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Probiotics, prebiotics, and low FODMAP diet for irritable bowel syndrome – What is the current evidence?

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ABSTRACT

Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders worldwide. While the pathogenesis is not clearly understood, current research points to the role of the gut microbiome and alterations in the diversity of the microbiota. Probiotics, prebiotics, and low FODMAP diet are therapeutic means associated with modification of the gut microbiome for the alleviation of IBS symptoms.

This narrative review assesses the current evidence on the efficacy of these treatment options based on findings from recent systematic reviews and meta-analyses published from October 2013 to October 2018.

There is a general agreement in the 11 included systematic reviews and meta-analyses that probiotic therapy is safe and can be effective in improving overall IBS symptom scores and abdominal pain in the general IBS population. Nonetheless, conflicting findings remain and no recommendation on the specific species/strains or combination can be made.

Short-term restriction of FODMAP in the diet can improve IBS symptoms as per the findings of 7 systematic reviews and meta-analyses, even though the quality of the evidence remains questionable. Inappropriate use of the low FODMAP diet can potentially impact health negatively. As such, a low FODMAP diet is only recommended as a second line treatment guided by qualified clinicians with specialized training.

Despite preclinical studies of some prebiotics demonstrated the potential use in improving gut microbiome and intestinal inflammatory response, the beneficial effect of prebiotics for IBS remains theoretical. Two systematic reviews found no evidence to support the clinical use of prebiotics for IBS.

1. Introduction

Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders with a global prevalence of about 11%.[1] This condition affects more women than men. IBS is defined by recurring abdominal pain associated with defecation and/or a change in bowel habits, typically accompanied by symptoms of abdominal bloating/distension.[2] The diagnosis of one of the specific IBS subtypes depends on the predominant bowel habits, such as constipation, diarrhea, multi-type, or unspecified IBS.[2–5] The current diagnostic criteria for IBS (Rome IV) are summarized in Table 1. While the pathogenesis is not clearly understood, current research points to the role of the gut microbiome and alterations in the diversity of the microbiota (referred to as 'dysbiosis'), specifically a decrease in *Lactobacillus* and *Bifidobacterium* species.[4–6] Dysbiosis activates the immune system and leads to low-grade inflammation of the gut, and thus disrupts the gut-brain axis interaction.[3,5,6] Probiotics, prebiotics, and low FODMAP diet are therapeutic means associated with modification of the gut microbiome for the alleviation of IBS symptoms. These therapies have received much research focus in recent years.[6–10]

This review aims to assess the current evidence on the efficacy of these treatment options for IBS. We conducted searches in research databases (Pubmed, Cochrane Library, Scopus, and Web of Science) to identify relevant studies with the keywords (prebiotics OR probiotics OR FODMAP AND irritable bowel syndrome). With the bulk of available clinical trials and reviews on this topic, we selected only the systematic reviews and meta-analyses of human clinical trials published within the 5-year period from October 2013 to October 2018. Our search yielded 267 unique records after removing the duplicates. After screening and assessing for eligibility, a total of 18 studies are included for information synthesis and a narrative review.

2. Probiotics

According to the World Health Organization definition, probiotics are living bacteria which confer health benefits on the host when

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Table 1
Diagnostic Criteria for Irritable Bowel Syndrome (Rome IV).

Diagnostic Criteria for IBS:
Recurrent abdominal pain on average at least 1 day/week in the last 3 months, associated with 2 or more of the following *:
☐ Related to defecation *(i.e. either increasing or improving pain)*
☐ Associated with a change in stool frequency
☐ Associated with a change in stool form (appearance)
* *Criterion fulfilled for the last 3 months with symptoms onset at least 6 months prior to diagnosis.*
IBS subtypes:
☐ IBS-C: constipation predominant
☐ IBS-D: diarrhea predominant
☐ IBS-M: mixed IBS, both constipation and diarrhea are present
☐ IBS-U: unclassified IBS

administered in adequate amount.[11,12] Some commonly used probiotics today are Gram-positive species such as the *Lactobacillus* and *Bifidobacterium*, as well as some Gram-negative, most notably, *Escherichia coli* Nissle 1917.[11] The health-promoting benefits of probiotics include preventing the colonization or curbing the growth of pathogenic bacteria, enhancing epithelial barrier functions, stimulating the host immune response, and modulating the inflammatory gene expression in the gut.[12,13] The potentials for probiotics to modulate gut microbiome and thus correct the dysbiosis support its use in IBS.[14–16]

