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Low-FODMAP Diet Is Associated With Improved Quality of Life in IBS Patients—A Prospective Observational Study

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Abstract

Background: The low fermentable oligosaccharide, disaccharide, monosaccharide, and polyol (FODMAP) diet is effectively manages irritable bowel syndrome (IBS) symptoms. Long-term low-FODMAP studies rarely report quality of life (QoL). We aimed to determine the effect of low-FODMAP diet on long-term QoL, gastrointestinal (GI) and non-GI symptoms in IBS patients. *Methods:* A prospective observational study of IBS patients referred for low-FODMAP dietary advice was performed. The primary outcome of QoL and secondary outcomes of GI symptoms, anxiety/depression, fatigue, sleep quality, and happiness were obtained at baseline, 6 weeks (T6), and 6 months (T26). *Results:* 111 patients were recruited. 91.0%, 71.6%, and 50.5% of participants completed baseline, T6, and T26 assessments, respectively. There were significant improvements in QoL from baseline at T6 and T26 (both $P < 0.001$). Significant reductions were seen in GI symptoms at T6 and T26 (both $P < 0.001$), fatigue at T6 and T26 (both $P < 0.003$), and anxiety at T6 and T26 (both $P < 0.007$), compared with baseline. A significant reduction was seen for depression ($P < 0.010$) from baseline at T26, and a significant increase was seen for both happiness and vitality (both $P < 0.04$) from baseline at T26. There was a significant correlation between GI symptom response and change in QoL, anxiety, depression, and fatigue (all $P < 0.034$). *Conclusion:* Low-FODMAP diet was associated with improved long-term QoL and GI symptoms, reduced fatigue and anxiety/depression, and increased happiness and vitality. These data support a wider range of benefits for IBS patients consuming a low-FODMAP diet. (*Nutr Clin Pract.* 2019;34:623–630)

Keywords

anxiety; depression; diarrhea; diet therapy; fatigue; FODMAP; irritable bowel syndrome; quality of life

Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) disorder characterized by abdominal pain and altered bowel habits (diarrhea or constipation).[1] In industrialized countries, IBS is one of the most common GI disorders presenting to general practitioners (GPs).[2,3] Its prevalence ranges from 7% to 20% globally, with a higher prevalence found in women and those under the age of 50 years.[2,4] Economically, IBS and related comorbidities place a significant burden on healthcare systems, societies, and individuals.[5,6]

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Conflicts of interest: C. H., J. L., L. O.'B., and J. S. B. are professional and registered dietitians who give dietary advice to patients with IBS in a private clinic on a regular basis. R. B. G. is a consultant gastroenterologist with a research and clinical interest in luminal gastroenterology including IBS. He is a director of Digestive Health Services Ltd, a private clinic specializing in gastrointestinal diagnostics.

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The pathophysiology of IBS and its comorbidities are incompletely understood, although a range of factors has been implicated, including alterations in the gut microbiome, immune system, motility and permeability, gut-brain interactions, genetics, and psychosocial factors.[1] Additionally, visceral afferent hypersensitivity may be increased in individuals with IBS compared with controls.[7] Visceral afferent hypersensitivity can predispose to symptoms in individuals with IBS caused by triggers such as stress or specific dietary factors.

IBS is associated with significant reductions in quality of life (QoL) and increased psychological distress including depression and anxiety.[8-10] These non-GI manifestations of IBS have been shown to play an enormous role in the morbidity experienced by IBS patients.[11,12]

IBS patients frequently identify diet as being a common trigger for symptoms and target for symptomatic therapy.[13] There has been a range of dietary interventions suggested for the treatment of IBS. However, the nature of whole-diet studies and inability to blind participants to such interventions inevitably leads to concerns regarding study quality.[14] The low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) diet has gained much attention recently as researchers and clinicians work to describe the mechanisms by which whole foods may lead to symptoms in those with IBS. FODMAPs are poorly absorbed and osmotically active short-chain carbohydrates that attract water into the small-intestinal lumen and are readily fermented by the colonic microbiota. There is evidence that subsequent increase in water and gas in the gut lumen is associated with luminal distention, which may trigger symptoms in patients with visceral hypersensitivity.[15-19]

