and non-fermentable fiber contributes (0 kJ/g) (40). **Table 2** lists popular commercially available supplements by type of fiber.

How fiber affects GI function

Fiber has been advocated for improved bowel function since the early 1970s (41). In a 1980 *Nature* article, Stephen and Cummings (42) demonstrated that the actions of soluble and insoluble fibers in the colon depend on the extent to which they are digested. In an elegant study they showed that insoluble fiber alters colonic function by increasing fecal water content and fecal bulk. The mechanism for this effect was unclear, however, as insoluble fiber has no appreciable water holding capacity, is minimally fermented (no appreciable increase in biomass), and accelerates colonic transit in germ-free rats (43,44). It was later determined that insoluble fiber (e.g., wheat bran) increases fecal mass and colonic transit rate through mechanical stimulation/irritation of gut mucosa, inducing secretion and peristalsis (45). An additional study showed that both particle size and shape were important, with large, coarse particles providing greater laxative efficacy than fine, smooth particles (no effect) (46). Taken together, these data support that insoluble fiber can have a significant laxative effect, but only if the particles are of sufficient size and coarseness.

Soluble non-viscous fiber and soluble viscous fiber that is readily fermented increase stool bulk by increasing biomass and fermentation by-products, such as gas and SCFAs (42). On the basis of such observations, it has been proposed that fiber improves FGIDs through the acceleration of oro-anal transit and by decreasing intra-colon pressure (47,48). Of course, it is also possible that it is through secondary effects on the microbiota, low-grade inflammation, or permeability that fiber exerts effects on sensation as well as transit (**Figure 1**) (49). The consumption of fiber may actually retard gas transit, by decreasing bolus propulsion to the rectum (50). Thus, in addition to increasing gas production by colonic flora, fiber ingestion may elicit gaseous or bloating symptoms by promoting gas retention.

Soluble viscous fiber that is minimally fermented has a high water-holding/gel-forming capacity that is preserved throughout the large bowel, normalizing stool form (softens hard stool in constipation, firms loose/liquid stool in diarrhea) (51,52). Viscous fibers that are FDA approved for laxation include methylcellulose, calcium polycarbophil, and psyllium. Stool consistency is highly correlated with stool water content, and a relatively small change in stool water content (increase of 4.7%) can lead to a relatively large stool softening effect (4.6-fold difference in viscosity) (51).

Fiber also has extra-colonic effects, and the data on gastric emptying are mixed (53–57). In general, high doses (≥ 7 g) of wheat bran, inulin, and psyllium tend to delay gastric emptying, whereas lower doses do not show a significant effect. Delayed gastric emptying may be due to increased viscosity of gastric contents, which reduces pyloric flow. Increased viscosity reduces sedimentation of solids in liquids and thus impairs the ability of the antrum to preferentially empty liquids faster than solids (58,59). This delay in gastric emptying, together with a possible impairment of nutrient absorption in the small intestine may delay intragastric redistribution, which normally occurs as nutrients enter the duodenum (60). This could explain the tendency towards the higher antral/fundal ratios seen with bran, leading to the sensation of distension and bloating (61).

Effects of SCFAs

Using *in vitro* fermentation models to produce estimates of *in vivo* fiber fermentation, there is evidence that soluble fibers increase the rate of fermentation, increase SCFA production, lower pH, and increase hydrogen gas production (62). In fact, differences in fermentation rates, gas production, and SCFA production have been observed for various fiber preparations (wheat dextrin, psyllium, inulin), which may in turn explain their clinically observed different gastrointestinal tolerances. Of the SCFAs, butyrate is the preferred energy source for the colonic mucosa cells and exerts effects on myenteric neurons and motility (63), supporting one mechanism by which a high fiber diet accelerates colonic transit (64). Recent work has found that specific SCFAs such as butyrate alter the proportion of ChAT immune reactive myenteric neurons and increase cholinergic-mediated colonic circular smooth muscle contraction in animals (63). Butyrate has also been shown to suppress colonic inflammation by the inhibition of the IFN- γ /STAT1 signaling pathway (65–67).

SCFAs may also be shown to exert effects on the GI tract outside the colon. Exposure of the proximal colon in healthy

Table 1. Naturally occurring fiber types

Fiber type	Chain length	Sources	Potential benefits for IBS ^a	Potential risks for IBS ^a
Soluble highly fermentable oligosaccharides (includes FOS, GOS) 	Short-chain carbohydrates	<ul style="list-style-type: none"> Legumes/pulses Nuts and seeds Wheat, rye Onions, garlic, artichoke 	<ul style="list-style-type: none"> Laxation: weak laxative effect. Transit time: does not hasten transit time. Balance of bacteria: selective growth of certain microbiota, e.g., Bifidobactia. SCFA: very rapidly fermented in terminal ileum and proximal colon to produce SCFA. Gas production: high 	<ul style="list-style-type: none"> In patients with IBS the rapid fermentation may contribute to gas, flatus and gastrointestinal symptoms. A number of studies have been undertaken in IBS—with mixed results (37).
Soluble highly fermentable 'fiber' (e.g., RS, pectin, guar gum, and inulin) 	Long-chain carbohydrates	<ul style="list-style-type: none"> Legumes/pulses Rye bread, barley Firm bananas Buckwheat groats (kashi), millet, oats Cooked and cooled-pasta, potato and rice. 	<ul style="list-style-type: none"> Laxation: Mild laxative effect. Transit time: Does not hasten gut transit. Can slow absorption from the small intestine. Balance of bacteria: Increases overall bacterial species but not selective for bifidobacteria. SCFA: Rapidly fermented in proximal colon to produce SCFA. RS is good an excellent substrate for the production of the SCFA butyrate. Gas production: moderate 	<ul style="list-style-type: none"> In patients with IBS the rapid fermentation may contribute to gas, flatus, and gastrointestinal symptoms No well-designed studies have been undertaken in IBS.
Intermediate soluble fermentable 'fiber' (psyllium/ispaghula) and oats. 	Long-chain carbohydrates	Seed of the plant <i>Plantago ovata</i> , and oats	<ul style="list-style-type: none"> Laxation: good laxative effect. Transit time: does hasten transit time. Balance of bacteria: increases overall bacterial species but little evidence for selective growth SCFA: moderately fermented along length of colon to produce SCFA. Gas production: moderate. 	<ul style="list-style-type: none"> In patients with IBS studies have shown some positive effect on laxation. Side-effects of gas/flatus has produced mixed results for some patients with IBS (38).
Insoluble slowly fermentable 'fiber' (e.g., wheat bran, lignin (flax), fruit, and vegetables) 	Long-chain carbohydrates	<ul style="list-style-type: none"> Some vegetables and fruit Wheat bran Wholegrain cereal Rye Brown rice, wholemeal pasta, quinoa Flax seed. 	<ul style="list-style-type: none"> Laxation: good laxative effect. Transit time: does hasten transit time. Balance of bacteria: increases overall bacterial species but little evidence for selective growth SCFA: slowly fermented to produce SCFA along the length of the colon. Gas production: moderate-high 	<ul style="list-style-type: none"> In patients with IBS wheat bran has not been shown to be effective. A major side-effect has been excessive gas/wind and bloating (39). This may be due to the presence of high quantities of fructans also associated with the wheat bran (40). Symptoms associated with wheat bran may not be acceptable to many patients.
Insoluble, non-fermentable 'fiber' (e.g. cellulose, sterculia, and methylcellulose) 	Long-chain carbohydrates	<ul style="list-style-type: none"> High fiber grains and cereals Nuts, seeds Skins of fruit and vegetables. 	<ul style="list-style-type: none"> Laxation: good laxative effect. Transit time: does hasten transit time. Balance of bacteria: no evidence for selective growth. SCFA: poorly fermented. Gas production: low 	<ul style="list-style-type: none"> Less gas/wind forming properties This fiber type may have better characteristics for treating constipation in IBS patients. However, few well designed studies have been conducted.

