

Evaluation of efficacy of low Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols (FODMAP) diet in management of irritable bowel syndrome (IBS): An updated Meta-Analysis of RCT's

Abstract

Irregular Bowel Syndrome (IBS) is a common gastrointestinal disorder causing chronic abdominal pain, bloating and altered bowel habits with inadequate treatments integrating into daily life of patient care. The low FODMAP (Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols) diet has emerged as a dietary intervention to help alleviate IBS-related symptoms. This updated meta-analysis seeks to investigate further the effectiveness of a low FODMAP diet in reducing gastrointestinal symptoms and improving quality of life among patients with IBS. This systematic review and meta-analysis identified 18 RCTs that included as primary outcomes the presence of gastrointestinal symptoms, severity of abdominal pain, quality end life. Outcomes: there is sufficient evidence that the FODMAP diet provided greater relief of IBS symptoms, including abdominal pain and bloating; with improvements in quality of life compared to other dietary interventions. Although the diet has shown some usefulness, concerns exist regarding long-term compliance as well as nutritional adequacy. However, these analyses highlight the need for personalized IBS management and suggest that more research is required to determine long-term outcomes and adherence of a LFD.

Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder with no single, well-established pathophysiology and characterized by chronic abdominal pain, bloating, and altered defecation habits that severely affect the quality of life in its patients [1]. Irritable bowel syndrome is a multifactorial condition in which pathophysiological interactions between the gut-brain axis, diet and microbiome come into play [2,3]. IBS management has traditionally focused on dietary interventions, and the low Fermentable Oligosaccharides, Disaccharides,

Monosaccharides And Polyols (FODMAP) diet is one of these diets that have shown efficacy in reducing IBS symptoms [4,5].

The low FODMAP diet was initially developed as a treatment to alleviate gastrointestinal symptoms by reducing the consumption of fermentable poorly absorbed short-chain carbohydrates [6,7]. These poorly absorbed carbohydrates ferment in the large intestine through action of gut bacteria causing gas production, and increased fluid due to its osmotic effects resulting in retention, so both contribute to IBS symptoms [8]. A number of randomized controlled trials (RCTs) suggested that a low FODMAP diet can alleviate typical IBS symptoms in patients with this disorder, e.g. bloating, abdominal pain and stool consistency [9].

Although more evidence is building on the benefits of this diet, there are studies with variable results [30], probably influenced by different designs and evaluation methods applied to distinct populations. In addition, this very low caloric nature of the diet might deter long-term sticking with and may undermine nutritional adequacy [10, 11]. An updated meta-analysis is therefore needed to offer a comprehensive evaluation of the effectiveness of LLFD in IBS care and, given that there may exist potential effect-modifiers affecting its efficacy.

Although the low FODMAP diet has been widely accepted as a treatment modality for irritable bowel syndrome (IBS), variation in reported outcomes and concern about long-term sustainability have led to investigation of alternatives. A comprehensive systematic review of all RCTs is required to establish the efficacy of a low FODMAP diet, as well as identify limitations in current evidence that may help with formulating future research and clinical practice.

Aims

This study aims to evaluate the efficacy of the low FODMAP diet in reducing gastrointestinal symptoms, particularly abdominal pain and bloating, and improving the quality of life in patients with IBS. Additionally, the study seeks to identify factors that may modulate the effectiveness of the low FODMAP diet, such as patient demographics, adherence to the diet, and the presence of comorbidities.

Research Question

In patients with irritable bowel syndrome (IBS), what is the efficacy of the low FODMAP diet compared to other dietary interventions or controls in reducing gastrointestinal symptoms and improving quality of life?

METHODS

Study Design

The "Reporting Items for Systematic Review and Meta-Analysis (PRISMA)" guidelines was followed in this study [12]. Our study was a meta-analysis of already published RCT trials so, there is no need for additional ethical review.

Study Question

In patients with irritable bowel syndrome (IBS), what are the efficacy outcomes of low Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols (FODMAP) diet? The recent study used the Population Intervention Control Outcome (PICO) framework [25] to guide the search (Table 1).

Table no. 1: PICO framework for research question of recent study

PICO	Description
Population	Patients diagnosed with irritable bowel syndrome (IBS)
Intervention	low Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols (FODMAP) diet
Control	Other dietary intervention or control
Outcome	Intensity of GI symptoms, abdominal pain, quality of life (QoL)

.Search Strategy

PRISMA criteria were followed in the extraction of research papers relevant to the study's objectives, which include "Evaluation of efficacy of low Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols (FODMAP) diet in management of irritable bowel syndrome (IBS)" from several databases (1). The Cochrane Library, PubMed, EMBASE, and Clinicaltrials.gov electronic databases were used in this investigation. "low Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols" OR "FODMAP diet" OR "low fat diet") AND "GI symptoms" OR "Gastrointestinal symptoms" OR "IBS-SS score" OR

"abdominal pain" OR "QOL" were the MeSH keywords used for data extraction. The study timeframe was set to run from January 2010 to July 2024.

Selection Criteria

PRISMA criteria were followed in the selection and screening of research publications [24]. The screening of research articles for this study was aided by the predetermined selection criteria.

Inclusion Criteria

This research only included publications that satisfied the following requirements: 1. Research or randomized controlled trials with individuals with IBS diagnosis 2. Research pertaining to the low-FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) diet intervention 3. Research examines the effects on the severity of GI symptoms, discomfort in the abdomen, and enhancements in quality of life. 4. research using randomized controlled trials, or RCTs, as a basis 5). studies with full text published in English.

Exclusion Criteria:

Only the following studies were not included: 1. Research on people with different gastrointestinal (GI) conditions 2. Research on other dietary approaches to treating IBS other than reducing FODMAP intake 3. Research talk on the results rather than the severity of GI symptoms, stomach discomfort, and QOL 4 improvements. Systematic reviews, meta-analyses, scoping reviews, symposia, and case studies that have already been published 5. studies with duplicate publications or non-full-text articles that were published in languages other than English.

Data Extraction

For each eligible paper, we extracted the demographic information related to authors, year of study, country, study population, sample size, study design, and primary outcomes such as Intensity of GI symptoms, abdominal pain, quality of life (QoL) from selected articles after the selection and screening of research articles, as table no. 2.

