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Low FODMAP Diet in the Treatment of Irritable Bowel Syndrome: A Systematic Review and Meta-Analysis

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Abbreviations: ANS - autonomic nervous system; CI - confidence interval; FODMAP(s) - Fermentable, Oligo-, Di-, Mono-saccharides and Polyols; FOS - fructo-oligosaccharides; GOS - galacto-oligosaccharides, GI - gastrointestinal; GIS - Global Improvement Scale; IBS - Irritable bowel syndrome; HADS - Hospital Anxiety and Depression Scale; IBS-D – diarrhea predominant IBS; IBS-GAI - IBS Global Assessment of Improvement; IBS-QOL – Irritable Bowel Syndrome Quality of Life questionnaire; IBS-SSS - IBS Symptom Severity Scale; LFD – Low FODMAP Diet; mNICE – modified guidelines from the National Institute for Health and Care Excellence; NRS - Numeric Rating Scale; RCT(s) - Randomized controlled trial(s); SF-36 - Health-Related Quality of Life Short Form 36; SMD - Standardized mean differences; STAI - state and trait anxiety inventory; VAS – Visual Analogue scale; VSI - Visceral Sensitivity Index.

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ABSTRACT

The aim of this review was to systematically assess and meta-analyze the effects of low FODMAP diet (LFD) on severity of symptoms, quality of life and safety in patients with irritable bowel syndrome (IBS). The databases MEDLINE/PubMed, Scopus and the Cochrane Library were screened through 19th January 2016. Randomized controlled trials (RCTs) comparing LFD to other diets were included when 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 differences (SMD) and 95% confidence intervals (CI) were calculated. Nine RCTs with a total of 596 subjects were included. Three RCTs compared LFD to habitual diet, two RCTs provided all meals and compared LFD to western diet, one RCT each compared LFD to a diet high in FODMAPs or a sham diet and two RCTs to other diet recommendations for IBS. Meta-analysis revealed significant group differences for LFD compared to other diets on 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 on health-related quality of life (SMD=0.36; 95%CI=0.10 to 0.62; p=0.007). Three studies reported a significant reduction in luminal Bifidobacteria after LFD. Adverse events were assessed in three RCTs only, no intervention-related adverse events were reported.

Finally, this meta-analysis found evidence for short-term efficacy and safety of LFD in patients with irritable bowel syndrome. However only preliminary recommendation for LFD can be made until long term effects are investigated.

Keywords: Irritable Bowel Syndrome, FODMAP diet, gut microbiota, Meta-analysis

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 correlation between pathophysiology and symptoms is lacking for most cases, patients experience abdominal pain and a negative impact on quality of life. IBS is the most common functional gastrointestinal (GI) [1] and diagnosis of IBS is based on Rome criteria [2].

Although nearly 60 % of patients claim that certain foods trigger their symptoms, IBS patients who eliminate those foods, often only find minor symptom improvements [3]. A novel treatment option for 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- and fructo-oligosaccharides (GOS, FOS), lactose (disaccharide), fructose (monosaccharide) and sorbitol (polyol). These carbohydrates are poorly absorbed in the small intestine which leads to an increased intestinal osmolality and causes gas production due to their rapid fermentation and osmotic action [4]. Therefore, the mechanism behind the low FODMAP diet lies in reducing the fermentable load and liquid volume delivered to the colon, to reduce gas production and luminal distension associated with gastrointestinal symptom relief in IBS patients [5]. Primary purpose of this study is to review and meta-analyze the effectiveness of such a diet in the treatment of functional gastrointestinal symptoms in IBS patients, while the secondary goal is to determine the safety of the treatment and the influence on the microbiome.

METHODS

PRISMA guidelines for systematic reviews and meta-analyses [6] and the recommendations of the Cochrane Collaboration [7] were followed.

Eligibility criteria

Types of studies

Randomized controlled trials (RCTs) and randomized cross-over studies were eligible.

Types of participants

Adults, adolescents and children with irritable bowel syndrome were eligible if they were diagnosed by Rome Criteria [8]. Studies involving participants with comorbid physical or mental disorders were eligible for inclusion.

Types of interventions

Experimental

Dietary interventions including the application of a low FODMAP diet were eligible. No restrictions were made regarding duration of the program. Studies with co-interventions were allowed.