FOS, fructo-oligosaccharides; GOS, galacto-oligosaccharides; IBS, irritable bowel syndrome; RS, resistant starch; SCFA, short chain fatty acids.

Information given in this table is a simplified overview that summarizes the different physiological effects of the different fiber types. More detailed information about this area may be obtained by key reviews cited in this paper (26–35,42–44,73,74,77).

^aUsing standard (not excessive) doses of these carbohydrates.

Table 2. Commercially available fiber preparations

Fiber category	Type	Brand	Serving size	Amount of fiber per serving
Soluble highly fermentable oligosaccharides	FOS	Orafti-P95	Powder 8g/day	7.5g
Soluble highly fermentable fiber	Inulin	FiberChoice	2 Tablets	4–5g
		Fibersure	1 teaspoon	
	Benefiber (Canada)	Varies		
	Wheat dextrin	Benefiber (USA)	2 Teaspoon powder	3g
	Partially hydrogenated guar gum (PHGG) Resistant starch	Benefiber (formerly) Hi-Maize	Powder 15–20g powder	7–9g
Soluble intermediate fermentable fiber	Ispaghula/psyllium Oat Bran	Metamucil	1 Tsp	3g
		Konsyl	Powder, caplet, wafer	4g (2g soluble)
		Quaker oats	40g dry	
Insoluble, minimally fermentable fiber	Wheat Bran	Available in supermarket	– 15g Coarse powder	6.5g
			– 19g Bran-pellets	4.5g
Insoluble, non-fermentable fiber	Methylcellulose ^a	Citrucel	Varies	0.5–2g
	Karaya gum/sterculia ^b	Normacol Normafib	1–2 Sachets daily or bid	7g Per sachet

FOS, fructo-oligosaccharides.
^aDerivatives of insoluble fibers (e.g., esters of cellulose) are generally used. These derivatives are soluble in cold water.
^bSterculia gum is available as granules which should be swallowed whole with plenty of water.

volunteers to SCFAs results in marked dose-dependent relaxation of the proximal stomach, and triggers transient LES relaxations (68,69). Similar effects have been observed in patients with gastroesophageal reflux disease on a diet high in indigestible carbohydrates (10 g fiber/day), significantly increasing the rate of transient LES relaxations, number of acid reflux episodes, and symptoms of gastroesophageal reflux disease (70).

Interaction with microbiota

There is also evidence that changes in the complex gastrointestinal environment by ingested fiber influence fecal microbiota profiles, perhaps because of the varied production of SCFAs and/or decreases in colonic pH, promoting the growth of beneficial bacteria (Figure 1). Short-chain carbohydrates (inulin, fructo-oligosaccharides/galacto-oligosaccharide) and other soluble fibers are fermented in the distal small intestine and proximal colon by endogenous bacteria to energy and metabolic substrates (SCFAs), and the presence of these carbohydrates may produce selective changes in the composition of the microbiota, inducing different fermentation patterns. As such, carbohydrates such as inulin are regarded as prebiotics, which may stimulate or alter the preferential growth of health-promoting species already residing in the colon (especially, but not exclusively, lactobacilli and bifidobacteria) (71–75), leading to potential benefits in irritable bowel syndrome (IBS) (76).

Fiber for chronic constipation

In addition to adequate fluid intake and exercise, a high fiber diet is often the first recommendation a patient will receive for chronic

constipation, as a lack of dietary fiber is believed to contribute to constipation (77–79). Although 50% of patients think fiber does not completely relieve their constipation and almost two-thirds of respondents are not completely satisfied with the ability of fiber to improve their quality of life (80), current guidelines recommend the use of fiber in both dietary and supplement form for the early management of constipation (81) (Table 3 (82)). It is apparent from trials identified by systematic reviews that there is a relative paucity of high quality evidence to support this approach, especially for insoluble fiber. Soluble fiber is thought to increase stool bulk and weight and therefore stool frequency (3,83). Insoluble fiber such as bran is thought to accelerate intestinal transit time, thereby increasing stool frequency (43,45,84). Finally, there is a particular lack of evidence of efficacy of fiber for individual constipation subtypes (obstructive, metabolic, neurological, diet-related, myogenic, drug-related, and pelvic floor dysfunction). Thus, the remainder of this discussion will focus on fiber as a treatment for chronic idiopathic constipation (CIC), or constipation unrelated to anatomic, medication-related, or readily identifiable physiological causes.

Fiber supplements. In an attempt to make sense of the divergent data addressing the role of fiber as a treatment for constipation, a number of systematic reviews and meta-analyses with varying selection criteria have been published (2,85,86). These analyses have found that most studies suffer from small sample sizes and poor study design with non-rigorous outcomes and high risk of bias. Acknowledging the inherent heterogeneity of the data, there does appear to be a significant improvement in constipation symptoms

Table 3. Commonly used therapeutics for constipation and level and grade of evidence (82)

Treatment modalities commonly used for constipation	Recommendation level and grade of evidence
Bulking agents	
• Psyllium/ispaghula	Level II; grade B
• Calcium polycarbophil	Level III; grade C
• Bran	Level III; grade C
• Methylcellulose	Level III; grade C

and abdominal discomfort compared with placebo for soluble fiber (psyllium, inulin). The paucity of high quality data highlights the need for further large, methodologically rigorous, randomized controlled trials (RCTs) utilizing validated outcome measures as defined by the Rome Foundation and regulatory agencies such as the US Food and Drug Administration and the European Medicines Agency (87).

