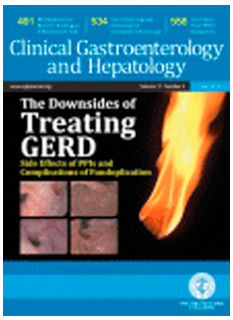

Efficacy and Acceptability of Dietary Therapies in Non-Constipated Irritable Bowel Syndrome: A Randomized Trial of Traditional Dietary Advice, the Low FODMAP Diet and the Gluten-Free Diet

Anupam Rej, David S. Sanders, Christian C. Shaw, Rachel Buckle, Nick Trott, Anurag Agrawal, Imran Aziz

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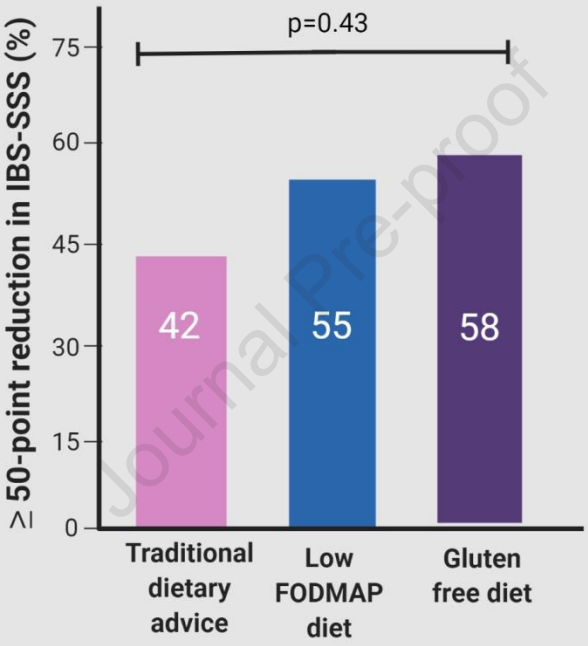
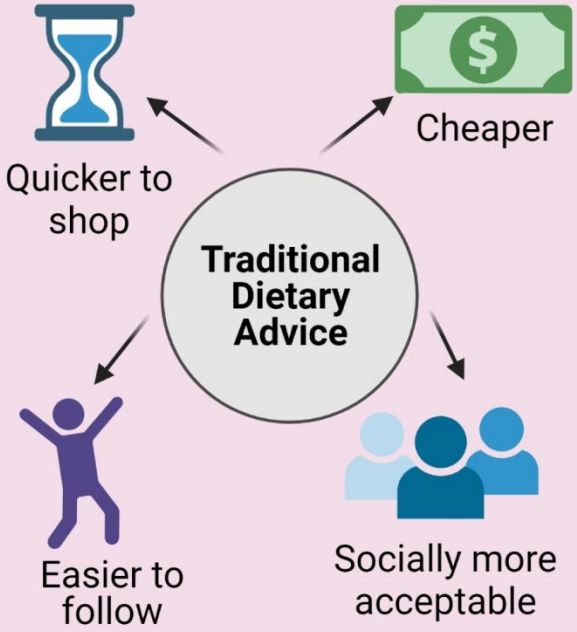
Efficacy and Acceptability of Dietary Therapies in Non-Constipated IBS

Diet is a key trigger for symptoms in IBS

Comparable efficacy of dietary therapies



Acceptability of Dietary Therapies



All three diets are effective in non-constipated IBS, but traditional dietary advice is the most patient-friendly with regards to cost and convenience

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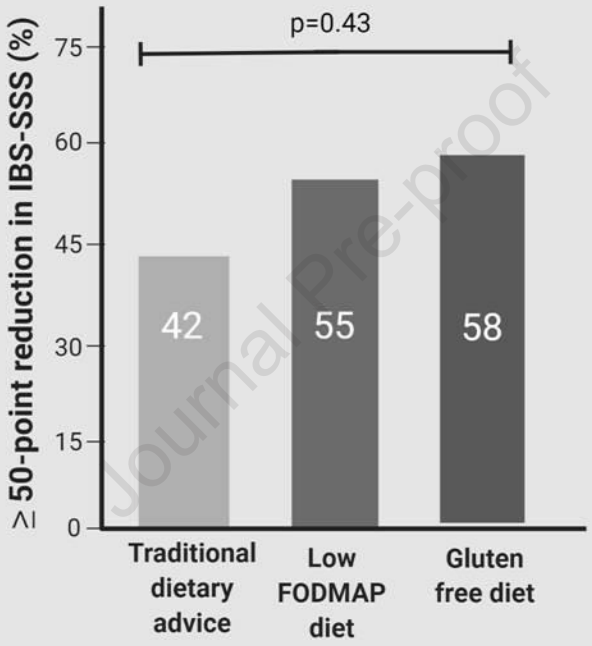

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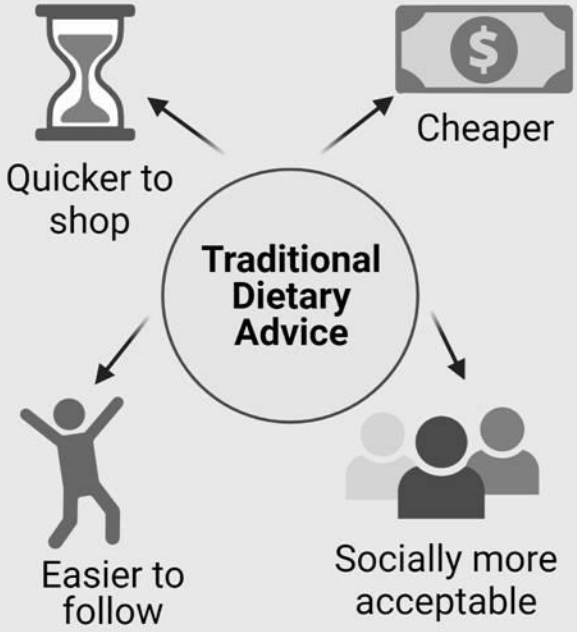

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Efficacy and Acceptability of Dietary Therapies in Non-Constipated Irritable Bowel Syndrome: A Randomized Trial of Traditional Dietary Advice, the Low FODMAP Diet and the Gluten-Free Diet

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Contributions: DSS, AR and IA conceived the study. AR, DSS, CCS, RB, NT, AA and IA contributed to the study design and its conduct. AR, CCS, RB and NT collected and inputted data. AR analyzed the data and wrote the initial manuscript with IA. All authors had access to the study data, revised the manuscript and approved the final version of the article. IA is guarantor of the article.