Restriction of FODMAPs from the diet is associated with GI symptom improvement in up to 80% of IBS patients, which has been demonstrated in a range of retrospective and prospective studies.[20-23] Systematic reviews and meta-analyses also suggest short-term efficacy of low-FODMAP diet for the treatment of IBS.[24,25] However, there are limited data concerning the effect of low-FODMAP diet on global and non-GI outcomes such as QoL, anxiety, depression, vitality, and happiness.

Recently, Eswaran et al described the results of a randomized controlled trial of low-FODMAP diet compared with standard dietary advice, including a substudy describing QoL, anxiety, depression, and sleep as outcomes after 4 weeks of follow-up. Significant improvements were seen in each of these outcomes.[26] Similarly, Staudacher et al demonstrated improvements in some aspects but not overall QoL for low-FODMAP diet compared with a sham diet but also only after 4 weeks of follow-up.[27] Pedersen et al also performed a short-term (6-week) study of low-FODMAP diet compared with a probiotic diet and showed no improvement in QoL.[28] Finally, Harvie et al demonstrated an increase in QoL after 6 months of low-FODMAP diet in a relatively small cohort.[37] However, all in all, there are no or limited published data on these and related endpoints over longer time frames. This is important given the chronic nature of IBS and its significant impact on QoL, anxiety, and depression. In comparison, Maagaard et al described a range of endpoints in a mixed cohort of IBS and inflammatory bowel disease (IBD) patients over a mean follow-up of 16 months. However, this was performed retrospectively with no baseline data available prior to the intervention.[29]

Given the limited data concerning the effect of low-FODMAP diet on non-GI outcomes such as QoL, depression, anxiety, vitality, and happiness in patients with IBS, we aimed to measure these outcomes prospectively in IBS patients undergoing low-FODMAP diet intervention for up to 6 months.

Methods

Participants

The current study was a prospective observational nonrandomized study. Participants, who were referred to a dietitian for dietary consultation on the low-FODMAP diet, were recruited during a period of 12 months in private dietary centers in Christchurch (New Zealand) and Melbourne (Australia). Patients between 16 and 75 years of age at the time of recruitment and who had been referred to a dietitian for treatment of their IBS symptoms with the low-FODMAP diet by a GP or gastroenterologist were eligible for inclusion. Patients had to meet the Rome III criteria for IBS. Exclusion criteria comprised coexistence of the following: significant GI disease (eg, celiac disease, IBD, bowel resection), type 1 or 2 diabetes mellitus, pregnancy, or a previous and unsuccessful attempt to alleviate GI symptoms with the low-FODMAP diet while under the guidance of a trained dietitian.

All participants were either recruited at their initial appointment with a dietitian or at breath-testing sessions prior to their appointment with a dietitian where this had been arranged. All participants provided written informed consent and additional medical and nutrition details, including a list of current medication, medical history, use of dietary supplements (eg, fiber, probiotics, and laxatives), and lifestyle characteristics. Follow-up evaluations occurred at week 6 (T6) and at week 26 (T26) following the intervention.

Dietary Advice

Participants consulted a dietitian experienced in the delivery of the low-FODMAP diet at baseline for treatment of IBS symptoms. During this initial 60-minute appointment, a global explanation of the physiology and mechanisms of the low-FODMAP diet in IBS patients was explained. In

addition, a requested 7-day food diary of patients' normal dietary habits was reviewed and subsequently compared to the dietary components of the low-FODMAP diet. Adjustments were made when necessary and communicated to the participant. Complementary written information on the low-FODMAP diet was provided to stimulate understanding and adherence. This information included a list of foods that should be avoided, foods that could be eaten in small amounts, and foods that could be eaten at all times; a low-FODMAP shopping list including products from popular and broadly available brands; and recipes of low-FODMAP meals. A follow-up consultation was conducted at 6 weeks to teach participants how to identify food triggers and how to modify their diet to include high-FODMAP foods they are able to tolerate. This protocol has been used in previous studies that have assessed low-FODMAP diet efficacy.[21,30]