The most recent summary of available RCTs studying the effects of both soluble and insoluble fiber in patients with CIC was performed in 2011 by Soares *et al* (88). Six studies were found eligible for inclusion, including one RCT, which utilized a cross-over design. It should be noted that studies which recruited patients with drug-induced constipation, institutionalized patients, or those that enrolled a heterogeneous group of patients (e.g., both CIC and IBS with constipation (IBS-C)) were excluded. None of these was at low risk of bias, the majority of them were small, and none accounted for baseline dietary fiber consumption or change in fiber consumption during the study. Amounts of fiber in these studies ranged between 10–20g of fiber/day with a treatment duration from 2 to 8 weeks. The settings were mostly tertiary care centers and subjects were predominantly female. Four of the eligible trials used soluble fiber (3 with psyllium, 1 with inulin and malto-dextrin) (89–92). The largest trial was a single-blind RCT with 201 primary care patients who underwent treatment over a 2-week period (89). Eighty-seven percent of patients allocated to psyllium reported an improvement in symptoms, compared with 47% of patients receiving placebo ($P < 0.001$). There was also a significant response in abdominal pain/discomfort and straining on defecation. Similar effects were seen among the other three trials of soluble fiber. In one study, pain with defecation was significantly reduced with psyllium, but 18% of psyllium patients reported abdominal pain as a side effect as compared with 0% of placebo (90).

Two studies used insoluble fiber, wheat bran in one study (93) and rye bread in the other (94). In the 24 patients recruited to receive 20g of bran per day or placebo, no statistically significant difference in response (defined as having no further straining at stool) occurred with active treatment. For the rye bread study, 29 female participants consumed rye bread (37g/day fiber) or low fiber bread (6.6g/day fiber) over a 3-week period. Following the intervention period, the mean difference in number of stools per day was 0.3 higher for the patients randomized to rye bread compared with those assigned to low-fiber bread ($P = 0.001$).

Difficulty of defecation was also significantly reduced with rye bread ($P < 0.001$), and stools were softer ($P < 0.001$). However, there were higher symptoms scores for gastrointestinal side effects such as abdominal pain, flatulence, borborygmi, and bloating with rye bread compared with low fiber bread (mean difference in scores = 1.6, $P < 0.001$). Note that rye is partially fermentable, and the high dose (37g/day) was started day 1 without a gradual introduction of fiber.

Little human data exist on other commercially available fiber preparations (Table 3). For example, one study of methylcellulose in constipated patients resulted in statistically significant increases in stool frequency, water content, and fecal solids but this was neither randomized or placebo controlled (95).

Fiber effects on constipation subtype. Non-response to supplementary fiber may be a marker of refractory constipation or constipation subtype, though there are few studies that have assessed the efficacy of fiber for slow transit constipation or dyssynergic defecation. One non-randomized study demonstrated 88% of patients with slow transit and 63% of patients with a disorder of defecation did not respond to dietary fiber treatment (30g of fiber per day), whereas 85% of patients without a pathological finding improved or became symptom free (96). Approximately half of patients with symptoms refractory to supplementary fiber have a prolonged intestinal transit time (97). Thus, fiber intake is not a panacea for all CIC patients.

Dietary fiber. Patients often find fiber supplements inconvenient and unpalatable with the occurrence of gas or bloating often a reason for lack of compliance or discontinuation of therapy (98). Comparatively, few clinical trials have evaluated dietary fiber that is naturally occurring as opposed to supplemental fiber, likely because food contains not only fiber but other non-absorbable sugars (i.e., polyols, fructans, and galacto-oligosaccharides) or chemicals, which may exert laxative effects. For example, a recent prospective, randomized-controlled 8-week single-blind cross-over study examined treatment with dried plums (prunes, 6g/day fiber) compared with psyllium (6g/day fiber) in 40 patients (99). Dried plums not only contain fiber but also sorbitol and fructans, non-absorbable carbohydrates that, when fermented by colonic bacteria, create an osmotic load that can dramatically alter stool frequency and consistency (100). Treatment with dried plums resulted in a greater improvement in constipation symptoms as reflected by a significant increase in the number of complete spontaneous bowel movements and in stool consistency (softer stools) when compared to treatment with psyllium. Also, more subjects reported subjective improvement in overall constipation symptoms, although the mean global constipation symptom scores were similar between groups and psyllium also improved constipation symptoms when compared with baseline.

Conclusion. As there may be some benefit and little risk of serious adverse events, increasing dietary fiber or the addition of fiber supplements seems a reasonable initial strategy in the management of CIC patients. Patients may enjoy improvements in bowel

movement frequency and consistency. Effects on other symptoms commonly reported by CIC patients such as abdominal pain or bloating are more variable. Non-evidence based but practical advice on initiating therapy with fiber supplements includes starting at a nominal dose and slowly titrating up as tolerated over the course of weeks to a target dose of 20–30 g of total dietary and supplementary fiber per day (Table 2). It is also reasonable to recommend clearing hard stool with an osmotic laxative before initiating fiber therapy, which may avoid cramping pain. Occasionally, patients will experience marked worsening of their constipation related symptoms with fiber. When this occurs, there are some data to suggest that significantly delayed colon transit or dyssynergic defecation might be present (96,97).

Fiber for IBS. Historically, increasing dietary fiber intake has been a standard recommendation for patients with IBS, but the efficacy of fiber for IBS is more nuanced than appreciated by most clinicians. Ever since Burkitt *et al.* (41) first suggested that fiber might protect people in rural areas from certain gastrointestinal disorders, the practice of advising fiber supplementation in FGIDs has become widespread and remains standard operating procedure. However, the use of fiber for IBS has historically been, and still remains, controversial. Although some believe that the highly processed, low fiber western diet is at the root of IBS, others believe that “roughage” can exacerbate or even cause IBS symptoms (41,101). These divergent views are likely the result of the inherent heterogeneity of IBS, confusion as to what we refer to as fiber, the paucity of high quality studies, and conflicting historical data. In 1977, Manning *et al.* (102) examined the effect of a 6-week high- or low-fiber diet on abdominal pain and bowel frequency in 26 IBS patients. Participants in this single-blind RCT ingested an additional 20 g of wheat bran per day on the high fiber diet. The investigators found significant improvement in pain frequency ($P < 0.05$) and pain severity ($P \sim 0.01$). Bowel habit was regarded as “improved” in the high fiber group ($P < 0.05$), and bowel frequency improved modestly as well ($P < 0.02$). Another seminal RCT of psyllium in 80 IBS patients significantly improved constipation ($P = 0.026$) and transit time ($P = 0.001$) but did not significantly improve bloating and abdominal pain (103). A subsequent non-randomized study investigated the utility of “high-fiber” diets (30 g of fiber/day) for the treatment of 72 IBS patients (all subtypes). This study reported improvement in hard stools, bowel frequency, and urgency but no change in abdominal distension, diarrhea, or flatulence (104). Finally, an often-cited patient survey of 100 IBS patients found that 55% felt worse and only 10% felt better on bran (105).