Study Outcomes

The primary outcomes of this study were Intensity of GI symptoms, abdominal pain, quality of life (QoL). The primary objective was to determine the severity of IBS symptoms, ideally using

the well-researched and commonly used IBS Severity Scoring System (IBS-SSS). The IBS-SSS questionnaire evaluates how severe GI symptoms are over a period of ten days, with particular attention to issues with distension, frequency and consistency of stools, and impairment with day-to-day functioning. Higher scores denote more severe symptoms. Each of these elements is rated on a visual analog scale ranging from 0 to 100, summing up to a total aggregate score of 0 to 500. Included were studies that used validated and non-validated VAS and Likert scales in addition to other measures of symptom severity. Abdominal discomfort was utilized as an outcome of interest when there was no documented assessment of the total severity of the symptoms.

Risk of Bias Assessment

The Cochrane risk of bias assessment technique (2) was used to assess the bias risk of the included RCTs. The investigation of the bias was divided into seven categories: allocation concealment, bias in other areas, blinding staff and participants for performance, biased reporting or bias in other areas, blinding result evaluation or bias detection. Three categories were created from the ratings for each domain: uncertain, high risk, and low risk.

Statistical Analysis

In this study, pooled analysis was performed using the RevMan (Review Manager) software version 5.4 (Cochrane Collaboration, United Kingdom). In this study, two measures were examined: the odd ratio (OR) and the mean difference of the expected outcomes after decreasing FODMAP. Mantel-Haenszel random effects techniques were used for the pooled analysis. Furthermore, the Q test and I² statistics were used to quantify the heterogeneity. Consideration was given to significant heterogeneity if the I² value exceeded 50%. If the p-value was greater than 0.05, a significant difference was deemed to exist. I² statistics were used to calculate the degree of heterogeneity (mild, 0–30%; moderate, 31–50%; extreme, >50%). Determining publishing bias was made possible by the reporting of funnel pooled estimates.

RESULTS

Search Results

About 5954 studies were identified from above mentioned 4 databases with 4262 duplicates to fulfill research aims related to the title “Evaluation of efficacy of low Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols (FODMAP) diet in management of irritable bowel syndrome (IBS)”. The primary screening was performed on 692 articles and 302 were excluded. About 390 research articles were retrieved after the removal of 206 studies. The eligibility criteria were applied to 84 research papers and only 18 studies met the eligibility criteria. About 66 research papers were excluded: 29 were excluded due to non-RCT trials, 21 studies discussing other interventions, 6 were not discussing desired outcomes, 5 were secondary analyses, and 5 were excluded due to other reasons such as non-English and non-full articles. Finally, 18 RCT were included in this study

