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Effects of Gluten-Free and Low-FODMAP Dietary Interventions on IBS and Cardiometabolic Health: Evidence from Clinical Trials and Meta-Analysis

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Abstract

Background: Irritable bowel syndrome (IBS) affects a substantial proportion of the global population, prompting investigation into dietary interventions as therapeutic strategies. Gluten-free diets (GFD) and low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) diets (LFD) have emerged as potential treatments, yet their efficacy and broader health implications remain subjects of ongoing research.
Objective: This comprehensive review synthesizes evidence from clinical trials and meta-analyses to evaluate the effects of GFD and LFD on IBS symptom management and cardiometabolic health outcomes.
Methods: A systematic literature search identified 75 studies on GFD and IBS, 83 studies on LFD and IBS, and 71 studies on cardiometabolic outcomes. Studies included randomized controlled trials (RCTs), systematic reviews, and meta-analyses published through 2026. Primary outcomes included IBS symptom severity scores, quality of life measures, and cardiometabolic parameters including lipid profiles, blood pressure, glucose metabolism, and body composition.
Results: LFD demonstrated robust efficacy in reducing IBS symptoms, with meta-analyses showing significant improvements in IBS Symptom Severity Scale (IBS-

SSS) scores (standardized mean difference [SMD] −0.66, 95% CI −0.88 to −0.44) and quality of life. GFD showed more variable results, with some trials reporting significant symptom improvement while meta-analyses indicated insufficient evidence for routine recommendation. Combined LFD-GFD approaches showed enhanced efficacy for bloating and pain reduction. Regarding cardiometabolic outcomes, GFD demonstrated mixed effects, with some studies showing improvements in HDL cholesterol and triglycerides, while others reported increased total cholesterol and potential nutritional concerns. LFD research has primarily focused on gastrointestinal outcomes with limited cardiometabolic data.

Conclusions: LFD represents an evidence-based dietary intervention for IBS symptom management, while GFD efficacy remains controversial and may be limited to specific patient subgroups. The cardiometabolic safety profile of both diets requires further investigation, particularly for long-term adherence. Clinicians should consider individualized dietary approaches with appropriate nutritional monitoring.

Introduction

Irritable bowel syndrome (IBS) is a prevalent functional gastrointestinal disorder characterized by recurrent abdominal pain, bloating, and altered bowel habits, affecting approximately 10-15% of the global population (Savarino et al., 2022). The multifactorial etiology of IBS, involving visceral hypersensitivity, altered gut motility, intestinal dysbiosis, and psychosocial factors, has prompted investigation into diverse therapeutic approaches. Among these, dietary interventions have gained considerable attention as non-pharmacological strategies for symptom management.

Two dietary approaches have emerged as particularly prominent in IBS management: the gluten-free diet (GFD) and the low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) diet (LFD). The GFD, traditionally prescribed for celiac disease, has been explored in non-celiac IBS populations based on observations of symptom improvement following gluten restriction (Biesiekierski et al., 2011). The LFD, developed specifically for IBS management, restricts short-chain carbohydrates that are poorly absorbed in the small intestine and rapidly fermented by colonic bacteria, thereby reducing gas production and osmotic effects (Altobelli et al., 2017).

While the primary focus of these dietary interventions has been gastrointestinal symptom relief, emerging evidence suggests potential implications for broader metabolic health. The increasing adoption of GFD among individuals without celiac disease has raised questions about its effects on cardiovascular risk factors, body composition, and metabolic parameters (Kim et al., 2017). Similarly, the restrictive nature of LFD and its impact on gut microbiota composition may have consequences beyond symptom management.

Despite growing research interest, several critical questions remain unanswered. First, the comparative efficacy of GFD versus LFD in IBS symptom management lacks comprehensive synthesis. Second, the mechanisms underlying symptom improvement—whether attributable to gluten, FODMAPs, or other dietary components—remain incompletely understood. Third, the cardiometabolic safety profile of these restrictive diets, particularly with long-term adherence, requires systematic evaluation.

This comprehensive review addresses these gaps by synthesizing evidence from clinical trials and meta-analyses to evaluate: (1) the efficacy of GFD in IBS symptom management, (2) the efficacy of LFD in IBS symptom management, (3) the comparative effectiveness of these dietary approaches, and (4) the effects of both diets on cardiometabolic health outcomes. By integrating findings from multiple high-quality studies, this review aims to provide evidence-based guidance for clinicians and inform future research directions in dietary management of IBS.

Background and Theoretical Foundations

Pathophysiology of IBS and Dietary Triggers

IBS represents a complex disorder of gut-brain interaction, characterized by visceral hypersensitivity, altered gastrointestinal motility, immune activation, and dysbiosis of the intestinal microbiota (Savarino et al., 2022). The role of dietary components in triggering or exacerbating IBS symptoms has been increasingly recognized, with patients frequently reporting symptom onset or worsening following food intake.

The mechanisms by which dietary components influence IBS symptoms are multifaceted. FODMAPs, a group of short-chain carbohydrates including fructose, lactose, fructans, galactans, and polyols, exert osmotic effects in the small intestine and undergo rapid fermentation by colonic bacteria, leading to increased gas production, luminal distension, and activation of mechanoreceptors in viscerally hypersensitive individuals (Black et al., 2021). This mechanistic understanding forms the theoretical basis for LFD in IBS management.

The role of gluten in non-celiac IBS remains more controversial. While celiac disease involves a well-characterized immune-mediated response to gluten proteins, the concept of non-celiac gluten sensitivity (NCGS) in IBS patients lacks definitive biomarkers and mechanistic clarity (Shahbazkhani et al., 2015). Some researchers have proposed that symptom improvement attributed to gluten restriction may actually result from concurrent reduction in fructans, which are present in wheat and other gluten-containing grains (Hekmatdoost, 2022).

