



Review

Low fermentable, oligo-, di-, mono-saccharides and polyol diet in the treatment of irritable bowel syndrome: A systematic review and meta-analysis



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ABSTRACT

Objectives: The aim of this review was to systematically assess and meta-analyze the effects of a low fermentable, oligo-, di-, mono-saccharides and polyol (FODMAP) diet (LFD) on the severity of symptoms, quality of life, and safety in patients with irritable bowel syndrome (IBS).

Methods: The MEDLINE/PubMed, Scopus, and Cochrane Library databases were screened through January 19, 2016. Randomized controlled trials (RCTs) that compared LFD to other diets were included if they assessed symptoms of IBS or abdominal pain in patients with IBS. Safety, quality of life, anxiety, depression, and effect on gut microbiota were defined as secondary outcomes. Standardized mean difference (SMD) and 95% confidence interval (CI) were calculated.

Results: Nine RCTs with a total of 596 subjects were included. Three RCTs compared LFD with a habitual diet, two RCTs provided all meals and compared LFD with a western diet, one RCT each compared LFD with a diet high in FODMAPs or a sham diet, and two RCTs compared with other diet recommendations for IBS. A meta-analysis revealed significant group differences for LFD compared with other diets with regard to gastrointestinal symptoms (SMD = -0.62; 95% CI = -0.93 to -0.31; $P = 0.0001$), abdominal pain (SMD = -0.50; 95% CI = -0.77 to -0.22; $P = 0.008$), and health-related quality of life (SMD = 0.36; 95% CI = 0.10–0.62; $P = 0.007$). Three studies reported a significant reduction in luminal bifidobacteria after LFD. Adverse events were assessed in three RCTs only and no intervention-related adverse events were reported.

Conclusions: This meta-analysis found evidence of the short-term efficacy and safety of LFD in patients with IBS. However, only a preliminary recommendation for LFD can be made until long-term effects are investigated.

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Background

Irritable bowel syndrome (IBS) describes a group of symptoms that include abdominal pain or discomfort and changes in bowel movement patterns and defecation. Although a correlation between pathophysiology and symptoms lacks for most cases, patients experience abdominal pain and a negative

impact on their quality of life. IBS is the most common functional gastrointestinal (GI) disease [1] and a diagnosis of IBS is based on the Rome criteria [2].

Although nearly 60% of patients claim that certain foods trigger their symptoms, patients with IBS who eliminate those foods often find only minor symptom improvements [3]. A novel treatment option for patients with IBS is the low fermentable, oligo-, di-, mono-saccharides and polyol (FODMAP) diet, which focuses on the restriction of fermentable, short-chain carbohydrates including galacto-oligosaccharides (GOS) and fructo-oligosaccharides (FOS), lactose (disaccharide), fructose (monosaccharide), and sorbitol (polyol). These carbohydrates are absorbed poorly in the small intestine, which leads to an

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increased intestinal osmolality and causes gas production due to rapid fermentation and osmotic action [4]. Therefore, the mechanism behind the low FODMAP diet lies in the reduction of the fermentable load and the liquid volume that is delivered to the colon to reduce gas production and luminal distension that is associated with GI symptom relief in patients with IBS [5].

The primary purpose of this study is to review and meta-analyze the effectiveness of such a diet in the treatment of functional GI symptoms in patients with IBS. The secondary goal is to determine the safety of the treatment and the influence on the microbiome.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for systematic reviews and meta-analyses [6] and the recommendations by the Cochrane Collaboration [7] were followed.

Eligibility criteria

Types of studies

Randomized controlled trials (RCTs) and randomized crossover studies were eligible for inclusion in the meta-analysis.

Types of participants

Adults, adolescents, and children with IBS were eligible if they were diagnosed with use of the Rome criteria [8]. Studies that involved participants with comorbid physical or mental disorders were also eligible for inclusion.

Types of interventions

Experimental. Dietary interventions including the application of a low FODMAP diet were eligible. No restrictions were made with regard to the duration of the program. Studies with cointerventions were allowed.

Control. Habitual diet or standard dietary intervention was included in the meta-analysis.

Types of outcome measures

To be eligible, RCTs had to assess at least one primary outcome: Severity of IBS symptoms as measured by patient-rated scales such as the IBS Severity Scoring System (IBS-SSS) [9] or any other validated scale, or abdominal pain or discomfort as measured through means such as a Numeric Rating Scale. The secondary outcomes included quality of life or well-being as measured by any generic or disease-specific validated scale such as the Health-Related Quality of Life Short Form 36 [10] or the IBS Quality of Life Questionnaire [11], anxiety or depression as measured by any validated scale such as the Hospital Anxiety and Depression Scale (HADS) [12], analysis of gut microbiota, and the safety of the intervention as assessed by the number of patients with adverse events.