Control

Habitual diet or standard dietary intervention.

Types of outcome measures

To be eligible, RCTs had to assess at least one primary outcome:

1. Severity of IBS-symptoms, measured by patient-rated scales, such as the Irritable Bowel Syndrome – Severity Scoring System (IBS-SSS) [9], or any other validated scale.

2. Abdominal pain or discomfort measured through means such as a Numeric Rating Scale (NRS).

Secondary outcomes included:

1. Quality of life or well-being measured by any generic or disease-specific validated scale such as the (SF-36) [10] or (IBS-QOL) [11].

2. Anxiety or depression measured by any validated scale such as Hospital Anxiety and Depression Scale (HADS) [12].

3. Analysis of gut microbiota.

4. Safety of the intervention assessed as number of patients with adverse events.

Search methods

MEDLINE/PubMed, Scopus and the Cochrane Library, databases were searched from their inception through 19th January 2017. The literature search was constructed around search terms for “FODMAP” or “fermentable oligosaccharides disaccharides monosaccharides and polyols” and search terms for “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 identified during literature search were screened and potentially eligible articles were read in full to determine whether they met 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, co-interventions, outcomes (e.g. 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 consensus was reached. If necessary, the study authors were contacted for additional information.

Risk of bias in individual studies

Two authors independently assessed risk of bias using the risk of bias tool proposed by the Cochrane Collaboration [7]. This tool assesses risk of bias on the following domains: selection bias, performance bias, attrition bias, reporting bias, and detection bias using 12 criteria. Risk of bias was assessed for each criterion as 1) low risk of bias, 2) unclear, 3) high risk of bias. Discrepancies were discussed with a third review author until consensus was reached.

Data analysis

Assessment of effect size

If at least 2 studies assessing a specific outcome were available, meta-analyses were conducted using Review Manager 5 software (Version 5.1, The Nordic Cochrane Centre, Copenhagen) by a random effects model [10] using the generic inverse variance method. For continuous outcomes, standardized mean differences (SMDs) with 95% confidence intervals (CIs) were calculated as the difference in means between groups divided by the pooled standard deviation (SD). SMDs were calculated as Hedge's g using a standardized Excel spreadsheet. For dependent samples (ie, crossover trials), the calculation was adapted for intercorrelations between groups. Where no correlation was reported, it was estimated as 0.7. Where no SDs were available, they were calculated from standard errors, CIs, 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 (eg, decreased gastrointestinal symptoms) except for quality of life where a positive SMD was defined to indicate beneficial effects (ie, 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; SMD of 0.5 to 0.8, medium; and SMD greater than 0.8, large effect sizes.

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 statistical heterogeneity between studies. The magnitude of heterogeneity was categorized as I^2=0-25%: low heterogeneity; I^2=26-50%: moderate heterogeneity; I^2=51-75%: substantial heterogeneity; and I^2=76-100%: considerable heterogeneity.[7, 13] The Chi^2 test was used to assess whether differences in results were compatible with chance alone. Given the low

power of this test when only few studies or studies with low sample size are included in a meta-analysis, a P-value ≤ 0.10 was regarded to indicate significant heterogeneity [7].

Sensitivity analyses

To test the robustness of significant results, sensitivity analyses were conducted for studies with high versus low risk of bias at the following domains: selection bias (random sequence generation and allocation concealment), detection bias (blinding of outcome assessment), and attrition bias (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 a RCT design and/or low FODMAP diet was not an intervention. One further RCT was excluded as it used the low FODMAP diet only to wash-out symptoms in the initial stage of the investigation on the effects of diets high or low in gluten [14]. Nine full-text articles (RCTs) with a total of 596 subjects were finally included for qualitative analysis [15-23]. One randomized cross-over trial was excluded from quantitative synthesis as data was not displayed as mean and SD and further information from the authors could not be retrieved [24]. Of those, 561 patients matched the intervention criteria and were included in the meta-analysis (Figure 1).

