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TITLE PAGE

Title: Efficacy of Dietary Interventions in Irritable Bowel Syndrome: Systematic Review and Network Meta-analysis.

Short title: Network Meta-analysis of Dietary Interventions for IBS.

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Abbreviations:

BDA	British Dietetic Association
CI	confidence interval
CINeMA	Confidence in Network Meta-Analysis framework
FDA	Food and Drug Administration
FODMAP	fermentable oligosaccharides, disaccharides, and monosaccharides, and polyols
IBS	irritable bowel syndrome
IBS-C	IBS with constipation
IBS-D	IBS with diarrhoea
NICE	National Institute for Health and Care Excellence
RCT	randomised controlled trial
RR	relative risk

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SUMMARY

Background: Patients with irritable bowel syndrome (IBS) are often interested in dietary interventions as a means of managing their symptoms. The relative efficacy of available diets for the management of IBS is unclear.

Methods: We performed a network meta-analysis. We searched the medical literature through to 7th February 2025 to identify RCTs comparing an active dietary intervention requiring changes to intake of more than one food in IBS with either a control intervention, such as habitual diet, sham diet, a high FODMAP diet, or alternative miscellaneous dietary advice, or any other active dietary intervention requiring changes to intake of more than one food. We judged efficacy using dichotomous assessments of improvement in global IBS symptoms or improvement in individual IBS symptoms, including abdominal pain, abdominal bloating or distension, and bowel habit. We pooled data using a random effects model, with efficacy of each intervention reported as pooled relative risks (RRs) with 95% confidence intervals (CIs). We ranked interventions according to their P-score, which measure the mean extent of certainty that one intervention is better than another, averaged over all competing interventions.

Findings: We identified 28 eligible RCTs (2338 patients) of 11 different dietary interventions compared with four control interventions, of which six (low FODMAP diet, British Dietetic Association/National Institute of Health and Care Excellence (BDA/NICE) diet, lactose-reduced diet, starch- and sucrose-reduced diet, a "personalised" diet, and a Mediterranean diet) were studied in more than one trial. For global symptoms in 28 RCTs, when considering only the dietary interventions studied in more than one trial, a starch- and sucrose-reduced diet, ranked first (RR of global IBS symptoms not improving = 0.41; 95% CI 0.26-0.67, P-score 0.84) in two RCTs, a low FODMAP diet fourth (RR = 0.51; 95% CI 0.37-0.70, P-score 0.71) in 24 trials, and BDA/NICE diet tenth (RR = 0.62; 95% CI 0.43-0.90, P-score 0.44) in

eight RCTs, versus habitual diet. For abdominal pain in 26 trials, when considering only the dietary interventions studied in more than one RCT, a starch- and sucrose-reduced diet ranked second (RR of abdominal pain not improving = 0.54; 95% CI 0.33-0.90, P-score 0.73) in two trials, and a low FODMAP diet fifth (RR = 0.61; 95% CI 0.42-0.89, P-score 0.64) in 23 RCTs, versus habitual diet. For abdominal bloating or distension in 26 trials, when considering only the dietary interventions studied in more than one RCT, only a low FODMAP diet (RR of abdominal bloating or distension not improving = 0.55; 95% CI 0.37-0.80, P-score 0.64), which was assessed in 23 trials, was superior to habitual diet and ranked fifth. For bowel habit in 23 RCTs, none of the dietary interventions was superior to any of the control interventions, but a low FODMAP diet was superior to BDA/NICE diet (RR of bowel habit not improving = 0.79; 95% CI 0.63-0.99).

Interpretation: In terms of dietary interventions for IBS, the most evidence exists for a low FODMAP diet, but other promising therapies are emerging and should be the subject of further study. All comparisons across the network were rated low or very low confidence, except for direct comparisons between a low FODMAP diet or a starch- and sucrose-reduced diet and habitual diet, both of which were rated as moderate.

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RESEARCH IN CONTEXT

Evidence before this study

Many people with irritable bowel syndrome (IBS) report food-related symptoms and patients are interested in non-pharmacological approaches to managing symptoms, including dietary interventions. However, it is less clear which dietary interventions are effective for a particular symptom in IBS, or whether they are superior to a control intervention. Although it is only 3 years since our network meta-analysis examining the efficacy of a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs), a comprehensive search of the medical literature using MEDLINE, EMBASE, EMBASE Classic, and the Cochrane central register of controlled trials from 1946 to 7th February 2025, and including foreign language articles, identified multiple randomised controlled trials (RCTs) of dietary interventions in IBS published since the conduct of the prior network meta-analysis. This provided the rationale for this systematic review and network meta-analysis. We aimed to examine whether inclusion of trials of dietary interventions studied more recently, as well as additional trials of a low FODMAP diet or a diet based on advice from the British Dietetic Association (BDA) and the National Institute of Health and Care Excellence (NICE), changed the conclusions of our previous network meta-analysis. We also wanted to assess whether we could identify any promising interventions to be taken forward to definitive RCTs in IBS.

Added value of this study

We did a contemporaneous systematic review and network meta-analysis of RCTs of active dietary interventions requiring changes to intake of more than one food, compared with either a control intervention, such as habitual diet, sham diet, a high FODMAP diet, or alternative

miscellaneous dietary advice, or any other active dietary intervention requiring changes to intake of more than one food, in adult patients with IBS. We identified 28 eligible trials, including 2338 patients. In terms of global symptoms data from all 28 RCTs were included. Among dietary interventions that were superior to habitual diet and whose efficacy was studied in more than one RCT, a starch- and sucrose-reduced diet ranked first (RR of global IBS symptoms not improving = 0.41; 95% CI 0.26 to 0.67, P-score 0.84) in two trials including 217 patients in total, a low FODMAP diet ranked fourth (RR = 0.51; 95% CI 0.37 to 0.70, P-score 0.71) in 24 trials including 1803 patients in total, and the BDA/NICE diet ranked tenth (RR = 0.62; 95% CI 0.43 to 0.90, P-score 0.44) in eight RCTs including 710 patients in total. For abdominal pain, data were available from 26 trials. Among interventions that were superior to habitual diet and whose efficacy was studied in more than one RCT a starch- and sucrose-reduced diet (RR of abdominal pain not improving = 0.54; 95% CI 0.33 to 0.90, P-score 0.73) ranked second in two trials including 217 patients in total and a low FODMAP diet (RR = 0.61; 95% CI 0.42 to 0.89, P-score 0.64) ranked fifth in 23 RCTs including 1773 patients in total. When abdominal bloating or distension was considered, again data were available for 26 RCTs, and among interventions whose efficacy was studied in more than one RCT only a low FODMAP diet (RR of abdominal bloating or distension not improving = 0.55; 95% CI 0.37 to 0.80, P-score 0.64) was superior to habitual diet, ranking fifth in 23 trials including 1773 patients in total. Finally, for bowel habit, in 23 trials, none of the dietary interventions were superior to habitual diet, although a low FODMAP diet was superior to BDA/NICE diet (RR of bowel habit not improving = 0.79; 95% CI 0.63 to 0.99) in 21 trials including 1666 patients in total. Findings were similar when only trials that either included patients with IBS with diarrhoea or stated that they excluded patients with IBS with constipation were included in the analyses.

Implications of all the available evidence

This systematic review and network meta-analysis demonstrates that, in terms of dietary interventions for IBS, the most evidence exists for a low FODMAP diet, which was superior to habitual diet for almost all symptom endpoints studied, and superior to several other control interventions. In addition, BDA/NICE diet was superior to habitual diet for global symptoms. Other dietary interventions that may be promising, and which are emerging, include a starch- and sucrose-reduced diet, a FODMAP-simple diet, and a gluten-free diet. Some of these may be considerably easier to implement than a low FODMAP diet and should be studied in definitive trials. For global symptoms, all direct and indirect comparisons across the network were rated as either low or very low confidence, except for the direct comparisons between a low FODMAP diet and habitual diet and between a starch- and sucrose-reduced diet and habitual diet, both of which were rated as moderate confidence.

INTRODUCTION

Irritable bowel syndrome (IBS) is characterised by abdominal pain that is associated with defaecation and either altered stool form or altered stool frequency.[1,2] The prevalence globally, according to the Rome IV criteria, is 5%.[3,4] IBS is chronic with a relapsing and remitting natural history.[5] As a result, costs to the health service and society are considerable,[6,7] and there is a substantial impact of symptoms on quality of life and social functioning.[7,8] Up to 80% of people with IBS report food-related symptoms.[9,10] It is, therefore, not surprising that patients often express a preference for dietary treatments as a means of improving their symptoms.[11]

Fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) are present in a range of foods, including wheat, some fruits, vegetables, and legumes, and artificial sweeteners. FODMAPs are either poorly absorbed, such as fructose, polyols, or lactose, or indigestible, such as fructans or galacto-oligosaccharides. This means they either increase small intestinal water content, via their osmotic effects, or undergo microbial fermentation in the colon.[12,13] These are the major proposed mechanisms by which they generate gastrointestinal symptoms. There have been multiple randomised controlled trials (RCTs) of a low FODMAP diet in IBS and, in our previous network meta-analysis from 2022,[14] a low FODMAP diet ranked first for global symptoms in IBS and was superior to all comparators studied, which included alternative dietary advice for IBS from the British Dietetic Association (BDA),[15] and the National Institute of Health and Care Excellence (NICE).[16] These both include advice to consume small regular meals, avoid skipping meals or eating late at night, reduce tea, coffee, alcohol, and carbonated drinks, and limit the intake of rich or fatty food.

However, other dietary interventions have been studied in RCTs in IBS in recent years. Wheat may contribute to IBS symptoms due to the effects of gluten on epithelial

barrier integrity,[17] fructans acting as FODMAPs,[18] or amylase trypsin inhibitors, which may induce immune activation.[19] A gluten-free diet has, therefore, been proposed as a potential treatment. A Mediterranean diet has been shown to have multiple health benefits, including reductions in cardiovascular and cancer risk,[20] and has been tested recently in IBS. Some studies show that fructans and galacto-oligosaccharides are the main FODMAPs that induce gastrointestinal symptoms in IBS,[18] which has led to an interest in a FODMAP-simple diet, where only these two FODMAPs are excluded. Reducing dietary intake of individual carbohydrates, such as lactose or fructose, may be beneficial for those with disaccharidase deficiency or fructose intolerance. There is also evidence that congenital sucrase-isomaltase deficiency may be more common among people with IBS than healthy individuals,[21] and that, in these individuals, symptoms improve with dietary reductions in starch and sucrose.[22] Finally, there is preliminary evidence that replacing wheat-based products such as bread and pasta, with products made from tritordeum, a Spanish cereal hybridised from durum wheat and barley with lower levels of gliadins and fructans, may improve symptoms in IBS.[23]

We, therefore, performed a network meta-analysis to examine the relative efficacy of all these dietary interventions, which require changes to intake of more than one food, in IBS. Network meta-analysis allows direct comparisons of interventions that have been compared head-to-head, as well as indirect comparisons, where no head-to-head evidence exists, to be made across different RCTs, increasing the number of participants' data available for analysis. It also allows a credible ranking system of the relative efficacy of all these different interventions to be developed, including potentially active interventions that have been used as control interventions in some RCTs, such as a BDA/NICE diet, even in the absence of trials making direct comparisons.