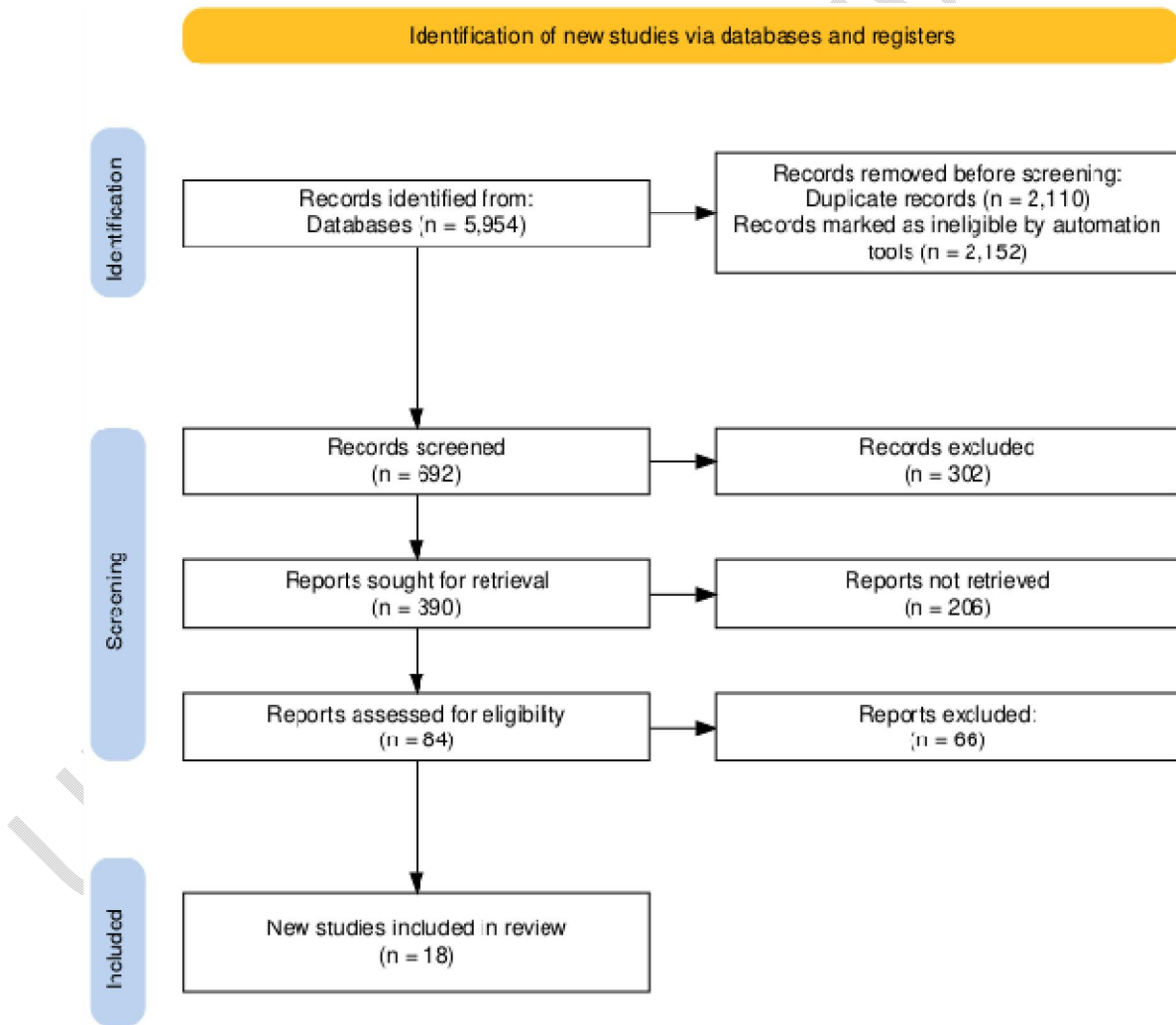


Fig no. 1: Flow chart of PRISMA Guidelines for screening and selection

Description of Included Studies

The characteristics of all included studies were summarized in Table. 2. All included studies discussed the patients (>18 years old) with a diagnosis of irritable bowel syndrome (IBS). A total of 1167 IBS patients were included from 18 RCTs in this study. All patients in intervention groups received low FODMAPs (9 g/day) and placebo groups received traditional dietary interventions such as Australian diet, gluten free diet etc. To produce heterogeneity, RCTs were taken from 12 different countries, such as 2 studies from USA, 2 studies from Australia, 4 studies from UK, 2 studies from Iran, 1 from Sweden, 1 from Switzerland, 1 from New Zealand, 1 from Thailand, 1 from Denmark, 1 from Italy, 1 study from India and 1 from the Canada. The median duration of follow-up was 4 weeks.

UNDER PEER RE

Table 2: Characteristics of the included studies

Author, year	Country	Study population	Study design	Study follow up	Intervention	GI symptoms	Abdominal pain	Quality of Life
Bohen et al., 2015 (14)	Sweden	75 IBS patients (Age; 18-69 years) Intervention: 33 Control: 34	RCT	4 weeks	Low FODMAP diet (3.8 ± 3.3 g/d)	Responders T: 19 P: 17 T: 246 ± 127 P: 236 ± 78 ;	T: 14.0 ± 1.4 P: 23.2 ± 2.1	T: 17.7 ± 11.1 P: 10.3 ± 4.1
Chumpitazi et al., 2015 (15)	USA	52 IBS patients Intervention: 33 Control: 33	RCT	1 week	Low FODMAPs (9 g/day)	Responders T: 8 P; 10	T: 1.1 ± 0.2 P: 1.7 ± 0.4	
Eswaran et al., 2016 (16)	USA	92 IBS patients 45 in intervention 39 in placebo	RCT	4 weeks	Low FODMAPs (9 g/day)	Responders T: 23 P: 9 T: 3.38 ± 2 P: 4.41 ± 2.2		T: 69.3 ± 13.97 P: 59.4 ± 12.05
Halmos et al., 2014 (17)	Australia	30 IBS patients 30 in intervention 30 in placebo	RCT	42 days		T: 22.8 ± 32.4 P: 44.9 ± 44.10		
Harvie et al., 2017 (18)	New Zealand	50 patients of IBS 23 in intervention 27 in placebo	RCT	3 months	Low FODMAPs (9 g/day)	T: 128.8 ± 82.5 P: 206.31 ± 69.59	T: 17 ± 17 P: 33 ± 26	T; 83 ± 13.4 P: 73.3 ± 14.4
McIntosh et al., 2017 (19)	Canada	37 IBS patients 19 in intervention 18 in placebo	RCT	3 weeks	Low FODMAPs (9 g/day)	T: 208 ± 74.8 P: 290 ± 106		
Ong et al., 2010 (20)	Australia	30 IBS patients 15 in intervention	RCT	8 weeks	Low FODMAPs (9 g/day)	T: 2.52 ± 2.01 P: 5.83 ± 2.01		

		15 in placebo						
Paduano et al., 2019 (21)	Italy	30 in intervention 34 in placebo	RCT	4 weeks	Low FODMAPs (9 g/day)	T: 16 ± 8 P: 19 ± 9		T: 83 ± 14 P: 79 ± 14
Pacharatrakul, 2019 (22)	Thailand	70 Seventy patients with moderate-to-severe IBS 30 in intervention 32 in placebo	RCT	4 weeks		Responders T: 11 P: 5 T: 38.5 ± 20.0 P: 53.5 ± 19.2	T: 2.5 (0.8–4.8) P: 5 (2.6–6.7)	
Pedersen et al., 2014 (23)	Denmark	42 in intervention 40 in placebo	RCT	6 weeks	Low FODMAPs (9 g/day)	T: 198.4 ± 101.1 P: 288.39 ± 98.6		T: 8 ± 18 P: 7 ± 17
Staudacher et al., 2012 (24)	UK	41 IBS patients 19 in intervention 22 in control	RCT	4 weeks	Low FODMAPs (9 g/day)	T: 1.1 ± 0.47 P: 1.7 ± 0.52		
Staudacher et al., 2017 (25)	UK	104 IBS patients 51 in intervention 51 in placebo	RCT	4 weeks	low FODMAP diet group (9·9 g/d)	T: 173 (95) P: 207 (98)	T: 0.9 (0.7) P: 1.0 (0.7)	T: 72.4 (19.7) P: 68.6 (20.7)
Zahedi et al., 2017 (26)	Iran	110 patients with IBS-D 55 in intervention 55 in placebo	RCT	6 weeks	low FODMAP diet group (9·9 g/d)	T: 108 ± 63.82 P: 149.75 ± 51.39		T: 7.3 ± 8.78 P: 5.35 ± 9.19
Goyal et al., 2021 (27)	India	166 patients with IBS-D 83 in intervention 83 in placebo	RCT	16 weeks	low FODMAP diet group (9·9 g/d)	Responders T: 32 P: 20 T: 98.7 P: 156.9		
Mohseni et al., 2022 (28)	Iran	49 patients with IBS 24 in intervention 25 in placebo	RCT	6 weeks	low FODMAP diet group (9·9 g/d)	T: 132 P: 149	T: 29 P: 63	T: 32 P: 23
Kruger et al., 2020 (29)	Switzerland	29 patients with IBS 14 in intervention 15 in placebo	RCT	21 days	low FODMAP diet group (9·9 g/d)	T: 63 P: 51	T: -2.8 P: 2.7,	

Wilson et al., 2020 (30)	UK	69 IBS patients	RCT	4 weeks	low FODMAP diet group (9.9 g/d)		T: 1.3 P: 15.6	
Prince et al., 2016 (31)	UK	88 in intervention 88 in placebo	RCT	6 weeks	low FODMAP diet group (9.9 g/d)	T: 0.75 P: 1.20		