We found a total of 11 systematic reviews and/or meta-analyses [17,18,27,17–27] published over the last 5 years. The characteristics of these studies are summarized in Table 2. Three studies [17,22,27] stand out in terms of the breadth of inclusion and depth of the analysis. The first is published in 2014 by Ford et al.[17] to inform the American College of Gastroenterology's monograph on the management of IBS. This study found probiotics to be better than placebo in reducing the persistence of IBS symptoms and had beneficial effects on global IBS, abdominal pain, bloating, and flatulence scores based on the results of 35 randomized control trials (RCTs). A diverse range of both single and multi-strains probiotics was used as interventions and it was unclear which individual species and strains were the most beneficial.[17] Ford et al.[27] updated their systematic review in 2018 to include up to 53 RCTs. This updated study found the use of specific combinations of probiotics or specific species and strains did suggest a significant improvement in IBS symptom scores and abdominal pain, however, the authors had reservations about drawing any definitive conclusions about their efficacy. The British Dietetic Association published a systematic review of 35 RCTs extracted from 9 systematic reviews in 2016.[22] This study indicated that no strain or dose-specific probiotic was consistently effective to improve any IBS symptoms or quality of life (QoL) and thus no recommendation on any specific probiotic for IBS management in adults could be made. Nevertheless, taking probiotics was considered safe and IBS patients were advised to select one product at a time and to monitor the effects if they chose to try probiotics.[22]

The inconsistency in treatment efficacy of probiotics also reflected in findings of other systematic reviews. Two meta-analyses by Didari et al.[19] and Hu et al.[20] found probiotics to have beneficial effects in IBS patients over placebo, especially in the reduction of pain and symptom severity scores but not QoL. Whereas the meta-analysis conducted by Zhang et al.[23] reported a significant improvement in overall symptom response and QoL, but not individual IBS symptoms, with probiotic therapy. In contrast to Ford et al.[27] Zhang et al.[23] suggested that single probiotic (rather than combinations) at a low dose and with a short treatment duration appeared to be more effective.

The efficacy of single strain or species was meta-analyzed in 3 studies. Tiequn et al.[21] found treatment with *Lactobacillus* strains was more effective than placebo based on the results from 6 RCTs, whereas Cayzeele-Decherf et al.[24] concluded that *Saccharomyces cerevisiae* CNCM I-3856 could significantly improve abdominal pain/discomfort in IBS patients over placebo based on the results of only 2 RCTs. Yuan et al. [25], however, reported that the efficacy of *Bifidobacterium infantis* 35624 was no better than placebo.

In pediatric IBS patients, probiotics appeared to be effective in reducing abdominal pain symptoms based on the results from 4 RCTs as reported by Korterink et al.[18] Our search also located a Cochrane Systematic Review protocol.[28] which aims to assess the efficacy and safety of probiotics for the treatment of IBS in children. In time, this Cochrane review will add to the understanding of therapeutic use of probiotics in this subpopulation of IBS.

Among patients with chronic fatigue syndrome and myalgic encephalomyelitis, which often suffered from symptoms of irritable bowel, Corbitt et al.[26] found inconclusive evidence for the use of probiotics due to limited, poor-quality data.

Hitherto, there is a general agreement in these systematic reviews and meta-analyses that probiotics treatment can be effective in improving overall IBS symptom scores and abdominal pain in the general IBS population. Nonetheless, conflicting findings remain.