Endpoints

The primary endpoint was the difference in QoL score measured with the IBS-QoL questionnaire between the final follow-up (T26) and baseline. The IBS-QoL consists of 34 items that produce an overall score and 8 subscale scores including dysphoria, interference with activity, body image, health worry, food avoidance, social reaction, sexual activity, and relationships. Secondary endpoints comprised changes in GI symptoms, symptoms of depression and anxiety, fatigue, sleep, vitality, and happiness at both follow-up points (T6 and T26). Additional secondary endpoints included correlations between changes in GI symptoms and non-GI outcomes.

Assessment

Participants completed an online questionnaire at baseline and were subsequently introduced to the low-FODMAP diet. At the first follow-up point, after 6 weeks on the low-FODMAP diet, participants were sent the second questionnaire via email. Participants were also invited to attend a follow-up consultation with a dietitian as part of standard treatment. Six months from the start of the low-FODMAP diet, participants were sent the third questionnaire. All 3 validated questionnaires comprised the IBS-QoL, Gastrointestinal Symptom Rating Scale (GSRS), State-Trait Personality Inventory (psychological indices concerning depression and anxiety), Fatigue Impact Scale (Fatigue), Karolinska Sleep Questionnaire (Sleep quantity and quality), Subjective Vitality Scale (Vitality), and the Happiness Measures (Happiness). The baseline questionnaire also included the Rome III criteria questionnaire.

Statistics

Statistical analysis was performed using IBM SPSS Statistics 23 (Armonk, NY, USA: IBM Corp.). Each variable at baseline was compared with its score at T6 and T26 to determine the effects of the low-FODMAP diet on medium- and long-term in individual variables. Parametric paired *t*-tests were performed on continues variables (IBS-QOL score, State-trait Personality Inventory score, Fatigue Impact Scale score, and Subjective Vitality Scale score). The Wilcoxon signed-rank test (nonparametric) was used for ordinal variables (GSRS, Karolinska sleep questionnaire, and the Happiness measure). Spearman's rank order test was used to investigate the correlation between changes in individual non-GI outcomes and changes in GI symptom score following low-FODMAP diet, as well as adherence to the low-FODMAP diet. All statistical significance was assessed at $P < 0.05$ (2-tailed).

The analyses were performed on a per-protocol basis but repeated using intention-to-treat analyses whereby those who did not complete follow-up assessments (nonrepliers) were assumed to have had no change from their baseline questionnaire.

The study received ethical approval from the University of Otago Human Ethics Committee (Ref H15/116) and the Monash University Human Research Ethics Committee (H15/116).

Table 1. Characteristics of the Participants.

Characteristics	Baseline n = 101	T6 n = 73	T26 n = 56
Female, n (%)	84 (83%)	63 (86%)	51 (91%)
Age (years), mean (SD)	41.9 (16.0)	44.3 (16.3)	45.6 (16.0)
Subtype IBS			
IBS-C; n (%)	12 (12%)	4 (6%)	4 (7%)
IBS-D; n (%)	42 (41%)	29 (39%)	25 (45%)
IBS-U; n (%)	4 (4%)	1 (1%)	1 (2%)
IBS-M; n (%)	44 (43%)	39 (54%)	26 (46%)

IBS-C, irritable bowel syndrome, constipation type; IBS-D, irritable bowel syndrome, diarrhea type; IBS-M, irritable bowel syndrome, mixed-type; IBS-U, irritable bowel syndrome, unsubtyped; T6, after 6 weeks; T26, after 26 weeks.