Development and Rationale of Dietary Interventions

The LFD was developed by researchers at Monash University based on systematic investigation of carbohydrate malabsorption and fermentation in IBS patients. The diet involves a three-phase approach: (1) strict restriction of high-FODMAP foods for 2-6 weeks, (2) systematic reintroduction to identify individual triggers, and (3) personalization to maintain symptom control while maximizing dietary variety (Schäfer, 2022). This structured approach distinguishes LFD from simple elimination diets and provides a framework for long-term dietary management.

The application of GFD to non-celiac IBS populations emerged from clinical observations and patient-reported symptom improvement following gluten restriction. Early studies suggested that a subset of IBS patients, particularly those with diarrhea-predominant symptoms and specific HLA genotypes (DQ2/8), might benefit from gluten restriction (Aziz et al., 2016). However, subsequent research has challenged the specificity of gluten as the causative agent, with some studies suggesting that fructans or other wheat components may be responsible for symptom provocation (Hekmatdoost, 2022).

Cardiometabolic Considerations

The potential cardiometabolic implications of restrictive diets have gained attention as adoption of GFD has increased among individuals without celiac disease. Gluten-containing whole grains are important sources of dietary fiber, B vitamins, and other micronutrients, and their restriction may have unintended nutritional consequences (Potter et al., 2018). Additionally, commercially available gluten-free products often contain higher levels of fat, sugar, and sodium while being lower in protein and fiber compared to their gluten-containing counterparts (Defeudis et al., 2023).

The metabolic effects of carbohydrate restriction, inherent in both GFD (through grain restriction) and LFD (through FODMAP restriction), may influence lipid metabolism, glucose homeostasis, and body composition. Understanding these broader health implications is essential for informed clinical decision-making, particularly for patients requiring long-term dietary management.

Methods

Literature Search Strategy

This comprehensive review synthesized evidence from three systematic literature searches conducted to identify relevant clinical trials and meta-analyses. The searches were performed across multiple databases including SciSpace, Google Scholar, and PubMed, covering publications through June 2026.

Search 1: Gluten-Free Diet and IBS The first search focused on gluten-free dietary interventions in IBS populations, using search terms including "gluten-free diet," "gluten restriction," "irritable bowel syndrome," "IBS," "clinical trial," and "meta-analysis." This search identified 75 unique papers after deduplication.

Search 2: Low-FODMAP Diet and IBS The second search targeted low-FODMAP dietary interventions in IBS, employing search terms including "low-FODMAP diet," "FODMAP restriction," "fermentable carbohydrates," "irritable bowel syndrome," "IBS," "clinical trial," and "meta-analysis." This search yielded 83 unique papers.

Search 3: Cardiometabolic Outcomes The third search examined cardiometabolic effects of both GFD and LFD, using search terms including "gluten-free diet," "low-FODMAP diet," "cardiovascular," "metabolic syndrome," "lipid profile," "blood pressure," "glucose metabolism," and "body composition." This search identified 71 unique papers.

Inclusion and Exclusion Criteria

Inclusion Criteria:

Randomized controlled trials (RCTs) investigating GFD or LFD in IBS populations
Systematic reviews and meta-analyses synthesizing evidence from multiple trials
Studies reporting validated outcome measures for IBS symptoms (e.g., IBS-SSS, IBS-QOL)
Studies examining cardiometabolic parameters in populations following GFD or LFD
Publications in English
Human studies

Exclusion Criteria:

Studies exclusively in celiac disease populations without IBS
Case reports and case series
Studies without validated outcome measures
Duplicate publications
Conference abstracts without full-text availability

Data Extraction

For each included study, the following data were systematically extracted:
Study design (RCT, crossover trial, systematic review, meta-analysis)
Sample size and participant characteristics
Intervention details (diet type, duration, implementation method)
Primary and secondary outcomes
IBS symptom measures (IBS-SSS, visual analog scales, individual symptom scores)
Quality of life measures (IBS-QOL)
Cardiometabolic parameters (lipid profiles, blood pressure, glucose metabolism, BMI)
Statistical findings (effect sizes, confidence intervals, p-values)
Study limitations and risk of bias

Quality Assessment

Study quality was assessed based on established criteria for RCTs and systematic reviews. For RCTs, considerations included randomization methods, allocation concealment, blinding procedures, completeness of outcome data, and selective reporting. For systematic reviews and meta-analyses, quality was evaluated using GRADE (Grading of Recommendations Assessment, Development and Evaluation) criteria where reported, and assessment of search comprehensiveness, study selection transparency, and statistical methods.

Synthesis Approach

Evidence synthesis followed a narrative approach organized by research question, with quantitative findings from meta-analyses prioritized where available. For IBS outcomes, studies were grouped by dietary intervention (GFD, LFD, combined approaches) and outcome measure. For cardiometabolic outcomes, findings were organized by parameter type (lipid metabolism, blood pressure, glucose homeostasis, body composition). Heterogeneity in study designs, populations, and outcome measures precluded additional quantitative meta-analysis; therefore, findings are presented descriptively with emphasis on high-quality systematic reviews and meta-analyses.

Results

Gluten-Free Diet Effects on IBS Symptoms

Randomized Controlled Trials

Multiple RCTs have investigated the efficacy of GFD in IBS populations with variable results. Zanwar et al. (2016) conducted a prospective, randomized, double-blind, placebo-controlled rechallenge trial involving 180 IBS patients who initially followed a GFD. Of these, 65 patients (36%) responded to the initial GFD phase. When these responders were randomized to either gluten rechallenge or placebo, the gluten group experienced significant worsening of overall symptoms, abdominal pain, bloating, and tiredness compared to placebo ($p < 0.05$).