3. Prebiotics

A prebiotic is “a substrate that is selectively utilized by host microorganisms conferring a health benefit”, as defined by the expert panel of the International Scientific Association for Probiotics and Prebiotics.[29] Unlike probiotics which are living organisms, prebiotics are non-viable dietary substances such as indigestible polysaccharides that serve as nutrients for microbiota with the goal of improving health. The potential health effects of prebiotics may include benefits to the gastrointestinal tract, cardiometabolic health, cognitive functions, and bone strength.[29] Prebiotics are selectively utilized by various groups of bacteria in the gut including *Lactobacillus* spp., *Bifidobacterium* spp., *Faecalibacterium prausnitzii*, *Anaerostipes* spp. and *Bilophila* spp., to name a few. The benefits of prebiotics to the host are thought to be mediated through the microbial metabolic products such as the short-chain fatty acids which appeared to be lower in IBS patients.[12,30] Inulin, fructan, galactooligosaccharides and oligosaccharides are some of the prebiotics that have been studied in clinical trials on their role in correcting dysbiosis and ameliorating IBS symptoms.[3] Prebiotics are also combined with probiotics for their potential synergistic action, and such combinations are called synbiotics.[31]

The two systematic reviews by Ford et al [17,27] (see Table 3) also reviewed the efficacy of prebiotics and synbiotics in IBS treatment. The earlier review did not include any RCT of prebiotics and only 2 RCTs (n = 185) of synbiotics were included. Even though both trials were individually positive, there was no statistically significant effect of synbiotics in IBS symptom reduction.[17] The updated review included 3 RCTs (n = 237) of prebiotics and no new RCT of synbiotics were found. All 3 RCTs found no significant difference between the treatment effects of prebiotics compared to placebo or control.[27]

One placebo-RCT that compared the use of oligo- and polysaccharides and reticulated protein combination in IBS treatment was excluded in Ford et al [27] due to the use of the reticulated protein of which its treatment effect from prebiotics cannot be separated. This RCT found the combination therapy of prebiotics and reticulated protein significantly improved abdominal pain, flatulence, and QoL of IBS patients over placebo.[32] Nonetheless, the dearth of evidence was apparent and Ford et al. [27] concluded that there was little evidence for the use of prebiotics or synbiotics in IBS.

4. Low FODMAP diet

FODMAP is the acronym for “Fermentable Oligo-, Di- and Monosaccharides And Polyols”. It refers to a group of short-chain carbohydrates that are fermented in the colon due to incomplete absorption by the small intestines.[33,34] FODMAPs can increase gastrointestinal motility, which decreases the small intestinal transit time and thus reduces the opportunity for absorption. Unabsorbed FODMAPs such as fructans,

Table 2
Summary of included reviews: Probiotics for irritable bowel syndrome.