METHODS

Search Strategy and Selection Criteria

We searched MEDLINE (1st January 1946 to 7th February 2025), EMBASE and EMBASE Classic (1st January 1947 to 7th February 2025), and the Cochrane central register of controlled trials. We searched conference proceedings (Digestive Diseases Week, American College of Gastroenterology, United European Gastroenterology Week, and the Asian Pacific Digestive Week) between 2001 and 2024 to identify trials published only in abstract form. Finally, we used bibliographies of all obtained articles to perform a recursive search. The search strategy is provided in the appendix page 2.

Eligible RCTs examined the effect of any dietary intervention that required changes to intake of more than one food in adults (≥18 years) with IBS of any subtype (see appendix page 3). These included a low FODMAP diet, a gluten-free diet, a FODMAP-simple diet, a fructose- or lactose-reduced diet, a Mediterranean diet, a starch- and sucrose-reduced diet, or any other dietary intervention, such as that from the BDA and NICE.[15,16] Trials had to compare an active dietary intervention requiring changes to intake of more than one food with either a control intervention, such as habitual diet, sham diet, a high FODMAP diet, or alternative miscellaneous dietary advice, or any other active dietary intervention that required changes to intake of more than one food. We included the first period of cross-over RCTs if they provided efficacy data prior to cross-over and considered definitions of IBS that included either a clinician's opinion, or those that met specific symptom-based criteria, for example the Rome criteria. We required a minimum treatment duration of 2 weeks. Trials that studied the addition or removal of a single food or challenge/re-challenge trials (e.g., adding in low FODMAP rye bread or "spiking" a diet with gluten) were ineligible.

Two investigators (MAC and ACF) conducted the literature search, independently from each other, using medical subject heading (MeSH) and free text terms. There were no language restrictions. We translated foreign language papers, where required. Two investigators (MAC and ACF) evaluated all abstracts identified by the search for eligibility independently from each other. We obtained all potentially relevant papers and evaluated them in detail independently, using pre-designed forms, to assess eligibility according to our pre-defined criteria. We resolved disagreements by discussion between investigators (MAC and ACF).

Outcome Assessment

We assessed the efficacy of all dietary interventions in IBS, compared with the various alternative control interventions or each other, in terms of failure to respond to therapy, according to several endpoints of interest reported below. Other outcomes assessed included adverse events (total numbers of adverse events, as well as adverse events leading to study withdrawal, and individual adverse events), if reported.

Data Extraction

Data extraction was performed independently by two investigators (CJB or MAC, and ACF). We extracted all data as dichotomous outcomes (response or no response to therapy) onto a Microsoft Excel spreadsheet (XP professional edition; Microsoft Corp, Redmond, WA, USA). We assessed efficacy according to the proportion of patients failing to achieve an improvement in the following: a) global symptoms of IBS; b) abdominal pain severity; c) abdominal bloating or distension severity; and d) bowel habit. For studies that reported a dichotomous assessment of response to therapy according to these endpoints, for example a 50-point decrease in the IBS-SSS or a 30% improvement in abdominal pain severity

(approximating Food and Drug Administration (FDA)-recommended endpoints in drug trials in IBS), we extracted these data from the article. Where studies reported more than one dichotomous assessment of the same endpoint, such as a 50-point decrease in the IBS-SSS or a 50% decrease in the IBS-SSS, we extracted the more stringent. Where studies reported mean individual symptom severity scores at baseline together with follow-up mean symptom severity scores and follow-up standard deviation for these endpoints for each intervention arm, we imputed dichotomous responder and non-responder data using methodology described previously by Furukawa *et al.*[24,25] For example, a 30% improvement in abdominal pain severity on the IBS-SSS is derived from the formula: number of participants in each treatment arm at final follow-up x normal standard distribution. The latter corresponds to: (70% of the baseline mean score – follow-up mean score) / follow-up standard deviation. We contacted first and senior authors of studies to provide additional information for individual trials, where required.

We also extracted the following data for each trial, where available: country of origin, setting (primary, secondary, or tertiary care), proportion of female patients, diagnostic criteria used to define IBS, and proportion of patients with IBS according to subtype. We also recorded duration of follow-up and the method of delivery of the dietary intervention(s) and any control intervention (i.e., dietary counselling, provision of most or all foods), in terms of the intervention itself and the length of the initial consultation, where reported. We extracted data as intention-to-treat analyses, assuming all dropouts to be treatment failures (i.e., no response to the dietary intervention or the comparator), wherever trial reporting allowed. If this was not clear from the original article, we performed an analysis on all patients with reported evaluable data.

Quality Assessment and Risk of Bias

We used the Cochrane risk of bias tool to assess this at the study level.[26] Two investigators (CJB or MAC, and ACF) performed this independently; we resolved disagreements by discussion. We recorded the method used to generate the randomisation schedule and conceal treatment allocation, as well as whether blinding was implemented for participants, personnel, and outcomes assessment, whether there was evidence of incomplete outcomes data, and whether there was evidence of selective reporting of outcomes.

Data Synthesis and Statistical Analysis

The network meta-analysis was performed using the frequentist model, with the statistical package "netmeta" (version 2.9-0, https://cran.r-project.org/web/packages/netmeta/index.html) in R (version 4.4.2). We reported the study according to the PRISMA extension statement for network meta-analyses,[27] to explore direct and indirect treatment comparisons of the efficacy and safety of each intervention. Network meta-analysis results usually give a more precise estimate, compared with results from standard, pairwise analyses,[28,29] and allows the ranking of interventions to inform clinical decision-making.[30]

We examined the symmetry and geometry of the evidence by producing a network plot with node size corresponding to number of study subjects, and connection size corresponding to number of studies using Stata version 18 (Stata Corp., College Station, TX, USA). We used "netmeta" to produce comparison adjusted funnel plots exploring publication bias or other small study effects, for all available comparisons. This is a scatterplot of effect size versus precision, measured via the inverse of the standard error. Symmetry around the effect estimate line indicates absence of publication bias, or small study effects.[31] We applied Egger testing to these,[32] where there were 10 or more RCTs, in line with recommendations.[33]

We summarised the effect of each comparison tested as a pooled relative risk (RR) with 95% confidence intervals (CIs), using a random effects model as a conservative estimate. We used a RR of failure to achieve each of the endpoints of interest, where if the RR was less than 1 and the 95% CI did not cross 1, there was a significant benefit of one dietary intervention over another. This approach is the most stable, compared with RR of improvement, or using the odds ratio, for some meta-analyses.[34]

Many meta-analyses use the I^2 statistic to measure heterogeneity.[35] This statistic is easy to interpret and does not vary with the number of studies. However, the I^2 value tends to increase with the number of included patients in the meta-analysis.[36] Therefore, we assessed global statistical heterogeneity using the τ^2 measure from the "netmeta" statistical package. Estimates of τ^2 greater than 0.04, 0.16, and 0.36 are considered to represent low, moderate, and high levels of heterogeneity, respectively.[37] We checked the correlation between direct and indirect evidence across the network via consistency modelling,[38] generating network heat plots. These have grey squares representing the size of the contribution of the direct estimate of one study design in columns, compared with the network estimate in rows.[39] The coloured squares around these represent the change in inconsistency between direct and indirect evidence in a network estimate in the row after relaxing the consistency assumption for the effect of one design in the column. Blue squares indicate that the direct evidence of the design in the column supports the indirect evidence in the row, red squares are "hotspots" of inconsistency between direct and indirect evidence, and yellow squares indicate no major inconsistency but some degree of disparity between direct and indirect evidence.

We ranked all dietary interventions and all comparators according to their P-score, which is a value between 0 and 1. P-scores are based solely on the point estimates and standard errors of the network estimates. They measure the mean extent of certainty that one intervention is better than another, averaged over all competing interventions.[40] Higher scores

indicate a greater probability that the intervention is ranked as best,[40] but the magnitude of the P-score should be considered, as well as the treatment rank. The mean P-score value is always 0.5 so, if individual interventions cluster around this value, they are likely to be of similar efficacy. However, it is also important to take the RR and corresponding 95% CI for each comparison into account when interpreting the results, rather than using only rankings.[41] In our primary analyses, we pooled data for the risk of being symptomatic at the final point of follow-up in each study for all included RCTs using an intention-to-treat analysis. In terms of IBS subtype of recruited patients, individual trials did one of three things: 1) limited their recruitment to patients with IBS with diarrhoea (IBS-D) only; 2) excluded patients with IBS with constipation (IBS-C) only; or 3) recruited patients with IBS irrespective of subtype. In the latter situation, efficacy according to IBS subtype was not reported in most trials. Hence, we were only able to perform an *a priori* subgroup analysis restricted to trials that either recruited only patients with IBS-D or stated that they excluded those with IBS-C and, hence, recruited only patients with IBS-D or IBS with mixed bowel habits (IBS-M).

For our analysis of global IBS symptoms, we used the Confidence in Network Meta-Analysis (CINeMA) framework to evaluate confidence in the indirect and direct treatment estimates from the network,[42] which is endorsed by the Cochrane Collaboration. This includes the Risk of Bias from Missing Evidence in Network Meta Analysis tool for evaluation of reporting bias.[43]

Role of the funding source

We received no funding for this network meta-analysis. All authors had full access to all data and accepted responsibility to submit for publication.

RESULTS

The search strategy, including all the dietary interventions for IBS of interest, generated 4805 citations, 52 of which appeared relevant and were retrieved for further assessment (Figure 1). Of these, we excluded 24 that did not fulfil eligibility criteria, leaving 28 eligible RCTs,[44-71] which included 2338 patients. Four of these were published as conference abstracts only.[54,55,64,68] Agreement between investigators for eligibility of trials was excellent (kappa statistic = 0.90). There were 23 trials of low FODMAP diet,[44,46-54,57-65,67,68,70,71] eight RCTs of BDA/NICE diet,[47,48,53,55,60-62,65] two trials of a lactose-reduced diet,[45,58] two RCTs of a starch- and sucrose-reduced diet,[56,67] and two RCTs of a Mediterranean diet.[68,69] Two trials tested a "personalised" diet, one of which was done according to individual tolerance and preferences based on food diary records,[55] and in the second based on microbiome analysis and artificial intelligence algorithms.[70] One trial compared a combination of a low FODMAP diet and BDA/NICE diet with a low carbohydrate diet but, given that this intervention would lead, predominantly, to a reduction in FODMAP intake, we grouped it with the 23 trials of a low FODMAP diet.[66] The number of trials, and number of patients assigned to each dietary intervention is detailed in the appendix page 4.

Twenty-two trials delivered the dietary intervention through counselling (19 by a dietitian or nutritionist, three by a physician),[44,47-62,64,65,67,69,70] and four RCTs delivered the intervention through provision of most or all food for the duration of the study.[46,66,68,71] The mode of delivery was mixed in one trial of the tritordeum-based diet.[63] Food was provided for the tritordeum-based diet group and dietary advice was provided to the low FODMAP group. One trial did not describe how the intervention was delivered.[45] Twelve trials either recruited only patients with IBS-D or excluded those with IBS-C specifically.[44,48,52,53,59-64,68,71] Detailed characteristics of individual RCTs are provided in Table 1. Two trials recruited patients with

functional bowel disorders,[56,67] but we obtained data only for participants with IBS from the authors.

