

## Original Article

# Predicting response to the low FODMAP diet in irritable bowel syndrome: Current evidence and clinical considerations

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**Background and Objectives:** The low fermentable oligo-, di-, mono-saccharides and polyols (FODMAP) diet is an effective dietary intervention for irritable bowel syndrome (IBS), yet up to 50% of patients fail to respond adequately. Identifying reliable predictors of response could optimize treatment selection and improve treatment outcomes while avoiding unnecessary dietary restrictions. This narrative review examines current evidence for predictors of response to the low FODMAP diet and highlights gaps in knowledge that must be addressed to develop clinically useful indicators for routine practice. **Methods and Study Design:** We reviewed the literature on the low FODMAP diet, and studies investigating factors that may predict treatment response, including clinical, diagnostic, biological, biochemical, and microbial markers. **Results:** Several potential predictors to the low FODMAP diet have emerged, including baseline symptom severity, psychological factors (particularly depression), hydrogen breath test results, volatile organic compounds in fecal samples, and specific gut microbiota profiles. Clinical and psychological measures show the most immediate potential for implementation due to accessibility and established measurement tools. Biological markers, including breath testing, metabolomics, and microbiome analysis, show promise but require further validation in larger, diverse populations and standardization of methodologies. **Conclusions:** Despite promising research, significant gaps remain in developing reliable, accessible predictors of response to the low FODMAP diet. Future research should focus on validating simple clinical tools that combine symptom profiles with psychological assessment to guide treatment decisions. A personalized approach to dietary management of IBS based on reliable response predictors would optimize clinical outcomes while minimizing unnecessary dietary restriction and healthcare resource utilization.

**Key Words:** irritable bowel syndrome, FODMAP, diet therapy, treatment response, predictive markers

## INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic disorder of gut-brain interaction (DGBI) and is characterized by recurrent abdominal pain that is associated with defecation.<sup>1</sup> According to the Rome IV criteria, IBS diagnosis requires recurrent abdominal pain (at least weekly for three months) associated with at least two changes in defecation patterns. These criteria must be fulfilled for three months, with symptom onset occurring at least six months before diagnosis.<sup>1</sup> Bowel habits associated with IBS can be further classified as diarrhoea-predominant (IBS-D), constipation-predominant (IBS-C), a combination of both bowel habits (IBS-M), or un-subtyped (IBS-U).

Despite advances in IBS management, identifying effective treatments remains challenging due to the disorder's heterogeneous nature. The low fermentable, oligo-, di-, monosaccharide and polyol (FODMAP) diet has emerged as one of the most evidence-based dietary interventions, yet up to 50% of patients fail to respond adequately.<sup>2</sup> This represents a significant clinical challenge, as following this restrictive diet requires considerable patient effort and healthcare resources. Identifying reliable

predictors of response could optimize treatment selection, improving outcomes while avoiding unnecessary dietary restrictions. Recent research by Wu et al. demonstrates how gut-brain axis dysfunction underlies FODMAP-induced symptom generation, highlighting the complex interplay between physiological reactions and central processing that may determine treatment response.<sup>3</sup>

IBS has an estimated global pooled prevalence of 4.1%,<sup>4</sup> with higher rates among females, particularly those aged 18-39 years of age.<sup>4</sup> In the Asia-Pacific region, prevalence reaches 4.7%,<sup>5</sup> representing a significant

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Manuscript received 13 March 2025. Initial review completed 15 March 2025. Revision accepted 24 March 2025.

doi: 10.6133/apjcn.202506\_34(3).0012

## Highlight box

### LOW FODMAP DIET IN THE ASIA-PACIFIC CONTEXT

- IBS has an estimated prevalence of up to 4.7% in the Asia-Pacific region, representing a significant healthcare burden.<sup>4</sup>
- Cultural dietary patterns in many Asia-Pacific countries feature high FODMAP foods,<sup>7,9</sup> creating unique implementation challenges, for example:
  - Certain fruits high in polyols and fructose: mango, persimmon
  - Wheat-based products high in fructans: roti, naan, mee goreng, udon
  - Certain vegetables high in polyols, galacto- and fructo-oligosaccharides: mushrooms, soybeans, onion, garlic, legumes/pulses
- Limited availability of specialized dietitian services in some Asia-Pacific regions increases the importance of identifying reliable predictors of response.<sup>83</sup>
- Regional variations in gut microbiome profiles may influence response to the low FODMAP diet, suggesting potential for region-specific microbial predictors.<sup>84</sup>
- Traditional medical systems in the region often emphasize dietary approaches to gut health, potentially increasing acceptance of dietary interventions compared to pharmaceutical and herbal options.<sup>51</sup>