1st Author (Year)	Type	Inclusion	No. Studies (Study Size)	Outcome/Conclusion
Ford (2014)[17]	SR + MA	Placebo-RCTs with adults (age > 16); IBS diagnosis based on clinical opinion or specific diagnostic criteria (Manning, Kruis score, Rome I, II, or III); Minimum 7 days of therapy and follow-up.	Total: 35 (n = 3452) Combination = 19 (n = 1487) Lactobacillus = 8 (n = 542) Escherichia = 3 (n = 715) Bifidobacterium = 2 (n = 484) Bifidobacterium or Lactobacillus = 1 (n = 80) Saccharomyces = 1 (n = 90) Streptococcus = 1 (n = 54)	The RR of IBS symptoms persisting with probiotics versus placebo (based on 23 RCTs with n = 2575) was 0.79 (95 % CI: 0.70 – 0.89). Probiotics had beneficial effects on global IBS, abdominal pain, bloating, and flatulence scores. It remains unclear which individual species and strains are the most beneficial.
Korterink (2014)[18]	SR + MA	Placebo-RCTs with children and adolescents (age ≤18); IBS diagnosis based on Rome II or III or authors' definition. No restriction on dose or duration.	Total: 4 (n = 349) Combination = 1 (n = 59) Lactobacillus = 3 (n = 290)	Pooled RR for IBS abdominal pain symptoms with probiotics versus placebo was 1.62 (95% CI: 1.27–2.06). Probiotics are more effective than placebo in the treatment of pediatric IBS.
Didari (2015)[19]	SR + MA	All RCTs that considered improvement of IBS symptoms as the outcome of interest.	Total: 24 (n = 2282) Combination = 12 (n = 821) Lactobacillus = 7 (n = 550) Escherichia = 3 (n = 715) Bifidobacterium = 1 (n = 122) Saccharomyces = 1 (n = 74)	The RR of adequate general symptom improvement in IBS patients for seven included trials from six studies comparing probiotics with placebo was 2.14 (95%CI: 1.08 – 4.26). Probiotics reduce pain and symptom severity scores.
Hu (2015)[20]	MA	All double-blind placebo-RCTs with adults (age > 18); IBS diagnosis based on Rome II or III.	Total: 17 (n = 1700) Combination = 13 (n = 1204) Lactobacillus = 2 (n = 254) Escherichia = 1 (n = 120) Bifidobacterium = 1 (n = 122)	Results favor probiotics over placebo in improving the total IBS symptom scores, abdominal pain, distention, and defecation distention. No statistical difference in overall QoL and adverse effect ratio.
Tiequn (2015)[21]	MA	All RCTs investigated the efficacy of Lactobacillus therapy in patients with IBS that reported measurable outcomes.	Lactobacillus = 6 (n = 450)	The pooled RR for clinical improvement with Lactobacillus treatment was 7.69 (95% CI: 2.33 – 25.43). Lactobacillus treatment was associated with a significantly higher response rate than placebo in the overall population with IBS, without any side effects.
McKenzie (2016)[22]	SR of SR	All placebo-RCTs included in English-language SRs and MAs with adults (age ≥16, n ≥20) diagnosed with IBS (Manning, Rome I-III, or clinicians' diagnosis).	Total: 35 (n = 3452) Combination = 18 (n = 1568) Lactobacillus = 9 (n = 648) Escherichia = 2 (n = 417) Bifidobacterium = 2 (n = 438) Bifidobacterium or Lactobacillus = 1 (n = 77) Saccharomyces = 1 (n = 246) Streptococcus = 1 (n = 58)	No strain or dose specific probiotic was consistently effective to improve any IBS symptoms or QoL. Taking a probiotic product is considered safe, but unlikely to provide substantial benefit to IBS symptoms. Individuals are advised to select one product at a time and monitor the effects.
Zhang (2016)[23]	MA	Placebo-RCTs with IBS diagnosis based on the Rome III criteria with treatment duration > 7 days.	Total: 21 (n = 1639) Combination = 13 (n = 961) Lactobacillus = 6 (n = 484) Bifidobacterium = 1 (n = 122) Saccharomyces = 1 (n = 72)	Probiotic therapy was associated with more improvement than placebo administration in overall symptom response (RR: 1.82, 95 % CI 1.27 to 2.60) and QoL (SMD: 0.29, 95 % CI 0.08 to 0.50), but not in individual IBS symptoms. Single probiotic at a low dose and with a short treatment duration appear to be more effective.
Cayzeele-Decherf (2017)[24]	MA	Placebo-RCTs that studied the effect of *Saccharomyces cerevisiae* CNCM I-3856 supplementation on gastrointestinal symptoms in IBS subjects.	Saccharomyces = 2 (n = 579)	*S. cerevisiae* CNCM I-3856 significantly improved abdominal pain/discomfort. A 12.3% reduction of abdominal pain/discomfort was recorded relative to the placebo group.
Yuan (2017)[25]	MA	Placebo-RCTs that studied the effect of *Bifidobacterium infantis* 35,624 in adolescents and adults (age > 15) with IBS symptoms (Criteria: Rome I – III). Follow-up ≥ 1 months.	Total = 6 (n = 666) Bifidobacterium = 3 (n = 554) Combination = 2 (n = 112)	Combination probiotics containing *B. infantis* significantly reduced abdominal pain and bloating/distention compared to placebo, but not single probiotic *B. infantis*. The efficacy of single probiotic *B. infantis* on IBS has not been confirmed.