We obtained extra data from the investigators of 16 RCTs.[49,51-60,62-64,67,69] Risk of bias for all included trials is reported in the appendix page 5. We obtained supplementary information regarding risk of bias items from authors of seven RCTs.[54-56,58,64,67,68] No trials were at low risk of bias across all domains, although 17 RCTs were low risk of bias across all domains other than double blinding.[44,47,49-52,54-56,59-64,67,69] Blinding is problematic in dietary intervention trials, but three RCTs stated specifically that they were double-blind,[68,70,71] with two providing food as complete meals to both treatment arms.[68,71] Another five stated that they were single-blind with investigators analysing data blinded to treatment allocation,[45,48,54,60,64] nine that they were single-blind with patients blinded,[46,47,52,53,57,59,61,63,65] and one that both patients and investigators analysing data were blinded.[50] Patient blinding was usually achieved by avoiding specific reference to, or discussion of, the name of the diet or key dietary constituents under study. Endpoints used, or imputed, in each trial are provided in the appendix pages 6 to 7. Adverse events were reported in insufficient detail to allow pooling of data, with only eight RCTs providing these data.[44,52,61,65-67,69,71] Adherence was assessed formally in 11 trials,[45-47,52,59,60,63,66,69-71] with no differences reported between arms in nine, and a higher rate of adherence to a Mediterranean diet versus habitual diet in one RCT,[69] and to a FODMAP-simple diet versus low FODMAP diet in a second trial.[71]

Global IBS Symptoms

Twenty-three RCTs provided extractable dichotomous data,[44,46-56,58-63,66-69,71] and data were imputed for another five trials,[45,57,64,65,70] meaning that all 28 trials contributed data to this analysis. The network plot is provided in the appendix page 19. When data were pooled, there was low heterogeneity ($\tau^2 = 0.024$), and there was no evidence of funnel plot

asymmetry (Egger test, P = 0.24) (see appendix page 20). Compared with habitual diet, a starch- and sucrose-reduced diet ranked first (RR of global IBS symptoms not improving = 0.41; 95% CI 0.26 to 0.67, P-score 0.84), studied in two trials including 217 patients in total (Figure 2). This means that the probability of a starch- and sucrose-reduced diet being the most efficacious when all interventions were compared with each other was 84%. A gluten-free diet ranked second (RR = 0.45; 95% CI 0.25 to 0.81, P-score 0.78) and a tritordeum-based diet third (RR = 0.48; 95% CI 0.26 to 0.89, P-score 0.71), but these were studied in only one trial, with 114 and 72 patients included in total, respectively. Among other dietary interventions that were superior to habitual diet studied in more than one RCT, a low FODMAP diet ranked fourth (RR = 0.51; 95% CI 0.37 to 0.70, P-score 0.71) in 24 trials including 1803 patients in total. A FODMAP-simple diet ranked seventh (RR = 0.56; 95% CI 0.33 to 0.96, P-score 0.57) and a low carbohydrate diet eighth (RR = 0.57; 95% CI 0.35 to 0.94, P-score 0.55), but both in only one trial, including 35 patients and 202 patients in total, respectively. Finally, BDA/NICE diet ranked tenth (RR = 0.62; 95% CI 0.43 to 0.90, P-score 0.44) in eight RCTs including 710 patients in total. The network heat plot had no red "hotspots" of inconsistency (see appendix page 21). After direct and indirect comparison, both a starch- and sucrose-reduced diet and a low FODMAP diet were also superior to sham diet and a high FODMAP diet, and a low FODMAP diet was also superior to BDA/NICE diet (Table 2). None of the other dietary interventions were superior to any of the other interventions, including no significant difference between a starch- and sucrose-reduced diet and a low FODMAP diet. Using the CINeMA framework to evaluate confidence in the results of this endpoint, all direct and indirect comparisons across the network were rated as either low or very low confidence, except for the direct comparisons between a low FODMAP diet and habitual diet and between a starch- and sucrose-reduced diet and habitual diet, both of which were rated as moderate confidence (see appendix pages 8 to 14).

When we restricted the analysis to 12 trials including 879 patients, which either included patients with IBS-D only or excluded those with IBS-C specifically,[44,48,52,53,59-64,68,71] gluten-free diet ranked first (RR = 0.37; 95% CI 0.17 to 0.84, P-score 0.84) (see appendix page 22), followed by a tritordeum-based diet (RR = 0.39; 95% CI 0.17 to 0.88, P-score 0.79), but each of these were studied in only one RCT, including 114 patients and 72 patients in total, respectively. Low FODMAP diet ranked third (RR = 0.41; 95% CI 0.20 to 0.82, P-score 0.78), and was assessed in all 12 RCTs, and a FODMAP-simple diet fourth (RR = 0.45; 95% CI 0.21 to 0.97, P-score 0.62), but again in only one RCT including 35 patients in total. After indirect comparison, gluten-free diet and a low FODMAP diet were also superior to sham diet (see appendix page 15), and a low FODMAP diet was superior to BDA/NICE diet.

Abdominal Pain Severity

There were eight trials reporting data on effect on abdominal pain severity,[44,48,54,55,58,62,68,71] and data were imputed for a further 18 RCTs.[47,49-53,56,57,59-61,63-67,69,70] Therefore, in total, there were 26 RCTs, including 1988 patients, providing abdominal pain data. The network plot is provided in the appendix page 23. When data were pooled, there was low heterogeneity ($\tau^2 = 0.067$), but evidence of funnel plot asymmetry or other small study effects (Egger test, P = 0.050) (see appendix page 24). Compared with habitual diet, a FODMAP-simple diet ranked first (P-score 0.80) in one trial, including 35 patients in total, but this was not superior to habitual diet. A starch- and sucrose-reduced diet ranked second (RR of abdominal pain not improving = 0.54; 95% CI 0.33 to 0.90, P-score 0.73), studied in two RCTs including 217 patients in total, and a lactose-reduced diet third (P-score 0.69) in one trial including 320 patients in total, but again this was not statistically significantly superior to habitual diet (Figure 3). Of the other dietary interventions studied, only a low FODMAP diet (RR = 0.61; 95% CI 0.42 to 0.89, P-score 0.64), which ranked fifth and was

studied in 23 RCTs including 1773 patients in total, was superior to habitual diet. The network heat plot had no red "hotspots" of inconsistency (see appendix page 25). After direct and indirect comparison, a starch- and sucrose-reduced diet was also superior to a sham diet, and low FODMAP diet was superior to both a BDA/NICE diet and a sham diet (Table 3), but there were no other significant differences including between a starch- and sucrose-reduced diet and a low FODMAP diet.

When we restricted the analysis to 12 trials, which recruited 879 patients, that either included patients with IBS-D only or excluded those with IBS-C specifically,[44,48,52,53,59-64,68,71] a FODMAP-simple diet again ranked first but was not superior to habitual diet (RR = 0.45; 95% CI 0.12 to 1.73, P-score 0.86) (see appendix page 26). None of the dietary interventions were superior to habitual diet. However, low FODMAP diet remained superior to both BDA/NICE diet and sham dietary advice (see appendix page 16). There were no other significant differences between interventions.

Abdominal Bloating or Distension Severity

There were seven trials reporting data on effect on abdominal bloating or distension severity,[44,54,55,58,62,68,71] and data were imputed for a further 19 RCTs.[47-53,56,57,59-61,63-67,69,70] Therefore, in total, there were again 26 RCTs, including 1988 patients, providing abdominal bloating or distension data. The network plot is provided in in the appendix page 27. There was low heterogeneity ($\tau^2 = 0.081$), but evidence of funnel plot asymmetry or other small study effects (Egger test, P = 0.0090) (see appendix page 28). Compared with habitual diet, a FODMAP-simple diet ranked first (RR of abdominal bloating or distension severity not improving = 0.35; 95% CI 0.13 to 0.96, P-score 0.84) (Figure 4), but again only in one RCT including 35 patients in total. Of the other dietary interventions studied, a low FODMAP diet (RR = 0.55; 95% CI 0.37 to 0.80, P-score 0.64), which ranked fifth in 23 RCTs including

1773 patients in total, was superior to habitual diet. The network heat plot had no red "hotspots" of inconsistency (see appendix page 29). After direct and indirect comparison, a low FODMAP diet was also superior to BDA/NICE diet (Table 4). There were no other significant differences.

When we restricted the analysis to 12 trials, which recruited 879 patients, that either included patients with IBS-D only or excluded those with IBS-C specifically,[44,48,52,53,59-64,68,71] a FODMAP-simple diet again ranked first but was not superior to habitual diet (RR = 0.30; 95% CI 0.09 to 1.05, P-score 0.88) (see appendix page 30). None of the dietary interventions were superior to habitual diet. However, low FODMAP diet remained superior to BDA/NICE diet and a FODMAP-simple diet was superior to Mediterranean diet (see appendix page 17). There were no other significant differences between interventions.

Improvement in Bowel Habit

Six trials provided data on effect on improvement in bowel habit,[48,54,58,62,68,71] and data were imputed for a further 17 RCTs.[47,49-53,56,59-61,63-67,69,70] Therefore, in total, there were 23 RCTs, including 1811 patients, providing data on bowel habit. The network plot is provided in in the appendix page 31. When data were pooled, there was low heterogeneity ($\tau^2 = 0.066$), but evidence of funnel plot asymmetry or other small study effects (Egger test, $P < 0.0001$) (see appendix page 32). In terms of dietary interventions, a starch- and sucrose-reduced diet ranked second, studied in two trials including 217 patients in total (RR of bowel habit not improving = 0.70; 95% CI 0.43 to 1.13, P-score 0.73) and a low FODMAP diet third in 21 trials including 1666 patients in total (RR = 0.76; 95% CI 0.55 to 1.05, P-score 0.69), compared with habitual diet (Figure 5). However, none of the dietary interventions were superior to habitual diet. The network heat plot had no red "hotspots" of inconsistency (see appendix page 33). After direct and indirect comparison, low FODMAP diet was superior to

BDA/NICE diet (RR of bowel habit not improving = 0.79; 95% CI 0.63-0.99), but there were no other significant differences between any of the dietary interventions (Table 5), including between a starch- and sucrose-reduced diet and a low FODMAP diet.

When restricting the analysis to 11 trials, which recruited 838 patients , that either included patients with IBS-D only or excluded those with IBS-C specifically,[48,52,53,59-64,68,71] none of the trials used habitual diet as the comparator. A low FODMAP diet ranked first but was not superior to sham diet (RR = 0.79; 95% CI 0.53 to 1.17, P-score 0.76) (see appendix page 34). None of the dietary interventions were superior to sham diet, although again low FODMAP diet was superior to BDA/NICE diet (see appendix page 18).