Conflict of interests: DSS receives an educational grant from Schaer (a gluten-free food manufacturer). The remaining authors have no declarations

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Ethical Approval: The study was carried out in accordance with the Declaration of Helsinki and was approved by HRA and Health and Care Research Wales (HCRW) [REC reference 19/WM/0069]. Written informed consent was obtained from patients. The study commenced in August 2019 and was completed in May 2021. The clinical trials.gov number is NCT04072991.

ABSTRACT

BACKGROUND & AIMS: Various diets are proposed as first-line therapies for non-constipated irritable bowel syndrome (IBS) despite insufficient or low-quality evidence. We performed a randomized trial comparing traditional dietary advice (TDA) against the low FODMAP diet (LFD) and gluten-free diet (GFD).

METHODS: Patients with Rome IV-defined non-constipated IBS were randomized to TDA, LFD, or a GFD (the latter allowing for minute gluten cross-contamination). The primary endpoint was clinical response after 4 weeks of dietary intervention, as defined by ≥50-point reduction in IBS symptom severity score (IBS-SSS). Secondary endpoints included i) changes in individual IBS-SSS items within clinical responders, ii) acceptability and food-related quality of life with dietary therapy, iii) changes in nutritional intake, iv) alterations in stool dysbiosis index, and v) baseline factors associated with clinical response.

RESULTS: The primary endpoint of ≥50-point reduction in IBS-SSS was met by 42% (n=14/33) undertaking TDA, 55% (n=18/33) for LFD, and 58% (n=19/33) for GFD; p=0.43. Responders had similar improvements in IBS-SSS items regardless of their allocated diet. Individuals found TDA cheaper (p<0.01), less time-consuming to shop (p<0.01), and easier to follow when eating out (p=0.03) than the GFD and LFD. TDA was also easier to incorporate into daily life than the LFD (p=0.02). Overall reductions in micro- and macro- nutrient intake did not significantly differ across the diets. However, the LFD group had the greatest reduction in total FODMAP content (27.7g/day pre-intervention to 7.6g/day at week 4) compared with the GFD (27.4/g/day to 22.4g/day) and TDA (24.9g/day to 15.2g/day); p<0.01. Alterations in stool dysbiosis index were similar across the diets, with 22-29% showing reduced dysbiosis, 35-39% no change, and 35-40% increased dysbiosis; p=0.99. Baseline clinical characteristics and stool dysbiosis index did not predict response to dietary therapy.

CONCLUSION: TDA, LFD and GFD are effective approaches in non-constipated IBS, but TDA is the most patient-friendly in terms of cost and convenience. We recommend TDA as the first-choice dietary therapy in non-constipated IBS, with a LFD and GFD reserved according to specific patient preferences and specialist dietetic input.

Clinical trials number: NCT04072991

Keywords: irritable bowel syndrome; diet; acceptability; nutrition; microbiome

INTRODUCTION

Irritable bowel syndrome (IBS) is a common functional bowel disorder characterized by chronic abdominal pain, bloating, and altered bowel habit.[1] Dietary therapies are frequently recommended in IBS, given that over 80% of individuals report food-related symptoms,[2] with almost 63% wanting to know which food(s) they should avoid.[3]

The last decade has seen three diets popularized for non-constipated IBS, which are (i) traditional dietary advice (TDA), (ii) a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (LFD), and (iii) a gluten-free diet (GFD).[4] Of these, TDA is the first-line dietary therapy within the United Kingdom, and is based upon guidance provided by the National Institute for Health and Care Excellence and the British Dietetic Association.[5-7] Its principles include adopting healthy, sensible eating patterns, such as having regular meals, never eating too little/too much, maintaining adequate hydration, and reducing the intake of, i) alcohol/caffeine/fizzy drinks, ii) fatty/spicy/processed foods, iii) fresh fruit to a maximum of 3 per day, iv) fiber and other commonly consumed gas-producing foods (e.g. beans, bread, sweeteners, etc), and v) addressing any perceived food intolerances (e.g. dairy). The LFD is the second-line dietary therapy for IBS within the United Kingdom,[5-7] although in North America it is first-line.[8,9] FODMAPs are short-chain fermentable carbohydrates found in a variety of fruits, vegetables, dairy products, artificial sweeteners, and wheat. They increase small intestinal water volume and colonic gas production that, in those with visceral hypersensitivity, induces gastrointestinal symptoms.[7] The LFD initially eliminates all FODMAPs for 4-6 weeks, followed by their gradual re-introduction and personalization. Finally, taking a GFD without celiac disease has become a global phenomenon, with ~10% of the population reporting gluten-based products to provoke intestinal symptoms compatible with IBS.[10] The mechanism for symptom improvement on a GFD are extensively debated but appear, in the main, not to be via the removal of gluten *per se*, but rather through reducing fructan content (a FODMAP) due to wheat exclusion.[11]

Whilst heavily promoted, these diets are limited in evidence.[7,12] Recommendations for TDA are mainly based on clinical experience and the potential mechanisms by which these foods may induce symptoms, as opposed to randomized controlled trials.[6] With regards to a LFD, historical

and contemporary reviews report an efficacy approaching ~75%,[13,14] although a 2018 systematic review and meta-analysis of randomized controlled trials concluded there to be low quality evidence, mainly to due small sample sizes and significant heterogeneity between studies.[12] Interestingly, the few studies that compared the LFD with TDA demonstrated the least magnitude of effect,[12] with a response rate of 40-50%, although some debated whether the LFD was (sub)optimally delivered and its efficacy underestimated.[15-17] Additional studies have since been performed,[18-20] with a 2021 network meta-analysis ranking the LFD first amongst the dietary therapies for IBS, deeming it superior to TDA.[21] Yet, trials of TDA were limited to five studies, had far fewer participants compared with a LFD, and some modified its recommended instructions; **see Supplementary Table 1**.[16-21] For example, four-of-five studies did not advise patients to reduce commonly consumed gas-producing foods,[17-20] which contradicts the TDA concept and conceivably underestimates its efficacy. While it may be argued that TDA overlaps with the LFD, they are appreciable differences in that the former advises reducing commonly consumed gas-producing foods, whereas the latter initially eliminates them all. A GFD in IBS has also come under scrutiny as, despite reports of ~70% efficacy, a systematic review and meta-analysis identified only two randomized trials and concluded insufficient evidence.[4,12]