(*continued on next page*)

Table 2 (*continued*)

1st Author (Year)	Type	Inclusion	No. Studies (Study Size)	Outcome/Conclusion
Corbitt (2018)[26]	SR	Intervention studies of adult patients (age > 18) with IBS or CFS/ME that evaluated the effectiveness of probiotics on IBS symptoms, QoL, and other secondary outcomes.	Total: 25 (n = 2437) Combination = 14 (n = 1183) Lactobacillus = 5 (n = 580) Escherichia = 2 (n = 234) Bifidobacterium = 2 (n = 189) Saccharomyces = 2 (n = 251)	There is a role for probiotics in the management of IBS, but the role of probiotics in the management of irritable bowel and gastrointestinal symptoms in the CFS/ME patient is inconclusive due to limited, poor-quality data.
Ford (2018)[27]	SR + MA	Placebo-RCTs with adults (age > 16); IBS diagnosis based on clinical opinion or specific diagnostic criteria (Manning, Kruis score, Rome I-IV); Minimum 7 days of therapy and follow-up.	Total: 53 (n = 5545) Combination = 29 (n = 2263) Lactobacillus = 11 (n = 1094) Escherichia = 3 (n = 715) Bifidobacterium = 3 (n = 528) Bifidobacterium or Lactobacillus = 1 (n = 80) Saccharomyces = 5 (n = 811) Streptococcus = 1 (n = 54)	Combination probiotics were assessed to have a significant effect on IBS symptoms (RR = 0.79; 95% CI 0.68-0.91). Specific combinations of probiotics, or specific species and strains, appeared to have beneficial effects on global IBS symptoms and abdominal pain, but it was not possible to draw definitive conclusions about their efficacy.

Abbreviation. Chronic fatigue syndrome (CFS); Confidence interval (CI); Irritable bowel syndrome (IBS); Meta-analysis (MA); Myalgic encephalomyelitis (ME); Quality of life (QoL); Randomized-control trial (RCT); Relative risk (RR); Standard mean difference (SMD); Systematic review (SR).

fructose, polyols and lactose are osmotically active and attract water into the small intestines to increase its volume. Once in the colon, these FODMAPs undergo rapid fermentation and produce gas, especially hydrogen. These mechanisms cause luminal distension and can lead to functional gastrointestinal symptoms in individuals with visceral hypersensitivity.[34–38] A high FODMAP diet is also associated with dysbiosis, inflammation, barrier dysfunction, and visceral hypersensitivity, all of which are implicated in the pathology and exacerbation of IBS.[39–41] The clinical intervention with a low FODMAP diet involves restricting FODMAP intake for 4–8 weeks to test for symptom response. When symptom reduction is achieved, some FODMAP carbohydrates are then reintroduced into the diet individually to test for tolerance with the aim to achieve long-term symptom control with nutritionally adequate diet.

Our search identified 7 systematic reviews and/or meta-analyses,[42–48] all published within the last 3 years. The characteristics of these reviews are summarized in Table 4. Marsh et al.[42] included 20 human studies of different design and found a low FODMAP diet to significantly improve IBS symptom severity and QoL of patients in 6 RCTs and a non-randomized study. Other non-controlled clinical studies have also shown low FODMAP diet to be effective in reducing abdominal pain and bloating in IBS patients. The British Dietetic Association[43] also found evidence supporting the use of dietitian-led low FODMAP diet to improve overall symptoms of IBS and recommended low FODMAP diet as a second-line advice in the IBS algorithm for clinical practice. A meta-analysis by Altobelli et al.[44] found a low FODMAP diet to have a favorable impact on IBS symptoms, especially abdominal pain and bloating. However, the superiority of the low FODMAP diet compared to conventional IBS diet/remedies remained unclear.[44] Similarly, Pourmand et al.[46] found no significant difference between the efficacy of a low FODMAP diet versus that of traditional remedies for IBS. However, another meta-analysis by Varju et al.[47] reported that even though both conventional IBS and low FODMAP diets proved to be effective in IBS, values of post-diet IBS Symptom Severity Score were significantly lower in the low FODMAP group.

