Spring 2019

The evidence for the low-FODMAP diet in managing symptoms of Irritable Bowel Syndrome

Elizabeth Foley
Iowa State University

The Evidence for the Low-FODMAP Diet in Managing Symptoms of Irritable Bowel Syndrome

In partial fulfillment of requirements for the Masters of Family and

Consumer Sciences in Dietetics

Iowa State University

Elizabeth Foley

February 2019

ABSTRACT

Background: Irritable bowel syndrome (IBS) is a very common gastrointestinal disorder, with significant impact on quality of life. Until recently, there has been little evidence-base for treating GI symptoms through dietary therapy; clinical treatment is often unsuccessful or unsatisfactory. The low-FODMAP diet (LFD) has emerged as a potential therapy for alleviating GI symptoms.

Purpose: The purpose of this project is to evaluate the most current literature to determine the effectiveness of the low-FODMAP diet in managing the characteristic symptoms of IBS and to potentially identify a subset of the IBS population most likely to benefit from this approach. Ideally, this information may be translated into evidence-based and effective clinical treatment.

Methods: An electronic search was performed of the Academic Search Complete/EBSCO, Google Scholar, and PubMed databases to find related peer-reviewed, full-text articles which pertained to the research question. Randomized, controlled trials, descriptive trials, and meta-analysis studies published between January 2010 and June 2018 were included. Using methodology based on the Evidence Analysis process, pertinent data was collected on each study and a quality rating was assigned to studies to determine their "weight" in providing evidence for the research purpose.

Results: There were 15 RCTs found and 11 of these RCTs received a positive quality rating. All of the positively rated RCTs except for one found benefit to the LFD relative to IBS symptom control, although two studies of neutral quality found the LFD to be similar in effectiveness to the alternative intervention given to the comparator group. Three observational or non-randomized studies also found significant benefit(s) to the LFD in improving IBS symptoms,

with two of these studies indicating potential longer-term benefit to the LFD. Abdominal pain, bloating, flatulence, and bowel habit status scores were commonly analyzed as variables of interest, and most studies found benefit to the LFD for these particular symptoms. Most studies did not analyze or include the IBS-C subtype.

Conclusions: The LFD may be a good approach to use for IBS patients in the alleviation of abdominal pain, bloating, flatulence, and other symptoms. There is little evidence to support the use of the LFD for IBS-C. Further research should elucidate long-term effects and potential risk vs. benefit analysis in utilizing this approach.

BACKGROUND & SIGNIFICANCE

Irritable Bowel Syndrome (IBS) is a very common gastrointestinal disorder, seen often in clinical practice. Prevalence for IBS, based on pooled study populations, is estimated around 11.2%, but pooled prevalence estimates vary globally by geographic location (from 1.1% to 45%) and also by diagnostic criteria.[1] Prevalence is also higher in women than men, and higher in persons younger than 50 years, as compared to those older than 50. There are at least three, and possibly four, subtypes of IBS – IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), and IBS with mixed bowel pattern (IBS-M). Some studies also include an IBS with unknown patterns (IBS-U). When considering only three subtypes, a meta-analysis on IBS prevalence showed that IBS-D may be the most prevalent and IBS-M the least prevalent.[1] However when considering studies that included the fourth subtype (IBS-U), the same meta-analysis showed the prevalence of each subtype to be evenly distributed amongst the four subtypes.

There is currently no diagnostic biomarker for IBS, and symptoms can overlap with other organic gastrointestinal diseases.[2] It is considered a functional bowel disorder, meaning that organic evidence of disease will not be present. As such, it is often, unfortunately, a diagnosis of exclusion of organic disease. It is the most commonly diagnosed gastrointestinal disorder, with significant impact on quality of life.[3] IBS is defined by the presence of symptoms such as abdominal pain or discomfort, bloating, and altered bowel patterns, in the absence of any organic disease. The most recently revised Rome IV criteria should be utilized for diagnosis, which requires assessing the frequency of abdominal pain in association with changes in stool frequency and form.[2] Subtyping can then be assessed utilizing the Bristol Stool Form Scale and assessment of frequency of stool types. In most patients, IBS presents as a chronic relapsing disease, with symptoms and dynamics that change over time.[3]

4

There are multiple comorbidities associated with IBS, ranging from somatic pain syndromes, other gastrointestinal disease, and psychiatric disorders, perhaps pointing to a shared pathogenesis.[3] Pathophysiology of the disease is complex and multifactorial, possibly indicating IBS may encompass a variety of distinct diseases that share similar symptoms. Factors contributing to IBS pathophysiology and symptoms may include altered pain perception and/or brain-gut interaction, dysbiosis, increased intestinal permeability, increased gut mucosal immune activation, and heightened visceral sensitivity.[3]

Within the clinical realm, diet is an undisputed factor to consider when treating IBS, and patients often associate their IBS symptoms with eating a meal.[3] Foods can trigger the functional bowel symptoms associated with IBS. However, there are several reasons why IBS can be difficult to treat with diet. Firstly, IBS is multi-faceted and symptoms may be triggered by contributors that are not diet-related (i.e., life stressors, antibiotics, infection). There is a well-known psychological component to IBS dynamics, linking psychological state to symptom fluctuation.[3] IBS may also be difficult to treat nutritionally because symptoms and/or dietary triggers may be very different depending on the subtype of IBS that is present. Current research is unclear as to the major distinctions for dietary treatment of IBS-C vs. IBS-D, however, some studies have found differences in symptom response to dietary management between these subtypes.[4] In addition, standard or "traditional" diet approaches are often not sufficient to resolve symptoms. It is not uncommon in clinical practice to see patients who have implemented "traditional" diet advice and yet still struggle with unresolved symptoms. Finally, depending on the type of diet therapy offered, recommended changes may be complicated and/or difficult for the patient to implement, especially long-term.

There is inconsistency within the clinical realm as to what type of dietary therapy is provided for IBS. In general, there is little evidence concerning the underlying mechanisms by which food triggers functional bowel symptoms, which makes it difficult to develop diagnostic tests to detect certain food triggers.[5] Historically, there has been little evidence for effectiveness of dietary interventions on IBS symptoms. A trial-and-error approach is often taken within clinical practice, which could be considered an ineffective or inefficient approach, not to mention frustrating for patients seeking symptom relief. Traditional dietary advice, which may focus on timing of meals and certain food-related triggers like caffeine and alcohol, (such as that laid out in the United Kingdom's National Institute for Health and Care Excellence or "NICE" guidelines[6]) may be commonly offered; however emphasis and scope can be very different from clinician to clinician, likely contributing to patient frustration. Advice offered in the primary care setting may be often very basic, given the usual limited timeframe for patient education. Because of the nature and mechanisms of IBS as currently understood, there is likely a need for recommendations to be tailored to the individual's situation and symptoms.

Only within recent years, published literature has quickly multiplied in utilizing a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols—the low-FODMAP diet—to treat IBS symptoms. In fact, over the last 5-10 years, the low-FODMAP diet has become one of the most well-studied diets for functional bowel disorders, with numerous randomized controlled trials conducted in several geographic locations worldwide.[7] The low-FODMAP diet involves the restriction of 4 groups of short-chain fermentable carbohydrates which include the following: 1) oligosaccharides, fructans, and galacto-oligosaccharides—found in wheat and rye products, legumes, nuts, artichokes, onions and garlic; 2) the disaccharide lactose—found in milk products; 3) the monosaccharide fructose—found in fruits such as apples,

pears, watermelon, mango, as well as honey and some vegetables; and 4) polyols like mannitol and sorbitol--found in apples, pears, stone fruits, cauliflower, and mushrooms—as well as artificial sweeteners like xylitol.[8]

Restriction of individual carbohydrates (i.e., lactose or fructose) for the treatment of IBS symptoms is not a novel concept and has been commonly used for years; however, the collective and broader restriction of all of the aforementioned short-chain carbohydrates is what has been studied more recently.[5] Elimination or restriction of these carbohydrates is based on the idea that many of these carbohydrates enter the colon because of a lack of hydrolysis (fructans and galacto-oligosaccharides), incomplete hydrolysis (lactose), or incomplete absorption (fructose and polyols). These incompletely digested and highly fermentable carbohydrates are then potentially exacerbating IBS symptoms by increasing small intestinal water volume (i.e., osmotic effect of fructose and polyols[8]), small intestinal motility and colonic gas production.[5] Through reducing gas production and water, luminal distention may be limited, potentially reducing symptoms like bloating, pain, and excessive gas. Additive and dose-dependent effects of these carbohydrates may then be plausible.[5] Interestingly, there is evidence that it is not technically malabsorption, greater gas production, or visceral distention that drives IBS symptoms, but it is colonic hypersensitivity to distention that results in carbohydrate-related symptoms in these patients.[9-10]

The low-FODMAP diet begins as an elimination diet but is not intended to remain extremely restrictive. Seen as a whole, the diet is not a lifelong diet, but rather an approach to drastically drop FODMAP intake to a level at which they do not induce gastrointestinal symptoms followed by careful reintroduction and personalization of the diet.[2] Ideally, the diet implementation is executed via three important stages/clinical visits: 1) an initial clinical visit for

7

assessment, careful explanation and counseling on FODMAP restriction, 2) a second visit for re-assessment of diet/symptoms and counseling on FODMAP reintroduction to identify triggers, and 3) long-term personalization whereby a less restrictive diet is consumed. The restrictive phase typically lasts around 4 weeks but the process of re-challenge and personalization may require a lengthier commitment to the approach. The important aim in the multiple steps outlined above involves finding a balance between adequate symptom control and diverse dietary intake.[11]

PURPOSE

Based on the clinical picture of IBS presented thus far and the recent and rapidly accumulating works concerning low-FODMAP dietary therapy, it is necessary to review current research for the most updated evidence on the effectiveness of this approach. The purpose of this project is to evaluate the most current literature to determine the effectiveness of the low-FODMAP diet in managing the characteristic symptoms of IBS and to potentially identify a subset of the IBS population that is most likely to benefit from this approach. This information will not only provide dietetic professionals with the most updated evidence of this potential nutrition therapy, but may also serve to identify a critical learning need for those nutrition providers who give services to patients affected by IBS. Ideally, the information gained by this review will also serve to provide more consistency amongst healthcare providers and will translate into better care for IBS patients.

OUTLINE

The proposed literature review will discuss:

a) Low-FODMAP dietary interventions within the literature.

b) Control and comparator groups utilized with the low-FODMAP diet.

c) Tools utilized to measure IBS symptoms.

d) Key trends in symptom response to the low-FODMAP approach.

e) Individual symptom response to the low-FODMAP approach.

f) Evidence for the diet in relation to different IBS subtypes.