Additionally, some previous IBS dietary trials have been feeding studies which, despite being a powerful proof-of-concept tool,[12] do not address the challenges placed upon patients to incorporate the diets into their everyday personal and social life. This may be of relevance with the conceivably more complex LFD and GFD, which also require specialist dietetic input prior to implementation and incur substantial pressures on publicly-funded healthcare services.[7] Concerns have also been raised that restrictive diets may induce potentially detrimental nutritional and stool microbial changes.[4]

In summary, there is no pragmatic head-to-head trial comparing the efficacy and acceptability of the LFD and GFD against TDA. We hypothesized that the LFD and GFD will be superior to TDA in improving IBS symptoms, and performed a randomized trial to address this. We also investigated the acceptability, nutritional and stool microbial changes associated with these diets. Finally, we evaluated whether baseline factors predict a response to dietary intervention, as this could lead to future provision of personalized care.

METHODS

Participants and Setting

All authors had access to the study data and reviewed and approved the final manuscript. Patients were recruited via two secondary-care centers in the United Kingdom. The inclusion criteria were adults aged ≥18 years with Rome IV IBS-diarrhea (IBS-D) or mixed-type (IBS-M), and an IBS-symptom severity score (IBS-SSS) of >75. The exclusion criteria are in the **Supplementary material**.

Randomization

Patients were allocated TDA, the LFD or GFD (the latter not being strict like in celiac disease, as gluten cross-contamination was allowed, e.g. sharing the same household toaster). Individuals were block-randomized into groups of up to 5, with diets given in a 1:1:1 ratio. The randomization was computer-generated and performed by an individual not involved in recruitment or treatment. Participants were seen face-to-face by specialist dietitians, where they were educated on their allocated diet via a standardized 45-60 minute presentation, including time for questions, followed by appropriate dietary information sheets. However, following the onset of COVID-19, delivery of dietetic advice was transferred to a web-based live virtual consult, with the same information provided as with face-to-face. Participants commenced their allocated diet for 4 weeks, with outcomes at week 4 compared with baseline.

Questionnaires

Participants provided baseline demographic data. Their socioeconomic status was also determined, using the Index of Multiple Deprivation (IMD) 2019 scale, as this may contribute towards an individual's biopsychosocial model and their response to dietary therapy.

The following questionnaires were completed pre- and post- dietary intervention, with further information provided in **Supplementary Materials**:

a) IBS symptom severity score (IBS-SSS).
b) Hospital Anxiety and Depression Scale.
c) Patient health questionnaire-12 non-GI somatic symptoms scale.
d) IBS quality of life (QOL) questionnaire.
e) Acceptability of dietary restriction questionnaire.

f) Food-related QOL questionnaire.
g) Comprehensive Nutrition Assessment Questionnaire (CNAQ).

Stool samples

Participants provided stool samples pre- and post-dietary intervention. However, this process was temporarily suspended at the start of COVID-19 and resumed once allowed. Hence, stool samples were collected in around half of cases. Data was analyzed using the GA-map™ Dysbiosis Test, with bacterial profiles assigned a dysbiosis index (DI) on a scale from 0-5, with >2 indicating a bacteria composition differing from a healthy normobiotic reference range and, as such, considered dysbiotic. Further information regarding stool sample analysis is in **Supplementary Materials.**

Endpoints

The primary endpoint was % clinical responders after 4 weeks of dietary intervention, as defined by ≥50-point reduction in IBS-SSS which has been shown to represent a clinically significant improvement. Secondary endpoints included i) changes in individual IBS-SSS items in those with a clinical response, ii) changes in anxiety, depression, somatization, quality of life, nutritional intake, gut microbiota, and iii) acceptability and food-related quality of life associated with dietary therapy. An assessment was also made on whether baseline factors (age, gender, IMD, mood, somatization, stool DI) might be associated with clinical response to dietary therapy.

Sample size & Statistical analysis

The sample size calculation considered the aforementioned ambiguities regarding the true efficacy of a LFD or GFD, with some groups reporting ~75% response,[13,14,22,23] and questioning the lower response rates from randomized trials.[15] Further, detecting a large effect-size might be desirable if demanding diets (i.e. LFD/GFD) were to be considered first-choice over the relatively straightforward TDA. Assuming a response rate of 75% with LFD or GFD, and 40% with TDA, 31 subjects per arm were required to detect a 35% difference with 80% power at α=0.05. To accommodate 10% dropout rate, we aimed for 33 individuals per arm. Of note, the effect-size is comparable to previous studies,[16,17] and those published recently.[18-20]

Full details on statistical analyses are in **Supplementary Materials**. The p-value was significant at <0.05, with post-hoc bonferonni corrections performed as required.

RESULTS

Of 114 participants recruited, 101 commenced dietary intervention (TDA=35, LFD=33, GFD=33), with two excluded as lost to follow-up. A total of 99 participants, 33 per arm, completed the study (**Supplementary Figure 1)**. There was no difference in baseline variables across groups **(Supplementary Table 2**). The mean-age was 37 years, with 71% female, 88% white, 75% IBS-D and 25% IBS-M. The mean baseline IBS-SSS was 301, with 9% having mild IBS, 47% moderate IBS, and 45% severe IBS (p=0.5 across groups).

Clinical Response

The primary endpoint of ≥50-point reduction in IBS-SSS was met by 42% (n=14/33) taking TDA, 55% with LFD (n=18/33), and 58% with GFD (n=19/33), with no significant difference across groups; p=0.43 **(Figure 1)**.

Of those who experienced ≥50-point reduction in IBS-SSS, there were significant within-group improvements in individual IBS-SSS items. This was seen with each dietary therapy but with no significant difference across groups **(Table 1**).