Shahbazkhani et al. (2015) reported similar findings in a double-blind randomized placebo-controlled trial of 72 IBS patients who completed a six-week GFD. Following randomization to gluten or placebo, 83.8% of patients in the placebo group maintained symptom control compared to only 25.7% in the gluten-containing group ($p < 0.001$). All symptoms, particularly bloating and abdominal pain, significantly increased in the gluten group upon rechallenge.

Algera et al. (2022) conducted an RCT examining GFD effects on symptoms and gut microenvironment in IBS patients. The study demonstrated that GFD reduced symptoms in some patients, though the mechanisms underlying this improvement remained unclear. The study highlighted the heterogeneity of treatment response, suggesting that GFD benefits may be limited to specific patient subgroups.

A three-arm RCT by Rej et al. (2022) compared traditional dietary advice, LFD, and GFD in 99 non-constipated IBS patients. The GFD achieved a ≥50-point reduction in IBS-SSS for 58% of participants, with no significant difference compared to the other dietary interventions ($p = 0.43$). Responders showed significant within-group improvements in abdominal pain severity, abdominal distention, and satisfaction with bowel habits.

Hajiani et al. (2019) randomized 140 IBS patients to either GFD or regular diet for 12 weeks. The GFD group showed significantly greater improvements in intestinal gas, fecal consistency, urgent need for defecation, and incomplete evacuation compared to controls ($p < 0.05$). Abdominal pain and bowel movement frequency were also better controlled in the GFD group.

However, not all studies have demonstrated clear benefits. Saadati et al. (2022) conducted a randomized single-blind controlled trial examining gluten challenge effects in 50 IBS patients following a low-FODMAP strict GFD. While the strict GFD significantly improved pain severity ($p = 0.02$) and bloating ($p = 0.03$) after 6 weeks, the high-gluten group also showed significant decreases in total symptom scores ($p = 0.05$), complicating interpretation of gluten-specific effects.

Meta-Analyses and Systematic Reviews

Meta-analytic evidence for GFD in IBS has been mixed. Arabpour et al. (2023) conducted a GRADE-assessed systematic review and meta-analysis of nine controlled trials. The analysis found that GFD was unable to significantly reduce overall IBS symptoms (SMD −0.31, 95% CI −0.92 to 0.31), bloating (SMD −0.37, 95% CI −1.03 to 0.30), or improve quality of life (SMD −0.12, 95% CI −0.64 to 0.39). However, GFD showed a slight trend toward reducing abdominal pain (SMD −0.68, 95% CI −1.36 to −0.00). Notably, LFD significantly outperformed GFD in reducing IBS-SSS (SMD 0.66, 95% CI 0.31 to 1.01) and improving quality of life (SMD −0.36, 95% CI −0.70 to −0.01).

Dionne et al. (2018) concluded in their systematic review and meta-analysis that there is insufficient evidence to recommend GFD for reducing IBS symptoms, while very low-quality evidence suggested LFD effectiveness. This assessment highlighted the limited number and quality of GFD trials available for meta-analysis.

A network meta-analysis by Lei et al. (2025) including 44 eligible articles ranked GFD fourth in relieving IBS symptoms (SUCRA 54.3%) and fourth in reducing total IBS-SSS (SUCRA 28.3%). For quality of life improvement, GFD ranked second (SUCRA 57.0%), though it remained inferior to LFD and combination approaches.

Haghbin et al. (2024) conducted a systematic review and network meta-analysis of 23 RCTs involving 1,689 IBS patients. Direct meta-analysis revealed no statistically significant difference in any IBS score between GFD and either LFD or standard diet. While LFD showed superiority over standard diet in IBS-SSS (MD −46.29, 95% CI −63.72 to −28.86, $p < 0.01$) and IBS-QOL (MD 4.06, 95% CI 0.72 to 7.41, $p = 0.02$), specific improvements for GFD alone were not statistically significant in direct comparisons.

Mechanistic Considerations

An important mechanistic question concerns whether symptom improvement attributed to GFD results from gluten restriction per se or from concurrent reduction in fructans present in wheat. Hekmatdoost (2022) addressed this question in a double-blind, placebo-controlled RCT of 49 IBS patients randomized to low-FODMAP diet with either gluten powder or rice flour placebo. Both groups showed significant improvements in IBS-SSS, abdominal pain, distension, and quality of life ($p < 0.05$), with only 5 patients in the gluten group reporting symptom exacerbation. The authors concluded that symptom exacerbation after wheat and barley consumption is primarily due to fructan content rather than gluten in most patients.

Savarino et al. (2022) reviewed evidence from a 4-week RCT of 45 IBS-D patients, finding higher daily stool frequency in those consuming gluten compared to GFD, with more pronounced effects in HLA-DQ2 or -DQ8 positive patients. However, a meta-analysis of two trials showed no statistically significant benefit for GFD (RR 0.42, 95% CI 0.11-1.55, $I^2 = 88\%$), with the authors noting that any benefit may relate to decreased fructan rather than gluten itself.

Low-FODMAP Diet Effects on IBS Symptoms

Randomized Controlled Trials

The evidence base for LFD in IBS is substantially more robust than for GFD, with numerous high-quality RCTs demonstrating efficacy. Böhn et al. (2015) conducted an RCT comparing LFD to traditional dietary advice in IBS patients. The LFD group showed reductions in IBS severity scores of 50% or more compared to baseline in 62% of patients (23/37), compared to 46% (17/37) in the traditional IBS diet group.

Schumann et al. (2018) performed a single-blind RCT comparing yoga to LFD in 59 IBS patients over 12 weeks. Within-group comparisons showed statistically significant reductions in gastrointestinal symptoms (IBS-SSS) at both 12 and 24 weeks for the LFD group (all $p < 0.001$). However, no statistically significant difference was found between LFD and yoga groups at either time point (12 weeks: Δ = 31.80, 95% CI −11.90 to 75.50, $p = 0.151$; 24 weeks: Δ = 33.41, 95% CI −4.21 to 71.04, $p = 0.081$).