UNDER PEER REVIEW

	Adequate sequence generation?	Allocation concealment?	Blinding?	Incomplete outcome data addressed?	Free of selective reporting?	Free of other bias?
Bohen et al., 2015	+		+	-		-
Chumpitazi et al., 2015		+	+		-	-
Eswaran et al., 2016	+	-	+	+	-	
Goyal et al., 2021	-	-	+	+		+
Halmos et al., 2014	+	-	+	+	-	
Harvie et al., 2017	+	+	-	+	-	+
Kruger et al., 2020	+	-		+	-	
McIntosh et al., 2017		-	+	-	-	-
Mohseni et al., 2022	+	+	-	-		+
Ong et al., 2010	+	-	-		+	+
Paduano et al., 2019	-	+	-		+	-
Patcharatrakul, 2019	+	+	+	-	-	-
Pedersen et al., 2014	+	-	+	-	+	+
Prince et al., 2016	-	+	+		-	-
Staudacher et al., 2012	+	-	+	+	-	
Staudacher et al., 2017	+	-	+	+	-	
Wilson et al., 2020	+	-	+	+	-	+
Zahedi et al., 2017	+	-	-	+	+	+

Figure 2 Risk of bias assessment

Primary outcomes

1. GI symptoms (IBS-SS scores)

Among 18 RCT's related to low FODMAP diet, 16 studies discussed the IBS-SS scores related to GI symptoms among intervention groups as outcomes [14, 16-29, 31]. The pooled analysis showed that low FODMAP diet improved the GI symptoms among intervention group as compared to placebo (mean difference; -6.77 (-8.88, -4.67), CI: 95%) and heterogeneity (df = 15 ($P < 0.00001$); $I^2 = 96\%$), as shown in figure 3 and 4.

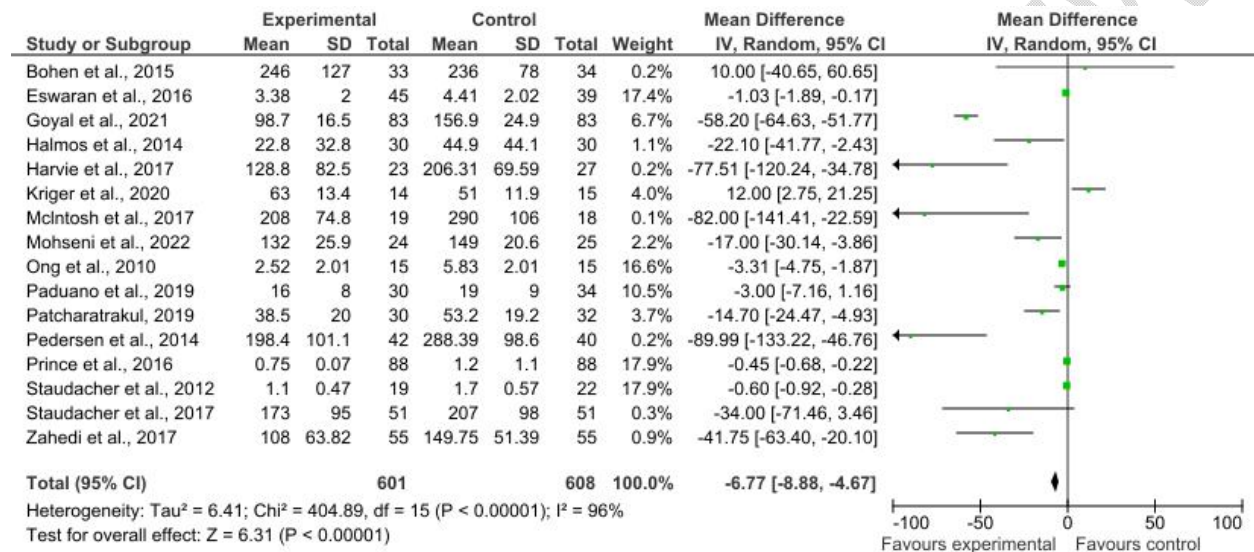


Figure 3 GI symptoms (IBS-SS scores) [14, 16-29, 31].

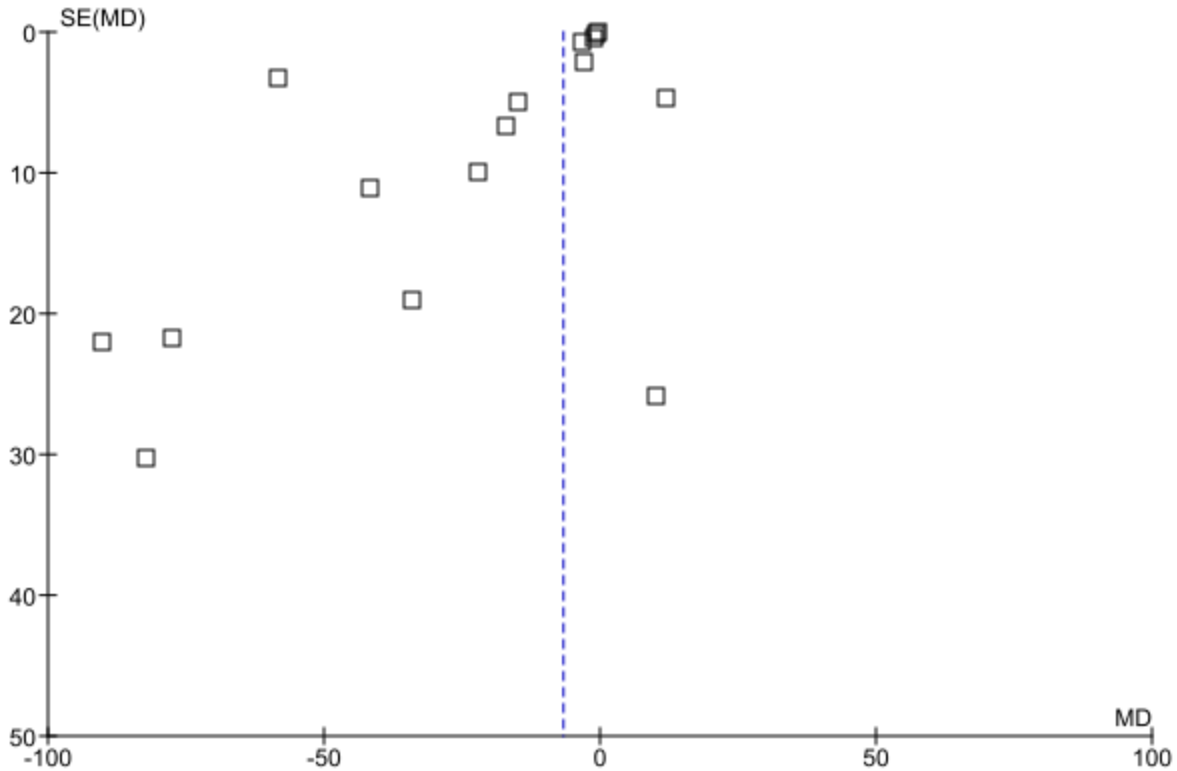


Figure 4 pooled analysis of GI symptoms (IBS-SS scores)[14, 16-29, 31].