A ≥50-point reduction in IBS-SSS was seen in 52% (n=15/29) receiving face-to-face consult vs. 51% (n=36/70) receiving live virtual consult; p=0.98. This was seen to a similar extent irrespective of the allocated dietary therapy (data not shown).

A ≥50-point reduction in IBS-SSS was seen in 54% (n=40/74) with IBS-D vs. 44% (n=11/25) with IBS-M, with no difference between groups; p=0.38. There was no statistical difference in response rates between IBS-D vs. IBS-M based on a particular dietary therapy (data not shown).

Impact on mood, somatization, and IBS-QOL

Individuals allocated a LFD had a significant improvement in depression compared with TDA. Changes in anxiety, somatization, and IBS QOL did not differ across groups, except for the LFD having a significant improvement in dysphoria compared with TDA and GFD (**Supplementary Table 3)**.

Acceptability of dietary restriction and food-related QOL

Individuals found TDA cheaper ($p<0.01$), less time-consuming to shop ($p<0.01$), and easier to follow when eating out at family and friends ($p=0.03$) compared with a GFD and LFD. Individuals found TDA and GFD easier to incorporate into their life than the LFD ($p=0.02$); **Table 2**.

The proportion of individuals who would consider continuing the diets were 70% (n=23) for TDA, 67% (n=22) for LFD and 61% (n=20) for GFD, with no difference across groups ($p=0.73$).

Nutritional intake and FODMAP composition

While macro- and micro- nutrients reduced within each dietary group, there was no significant difference across groups besides a trend towards more fiber reduction on the LFD compared with the GFD and TDA ($p=0.06$) [**Table 3**].

The proportion of individuals meeting recommended Dietary Reference Values (DRVs) for macronutrients did not change pre- to post- intervention for any of the diets. However, DRVs for the micronutrients of potassium and iron were significantly reduced with TDA, whereas thiamine and magnesium were significantly reduced with the LFD and GFD. The majority of individuals across all three diets failed to meet DRVs for total energy intake both pre- and post-intervention [**Supplementary Table 4**].

Significant within-group reduction in total FODMAP intake occurred with all three diets; **Table 4**. However, the greatest reduction was with a LFD (27.7g/day pre-intervention to 7.6g/day at week 4) compared with TDA (24.9g/day to 15.2g/day) and GFD (27.4g/day to 22.4g/day); $p<0.01$.

As expected, the LFD led to significant reductions in each individual FODMAP component, while with TDA it was for fructo-oligosaccharides, lactose and mannitol, and with the GFD it was for fructo- and galacto- oligosaccharides. The LFD led to a significantly greater reduction in fructo-oligosaccharides, galacto-oligosaccharides and mannitol compared with TDA, and a significantly greater reduction in lactose, excess fructose and mannitol compared with the GFD [**Table 4**].

Stool Analysis

A total of 55 paired stool samples were analyzed (TDA=18, LFD=17, GFD=20). Changes in DI did not differ across groups (p=0.99), with 22-29% having an improvement, 35-39% having no change, and 35-40% having worsening DI (**Figure 2).** Changes in DI did not differ between responders and non-responder**s (**S**upplementary Table 5**).

No significant changes in functional bacterial profiles were noted (**Supplementary Table 6),** with specific alterations in bacterial abundance reported in **Supplementary Tables 7-9.**

Factors associated with clinical response

Age, gender, IBS-subtype, IMD, somatization, and mood did not predict response to dietary therapies **(Supplementary Table 10**), and nor did baseline stool DI **(Supplementary Figure 2)**.

DISCUSSION

This is the first randomized trial comparing the efficacy and convenience of TDA, LFD and GFD in non-constipated IBS. The pragmatic study design, whereby the responsibility was left upon patients to undertake the diets following appropriate education, means our findings can be generalized. The main results are that the diets did not significantly differ in clinical efficacy, with 42-58% experiencing a ≥50-point reduction in IBS-SSS. Responders had similar improvements in IBS-SSS items regardless of their allocated diet. Individuals found TDA cheaper, less time-consuming to shop, and easier to follow when eating out than the GFD and LFD. It was also easier to implement into everyday life than the LFD. Neither clinical characteristics nor stool dysbiosis index predicted response to dietary therapy. Finally, the modes of dietary education, either face-to-face or virtual, were equally effective.

Our study has notable strengths. First, it is amongst the largest studies assessing dietary therapies in IBS.[12] Second, we provided dietary education as per recommended instructions,[5,6] whereas four-of-five previous randomized trials of TDA have been limited to providing a modified or incomplete version.[17-20] This could partly explain TDA being ranked inferior to a LFD in a recent network meta-analysis.[21] Our findings shed further clarity on the efficacy of TDA and are in line with a Swedish randomized trial that provided TDA instructions as per guidance and noted no difference versus the LFD.[16] The added value of our study is its assessment of dietary acceptability, as well as evaluating a GFD which has become increasingly popular in modern times. While a recent Italian study demonstrated similar clinical efficacy between the LFD, GFD and a balanced Mediterranean diet, with 86% of patients subsequently expressing a preference for the latter, it was limited to being a small non-randomized trial of 42 patients and the Mediterranean diet did not resemble TDA.[24]

Third, objective evidence to support dietary adherence can be inferred from the reductions seen in specific FODMAPs. For example, there was a marked reduction in all FODMAPs within the LFD group (27.7g/day to 7.6g/day, with <12g per day being the desired cut-off),[25] appropriate reductions with the GFD (i.e. fructo- and galacto- oligosaccharides), and for TDA a decrease in fructo-oligosaccharides, lactose and mannitol (which is to be expected when reducing some gas-producing foods e.g. bread, fruits, dairy, and sweeteners).

Fourth, due to COVID-19, dietary education moved away from face-to-face to virtual consults, and was also provided in group settings. We found similar clinical efficacy to dietary therapy irrespective of the mode of educational delivery, and with response rates in the group setting being comparable to studies where patients have been seen individually.[16,17] Moving forward, this delivery of care model will have cost-saving implications for healthcare services, and alleviate concerns patients may have attending health centers in the current climate.