LITERATURE SEARCH/METHODS

The literature utilized in this review was gathered using an electronic search of the Academic Search Complete/EBSCO, Google Scholar, and PubMed databases to find related peer-reviewed, full-text articles. Keywords for the search included IBS, irritable bowel syndrome, and functional bowel/gut, combined with diet, food, nutrition, meal, lifestyle and/or treatment. Titles and abstracts were reviewed to determine applicability to the research question. Preference was given for including experimental studies with randomized, controlled designs to best contribute to the development of evidence-based guidelines; however, descriptive studies were also included if results or methods are applicable to the research question. Meta-analyses pertaining to the research question were included. Reference lists of included studies were cross-referenced for other studies of potential relevance. Only recent articles published between January 2010 and June 2018 were considered for this review. The Evidence Analysis Manual's "Search Plan & Results Template" was utilized to organize articles to be included or excluded from the review. Inclusion and exclusion criteria for articles are listed in Table 1 below.

Table 1: Inclusion vs. Exclusion Criteria

Inclusion Criteria`	Exclusion Criteria
Full-text articles	Articles with only abstract available
Peer-reviewed	Secondary reports (other than meta-analysis)
Primary research or Meta-analysis	Studies performed on children or patients <18 years of age
Published between Jan 2010 and June 2018	Studies performed on patients without clearly diagnosed IBS
Studies done on adults (age 18+)	Studies which did not formally assess IBS symptom response after low-FODMAP intervention
Studies performed on patients formally/clinically diagnosed with IBS (i.e., Rome criteria)	
Formally validated or clear method/tool utilized to measure IBS symptoms	
Valid and well-defined method of intervention	

A total of 26 studies, 22 primary reports and 4 meta-analyses, were included for review and were critically appraised using methodology based on the Evidence Analysis process. The Evidence Analysis Library's (EAL) "Worksheet Template" (see Appendix A) was utilized to collect pertinent data on each study. Once this data was extracted from each study, the EAL's "Quality Criteria Checklist" for either Primary Research or Review Articles (whichever was appropriate) was utilized to assign a quality rating to each study (see Appendices B and C). Studies were given a quality rating of positive, neutral, or negative, based on the score they obtained from the quality criteria checklist. Of the 26 studies included in the critical appraisal process, 22 of them (18 primary reports and 4 meta-analysis studies) obtained either a positive or netural score, and thus were considered in determining the "weight" of evidence for the research question. The 4 studies that were assigned a negative quality rating were not considered in weighing the evidence; thus these studies were not summarized in the study "Overview Table" (see Appendix D).

LITERATURE REVIEW

From the literature search as described previously, there were 15 original research articles identified describing randomized controlled trials (RCTs) which were relevant to the research question.[12-26] Of these RCTs, the majority of them (11 out of 15 studies) received a positive quality rating[12-22] and the remaining (4 out of 15) received a neutral quality rating.[23-26] All of the positively rated RCTs except for one[15] found some benefit to the low-FODMAP diet (LFD) in regards to IBS symptom control, although two studies of neutral quality found the LFD to be similar in effectiveness to the alternative intervention given to the comparator group.[25-26] In addition to the RCTs, there were two observational studies[27-28] and one non-randomized controlled trial[29] that were identified as relevant and rated of neutral quality. These three studies also found significant benefit(s) to the LFD in improving IBS symptoms, with the two observational studies indicating potential longer-term benefit to the LFD.

Interventions

The interventions utilized for a LFD in these studies primarily consisted of one-on-one verbal and written diet education. A trained dietitian or group of dietitians typically provided all dietary counseling, with 1-3 sessions of 30-60 minutes each. It is important to note that most of these clinical studies did not include the FODMAP reintroduction stage of the diet; rather, the intervention period only included the elimination phase of the diet. Thus there is little evidence available of the "long-term" effectiveness of the LFD, which ideally should include the three stages of 1) initial elimination, 2) reintroduction, and 3) personalization (as discussed previously).[11] However, there were three "long-term" studies identified which did clearly include FODMAP reintroduction in their methods. [21, 27-28] These studies analyzed longer-term data on

IBS symptoms in response to LFD education, with follow-up data ranging from 6-18 months after study initiation.

Three of the studies selected for review provided low-FODMAP food for dietary intervention – all three were randomized, controlled, cross-over trials.[16,20,24] Both Halmos et. al[16] and Ong et. al[24] provided subjects with all daily food; the former provided food for 21 days of treatment and the latter provided food for a short two-day intervention. Laatikainen et. al[20] only provided subjects with a certain number of bread slices (low-FODMAP vs. regular rye bread) and allowed a habitual diet to continue. The studies providing subjects with all food certainly present a strength for dietary control and an opportunity for examining the specific role of FODMAPs, especially as the intervention and control diets seemed to be well-matched for various potential nutrient confounders. However, as Halmos et. al[16] points out, this type of study design is not representative of reality and has limited applicability to real-life clinical treatment. Further, these studies did not or could not control for gluten intake, which could be a confounding dietary factor when studying symptomatology of IBS. Interestingly, when wheat intake is lowered, both fructans (a FODMAP) and gluten are reduced, making it more difficult to ascertain the true cause of symptom relief.[4]

Control/Comparator Groups

The low-FODMAP diet has been compared to many different alternative intervention diets or "control" diets. In fact, the RCTs examined are significantly heterogeneous in their methodology, in large part due to the comparator diet which is used to contrast the LFD. Four studies[13-15,29] compared the LFD to what is considered "traditional" dietary therapy based on NICE guidelines; although one of these studies modified NICE guidelines so that no FODMAP

food was excluded in their traditional diet group.[14] It is important to note that there is some potential overlap between NICE guidelines and LFD therapy, i.e., there are a few FODMAP foods restricted in the NICE guidelines, although not nearly as restrictive as the LFD. Three studies[18,21,25] compared the LFD to a habitual diet, or a non-intervention control group (no placebo control). One study[16] (previously mentioned) compared the LFD to a typical Australian diet but provided placebo control by providing blinded subjects with all daily food during the study period (however, the authors note they may have over-estimated some FODMAP content in the provided typical diet). Three studies compared the LFD to a high-FODMAP diet, with one providing all food for a short time-period,[24] another providing high-FODMAP dietary advice,[12] and another comparing high intake of one particular FODMAP (fructo-oligosaccharides supplement vs. placebo supplement) with the LFD.[22] One study compared the LFD to a specific carbohydrate diet,[17] one compared effectiveness to a yoga-based intervention,[26] one compared to a probiotic supplement (in addition to non-intervention group),[25] one compared low-FODMAP vs. regular rye bread in a habitual diet,[20] and one compared the LFD to a "sham" diet which was designed to be a similar diet in the restrictive sense.[19]

Krogsgaard et. al[30] performed a systematic review (2016) using nine RCTs which examined the role of the LFD on IBS symptoms. This review notes that choosing a control group for this type of research is very challenging; there are truly no established evidence-based treatment options for IBS with which to compare to the LFD. The review by Krogsgaard et. al criticizes the control groups in most studies do not allow discrimination of the true effect of the diet, and control groups utilized in future research should be chosen based on proven efficacy (and/or role as standard of care); true placebo control is also essential for this type of research. This is important as placebo response may be high and ranges from 3% to 84% in published

trials.[31] Interestingly, there have been at least two RCTs published in the last two years that have offered placebo-control and were able to show some significant benefits for the LFD approach.[19,22]

Tools for Measuring Symptom Effect

Within the research, there have been many tools utilized to measure IBS symptom change in response to the LFD and other interventions. All of the tools utilized are self-rated scales for the patient to complete. Perhaps the most popular is the formally validated symptom questionnaire, the IBS-Symptom Severity Score or IBS-SSS. This score can provide a measure of overall symptom severity, and consists of five questions regarding abdominal pain severity, abdominal pain frequency, abdominal bloating, bowel habit dissatisfaction and interference with quality of life on a visual analogue scale (VAS) from 0-100.[32] There were 9 RCTs examined that utilized the IBS-SSS scale to measure symptom response, although it was not always utilized as the primary endpoint.[12-13,15,19-22,25-26] Other VAS scales have also been used to measure various GI symptoms (0-10mm or 0-100mm scales).[16-17,20,22] Another scale validated in the IBS population to measure symptom response is the GI Symptom Rating Scale or GISRS.[18] This scale has been utilized to measure various GI symptoms using a 4-point scale.[18-19,27] Various non-validated Likert scales have been used to measure a number of IBS-related symptoms or symptom changes retrospectively.[24,28-29] In addition to measuring individual/total symptoms or the change in symptoms, other important endpoints have been used to examine the effects of the LFD, including a "global symptom question" (yes/no question regarding being adequately controlled),[18-19,22,27] an "adequate relief" question,[14] bowel habit status scores (using Bristol Stool Chart or King's Stool Chart),[13-16,18-19,27] and the IBS-QOL (measures important impact of IBS on quality of life).[19-21,23,25]

15

Most of the RCTs examined for this review did report positive effects of the LFD on IBS symptoms. As discussed, reduction in IBS-SSS score(s) was one of the primary or secondary outcomes of most of the RCTs reviewed. One of the largest RCTs (n=101) by Zahedi et. al[13] compared LFD education to traditional dietary advice (similar to NICE guidelines) and found that although both interventions reduced IBS-SSS scores and improved bowel habit status scores (stool consistency and frequency), the LFD produced a greater reduction in all of these measurements. In this Iranian population which only included IBS-D patients, all of the individual item symptom scores (included on the IBS-SSS) were significantly decreased in the LFD group vs. the traditional diet group. Another study with a larger sample size (n=104 in ITT analysis) by Staudacher et. al[19] measured IBS-SSS scores and compared the LFD with a placebo sham diet. These authors reported not only were total symptoms scores reduced in the LFD group, but 73% of patients reported a global clinical response or made what is referred to as "clinically meaningful improvement" based on IBS-SSS (reduction in total score of >50) vs. 42% in the sham diet group. This study examined all subtypes of IBS except IBS-C (and majority of subjects had IBS-D). Another smaller study by Harvie et. al[21] found significantly lower IBS-SSS scores and increased IBS-QOL scores for a LFD group (dietary education) after three months with sustained reductions at 6 months; however, this study compared the LFD in all IBS sybtypes to a parallel, non-intervention control group where placebo effect was not mitigated. In addition, an interesting smaller, double-blinded placebo-controlled crossover trial (n=20) by Hustoft et. al[22] examined subjects educated to a LFD diet and then supplemented with either an average daily amount of FODMAPs (via a fructo-oligosaccharide pill) or placebo. Not only did all participants see a significant drop in IBS-SSS score after 3 weeks on the LFD, but

16

symptoms were significantly greater in the FODMAP group vs. the placebo after the double-blinded supplement was given. A "global" question regarding symptom relief was also an outcome of this study, and 80% of participants reported symptom relief in response to placebo (LFD) vs. 30% to the FODMAP-supplemented group.