2. Abdominal pain (VAS scores)

Among 18 RCT's related to low FODMAP diet, 8 studies discussed the abdominal pain intensity by VAS scores among intervention groups as outcomes [14, 15, 17,22, 25, 27, 28, 29]. The pooled analysis showed that low FODMAP diet improved the abdominal pain intensity among intervention group as compared to placebo (mean difference; -6.86 (-9.25, -4.47), CI: 95%) and heterogeneity (Heterogeneity: $df = 7$ ($P < 0.00001$); $I^2 = 99\%$) as shown in figure 5 and 6.

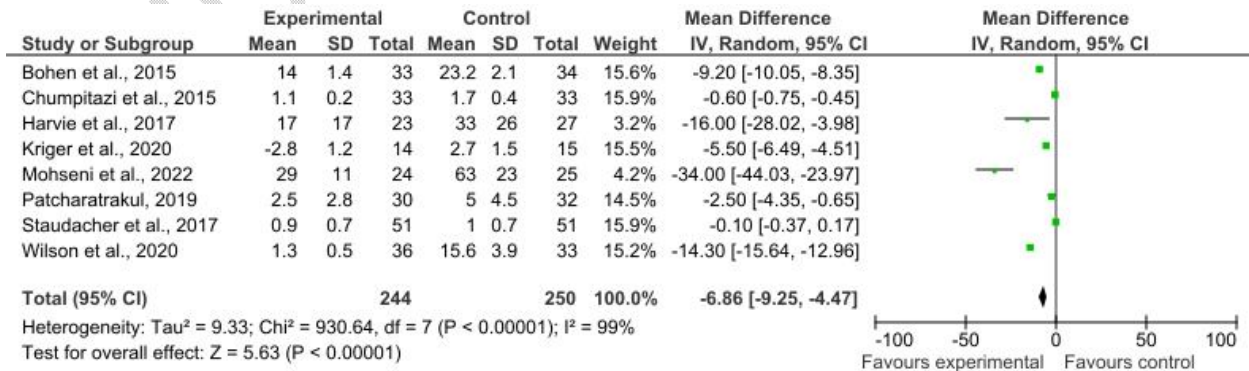


Figure 5 Abdominal pain (VAS scores)[14, 15, 17,22, 25, 27, 28, 29].

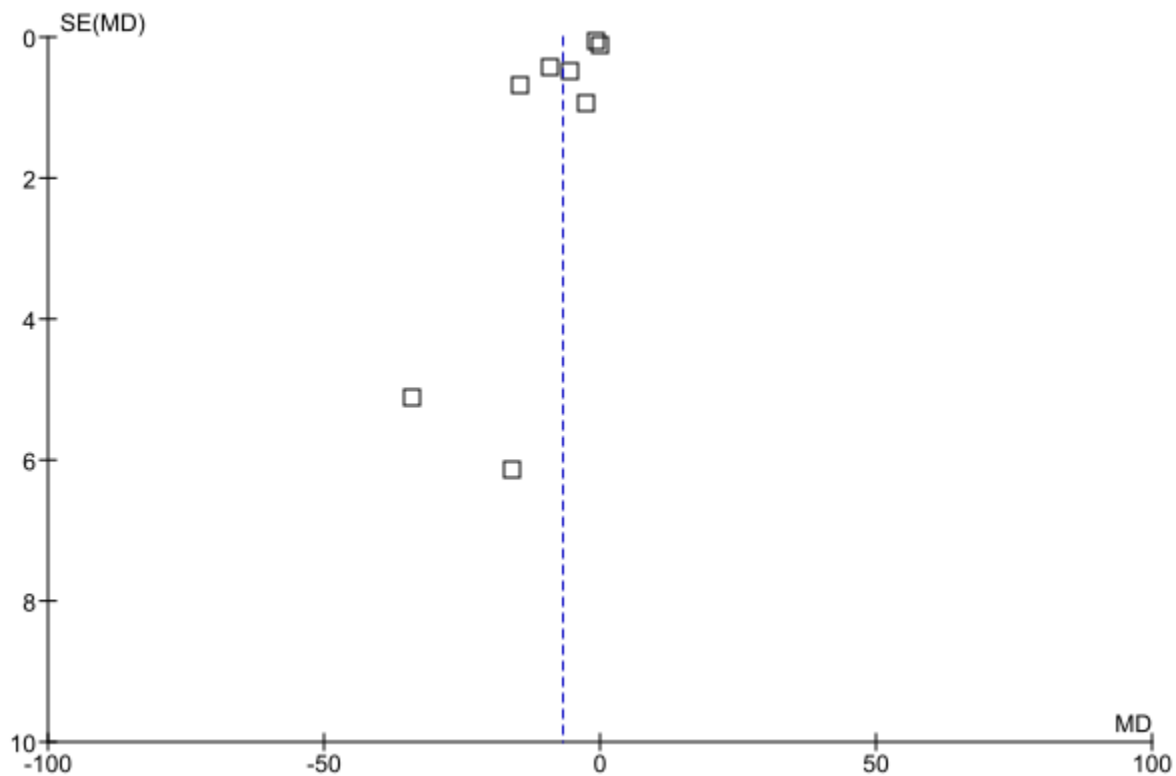


Figure 6 pooled analysis for Abdominal pain [14, 15, 17, 22, 25, 27, 28, 29].

3. Quality of Life (QoL)

Among 18 RCT's related to low FODMAP diet, 8 studies discussed the quality of life (QoL) among intervention groups as outcomes [14, 16, 21, 23, 25, 26, 28]. The pooled analysis showed that low FODMAP diet improved the quality of life among intervention group as compared to placebo (mean difference; 6.61 [3.42, 8.78], CI: 95%) and heterogeneity (Heterogeneity: $df = 7$ ($P = 0.02$); $I^2 = 57\%$) as shown in figure 7 and 8.