Current national guidelines demonstrate some differences regarding dietary therapies in IBS.[7-9] Whereas British guidelines recommend TDA as the first choice followed by a LFD, the North American guidelines only mention a LFD.[7-9] Due to insufficient evidence, neither recommends a GFD although our study (amongst other recent publications) suggests it deserves future re-evaluation.[4] On balancing the efficacy and acceptability of dietary therapies, plus the demands they place upon healthcare services, we suggest TDA be considered first. The LFD and GFD, while beneficial, are costlier, harder to follow, and more inconvenient. Furthermore, their implementation requires specialized and extensive dietetic input which incurs a substantial burden on healthcare services. Indeed, even within countries with highly established healthcare systems (e.g. United Kingdom and United States), there is inequity of gastrointestinal dietetic services available across regions,[26] and a failure to correctly implement a LFD despite it frequently being recommended and prescribed.[27] Given that IBS is a global condition then arguably countries with less established healthcare systems may be falling even shorter of optimally delivering a LFD. Hence, we suggest a GFD or LFD be reserved according to specific patient preferences and with specialist dietetic input. It would also be of interest to evaluate their efficacy in patients not responding to TDA. However, as costs are critical determinants of IBS treatment value to patients and providers, alternate cheaper options should also be considered (e.g. antispasmodics, neuromodulators).[28]

The diets reduced total FODMAP intake, mostly in the LFD group compared with TDA and GFD. This suggests a degree of overlap and that moderate FODMAP restriction, as seen with TDA and a GFD, may be similarly effective as a strict LFD. To reintroduce FODMAPs to tolerance, and avoid over-restriction, it is important to emphasize that the LFD is altogether a 3-

stage process and that after its strict 4-6 week elimination phase comes re-introduction and personalization, all done under dietetic supervision.[6,7] However, real-world Canadian healthcare experience suggests that only 40% satisfactorily complete all 3-phases of the LFD program, implying that a proportion might remain within the strict elimination phase, are at risk of developing overly restrictive eating patterns and nutritional inadequacies.[25] There are suggestions that a 'bottom-up' or "FODMAP-gentle" approach to the LFD may overcome its extensive 3-phase program.[4] For example, in the long-term, many patients on a personalized LFD reduce fructan intake to manage their symptoms, and facilitate this through purchasing gluten- or wheat- free products.[29] This raises the hypothesis that a GFD might be an option before considering the complete LFD programme. Other reasons for a GFD in IBS are in antigliadin antibody positive patients, as well those with non-celiac gluten/wheat sensitivity.[10,30] Our study, amongst another recent publication, suggests that a GFD in IBS does not need to be strict as that seen in celiac disease.[30] However, as the GFD generally comes in one form, future studies should determine the level of gluten restriction required to derive symptom benefit, regardless of whether they start with this diet or reach it via a personalized LFD.

The study limitations are similar to previous randomized trials in that dietary intervention was of 4-week duration and long-term outcomes are relatively unknown.[12] A few studies have demonstrated ongoing efficacy with a GFD and personalized LFD,[23,29] although as mentioned there is currently no guidance regarding gluten re-introduction. The study was also powered to detect a large 35% difference in clinical benefit between the LFD and GFD compared with TDA, thus underpowered to detect smaller yet significant differences, potentially leading to a type II error. Interestingly, when combining our results with that of a similarly designed and powered Swedish study,[16] essentially doubling the sample size to ~70 patients per arm, the proportion of responders with a ≥50 point reduction in IBS-SSS is ~44% (range 42-46%) with TDA, and ~53% with LFD (range 50-55%), suggesting a difference of 9%. In our study, a GFD showed 16% gain over TDA. To ascertain if a 9% to 16% therapeutic gain with a LFD and GFD is significant over TDA then, based on our primary endpoint, studies with a sample size of over 950 and almost 300 patients would be needed, respectively. However, whether this would lead to TDA being displaced from pole position is debatable given its relative simplicity and minimal healthcare service requirements, and that the LFD and GFD are still viable options that can be

considered afterwards. In addition, while our study was geared towards comparing different diets head-to-head, their true benefit (if any) over placebo is unknown in the absence of a control group. Pharmacological trials in IBS suggest a pooled placebo response rate of approximately 30%,[31] but this is yet to be adequately explored with dietary interventions. We also excluded patients with IBS-constipation on the presumption that reducing FODMAP intake might aggravate constipation and worsen overall symptoms; however, there is emerging data to suggest a LFD might benefit this patient group and, alongside the other dietary interventions, merits further independent study.[16] Other limitations relating to the tools used to assess nutritional intake and nutritional considerations when prescribing dietary therapies are detailed in **Supplementary Discussion**. Here we also discuss issues regarding the stool normobiotic reference range, and that only 50% of stool samples were collected, which precludes firm conclusions on the stool dysbiosis index being made.

In conclusion, TDA, GFD and a LFD are effective approaches in non-constipated IBS. We recommend TDA as the first-choice dietary option due to its widespread availability and patient friendliness. The LFD or GFD are alternative options based on specific patient preferences and with specialist dietetic counseling.

Table 1: Change in IBS-SSS, and its individual items, in patients responding to dietary therapy (n=51 of 99)

Table 2: Acceptability of Dietary Restriction and Food Related Quality of Life

Table 3: Nutritional intake at baseline and week 4 of dietary therapy

Table 4: FODMAP intake at baseline and week 4 of dietary therapy

Figure 1: Response rate to dietary therapies

Figure 2: Change in stool dysbiosis index

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Table 1: Change in IBS-SSS, and its individual items, in patients responding to dietary therapy (n=51 of 99)

IBS-SSS and its individual items, mean (SD)	Intervention									Difference in reduction across groups *p-value*
	TDA (n=14)			LFD (n=18)			GFD (n=19)			
	Baseline	Week 4	Within-group change*	Baseline	Week 4	Within-group change*	Baseline	Week 4	Within-group change*	
IBS-SSS	330 (74)	199 (93)	131	311 (80)	148 (87)	163	299 (73)	180 (89)	119	0.13
Abdominal pain severity	51 (22)	28 (30)	23	55 (23)	18 (17)	37	52 (22)	25 (21)	27	0.11
Number of days in pain every 10 days	6.1 (2.5)	3.5 (3.2)	2.6	6.0 (2.9)	3.1 (2.3)	2.9	6.4 (1.8)	3.7 (2.6)	2.7	0.93
Abdominal distention severity	63 (24)	28 (26)	35	54 (32)	22 (23)	32	49 (24)	21 (22)	28	0.61
Satisfaction with bowel habits	78 (19)	58 (30)	20	75 (25)	44 (32)	31	71 (24)	52 (28)	19	0.50
Interference with life in general	76 (15)	50 (26)	26	67 (22)	33 (28)	34	63 (22)	44 (32)	19	0.17