Search methods

The MEDLINE/PubMed, Scopus, and Cochrane Library databases were searched from their inception through January 19, 2017. The literature search was constructed around search terms for “FODMAP” or “fermentable oligosaccharides disaccharides monosaccharides and polyols” and “irritable bowel syndrome” or “IBS”. For PubMed, the following search strategy was used: (“Irritable Bowel Syndrome”[MeSH] OR “Irritable bowel syndrome”[Title/Abstract] OR “IBS”[Title/Abstract]) AND (“FODMAP”[Title/Abstract] OR “FODMAPS”[Title/Abstract] OR “fermentable oligosaccharides disaccharides monosaccharides and polyols”[Title/Abstract]) AND (“Randomized Controlled Trial”[Publication Type] OR “controlled clinical trial”[Publication Type] OR randomized[Title/Abstract] OR placebo[Title/Abstract] OR random[Title/Abstract] OR randomly[Title/Abstract] OR trial[Title/Abstract] OR group[Title/Abstract]). The search strategy was adapted for each database as necessary.

Abstracts that were identified during the literature search were screened and articles that were potentially eligible were read in full to determine whether they met the eligibility criteria.

Data extraction and management

Data on patients (e.g., age, diagnosis), methods (e.g., randomization, allocation concealment), interventions (e.g., duration, administration of diet, dietary adherence), control interventions (e.g., type, cointerventions, outcomes [outcome measures, assessment time points]), and results were extracted independently by two authors using an a priori developed data extraction form.

Discrepancies were discussed with a third review author until a consensus was reached. If necessary, the study authors were contacted for additional information.

Risk of bias in individual studies

Two authors independently assessed the risk of bias with the risk-of-bias tool as proposed by the Cochrane Collaboration [7]. This tool assesses the risk of bias using 12 criteria on the domains of selection, performance, attrition, reporting, and detection. The risk of bias was assessed for each criterion as low risk, unclear, or high risk. Discrepancies were discussed with a third review author until a consensus was reached.

Data analysis

Assessment of effect size

If at least two studies assessing a specific outcome were available, meta-analyses were conducted using Review Manager 5 software Version 5.1 (The Nordic Cochrane Centre, Copenhagen, Denmark) by a random effects model [10] using the generic inverse variance method. For continuous outcomes, the standardized mean difference (SMD) with 95% confidence interval (CI) was calculated as the difference in means between the groups divided by the pooled standard deviation (SD). SMDs were calculated as Hedge’s *g* using a standardized Excel spreadsheet. For dependent samples (i.e., crossover trials), the calculation was adapted for intercorrelations between the groups. For articles where no correlation was reported, the SMD was estimated as 0.7. When unavailable, the SD was calculated from standard errors, CI, or *t*-values, or attempts were made to obtain the missing data from the trial authors by e-mail. A negative SMD was defined to indicate beneficial effects of the low FODMAP diet compared with the control intervention for all outcomes (e.g., decreased GI symptoms) except for quality of life where a positive SMD was defined to indicate beneficial effects (i.e., increased quality of life). Cohen’s categories were used to evaluate the magnitude of the overall effect size as follows: SMD of 0.2 to 0.5, small effect size; SMD of 0.5 to 0.8, medium effect size; and SMD greater than 0.8, large effect size.

Assessment of heterogeneity

The I^2 statistics, a measure of how much variance between studies can be attributed to differences between studies rather than chance, was used to analyze the statistical heterogeneity between the studies. The magnitude of the heterogeneity was categorized as $I^2 = 0\%$ to 25%, low heterogeneity; $I^2 = 26\%$ to 50%, moderate heterogeneity; $I^2 = 51\%$ to 75%, substantial heterogeneity; and $I^2 = 76\%$ to 100%, considerable heterogeneity [7,13]. The χ^2 test was used to assess whether differences in the results were compatible with chance alone. Given the low power of this test when only few studies or studies with a low sample size are included in a meta-analysis, a *P* value ≤ 0.10 was regarded as significant heterogeneity [7].

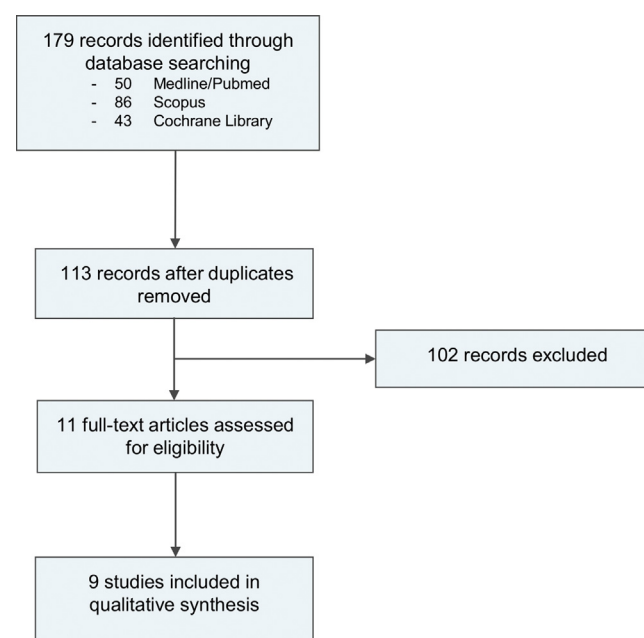


Fig. 1. Flow-chart of the literature search and study selection.