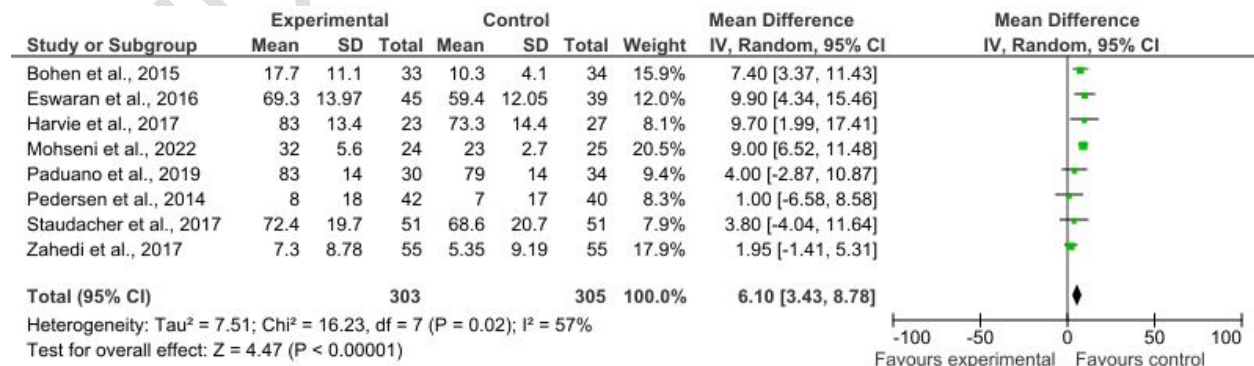


Figure 7 Quality of life [14, 16, 21, 23, 25, 26, 28].

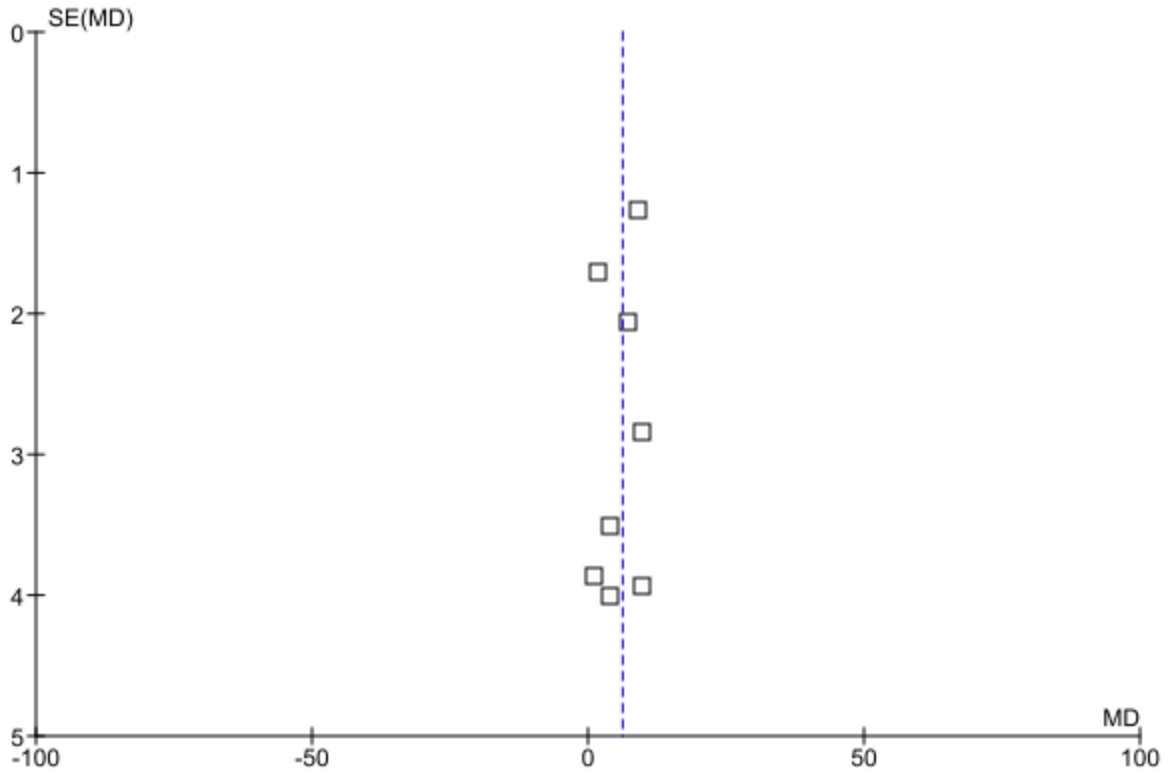


Figure 8 pooled analysis for quality of life [14, 16, 21, 23, 25, 26, 28].

Discussion

The low FODMAP diet has been widely studied as a successful dietary intervention for the treatment of Irritable Bowel Syndrome (IBS) symptoms. We aimed to assess the efficiency of a low FODMAP diet in reducing gastrointestinal symptoms such as abdominal pain, bloating and improving quality of life among people diagnosed with IBS. The strong support for the efficacy of a low FODMAP diet assessed in this meta-analysis is likely due to endpoints being drawn from 18 randomized controlled trials (RCTs).

Efficacy of the Low FODMAP Diet on Gastrointestinal Symptoms

A pooled analysis of these studies showed a significant improvement in the severity of gastrointestinal symptoms, such as abdominal pain, bloating and stool consistency in IBS patients following low FODMAP diet vs. other dietary strategy or controls. For example, after following a low FODMAP diet for 4 weeks there was a significantly lower IBS-SS score (mean difference; -6.77, CI: -8.88 to -4.67, $P < 0.05$) indicating an improvement in symptom severity

compared with baseline [14, 16]. These results are in keeping with earlier works that have shown the importance of fermentable carbohydrates as a trigger for IBS symptoms, related to osmotic effects and rapid fermentation by gut bacteria (Halmos et al., 2014; Ong et al., 2010).