There is some evidence indicating the LFD has an advantage over other potential nutrition therapies. There were four studies identified which compared the LFD to other diet therapies, three of which compared LFD education to NICE guidelines[13-14,29] and one of which compared LFD education to a Specific Carbohydrate Diet (SCD).[17] One RCT and one non-randomized controlled trial found significant advantages for the LFD as compared to NICE guidelines.[13,29] Another study by Eswaran et. al[14] compared modified NICE instructions (which did not exclude any high FODMAP foods) with LFD education and found no difference in rates of "adequate relief" for IBS-D symptoms, but significantly greater reductions in abdominal pain, bloating, stool consistency, frequency and urgency with the LFD (as measured by numerical rating scale). Another study used a VAS scale and found significant reductions in abdominal pain and bloating in IBS patients after LFD education, as compared to no significant benefit with the use of the SCD.[17]

On the other hand, there is certainly some evidence that although the LFD is effective, it is similar in effectiveness to other interventions. A single-blinded RCT performed with Swedish subjects (n=67) compared groups who had been educated to the LFD vs. educated to traditional dietary advice (NICE guidelines).[15] Although IBS-SSS scores suggest symptom severity was reduced in both groups, changes relative to baseline did not actually differ between groups and approximately 50% of the subjects in both groups responded well to treatment. It is interesting to note that the group given traditional dietary advice also excluded some FODMAP-containing

foods, as per NICE guidelines. Another relatively large study (n=108) by Pedersen et. al[25] allocated patients to one of three groups: 1) LFD education (with some reintroduction education); 2) probiotic supplementation with habitual diet; or 3) control group with access to web-based general IBS education. Again, each of the 3 groups had a significant reduction of IBS-SSS scores; however, the probiotic and the LFD group both had significant reductions compared to control (although LFD group appeared to have greater advantage than the probiotic group when comparing changes in IBS-SSS over the 6-week study period). Schumann et. al[26] also found similar reductions in IBS-SSS score when comparing LFD education to yoga therapy over a 12-week intervention period. As these studies suggest, placebo response is very obviously present in this type of research and is an essential factor to consider when determining the true effectiveness of this diet.

There were two studies examined which compared the use of a LFD with a high-FODMAP diet (above normal average intake). As Krosgaard et. al[30] notes, this comparison is not clinically relevant, as the control arm does not serve as a placebo or as a potential treatment option. However, these types of studies serve to further understanding on the effects of FODMAPs in IBS patients. McIntosh et. al[12] reported a significant decrease in symptom scores (IBS-SSS) in patients educated to the LFD and a non-significant increase in symptoms in IBS patients educated to a high-FODMAP diet. Interestingly, these authors observed a positive correlation between dietary FODMAPs and increasing GI symptoms. Another study used a randomized crossover trial with 15 healthy subjects and 15 IBS patients to compare a LFD to a high-FODMAP diet, with all food provided for a 2-day period.[24] Using a 4-point Likert scale, these authors found a high-FODMAP diet significantly worsened symptoms for both patient populations, although the healthy population had worsened symptoms only due to increased

flatus. In addition to lower GI symptoms, IBS patients also reported increased upper GI symptoms and lethargy in response to this short-trial of high-FODMAP foods. These trials elucidate some of the potential mechanism behind FODMAP foods and their potential for symptom induction in IBS patients.

Individual Symptom Response

Within the clinical realm, in addition to general symptom response, it is arguably most helpful to use the literature to identify those specific symptoms which a LFD is most likely to alleviate. This helps clinicians target those IBS patients who would potentially have the greatest benefit to this approach. Although there are differences between studies in regards to specific symptoms measured, most studies evaluating the LFD assess at least some measure of individual GI symptoms. Many studies measure individual symptoms such as those included in the IBS-SSS (abdomen pain intensity/frequency, distention, dissatisfaction of bowel habit, and interference on life in general) and lower GI symptoms were most commonly assessed. Eswaran et. al[14] and several others[12-13,16,18-19,27-29] have demonstrated the benefit of a LFD on both abdominal pain and bloating, in particular. Flatulence, although not as frequently measured, also appears to be reduced with a LFD.[16,18-20, 27-29] Several studies have investigated bowel habit status scores and found benefit in favor of the LFD, with five of these studies reporting benefit to stool frequency[13-14, 16,18,27] and six improving stool consistency.[13-14,16, 18-19,27] One other study did find benefit to the LFD in reduction of stool frequency but results were not significantly better than the comparison group (traditional IBS/NICE dietary guidelines).[15] It is also essential to note that most of these studies enrolled primarily IBS-D patients and many did not analyze results by IBS subtype. One cited study which examined bowel habit status scores found the improvement in these scores was only present when analyzing IBS-D subtype.[16]

Other symptoms examined and perhaps less common within the literature include upper GI symptoms (nausea/vomiting, belching/gas), borborygmi (stomach rumbling), urgency, fatigue/tiredness, and IBS-related quality of life. Staudacher et. al[18] and Laatikainen et. al[20] reported reductions in borborygmi with either a LFD vs. habitual diet and low-FODMAP bread vs. regular rye bread, respectively. The former also reported benefit to the LFD for stool urgency, as did another RCT comparing LFD to modified NICE guidelines.[14] At least two studies have examined upper GI symptoms relative to FODMAPs; one found significant reduction of belching/gas and nausea/vomiting scores with a LFD, with a subsequent increase in these scores with supplementation of a certain FODMAP (FOS).[22] Another study also demonstrated increased upper GI symptoms (heartburn and nausea) with a high-FODMAP diet as compared to a low-FODMAP diet, whereas healthy controls did not have this response to increased FODMAPs.[24] In this study IBS patients also reported increased tiredness when fed a high-FODMAP diet. Finally, IBS-related quality of life was reported in response to low-FODMAP interventions in several of the studies via the IBS-QOL assessment. Four studies[19,21,23,25] utilizing IBS-QOL as an outcome observed increased quality of life after low-FODMAP interventions. One was only able to demonstrate improvement in a few individual areas of the QOL assessment[19] and another could only show improved QOL in the IBS-D subtype.[25] Another study failed to show any significant difference in QOL, although this study only intervened via provision of low-FODMAP vs. regular bread and did not target a full-diet adjustment.[20]

There were four meta-analyses identified, each with its own methodology to analyze a LFD approach in managing IBS symptoms.[32-35] The earliest meta-analysis by Marsh et. al[33] analyzed IBS-SSS and IBS-QOL scores in a total of 22 studies (6 RCTs and 16 non-randomized

interventions) and showed a positive association between the LFD and significant decrease in IBS-SSS score. This study reported abdominal pain and bloating were the symptoms which showed the most improvement in the RCTs and bloating, flatulence, pain, diarrhea, nausea and constipation (respectively) showed the most improvement in non-randomized interventions. A study by Varju et. al[32] also analyzed IBS-SSS scores, but in only controlled and uncontrolled studies which utilized LFD vs. a control group consisting of a standard IBS diet. This study found a LFD diet to be superior to a standard IBS diet in improving IBS-SSS score; however, it should be noted that standard IBS diet groups were very heterogeneous, with only two out of ten studies detailing exact food contents. Another meta-analysis by Altobelli et. al[35] examined 6 RCTs and 6 cohort studies, aiming to examine a LFD vs. traditional IBS diet, a LFD vs. medium- or high-FODMAP diet, and a LFD without comparator in cohort studies. This analysis reported LFD significantly reduced pain and bloating in all types of studies, with the additional benefit of improvements in stool frequency in the LFD v. traditional IBS diet studies (but no improvement in stool consistency). Finally, the most recent of meta-analyses by Schumann et. al[34] looked only at 9 RCTs (n=561 patients) which compared LFD to other diets and included a variety of patient-rated scales. Again, group differences were found for the LFD as compared to any control for GI symptoms and abdominal pain, and secondary outcome analysis found short-term improvements in quality of life. This study noted improvements were mainly seen with IBS-D patients. Authors of these meta-analysis studies note limitations to the current research, including inadequate blinding for the outcome assessment,[34-35] a general high risk for performance bias,[34] lack of adequate information on IBS subtypes,[32-34] limited ability to generalize findings to all geographic regions and to the male gender,[34] lack of control of dietary adherence,[33-34] and wide variation of study duration.[33]

IBS Subtype Analysis

There is currently a lack of evidence for the LFD in treating all IBS subtypes. In particular, the constipation-predominant IBS subtype has not been adequately studied for more conclusive results. There were six RCTs within this literature review that specifically excluded IBS-C subtypes[13-14,18-20,22] and two of these studies only included patients with IBS-D.[13-14] Several studies either had too few IBS-C patients to perform subgroup analysis or simply did not perform/publish a subgroup analysis,[12,17,21,24,27-29] although de Roest et. al[28] did report long-term improvement in constipation as well as other symptoms. Bohn et. al[15] included some analysis of subtypes in their RCT, but were unable to demonstrate a difference between IBS subtypes; the authors admit the trial was not powered to detect subgroup differences. Pedersen et. al[25] demonstrated benefits in symptom reduction in IBS-D and IBS-M patients, but no benefits were found for IBS-C patients. Halmos et. al[16] found similar beneficial results in pain, bloating, flatulence and satisfaction with stool consistency in both IBS-C and IBS-D subtypes, but only IBS-D subtypes had improvements in fecal frequency. Collectively, literature concerning the effectiveness of the LFD in constipation-predominant IBS appears sparse and inconclusive. It has been argued that as pain, bloating and flatulence may be found in all subtypes, it is possible that the LFD may still be helpful for IBS-C patients.[15] Although the LFD could lessen the discomfort often present in association with constipation, reduction of FODMAPs could also potentially reduce one's fiber intake, aggravating transit issues and contradicting benefit of the LFD.[36] Interestingly, a long-term follow-up study found a greater proportion of patients on an "adapted FODMAP" diet (who had already gone through the reintroduction phase of the diet) met fiber requirements than those who returned to a "habitual" diet.[27] However, more longer

term studies are needed to assess the adequacy of fiber and other nutrients after all phases of the LFD have been implemented.