Jeitler et al. (2021) conducted a two-armed multicenter RCT comparing Ayurvedic nutritional therapy to conventional nutritional therapy including LFD in 69 IBS patients. The LFD showed clinically meaningful responses in 50-86% of patients. Meta-analytic evidence cited in the study indicated greater likelihood of reducing abdominal pain (OR 1.81), abdominal bloating (OR 1.75), and general gastrointestinal symptoms (OR 1.81) compared to controls.

4.2.2 Meta-Analyses and Systematic Reviews

Multiple high-quality meta-analyses have consistently demonstrated LFD efficacy in IBS. Black et al. (2021) performed a network meta-analysis of 13 eligible RCTs involving 944 patients. LFD ranked first for all endpoints studied, including abdominal pain severity, abdominal bloating or distension severity, and bowel habit. LFD was superior to habitual diet for global IBS symptoms (RR of symptoms not improving = 0.67, 95% CI 0.48 to 0.91) and superior to British Dietetic Association/National Institute for Health and Care Excellence (BDA/NICE) dietary advice for abdominal bloating or distension (RR = 0.72, 95% CI 0.55 to 0.94).

Altobelli et al. (2017) conducted a meta-analysis including 3 RCTs comparing LFD to traditional IBS diets, 3 RCTs comparing LFD to high-FODMAP diets, and 6 cohort studies. LFD significantly reduced abdominal pain (OR = 0.44) and bloating (OR = 0.32) compared to traditional diet in RCTs, with no statistical heterogeneity. Comparing LFD to high-FODMAP diets showed even greater reductions in abdominal pain (OR = 0.17) and bloating (OR = 0.13). Cohort studies demonstrated significant reductions in abdominal pain (effect size [ES] = −0.59) and bloating (ES = −0.64) after treatment compared to baseline.

Lanen et al. (2021) performed a systematic review and meta-analysis of 12 papers comprising 772 subjects. LFD significantly reduced IBS severity by a moderate-to-large extent compared to control diet (SMD −0.66, 95% CI −0.88 to −0.44, $I^2 = 54\%$). Studies using the validated IBS-SSS questionnaire showed a mean reduction of 45 points (95% CI −77 to −14, $I^2 = 89\%$). This reduction in gastrointestinal symptoms was consistent across various subgroups, including different levels of adherence, age, intervention duration, and IBS subtype.

Varjú et al. (2017) conducted a meta-analysis of 10 eligible studies, finding that LFD significantly improved general IBS symptoms compared to standard IBS diet. Post-diet IBS-SSS values were significantly lower in the LFD group ($p = 0.002$), demonstrating superiority to regular IBS dietary therapy.

An umbrella review by Bogdanowska-Charkiewicz et al. (2026) systematically evaluated 16 meta-analyses including 141 studies and 9,904 patients. LFD significantly reduced IBS symptom scores on IBS-SSS (SMD −0.599, 5 meta-analyses, 3,761 patients) and improved quality of life (SMD = 0.259, $p < 0.0001$, 5 meta-analyses, 3,576 patients). No significant effect was found on abdominal pain, stool consistency, or stool frequency when analyzed separately, though the overall symptom severity improvement was robust.

Long-Term Outcomes

Pouladi et al. (2025) conducted a systematic review and meta-analysis of five studies with 324 patients examining long-term LFD outcomes. Long-term LFD significantly reduced overall gastrointestinal symptoms (SMD −1.97, 95% CI −3.63 to −0.30) and improved psychological well-being, specifically reducing anxiety (SMD −0.40, 95% CI −0.65 to −0.15) and depression (SMD −0.28, 95% CI −0.53 to −0.03). Additionally, long-term LFD improved quality of life (mean difference 0.53, 95% CI

0.24 to 0.83), though it did not improve sleep quality (SMD −0.13, 95% CI −0.39 to 0.12).

Schäfer (2022) reviewed recent evidence indicating that at least 50% of individuals experience symptom relief following the complete three-phase LFD approach (restriction, reintroduction, and personalization) in the long term. Uncontrolled follow-up studies supported sustained benefits with personalized FODMAP restriction.

Comparative Efficacy: GFD vs. LFD

Direct comparative studies have consistently favored LFD over GFD for IBS symptom management. Rej et al. (2022) found no significant difference in response rates between GFD (58%), LFD, and traditional dietary advice ($p = 0.43$), though all three approaches showed within-group improvements. However, this study's design may have limited power to detect differences between active interventions.

The meta-analysis by Arabpour et al. (2023) provided more definitive comparative evidence, showing that LFD significantly reduced IBS-SSS (SMD 0.66, 95% CI 0.31 to 1.01) and improved quality of life (SMD −0.36, 95% CI −0.70 to −0.01) compared to GFD. This suggests that LFD provides superior symptom control compared to GFD in head-to-head comparisons.

Network meta-analyses have consistently ranked LFD higher than GFD across multiple outcome measures. Lei et al. (2025) ranked LFD combined with probiotics highest (SUCRA 80.4%), followed by LFD alone (SUCRA 70.8%), with GFD ranking fourth (SUCRA 54.3%) for overall symptom relief. Similarly, Yu et al. (2022) found that symptom flare-ups were significantly lower with GFD than high-gluten diets, but LFD showed superior effects alongside starch- and sucrose-reduced diets.

Combined Low-FODMAP and Gluten-Free Diet Approaches

Several studies have investigated whether combining LFD with GFD provides additional benefits beyond either approach alone. Zhang et al. (2024) conducted a systematic review and meta-analysis of 4 RCTs and 4 cohort studies involving 437 patients (221 on combined LF-GFD, 216 on GFD alone). The combined LF-GFD significantly alleviated VAS bloating scores (RR = −0.58, 95% CI −0.92 to −0.23, $p = 0.0010$) and VAS pain scores (RR = −0.42, 95% CI −0.66 to −0.19, $p = 0.005$) compared to GFD alone. Combined LF-GFD also showed significant improvement in IBS-SSS scores (MD = −1.42, 95% CI −2.74 to −0.10, $p = 0.03$) and IBS-QOL scores (MD = 3.75, 95% CI 0.98 to 6.53, $p = 0.008$). Additionally, the combined approach decreased depression (SDS) and anxiety (SAS) scores ($p < 0.00001$ and $p < 0.0001$, respectively).

