

CLINICAL—ALIMENTARY TRACT

A Diet Low in FODMAPs Reduces Symptoms of Irritable Bowel Syndrome

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BACKGROUND & AIMS: A diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) often is used to manage functional gastrointestinal symptoms in patients with irritable bowel syndrome (IBS), yet there is limited evidence of its efficacy, compared with a normal Western diet. We investigated the effects of a diet low in FODMAPs compared with an Australian diet, in a randomized, controlled, single-blind, cross-over trial of patients with IBS. **METHODS:** In a study of 30 patients with IBS and 8 healthy individuals (controls, matched for demographics and diet), we collected dietary data from subjects for 1 habitual week. Participants then randomly were assigned to groups that received 21 days of either a diet low in FODMAPs or a typical Australian diet, followed by a washout period of at least 21 days, before crossing over to the alternate diet. Daily symptoms were rated using a 0- to 100-mm visual analogue scale. Almost all food was provided during the interventional diet periods, with a goal of less than 0.5 g intake of FODMAPs per meal for the low-FODMAP diet. All stools were collected from days 17–21 and assessed for frequency, weight, water content, and King's Stool Chart rating. **RESULTS:** Subjects with IBS had lower overall gastrointestinal symptom scores (22.8; 95% confidence interval, 16.7–28.8 mm) while on a diet low in FODMAPs, compared with the Australian diet (44.9; 95% confidence interval, 36.6–53.1 mm; $P < .001$) and the subjects' habitual diet. Bloating, pain, and passage of wind also were reduced while IBS patients were on the low-FODMAP diet. Symptoms were minimal and unaltered by either diet among controls. Patients of all IBS subtypes had greater satisfaction with stool consistency while on the low-FODMAP diet, but diarrhea-predominant IBS was the only subtype with altered fecal frequency and King's Stool Chart scores. **CONCLUSIONS:** In a controlled, cross-over study of patients with IBS, a diet low in FODMAPs effectively reduced functional gastrointestinal symptoms. This high-quality evidence supports its use as a first-line therapy. Clinical Trial number: ACTRN12612001185853.

Keywords: Clinical Trial; Food Intolerance; Abdominal Pain; Short-Chain Carbohydrates.

Despite irritable bowel syndrome (IBS) being the most common gastrointestinal condition presenting to gastroenterologists, therapy has been unsatisfactory. The majority of patients note food as a trigger of symptoms.^{1,2} Diet as a therapy, however, has not been a central platform for management, mainly because the evidence base for reduction or exclusion of specific foods such as wheat and dairy³ has been poor.

A diet with increasing evidence of efficacy for the management of IBS is the low fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) diet.⁴ FODMAPs⁵ are poorly absorbed short-chain carbohydrates including fructose (in excess of glucose), lactose, polyols, fructans, and galacto-oligosaccharides. Although individually shown to contribute to IBS symptoms,^{6–8} the concept of considering all of these sugars collectively as a treatment for IBS is relatively new.⁵ The potential benefits of restricting a spectrum of FODMAPs in the diet was first shown in a retrospective study that showed that 74% of selected patients with both IBS and fructose malabsorption responded well to restriction of fructose and fructans (and polyols if the patients noted symptom induction) of 2–40 months' duration.⁹ This then was followed up with a randomized, double-blinded, placebo-controlled, rechallenge trial using fructose and fructan, alone and in combination, in selected patients with IBS and fructose malabsorption who had responded to the diet.¹⁰ Symptoms were induced in 4 of 5 study participants on the individual and combined FODMAP solutions compared with fewer than 1 in 5 with placebo (glucose). The symptoms were dose-dependent and fructose and fructans had additive effects.¹⁰

Understanding of FODMAPs encompasses mechanisms of action, being luminal distension from their osmotic

Abbreviations used in this paper: FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, and polyol; FWC, fecal water content; IBS, irritable bowel syndrome; IBS-C, constipation-predominant irritable bowel syndrome; IBS-D, diarrhea-predominant irritable bowel syndrome; IBS-M, mixed diarrhea and constipation irritable bowel syndrome; IBS-U, neither diarrhea nor constipation irritable bowel syndrome; KSC, King's Stool Chart; VAS, visual analogue scale.

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effect¹¹ and rapid fermentation preferentially to hydrogen.¹² These findings, together with support of continually expanding food composition analysis, have led to widespread application of the low FODMAP diet to manage IBS symptoms throughout Australia and New Zealand, and in some parts of Europe and North America. In fact, a research center in the United Kingdom found the low FODMAP diet to be superior to their national guidelines in IBS management in a nonrandomized, comparative study.¹³

Despite the extensive use of this therapy, the only blinded, randomized, controlled trial of efficacy for the low FODMAP diet in unselected IBS subjects comprised a 2-day interventional trial comparing low FODMAP with a very high FODMAP diet in 15 patients with IBS¹²; few studies have included healthy controls. There is, therefore, a large gap in high-quality evidence of the efficacy of the low FODMAP diet compared with a diet of normal FODMAP content in unselected patients with IBS.

The present study aimed to fill the major gaps in evidence for the efficacy of the low FODMAP diet by performing a randomized, controlled, cross-over trial. This trial compared gastrointestinal symptoms over 3 weeks of a low FODMAP diet with moderate FODMAP intake on a typical Australian diet in unselected patients with IBS who had not previously received advice from a dietitian. As is best practice to investigate the effects of a specific dietary manipulation, all food was provided to patients who were naive to the diet.¹⁴ To determine the specificity of any observed effects to patients with IBS, a healthy control population also was included in the interventional study.

Materials and Methods

Participants

Patients with IBS according to Rome III criteria¹⁵ and healthy controls without gastrointestinal symptoms were recruited between April 2009 and June 2011 via advertisements in breath testing centers, community newspapers, and through word of mouth. Exclusion criteria comprised exclusion of celiac disease by duodenal biopsy and/or negative celiac serologic testing while consuming a gluten-rich diet and/or negative HLA-DQ2/DQ8 for IBS patients, previous abdominal surgery, and comorbid conditions such as diabetes. All patients must not have previously visited a dietitian for dietary management of IBS or currently taking any other therapies for IBS. Patients were not permitted to take pharmacologic agents to alter their symptoms (such as laxatives or antidiarrheal agents). Patients with IBS were assessed by a gastroenterologist to ensure inclusion and exclusion criteria were met and further investigations were performed if organic disease was implicated. Patients with IBS were subclassified further as diarrhea-predominant (IBS-D), constipation-predominant (IBS-C), those with both diarrhea and constipation (IBS-M), and those with neither diarrhea nor constipation (IBS-U).¹⁵ Past medical investigations were documented including results of any breath tests performed for sugar malabsorptions.