Limitations

There were several important limitations identified in the current body of research for the LFD as it relates to IBS symptom control. Firstly, results cannot be generalized to all populations. As discussed in the previous section, these results were seen for the IBS population, and more specifically, mostly for those without the constipation-predominant subtype (diarrhea-predominant and mixed subtypes are more likely to benefit from this approach). In addition, the studies discussed were seen in mostly the US,[14,23] New Zealand,[21,28] Scandinavia,[15,20,22] Europe,[17-19,25-27,29] Australia,[16,24] Iran,[13] and Canada.[12] Results may then not be generalized to all cultures or geographic locations. It is also possible that these results do not apply the same to males. A recent meta-analysis by Schumann et. al[34] indicated RCTs were 67-86% female. However, related studies may simply reflect a clinical reality, as prevalence of IBS has been estimated at 14% of females vs. 9% of males.[1] Finally, as with all dietary therapies, results are more likely to be seen when subjects have the physical and mental capability of adhering to the diet; thus results cannot be expected within the general population or within any socioeconomic status. Not surprisingly, a long-term observational study by de Roest et. al.[28] reported a significant positive correlation between adherence to the LFD and improvement in IBS symptoms. Any elimination or restrictive diet such as the LFD is unlikely to be helpful and could be potentially harmful if patients have obvious barriers to adherence (i.e., financial, cognitive limits, etc.). As almost all of the studies in this review incorporated dietitian-led education, there

is little to no evidence that the LFD should be provided by anyone but a trained dietitian who would presumably be able to adequately assess for the appropriateness of the approach.

Many of the studies within this review lack adequate blinding and generally suffer from risk of performance bias. Most of the RCTs attempted to blind participants to the intervention assignment, however, many did not formally assess the adequacy of the blinding. It may be likely that some patients were able to deduce the nature of the diet that they were on; this may become more likely as the LFD approach continues to gain more popularity. This risk of bias which intervenes with a formal LFD education could artificially inflate positive results, especially as placebo effect is so strong within this area of study. As a systematic review by Krogsgaard et. al[30] suggests, future studies should be assessing the adequacy of the blinding on the side of the participant. In addition, although there were two studies which afforded a design that could be double-blinded,[20,22] it is not realistic to blind the educator who gives the LFD education; thus, those studies which provided more clinically relevant situations (LFD education by a dietitian) may risk bias on the part of those giving the intervention. This risk of bias is likely unavoidable in these types of studies.

Another potential limitation of these studies that is worth noting is a general lack of control for dietary adherence. Of those studies that utilized LFD education and assessed nutrient/FODMAP intake,[14-15,18-19, 21] there was significantly less FODMAP intake in the LFD intervention group (i.e., intake was as expected after dietary intervention). However, these results cannot necessarily be generalized across studies. Typically, adherence was measured via a food diary implemented in the last several days of the intervention period; thus, strict control was not feasible. A meta-analysis published in 2016 by Marsh et. al[33] indicated a lack of studies providing adherence figures and quantities of FODMAPs ingested. A meta-analysis published in

24

2017 by Varju et. al[32] found similar issues with only 2 out of 10 studies detailing exact food contents. In general, future studies should include feasible methods of assessing dietary adherence, although strict control of dietary intake is challenging and/or unfeasible for research in the "realistic" clinical education setting.

Although not necessarily a limitation, it is important to note the variable study duration within these studies. There were few studies that looked at longer-term effects of the LFD, and most did not include a FODMAP reintroduction period. Most examined only the initial low-FODMAP phase, with widely different study durations. It appears the LFD may be effective for abdominal pain in as little as 2 days,[24] but study durations for the initial low-FODMAP phase lasted as long as three months.[21] One RCT found greatest symptom control was established about seven days after implementation of the LFD.[16] The meta-analysis by Marsh et. al[33] found the widely variable study duration may potentially act as a confounder of results, as results may be then more diversified. It is also possible that changes to the gut microbiota may play a role in symptom improvement and it has been suggested that these changes may take up to eight weeks to occur.[18] Long-term studies are greatly needed in this area of research, as this will help determine the true effectiveness and clinical meaning for the LFD.

Finally, it is evident from current research that an important limitation to the use of this diet is potentially unknown long-term side effects. Potential side effects of concern include nutrient inadequacies and detrimental gastrointestinal microbiota alterations. One longer-term study (6 months) found initial decreases in fiber intake but a subsequent increase after FODMAP reintroduction.[21] An observational study suggests a LFD can be nutritionally adequate up to 18 months after the dietary education, with no evidence of harm in the low-FODMAP group which maintained a selectively limited FODMAP diet.[27] Overall, there is a need for more research to

determine possible nutrient inadequacies long-term. Although there is evidence that the initial low-FODMAP phase can alter the microbiome in a potentially unfavorable way,[12, 18-19, 22] none of the studies were able to adequately assess long-term changes (after FODMAP reintroduction) to the microbiome. These long-term effects are a necessary research area and currently, they are likely the most important determinants and/or potential barriers to the clinical use of a LFD.

Discussion/Conclusion

The low-FODMAP diet has been a very popular research area in recent years, with encouraging results for those that suffer from symptoms of IBS. As IBS is such a common disorder with considerable clinical cost, effective treatments are no doubt going to be met with enthusiasm. A dietary approach is also considered a more acceptable approach and may be more welcome in current US culture than the pharmacological approach. This literature review has identified a considerable number of RCTs and some observational studies which have investigated the effect of the LFD on GI symptoms. Based on the articles included in this review, it appears that the LFD has significant benefits in reducing GI symptoms that accompany IBS, particularly abdominal pain, bloating, and flatulence. Bowel habit status scores (stool frequency and consistency) also seem to improve with the LFD, although this effect might not apply to the IBS-C subtype. It is possible that it has benefit in the alleviation of other upper GI symptoms and non-GI symptoms; however, more research needs to be performed in these areas. Quality of life also seems to improve for IBS patients on a LFD. In general, the evidence base is only strong for utilizing this approach in the IBS-D and IBS-M population. It is possible that patients with the IBS-C subtype may still have benefit, particularly with symptoms such as pain and bloating; however, there is not enough evidence for a definite conclusion.

There are certainly unknowns for the LFD approach which need further elucidation. It does appear that this approach is more effective than placebo or a standard IBS dietary therapy; however, more research should be done. Ideally, RCTs should be well-designed, with placebo control, adequate blinding of the participant and investigator, and adequate assessment of dietary intake, dietary adherence, and other possible confounders (medications/supplements,etc.). Admittedly, designing a study without these weaknesses is challenging and likely costly. Additional research should further analyze effects on all subtypes of IBS (particularly IBS-C) and on more diverse populations. Arguably, the most important need for further research lies in the long-term effects of the LFD, which would encompass all stages of the diet. The beginning stages of the long-term research do not indicate nutrient inadequacies, but point towards the potential for alteration of the gut microbiome. These areas should be investigated further.

In conclusion, the LFD may be a good approach to use for IBS patients in the alleviation of abdominal pain, bloating, flatulence, and other symptoms. Patients without IBS-C and with applicable GI complaints should likely be targeted for potential use of this dietary therapy. Further research should elucidate long-term effects and potential risk vs. benefit analysis in utilizing this approach.

REFERENCES

1. Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clin Gastroenterol Hepatol.* 2012;10(7):712-721.e714.
2. Whelan K, Martin LD, Staudacher HM, Lomer MCE. The low FODMAP diet in the management of irritable bowel syndrome: an evidence-based review of FODMAP restriction, reintroduction and personalisation in clinical practice. *J Hum Nutr Diet.* 2018;31(2):239-255.
3. Chey WD, Kurlander, J, Eswaran S. Irritable bowel syndrome: a clinical review. *JAMA.* 2015;313(9):949-958. doi:10.1001/jama.2015.0954. Accessed March 21, 2018.
4. McKenzie YA, Bowyer RK, Leach H, et. al. British Dietetic Association systematic review and evidence-based practice guidelines for the dietary management of irritable bowel syndrome in adults (2016 update). *J Hum Nutr Diet.* 2016; doi:10.1111/jhn.12385. Accessed March 23, 2018.
5. Staudacher HM, Whelan K. Altered gastrointestinal microbiota in irritable bowel syndrome and its modification by diet: probiotics, prebiotics and the low FODMAP diet. *Proc Nutr Soc.* 2016;75(3):306-318.
6. Irritable bowel syndrome in adults: diagnosis and management. National Institute for Health and Care Excellence website. https://www.nice.org.uk/guidance/cg61/chapter/1-Recommendations#dietary-and-lifestyle-advice. Updated April 2017. Accessed September 14, 2018.
7. Tuck CJ, Vanner SJ. Dietary therapies for functional bowel symptoms: Recent advances, challenges, and future directions. *Neurogastroenterol Motil.* 2018;30(1).
8. Barrett JS. How to institute the low-FODMAP diet. *J Gastroenterol Hepatol.* 2017;32 Suppl 1:8-10.
9. Wilder-Smith CH, Materna A, Wermelinger C, Schuler J. Fructose and lactose intolerance and malabsorption testing: the relationship with symptoms in functional gastrointestinal disorders. *Aliment Pharmacol Ther.* 2013;37(11):1074-1083.
10. Major G, Pritchard S, Murray K, et al. Colon Hypersensitivity to Distension, Rather Than Excessive Gas Production, Produces Carbohydrate-Related Symptoms in Individuals With Irritable Bowel Syndrome. *Gastroenterology.* 2017;152(1):124-133.e122.
11. Tuck C, Barrett J. Re-challenging FODMAPs: the low FODMAP diet phase two. *J Gastroenterol Hepatol.* 2017;32 Suppl 1:11-15.
12. McIntosh K, Reed DE, Schneider T, et al. FODMAPs alter symptoms and the metabolome of patients with IBS: a randomised controlled trial. *Gut.* 2017;66(7):1241-1251.
13. Zahedi MJ, Behrouz V, Azimi M. Low fermentable oligo-di-mono-saccharides and polyols diet versus general dietary advice in patients with diarrhea-predominant irritable bowel syndrome: A randomized controlled trial. *J Gastroenterol Hepatol.* 2018;33(6):1192-1199.

14. Eswaran SL, Chey WD, Han-Markey T, Ball S, Jackson K. A Randomized Controlled Trial Comparing the Low FODMAP Diet vs. Modified NICE Guidelines in US Adults with IBS-D. *Am J Gastroenterol.* 2016;111(12):1824-1832.

15. Böhn L, Störsrud S, Liljebo T, et al. Diet low in FODMAPs reduces symptoms of irritable bowel syndrome as well as traditional dietary advice: a randomized controlled trial. *Gastroenterology.* 2015;149(6):1399-1407.e1392.

16. Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology.* 2014;146(1):67-75.e65.

17. Vincenzi M, Del Ciondolo I, Pasquini E, Gennai K, Paolini B. Effects of a Low FODMAP Diet and Specific Carbohydrate Diet on Symptoms and Nutritional Adequacy of Patients with Irritable Bowel Syndrome: Preliminary Results of a Single-blinded Randomized Trial. *J Transl Int Med.* 2017;5(2):120-126.