Two systematic reviews questioned the quality of the available evidence. Assessing the risk of bias of 9 RCTs on the low FODMAP diet for IBS, Krogsgaard et al.[45] found a high risk of bias in all these trials. Furthermore, all trials were short-term ($\leq$6 weeks) in nature and none of the trials studied the subsequent reintroduction of FODMAP into the diet. Furthermore, the risk of placebo-response cannot be ruled out in all the RCTs. The latest systematic review by Dionne et al.[48] also found the overall quality of the data to be "very low" even though their meta-analysis showed low FODMAP diet did associate with reduced global symptom scores compared to control interventions.

From the findings of these systematic reviews, there is evidence supporting the use of low FODMAP diet, especially when guided by dietitians, to achieve symptomatic relief in IBS. However, the quality of the evidence remains questionable.

5. Discussion

Despite active research on the therapeutic management of IBS in recent years, treatment options supported by high-quality evidence remain scarce.[49] Probiotics, prebiotics, and low FODMAP diet are non-pharmaceutical therapies proposed for this complex condition. We found a good number of recent systematic reviews and meta-analyses on the efficacy of probiotics and low FODMAP diet for IBS but not prebiotics.

Systematic reviews and meta-analyses play an important role in evidence-informed practice as they provide clinicians with pre-filtered information that have been appraised and synthesized from relevant original studies. The fact that 11 systematic reviews and meta-analyses were published over the course of the past 5 years on the topic of probiotics for the treatment of IBS demonstrated the continuing research interest in the quest for evidence for therapies aimed at

Table 3
Summary of included reviews: Prebiotics for irritable bowel syndrome.

1st Author (Year)	Type	Inclusion	No. Studies (Study Size)	Outcome/Conclusion
Ford (2014)[17]	SR + MA	Placebo-RCTs with adults (age > 16); IBS diagnosis based on clinical opinion or specific diagnostic criteria (Manning, Kruis score, Rome I, II, or III); Minimum 7 days of therapy and follow-up.	Synbiotics = 2 (n = 185)	No statistically significant effect of synbiotics in reducing IBS symptoms, even though both trials were individually positive, owing to significant heterogeneity between studies.
Ford (2018)[27]	SR + MA	Placebo-RCTs with adults (age > 16); IBS diagnosis based on clinical opinion or specific diagnostic criteria (Manning, Kruis score, Rome I-IV); Minimum 7 days of therapy and follow-up.	Total: 5 (n = 422) Synbiotics = 2 (n = 185) Prebiotics = 3 (n = 237)	Data for both prebiotics and synbiotics were sparse, with neither appearing to be of particular benefit in IBS.

Abbreviation: Irritable bowel syndrome (IBS); Randomized-control trial (RCT); Systematic review (SR).

correction of dysbiosis for IBS. By and large, current evidence supports the use of probiotics to provide general symptomatic relief for IBS patients especially in the reduction of abdominal pain. The conflicting results observed in different clinical trials reflect the relative infancy of research and knowledge of how the gut microbiota influences IBS. It remains unclear whether probiotic combinations are more effective than single strain/species or vice versa. Also, none of the systematic reviews and meta-analyses can provide any clear indication of the minimum or the optimal quantity of probiotics required to achieve a clinically significant difference in treatment. Hence, more well-designed comparative RCTs are needed to explore the dose-response relationship of single-strain/species versus combination probiotics in treating specific symptom outcomes in different subtypes of IBS.

In terms of safety, supplementation with probiotics is considered safe in IBS with no concern raised in any of the included reviews. Furthermore, safety evaluations of probiotics also found overwhelming evidence suggesting probiotics to be generally safe, but warned against potential systemic infections in certain at-risk populations, such as the critically ill or immunocompromised.[50,51] However, as pointed out by Ford at al.[27], the longer-term impact and safety of repeated use of probiotics on the gut microbiota remains unclear. This should be an area of further research. In any case, we can expect probiotics to be a mainstay of IBS management in clinical practice with the choice of types and strengths of the probiotics depending largely on clinicians' experience along with the close monitoring of patients' symptom responses.