That the change in specific symptom burden of IBS like abdominal pain, was particularly impressive (mean difference; -6.86, CI: -9.25 to -4.47, $P < 0.05$) that significantly more improved VAS scores also maintained consistency among low FODMAP patients throughout different meta-analysis study localities (Patcharatrakul et al., 2019; Pedersen et al., 2014). This is consistent with previous work showing that reducing fermentable carbohydrate intake can decrease luminal distension and visceral hypersensitivity which are thought to be the primary causes of abdominal pain in patients with IBS [27].

Impact on Quality of Life

The improvement in gastrointestinal symptoms was also associated with enhanced quality of life (QoL) among IBS patients on the low FODMAP diet. The meta-analysis showed a significant increase in QoL scores (mean difference; 6.61, CI: 3.42 to 8.78, $P < 0.05$) [25, 26]. Improved symptom control directly correlates with better daily functioning and reduced psychological distress, contributing to overall well-being. This association is supported by studies that have observed positive changes in QoL scores following the adoption of the low FODMAP diet, emphasizing the diet's role in improving not just physical but also mental health aspects in IBS patients [30, 31].

Yet, the severely limited diet has raised questions of long-term repletion and possible nutrient in short supply. Such a dietary regime, if not well controlled, also increases the risk of imbalanced intake and deficiencies in essential nutrients since it eliminates foods from different food groups [18]. The diet has been demonstrated to benefit in a short-term basis, although more research is needed on its long term outcomes and nutritional support strategies are required for the purpose of maintaining disease control [28].

Comparison with Other Dietary Interventions

When compared with other dietary interventions, the low FODMAP diet consistently showed superior efficacy in reducing IBS symptoms. For instance, studies comparing the low FODMAP

diet with traditional dietary advice, such as the Australian diet or gluten-free diet, reported better outcomes in the low FODMAP group [20, 23]. The superior efficacy of the low FODMAP diet can be attributed to its targeted approach in reducing specific fermentable carbohydrates known to exacerbate IBS symptoms, whereas other diets may not adequately address the same triggers.

Nevertheless, not all IBS patients respond positively to the low FODMAP diet. However, the effectiveness of a diet is immensely determined by factors like gut microbiota variations at an individual level and psychological stressors such as adherence to said contributing dietary requirements [15]. This variability also hints to the fact that although a low FODMAP diet is an important tool for management of IBS, it may need careful modification on these diets among patients based upon their needs and/or likes [29].

Limitations and Future Research

Although the evidence in favor of a low FODMAP diet is compelling, this meta-analysis has its limitations that warrant consideration. It is possible that the heterogeneity among the included studies, particularly in regard to study design and duration as well as outcome measurements isn't considered by our findings. A further concern is the short duration of follow-up which was only 1–26 wk in most studies ranging up to 52 weeks [19].

We recommend more long-term studies that assess the sustainability and nutritional completeness of a low FODMAP diet for further research. In addition, the unraveling of the role that gut microbiota play in mediating response to low FODMAP diet may pave the way for personalized dietary interventions among IBS patients. The mechanisms by which the diet works and identifying how to predict who will respond, perhaps through identifying biomarkers that may be indicative of treatment response could pave the way for more targeted action on managing IBS.

Conclusion

This meta-analysis has confirmed the efficiency of low FODMAP diet on gastrointestinal symptoms and quality of life in IBS patients. This re-analysis suggests the diet is superior to most other dietary interventions, but that significant inter-individual variation in response will require metabolic biomarker-based tailoring of individual diets. Studies in the future should

focus on explaining long-term effects of this diet and perhaps steps to heighten its efficacy, whilst trying not to compromise dietary adequacy.

UNDER PEER REVIEW

References

1. Kolb JM, Molmenti CL, Patel SG, Lieberman DA, Ahnen DJ: Increased Risk of Colorectal Cancer Tied to Advanced Colorectal Polyps: An Untapped Opportunity to Screen First-Degree Relatives and Decrease Cancer Burden. *American Journal of Gastroenterology*. 2020, 115:980-988.<https://doi.org/10.14309/ajg.0000000000000639>
2. Hoffman JM: Irritable bowel syndrome: is the colonic mucosa to blame? *Neurogastroenterology & Motility*. 2012, 24:1051-1053.<https://doi.org/10.1111/nmo.12039>
3. Grover M, Herfarth H, Drossman DA: The Functional–Organic Dichotomy: Postinfectious Irritable Bowel Syndrome and Inflammatory Bowel Disease–Irritable Bowel Syndrome. *Clinical Gastroenterology and Hepatology*. 2009, 7:48-53.<https://doi.org/10.1016/j.cgh.2008.08.032>
4. Moayyedi P, Andrews CN, MacQueen G, et al.: Canadian Association of Gastroenterology Clinical Practice Guideline for the Management of Irritable Bowel Syndrome (IBS). *Journal of the Canadian Association of Gastroenterology*. 2019, 2:6-29.<https://doi.org/10.1093/jcag/gwy071>
5. Cash BD, Epstein M, Shah SM: In Patients with Irritable Bowel Syndrome–Mixed (IBS–M), a Novel Peppermint Oil Formulation Designed for Site Specific Targeting (PO–SST), in the Small Intestine, Improves the 8 Symptoms that Comprise the Total IBS Symptoms Score (TISS). *Gastroenterology*. 2017, 152.[https://doi.org/10.1016/s0016-5085\(17\)33120-7](https://doi.org/10.1016/s0016-5085(17)33120-7)
6. 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. *International Journal of Clinical Practice*. 2013, 67:895-903.<https://doi.org/10.1111/ijcp.12128>
7. Cox SR, Lindsay JO, Fromentin S, et al.: Effects of Low FODMAP Diet on Symptoms, Fecal Microbiome, and Markers of Inflammation in Patients With Quiescent Inflammatory Bowel Disease in a Randomized Trial. *Gastroenterology*. 2020, 158:176-188.e7.<https://doi.org/10.1053/j.gastro.2019.09.024>