18. Staudacher HM, Lomer MC, Anderson JL, et al. Fermentable carbohydrate restriction reduces luminal bifidobacteria and gastrointestinal symptoms in patients with irritable bowel syndrome. *J Nutr.* 2012;142(8):1510-1518.

19. Staudacher HM, Lomer MCE, Farquharson FM, et al. A Diet Low in FODMAPs Reduces Symptoms in Patients With Irritable Bowel Syndrome and A Probiotic Restores Bifidobacterium Species: A Randomized Controlled Trial. *Gastroenterology.* 2017;153(4):936-947.

20. Laatikainen R, Koskenpato J, Hongisto SM, et al. Randomised clinical trial: low-FODMAP rye bread vs. regular rye bread to relieve the symptoms of irritable bowel syndrome. *Aliment Pharmacol Ther.* 2016;44(5):460-470.

21. Harvie RM, Chisholm AW, Bisanz JE, et al. Long-term irritable bowel syndrome symptom control with reintroduction of selected FODMAPs. *World J Gastroenterol.* 2017;23(25):4632-4643.

22. Hustoft TN, Hausken T, Ystad SO, et al. Effects of varying dietary content of fermentable short-chain carbohydrates on symptoms, fecal microenvironment, and cytokine profiles in patients with irritable bowel syndrome. *Neurogastroenterol Motil.* 2017;29(4).

23. Eswaran S, Chey WD, Jackson K, Pillai S, Chey SW, Han-Markey T. A Diet Low in Fermentable Oligo-, Di-, and Monosaccharides and Polyols Improves Quality of Life and Reduces Activity Impairment in Patients With Irritable Bowel Syndrome and Diarrhea. *Clin Gastroenterol Hepatol.* 2017;15(12):1890-1899.e1893.

24. Ong DK, Mitchell SB, Barrett JS, et al. Manipulation of dietary short chain carbohydrates alters the pattern of gas production and genesis of symptoms in irritable bowel syndrome. *J Gastroenterol Hepatol.* 2010;25(8):1366-1373.

25. Pedersen N, Andersen NN, Végh Z, et al. Ehealth: low FODMAP diet vs Lactobacillus rhamnosus GG in irritable bowel syndrome. *World J Gastroenterol.* 2014;20(43):16215-16226.
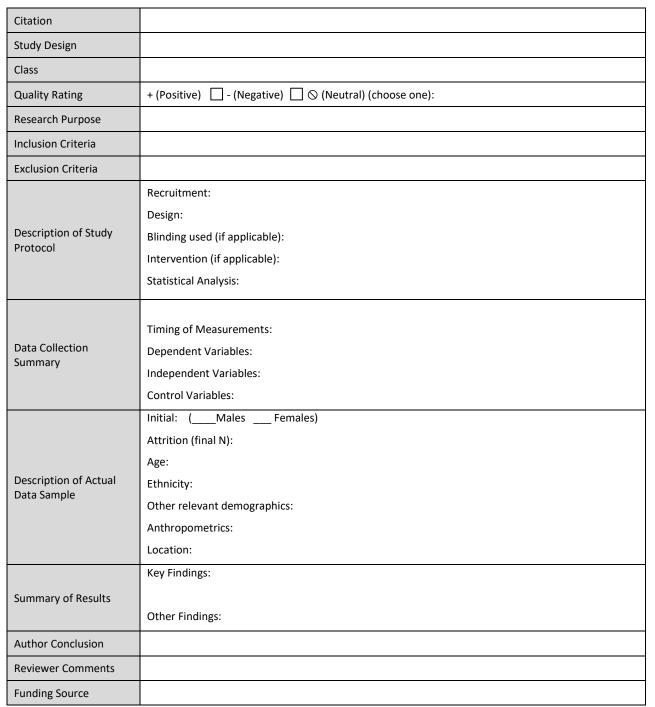
26. Schumann D, Langhorst J, Dobos G, Cramer H. Randomised clinical trial: yoga vs a low-FODMAP diet in patients with irritable bowel syndrome. *Aliment Pharmacol Ther.* 2018;47(2):203-211.
27. O'Keeffe M, Jansen C, Martin L, et al. Long-term impact of the low-FODMAP diet on gastrointestinal symptoms, dietary intake, patient acceptability, and healthcare utilization in irritable bowel syndrome. *Neurogastroenterol Motil.* 2018;30(1).
28. de Roest RH, Dobbs BR, Chapman BA, et al. The low FODMAP diet improves gastrointestinal symptoms in patients with irritable bowel syndrome: a prospective study. *Int J Clin Pract.* 2013;67(9):895-903.
29. Staudacher HM, Whelan K, Irving PM, Lomer MC. Comparison of symptom response following advice for a diet low in fermentable carbohydrates (FODMAPs) versus standard dietary advice in patients with irritable bowel syndrome. *J Hum Nutr Diet.* 2011;24(5):487-495.
30. Krogsgaard LR, Lyngesen M, Bytzer P. Systematic review: quality of trials on the symptomatic effects of the low FODMAP diet for irritable bowel syndrome. *Aliment Pharmacol Ther.* 2017;45(12):1506-1513.
31. Enck P, Horing B, Weimer K, et al. Placebo responses and placebo effects in functional bowel disorders. Eur J Gastroenterol Hepatol. 2011;24:1-8.
32. Varjú P, Farkas N, Hegyi P, et al. Low fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) diet improves symptoms in adults suffering from irritable bowel syndrome (IBS) compared to standard IBS diet: A meta-analysis of clinical studies. *PLoS One.* 2017;12(8):e0182942.
33. Marsh A, Eslick EM, Eslick GD. Does a diet low in FODMAPs reduce symptoms associated with functional gastrointestinal disorders? A comprehensive systematic review and meta-analysis. *Eur J Nutr.* 2016;55(3):897-906.
34. Schumann D, Klose P, Lauche R, Dobos G, Langhorst J, Cramer H. Low fermentable, oligo-, di-, mono-saccharides and polyol diet in the treatment of irritable bowel syndrome: A systematic review and meta-analysis. *Nutrition.* 2018;45:24-31.
35. Altobelli E, Del Negro V, Angeletti PM, Latella G. Low-FODMAP Diet Improves Irritable Bowel Syndrome Symptoms: A Meta-Analysis. *Nutrients.* 2017;9(9).
36. Halmos EP. When the low FODMAP diet does not work. *J Gastroenterol Hepatol.* 2017;32 Suppl 1:69-72.

APPENDIX A

WORKSHEET TEMPLATE

Academy of Nutrition and Dietetics

Evidence Analysis Library® Worksheet Template

Academy of Nutrition and Dietetics

Citation	
Study Design	
Class	
Quality Rating	+ (Positive) ☐ - (Negative) ☐ ⊘ (Neutral) (choose one):
Research Purpose	
Inclusion Criteria	
Exclusion Criteria	
Description of Study Protocol	Recruitment: Design: Blinding used (if applicable): Intervention (if applicable): Statistical Analysis:
Data Collection Summary	Timing of Measurements: Dependent Variables: Independent Variables: Control Variables:
Description of Actual Data Sample	Initial: (____Males ___ Females) Attrition (final N): Age: Ethnicity: Other relevant demographics: Anthropometrics: Location:
Summary of Results	Key Findings: Other Findings:
Author Conclusion	
Reviewer Comments	
Funding Source	

Academy of Nutrition & Dietetics, Evidence Analysis Library/Evidence Analysis Manual

QUALITY CRITERIA CHECKLIST – PRIMARY

Quality Criteria Checklist: Primary Research

Symbols Used

+   **Positive:** Indicates that the report has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis.

--   **Negative:** Indicates that these issues have not been adequately addressed.

Ø   **Neutral:** Indicates that the report is neither exceptionally strong nor exceptionally weak.

Quality Criteria Checklist: Primary Research

RELEVANCE QUESTIONS					
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (NA for some Epi studies)	Yes	No	Unclear	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes	No	Unclear	N/A
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to dietetics practice?	Yes	No	Unclear	N/A
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes	No	Unclear	N/A
If the answers to all of the above relevance questions are "Yes," the report is eligible for designation with a plus (+) on the Evidence Quality Worksheet, depending on answers to the following validity questions.					
VALIDITY QUESTIONS					
1.	**Was the** <u>research question</u> **clearly stated?**	Yes	No	Unclear	N/A
	1.1 Was the specific intervention(s) or procedure (independent variable(s)) identified?				
	1.2 Was the outcome(s) (dependent variable(s)) clearly indicated?				
	1.3 Were the target population and setting specified?				
2.	**Was the** <u>selection</u> **of study subjects/patients free from bias?**	Yes	No	Unclear	N/A
	2.1 Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?				
	2.2 Were criteria applied equally to all study groups?				
	2.3 Were health, demographics, and other characteristics of subjects described?				
	2.4 Were the subjects/patients a representative sample of the relevant population?				
3.	**Were** <u>study groups comparable</u>**?**	Yes	No	Unclear	N/A
	3.1 Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)				
	3.2 Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?				
	3.3 Were concurrent controls used? (Concurrent preferred over historical controls.)				
	3.4 If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?				
	3.5 If case control study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)				
	3.6 If diagnostic test, was there an independent blind comparison with an appropriate				

		reference standard (e.g., "gold standard")?				
4.		**Was method of handling <u>withdrawals</u> described?**	Yes	No	Unclear	N/A
	4.1	Were follow up methods described and the same for all groups?				
	4.2	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)				
	4.3	Were all enrolled subjects/patients (in the original sample) accounted for?				
	4.4	Were reasons for withdrawals similar across groups?				
	4.5	If diagnostic test, was decision to perform reference test not dependent on results of test under study?				
5.		**Was <u>blinding</u> used to prevent introduction of bias?**	Yes	No	Unclear	N/A
	5.1	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?				
	5.2	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)				
	5.3	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?				
	5.4	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?				
	5.5	In diagnostic study, were test results blinded to patient history and other test results?				
6.		**Were <u>intervention</u>/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were <u>intervening factors</u> described?**	Yes	No	Unclear	N/A
	6.1	In RCT or other intervention trial, were protocols described for all regimens studied?				
	6.2	n observational study, were interventions, study settings, and clinicians/provider described?				
	6.3	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?				
	6.4	Was the amount of exposure and, if relevant, subject/patient compliance measured?				
	6.5	Were co-interventions (e.g., ancillary treatments, other therapies) described?				
	6.6	Were extra or unplanned treatments described?				
	6.7	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?				
	6.8	In diagnostic study, were details of test administration and replication sufficient?				
7.		**Were <u>outcomes</u> clearly defined and the <u>measurements valid and reliable</u>?**	Yes	No	Unclear	N/A
	7.1	Were primary and secondary endpoints described and relevant to the question?				
	7.2	Were nutrition measures appropriate to question and outcomes of concern?				
	7.3	Was the period of follow-up long enough for important outcome(s) to occur?				
	7.4	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?				
	7.5	Was the measurement of effect at an appropriate level of precision?				
	7.6	Were other factors accounted for (measured) that could affect outcomes?				
	7.7	Were the measurements conducted consistently across groups?				
8.		**Was the <u>statistical analysis</u> appropriate for the study design and type of outcome indicators?**	Yes	No	Unclear	N/A
	8.1	Were statistical analyses adequately described the results reported appropriately?				
	8.2	Were correct statistical tests used and assumptions of test not violated?				
	8.3	Were statistics reported with levels of significance and/or confidence intervals?				
	8.4	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?				
	8.5	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?				