Values presented as mean (SD)

*Significant within-group reductions for all IBS-SSS items

Table 2: Acceptability of Dietary Restriction and Food Related Quality of Life

	Agree *n (%)*			Neutral *n (%)*			Disagree *n (%)*			Comparison across groups *p-value*
	TDA	**LFD**	**GFD**	**TDA**	**LFD**	**GFD**	**TDA**	**LFD**	**GFD**	
Acceptability of dietary restriction										
I find it easy to buy suitable foods for my current diet at my normal supermarkets or shops	19 (58)	12 (36)	18 (55)	13 (39)	13 (39)	11 (33)	1 (3)	8 (24)	4 (12)	0.1
I am able to buy foods suitable for my current diet at my normal supermarkets or shops	23 (70)	18 (55)	26 (79)	7 (21)	11 (33)	6 (18)	3 (9)	4 (12)	1 (3)	0.3
I use high street/online specialty shops (e.g. health food shops) to buy food for my current diets	8 (24)	3 (9)	9 (27)	7 (21)	7 (21)	7 (21)	18 (55)	23 (70)	17 (52)	0.4
It takes extra time to shop for my current diet	13 (39)	26 (79)	23 (70)	7 (21)	4 (12)	8 (24)	13 (39)	3 (9)	2 (6)	<0.01[a]
I find food labelling is adequate to allow me to confidently choose suitable foods	18 (55)	20 (61)	28 (85)	13 (39)	9 (27)	3 (9)	2 (6)	4 (12)	2 (6)	0.04
The cost of my current diet is more expensive	16 (49)	27 (82)	27 (82)	8 (24)	3 (9)	6 (18)	9 (27)	3 (9)	0 (0)	<0.01[a]
Does eating out at restaurants make it more difficult for you to follow your current diet?	19 (58)	20 (61)	19 (58)	9 (27)	12 (36)	11 (33)	5 (15)	1 (3)	3 (9)	0.5
Does eating out at friends/families make it more difficult for you to follow your current diet?	17 (52)	22 (67)	22 (67)	7 (21)	10 (30)	9 (27)	9 (27)	1 (3)	2 (6)	0.03[a]
Does travel (overseas/United Kingdom) make it more difficult for you to follow your current diet?	18 (55)	15 (46)	13 (39)	11 (33)	16 (49)	18 (55)	4 (12)	2 (6)	2 (6)	0.5
Overall, I find my current diet tasty and enjoyable	17 (52)	14 (42)	13 (39)	11 (33)	9 (27)	18 (55)	5 (15)	10 (30)	2 (6)	0.04
I can incorporate my current diet easily into my life	18 (55)	11 (33)	15 (46)	13 (39)	11 (33)	15 (46)	2 (6)	11 (33)	3 (9)	0.02[b]
My current dietary needs have created stress with my family/friends	3 (9)	8 (24)	8 (24)	13 (39)	11 (33)	10 (30)	17 (52)	14 (42)	15 (46)	0.5
Food Related QOL										
Food and meals are positive elements of my life	17 (52)	17 (52)	22 (67)	13 (39)	6 (18)	8 (24)	3 (9)	10 (30)	3 (9)	0.05
I am generally pleased with my food	22 (67)	15 (46)	17 (52)	8 (24)	9 (27)	14 (42)	3 (9)	9 (27)	2 (6)	0.05
My life in relation to food and meals is close to my ideal	6 (18)	7 (21)	7 (21)	14 (42)	11 (33)	19 (58)	13 (39)	15 (46)	7 (21)	0.3
With regard to food, the conditions of my life are excellent	4 (12)	6 (18)	9 (27)	18 (55)	12 (36)	17 (52)	11 (33)	15 (46)	7 (21)	0.2
Food and meals give me satisfaction in daily life	20 (61)	15 (46)	18 (55)	9 (27)	6 (18)	10 (30)	4 (12)	12 (36)	5 (15)	0.1
I wish my meals were much more pleasant part of my life	11 (33)	20 (61)	13 (39)	11 (33)	7 (21)	13 (39)	11 (33)	6 (18)	7 (21)	0.2
When I think of my next meal, I only see problems, obstacles and disappointments	4 (12)	11 (33)	7 (21)	11 (33)	13 (39)	13 (39)	18 (55)	9 (27)	13 (39)	0.2

[a] Statistically significant difference between TDA vs. LFD and GFD on post hoc analysis.
[b] Statistically significant difference between LFD vs. TDA and GFD on post hoc analysis