Results

A total of 111 patients with IBS were enrolled in this study. A total of 101 (91.9%), 73 (66.0%), and 56 (50.5%) patients had completed the baseline, T6, and T26 assessments, respectively. Most of the patients who enrolled in the study were women (83.3%) with the mean age of 41.9 years. The characteristics of the 3 groups are described in Table 1.

QoL

A significant improvement was seen in total IBS-QoL from baseline (65.7) at both T6 (72.5, $P < 0.001$) and T26 (77.1, $P < 0.001$) (Figure 1 and Table S1). In addition, QoL was significantly improved in almost all subdomains at both

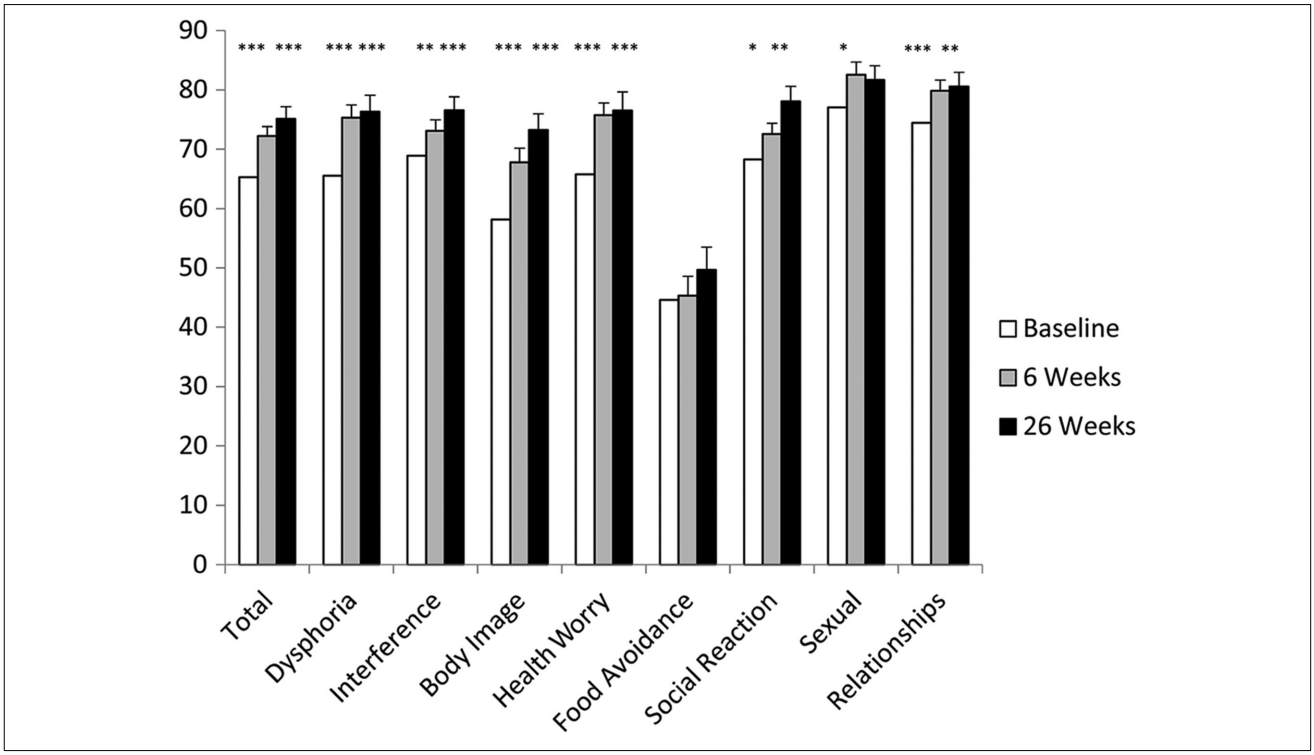

Figure 1. Total and subscore quality of life results for participants with IBS at baseline, 6 weeks, and 26 weeks. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$. IBS, irritable bowel syndrome.