8.6	Was clinical significance as well as statistical significance reported?		
8.7	If negative findings, was a power calculation reported to address type 2 error?		
9.	**Are <u>conclusions supported by results</u> with biases and limitations taken into consideration?**	Yes No Unclear N/A	
9.1	Is there a discussion of findings?		
9.2	Are biases and study limitations identified and discussed?		
10.	**Is bias due to study's <u>funding or sponsorship</u> unlikely?**	Yes No Unclear N/A	
10.1	Were sources of funding and investigators' affiliations described?		
10.2	Was there no apparent conflict of interest?		

MINUS/NEGATIVE (-)

If most (six or more) of the answers to the above validity questions are "No," the report should be designated with a minus (-) symbol on the Evidence Worksheet.

NEUTRAL (∅)

If the answers to validity criteria questions 2, 3, 6, and 7 do not indicate that the study is exceptionally strong, the report should be designated with a neutral (∅) symbol on the Evidence Worksheet.

PLUS/POSITIVE (+)

If most of the answers to the above validity questions are "Yes" (including criteria 2, 3, 6, 7 and at least one additional "Yes"), the report should be designated with a plus symbol (+) on the Evidence Worksheet.

Academy of Nutrition & Dietetics, Evidence Analysis Library/Evidence Analysis Manual

QUALITY CRITERIA CHECKLIST – REVIEW

Quality Criteria Checklist: Review Articles

Symbols Used	Explanation
+	**Positive –** Indicates that the report has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis
--	**Negative –** Indicates that these issues have not been adequately addressed.
⊘	**Neutral** – indicates that the report is neither exceptionally strong nor exceptionally week

Select a rating from the
drop-down menu ↓

Relevance Questions	
1. Will the answer if true, have a direct bearing on the health of patients?	Select a Rating
2. Is the outcome or topic something that patients/clients/population groups would care about?	Select a Rating
3. Is the problem addressed in the review one that is relevant to dietetics practice?	Select a Rating
4. Will the information, if true, require a change in practice?	Select a Rating

If the answers to all of the above relevance questions are "Yes," the report is eligible for designation with a plus (+) on the Evidence Quality Worksheet, depending on answers to the following validity questions.

Validity Questions	
1. Was the question for the review clearly focused and appropriate?	Select a Rating
2. Was the search strategy used to locate relevant studies comprehensive? Were the databases searched and the search terms used described?	Select a Rating
3. Were explicit methods used to select studies to include in the review? Were inclusion/exclusion criteria specified and appropriate? Were selection methods unbiased?	Select a Rating
4. Was there an appraisal of the quality and validity of studies included in the review? Were appraisal methods specified, appropriate, and reproducible?	Select a Rating
5. Were specific treatments/interventions/exposures described? Were treatments similar enough to be combined?	Select a Rating
6. Was the outcome of interest clearly indicated? Were other potential harms and benefits considered?	Select a Rating
7. Were processes for data abstraction, synthesis, and analysis described? Were they applied consistently across studies and groups? Was there appropriate use of qualitative and/or quantitative synthesis? Was variation in findings among studies analyzed? Were heterogeneity issued considered? If data from studies were aggregated for meta-analysis, was the procedure described?	Select a Rating
8. Are the results clearly presented in narrative and/or quantitative terms? If summary statistics are used, are levels of significance and/or confidence intervals included?	Select a Rating
9. Are conclusions supported by results with biases and limitations taken into consideration? Are limitations of the review identified and discussed?	Select a Rating
10. Was bias due to the review's funding or sponsorship unlikely?	Select a Rating

MINUS/NEGATIVE (-)
If most (six or more) of the answers to the above validity questions are "No," the review should be designated with a minus (-) symbol on the Evidence Quality Worksheet.
NEUTRAL (∅)
If the answer to any of the first four validity questions (1-4) is "No," but other criteria indicate strengths, the review should be designated with a neutral (∅) symbol on the Evidence Worksheet.
PLUS/POSITIVE (+)
If most of the answers to the above validity questions are "Yes" (must include criteria 1, 2, 3, and 4), the report should be designated with a plus symbol (+) on the Evidence Worksheet.

Academy of Nutrition & Dietetics, Evidence Analysis Library/Evidence Analysis Manual

APPENDIX D

OVERVIEW TABLE

Author/Year/ Study Design	Purpose	Population	Intervention	Key Outcomes	Conclusions	Limitations
			Primary Sources, Positive Quality Rating			
McIntosh et. al., 2016, Randomized, controlled, single-blinded trial	To compare the effects of low-FODMAP and high-FODMAP diets on symptoms, the metabolome, and microbiome of IBS patients.	Adults recruited from outpatient clinic in Ontario Canada who met Rome III criteria for IBS of any subtype & had symptoms for >6 months.	Either a high-FODMAP or low-FODMAP dietary education session (30-60 minutes) with a dietitian; specific written materials provided detailing allowed foods and sample meals.	Patients in low-FODMAP group had a signficant decrease in symptom scores (28%) utilizing IBS-SSS tool; patients on high-FODMAP diet had an increase in symptoms (7% increase, although not significant). Increases in dietary FODMAPs positively correlated with increasing symptoms. The lactulose breath test was not found to be a good predictor of diet responders.	FODMAP content is linked to IBS symptoms; there is a significant correlation between a quantitative measure of FODMAP content consumption and symptoms; changes in gut microbiota could be involved in symptom generation; a low-FODMAP diet could induce unhealthy changes at the microbial level.	There was no dietary intake assessment at baseline. Adequacy of the blinding of subjects was not formally monitored/ evaluated --it's possible they deduced the nature of the diet they were on.
Zahedi et. al, 2018, randomized, controlled, single-blinded trial	To compare the effect of low FODMAP diet vs "general diet advice" on quality of life and symptoms in patients with IBS-D.	Eligible patients referred to GI care clinic in Kerman, Iran meeting IBS-D criteria	Diet interventions via 45 min education with printed materials; Diet A: low-FODMAP diet intervention vs. Diet B: general IBS diet advice	Total scores of IBS-SSS, scores for individual item symptoms, and bowel habit status scores (Bristol scale) were reduced in both groups; individual item symptoms & bowel habit status scores improved significantly more in low-FODMAP group.	Both low-FODMAP and generalized dietary advice in IBS-D patients led to improvement of GI symptoms; low-FODMAP diet has greater benefit in reducing symptoms.	Results NOT generalizable to other IBS subtypes; single-blinded only; food intake not provided and thus not strictly controlled.

			originating from British Dietetic Association (caffeine, alcohol, small frequent meals, etc.)			
Eswaran et. al, 2016, Randomized, controlled, single-blind trial	To assess the impact of the low-FODMAP diet vs. modified NICE guidelines in patients with IBS-D	US patients with IBS-D who presented consecutively to GI and primary care clinics and/or recruited via advertisements.	Low-FODMAP dietary instruction vs. modified NICE instructions (which did not exclude high FODMAP foods).	The dietary interventions resulted in similar rates of "adequate relief" for IBS-D symptoms (52% low FODMAP vs 41% NICE guidelines); no significant difference as well in proportion of composite end point responders; however, low-FODMAP diet resulted in significantly greater reductions in average daily scores of abdominal pain, bloating, consistency, frequency, and urgency as compared to the NICE diet.	Both interventions led to adequate relief of overall symptoms in 40-50% of patients with IBS-D; the low-FODMAP diet led to significantly greater benefit particularly for abdominal pain and bloating, thus supporting a role for the diet in management of IBS-D patients.	Underpowered to detect modest difference in clinical benefit -- authors indicate likelihood of Type II error for their primary endpoint of "adequate relief"; food not provided to subjects; possible for bias to be introduced through patient deducing diet type or dietitian giving education.
Bohn et. al, 2015, randomized, controlled, single-blinded study	To compare the effects of a low-FODMAP diet vs. traditional dietary advice on IBS symptoms in outpatients.	Subjects with all subtypes of IBS, enrolled from GI outpatient clinics in Sweden	Patients received verbal & written instruction regarding either low-FODMAP diet or traditional IBS diet stemming from NICE guidelines (included some	IBS symptom severity reduced in both groups; the change in IBS-SSS relative to baseline did not differ between groups; a similar proportion of patients were defined as "responders" in both the treatment groups (~50% in each group).	Dietary advice provided to patients with IBS in the clinical setting reduces symptoms but there are not obvious differences between a low-FODMAP vs. a traditional IBS diet	Possible that supplements/probiotic intake could have confounded results (these were not controlled for); some FODMAP-containing foods were likely excluded in traditional IBS diet

			exclusion of FODMAP-containing foods).		education; it seems possible that dietary advice can produce desired effects (per food diaries); calorie/nutrient intake need to be monitored, especially long-term.	making diets more similar; no mention that investigators analyzing the data were blinded.
Halmos et. al, 2014, Randomized, controlled, single-blind, cross-over trial	To compare GI symptoms over 3 weeks of a low-FODMAP diet with moderate FODMAP intake (on a typical Australian diet) in patients with IBS who had never had advice from a dietitian.	Patients with any subtype of IBS and healthy controls without GI symptoms / Australia	Almost all daily food (3 meals & 3 snacks) was provided to subjects for 21 days of treatment, followed by 21-day washout, followed by the other 21-day treatment. Diets consisted of a low-FODMAP diet (<.5g FODMAP per sitting) vs. typical Australian diet, moderate in FODMAP content.	Overall GI symptoms were significantly less on the low-FODMAP diet and greater on the typical Australian diet, compared with baseline (measured via VAS scale). Bloating, pain and flatulence was also significantly improved on the low-FODMAP diet. Patients of all IBS subtypes had greater satisfaction with stool consistency although IBS-D subjects were the only subtype with altered fecal frequency and King's Stool Chart scores.	The low-FODMAP diet is effective to treat functional GI symptoms of IBS with symptoms being halved as compared to a typical Australian diet. This study supports the notion that the low-FODMAP diet works in the vast majority of IBS patients.	Oligosaccharide and polyol content of typical Australian diet provided was likely over-estimated (when comparing to subjects' baseline diet), leading to worse symptoms; potential difficulty with subject blinding related to the influence of change in symptoms; gluten could not be matched in diets-- may be a confounding factor.