Table 1
Characteristics of the studies included in the meta-analysis

Reference	Origin: Country	Sample: 1. Sample size 2. Age (mean) 3. Sex 4. Ethnicity 5. Diagnostic criteria	Intervention: 1. Intervention 2. Program length 3. Study design	Control group: 1. Intervention 2. Program length	Follow-up: Outcome assessment	Outcome measures: 1. GI symptoms 2. Abdominal pain 3. Life Quality 4. Anxiety 5. Depression 6. Safety	Results: Low FODMAP diet compared with control group
Böhn et al. [15]	Sweden	1. N = 75 (intervention n = 38, control n = 37) 2. 18–69 y (42.5 y) 3. 31 f 4. NR 5. Rome III, all subtypes	1. Low FODMAP diet (3.8 ± 3.3 g/d) 2. 4 wk; dietary advice 3. Single-blind parallel design	1. Diet usually recommended for IBS (13.5 ± 8.7 g/d) 2. 4 wk dietary advice	4 wk	1. IBS-SSS 2. IBS-SSS subscale 3. NA 4. VSI 5. NA 6. NR	The severity of IBS symptoms was reduced in both groups without a significant difference between the groups. Food diaries demonstrated a good adherence to the dietary advice. Eight patients dropped out prematurely during the intervention period. Reporting of adverse events was lacking.
Chumpitazi et al. [16]	USA	1. N = 52 (intervention n = 16; control n = 17) 2. 7–17 y (NR) 3. 22 f 4. NR 5. Rome III	1. Low FODMAP diet (max. 9 g/d) 2. 48 h, meals provided 3. Double-blind crossover	1. TACD (max. 50 g/d) 2. 48 h	48 h	1. Likert Scale 2. Likert Scale 3. NA 4. HADS-A 5. HADS-D 6. Adverse events	During LFD, significantly less abdominal pain occurred vs. the TACD. The total composite GI score was significantly lower on LFD vs. TACD. Compliance between both diets was similar. Nineteen children dropped out of the study and 74% left the study before the start of any intervention. No adverse events occurred.
Eswaran et al. [23]	USA	1. N = 92 (intervention n = 50 control n = 42) 2. 19–75 y (42.6 y) 3. 65 f 4. 74% Caucasian 5. Rome III, IBS-D	1. Low FODMAP diet 2. 4 wk; dietary advice 3. Single-blind parallel design	1. mNICE guidelines 2. 4 wk; dietary advice	4 wk	1. Adequate relief, Bristol stool scale 2. NRS 3. NA 4. NA 5. NA 6. Adverse events	The LFD group had a significantly lower intake in FODMAPs after 4 wk. There were no significant differences between the groups for the Adequate Relief. Significant difference in favor of the LFD group occurred for abdominal pain and stool consistency. Seven patients left the study prematurely (LFD: 5; mNICE: 2). No adverse events occurred as reported by the investigators.
Halmos et al. [17]	Australia	1. N = 33 (crossover design) 2. 29–53 y (41.0 y) 3. 21 f 4. NR 5. Rome III, all subtypes	1. Low FODMAP diet (Ø 3.1 g/d) 2. 21 d; meals provided 3. Single-blind crossover	1. Normal western (Australian) diet (Ø 23.7 g/d) 2. 21 d; meals provided	21 d, wash-out at least 21 d	1. VAS 2. VAS 3. NA 4. NA 5. NA 6. NA 7. NA	Patients with IBS had lower overall GI symptoms and pain scores while on a low FODMAP diet compared with a western Australian diet. Three participants exited the study before commencing the second diet. Adverse events were not assessed.
Harvie et al. [22]	New Zealand	1. N = 50 (intervention n = 23; control n = 27) 2. 20–66 y (41.8 y) 3. 43 f 4. 96% Caucasian 5. Rome III, subtypes IBS-D, IBS-C, IBS-M	1. Low FODMAP diet 2. 3 mo 3. FODMAP content: 10.0 ± 7.9 g/d; dietary advice 4. Unblinded parallel design	1. Usual diet 2. 3 mo 3. FODMAP content: 27.1 ± 15.6 g/d; waitlist	3 mo	1. IBS-SSS 2. IBS-SSS subscale 3. IBS-QOL 4. NA 5. NA 6. NR	A significant relationship between change in FODMAP content and reduction in symptom severity was shown. There was also a tendency toward a change in total FODMAP content and in IBS quality of life. Four patients dropped out prematurely. Reporting of adverse events was lacking.
McIntosh et al. [18]	Canada	1. N = 40 (intervention n = 20; control n = 20) 2. 24–83 y (50.9 y) 3. 32 f 4. NR 5. Rome III, all subtypes	1. Low FODMAP diet 2. 3 wk; dietary advice, booklet with sample meals 3. Single-blind parallel design	1. High FODMAP diet 2. 3 wk; dietary advice, booklet with sample meals	3 wk	1. IBS-SSS 2. IBS-SSS subscale 3. NA 4. NA 5. NA 6. NR	Comparison of IBS-SSS scores postdiet scores showed a significant reduction in the low compared with the high FODMAP group for GI symptoms and abdominal pain. Compliance with the diets was good. Reporting of adverse events was lacking.