Study Protocol

During a habitual baseline week, participants recorded their dietary intake in a food diary and included details about ingredients, brands of foods (if appropriate), cooking methods, and quantity consumed. Participants recorded their baseline symptoms daily.

Participants then were randomized according to a computer-generated order to receive 21 days of a diet low in FODMAPs or 21 days of a diet containing FODMAP content of a typical Australian diet.¹⁶ Participants were blinded to the diets and almost all food was provided. After this 21-day diet, each participant entered a washout period of at least 21 days in which they resumed their usual diet and then crossed-over to the alternate diet. The second interventional diet was not commenced until the symptoms had returned to the same level as during the baseline period, as determined by direct questioning by a study investigator. From days 17 to 21 of both interventional periods, participants collected all feces. Participants were instructed to collect each stool in a supplied plastic container and to avoid urine contamination. The containers were sealed and immediately stored in a supplied portable -4°C freezer. Each container was marked with the date and time of stool passage. The freezers were transported and delivered to the laboratory within the week after the 5-day collection.

On day 19 of both interventional diets, participants collected hourly breath samples from 12 midday to 8 PM into breath collection bags and the content of hydrogen was analyzed via a Quintron BreathTracker Digital Microlyzer (Quintron Instrument Company, Milwaukee, WI).

All participants provided written informed consent before commencement of the study. The study protocol was approved by the Eastern Health and Monash University Human Research and Ethics Committees. The protocol was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12612001185853). All authors had access to the study data and reviewed and approved the final manuscript.

Interventional Diets

Almost all food, comprising 3 main meals and 3 snacks daily, was provided. Detailed meal plans specifying meals and quantities were supplied (Supplementary Table 1 and Supplementary Figure 1). However, participants were instructed to eat to their appetite, and additional food lists were provided so that they could purchase fresh perishable items and additional food if participants wanted more. The supplemented foods contained at least one FODMAP for those following the typical Australian diet or were low FODMAP of ≤ 0.5 g per sitting as previously described on the low FODMAP diet.¹⁰ If participants ate a meal outside of their home or wanted to include foods that were not specified on the supplied lists, they contacted the study investigator for guidance.

The study investigator (E.P.H.) and university research chef, assisted by 2 hospitality students, prepared all food in commercial kitchens. Meals were provided as frozen complete meals with instructions to thaw and warm either via microwave or oven. They were free of charge and delivered to participants' homes weekly. All food consumed was recorded in food diaries and adherence to the diet was based on these records. If a participant consumed a high FODMAP meal during the low FODMAP diet or had a day of no high FODMAP-

containing foods¹⁷⁻¹⁹ during the typical Australian diet, that participant was considered noncompliant for that day.

The interventional diets were analyzed for energy, macronutrients, sugars, starch, and fiber via FoodWorks (Xyris Software Pty, Ltd, Brisbane, Queensland, Australia). Resistant starch was estimated from published data²⁰⁻²³ and both diets contained gluten. A daily average of 3 g psyllium and 5 g Hi-Maize 220 (National Starch & Chemical Company, Bridgewater, NJ) were mixed in with the meals of the low FODMAP diet to match the diets for fiber and resistant starch, respectively. The meal plans were aimed to provide an average of 8 MJ/day and to meet the recommended servings of all food groups according to the Australian dietary guidelines.²⁴ Both diets also aimed to be low in lactose (<5 g per sitting).²⁵ Because lactose is present in much higher concentrations in the diet than all other FODMAPs, the presence of lactase deficiency and subsequent malabsorption of large loads of lactose may mask the influence of the other FODMAPs. Dietary concentrations and absorption of all other FODMAPs is less variable.²⁶ The low FODMAP diet aimed to keep oligosaccharide, fructose in excess of glucose, and polyol content of less than 0.5 g each per sitting based on previously published data,¹⁰ and the typical Australian diet aimed to mimic the FODMAP content previously estimated by a validated food frequency questionnaire to be typically a daily content of 4.4 g oligosaccharides and 2.6 g polyols.¹⁶ The FODMAP content for all provided food underwent FODMAP analysis via high-performance liquid chromatography and enzymatic assays.

Gastrointestinal Symptoms

Gastrointestinal symptoms were measured daily during the baseline week and interventional diet periods using a 100-mm visual analogue scale (VAS), where 0 indicated no symptoms and 100 represented the worst symptoms ever experienced. The VAS score was used to measure overall gastrointestinal symptoms, abdominal pain, bloating, passage of wind, and dissatisfaction with stool consistency as previously applied.¹⁰ Differences of 10 mm or more arbitrarily were considered clinically significant.

Fecal Assessment

A single independent observer noted the fecal frequency, weighed each stool, and rated each stool using the validated King's Stool Chart (KSC),²⁷ which considers fecal frequency, consistency, and weight, and converts it to a daily numeric score. A higher score indicates more frequent, looser, and heavier stools.

To assess fecal water content (FWC), the 5-day fecal samples were defrosted, pooled, and thoroughly mixed, and then transferred into a small specimen container. Each sample was weighed and freeze-dried using Operon (Thermo Fisher Scientific Australia; Scoresby, Victoria, Australia), and then reweighed, which enabled the calculation of wet weight and dry weight. The FWC was expressed as a percentage.

End Points

The primary end point was the difference in overall gastrointestinal symptoms on the low FODMAP compared with a typical Australian diet averaged over the last 14 days of each

of the interventional dietary periods in the IBS cohort measured by the 100-mm VAS.

Secondary end points included differences in specific symptoms of abdominal pain, bloating, passage of wind, and dissatisfaction with stool consistency on the low FODMAP compared with a typical Australian diet averaged over the last 14 days of each diet in both the IBS and healthy cohorts measured by the 100-mm VAS; differences in gastrointestinal symptoms between the baseline and interventional dietary periods; and differences in fecal frequency, weight, FWC, and KSC score on the last 5 days of the low FODMAP diet compared with a typical Australian diet in the IBS and healthy cohorts.