Naseri et al. (2021) conducted a clinical trial of 30 IBS patients completing a 6-week LF-GFD intervention. The combined approach showed significant reduction in IBS-SSS compared to baseline ($p = 0.001$), alongside decreased fecal calprotectin levels ($p = 0.001$) and normalization of gut microbiota composition, including increased Bacteroidetes and decreased Firmicutes to Bacteroidetes ratio ($p = 0.001$).

Saadati et al. (2022) examined a low-FODMAP strict GFD in 50 IBS patients, finding significant decreases in pain severity ($p = 0.02$) and bloating ($p = 0.03$) after 6 weeks in the GFD group. Between-group analysis showed significant differences for pain severity ($p = 0.02$), pain frequency ($p = 0.04$), and impact on community function ($p = 0.02$) at study end.

These findings suggest that combined LF-GFD approaches may provide incremental benefits over either diet alone, particularly for bloating, pain, and psychological symptoms. However, the increased restrictiveness of combined approaches raises concerns about nutritional adequacy, dietary adherence, and quality of life implications.

Cardiometabolic Effects of Gluten-Free Diet

Lipid Metabolism

The effects of GFD on lipid profiles have shown considerable heterogeneity across studies. Rohani et al. (2024) conducted a systematic review and meta-analysis of 19 articles, finding that GFD significantly improved high-density lipoprotein (HDL) levels (weighted mean difference [WMD] 4.80 mg/dL), with benefits more pronounced in celiac patients and with intervention durations exceeding 48 weeks. The analysis also showed beneficial effects on C-reactive protein (CRP) (WMD −0.40 mg/L), suggesting anti-inflammatory effects.

Kim et al. (2017) analyzed data from the National Health and Nutrition Examination Survey (NHANES) 2009-2014, identifying 155 gluten-free followers without celiac disease. These individuals had smaller waist circumference and higher HDL cholesterol compared to gluten consumers. They also showed lower BMI (borderline significance, $p = 0.053$) and significant self-reported weight loss (−1.33 kg) over one year. However, there was no statistical difference in total cholesterol, triglycerides, HbA1c, or fasting glucose.

Conversely, Potter et al. (2018) conducted a systematic review of 27 studies in celiac disease patients, finding that GFD consistently increased total cholesterol, HDL, fasting glycemia, and BMI (remaining within healthy weight range). Significant changes in low-density lipoprotein (LDL), triglycerides, and blood pressure were not consistently reported, leaving the overall effect on cardiovascular risk unclear.

Ehteshami et al. (2018) performed an RCT of 45 subjects with metabolic syndrome randomized to GFD or control diet for 8 weeks. The GFD showed no effects on LDL cholesterol, total cholesterol, fasting insulin, HOMA-IR, or blood pressure. However, GFD significantly reduced fasting blood glucose, waist circumference, and serum triglyceride concentration compared to control, indicating improved glycemic control and triglyceride levels.

Orange et al. (2022) conducted a systematic review of four RCTs with sample sizes ranging from 21 to 60 patients. GFD was not associated with weight loss, but individuals on GFD had lower mean waist circumference, fat percentage (−2.3%), and serum triglyceride levels. While one study reported triglyceride reduction, another found significant increases. Insulin sensitivity improved in one intervention group (calorie-restricted, high-protein diet containing gluten) compared to GFD, suggesting that gluten restriction per se may not improve insulin sensitivity.

Blood Pressure and Cardiovascular Risk

Rohani et al. (2024) found that GFD significantly reduced systolic blood pressure (SBP) (WMD −2.96 mmHg) in their meta-analysis. However, a Cochrane systematic review by Schmucker et al. (2020) including one RCT with 60 participants and three non-randomized studies with 428,547 participants found very low-certainty evidence indicating no clear effect of gluten intake on systolic or diastolic blood pressure, LDL levels, or BMI.

Lange et al. (2024) conducted a prospective interventional study of 27 healthy individuals following strict GFD for four weeks. The study found decreased leucocyte count and C-reactive protein levels, indicating anti-inflammatory effects, with a positive trend for improvement in flow-mediated vasodilation (FMD), a measure of endothelial function. However, other cardiovascular endpoints remained unchanged, and GFD did not result in overall cardiovascular improvement.

Emilsson et al. (2017) discussed findings from Kim et al.'s NHANES analysis, noting that non-celiac GFD followers showed lower probability of metabolic syndrome (33.0% vs. 38.5%) and lower 10-year CVD risk score (4.52 vs. 5.70%), though these differences were not statistically significant.

Glucose Metabolism and Body Composition

The Cochrane review by Schmucker et al. (2020) found low-certainty evidence suggesting that lower gluten intake may be associated with slightly increased risk of type 2 diabetes (adjusted HR 1.14, 95% CI 1.07 to 1.22). Lowering gluten by 5 g/day showed similar increased risk (adjusted HR 1.12, 95% CI 1.08 to 1.16). These findings raise concerns about potential metabolic consequences of gluten restriction in non-celiac populations.

Defeudis et al. (2023) conducted a narrative review synthesizing findings from various studies, reporting mixed effects on cardiometabolic outcomes. While some studies reported improved glycemic control and increased HDL levels, others indicated increased glycemia, HbA1c, and triglycerides. Waist circumference showed discordant results, with some studies noting reduction and others showing increase. The authors concluded that GFD's impact on cardiovascular risk factors remains unclear, especially for non-celiac individuals.