DISCUSSION

We performed a systematic review and network meta-analysis of various dietary interventions for IBS, comparing their efficacy against multiple other dietary interventions, as well as control interventions, for the treatment of global symptoms, abdominal pain, abdominal bloating or distension, and bowel habit. Overall, although some of the dietary interventions studied more recently, including a starch- and sucrose-reduced diet, a gluten-free diet, a tritordeum-based diet, and a FODMAP-simple diet were ranked highly in the network in some analyses, these were studied in only one or two trials including small numbers of patients, and their findings should be viewed as preliminary, rather than confirmatory. Larger, definitive trials of these interventions are needed. Otherwise, a low FODMAP diet was superior to BDA/NICE diet for all endpoints studied, habitual diet for all endpoints studied other than effect on bowel habit, and a sham diet for global symptoms and abdominal pain. In addition, BDA/NICE diet, which was studied in eight trials, was superior to habitual diet for global symptoms. When we restricted the analysis to trials either recruiting only patients with IBS-D or excluding patients with IBS-C, a low FODMAP diet was superior to BDA/NICE diet for all endpoints, a sham diet for global symptoms and abdominal pain, and habitual diet for global symptoms. Only eight trials reported adverse events data, meaning analysis was not possible.[44,52,61,65-67,69,71]

The literature search, eligibility assessment, data extraction, and data imputation were conducted in duplicate and independently, with any discrepancies resolved by consensus. To reduce the likelihood that the benefit of any of the dietary interventions were overestimated, we used an intention-to-treat analysis, assuming all dropouts failed therapy, and pooled data with a random effects model. We also contacted authors of 16 RCTs to obtain supplementary symptom data.[49,51-60,62-64,67,69] obtained further information regarding risk of bias items from authors of seven trials,[54-56,58,64,67,68] and imputed dichotomous responder data, using means

and standard deviations according to validated methods,[24,25] for some RCTs for the symptom endpoints studied. This meant we were able to pool symptom data for between 1811 and 2338 patients in our analyses, as well as to study the effect of the various dietary interventions on individual symptoms of abdominal pain severity, abdominal bloating or distension severity, and improvement in bowel habit, and in only patients without IBS-C. We extracted or imputed endpoints that were relatively standardised between trials, and which are closely aligned to those recommended by the FDA.

No trials were at low risk of bias across all domains, although 17 RCTs were low risk of bias across all domains other than double blinding.[44,47,49-52,54-56,59-64,67,69] Blinding can be difficult in dietary intervention trials. These inherent challenges mean that the confidence in the evidence for global symptoms according to the CINeMA framework was low to very low for all comparisons other than the direct comparisons between a low FODMAP diet and habitual diet and between a starch- and sucrose-reduced diet and habitual diet. In addition, as part of the CINeMA analysis, confidence in all indirect comparisons was downgraded due to incoherence in the direct treatment estimates of some studies. This means that the confidence intervals around the RR extended across the line of null effect in both directions beyond the range of equivalence, compatible with the possibility of clinically important treatment effects in both directions. However, importantly, this was not the case for direct comparisons for a low FODMAP diet versus BDA/NICE diet, gluten-free diet, habitual diet, starch- and sucrose-reduced diet, Mediterranean diet, or a "personalised" diet, BDA/NICE diet versus gluten-free diet or "personalised" diet, and a starch- and sucrose-reduced diet versus a habitual diet.

We did not consider RCTs of IgG-based elimination diets in the network.[72,73] This was because our *a priori* intervention of interest was diets that lead to changes in the intake of more than one food. This was the case for all trials we included, including those using

"personalised" diets as the control intervention.[55,70] In contrast, there is the possibility that in RCTs using an IgG elimination-based diet a proportion of participants were required to exclude only one food based on IgG testing. These trials could be the subject of a future meta-analysis. There may have been variability in the way the same dietary interventions were applied across trials, due to differences in their study design and the experience of the investigators. In addition, aspects of the design of some RCTs were suboptimal. For example, the tritordeum-based diet trial used a different mode of delivery for each of the two arms, with dietary counselling for the low FODMAP arm but provision of food for the tritordeum-based diet arm.[23] This may have had differential impacts on adherence, although the investigators reported there was no difference in adherence between treatment arms. Furthermore, adherence was assessed formally in only 11 trials.[45-47,52,59,60,63,66,69-71] Twelve of 28 RCTs either recruited only patients with IBS-D or excluded those with IBS-C specifically,[44,48,52,53,59-64,68,71] and in trials that recruited unselected patients with IBS efficacy according to predominant bowel habit was not reported, meaning that the efficacy of the dietary interventions in IBS-C is uncertain. There was evidence of funnel plot asymmetry in some of our analyses, suggesting publication bias or other small study effects. Most eligible RCTs were of a relatively short duration. The utility of examining the efficacy of a dietary intervention over only 4 weeks in a chronic condition like IBS is, perhaps, limited.[5] Only two RCTs examined the effect of all three stages of the low FODMAP diet (i.e., restriction, reintroduction, and personalisation) on IBS symptoms.[61,66] One of these demonstrated a significant difference in responder rates favouring a low FODMAP diet compared with BDA/NICE diet.[61] The second RCT also reported symptom data at 6 months, again after all three phases of the low FODMAP diet, with no difference in efficacy versus a low carbohydrate diet.[66] Despite the fact that most patients with IBS are diagnosed and managed in primary care,[74] only four of the trials were conducted partially in primary care.[49,56,67,69]

Nevertheless, the results of this network meta-analysis are useful to inform treatment decisions and to highlight potentially efficacious dietary interventions for further definitive study, some of which may be relatively easily to implement across various care settings. They can also be used to inform future updates of IBS management guidelines.[16,75,76]

In our previous network meta-analysis,[14] low FODMAP diet was superior to habitual, sham, and BDA/NICE diet for global symptoms, sham diet for abdominal pain, BDA/NICE diet for abdominal bloating or distension, but to none of the comparator interventions for bowel habit. In this network meta-analysis, including 28 RCTs, low FODMAP diet was superior to habitual, sham, and BDA/NICE diet for both global symptoms and abdominal pain, habitual and BDA/NICE diet for abdominal bloating and distension, and BDA/NICE diet for bowel habit. These results, therefore, confirm that a low FODMAP diet is an efficacious treatment for IBS in secondary and tertiary care. Of note, BDA/NICE dietary advice was not superior to any of the control interventions in our previous analyses, but in this network meta-analysis appeared superior to habitual diet for global symptoms. This means there is now indirect evidence to support its use as a first-line dietary approach, which may be important as this diet has been reported to be acceptable to patients, and easier to implement and less expensive than a low FODMAP diet.[62] Nevertheless, there was no evidence that BDA/NICE diet was superior to a sham diet and, therefore, adequately powered sham-controlled trials of this diet are still required. Interestingly, a starch- and sucrose-reduced diet and a gluten-free diet are likely to reduce intake of FODMAPs, highlighting the potential issue of dietary confounding, as well as the importance of measuring adherence and dietary intake in RCTs, including FODMAPs. Only the trial of a gluten-free diet assessed FODMAP intake.[62] Either habitual or high FODMAP diet ranked last in all analyses. This is not surprising as habitual diet is, effectively, a no treatment control and it is likely that, for patients taking part in a clinical trial, being randomised to continue usual diet will be

disappointing and, therefore, associated with an expectation that symptoms will not improve. Similarly, given the known effects of FODMAPs in patients with IBS,[12] a high FODMAP diet is likely to exacerbate symptoms rather than improve them. The limitations of comparator interventions identified in the previous network meta-analysis remain, as there were still only three trials comparing an active dietary intervention with a placebo (sham) diet. Placebo diet or a BDA/NICE diet would be preferable as a comparator in future RCTs, and both would facilitate design of a trial in which participants are blinded.

Therapeutic dietary restriction for IBS is not recommended long-term, to minimise risk of nutritional inadequacy and potential effects on the microbiome.[77,78] Only two RCTs incorporated phases of restriction and liberalisation of the diet into their design,[61,66] meaning that the longer term effects of dietary interventions involving multiple phases remains unclear. Importantly, a dietitian or nutritionist provided advice in 19 of the 22 included RCTs in which the diet was delivered by counselling.[44,47-62,64-67,69,70] Our findings, therefore, support the use of dietary interventions under the supervision of a clinician with expertise in dietetics or nutrition. The clinical efficacy, dietary adequacy, and safety of patients in response to physician-delivered dietary counselling requires future study. The fact that many RCTs of a low FODMAP diet implemented this as a dietitian- or nutritionist-delivered intervention means that supervision is likely to be implicated in its efficacy. However, this has implications for access in clinical practice. Alternative approaches to delivering the low FODMAP diet, such as via a smartphone app,[79] require further efficacy and safety evaluation to confirm their place in management of IBS. When implementing and supervising dietary interventions dietitians assess for red flags, in the context of restrictive diets, and monitor nutritional adequacy, which an app cannot do. It remains important to point out that RCTs of dietary interventions in IBS in primary care are lacking, which is in contrast with their placement in current NICE guidance for the management of IBS.[16]

In summary, this systematic review and network meta-analysis has demonstrated that, in terms of dietary interventions for IBS, the most evidence exists for a low FODMAP diet, which was effective for almost all symptom endpoints studied, compared with several control interventions, and for BDA/NICE diet, which was superior to habitual diet for global symptoms. Findings were similar when the analysis was restricted to trials recruiting only patients with IBS-D or mixed bowel habits. Other dietary interventions that appear promising include a FODMAP simple diet, a gluten-free diet, and a starch- and sucrose-reduced diet. Although these may be considerably easier to implement than a low FODMAP diet, they are also predominantly restrictive in nature and should be the subject of definitive trials before recommendations are made for clinical practice. Given the issues we identified with RCTs to date, future trials in this field should assess dietary adherence and potential dietary confounding, report complete adverse events data, and evaluate acceptability to patients.

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AUTHORSHIP STATEMENT

Specific author contributions: MSC, HMS, CJB, and ACF conceived and drafted the study. MSC, HMS, CJB, and ACF analysed and interpreted the data. ACF, CJB, and HMS drafted the manuscript. All authors edited and approved the final draft of the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Guarantor: *ACF is guarantor.*

DISCLOSURES

Melanie S. Cuffe: none. Heidi M Staudacher: none. Imran Aziz: none. Enrique Coss-Adame: none. Claudia Krieger-Grubel: none. Ana Maria Madrid: none. Bodil Ohlsson: none. Christopher J. Black: none. Alexander C. Ford: none.

ETHICS COMMITTEE APPROVAL

Not required.

DATA SHARING STATEMENT

Trial level data are already in the public domain, but we would consider reasonable requests to share the trial level data we extracted or imputed with others. No other data are available.

REFERENCES

1. Ford AC, Sperber AD, Corsetti M, Camilleri M. Irritable bowel syndrome. *Lancet* 2020; **396**: 1675-88.

2. Mearin F, Lacy BE, Chang L, et al. Bowel disorders. *Gastroenterology* 2016; **150**: 1393-407.

3. Sperber AD, Bangdiwala SI, Drossman DA, et al. Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome Foundation global study. *Gastroenterology* 2021; **160**: 99-114.

4. Oka P, Parr H, Barberio B, Black CJ, Savarino EV, Ford AC. Global prevalence of irritable bowel syndrome according to Rome III or IV criteria: A systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2020; **5**: 908-17.

5. Ford AC, Forman D, Bailey AG, Axon ATR, Moayyedi P. Irritable bowel syndrome: A 10-year natural history of symptoms, and factors that influence consultation behavior. *Am J Gastroenterol* 2008; **103**: 1229-39.

6. Goodoory VC, Ng CE, Black CJ, Ford AC. Direct healthcare costs of Rome IV or Rome III-defined irritable bowel syndrome in the United Kingdom. *Aliment Pharmacol Ther* 2022; **56**: 110-20.

7. Goodoory VC, Ng CE, Black CJ, Ford AC. Impact of Rome IV irritable bowel syndrome on work and activities of daily living. *Aliment Pharmacol Ther* 2022; **56**: 844-56.

8. Goodoory VC, Guthrie EA, Ng CE, Black CJ, Ford AC. Factors associated with lower disease-specific and generic health-related quality of life in Rome IV irritable bowel syndrome. *Aliment Pharmacol Ther* 2023; **57**: 323-34.