Pedersen	Denmark	<ol style="list-style-type: none"> 1. N = 127 (LFD n = 23; probiotic n = 41; control n = 13) 2. 18–73 y (34.6 y) 3. 90 f 4. NR 5. Rome III, subtypes IBS-D, IBS-C, IBS-A 	<ol style="list-style-type: none"> 1. Low FODMAP diet 2. 6 wk; dietary advice 3. Unblinded parallel design 	<ol style="list-style-type: none"> 1. Normal western (Danish) diet (habitual diet) 2. Probiotic supplementation with two capsules lactobacillus rhamnosus GG daily (6 billion per capsule) 3. 6 wk 	6 wk	<ol style="list-style-type: none"> 1. IBS-SSS 2. IBS-SSS subscale 3. IBS-QOL 4. NA 5. NA 6. NR 	Statistically significant reduction in IBS-SSS scores in the LFD group compared with normal diet. No significant effects in the probiotics group compared with normal diet. Eight patients discontinued participation from the low FODMAP diet, three from the normal diet, and four from the probiotics group. A report of adverse events was missing.
Staudacher et al. [20]	UK	<ol style="list-style-type: none"> 1. N = 41 (intervention n = 23; control n = 13) 2. NR (34.6 y) 3. 27 f 4. NR 5. Rome III, IBS-D 	<ol style="list-style-type: none"> 1. Low FODMAP diet (Ø 17.7 g/d) 2. 4 wk; dietary counseling by the same experienced dietitian; weekly contact via email or phone 3. 7-d food diary at baseline and final week 4. Unblinded parallel design 	<ol style="list-style-type: none"> 1. Habitual diet (Ø 29.6 g/d) 2. 4 wk 	4 wk	<ol style="list-style-type: none"> 1. Validated GI Symptom Rating Scale, Global Symptom Question 2. 4-Point Subscale of the Symptom Rating Scale 3. NA 4. NA 5. NA 6. Adverse Events 	Significantly more patients in the intervention group reported adequate symptom control and lower incidence of abdominal pain compared with control group. Patients in the intervention group had a significant reduction in scores for overall symptoms compared with the controls. Six patients dropped out of the study. Four patients had adverse events (two in the intervention, two in the control group), none of which were related to the trial.
Staudacher et al. [21]	UK	<ol style="list-style-type: none"> 1. N = 104 (intervention n = 51; control n = 53) 2. NR (34.4 y) 3. 70 f 4. 86 Caucasian 5. Rome III, IBS-D, IBS-M, IBS-U 	<ol style="list-style-type: none"> 1. Low FODMAP diet 2. 4 wk; dietary advice 3. Unblinded parallel design 	<ol style="list-style-type: none"> 1. Sham diet 2. 4 wk; dietary advice 	4 wk	<ol style="list-style-type: none"> 1. IBS-SSS, GSRS 2. IBS-SSS subscale 3. IBS-QOL 4. NA 5. NA 6. NR 	LFD resulted in a significantly lower IBS-SSS score than sham diet after intention to treat analysis and more patients on the LFD achieved the 14-point minimal clinical important difference for IBS-QOL scores. Reporting of adverse events was lacking.