T6 and T26. Only the food avoidance ($P = 0.270$) and sexual ($P = 0.055$) subdomains did not improve significantly at T26.

GI symptoms, as measured using the GSRS, significantly improved from baseline (3.08) to T6 (2.51, $P < 0.001$) and T26 (2.50, $P < 0.001$) (Table 2). Significant improvement was seen in all GI symptoms with the exception of constipation ($P = 0.198$ and $P = 0.501$) and nausea ($P = 0.068$ and $P = 0.098$) for T6 and for T26, respectively (Table S2).

Improvement of Other Non-GI Symptoms

A significant improvement was seen for a range of other non-GI symptoms. Fatigue, as measured using the fatigue impact scale, improved significantly from baseline (45.8) to T6 (37.2, $P < 0.001$) and T26 (35.5, $P = 0.003$). This improvement in fatigue was seen across cognitive, physical, and social subdomains out to T26 ($P < 0.016$, $P < 0.014$, and $P < 0.003$, respectively) (Table S3). Anxiety, as measured using the State-Trait Personality Inventory, improved

Table 2. Overview of Scores at T6 and T26.

Symptom	n	Baseline Mean (SD)	n	T6 Mean (SD)	*P* (2-Tailed)	n	T26 Mean (SD)	*P* (2-Tailed)
QoL (total)	101	65.7 (19.5)	72	72.5 (19.7)	<0.001[a]	56	77.1 (19.8)	<0.001
GI (total)	101	3.08 (0.94)	73	2.51 (0.94)	<0.001[b]	56	2.5 (1.1)	<0.001
Fatigue (total)	98	45.8 (32.3)	70	37.2 (29.6)	<0.001[a]	53	35.5 (30.4)	0.003
Depression	99	19.5 (5.9)	71	18.6 (5.7)	0.090[a]	54	18.3 (5.8)	0.010
Anxiety	99	20.6 (5.5)	71	19.1 (5.5)	0.004[a]	54	19.0 (5.3)	0.007
Happiness	93	62.0 (18.8)	66	64.4 (17.2)	0.319[b]	49	66.6 (15.4)	0.035
Sleep	97	11.4 (5.2)	70	10.8 (4.8)	0.502[b]	51	10.5 (4.6)	0.239
Vitality	93	27.6 (9.2)	69	28.3 (9.3)	0.592[a]	49	30.8 (9.7)	0.032

GI, gastrointestinal symptoms; QoL, quality of life; T6, after 6 weeks; T26, after 26 weeks.
[a]Paired *t*-test performed on the T6 and T26 scores.
[b]Wilcoxon Signed Ranks Test performed on the T6 and T26 scores.

Table 3. Intention-to-Treat Analyses for Study Outcomes at T6 and T26.

Symptom	n	Baseline Mean (SD)	n	T6 Mean (SD)	*P* (2-Tailed)	*P* (2-Tailed) Assuming Nonrepliers did not Change Symptoms	n	T26 Mean (SD)	*P* (2-Tailed)	*P* (2-Tailed) Assuming Nonrepliers Did Not Change Symptoms
QoL (total)	101	65.7 (19.5)	72	72.5 (19.7)	<0.001[a]	<0.001[a]	56	77.1 (19.8)	<0.001[a]	0.018[a]
GI (total)	101	3.08 (0.94)	73	2.51 (0.94)	<0.001[b]	<0.001[b]	56	2.5 (1.1)	<0.001[a]	0.451[b]
Fatigue (total)	98	45.8 (32.3)	70	37.2 (29.6)	<0.001[a]	<0.001[a]	53	35.5 (30.4)	0.003[b]	0.08[b]
Depression	99	19.5 (5.9)	71	18.6 (5.7)	0.090[a]	<0.001[a]	54	18.3 (5.8)	0.010[b]	0.973[a]
Anxiety	99	20.6 (5.5)	71	19.1 (5.5)	0.004[a]	<0.001[a]	54	19.0 (5.3)	0.007[a]	0.756[a]
Happiness	93	62.0 (18.8)	66	64.4 (17.2)	0.319[b]	0.319[b]	49	66.6 (15.4)	0.035[b]	0.395[b]
Sleep	97	11.4 (5.2)	70	10.8 (4.8)	0.502[b]	0.753[b]	51	10.5 (4.6)	0.239[b]	0.973[b]
Vitality	93	27.6 (9.2)	69	28.3 (9.3)	0.592[a]	0.368[a]	49	30.8 (9.7)	0.032[a]	0.121[a]