9. Bohn L, Storsrud S, Tornblom H, Bengtsson U, Simren M. Self-reported food-related gastrointestinal symptoms in IBS are common and associated with more severe symptoms and reduced quality of life. *Am J Gastroenterol* 2013; **108**: 634-41.

10. Ford AC, Staudacher HM, Talley NJ. Postprandial symptoms in disorders of gut-brain interaction and their potential as a treatment target. *Gut* 2024; **73**: 1199-211.

11. Sturkenboom R, Keszthelyi D, Masclee AAM, Essers BAB. Discrete choice experiment reveals strong preference for dietary treatment among patients with irritable bowel syndrome. *Clin Gastroenterol Hepatol* 2022; **20**: 2628-37.

12. Shepherd SJ, Parker FC, Muir JG, Gibson PR. Dietary triggers of abdominal symptoms in patients with irritable bowel syndrome: Randomized placebo-controlled evidence. *Clin Gastroenterol Hepatol* 2008; **6**: 765-71.

13. Staudacher HM, Whelan K. The low FODMAP diet: Recent advances in understanding its mechanisms and efficacy in IBS. *Gut* 2017; **66**: 1517-27.

14. Black CJ, Staudacher HM, Ford AC. Efficacy of a low FODMAP diet in irritable bowel syndrome: systematic review and network meta-analysis. *Gut* 2022; **71**: 1117-26.

15. 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; **29**: 549-75.

16. Hookway C, Buckner S, Crosland P, Longson D. Irritable bowel syndrome in adults in primary care: Summary of updated NICE guidance. *BMJ* 2015; **350**: h701.

17. Ajamian M, Rosella G, Newnham ED, Biesiekierski JR, Muir JG, Gibson PR. Effect of gluten ingestion and FODMAP restriction on intestinal epithelial integrity in patients with irritable bowel syndrome and self-reported non-coeliac gluten sensitivity. *Mol Nutr Food Res* 2021; **65**: e1901275.

18. Eswaran S, Jencks KJ, Singh P, Rifkin S, Han-Markey T, Chey WD. All FODMAPs aren't created equal: Results of a randomized reintroduction trial in patients with irritable bowel syndrome. *Clin Gastroenterol Hepatol* 2025; **23**: 351-8.e5.

19. Zevallos VF, Raker V, Tenzer S, et al. Nutritional wheat amylase-trypsin inhibitors promote intestinal inflammation via activation of myeloid cells. *Gastroenterology* 2017; **152**: 1100-13.e12.

20. Guasch-Ferré M, Willett WC. The Mediterranean diet and health: A comprehensive overview. *J Intern Med* 2021; **290**: 549-66.

21. Henstrom M, Diekmann L, Bonfiglio F, et al. Functional variants in the sucrase-isomaltase gene associate with increased risk of irritable bowel syndrome. *Gut* 2018; **67**: 263-70.

22. Nilholm C, Larsson E, Roth B, Gustafsson R, Ohlsson B. Irregular dietary habits with a high intake of cereals and sweets are associated with more severe gastrointestinal symptoms in IBS patients. *Nutrients* 2019; **11**: 1279.

23. Russo F, Riezzo G, Linsalata M, et al. Managing symptom profile of IBS-D patients With tritordeum-based foods: Results from a pilot study. *Front Nutr* 2022; **9**: 797192.

24. Samara MT, Spineli LM, Furukawa TA, et al. Imputation of response rates from means and standard deviations in schizophrenia. *Schizophr Res* 2013; **151**: 209-14.

25. Furukawa TA, Cipriani A, Barbui C, Brambilla P, Watanabe N. Imputing response rates from means and standard deviations in meta-analyses. *Int Clin Psychopharmacol* 2005; **20**: 49-52.

26. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.4 (updated August 2023). Cochrane, 2023. Available from www.training.cochrane.org/handbook. 2023. Accessed 14th January 2025.

27. Hutton B, Salanti G, Caldwell DM, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: Checklist and explanations. *Ann Intern Med* 2015; **162**: 777-84.

28. Salanti G, Higgins JP, Ades AE, Ioannidis JP. Evaluation of networks of randomized trials. *Stat Methods Med Res* 2008; **17**: 279-301.

29. Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: Many names, many benefits, many concerns for the next generation evidence synthesis tool. *Res Synth Methods* 2012; **3**: 80-97.

30. Salanti G, Ades AE, Ioannidis JP. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: An overview and tutorial. *J Clin Epidemiol* 2011; **64**: 163-71.

31. Chaimani A, Higgins JP, Mavridis D, Spyridonos P, Salanti G. Graphical tools for network meta-analysis in STATA. *PLoS One* 2013; **8**: e76654.

32. Egger M, Davey-Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; **315**: 629-34.

33. Sterne JA, Sutton AJ, Ioannidis JP, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011; **343**: d4002.

34. Deeks JJ. Issues in the selection of a summary statistic for meta-analysis of clinical trials with binary outcomes. *Stat Med* 2002; **21**: 1575-600.

35. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; **327**: 557-60.

36. Rucker G, Schwarzer G, Carpenter JR, Schumacher M. Undue reliance on I(2) in assessing heterogeneity may mislead. *BMC Med Res Methodol* 2008; **8**: 79.

37. da Costa BR, Juni P. Systematic reviews and meta-analyses of randomized trials: Principles and pitfalls. *Eur Heart J* 2014; **35**: 3336-45.

38. Higgins JP, Jackson D, Barrett JK, Lu G, Ades AE, White IR. Consistency and inconsistency in network meta-analysis: Concepts and models for multi-arm studies. *Res Synth Methods* 2012; **3**: 98-110.

39. Krahn U, Binder H, Konig J. A graphical tool for locating inconsistency in network meta-analyses. *BMC Med Res Methodol* 2013; **13**: 35.

40. Rucker G, Schwarzer G. Ranking treatments in frequentist network meta-analysis works without resampling methods. *BMC Med Res Methodol* 2015; **15**: 58.

41. Morton SC, Murad MH, O'Connor E, et al. AHRQ methods for effective health care. Quantitative synthesis-an update. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville (MD): Agency for Healthcare Research and Quality (US); 2018.

42. Nikolakopoulou A, Higgins JPT, Papakonstantinou T, et al. CINeMA: An approach for assessing confidence in the results of a network meta-analysis. *PLoS Med* 2020; **17**: e1003082.

43. Chiocchia V, Nikolakopoulou A, Higgins JPT, et al. ROB-MEN: A tool to assess risk of bias due to missing evidence in network meta-analysis. *BMC Med* 2021; **19**: 304.

44. 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**: 1510-8.

45. Moritz K, Hemmer W, Jung P, et al. Effect of a fructose and lactose elimination diet in patients with irritable bowel syndrome: A randomized double-blind placebo-controlled study. *Journal of Gastroenterology and Hepatology Research* 2013; **2**: 833-9.

46. 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.

47. Bohn L, Storsrud 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**: 1399-407.e2.

48. 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**: 1824-32.

49. 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**: 4632-43.

50. 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**: 1241-51.

51. Pedersen N, Ankersen DV, Felding M, et al. Low-FODMAP diet reduces irritable bowel symptoms in patients with inflammatory bowel disease. *World J Gastroenterol* 2017; **23**: 3356-66.

52. Staudacher HM, Lomer MCE, Farquharson FM, et al. Diet low in FODMAPs reduces symptoms in patients with irritable bowel syndrome and probiotic restores *Bifidobacterium* species: A randomized controlled trial. *Gastroenterology* 2017; **153**: 936-47.

53. 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**: 1192-9.

54. Carrasco G, Vera DB, Gotteland M, Madrid AM. Low-FODMAP diet improve symptoms and quality of life in patients with irritable bowel syndrome? *Neurogastroenterol Motil* 2019; **31 (Supplement 4)**.

55. Coss-Adame E, de la Torre MFH, Cedillo MFG, Hernandez EM, Villegas-Cervantes V, Milke-Garcia Md. Randomized clinical trial to compare two dietary interventions in the improvement of symptoms and quality of life in patients with irritable bowel syndrome. *Gastroenterology* 2019; **156 (Supplement 1)**: S478.

56. Nilholm C, Roth B, Ohlsson B. A dietary intervention with reduction of starch and sucrose leads to reduced gastrointestinal and extra-intestinal symptoms in IBS patients. *Nutrients* 2019; **11**: 1662.

57. Patcharatrakul T, Juntrapirat A, Lakananurak N, Gonlachanvit 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**: 2856.

58. 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. *Clin Nutr ESPEN* 2020; **40**: 83-9.

59. Wilson B, Rossi M, Kanno T, et al. β-galactooligosaccharide in conjunction with low FODMAP diet improves irritable bowel syndrome symptoms but reduces fecal *Bifidobacteria*. *Am J Gastroenterol* 2020; **115**: 906-15.

60. Zhang Y, Feng L, Wang X, et al. Low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols diet compared with traditional dietary advice for diarrhea-predominant irritable bowel syndrome: A parallel-group, randomized controlled trial with analysis of clinical and microbiological factors associated with patient outcomes. *Am J Clin Nutr* 2021; **113**: 1531-45.

61. Goyal O, Batta S, Nohria S, et al. Low fermentable oligosaccharide, disaccharide, monosaccharide, and polyol diet in patients with diarrhea-predominant irritable bowel syndrome: A prospective, randomized trial. *J Gastroenterol Hepatol* 2022; **37**: 301-9.

62. Rej A, Sanders DS, Shaw CC, et al. Efficacy and acceptability of dietary therapies in non-constipated irritable bowel syndrome: A randomized trial of traditional dietary advice, the low FODMAP diet, and the gluten-free diet. *Clin Gastroenterol Hepatol* 2022; **20**: 2876-87.e15.

63. Russo F, Riezzo G, Orlando A, et al. A comparison of the low-FODMAPs diet and a tritordeum-based diet on the gastrointestinal symptom profile of patients suffering from irritable bowel syndrome-diarrhea variant (IBS-D): A randomized controlled trial. *Nutrients* 2022; **14**: 1544.

64. Wu P, Wang Y-P, Hsieh J-C, Cheng C-M, Lu C-L. Low FODMAP diet attenuates the symptoms and alters brain activity in non-constipated IBS patients: Preliminary reports from a randomized sham-controlled trial. *Gastroenterology* 2023; **164 (Supplement)**: S409.

65. Liu Y, Jin D, He T, et al. Effect of the combined intervention of low-FODMAPs diet and probiotics on IBS symptoms in Western China: A randomized controlled trial. *Food Sci Nutr* 2024; **12**: 3993-4004.

66. Nybacka S, Törnblom H, Josefsson A, et al. A low FODMAP diet plus traditional dietary advice versus a low-carbohydrate diet versus pharmacological treatment in irritable bowel syndrome (CARBIS): A single-centre, single-blind, randomised controlled trial. *Lancet Gastroenterol Hepatol* 2024; **9**: 507-20.

67. Roth B, Nseir M, Jeppsson H, D'Amato M, Sundquist K, Ohlsson B. A starch- and sucrose-reduced diet has similar efficiency as low FODMAP in IBS-A randomized non-inferiority study. *Nutrients* 2024; **16**: 3039.

68. Singh P, Iram S, Chey S, et al. Does the Mediterranean diet have similar efficacy as a low FODMAP diet in irritable bowel syndrome? Results from a pilot randomized controlled trial. *Gastroenterology* 2024; **166 (Supplement)**: S307-S8.