Study characteristics

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

Setting and participant characteristics

Of the 9 RCTs that were included, 1 originated from Australia [17], 1 from New Zealand [22], 2 from USA [16, 23], 1 from Canada,[18] and 4 from Europe [15, 19-21]. Patients were recruited from gastroenterology clinics [15, 18, 20, 22, 23], internet announcements and/or advertisement 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 or constipation, mixed/alternating symptoms or of unspecified type (IBS-D, IBS-C, IBS-M/A, IBS-U), except for 2 RCTs that only included IBS-D and/or symptoms of bloating [20, 23]. Patients' age ranged from 7 years to 83 years with a median age of 39.5 years. 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 antibiotics, intake of probiotics, stool bulking agents, narcotic analgesic and lactulose. Patients were also excluded if on Paleolithic or gluten-free diet, low FODMAP or low carbohydrate diet.

Intervention characteristics

Two RCTs compared LFD to habitual diet [20, 22], one RCT compared it to a diet generally recommended for IBS [15] and two studies provided all meals and compared LFD to western diet (American/Australian) [16, 17]. One study compared LFD to a diet high in FODMAPs [18] and one trial compared it to a sham diet [21]. One RCTs measured LFD up to usual diet recommendations for IBS [15] and one RCT compared the LFD to modified NICE guidelines [23]. In the 7 interventions that did not provide meals, dietary advice was given by an experienced dietician.

Outcome measures

Symptoms of IBS were assessed in all RCTs for gastrointestinal symptoms and pain using Likert Scale [16], Visual Analogue Scale [14, 17], Numeric Rating Scale [23], GI Symptom Rating Scale [20, 21], Adequate Relief Question [23] or Irritable Bowel Syndrome – Severity Scoring System (IBS-SSS) [15, 18, 19, 21, 22]. Quality of life was assessed in 2 studies using the Irritable Bowel Syndrome Quality of Life (IBS-QOL) questionnaire [19, 21, 22]. Anxiety was assessed in 2 RCTs using the Hospital Anxiety and Depression Scale (anxiety subscale, HADS-A) [16] and the Visceral Sensitivity Index (VSI). Depression was assessed through Hospital Anxiety and Depression Scale (depression subscale, HADS-D) in 1 RCT [16]. While all RCTs reported short-term effects, no RCT reported long-term effects. Stool microbiota composition was analyzed by 16S rRNA gene profiling by 4 studies [16, 18, 20, 21].

Risk of bias in individual studies

Risk of bias in individual studies is shown in figure 2. All studies reported adequate random sequence generation, but five 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 outcome assessment was sufficient in three studies [18, 21, 23]. 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 had also to be considered concerning other bias in two studies [22, 23].

Analysis of overall effect

Results of the meta-analysis are displayed in figures 3-5.

Primary outcomes

The meta-analysis revealed significant group differences for LFD compared to any control on gastrointestinal 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).

While one study found no difference between IBS-D and IBS-C patients [17], improvements in IBS symptoms were less for patients with IBS-C in two studies [15, 19]. Investigating mainly IBS-C subtypes, Chumpitazi et al. identified only 8 responders to the LFD out of 33 participants [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 to any control on health-related quality of life (SMD=0.36; 95%CI=0.10 to 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 in between groups.

Four of the included RCTs assessed gut bacteria via 16SrRNA-profiling. Staudacher et al. demonstrated a reduction in concentration and proportion of luminal Bifidobacteria after 4 weeks of LFD [20, 21] but not when combined with probiotics [21]. In accordance, McIntosh et al. found a decrease in Bifidobacteria after LFD. 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.

Safety

Three studies provided safety-related data, 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 were considered related to the intervention.

Sensitivity analysis

Results for gastrointestinal symptoms and abdominal pain did not change when only RCTs with low risk of selection bias, detection bias, or attrition bias were included; the effects were thus 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 sensitivity analyses for detection bias. Assessment of publication bias was initially planned using funnel plots generated by Review Manager software; however, as fewer than 10 studies were included in each meta-analysis, funnel plots could not be analysed.