Fiber intake in IBS. A recent survey found that most general practitioners believe that fiber deficiency is the main cause of IBS symptoms and 94% would institute dietary therapy based on this assumption (106). However, patients with FGIDs do not seem to consume less dietary fiber than healthy controls, suggesting symptoms are unlikely to be related to altered diet composition (107). A recent Swedish abstract that compared the nutrition intake in patients with IBS with the general population actually found the

intake of dietary fiber to be higher in the IBS group (19 vs. 16 g/day, $P < 0.001$) compared with controls (108). The authors concluded that although IBS patients may have a self-imposed limited diet and avoid trigger foods, their mean average daily fiber intake is essentially similar to that of a matched healthy control population and in accordance with current nutrition recommendations.

Fiber supplements in IBS. The use of fiber or bulking agents for treatment of IBS has been summarized in two meta-analyses (109,110), four systematic reviews (37,111–113), and two comprehensive narrative reviews (114,115). All noted significant quality shortcomings in the published studies, including heterogeneous patient populations, varied outcome measures, different types of fiber supplements, small sample size, and difficulties with blinding. Other widely variable factors included the amount of soluble (5–30 g) and insoluble (4.1–36 g) fiber added to the diet and the duration of study intervention (3–16 weeks). Most of the trials that report the use of these agents do not adhere to the recommendations made by the Rome foundation for the design of treatment trials for the functional GI disorders (87), although this is largely because the majority of these trials were conducted long before these guidelines were in place. Finally, most studies evaluated supplementary fiber and not increased dietary fiber, and rarely reported on IBS subtype or baseline dietary fiber consumption.

The most recent Cochrane analysis concluded that bulking agents were not beneficial for the treatment of IBS (112). This analysis, which included 12 papers with an intervention period lasting 4–16 weeks, reiterated the problems with the quality of available data. The authors’ conclusions from the pooled data suggested that bulking agents provided no benefit for the treatment of IBS. The studies either showed no significance or did not address specific outcomes, including abdominal pain, improvement in global assessment, and IBS symptom scores. Only seven of the included studies had more than 30 patients and all studies had quality limitations (i.e., method of randomization, double-blinding, concealment of treatment allocation, description of withdrawals).

In a systematic review and meta-analysis by Ford *et al.*, (109) 12 trials and 591 patients were included that evaluated the efficacy of various forms of fiber with placebo or, in one study, a low fiber diet as treatment for IBS. Only 3 of these 12 studies reported on IBS subtype. Two of the studies included only IBS-C patients and another had 49% IBS-C patients. The fiber preparations used included bran (five studies), ispaghula/psyllium (six studies), and one unspecified. Overall, 52% of IBS patients assigned to fiber had persistent symptoms or no improvement in symptoms after treatment compared with 57% assigned to placebo or a low fiber diet (relative risk (RR) 0.87, 95% confidence interval (CI) = 0.76–1.00, $P = 0.05$). There was no statistically significant heterogeneity detected between studies ($I^2 = 14.2\%$, $P = 0.31$). The number needed to treat (NNT) with fiber to prevent one patient with persistent symptoms was 11 (95% CI = 5–100). There was no evidence of funnel plot asymmetry, suggesting no publication bias. However, only seven of the 12 studies scored 4 or more on the Jadad scale. When only these seven higher quality studies were included in the

analysis, the borderline treatment benefit for fiber was no longer evident (RR of persistent symptoms (0.90, 95% CI=0.75–1.08).

The data would suggest that all types of fiber supplementation are not created equally, at least not as it pertains to the treatment of IBS. In five studies (221 patients), which compared insoluble bran with placebo or a low fiber diet, bran failed to improve overall IBS symptoms (RR of persistent or unimproved symptoms 1.02, 95% CI=0.82–1.27) (109). On the other hand, six studies (321 patients) evaluated soluble fiber (ispaghula/psyllium) vs. placebo. Ispaghula was effective at improving overall IBS symptoms (RR of persistent or unimproved symptoms 0.78, 95% CI=0.63–0.96). The NNT for ispaghula to prevent one patient from experiencing persistent symptoms was 6 (95% CI=3–50). There was no evidence of funnel plot asymmetry and 5/6 studies scored 4 or more on the Jadad scale.

One key difference between the Ford and Cochrane reviews was the method of analysis (109,112). Both analyses had similar strict inclusion criteria, but Ford *et al.* (109) did not use an intention-to-treat analyses, and used persistent symptoms after treatment as an outcome measure. This may explain why this group found psyllium to have a small but statistically significant benefit for IBS.

The most recent comparative effectiveness trial evaluated the relative efficacy of psyllium/ispaghula, 10 g ($n=85$), bran, 10 g ($n=97$), or rice flour (placebo) ($n=93$), twice daily (mixed with food, preferably yogurt) over 12 weeks in 164 primary care IBS patients (116). This study was not included in the reviews mentioned above. At 1 month, 57% of patients taking psyllium experienced adequate symptom relief for 2/4 weeks of treatment compared with 40% with bran (NNT=6, 95% CI=4–104) and 35% with placebo (NNT=5, 95% CI=3–15). The difference between psyllium and placebo, however, was no longer significant at 3 months. Bran provided benefits over placebo only at 3 months. Over 60% of subjects randomized to psyllium or bran reported moderate adverse events, the most common of which were constipation and diarrhea. Interpretation of the results at 2 and 3 months of treatment are complicated by the high drop-out rates (29% and 40%, respectively). The overall likelihood of side effects was similar among the three groups.

It is important to recognize that most of the data on the efficacy of fiber for IBS come from referral centers. Studies conducted in referral centers are likely to be biased against fiber supplementation, as patients who improve with fiber are less likely to be referred to a tertiary care center. Thus, it is possible that results of trials evaluating from referral centers could underestimate the benefits of fiber for IBS. Only a few studies have included primary care patients exclusively (105,116), and only one has addressed this potential difference in response specifically. Miller *et al.* (117) recruited consecutive patients meeting Rome I criteria for IBS from primary and secondary clinics until 100 had completed questionnaires. Twenty-seven percent of primary care patients said that bran had improved their symptoms compared with 22% who claimed it had made them worse. Ten percent of secondary care patients attributed improvement to bran, while 55% of these patients felt it exacerbated their symptoms. About half of primary care patients (51%), reported that bran had no positive or negative effect on their symptoms compared with 33% of secondary

patients reporting no change. In primary-care, psyllium led to improvement in 25%, deterioration in 19% and no change in 56%, which was not significantly different to secondary-care. The authors concluded that although the approach of advising bran for patients with IBS is not especially beneficial, it may be better tolerated in primary care settings.