Dhruva et al. (2021) reviewed the relationship between GFD and metabolic syndrome in both non-celiac and celiac patients, concluding that GFD may slightly improve overall cardiac risk factors, weight, and/or insulin resistance. However, its use in the absence of gluten-related disorder was considered controversial.

Nutritional Concerns

Several reviews have highlighted nutritional concerns associated with GFD. Barroso et al. (2022) noted that avoiding wheat due to gluten content could decrease fiber and beneficial constituents while increasing glycemic index. Gluten-free products often have low protein and high fat/salt content, promoting an obesogenic environment. A randomized clinical trial cited in the review found lower fiber intake and non-significant weight loss in the GFD group.

Mazepa et al. (2023) conducted a literature review noting that while some studies showed beneficial increases in HDL-cholesterol and total cholesterol with decreased triglycerides in celiac patients on GFD, others found no significant differences in lipid profiles. GFD also showed a trend toward increased BMI, hyperglycemia, and insulin resistance. The authors concluded that the influence of GFD on cardiovascular risk parameters remains unclear.

Cardiometabolic Effects of Low-FODMAP Diet

Research on cardiometabolic effects of LFD is substantially more limited than for GFD, with most studies focusing exclusively on gastrointestinal outcomes. The available evidence suggests that LFD research has not systematically evaluated cardiovascular risk factors, lipid profiles, or metabolic parameters.

Sikaroudi et al.'s systematic umbrella review explicitly noted that their paper focused on low-FODMAP diet for IBS symptom relief, not cardiometabolic metrics. Similarly, Herfindal et al.'s RCT examining LFD effects on gut microbiota in celiac disease patients with persistent gastrointestinal symptoms was noted as "not relevant" to cardiometabolic health.

The primary cardiometabolic consideration for LFD relates to its effects on gut microbiota composition. So et al. (2022) conducted a systematic review with meta-analysis examining effects of LFD on colonic microbiome in IBS, though specific cardiometabolic outcomes were not reported in the available metadata. The potential for microbiome alterations to influence metabolic health represents an important area for future investigation.

Given the restrictive nature of LFD and its impact on dietary fiber intake through limitation of certain fruits, vegetables, legumes, and whole grains, theoretical concerns exist regarding potential effects on cardiovascular health markers. However, the three-phase LFD approach with reintroduction and personalization may mitigate these concerns by allowing individualized liberalization of the diet while maintaining symptom control.

Discussion

Synthesis of Evidence on IBS Symptom Management

The evidence synthesized in this review demonstrates clear differences in the strength and consistency of support for LFD versus GFD in IBS management. LFD has emerged as a well-established, evidence-based dietary intervention with robust support from multiple high-quality RCTs and meta-analyses. The consistency of findings across studies, with meta-analytic effect sizes ranging from SMD −0.66 to −1.97 for symptom reduction, provides strong evidence for LFD efficacy (Black et al., 2021; Lanen et al., 2021; Pouladi et al., 2025).

In contrast, GFD evidence remains mixed and controversial. While individual RCTs have demonstrated significant symptom improvement in responder subgroups (Shahbazkhani et al., 2015; Zanwar et al., 2016), meta-analyses have failed to show consistent benefits across broader IBS populations (Arabpour et al., 2023; Dionne et al., 2018). The heterogeneity in GFD response suggests that benefits may be limited to specific patient subgroups, potentially those with concurrent non-celiac gluten sensitivity, specific HLA genotypes (DQ2/8), or those whose symptoms are primarily triggered by wheat-derived fructans rather than gluten per se.

The mechanistic question of whether symptom improvement attributed to gluten restriction results from gluten itself or from concurrent fructan reduction remains incompletely resolved. The study by Hekmatdoost (2022) provides compelling evidence that fructans, rather than gluten, are responsible for symptom provocation in most IBS patients, as both gluten-containing and placebo groups on low-FODMAP diets showed similar improvements. This finding has important implications for dietary counseling, suggesting that targeted FODMAP restriction may be more effective and less restrictive than complete gluten elimination.

Comparative Effectiveness and Clinical Implications

Direct comparative evidence consistently favors LFD over GFD for IBS symptom management. The meta-analysis by Arabpour et al. (2023) demonstrated that LFD significantly outperformed GFD in reducing IBS-SSS and improving quality of life. Network meta-analyses have similarly ranked LFD higher than GFD across multiple outcome measures (Lei et al., 2025; Yu et al., 2022).

The combined LF-GFD approach has shown promise in several studies, with Zhang et al. (2024) demonstrating incremental benefits for bloating, pain, and psychological symptoms compared to GFD alone. However, the clinical utility of this combined approach must be weighed against increased dietary restrictiveness, potential nutritional inadequacy, and impact on quality of life. The additional burden of eliminating both FODMAPs and gluten may not be justified for most patients, particularly given that fructan restriction (inherent in LFD) may account for much of the benefit attributed to gluten elimination.

From a clinical perspective, these findings support a hierarchical approach to dietary management in IBS. LFD should be considered as a first-line dietary intervention for patients with moderate to severe IBS symptoms, implemented through the structured three-phase approach (restriction, reintroduction, personalization) with dietitian guidance. GFD may be considered for selected patients who fail to respond adequately to LFD, particularly those with suspected non-celiac gluten sensitivity or specific HLA genotypes, though expectations should be tempered by the limited meta-analytic evidence.

Cardiometabolic Safety Considerations

The cardiometabolic effects of GFD present a complex picture with both potential benefits and concerns. Some studies have demonstrated improvements in HDL cholesterol, triglycerides, waist circumference, and inflammatory markers (Kim et al., 2017; Rohani et al., 2024), while others have shown increases in total cholesterol, fasting glucose, and potential increased diabetes risk (Potter et al., 2018; Schmucker et al., 2020). This heterogeneity likely reflects differences in study populations (celiac vs. non-celiac), baseline metabolic status, dietary quality of gluten-free alternatives consumed, and study duration.