Table 3: Nutritional intake at baseline and week 4 of dietary therapy

Nutritional parameter	Intervention						Difference in reduction across groups *p-value*
	TDA		LFD		GFD		
	Baseline	Week 4	Baseline	Week 4	Baseline	Week 4	
Energy *kcal/d*	2373 (1774-2923)	1861 (1579-2411)	2338 (1574-2764)	1738 (1210-2231)	2366 (2030-2928)	1958 (1406-2770)	0.63
Protein *g/d*	104.2 (81.6-160.4)	90.9 (65.6-108.6)	97.1 (74.1-118.6)	80.4 (51.6-95.7)	99.7 (74.4-132.6)	79.1 (61.5-105.3)	0.52
Carbohydrate *g/d*	268 (224-342)	222 (203-320)	277 (211-357)	223 (141-277)	307 (231-375)	227 (174-306)	0.55
Fat g/d	86.8 (57.9-112.2)	65.3 (44.5-87.8)	82.3 (56.9-114.9)	64.6 (43.5-95.2)	86.1 (71.0-115.8)	77.9 (49.3-113.0)	0.66
Dietary fibre *g/d*	32.6 (27.4-40.7)	28.5 (21.4-35.4)	23.5 (16.8-44.1)	18.7 (14.3-31.7)	32.7 (23.4-39.3)	25.9 (21.1-35.0)	0.06
Folate *mcg/d*	449 (351-583)	353 (273-496)	362 (219-592)	291 (175-407)	392 (311-524)	335 (254-496)	0.22
Thiamine *mg/d*	1.70 (1.38=2.73)	1.40 (1.10-1.73)	1.40 (1.00-2.40)	1.00 (0.60-1.45)	1.50 (1.30-2.55)	1.10 (0.80-1.70)	0.13
Riboflavin *mg/d*	2.50 (1.70-4.25)	2.00 (1.20-2.63)	1.90 (1.43-3.28)	1.65 (1.13-2.53)	2.10 (1.80-3.70)	2.00 (1.30-2.90)	0.12
Niacin *mg/d*	24.0 (16.1-30.3)	19.6 (16.6-23.9)	19.1 (13.3-25.3)	14.8 (11.5-20.9)	20.2 (18.6-27.7)	17.7 (15.1-23.2)	0.72
Vitamin C *mg/d*	185 (143-280)	172 (115-250)	111 (78-251)	94 (73-213)	163 (124-244)	150 (117-204)	0.16
Sodium *mg/d*	2772 (1695-3204)	1947 (1516-2485)	2220 (1641-2915)	1761 (1372-2642)	2424 (1980-3217)	1910 (1446-2902)	0.97
Potassium *mg/d*	4394 (3739-5620)	3704 (2967-4807)	4042 (2819-5077)	3119 (2097-3813)	4039 (3469-5370)	3518 (2582-4577)	0.50
Magnesium *mg/d*	377 (288-517)	315 (252-423)	324 (238-440)	247 (169-333)	347 (292-426)	298 (234-379)	0.36
Calcium *mg/d*	1122 (917-2030)	896 (625-1357)	991 (714-2069)	888 (520-1330)	1057 (792-1699)	1049 (605-1510)	0.14
Phosphorus *mg/d*	1771 (1424-2569)	1476 (1202-1750)	1472 (1146-2111)	1365 (853-1793)	1606 (1200-2382)	1435 (1067-1956)	0.41
Iron *mg/d*	13.4 (9.4-14.3)	11.5 (9.4-14.3)	11.7 (8.5-15.6)	10.4 (6.5-14.1)	12.7 (10.0-16.0)	10.6 (8.6-13.9)	0.70
Zinc *mg/d*	11.8 (8.6-14.9)	10.7 (8.3-13.2)	11.0 (8.7-13.3)	11.1 (6.3-12.9)	11.2 (8.7-15.0)	10.9 (7.5-15.0)	0.70

Footnote; Values presented as median (IQR).

Significant within-group reductions seen with most macro- and micro- nutrients following dietary intervention, except for zinc (all diets), vitamin C (TDA and GFD), and fibre/folate/riboflavin (GFD)

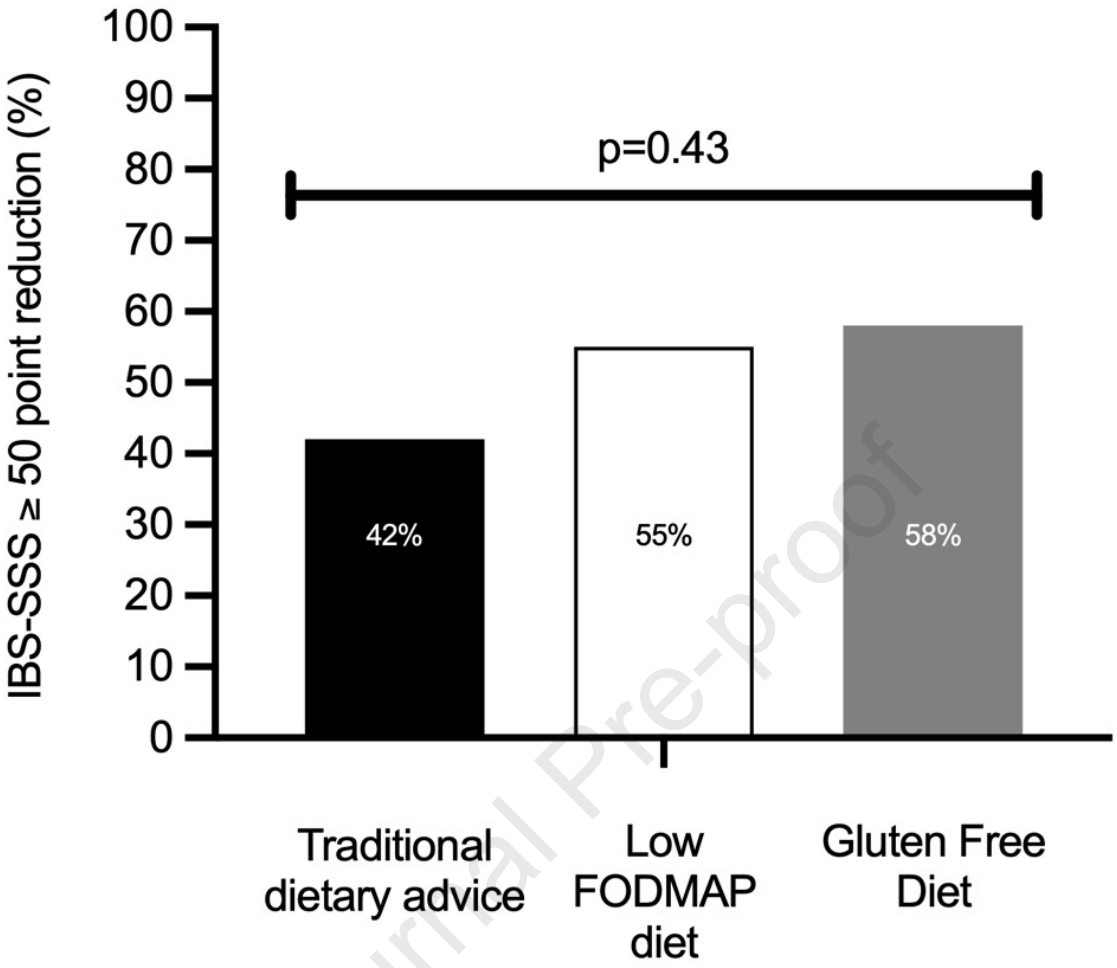
Table 4: FODMAP intake at baseline and week 4 of dietary therapy