8. Bellini M, Tonarelli S, Nagy AG, et al.: Low FODMAP Diet: Evidence, Doubts, and Hopes. *Nutrients*. 2020, 12:148. <https://doi.org/10.3390/nu12010148>
9. Hayes P, Corish C, O'Mahony E, Quigley EMM: A dietary survey of patients with irritable bowel syndrome. *Journal of Human Nutrition and Dietetics*. 2013, 27:36-47. <https://doi.org/10.1111/jhn.12114>
10. Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG: A Diet Low in FODMAPs Reduces Symptoms of Irritable Bowel Syndrome. *Gastroenterology*. 2014, 146:67-75.e5. <https://doi.org/10.1053/j.gastro.2013.09.046>
11. Black CJ, Staudacher HM, Ford AC: Efficacy of a low FODMAP diet in irritable bowel syndrome: systematic review and network meta-analysis. *Gut*. 2021, 71. <https://doi.org/10.1136/gutjnl-2021-325214>
12. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al.: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*. 2015, 4:1-9. <https://doi.org/10.1186/2046-4053-4-1>
13. Higgins JP, Altman DG: Assessing risk of bias in included studies. *Cochrane Handbook for Systematic Reviews of Interventions: Cochrane Book Series*. 2008:187-241.
14. Böhn L, Störsrud S, Liljebo T, Collin L, Lindfors P, Törnblom H, 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.e2. <https://doi.org/10.1053/j.gastro.2015.07.054>
15. Chumpitazi BP, Cope JL, Hollister EB, Tsai CM, McMeans AR, Luna RA, et al.: Randomised clinical trial: gut microbiome biomarkers are associated with clinical response to a low FODMAP diet in children with the irritable bowel syndrome. *Alimentary Pharmacology & Therapeutics*. 2015, 42(4):418-427. <https://doi.org/10.1111/apt.13306>
16. 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. *Official Journal of the American College of Gastroenterology | ACG*. 2016, 111(12):1824-1832. <https://doi.org/10.1038/ajg.2016.434>

17. 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.e5. <https://doi.org/10.1053/j.gastro.2013.09.046>
18. Harvie RM, Chisholm AW, Bisanz JE, Burton JP, Herbison P, Schultz K, et al.: Long-term irritable bowel syndrome symptom control with reintroduction of selected FODMAPs. *World Journal of Gastroenterology*. 2017, 23(25):4632-4643. <https://doi.org/10.3748/wjg.v23.i25.4632>
19. McIntosh K, Reed DE, Schneider T, Dang F, Keshteli AH, De Palma G, et al.: FODMAPs alter symptoms and the metabolome of patients with IBS: a randomised controlled trial. *Gut*. 2017, 66(7):1241-1251. <https://doi.org/10.1136/gutjnl-2015-311339>
20. Ong DK, Mitchell SB, Barrett JS, Shepherd SJ, Irving PM, Biesiekierski JR, et al.: Manipulation of dietary short chain carbohydrates alters the pattern of gas production and genesis of symptoms in irritable bowel syndrome. *Journal of Gastroenterology and Hepatology*. 2010, 25(8):1366-1373. <https://doi.org/10.1111/j.1440-1746.2010.06370.x>
21. Paduano D, Cingolani A, Tanda E, Usai P: Effect of three diets (low-FODMAP, gluten-free and balanced) on irritable bowel syndrome symptoms and health-related quality of life. *Nutrients*. 2019, 11(7):1566. <https://doi.org/10.3390/nu11071566>
22. Patcharatrakul T, Juntrapirat A, Lakananurak N, Gonlanchanvit S: Effect of structural individual low-FODMAP dietary advice vs. brief advice on a commonly recommended diet on IBS symptoms and intestinal gas production. *Nutrients*. 2019, 11(12):2856. <https://doi.org/10.3390/nu11122856>
23. Pedersen N, Andersen NN, Végh Z, Jensen L, Ankersen DV, Felding M, et al.: Ehealth: low FODMAP diet vs *Lactobacillus rhamnosus* GG in irritable bowel syndrome. *World Journal of Gastroenterology: WJG*. 2014, 20(43):16215-16226. <https://doi.org/10.3748/wjg.v20.i43.16215>
24. Staudacher HM, Lomer MC, Anderson JL, Barrett JS, Muir JG, Irving PM, et al.: Fermentable carbohydrate restriction reduces luminal bifidobacteria and gastrointestinal symptoms in patients with irritable bowel syndrome. *The Journal of Nutrition*. 2012, 142(8):1510-1518. <https://doi.org/10.3945/jn.112.159285>
25. Staudacher HM, Lomer MC, Farquharson FM, Louis P, Fava F, Franciosi E, 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. <https://doi.org/10.1053/j.gastro.2017.06.010>
26. 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. *Journal of Gastroenterology and Hepatology*. 2018, 33(6):1192-1199. <https://doi.org/10.1111/jgh.14120>
27. Goyal O, Batta S, Nohria S, Kishore H, Goyal P, Sehgal R, et al.: Low fermentable oligosaccharide, disaccharide, monosaccharide, and polyol diet in patients with diarrhea-predominant irritable bowel syndrome: a prospective, randomized trial. *Journal of Gastroenterology and Hepatology*. 2021, 36(8):2107-2115. <https://doi.org/10.1111/jgh.15560>
28. Mohseni F, Agah S, Ebrahimi-Daryani N, Taher M, Nattagh-Eshtivani E, Karimi S, et al.: The effect of low FODMAP diet with and without gluten on irritable bowel syndrome: a double blind, placebo controlled randomized clinical trial. *Clinical Nutrition ESPEN*. 2022, 47:45-50. <https://doi.org/10.1016/j.clnesp.2021.12.010>
29. Krieger-Grübel C, Hutter S, Hiestand M, Brenner I, Güsewell S, Borovicka J: Treatment efficacy of a low FODMAP diet compared to a low lactose diet in IBS patients: A randomized, cross-over designed study. *Clinical Nutrition ESPEN*. 2020, 40:83-89. <https://doi.org/10.1016/j.clnesp.2020.07.014>
30. Wilson B, Rossi M, Kanno T, Parkes GC, Anderson S, Mason AJ, et al.: β -Galactooligosaccharide in conjunction with low FODMAP diet improves irritable bowel syndrome symptoms but reduces fecal bifidobacteria. *Official Journal of the American College of Gastroenterology| ACG*. 2020, 115(6):906-915. <https://doi.org/10.14309/ajg.0000000000000562>
31. Prince AC, Myers CE, Joyce T, Irving P, Lomer M, Whelan K: Fermentable carbohydrate restriction (low FODMAP diet) in clinical practice improves functional gastrointestinal symptoms in patients with inflammatory bowel disease. *Inflammatory Bowel Diseases*. 2016, 22(5):1129-1136. <https://doi.org/10.1097/MIB.0000000000000715>

UNDER PEER REVIEW