Low FODMAP diet is another plausible treatment option for IBS supported by research evidence, although the quality of data is being contended due to the weak study methodologies (e.g. non-randomized trials) and high risk of bias in existing clinical trials. Undoubtedly, dietary restriction of suspected individual food triggers such as alcohol, spicy foods, or foods with high-fat contents, as well as increasing intakes of dietary fibers can also help to achieve symptom improvement.[52] It is still unclear whether a low FODMAP diet is superior to these proven dietary recommendations. More studies with better design and low risk of bias are needed to evaluate the efficacy of the low FODMAP diet compared to other IBS diet/remedies as well as placebo-control.

There are several issues with the low FODMAP diet as pointed out by some critics.[53,54] Firstly, this approach eliminates many staple foods, including wheat derivatives, lactose-containing dairy products as well as many vegetables, pulses, and fruits from the diet. IBS patients on the low FODMAP diet may be at risk of insufficient intake of micronutrients including calcium, iron, zinc, folate, B and D vitamins, natural antioxidants as well as dietary fibers in the longer term.[33] Additionally, certain FODMAP items, such as fructans and galacto-oligosaccharides, are considered prebiotics. The restriction may alter the balance of the gut microbiome, causing a reduction of the beneficial bacteria species in the short term and unknown health consequences in the long run.[53,54] Furthermore, with great emphasis placed on selection of food items, this approach may also contribute to the increased risk of development of disordered eating habits such as orthorexia nervosa, a condition characterized by "obsessional preoccupation with eating 'healthy foods', focusing on concerns regarding the quality and composition of meals".[53,55] Hence, inappropriate use of the low FODMAP diet can lead to negative health consequences. As such, a low FODMAP diet should remain a second-line dietary treatment option for IBS guided by qualified clinicians as per the recommendation of the British Dietetic Association.[43]

Despite preclinical studies of some prebiotics demonstrated the potential use in improving gut microbiome and intestinal inflammatory response,[56,57] the beneficial effect of prebiotics for IBS remain theoretical with few human trials available at present and limited efficacy demonstrated in the available RCTs. Furthermore, with certain prebiotics being FODMAP, there is also a possibility that prebiotics may exacerbate IBS symptoms. Hence, the current evidence does not support

Table 4
Summary of included reviews: Low FODMAP diet for irritable bowel syndrome.