GI, gastrointestinal symptoms; QoL, quality of life; T6, after 6 weeks; 26, after 26 weeks.
[a]Paired *t*-test performed on the T6 and T26 scores.
[b]Wilcoxon Signed Ranks Test performed on the T6 and T26 scores.

significantly from baseline (20.6) to T6 (19.1, $P = 0.004$) and T26 (19.0, $P = 0.007$).

Significant improvements from baseline were seen at T26 but not T6 for depression (State-Trait Personality Inventory, $P = 0.01$), happiness (Happiness Measures, $P = 0.035$), and vitality (Subjective Vitality Scale, $P = 0.032$), but no differences were seen for sleep (Karolinska Sleep Questionnaire, $P = 0.239$).

Intention-to-Treat Data

During the 6-month study period, a significant number of participants failed to complete all questionnaires out to T26, despite multiple reminders. Therefore, all analyses were repeated, including the nonrepliers, assuming that there had been no changes in the baseline score out to T6 and T26 time points as an intention-to-treat analysis. For the primary outcome of QoL, there remained a statistically significant improvement in the overall QoL ($P = 0.018$) at T26 in addition to the subdomains of interference with activity ($P = 0.025$), body image (0.006), and social reaction (0.006) (Table 3 and Table S4). Significant improvements in overall QoL and subdomains except food avoidance were present at T6 compared with baseline. However, using an intention-to-treat analysis, GI symptoms, fatigue, and anxiety were significantly improved at T6, but these improvements did not remain significant out to T26 (Table 3 and Tables S5 and S6).

GI Symptom Response and Non-GI Symptom Changes

We explored the relationships between changes in GI symptoms (assessed by GSRS) and nongastroenterological outcomes (Table 4). A significant correlation was found between changes in overall GI symptoms and changes in QoL, depression, and fatigue at both T6 ($P < 0.001$, $P < 0.008$, and $P < 0.001$, respectively) and T26 ($P < 0.001$, $P < 0.002$, and $P < 0.004$, respectively). However, such a relationship was only significant for changes in GI symptoms and anxiety between baseline and T26 ($r = 0.294$, $P < 0.028$) but not T6. No significant correlation was found between changes in overall GI symptoms and changes in happiness, sleep, and vitality from baseline at both T6 and T26.

Table 4. Correlation Between Changes in Overall Gastrointestinal Symptoms and Changes in Non-GI Symptoms.

	Δ GI Symptoms					
	T6			T26		
Δ Non-GI Symptoms	n	r	*P*[a]	n	r	*P*[a]
QoL	73	−0.564	0.000	56	−0.513	0.001
Anxiety	73	0.183	0.121	56	0.294	0.028
Depression	70	0.315	0.008	55	0.414	0.002
Fatigue	70	0.437	0.000	53	0.391	0.004
Happiness	67	0.213	0.401	50	−0.008	0.950
Sleep	67	−0.064	0.292	51	0.140	0.326
Vitality	67	0.092	0.295	49	−0.150	0.305

GI, gastrointestinal symptoms; QoL, quality of life; T6, after 6 weeks; T26, after 26 weeks.
[a]Spearman's rank order test performed on the T6 and T26 scores.