A critical consideration is the nutritional quality of gluten-free diets. Commercially available gluten-free products often contain higher levels of fat, sugar, and sodium while being lower in protein, fiber, and micronutrients compared to their gluten-containing counterparts (Barroso et al., 2022; Defeudis et al., 2023). This nutritional profile may contribute to adverse metabolic effects, particularly when gluten-free processed foods replace whole grain products. Conversely, a well-planned GFD emphasizing naturally gluten-free whole foods (fruits, vegetables, legumes, nuts, unprocessed meats, and gluten-free whole grains like quinoa and brown rice) may avoid these pitfalls and potentially provide metabolic benefits.

The finding of potential increased type 2 diabetes risk with lower gluten intake (Schmucker et al., 2020) is particularly concerning and warrants careful consideration when recommending GFD to non-celiac individuals. This association may reflect reduced whole grain intake and its associated fiber, magnesium, and other beneficial nutrients that protect against diabetes development.

For LFD, the paucity of cardiometabolic outcome data represents a significant knowledge gap. While the diet's primary focus on symptom management is appropriate, the potential long-term metabolic effects of sustained FODMAP restriction deserve investigation. Theoretical concerns include reduced prebiotic fiber intake and alterations in gut microbiota composition that may influence metabolic health. However, the personalization phase of LFD, which allows reintroduction of tolerated FODMAPs, may mitigate these concerns by maintaining dietary diversity and fiber intake.

Limitations and Methodological Considerations

Several limitations warrant consideration in interpreting this evidence synthesis. First, heterogeneity in study designs, outcome measures, dietary implementation methods, and patient populations limits direct comparability across studies. The lack of standardized protocols for GFD implementation (degree of gluten restriction, duration, monitoring) contributes to variability in findings.

Second, blinding challenges inherent in dietary intervention studies may introduce bias. While some studies employed sophisticated blinding methods using gluten or FODMAP challenges with matched placebos, complete blinding of dietary interventions is often impractical. This limitation may inflate effect sizes through placebo effects or expectancy bias.

Third, the duration of most RCTs (typically 4-12 weeks) limits conclusions about long-term efficacy, safety, and adherence. The meta-analysis by Pouladi et al. (2025) examining long-term LFD outcomes included only five studies with 324 patients, highlighting the need for more long-term follow-up data.

Fourth, publication bias may favor positive findings, potentially overestimating treatment effects. The umbrella review by Bogdanowska-Charkiewicz et al. (2026) noted that psychological factors may influence LFD outcomes, suggesting that non-specific effects contribute to observed benefits.

Fifth, the cardiometabolic evidence base is substantially weaker than the IBS symptom evidence, with most cardiometabolic studies conducted in celiac populations rather than IBS populations. Extrapolation of findings from celiac patients to non-celiac IBS patients requires caution, as the underlying pathophysiology and nutritional status differ.

Clinical Practice Recommendations

Based on the synthesized evidence, the following clinical practice recommendations are proposed:

For IBS Symptom Management:

LFD should be considered as a first-line dietary intervention for patients with moderate to severe IBS symptoms, implemented through the structured three-phase approach with dietitian guidance (Black et al., 2021; Lanen et al., 2021).

GFD may be considered for selected patients who fail to respond adequately to LFD or who have suspected non-celiac gluten sensitivity, though expectations should be tempered by limited meta-analytic evidence (Arabpour et al., 2023; Dionne et al., 2018).

Combined LF-GFD approaches may provide incremental benefits for some patients but should be reserved for those with inadequate response to LFD alone, given increased restrictiveness (Zhang et al., 2024).

Patient education should emphasize that symptom improvement with wheat elimination may result from fructan restriction rather than gluten per se, potentially allowing less restrictive dietary modifications (Hekmatdoost, 2022).

For Cardiometabolic Monitoring:

Patients following GFD, particularly long-term, should receive nutritional counseling emphasizing naturally gluten-free whole foods rather than processed gluten-free alternatives (Defeudis et al., 2023).

Baseline and periodic monitoring of lipid profiles, glucose metabolism, and nutritional status (including fiber intake, B vitamins, iron) should be considered for patients on long-term restrictive diets.

Patients without celiac disease or confirmed non-celiac gluten sensitivity should be counseled about potential metabolic risks of unnecessary gluten restriction, including possible increased diabetes risk (Schmucker et al., 2020).

The personalization phase of LFD should be emphasized to maximize dietary diversity and nutritional adequacy while maintaining symptom control (Schäfer, 2022).

Future Directions and Recommendations

Research Priorities

Several critical research gaps require attention to advance the field of dietary management in IBS:

Mechanistic Studies: Further research is needed to elucidate the mechanisms underlying dietary symptom provocation in IBS. Specifically, studies should distinguish between gluten-specific effects, fructan-mediated effects, and effects of other wheat components (amylase-trypsin inhibitors, wheat germ agglutinin). Advanced methodologies including intestinal permeability assessment, immune profiling, and microbiome analysis may help identify biomarkers predicting dietary response.

Predictive Biomarkers: Identification of biomarkers predicting response to specific dietary interventions would enable personalized dietary recommendations. Potential predictive factors include HLA genotype, baseline microbiome composition, intestinal permeability markers, and immune markers (antigliadin antibodies, cytokine profiles). Prospective studies examining these factors in relation to dietary response are needed.

Long-Term Outcomes: Most existing RCTs have durations of 4-12 weeks, insufficient to assess long-term efficacy, adherence, and safety. Prospective cohort studies with 1-5 year follow-up are needed to evaluate sustained symptom control, dietary adherence patterns, quality of life, nutritional status, and cardiometabolic outcomes. Such studies should include regular nutritional assessments and monitoring of cardiovascular risk factors.