69. Staudacher HM, Mahoney S, Canale K, et al. Clinical trial: A Mediterranean diet is feasible and improves gastrointestinal and psychological symptoms in irritable bowel syndrome. *Aliment Pharmacol Ther* 2024; **59**: 492-503.

70. Tunali V, Arslan N, Ermiş BH, et al. A multicenter randomized controlled trial of microbiome-based artificial intelligence-assisted personalized diet vs low-fermentable oligosaccharides, disaccharides, monosaccharides, and polyols diet: A novel approach for the management of irritable bowel syndrome. *Am J Gastroenterol* 2024; **119**: 1901-12.

71. Singh P, Chey SW, Nee J, Eswaran S, Lembo A, Chey WD. Is a simplified, less restrictive low FODMAP diet possible? Results from a double-blind, pilot randomized controlled trial. *Clin Gastroenterol Hepatol* 2025; **23**: 362-4.

72. Atkinson W, Sheldon TA, Shaath N, Whorwell PJ. Food elimination based on IgG antibodies in irritable bowel syndrome: A randomised controlled trial. *Gut* 2004; **53**: 1459-64.

73. Singh P, Chey WD, Takakura W, et al. A novel, IBS-specific IgG ELISA-based elimination diet in irritable bowel syndrome: A randomized, sham-controlled trial. *Gastroenterology* 2025; **doi:10.1053/j.gastro.2025.01.223**.

74. Thompson WG, Heaton KW, Smyth GT, Smyth C. Irritable bowel syndrome: The view from general practice. *Eur J Gastroenterol Hepatol* 1997; **9**: 689-92.

75. Ford AC, Moayyedi P, Chey WD, et al. American College of Gastroenterology monograph on management of irritable bowel syndrome. *Am J Gastroenterol* 2018; **113 (Suppl 2)**: 1-18.

76. Vasant DH, Paine PA, Black CJ, et al. British Society of Gastroenterology guidelines on the management of irritable bowel syndrome. *Gut* 2021; **70**: 1214-40.

77. 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**: 239-55.

78. So D, Loughman A, Staudacher HM. Effects of a low FODMAP diet on the colonic microbiome in irritable bowel syndrome: A systematic review with meta-analysis. *Am J Clin Nutr* 2022; **116**: 943-52.

79. Carbone F, Van den Houte K, Besard L, et al. Diet or medication in primary care patients with IBS: the DOMINO study - a randomised trial supported by the Belgian Health Care Knowledge Centre (KCE Trials Programme) and the Rome Foundation Research Institute. *Gut* 2022; **71**: 2226-32.

Table 1. Characteristics of Randomised Controlled Trials of Dietary Interventions for IBS.

Study	Country and setting	Duration	Dietary intervention(s)	Other dietary intervention or control intervention	Mode of delivery of the interventions	Number (%) female	Diagnostic criteria used for IBS, and number (%) with each subtype
Staudacher 2012 [44]	UK, tertiary care	4 weeks	19 patients assigned to a low FODMAP diet	22 patients advised to continue with their habitual diet	Dietary advice from a dietitian during a 45-minute appointment for both groups	27 (65.9%)	Rome III, subtype not stated but excluded patients with IBS-C
Moritz 2013 [45]	Austria, tertiary care	3 weeks	160 patients assigned to a fructose-reduced diet	160 patients assigned to a lactose-reduced diet	Not reported	320 (81.9%)*	Rome II, 28 (12.7%) IBS-C, 105 (47.5%) IBS-D, 88 (39.8%) IBS-M*
Halmos 2014 [46]	Australia, unclear	3 weeks	13 patients assigned to a low FODMAP diet	17 patients assigned to a typical Australian diet	Provision of all food and additional food lists to enable purchase of additional foods for both groups	21 (70.0%)	Rome III, 13 (43.3%) IBS-C, 10 (33.3%) IBS-D, 5 (16.7%) IBS-M

Bohn 2015 [47]	Sweden, secondary and tertiary care	4 weeks	38 patients assigned to a low FODMAP diet	37 patients assigned to BDA/NICE diet	Dietary advice from a dietitian and provision of written information for both groups	61 (81.3%)	Rome III, 22 (29.3%) IBS-C, 18 (24.0%) IBS-D, 35 (46.7%) IBS-M
Eswaran 2016 [48]	USA, tertiary care	4 weeks	50 patients assigned to a low FODMAP diet	42 patients assigned to BDA/NICE diet	Dietary advice from a dietitian and provision of teaching materials for both groups	65 (70.7%)	Rome III, 92 (100%) IBS-D
Harvie 2017 [49]	New Zealand, primary, secondary, and tertiary care	3 months	23 patients assigned to a low FODMAP diet	27 patients continued with their habitual diet	Dietary advice from a dietitian during a 1-hour appointment for the low FODMAP diet group	43 (86.0%)	Rome III, 5 (10.0%) IBS-C, 32 (64.0%) IBS-D, 14 (28.0%) IBS-M
McIntosh 2017 [50]	Canada, tertiary care	3 weeks	20 patients assigned to a low FODMAP diet	20 patients assigned to a high FODMAP diet	Dietary advice from a dietitian during a 30 to 60-minute appointment, sample food menus, and provision of written information for both groups	32 (86.5%)	Rome III, 2 (5.0%) IBS-C, 10 (25.0%) IBS-D, 23 (57.5%) IBS-M, 1 (2.5%) IBS-U

Pedersen 2017 [51]	Denmark, tertiary care	6 weeks	42 patients assigned to a low FODMAP diet	40 patients continued with their habitual diet	Dietary advice from a dietitian or nutritionist during a 1-hour appointment and additional food lists provided for the low FODMAP diet group	63 (76.8%)	Rome III, 12 (14.6%) IBS-C, 37 (45.1%) IBS-D, 28 (34.1%) IBS-M
Staudacher 2017 [52]	UK, tertiary care	4 weeks	51 patients assigned to a low FODMAP diet	53 patients assigned to a sham diet	Dietary advice from a dietitian of 10 minutes duration, based on provided food lists for both groups	70 (67.3%)	Rome III, 69 (66.3%) IBS-D, 24 (23.1%) IBS-M, 11 (10.6%) IBS-U
Zahedi 2018 [53]	Iran, secondary care	6 weeks	55 patients assigned to a low FODMAP diet	55 patients assigned to BDA/NICE diet	Dietary advice from a dietitian during a 45-minute appointment for both groups and provision of written information for the low FODMAP group	51 (50.5%)	Rome III, 110 (100%) IBS-D
Carassco 2019 [54]	Chile, tertiary care	6 weeks	17 patients assigned to a low FODMAP diet	16 patients continued with their habitual diet	Supervised by a nutritionist with monitoring via a patient journal for the low FODMAP diet group	33 (87.8%)	Rome IV, subtype not stated

Coss-Adame 2019 [55]	Mexico, tertiary care	4 weeks	35 patients assigned to BDA/NICE diet	35 patients assigned to a "personalised" diet	Supervised by a dietitian with monitoring via a patient food diary for the BDA/NICE diet group or specific dietary modifications according to individual tolerance and preferences based on a patient food diary for the "personalised" diet group	70 (85.7%)	Rome III, subtype not stated
Nilholm 2019 [56]	Sweden, primary, secondary, and tertiary care	4 weeks	67 patients assigned to a starch- and sucrose-reduced diet	19 patients continued with their habitual diet	Dietary advice from a physician during an appointment, and provision of written information for the starch- and sucrose-reduced diet group	86 (80.2%)	Rome IV, 20 (23.3%) IBS-C, 26 (30.2%) IBS-D, 37 (43.0%) IBS-M, 3 (3.5%) IBS-U

Patcharatrakul 2019 [57]	Thailand, secondary care	4 weeks	33 patients assigned to a low FODMAP diet	33 patients assigned to alternative dietary advice	Dietary advice from a physician during a 30-minute appointment, an example food menu, and provision of written information for the low FODMAP diet group or advice from a gastroenterologist during a 5-minute appointment for the alternative dietary advice group	47 (75.8%)	Rome III, subtype not stated
Krieger-Grubel 2020 [58]	Switzerland, secondary care	3 weeks	13 patients assigned to a low FODMAP diet	13 patients assigned to a lactose-reduced diet	Dietary advice from a dietitian and a telephone call to check adherence and clarify questions for both groups	26 (89.7%)	Rome IV, subtype not stated

Wilson 2020 [59]	UK, tertiary care	4 weeks	22 patients assigned to a low FODMAP diet	23 patients assigned to a sham diet	Dietary advice from a dietitian during a 1-hour appointment and provision of written information for the low FODMAP diet group and dietary advice during a 15 to 25-minute appointment and provision of written information for the sham diet group	25 (55.6%)	Rome III, 45 (66.7%) IBS-D, patients with IBS-C were excluded
Zhang 2021 [60]	China, tertiary care	3 weeks	54 patients assigned to a low FODMAP diet	54 patients assigned to BDA/NICE diet	Dietary advice from a dietitian during a 20-minute appointment and a menu plan to follow for both groups	51 (47.2%)	Rome III, 108 (100%) IBS-D
Goyal 2022 [61]	India, secondary care	4 weeks	52 patients assigned to a low FODMAP diet	49 patients assigned to BDA/NICE diet	Dietary advice from a dietitian and provision of written information for both groups	42 (41.6%)	Rome IV, 101 (100%) IBS-D

Rej 2022 [62]	UK, tertiary care	4 weeks	37 patients assigned to a low FODMAP diet, and 36 patients assigned to a gluten-free diet	41 patients assigned to BDA/NICE diet	Dietary advice from a dietitian during a 45- to 60-minute appointment and provision of written information for all three groups	114 (79.8%)*	Rome IV, 114 (100%) IBS-D or IBS-M
Russo 2022 [63]	Italy, tertiary care	12 weeks	36 patients assigned to a low FODMAP diet	36 patients assigned to a tritordeum-based diet	Dietary advice from a nutritionist during an appointment, a menu plan to follow, and provision of written information for the low FODMAP group and a controlled diet provided for the tritordeum-based diet group	72 (80.6%)	Rome III or IV, 72 (100%) IBS-D
Wu 2023 [64]	Taiwan, secondary care	6-8 weeks	16 patients assigned to a low FODMAP diet	15 patients assigned to a sham diet	Dietary advice from a dietitian during an appointment for both groups	31 (64.5%)	Rome III, 31 (100%) IBS-D or IBS-M
Liu 2024 [65]	China, secondary care	4 weeks	20 patients assigned to a low FODMAP diet	20 patients assigned to BDA/NICE diet	Dietary advice from a dietitian during an appointment for both groups	40 (not reported)	Rome IV, subtype not stated

Nybacka 2024 [66]	Sweden, tertiary care	4 weeks	101 patients assigned to a low FODMAP and BDA/NICE diet	101 patients assigned to alternative dietary advice consisting of a low carbohydrate diet	Dietary advice from a dietitian during an appointment, a menu plan to follow with all foods included in the recipes provided for free, and provision of written information for both groups	202 (81.9%)*	Rome IV, 84 (43.5%) IBS-C, 68 (35.2%) IBS-D, 32 (16.6%) IBS-M, 9 (4.7%) IBS-U*
Roth 2024 [67]	Sweden, primary, secondary, and tertiary care	4 weeks	64 patients assigned to a low FODMAP diet	67 patients assigned to a starch- and sucrose-reduced diet	Dietary advice from a physician during an appointment, a menu plan to follow, and provision of written information	131 (87.0%)	Rome IV, 26 (19.8%) IBS-C, 44 (33.6%) IBS-D, 54 (41.2%) IBS-M, 7 (5.3%) IBS-U
Singh 2024 [68]	USA, tertiary care	4 weeks	11 patients assigned to a low FODMAP diet	15 patients assigned to a Mediterranean diet	Provision of all food as complete meals to both groups	26 (not reported)	Rome IV, 26 (100%) IBS-D or IBS-M

Staudacher 2024 [69]	Australia, community	6 weeks	29 patients assigned to a Mediterranean diet	30 patients continued with their habitual diet	Dietary advice from a dietitian during a 20- to 30-minute appointment, a food hamper, and provision of written information for the Mediterranean diet group	59 (83.1%)	Rome IV, 17 (28.8%) IBS-C, 19 (33.3%) IBS-D, 20 (35.1%) IBS-M, 3 (5.1%) IBS-U
Tunali 2024 [70]	Turkey, tertiary care	6 weeks	74 patients assigned to a low FODMAP diet	75 patients assigned to a "personalised" diet based on microbiome analysis and artificial intelligence algorithms	Dietary advice from a dietitian during a 20-minute appointment and a 6-week menu plan for both groups	149 (60.3%)*	Rome IV, 56 (46.3%) IBS-C, 26 (21.5%) IBS-D, 39 (32.2%) IBS-M*
Singh 2025 [71]	USA, tertiary care	4 weeks	19 patients assigned to a low FODMAP diet	16 patients assigned to a FODMAP-simple diet	Provision of all food as complete meals to both groups	35 (not reported)	Rome IV, 35 (100%) IBS-D

*Proportions based on per protocol population.