Discussion

IBS patients have a reduced QoL and a higher prevalence of associated non-GI symptoms, including anxiety, depression, fatigue, and sleep disturbance, compared with healthy individuals. These effects contribute to the significant morbidity

associated with IBS. This prospective observational study aimed to assess the effect of the low-FODMAP diet on QoL in addition to related global health outcomes at 6 and 26 weeks following the dietary intervention. In this prospective observational study, the low-FODMAP diet was found to be associated with an increase in IBS-related QoL (on both per-protocol and intention-to-treat analyses) at both 6 weeks and 26 weeks. This is one of the first studies to prospectively measure QoL in an IBS study examining low-FODMAP diet for longer than 6 weeks following the implementation of the diet. Given the chronic nature of IBS, therapies with sustained efficacy are important and clinically relevant.

The efficacy of low-FODMAP diet in improving GI symptoms in people with IBS has been demonstrated in a range of retrospective, prospective, uncontrolled, and controlled studies from multiple centers around the world.[21-23,27,31,32] In addition to clinical efficacy, there has been increasing work demonstrating the mechanisms of action, including microbiological, MRI, breath test, and metabolite studies.[16,17,19,33] While the mechanism of action for the effect of low-FODMAP diet on gastroenterological symptoms becomes clearer, it is worthwhile to consider secondary benefits from improving GI symptoms in people with IBS. Traditionally, interventions that target GI symptoms have been evaluated using GI symptom scales and, possibly, disease-specific or generic QoL instruments. However, frequently patients may accrue benefits over and above these, particularly when there are comorbid conditions such as anxiety, depression, and fatigue. In the present study, low-FODMAP diet was associated with a significant reduction in anxiety, depression, and fatigue and significant increases in happiness and vitality. Furthermore, improvements in anxiety, depression, and fatigue were significantly correlated with improvements in GI symptoms.

Whereas improvements in QoL were seen in multiple domains, as one might expect there were not significant improvements in the domains of food "avoidance" and "sexual," albeit the latter only just missing a statistical significance. The impact of food avoidance should not be underestimated, as some patients find following strict dietary interventions particularly difficult. However, for any given individual, the benefits of a low-FODMAP diet should be balanced by its inconvenience. Furthermore, the initial rigorous dietary exclusion should be followed by a reintroduction phase in order to limit potential risks of any restrictive diet, including nutrition inadequacy and promotion of disordered eating.[34] A significant proportion (37.5%) of the participants demonstrated a clinically significant improvement in QoL as measured by the validated IBS-QOL instrument (>14 points) at 26 weeks after initiation of the diet.[35,36] The magnitude of improvement of QoL is also similar to that seen in other dietary intervention studies of low-FODMAP diet in IBS patients.[26,37]

In addition to the comparison of follow-up and baseline scores of repliers who completed the questionnaires per protocol, an intention-to-treat analysis was performed assuming that nonrepliers did not change in their baseline or short-term follow-up score. At the first follow-up point, at which 73 participants replied to the questionnaire, improvements in QoL, GI symptom score, depression, anxiety, and fatigue all remained significant. However, at T26, only the improvement in QoL score remained significant. The intention-to-treat analysis is a conservative estimate of effect, and it may be argued that the per-protocol analysis reflects clinical practice best, as only those who respond to the treatment will continue and nonresponders will try other therapy alternatives. The high rate of nonrepliers in this study may be explained by the lack of personal contact during the follow-up stages of our study, during which email and online questionnaires were used.

Of the subdomains of the GSRS questionnaire, only constipation and nausea did not improve significantly on the low-FODMAP diet at both follow-up points. The failure of a significant improvement in constipation scores may be due to the relatively low number of participants with constipation-type IBS compared with diarrhea-type IBS. In addition, the osmotic effects of FODMAPs, which are reduced on a low-FODMAP diet, make improvements in those with constipation-predominant symptoms less likely to respond.