Statistical Analysis

Power calculations were based on consensus opinion because previously published data were not suitable. The assumptions made were that the minimum detectable difference in the primary end point was 20 mm on the 100-mm VAS, and that the variance of that difference was 25 mm for an 80% power and a *P* value of .05. According to these assumptions, 27 IBS patients would be required for this positive treatment cross-over. No power calculations were conducted for healthy participants. Study recruitment continued until 30 IBS participants completed the study, at which time 8 healthy participants also had completed the study. Only participants who attempted both the low FODMAP and typical Australian diet were included in the analysis to enable better representation of the primary end point of symptom change between the 2 interventional diets. Symptom data of participants who ceased an interventional diet before the 21-day period were adjusted by carrying forward the last observation.

All descriptive data, including participant demographics, were parametric and presented as the mean and 95% confidence interval unless otherwise specified. A comparison of symptoms and fecal characteristics between participant groups was made by one-way analysis of variance with a post hoc Tukey multiple comparison analysis, and observations of differing treatment arms within participant groups were analyzed by paired *t* tests. Breath hydrogen data were nonparametric, summarized by area under the curve, and analyzed by Wilcoxon signed rank test. All statistical tests were analyzed with GraphPad Prism software (version 6; GraphPad Software, La Jolla, CA). A *P* value of .05 or less was considered statistically significant.

Results

Participants

Forty-five participants were recruited for the study. Seven participants (3 IBS and 4 healthy controls) quit the study before commencing their second diet and were excluded from analysis. Six of these 7 participants were female, with a median age of 28 years (interquartile range [IQR], 21-29 y), body mass index of 23.6 (IQR, 20.3-25.4), and none of them had undergone previous breath testing for fructose malabsorption. Five participants exited the study because the study protocol was too demanding (3 healthy participants exited after the first interventional diet, 1 IBS subject exited the study after 8 days of the low FODMAP diet, and 1 IBS subject exited the study after the baseline

Table 1. Comparison of Subject Demographics and Baseline Diet Characteristics Between IBS and Healthy Cohorts

	IBS (n = 30)	Healthy controls (n = 8)	P value
Demographics			
Female ^a	21 (70%)	6 (75%)	NS
Age, y ^b	41 (29–53)	31 (23–60)	NS
Body mass index ^b	24 (23–26)	24 (23–27)	NS
Fructose malabsorber ^c	17/22 (77%)	2/4 (50%)	NS
Baseline dietary intake			
Energy, MJ	9.1 [8.4–9.9]	8.3 [7.2–9.3]	NS
Protein, g	93.6 [84.1–103]	88.0 [74.2–102]	NS
Fat, g	87.8 [77.9–97.6]	78.8 [63.6–93.8]	NS
Carbohydrates, g	233 [205–260]	208 [158–259]	NS
Sugars, g	107 [87.8–127]	100 [63.4–137]	NS
Starch, g	138 [123–153]	116 [86.7–145]	NS
Fiber, g	24.0 [21.1–26.8]	20.6 [16.2–25.0]	NS
Total FODMAPs ^d	16.3 [14.1–18.5]	16.5 [11.4–21.8]	NS
Oligosaccharides, g	3.8 [3.3–4.3]	3.5 [2.7–4.3]	NS
Polyols, g	1.7 [1.3–2.1]	2.0 [0.7–3.3]	NS
Lactose, g	10.8 [8.5–13.1]	11.0 [7.0–15.1]	NS
Fructose, g	18.3 [13.9–22.7]	19.2 [8.6–29.8]	NS
Glucose, g	23.4 [17.4–29.3]	25.3 [13.2–37.4]	NS
Gluten	Present	Present	
Baseline gastrointestinal symptoms			
Overall	36.0 [29.5–42.5]	17.8 [4.0–31.7]	.012
Bloating	37.6 [29.6–45.6]	18.1 [4.9–31.2]	.022
Abdominal pain	35.5 [28.2–42.8]	14.8 [3.2–26.4]	.008
Passage of wind	39.0 [31.7–46.3]	23.1 [10.3–35.9]	.041
Dissatisfaction with stool consistency	35.1 [27.7–42.4]	21.2 [11.1–31.3]	.068

NOTE. Data are presented as mean [95% CI] and compared by unpaired *t* test except where specified. Statistically significant differences are shown in bold.

^an (percentage of total); the Fisher exact analysis was used.

^bMedian (IQR).

^cn/subjects who undertook breath hydrogen testing after ingestion of 35 g fructose (percentage of total); the Fisher exact analysis was used.

^dTotal FODMAP content does not include fructose in excess of glucose that cannot be estimated from the FoodWorks program.

diet), 1 healthy participant had an eating disorder emerge and exited the typical Australian diet after 12 days, and 1 IBS subject was removed for major protocol violation in which the participant did not adhere to the allocated low FODMAP diet for any of the 7 days that was completed before withdrawal. Of the remaining 38 participants, 30 had IBS and 8 were healthy controls. The IBS and healthy cohorts were well matched for sex, age, and body mass index, and 26 participants had breath hydrogen testing for fructose malabsorption (Table 1). Fourteen of the 22 IBS participants had performed breath testing before study enrolment and the remaining 8 participants performed breath testing shortly after study completion. Of the 4 healthy subjects who had performed fructose breath testing, 1 previously had participated in research involving breath

testing, 1 previously had been referred despite no presence of IBS, and 2 performed a breath test shortly after study completion. Of the 30 IBS participants, 10 had IBS-D, 13 had IBS-C, 5 had IBS-M, and 2 had IBS-U. Participants' baseline diets were similar with no obvious differences in any nutrients including energy, fiber, or FODMAPs (Table 1). All participants completed the study diets, except for 6 IBS participants who could not complete the typical Australian diet owing to unbearable symptoms. Their symptoms on exiting the study were carried forward for the remaining days on the typical Australian diet. In all participants, the level of symptoms returned to baseline levels during the washout period, but 5 participants with IBS extended this period for holidays and 3 for personal reasons. Three IBS and 1 healthy participant did not collect fecal samples on both diets, so fecal analysis was not included for these participants.

Interventional Diets

The nutritional composition of the interventional diets is shown in Table 2. The only quantified difference in nutrient content of the diets was the average daily intake of FODMAPs.