Although few adequately powered, methodologically rigorous studies have examined the role of commercially available fibers other than psyllium for the treatment of IBS symptoms, there are some data to suggest that preparations such as partially hydrolyzed guar gum (formerly Benefiber, Novartis Consumer Health Inc., Parsippany, NJ) and calcium polycarbophil (Fibercon, Pfizer, New York, NY) may be helpful and well tolerated (118–120). It should be noted that each caplet of calcium polycarbophil contains roughly 0.5g of fiber, thus multiple pills may be required to see an appreciable effect.

Dietary fiber. In contrast to the larger number of studies of fiber supplementation, few studies have examined the effect of increasing fiber intake in the form of ordinary foods (121–123). There are reports of improvement of IBS symptoms on both high-fiber and low-fiber diets, a result attributed to a placebo or Hawthorne effect. In fact, a number of contrarian studies had suggested that popular sources of dietary fiber, such as bran, cereals, vegetables, and fruits, might actually aggravate symptoms in IBS as these foods also contain large amounts of FODMAPs (e.g., fructans, excess fructose, galacto-oligosaccharide, and sugar polyols) (124). The symptoms that appeared to be aggravated most commonly were flatulence, bloating, and abdominal pain.

CONCLUSION

Success in finding an effective treatment strategy for treating functional GI disorders is a challenging area of clinical management. One of the aims of this review was to highlight the importance of assessing the fermentation characteristics of each fiber type when choosing a suitable strategy for patients. When fiber is recommended for FGIDs, use of a soluble supplement such as ispaghula/psyllium is best supported by the available evidence. In constipated patients, it can be helpful for pre-existing hard stool to be eliminated (e.g., with an osmotic laxative) before initiating fiber therapy. Fiber should be started at a nominal dose and slowly titrated up as tolerated over the course of weeks to a target dose of 20–30 g of total dietary and supplementary fiber per day. Even when used judiciously, fiber can exacerbate problems with abdominal distension, flatulence, constipation, and diarrhea (105,125,126). It is clear that rather than extrapolating from the studies undertaken in healthy individuals, further research in functional GI patients should be performed with rigorous endpoints, strict inclusion criteria, and IBS subtype in mind.

ACKNOWLEDGMENTS

The authors would specifically like to thank Dr John McRorie for his contributions and edits to the “Fiber metabolism” section of the manuscript.

CONFLICT OF INTEREST

Guarantor of the article: William D. Chey, MD, AGAF, FACG, FACP.

Specific author contributions: Dr Eswaran drafted the manuscript and prepared the tables. Dr Muir contributed to the writing, referencing, and preparation of the manuscript and tables. Dr Chey proofed and finalized the text. All authors approved the final draft submitted.

Financial support: None.

Potential competing interests: Dr Eswaran and Jane Muir have no potential competing interests. William D. Chey is a consultant for Nestlé/Prometheus.