Table 2. Summary Treatment Effects from the Network Meta-analysis for Failure to Achieve an Improvement in Global IBS Symptoms.

SSRD			1.11 (0.52; 2.37)										0.34 (0.19; 0.61)	
0.91 (0.45; 1.83)	**GFD**		0.92 (0.53; 1.61)						0.72 (0.43; 1.19)					
0.86 (0.41; 1.77)	0.94 (0.46; 1.92)	**TBD**	0.95 (0.56; 1.60)											
0.81 (0.49; 1.34)	0.89 (0.55; 1.45)	0.95 (0.56; 1.60)	**Low FODMAP diet**	1.09 (0.76; 1.58)	0.57 (0.27; 1.21)	0.90 (0.59; 1.38)	0.89 (0.61; 1.30)		0.79 (0.65; 0.95)	0.75 (0.34; 1.65)	0.77 (0.52; 1.14)	0.64 (0.45; 0.89)	0.61 (0.43; 0.87)	0.44 (0.22; 0.89)
0.76 (0.43; 1.37)	0.84 (0.48; 1.47)	0.89 (0.49; 1.63)	0.94 (0.69; 1.27)	**"Personalised" diet**					1.16 (0.70; 1.91)					
0.76 (0.36; 1.60)	0.83 (0.39; 1.79)	0.89 (0.40; 1.96)	0.93 (0.52; 1.69)	1.00 (0.51; 1.94)	**MD**								0.27 (0.11; 0.67)	
0.73 (0.38; 1.42)	0.80 (0.42; 1.53)	0.86 (0.44; 1.68)	0.90 (0.59; 1.38)	0.96 (0.57; 1.62)	0.97 (0.46; 2.01)	**FODMAP -simple diet**								
0.72 (0.38; 1.36)	0.79 (0.43; 1.47)	0.84 (0.44; 1.61)	0.89 (0.61; 1.30)	0.95 (0.58; 1.54)	0.95 (0.47; 1.93)	0.99 (0.56; 1.75)	**LCD**							
0.64 (0.24; 1.72)	0.70 (0.26; 1.87)	0.74 (0.27; 2.03)	0.78 (0.33; 1.84)	0.83 (0.34; 2.07)	0.84 (0.30; 2.37)	0.87 (0.33; 2.26)	0.88 (0.34; 2.25)	**FRD**		0.96 (0.69; 1.34)				
0.67 (0.39; 1.14)	0.73 (0.45; 1.18)	0.78 (0.45; 1.36)	0.82 (0.68; 0.98)	0.87 (0.64; 1.20)	0.88 (0.47; 1.63)	0.91 (0.57; 1.45)	0.92 (0.60; 1.41)	1.05 (0.44; 2.52)	**BDA/NICE diet**					
0.61 (0.24; 1.55)	0.67 (0.26; 1.69)	0.71 (0.28; 1.84)	0.75 (0.34; 1.65)	0.80 (0.34; 1.86)	0.80 (0.30; 2.15)	0.83 (0.34; 2.04)	0.84 (0.35; 2.03)	0.96 (0.69; 1.34)	0.91 (0.41; 2.05)	**LRD**				
0.62 (0.33; 1.18)	0.68 (0.37; 1.28)	0.73 (0.38; 1.40)	0.77 (0.52; 1.14)	0.82 (0.50; 1.34)	0.82 (0.40; 1.67)	0.85 (0.48; 1.52)	0.86 (0.50; 1.49)	0.98 (0.38; 2.51)	0.93 (0.61; 1.44)	1.02 (0.42; 2.47)	**Alternative diet**			

0.52 (0.28; 0.95)	0.57 (0.31; 1.03)	0.60 (0.32; 1.13)	0.64 (0.45; 0.89)	0.68 (0.43; 1.07)	0.68 (0.34; 1.35)	0.71 (0.41; 1.22)	0.72 (0.43; 1.20)	0.81 (0.32; 2.04)	0.78 (0.53; 1.14)	0.85 (0.36; 2.00)	0.83 (0.49; 1.40)	**Sham diet**		
0.41 (0.26; 0.67)	0.45 (0.25; 0.81)	0.48 (0.26; 0.89)	0.51 (0.37; 0.70)	0.54 (0.35; 0.84)	0.54 (0.30; 1.00)	0.56 (0.33; 0.96)	0.57 (0.35; 0.94)	0.65 (0.26; 1.62)	0.62 (0.43; 0.90)	0.68 (0.29; 1.59)	0.66 (0.40; 1.10)	0.80 (0.50; 1.28)	**Habitual diet**	
0.36 (0.15; 0.85)	0.39 (0.17; 0.92)	0.42 (0.17; 1.00)	0.44 (0.22; 0.89)	0.47 (0.22; 1.00)	0.47 (0.19; 1.18)	0.48 (0.21; 1.11)	0.49 (0.22; 1.10)	0.56 (0.18; 1.70)	0.53 (0.26; 1.10)	0.58 (0.20; 1.68)	0.57 (0.25; 1.28)	0.69 (0.31; 1.50)	0.86 (0.40; 1.86)	**High FODMAP diet**

Relative risk with 95% confidence intervals in parentheses. Comparisons, column versus row, should be read from left to right, and are ordered relative to their overall efficacy. The treatment in the top left position is ranked as best after the network meta-analysis of direct and indirect effects. Direct comparisons are provided above the dietary intervention labels, and indirect comparisons are below. Boxes shaded green denote a statistically significant difference.

BDA/NICE; British Dietetic Association/National Institute for Health and Care Excellence, FODMAP; fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, FRD; fructose-reduced diet, GFD; gluten-free diet, LCD; low carbohydrate diet, LRD; lactose-reduced diet, MD; Mediterranean diet, SSRD; starch- and sucrose reduced diet, TBD; tritordeum-based diet.

Table 3. Summary Treatment Effects from the Network Meta-analysis for Failure to Achieve an Improvement in Abdominal Pain Severity.

FODMAP -simple diet				0.71 (0.29; 1.78)									
0.81 (0.28; 2.31)	**SSRD**			1.00 (0.49; 2.05)							0.49 (0.26; 0.93)		
0.80 (0.24; 2.63)	0.99 (0.40; 2.49)	**LRD**		0.89 (0.42; 1.89)									
0.75 (0.23; 2.42)	0.93 (0.41; 2.11)	0.94 (0.33; 2.68)	**MD**	2.57 (0.60; 11.01)							0.45 (0.21; 0.94)		
0.71 (0.29; 1.78)	0.88 (0.53; 1.48)	0.89 (0.42; 1.89)	0.95 (0.46; 1.95)	**Low FODMAP diet**	1.31 (0.71; 2.41)	0.95 (0.51; 1.80)	0.79 (0.40; 1.55)	0.91 (0.50; 1.66)	0.79 (0.39; 1.58)	0.71 (0.55; 0.92)	0.70 (0.46; 1.06)	0.53 (0.32; 0.88)	0.47 (0.20; 1.06)
0.71 (0.25; 1.99)	0.88 (0.44; 1.77)	0.89 (0.36; 2.16)	0.94 (0.40; 2.24)	1.00 (0.62; 1.60)	**“Personalised" diet"**					1.06 (0.53; 2.11)			
0.68 (0.22; 2.07)	0.84 (0.37; 1.91)	0.85 (0.32; 2.28)	0.90 (0.35; 2.36)	0.95 (0.51; 1.80)	0.96 (0.43; 2.11)	**TBD**							
0.65 (0.22; 1.91)	0.81 (0.37; 1.74)	0.81 (0.31; 2.09)	0.86 (0.34; 2.17)	0.91 (0.52; 1.61)	0.92 (0.45; 1.87)	0.96 (0.41; 2.24)	**GFD**			0.75 (0.41; 1.36)			
0.65 (0.22; 1.94)	0.81 (0.37; 1.78)	0.81 (0.31; 2.13)	0.86 (0.34; 2.21)	0.91 (0.50; 1.66)	0.92 (0.43; 1.96)	0.96 (0.40; 2.28)	1.00 (0.44; 2.28)	**LCD**					
0.56 (0.18; 1.78)	0.70 (0.29; 1.66)	0.70 (0.25; 1.96)	0.75 (0.27; 2.04)	0.79 (0.39; 1.58)	0.79 (0.34; 1.83)	0.83 (0.32; 2.12)	0.87 (0.35; 2.13)	0.86 (0.35; 2.16)	**Alternative diet**				
0.53 (0.21; 1.38)	0.66 (0.37; 1.17)	0.66 (0.30; 1.47)	0.71 (0.33; 1.52)	0.75 (0.58; 0.96)	0.75 (0.46; 1.21)	0.78 (0.40; 1.55)	0.82 (0.47; 1.43)	0.82 (0.43; 1.56)	0.95 (0.45; 1.98)	**BDA/NICE diet**			

0.44 (0.16; 1.18)	0.54 (0.33; 0.90)	0.55 (0.24; 1.27)	0.58 (0.30; 1.13)	0.61 (0.42; 0.89)	0.62 (0.34; 1.12)	0.64 (0.31; 1.34)	0.67 (0.34; 1.33)	0.67 (0.33; 1.36)	0.78 (0.35; 1.71)	0.82 (0.52; 1.29)	**Habitual diet**		
0.38 (0.13; 1.08)	0.47 (0.23; 0.97)	0.47 (0.19; 1.17)	0.50 (0.21; 1.21)	0.53 (0.32; 0.88)	0.53 (0.27; 1.06)	0.56 (0.25; 1.25)	0.58 (0.27; 1.25)	0.58 (0.27; 1.27)	0.68 (0.29; 1.59)	0.71 (0.41; 1.25)	0.87 (0.47; 1.61)	**Sham diet**	
0.33 (0.10; 1.14)	0.41 (0.16; 1.09)	0.41 (0.14; 1.27)	0.44 (0.15; 1.32)	0.47 (0.20; 1.06)	0.47 (0.18; 1.21)	0.49 (0.17; 1.38)	0.51 (0.19; 1.39)	0.51 (0.18; 1.41)	0.59 (0.20; 1.74)	0.63 (0.26; 1.48)	0.76 (0.31; 1.87)	0.88 (0.33; 2.29)	**High FODMAP diet**

Relative risk with 95% confidence intervals in parentheses. Comparisons, column versus row, should be read from left to right, and are ordered relative to their overall efficacy. The treatment in the top left position is ranked as best after the network meta-analysis of direct and indirect effects. Direct comparisons are provided above the dietary intervention labels, and indirect comparisons are below. Boxes shaded green denote a statistically significant difference.