Symptoms

During the baseline period, the overall gastrointestinal symptoms in the IBS group were 36.0 mm on the VAS [95% CI, 29.5–42.5mm], which were of similar severity to previously published data.^{28,29} During the dietary intervention periods, the severity of overall gastrointestinal symptoms diverged, with the greatest difference seen after the first

Table 2. The Mean Daily Nutrition Information of Provided Low and Typical Australian FODMAP Diets

Per day	Typical Australian diet	Low FODMAP diet	P value
Energy, MJ	8.17 [7.37–8.97]	8.17 [7.09–9.24]	NS
Protein, g	96.1 [84.7–107]	98.1 [83.7–113]	NS
Fat, g	71.6 [49.4–93.8]	74.4 [51.9–97.0]	NS
Carbohydrate, g	219 [180–259]	215 [181–249]	NS
Sugars, g	120 [103–137]	122 [106–139]	NS
Starch, g	94.0 [52.8–135]	95.4 [59.7–131]	NS
Total dietary fiber, ^a g	29.7 [23.9–35.7]	30.4 [24.2–36.5]	NS
Fiber, g	25.9 [21.3–30.6]	23.4 [18.7–28.2]	NS
Resistant starch, g	3.74 [1.85–5.63]	6.93 [3.56–10.3]	NS
Total FODMAPs, g	23.7 [16.9–30.6]	3.05 [1.86–4.25]	<.001
Oligosaccharides, g	5.49 [2.34–8.65]	1.57 [0.47–2.66]	.009
Polyols, g	4.21 [2.57–5.85]	0.20 [-0.04 to 0.44]	.002
Lactose, g	1.35 [0.20–2.49]	0.05 [-0.01 to 0.10]	.033^b
Fructose in excess of glucose, g	12.7 [8.06–17.3]	1.24 [0.41–2.07]	.001
Gluten	Present	Present	

NOTE. Diets were matched for all nutrients except daily FODMAPs, indicated in bold (paired *t* test).

^aTotal dietary fiber comprises fiber and resistant starch.

^bAlthough there is a significant difference in lactose, 5 g lactose per sitting is considered well absorbed and tolerated in the majority of people.²⁵

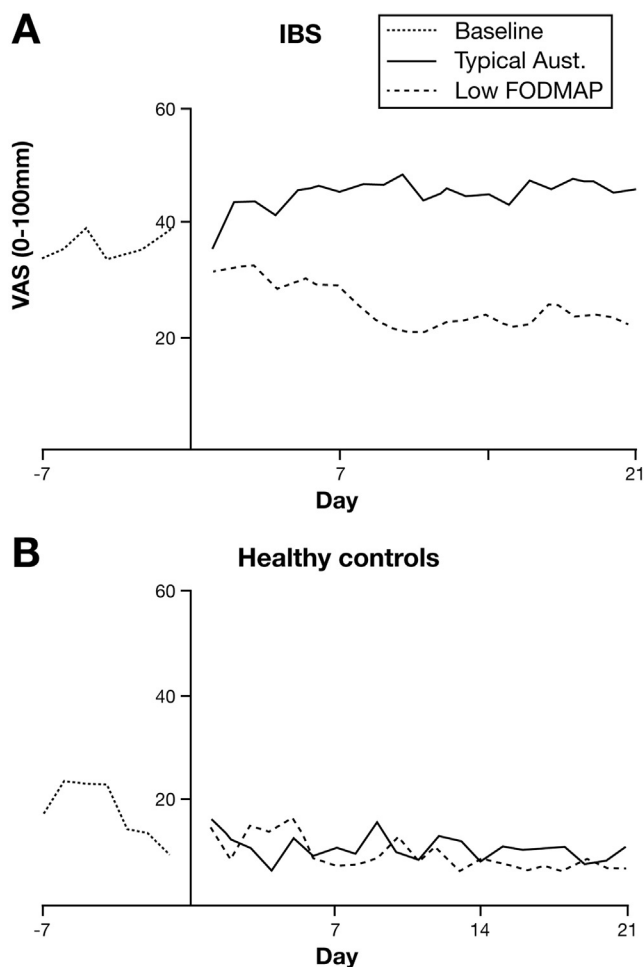


Figure 1. Mean overall gastrointestinal symptoms from the (A) IBS cohort and the (B) healthy cohort using a VAS during baseline, low FODMAP and typical Australian diets. Symptoms improved significantly on low FODMAP compared with baseline and the typical Australian diet for the IBS cohort. No differences were observed between any of the diets in the healthy cohort.

7 days, and thereafter was maintained (Figure 1A). Compared with baseline, the overall gastrointestinal symptoms in the last 14 days of the dietary intervention periods were less on the low FODMAP diet at 22.8 mm on the VAS [95% CI, 16.7–28.8 mm] ($P < .001$; repeated-measures analysis of variance) and greater on the typical Australian diet at 44.9 mm on the VAS [95% CI, 36.6–53.1 mm] ($P < .001$) (Figure 1A). The difference between the diets was statistically significant ($P < .001$). Improvement in overall gastrointestinal symptoms of more than 10 mm was observed in 21 of 30 participants (70%). This observation was of comparable proportion in IBS subjects with known positive fructose malabsorption (12 of 17; 70%), no fructose malabsorption (3 of 5; 60%), and those with no prior breath testing (6 of 8; 75%). Similar results were seen in abdominal pain, bloating, and passage of wind (Figure 2A–C), and dissatisfaction with stool consistency, in which the difference was observed in both the IBS-D and IBS-C subtypes (Figure 2D and E). The IBS-M and IBS-U subgroups were too small to analyze. The

scores for individual symptoms (bloating, abdominal pain, passage of wind, and dissatisfaction with stool consistency) as well as composite symptom scores of abdominal pain, bloating, and dissatisfaction with stool consistency are shown in Table 3.

The healthy subjects had very low scores at baseline for overall gastrointestinal symptoms 17.0 mm on the VAS [95% CI, 4.0–31.7mm]. During the dietary intervention arms, there was no evidence of any divergence of symptom severity between the diets. In fact, no change was observed for overall or individual symptoms (Figure 1C and Table 3).

Stool Analysis

The results of complete fecal samples that were collected over the last 5 days of each dietary period are shown in Supplementary Table 2.

Within the IBS group, no differences in the fecal indices were found across the subtypes with the exception of the KSC score, which was higher in the IBS-D group compared with the IBS-C group, but only on the typical Australian diet ($P = .002$). In the IBS-D subgroup, both the KSC score ($P < .001$) and the FWC ($P = .004$) were higher compared with healthy controls, again only on the typical Australian diet (Supplementary Figure 2).

As shown in Supplementary Table 2, the only significant differences in fecal characteristics were a lower KSC score and reduced stool frequency on the low FODMAP diet compared with the typical Australian diet in IBS-D subtype. No other differences were observed.

Adherence

Adherence to the diets was assessed through recorded food diaries. The median (range) number of days in which participants were adherent for the 42 days of the combined interventional diets was 41 (33–42) for the IBS and 42 (39–42) for the healthy cohort. If adherence for at least 17 days of the 21 days of controlled diet (>81% of the days) was arbitrarily considered compliant, then all participants were adherent to the typical Australian diet, and 80% of IBS participants (24 of 30) and 100% of healthy controls were adherent to the low FODMAP diet.