REFERENCES

- Bouchoucha M, Faye A, Savaireau B *et al*. Effect of an oral bulking agent and a rectal laxative administered alone or in combination for the treatment of constipation. *Gastroenterol Clin Biol* 2004;28:438–43.
- Ramkumar D, Rao SS. Efficacy and safety of traditional medical therapies for chronic constipation: systematic review. *Am J Gastroenterol* 2005;100:936–71.
- McRorie JW, Daggy BP, Morel JG *et al*. Psyllium is superior to docusate sodium for treatment of chronic constipation. *Aliment Pharmacol Ther* 1998;12:491–7.
- Mehmood MH, Aziz N, Ghayur MN *et al*. Pharmacological basis for the medicinal use of psyllium husk (*Ispaghula*) in constipation and diarrhea. *Dig Dis Sci* 2011;56:1460–71.
- Washington N, Harris M, Mussellwhite A *et al*. Moderation of lactulose-induced diarrhea by psyllium: effects on motility and fermentation. *Am J Clin Nutr* 1998;67:317–21.
- Wenzl HH, Fine KD, Schiller LR *et al*. Determinants of decreased fecal consistency in patients with diarrhea. *Gastroenterology* 1995;108:1729–38.
- Qvitzau S, Matzen P, Madsen P. Treatment of chronic diarrhoea: loperamide versus ispaghula husk and calcium. *Scand J Gastroenterol* 1988;23:1237–40.
- Heather DJ, Howell L, Montana M *et al*. Effect of a bulk-forming cathartic on diarrhea in tube-fed patients. *Heart Lung* 1991;20:409–13.
- Eherer AJ, Santa Ana CA, Porter J *et al*. Effect of psyllium, calcium polycarbophil, and wheat bran on secretory diarrhea induced by phenolphthalein. *Gastroenterology* 1993;104:1007–12.
- Murphy J, Stacey D, Crook J *et al*. Testing control of radiation-induced diarrhea with a psyllium bulking agent: a pilot study. *Can Oncol Nurs J* 2000;10:96–100.
- Smalley JR, Klish WJ, Campbell MA *et al*. Use of psyllium in the management of chronic nonspecific diarrhea of childhood. *J Pediatr Gastroenterol Nutr* 1982;1:361–3.
- Sherman DS, Fish DN. Management of protease inhibitor-associated diarrhea. *Clin Infect Dis* 2000;30:908–14.
- Fernandez-Banares F, Hinojosa J, Sanchez-Lombrana JL *et al*. Randomized clinical trial of *Plantago ovata* seeds (dietary fiber) as compared with mesalamine in maintaining remission in ulcerative colitis. Spanish group for the study of Crohn's disease and ulcerative colitis (GETECCU). *Am J Gastroenterol* 1999;94:427–33.
- Fujimori S, Gudis K, Mitsui K *et al*. A randomized controlled trial on the efficacy of synbiotic versus probiotic or prebiotic treatment to improve the quality of life in patients with ulcerative colitis. *Nutrition* 2009;25:520–5.
- Fujimori S, Tatsuguchi A, Gudis K *et al*. High dose probiotic and prebiotic cotherapy for remission induction of active Crohn's disease. *J Gastroenterol Hepatol* 2007;22:1199–204.
- Pittler MH, Ernst E. Dietary supplements for body-weight reduction: a systematic review. *Am J Clin Nutr* 2004;79:529–36.
- Salas-Salvado J, Farres X, Luque X *et al*. Effect of two doses of a mixture of soluble fibres on body weight and metabolic variables in overweight or obese patients: a randomised trial. *Br J Nutr* 2008;99:1380–7.
- Rodriguez-Moran M, Guerrero-Romero F, Lazcano-Burciaga G. Lipid- and glucose-lowering efficacy of *Plantago Psyllium* in type II diabetes. *J Diabetes Complications* 1998;12:273–8.
- Moreyra AE, Wilson AC, Koraym A. Effect of combining psyllium fiber with simvastatin in lowering cholesterol. *Arch Intern Med* 2005;165:1161–6.
- Romero AL, West KL, Zern T *et al*. The seeds from *Plantago ovata* lower plasma lipids by altering hepatic and bile acid metabolism in guinea pigs. *J Nutr* 2002;132:1194–8.
- de Bock M, Derraik JG, Brennan CM *et al*. Psyllium supplementation in adolescents improves fat distribution & lipid profile: a randomized, participant-blinded, placebo-controlled, crossover trial. *PLoS One* 2012;7:e41735.
- Anderson JW, Allgood LD, Turner J *et al*. Effects of psyllium on glucose and serum lipid responses in men with type 2 diabetes and hypercholesterolemia. *Am J Clin Nutr* 1999;70:466–73.
- Levin EG, Miller VT, Muesing RA *et al*. Comparison of psyllium hydrophilic mucilloid and cellulose as adjuncts to a prudent diet in the treatment of mild to moderate hypercholesterolemia. *Arch Intern Med* 1990;150:1822–7.
- Pastors JG, Blaisdell PW, Balm TK *et al*. Psyllium fiber reduces rise in postprandial glucose and insulin concentrations in patients with non-insulin-dependent diabetes. *Am J Clin Nutr* 1991;53:1431–5.
- Sierra M, Garcia JJ, Fernandez N *et al*. Therapeutic effects of psyllium in type 2 diabetic patients. *Eur J Clin Nutr* 2002;56:830–42.
- Slavin JL. Position of the American Dietetic Association: health implications of dietary fiber. *J Am Diet Assoc* 2008;108:1716–31.
- Cummings JH, Macfarlane GT. The control and consequences of bacterial fermentation in the human colon. *J Appl Bacteriol* 1991;70:443–59.
- Cummings JH, Macfarlane GT, Englyst HN. Prebiotic digestion and fermentation. *Am J Clin Nutr* 2001;73:415S–20S.
- Todesco T, Rao AV, Bosello O *et al*. Propionate lowers blood glucose and alters lipid metabolism in healthy subjects. *Am J Clin Nutr* 1991;54:860–5.
- Topping DL, Clifton PM. Short-chain fatty acids and human colonic function: roles of resistant starch and nonstarch polysaccharides. *Physiol Rev* 2001;81:1031–64.
- Roediger WE. Utilization of nutrients by isolated epithelial cells of the rat colon. *Gastroenterology* 1982;83:424–9.
- Flamm G, Glinsmann W, Kritchevsky D *et al*. Inulin and oligofructose as dietary fiber: a review of the evidence. *Crit Rev Food Sci Nutr* 2001;41:353–62.
- Davies GJ, Crowder M, Reid B *et al*. Bowel function measurements of individuals with different eating patterns. *Gut* 1986;27:164–9.
- McRorie J, Greenwood-Van Meerveld B, Rudolph C. Characterization of propagating contractions in proximal colon of ambulatory mini pigs. *Dig Dis Sci* 1998;43:957–63.
- Heizer WD, Southern S, McGovern S. The role of diet in symptoms of irritable bowel syndrome in adults: a narrative review. *J Am Diet Assoc* 2009;109:1204–14.
- Chouinard LE. The role of psyllium fibre supplementation in treating irritable bowel syndrome. *Can J Diet Pract Res* 2011;72:e107–14.
- Bijkerk CJ, Muris JW, Knottnerus JA *et al*. Systematic review: the role of different types of fibre in the treatment of irritable bowel syndrome. *Aliment Pharmacol Ther* 2004;19:245–51.
- Biesiekierski JR, Rosella O, Rose R *et al*. Quantification of fructans, galacto-oligosaccharides and other short-chain carbohydrates in processed grains and cereals. *J Hum Nutr Diet* 2011;24:154–76.
- Hunt R, Fedorak R, Frohlich J *et al*. Therapeutic role of dietary fibre. *Can Fam Physician* 1993;39:897–900, 3–10.
- Elia M, Cummings JH. Physiological aspects of energy metabolism and gastrointestinal effects of carbohydrates. *Eur J Clin Nutr* 2007;61(Suppl 1):S40–74.
- Burkitt DP, Walker AR, Painter NS. Effect of dietary fibre on stools and the transit-times, and its role in the causation of disease. *Lancet* 1972;2:1408–12.
- Stephen AM, Cummings JH. Mechanism of action of dietary fibre in the human colon. *Nature* 1980;284:283–4.
- Tomlin J, Read NW. The relation between bacterial degradation of viscous polysaccharides and stool output in human beings. *Br J Nutr* 1988;60:467–75.
- Riottot M, Sacquet E, Leprince C. Effect of wheat bran upon gastrointestinal transit in germ-free and conventional rats. *Digestion* 1984;29:37–41.
- Tomlin J, Read NW. Laxative properties of indigestible plastic particles. *BMJ* 1988;297:1175–6.
- Lewis SJ, Heaton KW. Roughage revisited: the effect on intestinal function of inert plastic particles of different sizes and shape. *Dig Dis Sci* 1999;44:744–8.
- Camilleri M. Management of the irritable bowel syndrome. *Gastroenterology* 2001;120:652–68.