Vincenzi et. al, 2017, Randomized, single-blinded, controlled trial	To assess efficacy of a low-FODMAP diet as compared to a specific carbohydrate diet on symptoms of outpatients with IBS, and to evaluate the nutritional adeqaucy of both diets.	Outpatients of Italian hospital clinics with IBS (presumably any subtype, although not specified)	Subjects were instructed by a dietitian to either eat a low-FODMAP diet or a specific carbohydrate diet and were given written instructional materials.	Patients with low-FODMAP diet had significant improvement in bloating and distention, while the SCD diet had a low & not significant improvement; comparable severity was shown in symptoms between 2 groups but a difference in symptoms after 12 days; low-FODMAP diet did not cause Vit D & folic acid deficiencies after 3 months.	IBS subjects benefitted from a low-FODMAP diet but NOT the specific carbohydrate diet, and a low-FODMAP diet does not seem to cause folic acid & vit D deficiencies.	No mention of assessment of blinding; not enough info given in this "preliminary results" study regarding statistical comparison for symptoms between the groups; no mention made of excluding those on "strict" diets already.
Staudacher et. al, 2012, randomized, unblinded, controlled trial	To investigate the effects of FODMAP restriction on the luminal microbiota, SCFA, & GI symptoms in IBS patients.	IBS patients with who met criteria for moderate/seve re symptoms (NOT those with primary constipation/I BS-C) from GI clinics in the UK	Participants randomly assigned to either low-FODMAP diet (dietitian-delivered education) or instructed to continue habitual diet; patients in both groups had weekly contact although "habitual" dieters were offered no advice.	Lower concentrations and proportions of bifidobacteria in intervention group vs. control at follow-up; more patients reported adequate symptom control in intervention group vs. control group (ITT: 68% vs. 23%); more patients in intervention group experienced reduction in bloating, borborygmi, urgency, and overall symptoms & also more had lower incidence of bloating, pain, and overall symptoms; intervention	Low-FODMAP diet is an effective management strategy for IBS, resulting in reductions in overall symptoms and bloating. However it can also result in significant reductions in luminal bifidobacteria after 4 weeks--long-term effects on health are unknown.	No blinding utilized; no control for placebo response in control group; results NOT generalizable to IBS-C as this population was not studied.

				group reported lower stool frequency & greater proportion of stools with normal consistency.		
Staudacher et. al, 2017, Randomized, placebo-controlled trial, w/ 2x2 factorial design	To investigate the effect of the low FODMAP diet compared with a placebo diet & to investigate whether low-FODMAP diet-induced microbiota alterations could be prevented through concurrent probiotic therapy compared with placebo.	IBS patients recruited in clinics at 2 hospitals in London, excluding IBS-C patients	Patients randomized to diet advice (sham diet or low-FODMAP) and supplement (placebo or multi-strain probiotic); 10 min diet education with weekly phone conversations; placebo diet designed to be similar to low-FODMAP as an exclusion diet, for similar intensity and duration & for similar nutrient intake and fiber.	For the ITT analysis, higher proportion reporting adequate symptom relief for low-FODMAP diet, although did not reach significance like the per protocol analysis showed (61% low-FODMAP diet, 39% sham diet). IBS-SSS significantly lower for patients on low-FODMAP diet. Bifidobacterium species abundance lower in fecal samples of those on low-FODMAP diet, but higher in patients given probiotic than those given placebo.	Low-FODMAP diet advice leads to improvement in overall and specific GI symptoms in IBS (2-3 greater odds of response to low-FODMAP compared with placebo); the low-FODMAP diet effect on bifidobacteria may be modified by concurrent probiotic therapy.	Keeping blinding intact (no mention of assessment of blinding); does not include IBS-C patients; collinearity-- changes in unmeasured dietary substrates that could have changed (gluten, etc.); dichotomous endpoint may not be best primary outcome given disparity between it and other non-dichotomous endpoints studied.
Laatikainen et. al, 2016, Randomized, double-blind, controlled crossover study	To determine if low-FODMAP rye bread would be better tolerated than regular rye bread in subjects with IBS.	73 patients with IBS (excluding IBS-C) recruited via the internet and from a private hospital clinic	Subjects were asked to follow usual diet; provided with and asked to consume both low-FODMAP rye bread and regular rye bread	As compared to the regular rye bread, the low-FODMAP rye bread (alone) caused less symptoms, with significantly less abdominal pain, flatulence, stomach rumbling, intestinal	Low-FODMAP rye bread caused less fermentation in the colon, less flatulence, less abdominal pain, less cramps, less stomach rumbling than the regular rye	Background diet not controlled/unable to measure total FODMAPs in diet; NOT generalizable to IBS-C patients.

		in Finland	for 4 weeks (7-8 slices during the 2nd-4th week).	cramps and total score of symptoms as measured by the weekly VAS. No differences in IBS-SSS or IBS-QoL scores between the groups.	bread. The low-FODMAP bread is also a feasible way to increase fiber.	
Harvie et. al, 2017, randomized, controlled trial (parallel)	Conduct an RCT to look at long-term effects of diet education on FODMAP intake, nutritional adequacy, symptom severity, quality of life & the effect of FODMAP reduction on GI microbiome.	IBS patients of any subtype in New Zealand	Low-FODMAP dietary education was provided by a dietitian in 3+ sessions (0-6 month timeframe), with FODMAP reintroduction at the 2nd visit. Group 1 received intervention immediately & started reintroduction at 3 months. Group 2 received intervention in the second three month period (no education in initial 3 month period).	Significantly lower IBS-SSS score & increased QOL score in group I (low-FODMAP) vs. group II (control) at 3 months; the reduced IBS-SSS was sustained at 6 months in group I (after reintroduction of FODMAPs) & replicated in group II. Fiber intake significantly decreased on low-FODMAP diet but increased again after reintroduction. No change seen in intestinal microbiome after participates adopted low-FODMAP diet.	A reduction in FODMAPs improves symptoms of IBS & the improvement can be maintained while reintroducing FODMAPs; fiber intake may decrease but only initially with dietitian-led intervention.	No sub-analysis for IBS-C so results not generalizable to this group; no blinding used so bias may be cofounding factor; the comparator group was not a true placebo group & were not expecting to get better over first 3 mo.; high attrition rate leading to small sample sizes at the end of study.

Hustoft et. al, 2017, Randomized, double-blinded, placebo-controlled crossover study	To investigate the effect of a low-FODMAP diet vs. high fructo-oligosaccharides (FOS) diet on symptoms, immune activation, gut microbiota composition & SCFAs in IBS patients.	Outpatients with IBS (excluding IBS-C) in a university hospital in Norway	Participants given oral and written low-FODMAP diet education (? If dietitian involved) to follow for 9 weeks. After 3 weeks, randomized to receive supplement of FOS (16g/day) for 10 days, a 3 week washout period, then supplement of placebo (16g maltodextrin) for 10 days, OR reverse sequence. Allocation double-blinded to minimize placebo/nocebo effects.	Significant improvement in all symptoms after 3 weeks of low-FODMAP diet & significantly more subjects reported symptom relief in response to the placebo supplement (80%) vs. the FOS supplement (30%). Levels of IL-6 & IL-8 decreased significantly with 3 week LFD, but no change in response to FOS supplement. Certain alterations in microbiota from both dietary interventions were observed (F. prausnitzii, Actinobacteria, Bifidobacterium).	This supports efficacy of LFD in reducing GI symptoms in IBS-D and IBS-M patients, as more patients reported symptom relief in response to placebo than FOS supplementation. The changes observed in proinflammatory cytokines, microbiota alterations, and decreased fecal levels of SCFAs may potentially have consequences for gut health.	No analysis of nutritive content or FODMAP content of diet-- at beginning or end (potentially skewing results); only 1 FODMAP - FOS - utilized for comparison (other FODMAPs may produce different results); no control group when comparing baseline to low-FODMAP diet - effects then may not be solely due to diet changes; correlations not found, however, this analysis may not be reliable due to small sample size. Only IBS-D & IBS-M patients included.
Primary Sources, Neutral Quality Rating						
Eswaran et. al, 2017, Randomized, controlled, single-blind	To investigate the effects of a low-FODMAP diet vs. traditional	Same as "Eswaran 2016" study	Same as "Eswaran 2016" study.	Magnitude of improvement in QOL score was significant greater in low-FODMAP arm vs. mNICE arm; the	Low-FODMAP diet produced significant improvements in QOL, anxiety and	Not powered for this secondary endpoint, thus, type II errors may have occurred;

trial; post-hoc analysis	dietary recommendations on health-related quality of life, anxiety and depression, work productivity and sleep quality in patients with IBS-D.			proportion of patients with "meaningful clinical response" in QOL score was greater in the low-FODMAP group; anxiety scores decreased in low-FODMAP group vs. mNICE group; activity impairment was significantly reduced with low-FODMAP group vs. mNICE group.	activity impairment compared with the mNICE guidelines -- extending benefits of Low-FODMAP diet beyond GI symptoms for IBS patients.	endpoints were measured at 4 weeks--long-term benefits not known; complete blinding not possible; limited to IBS-D patients.
Ong et. al, 2010, randomized, single-blind, crossover trial	To compare patterns of breath hydrogen, methane and symptoms in response to low vs. high-FODMAP diets.	15 healthy subjects & 15 IBS patients (any subtype), Australia	Subjects were provided with either a low- or high-FODMAP diet with diets matched for total energy, total starch, protein, fat, total dietary fiber and resistant starch.	Composite IBS symptom score (using Likert scale) significantly worse for IBS patients during the high-FODMAP diet (also worse for healthy subjects due to increased flatus) after 2 days; upper GI symptoms and lethargy also worse in IBS group during high-FODMAP diet.	Ingestion of FODMAPs leads to prolonged hydrogen production in healthy volunteers and in IBS patients in whom GI and and systemic symptoms were worsened. IBS patients produce more hydrogen.	Very short (2 days) and small study; did not study effects on IBS subtypes (hetereogeneous sample); the comparator group was not a control or placebo group; ? control for gluten content of food provided.
Pedersen et. al, 2014, Randomized, unblinded, controlled trial	To investigate the effects of a Low-FODMAP diet & a probiotic supplement (L. rhamnosus GG) as compared to a non-interventional control group	IBS patients of any subtype in Denmark	Patients allocated to 1 of 3 groups: low-FODMAP diet, probiotic (LGG), or non-intervention control group; low-FODMAP group given 1 hour education +	Significant reduction of IBS-SSS in all patients during intervention & in each treatment group; signficant reduction in IBS-SSS observed in LFD & LGG groups compared to control group when comparing mean score at week 6; a significant reduction in	Both the low-FODMAP diet & LGG supplementation is effective when treating IBS patients, especially in the IBS-D & IBS-A subtypes.	No blinding; no placebo; no measure of adherence to the diet & no background analyzation of diet characteristics in any group; low-FODMAP diet group had more