f, female; GI, gastrointestinal; GIS, Global Improvement Scale; HADS-A, Hospital Anxiety and Depression Scale (anxiety-related); HADS-D, Hospital Anxiety and Depression Scale (depression-related); IBS-D, diarrhea-predominant irritable bowel syndrome; IBS-GAI, Irritable Bowel Syndrome Global Assessment of Improvement; IBS-QOL, Irritable Bowel Syndrome Quality of Life Questionnaire; IBS-SSS, Irritable Bowel Syndrome Symptom Severity Scale; LFD, low fermentable, oligo-, di-, mono-saccharides and polyol diet; m, male; mNICE, modified guidelines from the National Institute for Health and Care Excellence; NA, not assessed; NR, not reported; NRS, Numeric Rating Scale; VAS, Visual Analogue Scale; VSI, visceral sensitivity index; TACD, typical American childhood diet

Sensitivity analyses

To test the robustness of significant results, sensitivity analyses were conducted for studies with a high versus a low risk of bias at the domains of selection (random sequence generation and allocation concealment), detection (blinding of outcome assessment), and attrition (incomplete outcome data). If present in the respective meta-analysis, subgroup and sensitivity analyses were also used to explore possible reasons for statistical heterogeneity.

Results

Literature search

The literature search retrieved 179 records of which 113 non-duplicate records were screened and 105 records were excluded because they did not use an RCT design and/or a low FODMAP diet was not an intervention. One RCT was excluded because it used the low FODMAP diet only to wash out symptoms in the initial stage of the investigation on the effects of diets that were high or low in gluten [14]. Nine full-text articles on RCTs with a total of 596 subjects were included for the qualitative analysis [15–23]. One randomized crossover trial was excluded from the quantitative synthesis because data were not displayed as mean and SD and further information from the authors could not be retrieved [24]. Of the included articles, 561 patients matched the intervention criteria and were included in the meta-analysis (Fig. 1).

Study characteristics

Characteristics of the sample, interventions, outcome assessment, and results are shown in Table 1.

Setting and participant characteristics

Of the nine RCTs that were included in the meta-analysis, one originated from Australia [17], one from New Zealand [22], two from the United States [16,23], one from Canada [18], and four from Europe [15,19–21]. Patients were recruited from gastroenterology clinics [15,18,20,22,23], internet announcements and/or advertisements in newspapers [15–17,22,23], private dietetics, and tertiary pediatric gastroenterological care [16]. Patients in all RCTs were diagnosed with IBS according to Rome-III criteria including subtypes with predominant symptoms of either diarrhea (IBS-D) or constipation (IBS-C), mixed/alternating symptoms (IBS-M/A), or of unspecified type (IBS-U) except for two RCTs that only included IBS-D and/or symptoms of bloating [20,23]. Patients' age ranged from 7 y to 83 y with a median age of 39.5 y. Between 67% and 86% (median: 71.0%) of patients in each study were female. McIntosh et al. [18] and Eswaran et al. [23] were the only studies to specify further exclusion criteria such as the use of antibiotic medications, intake of probiotic treatments, stool bulking agents, narcotic analgesic, and lactulose. Patients were also excluded if on a Paleolithic or gluten-free diet, low FODMAP, or low carbohydrate diet.

Intervention characteristics

Two RCTs compared LFD with a habitual diet [20,22], one with a diet that is generally recommended for patients with IBS [15], and two provided all meals and compared LFD with a Western diet (American/Australian) [16,17]. One study compared LFD with a diet that is high in FODMAPs [18] and another with a sham diet [21]. One RCT measured LFD up to the usual diet recommendations for patients with IBS [15], and one RCT compared the LFD with the modified guidelines from the National Institute for Health and Care Excellence [23]. In the seven interventions that did not provide meals, dietary advice was given by an experienced dietitian.

Outcome measures

Symptoms of IBS were assessed in all RCTs for GI symptoms and pain using the Likert Scale [16], Visual Analogue Scale [14,17], Numeric Rating Scale [23], GI Symptom Rating Scale [20,21], Adequate Relief Question [23], or IBS-SSS [15,18,19,21,22]. Quality of life was assessed in two studies using the IBS Quality of Life Questionnaire [19,21,22]. Anxiety was assessed in two RCTs with the HADS (anxiety subscale) [16] and the Visceral Sensitivity Index. Depression was assessed through the HADS (depression subscale) in one RCT [16]. Although all RCTs reported short-term effects, no RCT reported long-term effects. Stool microbiota composition was analyzed by 16S ribosomal ribonucleic acid gene profiling by four studies [16,18,20,21].