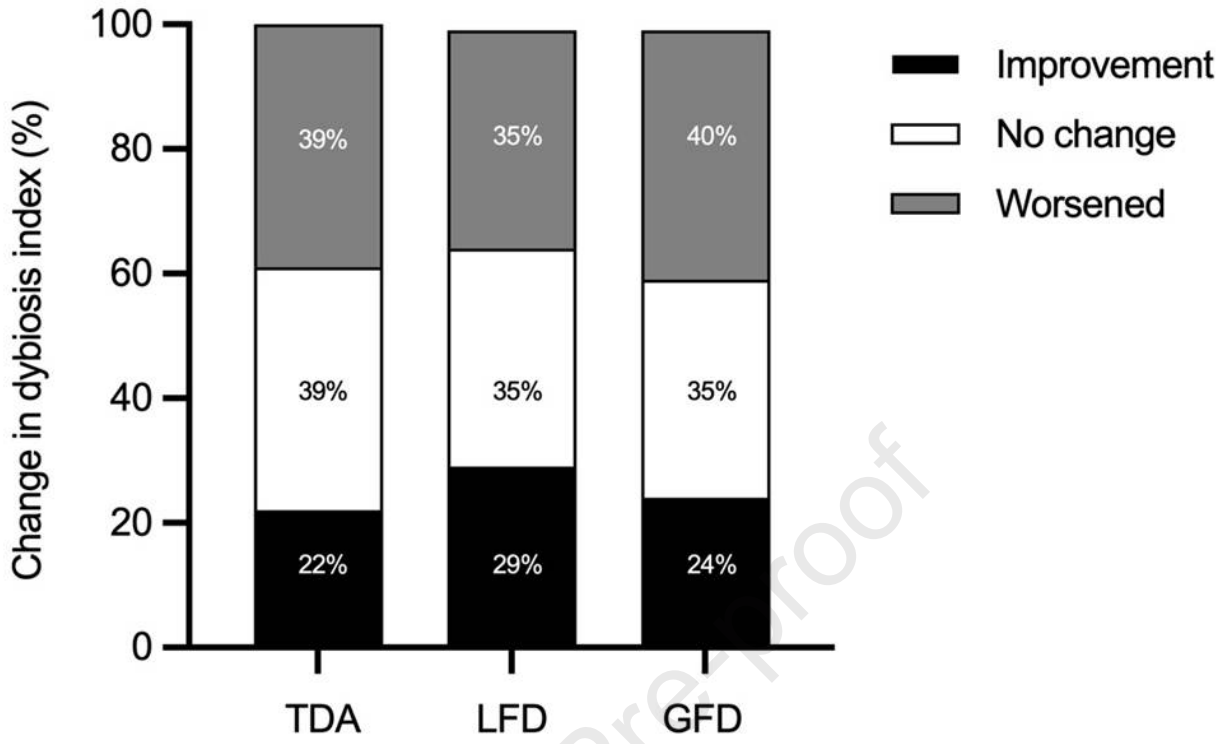
FODMAP	Intervention									Difference in change across groups *p-value*
	TDA			LFD			GFD			
	Baseline	Week 4	Baseline vs. Week 4 *p-value*	Baseline	Week 4	Baseline vs. Week 4 *p-value*	Baseline	Week 4	Baseline vs. Week 4 *p-value*	
Oligosaccharides										
Fructo-oligosaccharides g/d	3.8 (2.7-4.7)	2.9 (2.2-3.7)	<0.01	3.3 (1.8-6.2)	1.6 (0.8-2.5)	<0.01	3.9 (3.0-4.5)	2.4 (1.6-4.0)	<0.01	<0.01[a]
Galacto-oligosaccharidesg/d	1.1 (0.8-1.5)	1.1 (0.7-1.3)	0.05	1.2 (0.6-2.2)	0.6 (0.3-1.1)	<0.01	1.2 (0.9-2.2)	0.9 (0.7-1.6)	0.02	<0.01[a]
Disaccharides										
Lactose g/d	11.7 (4.3-26.4)	4.9 (1.0-15.0)	<0.01	12.5 (3.3-24.0)	1.9 (0.5-6.5)	<0.01	14.3 (7.0-26.0)	13.0 (4.6-22.0)	0.22	0.02[b]
Monosaccharides										
Excess fructose g/d	5.2 (2.6-7.0)	2.8 (1.7-6.8)	0.31	3.5 (2.0-10.4)	1.5 (0.8-3.5)	<0.01	4.0 (2.3-6.6)	4.0 (2.2-6.4)	0.95	<0.01[b]
Polyols										
Sorbitol g/d	1.9 (0.7-3.0)	1.4 (0.4-2.8)	0.18	1.3 (0.6-2.2)	0.3 (0.1-1.0)	<0.01	2.1 (1.1-3.2)	1.9 (0.9-3.4)	0.84	0.05
Mannitol g/d	0.8 (0.5-1.1)	0.6 (0.4-1.0)	<0.01	0.6 (0.3-0.8)	0.1 (0.0-0.3)	<0.01	0.7 (0.4-1.1	0.6 (0.3-1.1)	0.70	<0.01[a,b]
Total FODMAPs *g/d*	24.9 (13.8-53.4)	15.2 (9.1-28.0)	<0.01	27.7 (13.9-46.3)	7.6 (2.8-13.7)	<0.01	27.4	22.4	0.03	<0.01[a,b]

Values presented as medians (IQR)

[a] Statistically significant difference between LFD and TDA on post hoc analysis.

[b] Statistically significant difference between LFD and GFD on post hoc analysis.





WHAT YOU NEED TO KNOW

BACKGROUND

Dietary therapies are popular for the management of irritable bowel syndrome (IBS), yet data on their comparative efficacy and acceptability is limited.

FINDINGS

Traditional dietary advice is effective like the low FODMAP and gluten-free diet, but is more patient-friendly with regards to cost, time to shop, and ease of implementation.

IMPLICATIONS FOR PATIENT CARE

Traditional dietary advice should be considered the first-choice dietary therapy in IBS, with the low FODMAP and gluten-free diet reserved according to specific patient preferences and with specialist dietetic counseling.