BDA/NICE; British Dietetic Association/National Institute for Health and Care Excellence, FODMAP; fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, GFD; gluten-free diet, LCD; low carbohydrate diet, LRD; lactose-reduced diet, MD; Mediterranean diet, SSRD; starch- and sucrose reduced diet, TBD; tritordeum-based diet.

Table 4. Summary Treatment Effects from the Network Meta-analysis for Failure to Achieve an Improvement in Abdominal Bloating or Distension Severity.

FODMAP -simple diet			0.65 (0.26; 1.63)										
0.73 (0.24; 2.20)	**GFD**		0.81 (0.41; 1.61)								0.72 (0.37; 1.40)		
0.67 (0.23; 1.91)	0.92 (0.43; 1.98)	**"Personalised" diet**	0.72 (0.38; 1.37)								1.06 (0.51; 2.19)		
0.65 (0.26; 1.63)	0.89 (0.49; 1.63)	0.97 (0.59; 1.59)	**Low FODMAP diet**	1.00 (0.51; 1.97)	0.67 (0.30; 1.48)	0.95 (0.47; 1.91)	0.89 (0.40; 1.96)	0.86 (0.44; 1.70)	0.17 (0.02; 1.27)	0.77 (0.46; 1.31)	0.71 (0.55; 0.92)	0.69 (0.34; 1.41)	0.64 (0.43; 0.97)
0.65 (0.21; 2.04)	0.89 (0.36; 2.22)	0.97 (0.42; 2.24)	1.00 (0.51; 1.97)	**TBD**									
0.62 (0.21; 1.86)	0.86 (0.37; 1.99)	0.93 (0.43; 2.00)	0.96 (0.54; 1.72)	0.96 (0.39; 2.36)	**SSRD**								0.41 (0.20; 0.87)
0.61 (0.19; 1.96)	0.84 (0.33; 2.13)	0.92 (0.39; 2.16)	0.95 (0.47; 1.91)	0.95 (0.36; 2.52)	0.98 (0.40; 2.45)	**Alternative diet**							
0.58 (0.17; 1.95)	0.79 (0.29; 2.15)	0.86 (0.34; 2.19)	0.89 (0.40; 1.96)	0.89 (0.31; 2.52)	0.92 (0.35; 2.46)	0.94 (0.33; 2.70)	**LRD**						
0.56 (0.18; 1.76)	0.77 (0.31; 1.91)	0.83 (0.36; 1.93)	0.86 (0.44; 1.70)	0.86 (0.33; 2.26)	0.89 (0.37; 2.19)	0.91 (0.34; 2.42)	0.97 (0.34; 2.75)	**LCD**					
0.51 (0.15; 1.70)	0.70 (0.26; 1.87)	0.76 (0.31; 1.90)	0.79 (0.37; 1.70)	0.79 (0.28; 2.20)	0.82 (0.34; 1.99)	0.83 (0.29; 2.36)	0.89 (0.29; 2.67)	0.92 (0.33; 2.56)	**MD**				0.56 (0.27; 1.18)
0.50 (0.17; 1.46)	0.69 (0.31; 1.54)	0.75 (0.36; 1.55)	0.77 (0.46; 1.31)	0.77 (0.33; 1.83)	0.80 (0.37; 1.76)	0.82 (0.34; 1.97)	0.87 (0.34; 2.26)	0.90 (0.38; 2.13)	0.98 (0.39; 2.50)	**Sham diet**			

0.48 (0.19; 1.26)	0.67 (0.36; 1.22)	0.72 (0.44; 1.19)	0.75 (0.58; 0.96)	0.75 (0.36; 1.54)	0.78 (0.41; 1.46)	0.79 (0.37; 1.66)	0.84 (0.37; 1.93)	0.87 (0.42; 1.79)	0.95 (0.42; 2.13)	0.97 (0.54; 1.74)	**BDA/NICE diet**		
0.45 (0.14; 1.44)	0.61 (0.24; 1.57)	0.67 (0.28; 1.59)	0.69 (0.34; 1.41)	0.69 (0.26; 1.85)	0.71 (0.28; 1.80)	0.73 (0.27; 1.98)	0.77 (0.27; 2.25)	0.80 (0.30; 2.15)	0.87 (0.30; 2.50)	0.89 (0.36; 2.17)	0.92 (0.43; 1.97)	**High FODMAP diet**	
0.35 (0.13; 0.96)	0.49 (0.24; 1.00)	0.53 (0.28; 0.99)	0.55 (0.37; 0.80)	0.55 (0.25; 1.19)	0.57 (0.32; 1.01)	0.58 (0.26; 1.28)	0.62 (0.26; 1.48)	0.64 (0.29; 1.39)	0.69 (0.35; 1.39)	0.71 (0.37; 1.36)	0.73 (0.46; 1.15)	0.80 (0.35; 1.79)	**Habitual diet**

Relative risk with 95% confidence intervals in parentheses. Comparisons, column versus row, should be read from left to right, and are ordered relative to their overall efficacy. The treatment in the top left position is ranked as best after the network meta-analysis of direct and indirect effects. Direct comparisons are provided above the dietary intervention labels, and indirect comparisons are below. Boxes shaded green denote a statistically significant difference.

BDA/NICE; British Dietetic Association/National Institute for Health and Care Excellence, FODMAP; fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, GFD; gluten-free diet, LCD; low carbohydrate diet, LRD; lactose-reduced diet, MD; Mediterranean diet, SSRD; starch- and sucrose reduced diet, TBD; tritordeum-based diet.

Table 5. Summary Treatment Effects from the Network Meta-analysis for Failure to Achieve an Improvement in Bowel Habit.

"Personalised" diet		0.80 (0.45; 1.42)										
0.87 (0.41; 1.84)	**SSRD**	1.07 (0.56; 2.06)										0.61 (0.32; 1.14)
0.80 (0.45; 1.42)	0.92 (0.57; 1.49)	**Low FODMAP diet**	0.96 (0.52; 1.77)	0.83 (0.47; 1.46)	0.83 (0.46; 1.50)	0.84 (0.46; 1.53)	0.80 (0.45; 1.42)	0.78 (0.35; 1.73)	0.80 (0.55; 1.15)	0.79 (0.63; 0.99)	0.73 (0.37; 1.46)	0.84 (0.57; 1.23)
0.77 (0.33; 1.78)	0.88 (0.40; 1.93)	0.96 (0.52; 1.77)	**TBD**									
0.74 (0.36; 1.52)	0.84 (0.46; 1.56)	0.92 (0.59; 1.43)	0.96 (0.45; 2.05)	**MD**								0.73 (0.40; 1.36)
0.72 (0.33; 1.55)	0.83 (0.41; 1.67)	0.90 (0.54; 1.50)	0.94 (0.42; 2.09)	0.98 (0.50; 1.93)	**GFD**					0.83 (0.48; 1.44)		
0.68 (0.29; 1.55)	0.77 (0.36; 1.67)	0.84 (0.46; 1.53)	0.88 (0.37; 2.08)	0.92 (0.44; 1.94)	0.94 (0.43; 2.06)	**FODMAP -simple diet**						
0.64 (0.28; 1.44)	0.73 (0.34; 1.56)	0.80 (0.45; 1.42)	0.83 (0.36; 1.94)	0.87 (0.42; 1.80)	0.89 (0.41; 1.92)	0.95 (0.41; 2.18)	**LCD**					
0.62 (0.23; 1.67)	0.72 (0.28; 1.82)	0.78 (0.35; 1.73)	0.81 (0.30; 2.23)	0.85 (0.34; 2.11)	0.87 (0.34; 2.23)	0.92 (0.34; 2.51)	0.98 (0.36; 2.62)	**LRD**				
0.64 (0.32; 1.26)	0.73 (0.40; 1.34)	0.80 (0.55; 1.15)	0.83 (0.41; 1.70)	0.87 (0.49; 1.54)	0.89 (0.47; 1.66)	0.95 (0.47; 1.91)	1.00 (0.50; 1.98)	1.02 (0.43; 2.46)	**Sham diet**			
0.63 (0.34; 1.18)	0.73 (0.43; 1.24)	0.79 (0.63; 0.99)	0.83 (0.43; 1.60)	0.86 (0.52; 1.42)	0.88 (0.53; 1.45)	0.94 (0.49; 1.79)	0.99 (0.53; 1.86)	1.02 (0.44; 2.34)	0.99 (0.65; 1.53)	**BDA/NICE diet**		
0.59 (0.24; 1.44)	0.67 (0.29; 1.57)	0.73 (0.37; 1.46)	0.77 (0.30; 1.93)	0.80 (0.35; 1.81)	0.82 (0.35; 1.92)	0.87 (0.35; 2.17)	0.92 (0.37; 2.27)	0.94 (0.33; 2.71)	0.92 (0.42; 2.00)	0.93 (0.45; 1.91)	**High FODMAP diet**	

0.61 (0.32; 1.18)	0.70 (0.43; 1.13)	0.76 (0.55; 1.05)	0.79 (0.40; 1.59)	0.83 (0.53; 1.30)	0.84 (0.46; 1.55)	0.90 (0.46; 1.78)	0.95 (0.49; 1.86)	0.98 (0.41; 2.31)	0.95 (0.59; 1.55)	0.96 (0.65; 1.43)	1.04 (0.48; 2.22)	**Habitual diet**

Relative risk with 95% confidence intervals in parentheses. Comparisons, column versus row, should be read from left to right, and are ordered relative to their overall efficacy. The treatment in the top left position is ranked as best after the network meta-analysis of direct and indirect effects. Direct comparisons are provided above the dietary intervention labels, and indirect comparisons are below. Boxes shaded green denote a statistically significant difference.

BDA/NICE; British Dietetic Association/National Institute for Health and Care Excellence, FODMAP; fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, GFD; gluten-free diet, LCD; low carbohydrate diet, LRD; lactose-reduced diet, MD; Mediterranean diet, SSRD; starch- and sucrose reduced diet, TBD; tritordeum-based diet.

FIGURES

Figure 1. Flow Diagram of Assessment of Studies Identified in the Systematic Review.

Figure 2. Forest Plot for Failure to Achieve an Improvement in Global IBS Symptoms.

Note: The P-score is the probability of each intervention being ranked as best in the network.

Figure 3. Forest Plot for Failure to Achieve an Improvement in Abdominal Pain Severity.

Note: The P-score is the probability of each intervention being ranked as best in the network.

Figure 4. Forest Plot for Failure to Achieve an Improvement in Abdominal Bloating or Distension Severity.

Note: The P-score is the probability of each intervention being ranked as best in the network.

Figure 5. Forest Plot for Failure to Achieve an Improvement in Bowel Habit.

Note: The P-score is the probability of each intervention being ranked as best in the network.