Risk of bias in individual studies

The risk of bias in individual studies is shown in Figure 2. All studies reported adequate random sequence generation but five

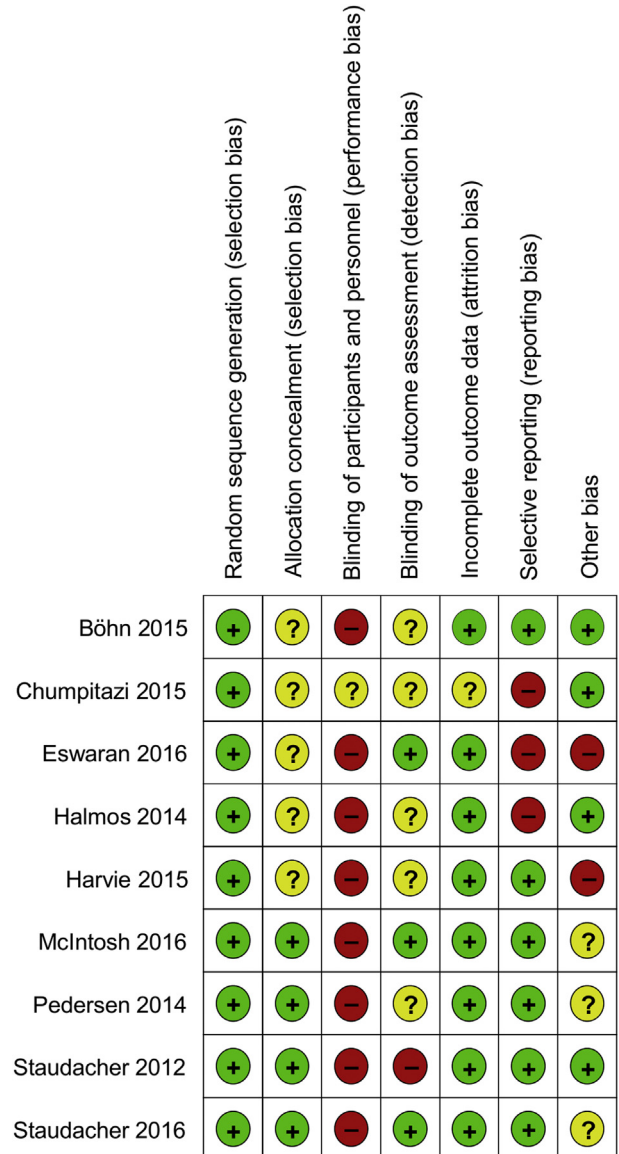


Fig. 2. Risk of bias for the included studies, rated as low risk (+), unknown risk (?), or high risk (-) for each category.

studies [15–17,22,23] did not report sufficient allocation concealment and none of the studies used/reported adequate blinding of participants and personnel. Blinding of the outcome assessment was sufficient in three studies [18,21,23]. A low risk was assessed for incomplete outcome data in all but one RCT [16]. Three RCTs were of high risk [16,17,23] for suspected selective reporting. High risk also had to be considered for other bias in two studies [22,23].

Analysis of overall effect

The results of the meta-analysis are displayed in Figures 3–5.

Primary outcomes

The meta-analysis revealed significant group differences for LFD compared with any control for GI symptoms (SMD = -0.62 ; 95% CI = -0.93 to -0.31 ; $P = 0.0001$; heterogeneity: $I^2 = 77\%$; $\chi^2 = 29.95$; $P = 0.0004$) and abdominal pain (SMD = -0.50 ; 95% CI = -0.77 to -0.22 ; $P = 0.008$; heterogeneity: $I^2 = 63\%$; $\chi^2 = 19.07$; $P = 0.0004$).

Although one study found no difference between patients with IBS-D and patients with IBS-C [17], improvements in IBS symptoms were less for patients with IBS-C in two studies [15,19]. While investigating mainly IBS-C subtypes, Chumpitazi et al. identified only eight responders of 33 participants to the LFD [16] while subjects of the remaining studies were primarily of IBS-D or IBS-M type [15,18,20–23].

Secondary outcomes

Evidence was found for short-term effects of LFD compared with any control on health-related quality of life (SMD = 0.36 ; 95% CI = 0.10 – 0.62 ; $P = 0.007$; heterogeneity: $I^2 = 14\%$; $\chi^2 = 3.48$; $P = 0.32$). One RCT measured anxiety and depression with the HADS questionnaire but no significant differences were found between the groups.

Four of the RCTs that were included assessed gut bacteria via 16S ribosomal ribonucleic acid profiling. Staudacher et al. demonstrated a reduction in concentration and proportion of luminal bifidobacteria after 4 wk of LFD [20,21] but not when combined with probiotic treatments [21]. In accordance, McIntosh et al. found a decrease in bifidobacteria after LFD [18]. Chumpitazi et al. solely assessed microbiota at baseline to identify potential responders and non-responders to the LFD according to individual gut bacteria profiles and found

responders to be enriched in microbes from several taxa with a larger saccharolytic potential [16].

Safety

Three studies provided safety-related data as assessed by adverse events [16,20,23]. Chumpitazi et al. and Eswaran et al. reported the absence of adverse events [16,23]. Staudacher et al. reported four adverse events: two in the intervention group (bronchitis, laryngitis) and two in the control group (exacerbation of asthma, pharyngitis) [20]. None of these events was considered related to the intervention.