48. Camilleri M, Heading RC, Thompson WG. Clinical perspectives, mechanisms, diagnosis and management of irritable bowel syndrome. *Aliment Pharmacol Ther* 2002;16:1407–30.
49. Hamer HM, Jonkers D, Venema K *et al*. Review article: the role of butyrate on colonic function. *Aliment Pharmacol Ther* 2008;27:104–19.
50. Gonlachanvit S, Coleski R, Owyang C *et al*. Inhibitory actions of a high fibre diet on intestinal gas transit in healthy volunteers. *Gut* 2004;53:1577–82.
51. McRorie J, Pepple S, Rudolph C. Effects of fiber laxatives and calcium docusate on regional water content and viscosity of digesta in the large intestine of the pig. *Dig Dis Sci* 1998;43:738–45.
52. Marlett JA, Fischer MH. The active fraction of psyllium seed husk. *Proc Nutr Soc* 2003;62:207–9.
53. Bergmann JF, Chassany O, Petit A *et al*. Correlation between echographic gastric emptying and appetite: influence of psyllium. *Gut* 1992;33:1042–3.
54. Rigaud D, Paycha F, Meulemans A *et al*. Effect of psyllium on gastric emptying, hunger feeling and food intake in normal volunteers: a double blind study. *Eur J Clin Nutr* 1998;52:239–45.
55. Bianchi M, Capurso L. Effects of guar gum, ispaghula and microcrystalline cellulose on abdominal symptoms, gastric emptying, oro-caecal transit time and gas production in healthy volunteers. *Dig Liver Dis* 2002;34(Suppl 2): S129–33.
56. Frost GS, Brynes AE, Dhillon WS *et al*. The effects of fiber enrichment of pasta and fat content on gastric emptying, GLP-1, glucose, and insulin responses to a meal. *Eur J Clin Nutr* 2003;57:293–8.
57. Kawasaki N, Suzuki Y, Urashima M *et al*. Effect of gelatinization on gastric emptying and absorption. *Hepatogastroenterology* 2008;55:1843–5.
58. Grimes DS, Goddard J. Gastric emptying of wholemeal and white bread. *Gut* 1977;18:725–9.
59. Meyer JH, Gu Y, Elashoff J *et al*. Effects of viscosity and fluid outflow on postcibal gastric emptying of solids. *Am J Physiol* 1986;250:G161–4.
60. Russell J, Bass P. Canine gastric emptying of fiber meals: influence of meal viscosity and antroduodenal motility. *Am J Physiol* 1985;249:G662–7.
61. Vincent R, Roberts A, Frier M *et al*. Effect of bran particle size on gastric emptying and small bowel transit in humans: a scintigraphic study. *Gut* 1995;37:216–9.
62. Timm DA, Stewart ML, Hospattankar A *et al*. Wheat dextrin, psyllium, and inulin produce distinct fermentation patterns, gas volumes, and short-chain fatty acid profiles *in vitro*. *J Med Food* 2010;13:961–6.
63. Soret R, Chevalier J, De Coppet P *et al*. Short-chain fatty acids regulate the enteric neurons and control gastrointestinal motility in rats. *Gastroenterology* 2010;138:1772–82.
64. Jouet P, Sabate JM, Coffin B *et al*. Fermentation of starch stimulates propagated contractions in the human colon. *Neurogastroenterol Motil* 2011;23:450–6, e176.
65. Zimmerman MA, Singh N, Martin PM *et al*. Butyrate suppresses colonic inflammation through HDAC1-dependent Fas upregulation and Fas-mediated apoptosis of T cells. *Am J Physiol Gastrointest Liver Physiol* 2012;302:G1405–15.
66. Klampfer L, Huang J, Sasazuki T *et al*. Inhibition of interferon gamma signaling by the short chain fatty acid butyrate. *Mol Cancer Res* 2003;1: 855–62.
67. Stempelj M, Kedinger M, Augenlicht L *et al*. Essential role of the JAK/STAT1 signaling pathway in the expression of inducible nitric-oxide synthase in intestinal epithelial cells and its regulation by butyrate. *J Biol Chem* 2007;282:9797–804.
68. Ropert A, Cherbut C, Rozé C *et al*. Colonic fermentation and proximal gastric tone in humans. *Gastroenterology* 1996;111:289–96.
69. Piche T, Zerbib F, Varannes SB *et al*. Modulation by colonic fermentation of LES function in humans. *Am J Physiol Gastrointest Liver Physiol* 2000;278:G578–84.
70. Piche T, des Varannes SB, Sacher-Huvelin S *et al*. Colonic fermentation influences lower esophageal sphincter function in gastroesophageal reflux disease. *Gastroenterology* 2003;124:894–902.
71. Roberfroid M. Prebiotics: the concept revisited. *J Nutr* 2007;137:830S–7S.
72. Gibson GR, Beatty ER, Wang X *et al*. Selective stimulation of bifidobacteria in the human colon by oligofructose and inulin. *Gastroenterology* 1995;108:975–82.
73. Bouhnik Y, Flourie B, Riottot M *et al*. Effects of fructo-oligosaccharides ingestion on fecal bifidobacteria and selected metabolic indexes of colon carcinogenesis in healthy humans. *Nutr Cancer* 1996;26:21–9.
74. Kleessen B, Sykura B, Zunft HJ *et al*. Effects of inulin and lactose on fecal microflora, microbial activity, and bowel habit in elderly constipated persons. *Am J Clin Nutr* 1997;65:1397–402.
75. Roberfroid MB, Van Loo JA, Gibson GR. The bifidogenic nature of chicory inulin and its hydrolysis products. *J Nutr* 1998;128:11–9.
76. Silk DB, Davis A, Vulevic J *et al*. Clinical trial: the effects of a trans-galactooligosaccharide prebiotic on faecal microbiota and symptoms in irritable bowel syndrome. *Aliment Pharmacol Ther* 2009;29:508–18.
77. Trowell H. Definition of dietary fiber and hypotheses that it is a protective factor in certain diseases. *Am J Clin Nutr* 1976;29:417–27.
78. Burkitt DP, Meisner P. How to manage constipation with high-fiber diet. *Geriatrics* 1979;34:33–5, 8–40.
79. Tucker DM, Sandstead HH, Logan Jr GM *et al*. Dietary fiber and personality factors as determinants of stool output. *Gastroenterology* 1981;81:879–83.
80. Johanson JF, Kralstein J. Chronic constipation: a survey of the patient perspective. *Aliment Pharmacol Ther* 2007;25:599–608.
81. Locke 3rd GR, Pemberton JH, Phillips SF. AGA technical review on constipation. American Gastroenterological Association. *Gastroenterology* 2000;119:1766–78.
82. Rao SS. Constipation: evaluation and treatment of colonic and anorectal motility disorders. *Gastroenterol Clin North Am* 2007;36:687–711, x.
83. Marteau P, Flourie B, Cherbut C *et al*. Digestibility and bulking effect of ispaghula husks in healthy humans. *Gut* 1994;35:1747–52.
84. Payler DK, Pomare EW, Heaton KW *et al*. The effect of wheat bran on intestinal transit. *Gut* 1975;16:209–13.
85. Tramonte SM, Brand MB, Mulrow CD *et al*. The treatment of chronic constipation in adults. A systematic review. *J Gen Intern Med* 1997;12: 15–24.
86. Jones MP, Talley NJ, Nuyts G *et al*. Lack of objective evidence of efficacy of laxatives in chronic constipation. *Dig Dis Sci* 2002;47:2222–30.
87. Irvine EJ, Whitehead WE, Chey WD *et al*. Design of treatment trials for functional gastrointestinal disorders. *Gastroenterology* 2006;130: 1538–51.
88. Soares NC, Ford AC. Systematic review: the effects of fibre in the management of chronic idiopathic constipation. *Aliment Pharmacol Ther* 2011;33:895–901.
89. Fenn GC, Wilkinson PD, Lee CE *et al*. A general practice study of the efficacy of Regulan in functional constipation. *Br J Clin Pract* 1986;40: 192–7.
90. Ashraf W, Park F, Lof J *et al*. Effects of psyllium therapy on stool characteristics, colon transit and anorectal function in chronic idiopathic constipation. *Aliment Pharmacol Ther* 1995;9:639–47.
91. Nunes F, Nunes C, Levis E. A double-blind trial of a celandin, aloevera and psyllium laxative preparation in adult patients with constipation. *Rev Bras Med* 2005;62:352–7.
92. Lopez Roman J, Martinez Gonzalez A, Luque A. Efecto de la ingesta de un preparado lacteo con fibra dietetica sobre el estreñimiento cronic primario idiopatico. *Nutr Hosp* 2008;23:12–9.
93. Badiali D, Corazziari E, Habib FI *et al*. Effect of wheat bran in treatment of chronic nonorganic constipation. A double-blind controlled trial. *Dig Dis Sci* 1995;40:349–56.
94. Hongisto SM, Paajanen L, Saxelin M *et al*. A combination of fibre-rich rye bread and yoghurt containing *Lactobacillus GG* improves bowel function in women with self-reported constipation. *Eur J Clin Nutr* 2006;60:319–24.
95. Hamilton JW, Wagner J, Burdick BB *et al*. Clinical evaluation of methylcellulose as a bulk laxative. *Dig Dis Sci* 1988;33:993–8.
96. Voderholzer WA, Schatke W, Muhldorfer BE *et al*. Clinical response to dietary fiber treatment of chronic constipation. *Am J Gastroenterol* 1997;92:95–8.
97. Mertz H, Naliboff B, Mayer E. Physiology of refractory chronic constipation. *Am J Gastroenterol* 1999;94:609–15.
98. Schiller LR. Review article: the therapy of constipation. *Aliment Pharmacol Ther* 2001;15:749–63.
99. Attaluri A, Donahoe R, Velestin J *et al*. Randomised clinical trial: dried plums (prunes) vs. psyllium for constipation. *Aliment Pharmacol Ther* 2011;33:822–8.
100. McRorie J, Zorich N, Riccardi K *et al*. Effects of olestra and sorbitol consumption on objective measures of diarrhea: impact of stool viscosity on common gastrointestinal symptoms. *Regul Toxicol Pharmacol* 2000;31:59–67.
101. Painter NS. Irritable or irritated bowel. *Br Med J* 1972;2:46.
102. Manning AP, Heaton KW, Harvey RF. Wheat fibre and irritable bowel syndrome. A controlled trial. *Lancet* 1977;2:417–8.
103. Prior A, Whorwell PJ. Double blind study of ispaghula in irritable bowel syndrome. *Gut* 1987;28:1510–3.