DISCUSSION

Summary of evidence

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

Despite the evidence supporting LFD efficacy, more than 25% of IBS subjects do not improve on the diet [25]. This meta-analysis shows that adherence to LFD significantly improves gastrointestinal symptoms. However, these improvements were investigated mostly for patients with diarrhea predominant IBS type [15, 19]. Symptom relief for diarrhea-type IBS is supposed to be 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 idiopathic constipation [26]. The LFD has been criticized for not providing sufficient sources of fiber, and further research is required to look into effects on single subtypes as well as conjunctive therapies benefitting constipation-type IBS. A strong association of psychiatric disorders in 94% of IBS patients 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 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 in IBS has 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 IBS so far. This review limited its assessment on two instruments, the IBS-SSS Symptom severity Score and the IBS-QOL for IBS quality of life, and included 6 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 score and improvement in IBS-QOL score in both RCTs and non-randomized interventions. The findings of our review are also in line with a descriptive review on LFD for IBS which considered 40 articles (31 original studies and 9 reviews) and

concluded that the LFD should be the first dietary approach in patients with IBS as they found it not only improve symptoms but also to provide relative ease of implementation [35].

External and internal validity

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

Strengths and weaknesses

Strengths of this review include the comprehensive literature search and the 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, results of this review cannot be extrapolated for long term effects. Results concerning gastrointestinal symptoms are based solely on subjective self-reported outcomes. It has to be considered, that the IBS-SSS may fail to detect changes in patients with mild IBS scoring lower than 175 [9]. Most importantly, safety of the intervention was insufficiently reported. Two unpublished studies were included which are according to the study coordinators in the process of submitting for publication. The usefulness of including unpublished trials is still under debate [7].

Implications for further research

Further trials should develop programs that agree on an effective duration for gastrointestinal symptom relief, suggested by the majority of research to occur within the first week of adherence. While 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 Severity Scoring System is preferable and the IBS Quality of Life measurement scale can be used to establish changes in health-related quality of life [39]. Another drawback of this review resulted from partly insufficient reporting of trial methodology, and authors of prospect research should improve the reporting of trials and follow commonly accepted reporting guidelines (e.g. CONSORT) [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 the patients. In contrast to study

interventions, the daily supply of patients with precooked 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 to improve quality of life in patients with irritable bowel syndrome. Still, long-term outcomes and 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 as compared to other modalities.

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Table 1: Characteristics of the included studies.

Reference	**Origin** *Country*	**Sample** *Sample size;* *mean age;* *gender;* *ethnicity;* *diagnostic criteria*	**Intervention** *Intervention;* *program length;* *study design*	**Control group** *Intervention;* *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 to control group:*
Böhn et al., 2015	Sweden	*Sample size:* n=75 (intervention n=38, control n=37) *Age:* 18-69; (42.5) *Gender:* 31 f *Ethnicity:* NR *Diagnostic criteria:* Rome III, all subtypes	Low FODMAP diet (3.8 ± 3.3 g/d) 4 weeks Dietary advice Single blind parallel design	Diet usually recommended for IBS (13.5 ± 8.7 g/d) 4 weeks Dietary advise	4 weeks	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. 8 patients dropped out prematurely during the intervention period. Reporting of adverse events was lacking.
Chumpitazi et al. 2015	USA	*Sample size:* n=52 (intervention n=16; control n=17) *Age:* 7-17 (mean NR) *Gender:* 22 f *Ethnicity:* NR *Diagnostic criteria:* Rome III	Low FODMAP diet (max. 9 g/d) 48 h Meals provided Double-blind crossover	Typical American childhood diet (TACD) (max. 50 g/d) 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 diet. The total composite GI score was significantly lower on LFD vs. TACD. Compliance between both diets was similar. 19 children dropped out of the study, 74% left the study prior to the start of any intervention. Adverse events did not occur.
Eswaran et al. 2016	USA	*Sample size:* n=92 (intervention n=50 control n=42) *Age:* 19-75 (mean 42.6) *Gender:* 65 f *Ethnicity:* 74% caucasian *Diagnostic criteria:* Rome III, IBS-D	Low FODMAP diet 4 weeks Dietary advise Single blind parallel design	mNICE guidelines 4 weeks Dietary advise	4 weeks	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 weeks. There was 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. 7 patients left the study prematurely (LFD: 5, mNICE: 2). No adverse events occurred as reported by the investigators.