Sensitivity analysis

Results for GI symptoms and abdominal pain did not change when only RCTs with low risk of selection, detection, or attrition bias were included. Thus, the effects were judged to be robust against potential methodological bias. Effects for quality of life were robust against selection and attrition bias but did not remain significant in the sensitivity analyses for detection bias. The assessment of the publication bias was initially planned using funnel plots generated by Review Manager software; however, because fewer than 10 studies were included in each meta-analysis, funnel plots could not be analyzed.

Discussion

Summary of evidence

In this systematic review of nine randomized trials, significant evidence for short-term benefits of diets that are low in FODMAPs was found for GI symptoms, abdominal pain, and quality of life in patients with IBS and no side effects were reported. Effects were robust against potential methodological bias.

Despite the evidence that supports LFD efficacy, more than 25% of patients with IBS do not improve on the diet [25]. This meta-analysis shows that adherence to LFD significantly improves GI symptoms. However, these improvements were investigated mostly for patients with IBS-D [15,19]. Symptom relief for patients with IBS-D is due to osmotic changes. Constipation underlies different intestinal mechanisms and has been associated with a lack of dietary fiber although additional fiber intake seems to be only moderately effective in patients with idiopathic constipation [26]. The LFD has been criticized for not providing sufficient sources of fiber and further research is

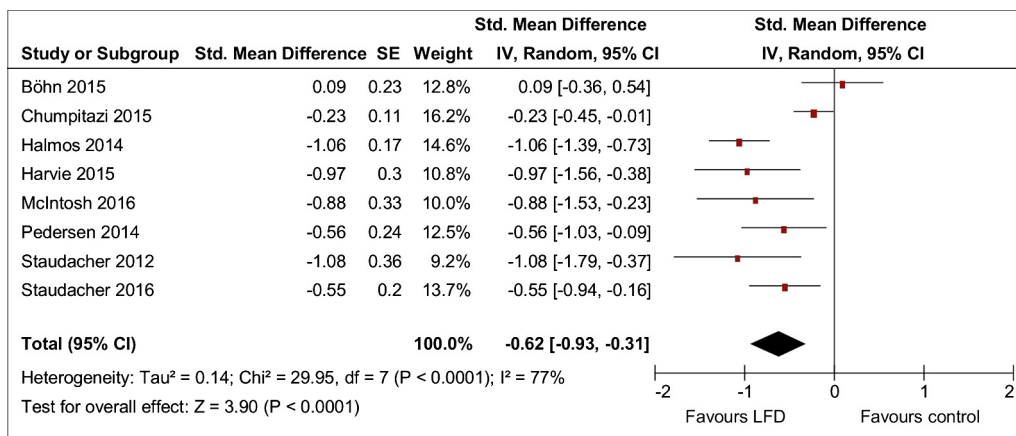


Fig. 3. Results of the meta-analysis for gastrointestinal symptoms in the low-FODMAP group versus control group.

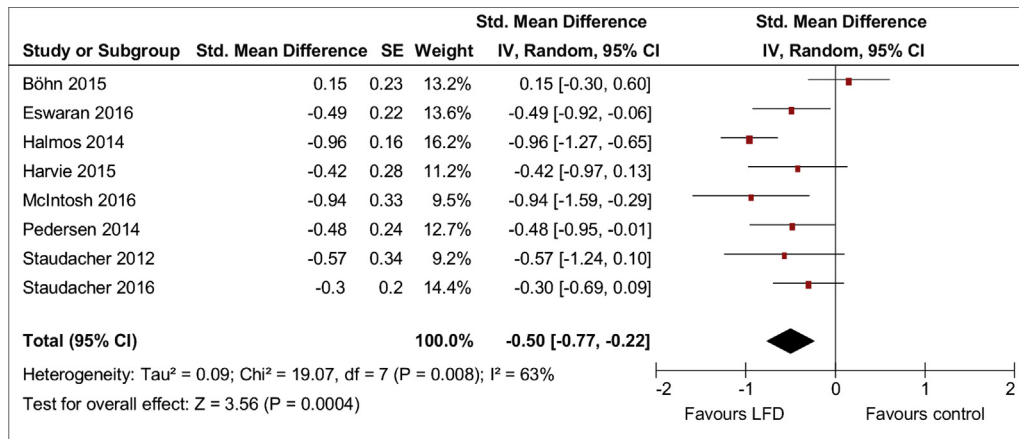


Fig. 4. Results of the meta-analysis for abdominal pain in the low-FODMAP group versus control group.

required to analyze effects on single subtypes as well as conjunctive therapies that benefit IBS-C. A strong association with psychiatric disorders in 94% of patients with IBS could be found [27,28], and further studies should investigate anxiety and depression as secondary outcomes.