Another method of assessing adherence was the hourly breath tests that were conducted on day 19 of the 2 controlled diets (Supplementary Figure 3). The area under the curve for breath hydrogen on the low FODMAP diet (22.8 IQR, 14.3–44.4 ppm · 8 h) was less in all participants than that on the typical Australian diet (80.9 IQR, 46.8–159.8 ppm · 8 h; $P < .001$).

Success of Blinding

To assess the blinding of the diets, each participant was asked to identify the diet that they thought was designed to manage IBS symptoms on completion of the study. Thirty-one of 38 participants answered the question. In the subject groups, 17% of the IBS and 71% of the healthy participants could not correctly identify the low FODMAP diet. There was also no order effect because the ratio of

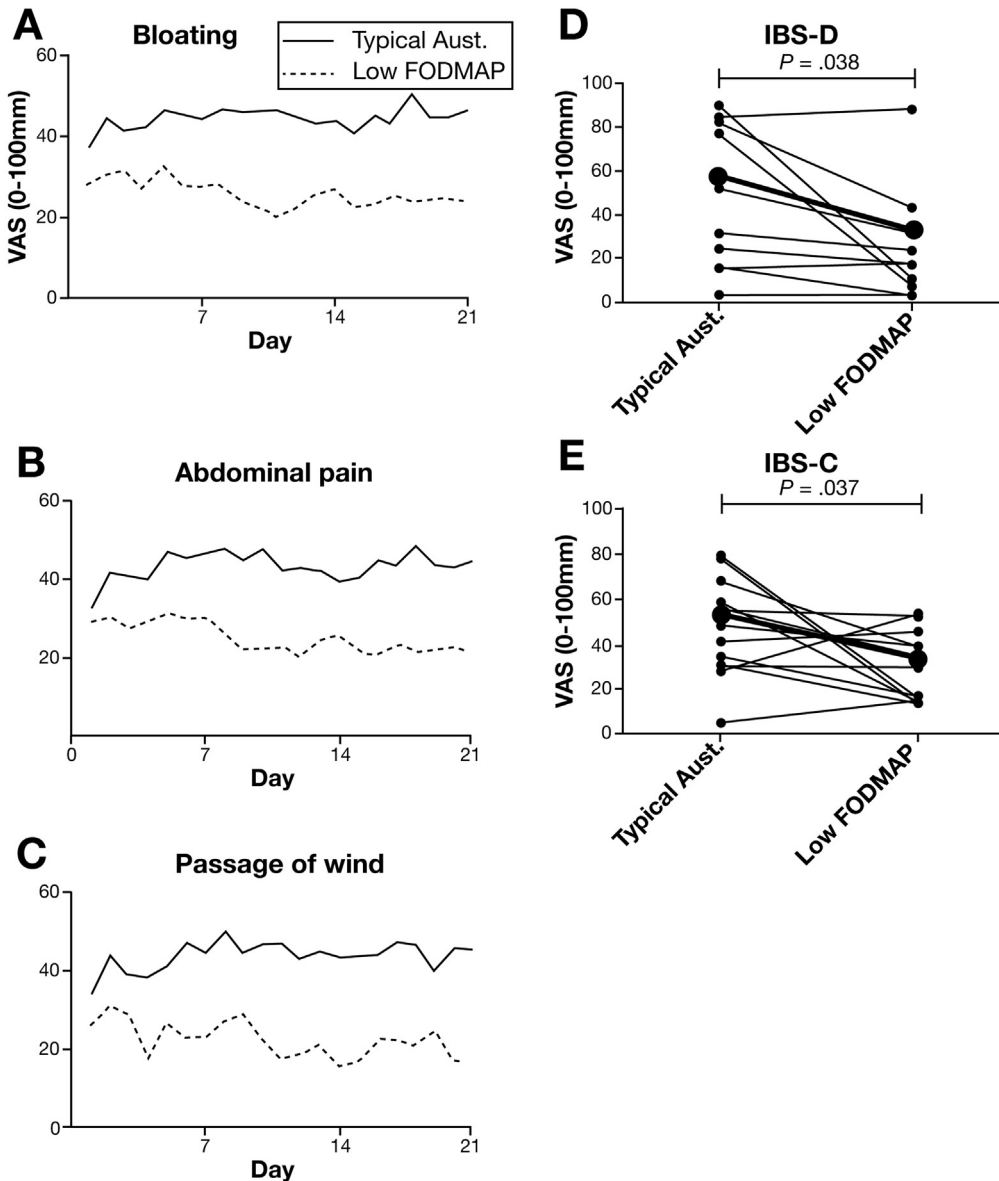


Figure 2. Mean symptoms of (A) bloating, (B) abdominal pain, and (C) passage of wind from the IBS cohort using a VAS while following a typical Australian and low FODMAP diet. Mean dissatisfaction with stool consistency in (D) IBS-D and (E) IBS-C after 8–21 days of typical Australian and low FODMAP diets are indicated with a *bold line*. Symptoms were significantly lower on low FODMAP compared with a typical Australian diet in all measured symptoms.

overall gastrointestinal symptoms on the low FODMAP to typical Australian diet was similar when the low FODMAP diet was given first (0.73; [95% CI], 0.41–1.04) compared with those participants in which it was given second (0.74; [95% CI], 0.46–1.01).

Discussion

Despite the growing popularity of the low FODMAP diet, efficacy data in unselected patients with IBS in which the effect of the diet on gastrointestinal symptoms is compared in a randomized, blinded manner with that of diet containing typical amounts of FODMAPs has been lacking. The results of the current study provide high-quality data to fill that gap. As highlighted by Figure 1, symptoms were more than halved in IBS subjects and all measured symptoms

were reduced to a level that arguably is considered good symptom control. The difference in symptoms between the 2 controlled diets was seen immediately and the greatest symptom control was achieved and maintained after 7 days of the low FODMAP diet. Interestingly, of the 70% of subjects who felt better on the low FODMAP diet, this encompassed subjects across all 4 subtypes of IBS. The presence of fructose malabsorption also had no bearing on the benefit of the low FODMAP diet. Because the interventional diets were provided and matched for all nutrients including fiber and resistant starch, results reflect the true influence of restricting dietary FODMAPs without confounding variables from other dietary components.