	in IBS; to evaluate feasibility of a web-based application & determine effects on IBS patients.		some re-introduction of foods during the 6-week study period; LGG group told to follow unchanged diet; all subjects had access to web-based program for IBS symptom tracking & education.	IBS-SSS found in patients with IBS-D & IBS-A (mixed or alternating) when treated with LFD or LGG.		interaction with dietitians (potential placebo response).
Schumann et. al, 2018, Randomized, single-blinded, controlled trial	To examine the effect of a yoga-based intervention vs. a low-FODMAP diet on gastrointestinal symptoms in IBS patients.	Individuals in Germany with any IBS subtype who responded to ads placed by the sponsoring organization/ University	Traditional hatha yoga group sessions (75 min) twice weekly for 12 weeks (with additional instruction to practice at home) vs. low-FODMAP diet education over 4 counseling sessions (60-90 min) and elimination phase that lasted 12 weeks.	No statistically signficant difference found between intervention groups in IBS-SSS score, at either 12 or 24 weeks; within-group comparisons showed significant effects for both yoga and low-FODMAP diet at both 12 and 24 weeks; comparable within-group effects occurred for other outcomes.	Both hatha yoga and a low-FODMAP diet can reduce GI symptoms and improve a range of other psychological and physiological health parameters in IBS patients; both treatments seem to be promising and safe. Further studies needed on longer-term effects, cost-effectiveness, and efficacy.	Inability to blind patients to interventions; lack of assessment of patient's baseline diet/diet knowledge; unable to control for other dietary confounders/diet intake between groups; no mention of control for medications/supplements.

O'Keeffe et. al, 2018, Prospective long-term follow-up (cohort) study	To assess the long-term impact of the Low-FODMAP diet on symptom response, FODMAP content of diet, nutritional adequacy, diet acceptability, food-related QOL & healthcare utilization in IBS patients.	Patients with any subtype of IBS recruited from primary/secondary care in the UK that had already undergone FODMAP education/reintroduction.	Past intervention had been initial low-FODMAP diet education and 6-week follow-up for reintroduction of FODMAP; long-term follow-up via postal questionnaire performed 6-18 months after the short-term follow-up.	At short-term follow-up, 61% of patients reported satisfactory symptom relief, with 57% reporting relief at long-term follow-up (70% of patients MAINTAINED their relief long-term); 82% continued to follow "adapted FODMAP" diet while 18% returned to their "habitual" diet -- no significant differences in this group for energy/nutrient intake, except folate & Vit A were higher in "adopted FODMAP" group; no differences in food-related QOL between groups; no differences for healthcare utilization or absenteeism; significantly more patients in the "adapted FODMAP" group ceased medication at long-term follow-up.	The low-FODMAP diet is clinically effective with 57% reporting long-term satisfactory response. A low-FODMAP diet can be nurtitionally adequate up to 18 months after initial education & patients find the diet acceptable. It does not adversely impact food-related QOL.	Only 27% of sample responded to survey (sample bias); uncontrolled and unblinded study; symptom evaluation was subjective (no biomarkers for IBS).
de Roest et. al, 2013, prospective, observational	To investigate whether a low-FODMAP diet leads to improved symptoms in patients with IBS via a prospective	IBS patients of any subtype who had received breath testing for lactose/fructose malabsorption	Hydrogen/methane breath testing performed on 3 separate days for lactulose, fructose, and lactose; individualized education/advice	Mean follow-up of 15.7 months. There was a significant positive change in almost all reported symptoms between baseline and follow-up, even when repeating the analysis with non-repliers	The Low-FODMAP diet is effective in improving symptoms in IBS patients, and those with fructose malabsorption are most likely to	Observational study with no placebo control; response rate was only 46.9%, which may reduce generalization of results; no control of other dietary

	evaluation using a symptom questionnaire.	and received low-FODMAP diet advice in clinical setting in New Zealand	on low-FODMAP diet consisting of initial visit and follow-up visit after 6 weeks (when info on reintroduction was provided). Patients were then contacted via mail or e-mail for additional follow-up information on safety & efficacy of the diet.	included; patients with fructose malabsorption were more likely to report improvement with certain symptoms than those without evidence of fructose malabsorption; most patients described ongoing adherence to the diet; there was a significant positive correlation between adherence and improvement in bloating, pain, flatulence, diarrhea, constipation, and energy levels.	benefit. Current strategy of diet advice by trained dietitians following breath testing provides good base for patients to understand and adhere to the diet.	variables, which may influence results.
Staudacher et. al, 2011, non-randomized controlled trial	To compare the clinical effectiveness of low-FODMAP diet to standard NICE guidelines as diet therapy for IBS in an outpatient service.	Consecutive adult patients (within outpatient service in UK) with any subtype of IBS and that returned for a follow-up visit	NICE general diet advice (and where indicated, specific NICE-based advice) vs. low-FODMAP advice; treatment group assignment was based on timeline/when subject was introduced to service.	More patients in low-FODMAP group reported satisfaction with their symptom response (76%) as compared to standard group (54%); composite symptom scores showed better response in the low-FODMAP group; significantly more patients in the low-FODMAP group reported decreased bloating, abdominal pain, and flatulence.	A low-FODMAP diet appears to be more effective than standard diet advice in reducing symptoms of IBS.	Group interventions not carried out at the same time, potential confounding variables not controlled for (meds, supplements, overall diet intake), potential for response bias.

Author/Year/ Study Design	Purpose	Population	Intervention	Key Outcomes	Conclusions	Limitations
			Review Articles, Positive Quality Rating			
Marsh et. al, 2016, Meta-analysis	To determine the evidence of efficacy of the low-FODMAP diet in the treatment of functional GI symptoms.	6 RCTs and 16 non-randomized interventions included in the analysis/ IBS & IBD patients	Pooled odds ratios & 95% CI calculated for the effect of LFD on IBS-SSS, IBS-QOL scores for both RCTs and non-randomized interventions.	In RCTs, greatest improvement was seen for abdominal pain and bloating & low-FODMAP diet showed greatest benefit in relief of GI symptoms; in non-randomized interventions, greatest improvement seen in bloating, then flatulence, pain, diarrhea, nausea and constipation, respectively. Pooled ORs in both study types showed positive association between low-FODMAP diet and significant decrease in IBS-SSS score. Both study types also showed significant improvement in IBS-QOL post- low-FODMAP intervention.	Adherence to low-FODMAP diet leads to overall improvement in function GI symptoms for IBS/IBD and a significant improvement in symptom severity and quality of life scores compared to IBS patients following a normal diet.	Both RCTs and non-randomized interventions had widely variable study duration; large heterogeneity of non-randomized interventions; lack of studies providing adherence figures and quantities of FODMAPs ingested; included non peer-reviewed data/abstracts; control in RCTs varied between studies; results specific to geographic locations studied.
Schumann, 2017, meta-analysis	1. Meta-analyze the effectiveness of Low-FODMAP diet in treating function GI symptoms in	9 articles on RCTs with a total of 561 patients matched intervention criteria and	Standardized mean differences with 95% CI were calculated to measure effect size when examining RCTs	Significant group differences for low-FODMAP diet compared with any control for GI symptoms and abdominal pain; low-FODMAP diet also had short-term	Significant evidence for short-term benefits of low-FODMAP diet on GI symptoms, abdominal pain, and quality of life	Improvements were investigated mostly for patients with IBS-D. No studies reported long-term effects. Findings not

	IBS patients. 2. Determine safety of treatment and influence on microbiome.	were included in the meta-analysis	that compared LFD to other diets and impact on severity of IBS symptoms (using IBS-SSS or other patient-rated scale). As secondary outcomes, safety, quality of life, anxiety, depression, and effect on gut microbiota were also analyzed.	favorable effects on health-related quality of life, as compared to control; none adverse events related to intervention were found.	in IBS patients, with no side effects reported. Effects were robust against potential methodological bias.	applicable to cultures outside of geographic regions studied & may not be fully applicable to male patients. Risk of bias in included studies unclear; general high risk of the studies found for performance bias.
Altobelli et. al, 2017, Meta-analysis	To compare 1) low-FODMAP diets and traditional IBS diets in RCTs, 2) low- and high-FODMAP diets in RCTs, and 3) baseline vs. post-intervention data in cohort studies with low-FODMAP diet treatment.	6 RCTs (3 compared traditional IBS diet vs. low-FODMAP, 3 compared low- to high-FODMAP diet), 6 cohort studies.	Odds ratios with 95% CI used as a measure of effect size for RCTs which examined low-FODMAP diet vs. traditional IBS diet or low-FODMAP diet vs. high-FODMAP diet; low-FODMAP diet intervention without comparator in cohort studies.	A low-FODMAP diet vs. a traditional IBS diet significantly reduced abdominal pain, bloating, and stool frequency (not stool consistency); significant reductions in pain and bloating also found in low-FODMAP diet vs. medium or high-FODMAP diet; cohort studies also demonstrated a significant reduction in pain and bloating with a low-FODMAP diet.	There is evidence that a low-FODMAP diet can have a favorable impact on IBS symptoms, particularly pain, bloating, and diarrhea. More research needs to be done to demonstrate whether a low-FODMAP diet is superior to conventional IBS diets, especially in long-term.	Relatively small number of primary studies; lack of blinding in studies; inadequate treatment duration of studies analyzed.

| Varju et. al, 2017, meta-analysis | To carry out a meta-analysis to determine whether a low-FODMAP diet improves symptoms of adult IBS patients more effectively than a traditional dietary intervention (without restriction of FODMAP content). | 7 controlled trials (5 RCTs, 1 single-blind crossover, 1 prospective controlled) & 3 non-controlled prospective trials of IBS patients | Enrolled controlled studies and non-controlled prospective trials that utilized LFD; control group had to use standard IBS diet. Mean differences with 95% CI calculated with outcome measure of IBS-SSS. | When comparing pre- and post-intervention scores between the control and low-FODMAP groups in the controlled trials, no statistically significant difference in pre-values between groups but significant difference in post-values, indicating low-FODMAP diet is better than control in improving IBS-SSS score. Significant heterogeneity in the meta-analysis. | A low-FODMAP diet significantly improves general symptoms and quality of life in patients with IBS. A low-FODMAP diet is more effective than standard IBS dietary therapy. | Standard IBS diet group NOT homogeneous and only 2 out of 10 studies detailed exact food contents; included 4 short supplements in analysis, no contact with authors for further info?; lack of data between IBS subtypes and in individual symptom improvement. |