To our knowledge, this is the first study that demonstrated the beneficial effect of the low-FODMAP diet on fatigue in ambulatory patients with IBS. Interestingly, sleep quality did not significantly improve in this study, suggesting that fatigue in IBS patients may be a consequence of the daily occurrence of GI symptoms and related activities (eg, pain, frequent toilet visits) rather than sleep disturbance. This assumption is supported by the correlation between GI symptom severity and fatigue.

Finally, this study assessed psychological characteristics in the form of symptoms of depression and anxiety and perceived feelings of happiness and vitality. Symptoms of depression were correlated with GI symptom severity. Although this finding may be due to the indirect effect of somatic symptom improvement on psychological well-being, a direct effect of gut symptoms on the brain may not be ruled out.

Although this study has demonstrated evidence of additional benefits of the low-FODMAP beyond the GI tract, there are limitations that need to be taken into consideration. Firstly, no blinding or randomization was performed in this study. Blinding is notoriously difficult to implement in dietary studies, as it is near impossible to blind participants to diet characteristics even when the complete diet is provided by the researchers. Furthermore, such blinding makes it difficult to assess dietary manipulation in a real-life setting, and blinding would not allow

for the personalization of the low-FODMAP diet that is required over time. After an initial 6-week introduction period, patients should carefully reintroduce high-FODMAP foods back into their diets under the guidance of skilled dietitians to ensure nutrition adequacy and optimal food choice; data suggest that a strict low-FODMAP diet may cause a reduction in energy intake and fiber, which can be corrected by adequately reintroducing high-FODMAP foods.[37] Another concern regarding a strict low-FODMAP diet is the reduction in relative abundance of certain species, such as *Bifidobacterium*, that may be beneficial to gut health compared with a normal diet.[34,38] It is unknown whether these findings bear any clinical implications, especially considering most patients will eventually reintroduce high-FODMAP foods. Theoretically, however, it is possible that on an individual level some patients may develop an altered GI microbiome on a long-term diet.

Second, there was no control group in this study. Therefore, observed differences could be due to a placebo effect. However, GI symptom rates and improvements were similar to other low-FODMAP studies in IBS populations, among them a number of studies that incorporated control groups. The IBS population of this study is also largely comparable to that of other (controlled) low-FODMAP diet studies. Then again, it must be noted that in the course of this study, the Rome IV criteria were published.[39] Although the revised Rome IV criteria share many similarities with the Rome III criteria used in this study, it is possible that future cohorts may slightly differ.

Thirdly, adherence to the low-FODMAP diet was not measured in this study. Thus, it is not possible to assess whether improvement in non-GI symptoms was correlated with low-FODMAP diet adherence. In the case of low adherence, this may indicate either a high placebo effect or potential gains in symptom improvement with better dietary guidance. However, as noted earlier, the observations of GI symptom improvement in this study are highly analogous to observations in most low-FODMAP diet studies, including studies that have assessed adherence in a real-life setting and found acceptable numbers.

In conclusion, this study demonstrates that non-GI symptoms of IBS patients are improved 6 months after trialing a low-FODMAP diet. Participants demonstrated a better QoL, less fatigue, and fewer symptoms of depression and anxiety. In addition, this study supports existing evidence of low-FODMAP diet efficacy in improving GI symptoms in IBS patients. They completed the low-FODMAP elimination component of the diet for 6 weeks but added higher-FODMAP foods over time, which was assessed at T26.

Statement of Authorship

R. B. Gearry, C. J. J. Mulder, and J. S. Barrett contributed to the conception and the design of the research. T. L. Kortlever contributed to the design of the research. T. L. Kortlever, S. Ten Bokkel Huinink, M. Offereins, J. Leeper, L. O'Brien, C. Hebblethwaite, J. S. Barrett, and R. B. Gearry contributed to the acquisition of data. T. L. Kortlever, S. Ten Bokkel Huinink, J. S. Barrett, and R. B. Gearry contributed to the analysis and interpretation of data. T.L. Kortlever, S. Ten Bokkel Huinink, and R. B. Gearry drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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