On evaluation of FODMAP intake on healthy controls, no difference was observed between the subjects' baseline diet and either of the controlled diets. Earlier studies have used

Table 3. Bloating, Abdominal Pain, Dissatisfaction With Stool Consistency, and Composite Scores of All Three Symptoms in IBS and Healthy Participants While Following Low FODMAP and Typical Australian Diets

Subject group	Diet	Bloating		Abdominal pain		Dissatisfaction with stool consistency		Composite scores	
		VAS (0–100 mm)		VAS (0–100 mm)		VAS (0–100 mm)		VAS (0–300 mm)	
IBS (n = 30)	Typical Australian	45.1 (35.1–55.0)	<i>P</i> < .001	43.8 (35.0–52.5)	<i>P</i> < .001	47.8 (37.6–57.9)	<i>P</i> < .001	137 (110–163)	<i>P</i> < .001
	Low FODMAP	24.2 (17.1–31.2)		22.5 (16.3–28.6)		25.9 (18.9–32.9)		73.1 (54.0–92.1)	
Healthy controls (n = 8)	Typical Australian	11.8 (5.9–17.8)	<i>P</i> = .742	9.6 (5.1–14.4)	<i>P</i> = .742	17.7 (7.5–27.9)	<i>P</i> = .547	38.7 (19.4–57.9)	<i>P</i> = .304
	Low FODMAP	10.4 (5.4–15.4)		9.1 (4.6–13.7)		10.1 (4.9–15.2)		29.6 (14.9–44.4)	

NOTE. Data from the last 14 days of the interventional diets were analyzed using repeated-measures analysis of variance. Statistically significant differences are shown in bold.

very high FODMAP diets or rechallenge solutions in comparison with a low FODMAP diet.^{8,10,12} However, it is known that FODMAPs will exert a laxative effect and increase gastrointestinal symptoms in the general population if taken in large enough doses.³⁰ Previous studies may have shown a biased benefit of the low FODMAP diet by exaggerating symptoms induced on the high FODMAP comparison.^{10,12} The typical Australian diet used in this study was designed to represent a usual dietary intake of FODMAPs, and, as such, was comparable with previously published data on the intake of healthy Australians.¹⁶ The importance of including healthy controls in this study was to ensure the typical Australian diet used did not induce symptoms in the general population. Indeed, symptoms remained low and were unaffected by the interventional study diets. In the subjects with IBS, symptoms still were greater on the typical Australian diet compared with participants on the baseline diet. This probably is because the oligosaccharide and polyol content of the diet fed to the patients was higher than their estimated intake on their baseline diet. This was a limitation of the present study and despite efforts to design a diet typical of the habitual intake of the recruited population, the oligosaccharide and polyol content was overestimated. Nevertheless, the FODMAP content of the typical Australian dietary arm was still much less than in previous studies in which high FODMAP intake was up to 4-fold greater,^{10,12} and the low FODMAP diet led to significantly lower levels of symptoms than observed during the baseline period. This reduction suggests that even if the FODMAP content of the typical Australian diet was overestimated, there was still a therapeutic benefit of the low FODMAP diet compared with their habitual diet in the patients studied.

Despite the significantly lower severity of gastrointestinal symptoms on the low FODMAP diet, little effect was seen on fecal indices. In fact, there was no clear impact of the low FODMAP compared with typical Australian diet on fecal frequency, weight, KSC score, or FWC, except in the IBS-D subjects, who had reduced fecal frequency and KSC

score on the low FODMAP diet. Unexpectedly, the score for subjective scoring of dissatisfaction of stool consistency was lower on the low FODMAP diet in all subtypes of IBS, despite the stool consistency being unchanged by altering FODMAP intake when assessed by the less subjective indices of FWC. This discrepancy may reflect differing perception of stool consistency when other symptoms, such as abdominal pain and bloating, were improved.

The strengths of the study included the comparison of the degree of symptom benefit of the low FODMAP diet compared with a typical Australian FODMAP intake, rather than high FODMAP intake. The measures put in place to minimize biased results such as recruiting FODMAP-naive patients and blinding participants to the provided diets also adds strength to the findings. In fact, assessment of blinding by questioning healthy subjects after the study and the lack of an order effect supported that the blinding was successful. The former method could not be applied to the patients with IBS because they were influenced by changes in symptoms. Despite no overt knowledge of the low FODMAP diet on enrolment questioning, it may be that the 14 IBS participants who had undergone breath testing before study enrolment had some prior knowledge because the breath testing protocol prescribes a diet low in FODMAPs and fiber for the day before testing. This may have been a point of reference for dietary identification. No differences were apparent in overall gastrointestinal symptoms in the interventional diets of IBS participants with prior breath testing compared with those with no prior breath testing. Baseline symptoms were also similar between those who had undergone breath testing and those who had not (data not shown).

Providing almost all food to participants facilitated a high degree of adherence to the study diets and the tightly controlled food consumption of the participants facilitated the accurate assessment of the influence of dietary FODMAPs rather than confounding factors on symptoms and fecal characteristics. The cross-over study design enabled a greater power of the study, particularly because each

participant acted as his/her own control, minimizing many potentially confounding variables. The application of such a design has been criticized in patients with IBS because of the uncertainties regarding a carry-over effect and the potential for patients withdrawing from the study substantially affecting the results.³¹ In the present study, the latter issue was not a major issue because only 3 patients in the IBS cohort dropped out after commencing the first dietary interventional arm. Furthermore, a carry-over effect on the severity of symptoms was not evident because symptoms appeared to return to the baseline level before crossing-over to the alternative diet within the planned washout period. However, potential changes in microbiota after the first diet and the possible unblinding of subjects when the second comparative diet was received both may have influenced the symptomatic response on the second diet. In addition, no formal protocol was in place to ensure symptoms returned to baseline severity. It was reassuring that no evidence of an order effect was identified.

A potential weakness was the way in which participants who stopped a dietary arm because of intolerable symptoms were handled. The assumed fixed symptom level that was carried forward from the 6 participants who ceased the typical Australian diet prematurely may inflate the mean symptom scores of this diet. Four of these 6 participants received the low FODMAP diet first, which again may accentuate the differences in symptoms between the controlled diets.

Although providing such a controlled diet is a strength in examining the role of FODMAPs in IBS, such a study design is not representative of reality. In life, the low FODMAP diet is dietitian-taught. Dietary restriction would have more varying degrees of compliance and depend on the patients' degree of understanding, food choices, and motivation for altering dietary habits, as well as the dietitians' advice on level of FODMAP restriction required. Furthermore, dietary fiber, including resistant starch, readily is found in high FODMAP foods such as wheat, rye, and legumes,²⁰ and, therefore, are at risk of being reduced on a low FODMAP diet if not supplemented. Dietary fiber accelerates transit and promotes laxation through contribution to fecal weight.^{32,33} A reduced fiber diet is likely to influence fecal characteristics and confound these study findings.