104. Lambert JP, Brunt PW, Mowat NA *et al*. The value of prescribed 'high-fibre' diets for the treatment of the irritable bowel syndrome. *Eur J Clin Nutr* 1991;45:601-9.
105. Francis CY, Whorwell PJ. Bran and irritable bowel syndrome: time for reappraisal. *The Lancet* 1994;344:39-40.
106. Bijkerk CJ, de Wit NJ, Stalman WA *et al*. Irritable bowel syndrome in primary care: the patients' and doctors' views on symptoms, etiology and management. *Can J Gastroenterol* 2003;17:363-8, quiz 405-6.
107. Saito YA, Locke III GR, Weaver AL *et al*. Diet and functional gastrointestinal disorders: a population-based case-control study. *Am J Gastroenterol* 2005;100:2743-8.
108. Bohn N, Storsrud S, Lindh A *et al*. Nutrition intake in patients with irritable bowel syndrome (IBS) compared with the general population. *Gastroenterology* 2011;140:S305.
109. Ford AC, Talley NJ, Spiegel BM *et al*. Effect of fibre, antispasmodics, and peppermint oil in the treatment of irritable bowel syndrome: systematic review and meta-analysis. *BMJ* 2008;337:a2313.
110. Lesbros-Pantoflickova D, Michetti P, Fried M *et al*. Meta-analysis: The treatment of irritable bowel syndrome. *Aliment Pharmacol Ther* 2004;20:1253-69.
111. Brandt LJ, Chey WD, Foxx-Orenstein AE *et al*. An evidence-based position statement on the management of irritable bowel syndrome. *Am J Gastroenterol* 2009;104(Suppl 1):S1-35.
112. Ruedert L, Quartero AO, de Wit NJ *et al*. Bulking agents, antispasmodics and antidepressants for the treatment of irritable bowel syndrome. *Cochrane Database Syst Rev* 2011, CD003460.
113. Jailwala J, Imperiale TF, Kroenke K. Pharmacologic treatment of the irritable bowel syndrome: a systematic review of randomized, controlled trials. *Ann Intern Med* 2000;133:136-47.
114. Zuckerman MJ. The role of fiber in the treatment of irritable bowel syndrome: therapeutic recommendations. *J Clin Gastroenterol* 2006;40:104-8.
115. Akehurst R, Kaltenthaler E. Treatment of irritable bowel syndrome: a review of randomised controlled trials. *Gut* 2001;48:272-82.
116. Bijkerk CJ, de Wit NJ, Muris JW *et al*. Soluble or insoluble fibre in irritable bowel syndrome in primary care? Randomised placebo controlled trial. *BMJ* 2009;339:b3154.
117. Miller V, Lea R, Agrawal A *et al*. Bran and irritable bowel syndrome: the primary-care perspective. *Dig Liver Dis* 2006;38:737-40.
118. Parisi G, Bottona E, Carrara M *et al*. Treatment effects of partially hydrolyzed guar gum on symptoms and quality of life of patients with irritable bowel syndrome. A multicenter randomized open trial. *Dig Dis Sci* 2005;50:1107-12.
119. Parisi GC, Zilli M, Miani MP *et al*. High-fiber diet supplementation in patients with irritable bowel syndrome (IBS): a multicenter, randomized, open trial comparison between wheat bran diet and partially hydrolyzed guar gum (PHGG). *Dig Dis Sci* 2002;47:1697-704.
120. Toskes PP, Connery KL, Ritchey TW. Calcium polycarbophil compared with placebo in irritable bowel syndrome. *Aliment Pharmacol Ther* 1993;7:87-92.
121. Aller R, de Luis DA, Izaola O *et al*. Effects of a high-fiber diet on symptoms of irritable bowel syndrome: a randomized clinical trial. *Nutrition* 2004;20:735-7.
122. Lucey MR, Clark ML, Lowndes J *et al*. Is bran efficacious in irritable bowel syndrome? A double blind placebo controlled crossover study. *Gut* 1987;28:221-5.
123. Villagra M, Boix J, Humbert P *et al*. Aleatory clinical study comparing otilonium bromide with a fiber-rich diet in the treatment of irritable bowel syndrome. *Ital J Gastroenterol* 1991;23:67-70.
124. Shepherd SJ, Parker FC, Muir JG *et al*. Dietary triggers of abdominal symptoms in patients with irritable bowel syndrome: randomized placebo-controlled evidence. *Clin Gastroenterol Hepatol* 2008;6:765-71.
125. Nanda RRJ, Smith H, Dudley CR, Jewell DP. Food intolerance and the irritable bowel syndrome. *Gut* 1989;30:1099-104.
126. King TS, Elia M, Hunter JO. Abnormal colonic fermentation in irritable bowel syndrome. *Lancet* 1998;352:1187-9.