Halmos et al., 2014	Australia	*Sample size:* n=33 (crossover design) *Age:* 29-53 (41.0) *Gender:* 21 f *Ethnicity:* NR *Diagnostic criteria:* Rome III, all subtypes	Low FODMAP diet (Ø 3.1 g/d) 21 days meals provided single blind cross-over	normal western (australian) diet, (Ø 23.7 g/d) 21 days meals provided	21 days, wash-out at least 21 days	1. VAS 2. VAS 3. NA 4. NA 5. NA 6. NA 7. NA	IBS patients had lower overall GI symptoms and pain scores while on a low FODMAP diet compared to a western Australian diet. 3 participants exited the study before commencing the second diet. Adverse events were not assessed.
Harvie et al. 2015	New Zealand	*Sample size:* n=50 (intervention n=23; control n=27) *Age:* 20-66 (41.8) *Gender:* 43 f *Ethnicity:* 96 % caucasian *Diagnostic criteria:* Rome III, subtypes IBS-D, IBS-C, IBS-M	Low FODMAP diet 3 months FODMAP content: 10.0 ± 7.9 g/d Dietary advise Unblinded Parallel design	Usual diet 3 months FODMAP content: 27.1 ± 15.6 g/d waitlist	3 months	1. IBS-SSS 2. IBS-SSS subscale 3. IBS-QOL 4. NA 5. NA 6. NR	A significant relationship between a change in FODMAP content and a reduction in symptom severity could be shown. There was also a tendency towards a change in total FODMAP content and a change in IBS Quality of life. 4 patients dropped out prematurely. Reporting of adverse events was lacking.
McIntosh et al., 2016	Canada	*Sample size*: n=40 (intervention n=20; control n=20) *Age*: 24-83 (50.9) *Gender:* 32 f *Ethnicity:* NR *Diagnostic criteria:* Rome III, all subtypes	Low FODMAP diet 3 weeks Dietary advise, booklet with sample meals Single blind parallel design	High FODMAP diet 3 weeks Dietary advise, booklet with sample meals	3 weeks	1. IBS-SSS 2. IBS-SSS subscale 3. NA 4. NA 5. NA 6. NR	Comparison of the IBS-SSS post diet scores showed a significant reduction in the low compared to the high FODMAP group for gastrointestinal symptoms and abdominal pain. Compliance with the diets was good. Reporting of adverse events was lacking.
Pedersen et al., 2014	Denmark	*Sample size:* n=127 (LFD n=23; probiotic n=41; control n=13) *Age:* 18-73 (34.6) *Gender:* 90 f *Ethnicity:* NR *Diagnostic criteria:* Rome III, subtypes IBS-D, IBS-C, IBS-A	Low FODMAP diet 6 weeks Dietary advice Unblinded parallel design	1. normal western (danish) diet (habitual diet) 2. probiotic supplementation with 2 capsules Lactobacillus rhamnosus GG daily (6 billion per capsule) 6 weeks	6 weeks	1. IBS-SSS 2. IBS-SSS subscale 3. IBS-QOL 4. NA 5. NA 6. NR	Statistically significant reduction in IBS-SSS score in the LFD group compared to normal diet. No significant effects in the probiotics group compared to normal diet. 8 patients discontinued participation from the low FODMAP diet, 3 from the normal diet and 4 from the probiotics group. A report of adverse events was missing.

Staudacher et al. 2012	UK	*Sample size:* n=41 (intervention n=23; control n=13) *Age:* Range NR (34.6) *Gender:* 27 f *Ethnicity:* NR *Diagnostic criteria:* Rome III, IBS-D	Low FODMAP diet (Ø 17.7 g/d) 4 weeks Dietary counselling by the same experienced dietician Weekly contact via email or phone 7 day food diary at baseline and final week Unblinded parallel design	Habitual diet (Ø 29.6 g/d) 4 weeks	4 weeks	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 to control group. Patients in the intervention group had a significant reduction in scores for overall symptoms compared to control. 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., 2016	UK	*Sample size:* n=104 (intervention n=51; control n=53) *Age:* Range NR (34.4) *Gender:* 70 f *Ethnicity:* 86 caucasian *Diagnostic criteria:* Rome III, IBS-D, IBS-M, IBS-U	Low FODMAP diet 4 weeks Dietary advise Unblinded parallel design	Sham diet 4 weeks Dietary advise	4 weeks	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.

Legend: d – day; 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 IBS; IBS-GAI - IBS Global Assessment of Improvement; IBS-QOL – Irritable Bowel Syndrome Quality of Life questionnaire; IBS-SSS - IBS Symptom Severity Scale; LFD – Low FODMAP 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 - The visceral sensitivity index; TACD - Typical American childhood diet