Because wheat, rye, and barley are FODMAP-containing grains, gluten, which also is present in these grains, inevitably also is reduced.³⁴ In the only studies to have examined gluten's effects independently of those of FODMAPs, symptoms induced were more severe in high vs zero gluten intake in one small parallel group study,³⁵ but no evidence of gluten-specific induction of symptoms (whether in high or low dose) was evident in a subsequent cross-over study in patients who believed themselves to be gluten-sensitive.²⁸ Nonetheless, because gluten could not be matched in the interventional diets, it could be a possible confounding factor.

In conclusion, the results of this study provide high-quality evidence that the low FODMAP diet is efficacious for treatment of functional gastrointestinal symptoms in unselected IBS with symptoms being halved compared with

a typical Australian diet. Furthermore, the symptomatic benefits of the low FODMAP diet are unlikely to be nonspecific because varying the intake of FODMAPs had no symptomatic effect on healthy controls. Self-assessed satisfaction with stool consistency also was improved in both IBS-D and IBS-C subgroups, although more objective markers were altered only in subjects with IBS-D. These results support the notion that the low FODMAP diet has efficacy in the vast majority of patients with IBS and support its use as a first-line therapy.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at <http://dx.doi.org/10.1053/j.gastro.2013.09.046>.

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Conflicts of interest

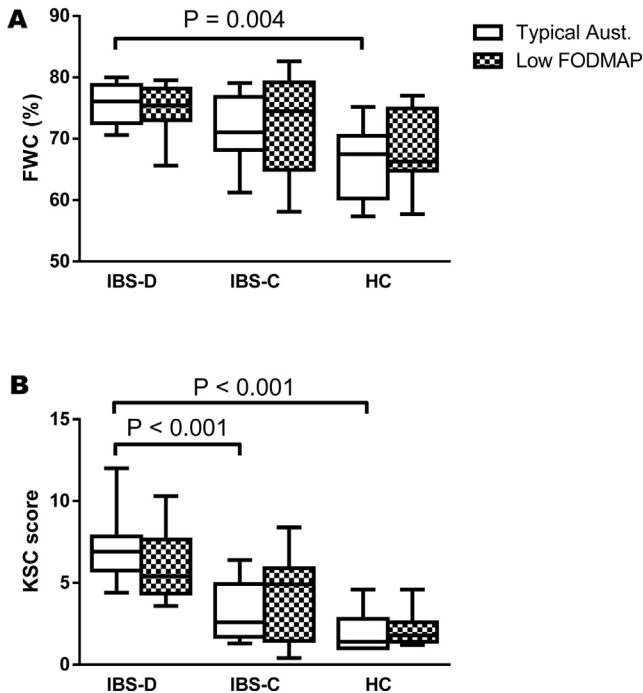
These authors disclose the following: Susan Shepherd has published a book on food intolerances and several cookbooks related to the topic of the article, and Peter Gibson has published a book on food intolerances. The remaining authors disclose no conflicts.

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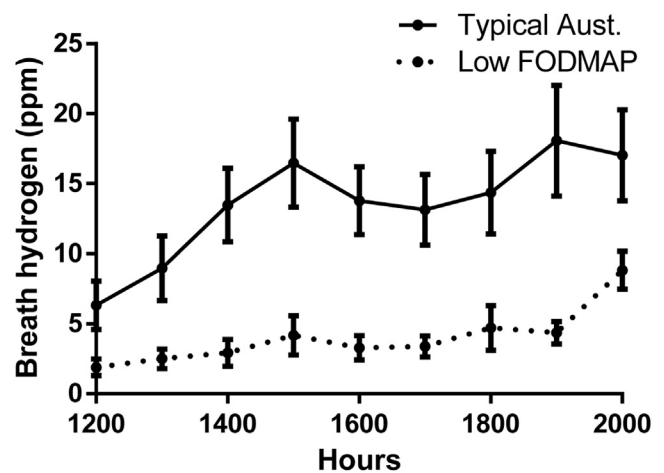
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Supplementary Figure 1. Photographs of example meals provided.



Supplementary Figure 2. Effects of dietary change on more objective markers of fecal characteristics across disease groups and IBS subtypes. (A) FWC was higher in the IBS-D cohorts compared with the healthy controls (HC) while following a typical Australian diet. (B) KSC scores were significantly higher in IBS-D participants compared with both IBS-C and healthy controls, indicating more frequent, looser, and heavier stools.



Supplementary Figure 3. Median breath hydrogen from 12 midday until 8 PM taken at hourly intervals following a typical Australian diet and low FODMAP diet in all participants (n = 28). The area under the curve indicates that less breath hydrogen was produced on the low FODMAP diet (median, 22.8 ppm; IQR, 14.3–44.4 ppm; 8 h) compared with the typical Australian diet (median, 80.9 ppm; IQR, 46.8–159.8 ppm; 8 h; $P < .001$; Wilcoxon signed rank test).

Supplementary Table 1. Weekly Meal Plans Detailing Meals and Quantities to Be Consumed for the Typical Australian Diet and Low FODMAP Diet