One of the presumed mediators of the efficacy of a diet that is low in FODMAPs is the gut microbiome [25], which is also suggested to be involved in the etiology of IBS and depression [29,30]. The potential benefits of bifidobacteria have been indicated [31,32] and patients with IBS may have lower concentrations of luminal and mucosal bifidobacteria [33]. As the LFD seems to lower gut bifidobacteria, further research should focus on this outcome.

Agreements with prior systematic reviews

Only one prior systematic review has assessed the effects of a low FODMAP diet in patients with IBS to date. This review limited its assessment to two instruments (IBS-SSS and IBS Quality of Life Questionnaire) and included six RCTs as well as 16 non-randomized trials [34]. In line with our more comprehensive review, this prior review found a significant decrease in IBS-SSS scores and an improvement in IBS Quality of Life Questionnaire scores in both RCTs and non-randomized interventions. The findings of our review are also in line with a descriptive review on LFD for IBS that considered 40 articles (31 original studies and nine reviews) and concluded that the LFD should be the first dietary approach in patients with IBS because it not only improves symptoms but also provides relative ease of implementation [35].

External and internal validity

All studies used the Rome criteria as a standard for eligibility; thus, standardizing the results. Overall, the risk of bias of the included studies was unclear. Only three studies reported adequate blinding of the outcome assessment [18,21] and a general high risk was found for performance bias. Mainly patients from Europe, Australia, New Zealand, and North America were included and female patients represented the majority of participants. Thus, the findings might be limited to geographic regions and not fully applicable to male patients [36].

Strengths and weaknesses

The strengths of this review include the comprehensive literature search and assessment of applicability of the results [37]. The primary limitation of this review is the limited overall sample size and the methodological heterogeneity of the studies. Further, none of the studies reported long-term effects, and the results of this review cannot be extrapolated for long-term effects. The results concerning GI symptoms are based solely on subjective self-reported outcomes. It must be considered that the IBS-SSS may fail to detect changes in patients with mild IBS who score lower than 175 [9]. Most importantly, the safety of the intervention was insufficiently reported. Two unpublished studies that are in the process of submission for publication according to the study coordinators were included. The usefulness of including unpublished trials is still under debate [7].

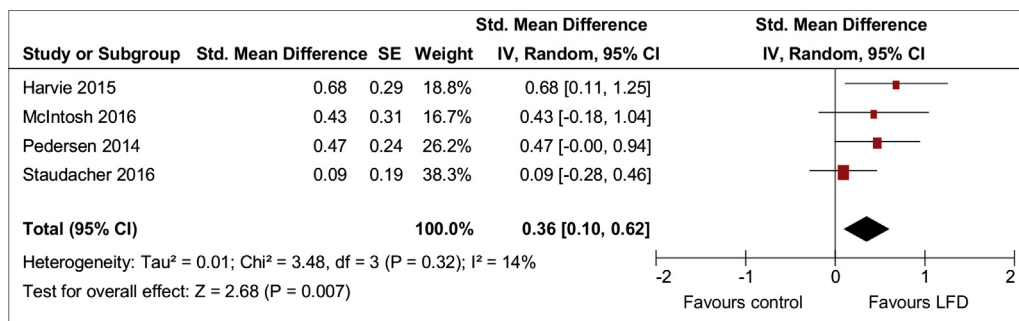


Fig. 5. Results of the meta-analysis for health-related quality of life in the low-FODMAP group versus control group.

Implications for further research

Further trials should develop programs that agree on an effective duration for GI symptom relief to occur within the first week of adherence as suggested by the majority of research. Although these effects seem to be due to osmotic changes, a stable adaption of gut microbiota to dietary changes is suggested to take more time [38]. For a more detailed IBS symptom assessment, the IBS-SSS is preferable and the IBS Quality of Life Questionnaire measurement scale can be used to establish changes in health-related quality of life [39]. Another drawback of this review resulted from the partially insufficient reporting of trial methodology and authors of prospect research should improve the reporting of trials and follow commonly accepted reporting guidelines (e.g., Consolidated Standards of Reporting Trials) [40]. Moreover, it is essential for further trials to survey dietary adherence, which is a driving factor for symptom relief. The LFD requires intensive meal planning by patients. In contrast with study interventions, the daily supply of patients with pre-cooked meals is not feasible in terms of time and costs in regular clinical practice.

Conclusion

This meta-analysis found evidence that the low-FODMAP diet is effective to relieve symptoms and improve the quality of life of patients with IBS. Still, long-term outcomes and the safety of low-FODMAP diets remain to be investigated. Further studies are required to evaluate its long-term effects on gut microbiota, cost effectiveness, and efficacy compared with other modalities.

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