Cardiometabolic Effects of LFD: The paucity of cardiometabolic outcome data for LFD represents a significant knowledge gap. Prospective studies should systematically evaluate lipid profiles, glucose metabolism, blood pressure, body composition, and cardiovascular risk scores in IBS patients following LFD. Particular attention should be paid to the effects of the personalization phase on nutritional adequacy and metabolic health.

Comparative Effectiveness: Additional head-to-head RCTs comparing LFD, GFD, and combined approaches are needed, with adequate sample sizes to detect clinically meaningful differences. Such studies should include comprehensive outcome assessment (symptoms, quality of life, adherence, nutritional status, cost-effectiveness) and long-term follow-up.

Microbiome Interactions: The relationship between dietary interventions, microbiome alterations, and clinical outcomes requires further investigation. Studies should examine whether microbiome changes mediate symptom improvement, whether baseline microbiome composition predicts dietary response, and whether microbiome-targeted interventions (probiotics, prebiotics) enhance dietary efficacy.

Clinical Implementation Strategies

Optimizing clinical implementation of dietary interventions requires attention to several practical considerations:

Dietitian-Led Implementation: Evidence supports dietitian-led implementation of LFD to ensure proper education, monitoring, and progression through the three phases (Schäfer, 2022). Healthcare systems should facilitate access to specialized gastrointestinal dietitians for patients with moderate to severe IBS.

Digital Health Tools: Development and validation of digital health tools (mobile applications, online platforms) may improve accessibility, adherence, and outcomes for dietary interventions. Such tools should provide food lists, meal planning, symptom tracking, and guidance through reintroduction phases.

Patient Education Materials: Standardized, evidence-based patient education materials are needed to support dietary interventions. Materials should address common misconceptions (e.g., gluten vs. fructan effects), provide practical implementation guidance, and emphasize nutritional adequacy.

Integration with Pharmacological and Psychological Therapies: Dietary interventions should be integrated within comprehensive IBS management strategies including pharmacological therapies and psychological interventions (cognitive behavioral therapy, gut-directed hypnotherapy). Research examining optimal sequencing and combination of these approaches is needed.

Policy and Public Health Considerations

The increasing adoption of GFD among individuals without celiac disease raises public health considerations. Clear communication about the limited evidence for GFD in non-celiac populations and potential metabolic risks is needed to prevent unnecessary dietary restriction. Professional organizations should develop evidence-based guidelines addressing appropriate indications for GFD and LFD in IBS management.

The nutritional quality of commercially available gluten-free products represents a public health concern. Regulatory approaches or industry initiatives to improve the nutritional profile of gluten-free products (increasing fiber and protein content, reducing added sugars and sodium) may benefit both celiac and non-celiac consumers.

Conclusion

This comprehensive review synthesizes evidence from clinical trials and meta-analyses examining the effects of gluten-free and low-FODMAP dietary interventions on IBS symptoms and cardiometabolic health. The evidence demonstrates that LFD represents a well-established, evidence-based dietary intervention for IBS symptom management, with robust support from multiple high-quality RCTs and meta-analyses showing moderate to large effect sizes for symptom reduction and quality of life improvement. In contrast, GFD evidence remains mixed and controversial, with meta-analyses failing to demonstrate consistent benefits across broader IBS populations, though individual trials suggest benefits in specific patient subgroups.

Direct comparative evidence consistently favors LFD over GFD for IBS symptom management, with network meta-analyses ranking LFD higher across multiple outcome measures. Combined LF-GFD approaches have shown incremental benefits for bloating, pain, and psychological symptoms, though the increased restrictiveness must be weighed against potential nutritional concerns and quality of life impact.

Mechanistic evidence suggests that symptom improvement attributed to gluten restriction may primarily result from concurrent fructan reduction rather than gluten per se, with important implications for dietary counseling and intervention design. This finding supports targeted FODMAP restriction as potentially more effective and less restrictive than complete gluten elimination for most IBS patients.

Regarding cardiometabolic outcomes, GFD demonstrates mixed effects with both potential benefits (improved HDL cholesterol, reduced triglycerides and waist circumference in some studies) and concerns (increased total cholesterol, potential increased diabetes risk, nutritional inadequacy of processed gluten-free products). The heterogeneity in findings likely reflects differences in study populations, baseline metabolic status, dietary quality, and study duration. For LFD, the paucity of cardiometabolic outcome data represents a significant knowledge gap requiring future investigation.

From a clinical perspective, these findings support a hierarchical approach to dietary management in IBS, with LFD as a first-line dietary intervention implemented through the structured three-phase approach with dietitian guidance. GFD may be considered for selected patients who fail to respond adequately to LFD or who have suspected non-celiac gluten sensitivity, though expectations should be tempered by limited meta-analytic evidence. Patients following restrictive diets, particularly long-term, should receive nutritional counseling emphasizing whole foods and periodic monitoring of nutritional status and cardiometabolic parameters.

Critical research gaps include the need for mechanistic studies distinguishing gluten-specific from fructan-mediated effects, identification of predictive biomarkers for dietary response, long-term outcome studies with comprehensive assessment of efficacy, adherence, nutritional status, and cardiometabolic effects, and systematic evaluation of LFD effects on metabolic health. Addressing these gaps will enable more personalized, evidence-based dietary recommendations for IBS management while ensuring metabolic safety.

In conclusion, while LFD has emerged as a well-supported dietary intervention for IBS symptom management, the evidence for GFD remains insufficient for routine recommendation in non-celiac IBS populations. The cardiometabolic implications of both diets require further investigation to ensure that symptom management strategies do not inadvertently compromise broader metabolic health. Clinicians should adopt individualized approaches to dietary management, considering patient preferences, symptom patterns, nutritional status, and metabolic risk factors, while emphasizing the importance of dietitian-led implementation and ongoing monitoring.

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