1st Author (Year)	Type	Inclusion	No. Studies (Study Size)	Outcome/Conclusion
Marsh (2016)[42]	SR & MA	Clinical studies with IBS patients (Criteria: Rome I – III & NICE) that pre- and post-intervention symptom severity score or QoL.	Total: 20 (n = 885) RCT = 6 (n = 354) non-RCT = 1 (n = 82) Cross-over trial = 3 (n = 89) Prospective observation = 2 (n = 120) Case-series = 7 (n = 170) Retrospective = 1 (n = 70)	A significant decrease in symptom severity scores and QoL for patients on low FODMAP diet observed in both RCTs and non-randomized intervention. The low FODMAP diet also found to reduce abdominal pain and bloating.
McKenzie (2016)[43]	SR	Clinical studies with adults (age ≥16) diagnosed with IBS (Criteria: Manning, Rome I-III, or clinician's diagnosis) with inclusion/avoidance of FODMAP in the diet as an intervention	RCT = 5 (n = 479)	A dietitian-led low FODMAP diet with a "restriction" phase for 3–6 weeks improved overall symptoms of IBS, IBS-D, and IBS-M but not IBS-C, abdominal pain, bloating, flatulence, satisfaction with stool consistency, borborygmi, urgency and life interference. Low FODMAP diet is included as a second-line advice in the IBS algorithm for clinical practice.
Altobelli (2017)[44]	MA	Clinical investigations involving the effect of a FODMAP diet on IBS patients.	Total: 12 (n = 600) RCT = 6 (n = 303) non-RCT = 2 (n = 89) Prospective observation = 4 (n = 208)	There is evidence that a low-FODMAP diet could have a favorable impact on IBS symptoms, especially abdominal pain and bloating. It remains unclear whether low-FODMAP diet is superior to traditional IBS diet, especially in the long term.
Krogsgaard (2017)[45]	SR	RCTs reported the effect of the low FODMAP diet on IBS symptoms. IBS diagnosis by clinicians or symptom-based diagnostic criteria.	RCT = 9 (n = 542)	RCTs on the low FODMAP diet have a high risk of bias. The diet has not been studied in any RCT for more than 6 weeks with reintroduction period. Current trials cannot rule out symptomatic effects due to a placebo response.
Pourmand (2017)[46]	SR	Human clinical trials examined the relationship or effect of a low FODMAP diet on IBS symptoms.	Total = 15 (n = 845) RCT = 5 (n = 590) non-RCT = 1 (n = 82) Cross-over trial = 1 (n = 52) Prospective observation = 3 (n = 121)	Most studies had reported a significant effect of low FODMAP diet on IBS symptoms; some studies reported no significant difference between low FODMAP diet and traditional remedies for IBS. Adherence to the diet was not associated with the severity of symptoms.
Varju (2017) [47]	MA	Include only RCTs, non-RCTs, and prospective observations examining the effect of low FODMAP diet in patients diagnosed with IBS (Criteria: Rome II-IV, or NICE) compared to traditional IBS diet.	Total = 10 (n = 845) RCT = 5 (n = 298) non-RCT = 1 (n = 56) Cross-over trial = 1 (n = 19) Prospective observation = 3 (n = 98)	Both traditional and low FODMAP diets proved to be effective in IBS, but values of post-diet IBS Symptom Severity Score were significantly lower (p = 0.002) in the low FODMAP group. Low FODMAP diet is superior to traditional IBS dietary therapy.
Dionne (2018) [48]	SR + MA	RCTs with adults (age ≥17) diagnosed with IBS (Criteria: Manning, Rome I-IV, or clinician's diagnosis) compared dietary exclusion of FODMAPs with placebo or usual diet. Minimum duration and follow-up: 7 days.	RCT = 7 (n = 397)	A low FODMAP diet was associated with reduced global symptoms compared with control interventions (RR = 0.69; 95% CI 0.54-0.88). Three RCTS that compared low FODMAP diet with rigorous control diets had the least heterogeneity and the least magnitude of effect. The overall quality of the data was "very low".

Abbreviation: Confidence interval (CI); Fermentable Oligo-, Di- and Mono-saccharides And Polyols (FODMAP); Irritable bowel syndrome (IBS); Meta-analysis (MA); The National Institute for Health and Care Excellence, United Kingdom (NICE); Quality of life (QoL); Randomized-control trial (RCT); Relative risk (RR); Standard mean difference (SMD); Systematic review (SR).

the administration of prebiotics for symptomatic relief in IBS. Nonetheless, the use of prebiotics to nourish and manipulate the gut microbiome to prevent the development of functional gastrointestinal disease remains a novelty worth further exploration. Much research is needed to understand the types and dose of prebiotics and the effects on pathological development and potential effects on IBS.

6. Conclusion

Current evidence from systematic reviews and meta-analyses supports the use of probiotics for symptomatic relief of IBS, however, no recommendation on the specific species/strains or combination can be made. Short-term restriction of FODMAP in the diet to improve IBS symptoms is also an evidence-based treatment option, but it must be guided by a qualified clinician with specialized training. Inappropriate use of the low FODMAP diet can potentially impact health negatively. As for prebiotics, there is no evidence of any clinical benefit for IBS.

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The Authors declare that there is no conflict of interest.

Author contribution

SCP conceived and designed the review. DC prepared the initial draft. SLO substantially reviewed and revised the paper. All authors reviewed and contributed to the final version of the manuscript.

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