Meals	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Typical Australian diet							
Breakfast	2× wheat biscuit-type cereal with 1/2 cup lactose-free milk, 2 slices wheat toast with spread (list provided)	1/3 cup muesli with 1/2 cup lactose-free milk, lactose-free yogurt	Cup wheat flakes and dried fruit cereal with 1/2 cup lactose-free milk, 1 cup lactose-free milk	2× wheat biscuit-type cereal with 1/2 cup lactose-free milk, 2 slices wheat toast with spread (list provided)	Cup wheat flakes and dried fruit cereal with 1/2 cup lactose-free milk, packaged peaches	Apple quick oats with 1/2 cup lactose-free milk, 1 cup lactose-free milk	Honey quick oats with 1/2 cup lactose-free milk, packaged peaches
Morning tea	Apple, drink (list provided)	1 slice watermelon, drink (list provided)	Apple, drink (list provided)	Pear, drink (list provided)	2 rye crackers with cheese, drink (list provided)	Pear, drink (list provided)	Lactose-free yogurt, drink (list provided)
Lunch	Vegetable frittata, 1/2 cup apple juice	Chicken risotto, 1/2 cup apple juice	Wheat sandwich (fillings list provided), 1/2 cup apple juice	Mini pizza, 1/2 cup apple juice	Tomato roulade, 1/2 cup apple juice	Chicken crepe, 1/2 cup apple juice	Wheat sandwich (fillings list provided), cup apple juice
Afternoon tea	Muffin, drink (list provided)	2 chocolate biscuits, drink (list provided)	Flavored potato chips, drink (list provided)	2 chocolate biscuits, drink (list provided)	Apple, drink (list provided)	2 rye crackers and cheese, drink (list provided)	Pear, drink (list provided)
Dinner	Salmon with vegetables and couscous	Ratatouille with 100 g pasta	Shepherd's pie, beetroot salad (recipe provided)	Chicken stir-fry with 1/2 packet noodles	Soy and ginger fish with vegetables	Chicken kebabs, beetroot salad (recipe provided)	Braised lamb shanks with vegetables
Supper	1 slice watermelon, drink (list provided)	1/2 cup cherries, drink (list provided)	1/2 mango, lactose-free yogurt	1 slice watermelon, drink (list provided)	Chocolate brownie, drink (list provided)	1 slice watermelon, drink (list provided)	Apple sorbet, drink (list provided)
Low FODMAP diet							
Breakfast	Cup corn flakes with 1/2 cup lactose-free milk, 2 slices spelt toast with spread (list provided)	Plain quick oats with 1/2 cup lactose-free milk, lactose-free yogurt	Cup rice bubbles with 1/2 cup lactose-free milk, 1 cup lactose-free milk	Cup corn flakes with 1/2 cup lactose-free milk, 2 slices spelt toast with spread (list provided)	Cup rice bubbles with 1/2 cup lactose-free milk, 2 kiwi fruit	Plain quick oats with 1/2 cup lactose-free milk, 1 cup lactose-free milk	Brown sugar and cinnamon quick oats with 1/2 cup lactose-free milk, 2 kiwi fruit
Morning tea	Orange drink (list provided)	1 slice cantaloupe, drink (list provided)	Banana, drink (list provided)	Orange drink (list provided)	2 rice cakes with cheese, drink (list provided)	Banana, drink (list provided)	Lactose-free yogurt, drink (list provided)
Lunch	Vegetable frittata, cup cordial	Chicken risotto, cup cordial	Spelt sandwich (fillings list provided), cup cordial	Mini-pizza, cup cordial	Tomato roulade, 1/2 cup cordial	Chicken crepe, cup cordial	Spelt sandwich (fillings list provided), cup cordial
Afternoon tea	Muffin, drink (list provided)	2 gluten-free chocolate biscuits, drink (list provided)	Potato chips, drink (list provided)	2 gluten-free chocolate biscuits, cup cordial	Orange drink (list provided)	2 rice cakes with cheese, cup cordial	Banana, drink (list provided)

Supplementary Table 1. Continued

Meals	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Dinner	Salmon with vegetables and quinoa	Ratatouille with 150 g gluten-free pasta	Shepherd's pie, Greek salad (recipe provided)	Chicken stir fry with 1/2 packet rice	Soy and ginger fish with vegetables	Chicken kebabs with potato, Greek salad (recipe provided)	Braised lamb shanks with vegetables
Supper	1 slice cantaloupe, drink (list provided)	Cup grapes, drink (list provided)	1/2 cup strawberries, lactose-free yogurt	1 slice cantaloupe, drink (list provided)	Chocolate brownie, drink (list provided)	1 slice cantaloupe, drink (list provided)	Raspberry sorbet, drink (list provided)

NOTE. Meal plans were provided with all specified food, except where indicated in **bold**, and delivered to IBS and healthy participants weekly. Meal plans were repeated 3 times each over the interventional period.

Supplementary Table 2. Daily Fecal Frequency, Weight, KSC Score, and FWC in IBS and Healthy Participants After Following a Low FODMAP and Typical Australian Diet for 17 to 21 Days

Subject group	Diet	Fecal frequency: stools/day			Fecal weight, g/day	FWC, % of total weight	KSC score ²⁷				
		0	1–2	3–4							
IBS (n = 27)	Australian	0	26	1	<i>P</i> = .108	123 (104–149)	<i>P</i> = .449	73.3 (71.4–75.2)	<i>P</i> = .628	5.2 (4.0–6.4)	<i>P</i> = .396
	Low FODMAP	2	24	1		118 (96–157)		73.5 (71.2–75.8)		4.7 (3.5–5.8)	
IBS-D (n = 8)	Australian	0	7	1	<i>P</i> = .018	164 (121–207)	<i>P</i> = .641	75.7 (72.9–78.5)	<i>P</i> = .633	7.2 (5.4–9.1)	<i>P</i> = .034
	Low FODMAP	0	8	0		152 (114–191)		74.7 (71.0–78.3)		6.1 (4.2–7.9)	
IBS-C (n = 12)	Australian	0	12	0	<i>P</i> = .120	126 (112–141)	<i>P</i> = .224	71.4 (67.7–75.1)	<i>P</i> = .639	3.3 (2.1–4.5)	<i>P</i> = .094
	Low FODMAP	2	9	1		122 (99–145)		72.3 (67.4–77.2)		4.4 (2.4–6.3)	
IBS-M (n = 5)	Australian	0	5	0	<i>P</i> = .136	106 (66–146)	<i>P</i> = .438	73.5 (69.9–77.2)	<i>P</i> = .668	6.3 (1.3–11.3)	<i>P</i> = .223
	Low FODMAP	0	5	0		123 (74–172)		74.0 (70.2–77.9)		3.8 (-0.4 to 8.0)	
IBS-U (n = 2)	Australian	0	2	0	<i>P</i> = .157	106 (-97 to 309)	<i>P</i> = .278	74.4 (69.5–79.3)	<i>P</i> = .902	4.3 (-22.4 to 31.0)	<i>P</i> = .500
	Low FODMAP	0	2	0		99 (-149 to 346)		75.0 (18.8–131)		2.6 (-2.5 to 7.7)	
Healthy controls (n = 7)	Australian	2	5	0	<i>P</i> = .088	132 (107–158)	<i>P</i> = .813	66.3 (60.7–71.8)	<i>P</i> = .688	1.9 (0.7–3.2)	<i>P</i> = .172
	Low FODMAP	1	6	0		135 (92–179)		67.8 (61.8–73.8)		2.2 (1.1–3.3)	

NOTE. Statistically significant differences are shown in **bold**.