healthcare burden with unique challenges, including variable healthcare access,<sup>6</sup> and diverse dietary patterns rich in FODMAPs, such as wheat-based products, certain fruits, and vegetables.<sup>7-9</sup> This disorder significantly reduces health-related quality of life (QoL) compared to healthy controls,<sup>10</sup> affecting work productivity, sleep, diet, social functioning. People with IBS experience greater absenteeism, presenteeism, and work productivity loss,<sup>10,11</sup> with a bi-directional relationship between work-related stress and gastrointestinal symptoms that can perpetuate symptom severity.<sup>12</sup>

## PATHOPHYSIOLOGY

The biopsychosocial model of DGBI emphasizes how genetic and environmental factors interact to influence both brain and gut function through bidirectional gut-brain communication.<sup>13</sup> This communication pathway connects psychological factors (mood, cognitive processes, emotions) with gastrointestinal function.<sup>13</sup> Several factors dysregulate the circuitry of the gut-brain axis, including genetic and environmental factors such as diet,<sup>13,14</sup> explaining why dietary interventions may need to be tailored based on physiological and psychological characteristics to achieve optimal symptom management. Recent research by Wu et al. has demonstrated that while FODMAPs increase small bowel motility and colonic gas similarly in both IBS patients and healthy controls, only IBS patients report increased symptoms,<sup>3</sup> underscoring how altered central processing of normal physiological responses can drive symptom generation in IBS.

### *Visceral hypersensitivity and central processing*

Visceral hypersensitivity, a key feature of IBS, involves heightened pain perception from normal gut stimuli.<sup>15</sup> Sensory information from the gastrointestinal tract is delivered to the central nervous system (CNS) via the vagal afferent nerves and spinal afferents.<sup>16</sup> Studies exploring rectal distention have shown that people with IBS experience greater pain perceptions and intensified pain sensations when assessed with a rectal barostat.<sup>17-20</sup> Dysregulated messaging between the brain and the gut may explain the presence of visceral hypersensitivity.

Visceral afferent nerves transmit sensory information from the gut to the CNS and can be classified by location, such as mucosal, mesenteric, or muscular, determining their functional properties.<sup>21</sup> Information transmitted via these nerves can cause visceral stimuli, such as intestinal barrier distortion, stretching or distension, to be perceived as pain. Additionally, these nerves modulate gastrointestinal motor and secretory function, and disturbances can lead to altered bowel function.<sup>22</sup> Experiencing frequent hypersensitivity may evoke concern and anxiety, further exacerbating symptoms through a self-reinforcing cycle.

### *Psychological factors and stress response*

Psychological comorbidity is common within IBS. A recent systematic review and meta-analysis showed an increased prevalence of anxiety symptoms (39.1%), anxiety disorders (23%), depressive symptoms (28.8%) and depressive disorders (23.3%) in IBS patients compared to healthy controls.<sup>23</sup> Stress is associated with increased IBS symptomatology, and people with IBS exhibit stress-induced emotional hyperresponsivity.<sup>24</sup>

The bidirectional communication between the gut and brain suggests that cognitive and emotional factors, like stress, anxiety, and depression, may affect IBS symptoms.<sup>25</sup> These psychological factors have been associated with intestinal function and motility, with a systematic review showing that psychological stress increased colonic motility in IBS, while increased emotional stress slowed small bowel motility.<sup>25</sup> The work by Biesiekierski et al. further highlights how psychological factors, particularly gastrointestinal-specific anxiety, can influence treatment responses in IBS, with implications for how patients might respond to different therapeutic approaches.<sup>26</sup>

### *Gut physiology and microbiome*

The intestinal barrier is essential for maintaining gastrointestinal homeostasis, gut immune function and selective uptake of critical nutrients.<sup>27</sup> Impairments to the intestinal barrier can activate the gut immune response, increasing symptom severity in DGBI.<sup>28,29</sup> Tight junction proteins in the epithelial layer help maintain intestinal barrier integri-

ty, but their expression can be decreased<sup>28</sup> by genetic and pathogenic factors.<sup>30</sup> Increased intestinal permeability has been observed in IBS-D, with participants having higher scores on anxiety and depression subscales.<sup>30</sup> Importantly, psychological factors such as depression, anxiety and stress can modulate the intestinal barrier function and increase intestinal permeability,<sup>30</sup> further illustrating the bidirectional nature of the gut-brain axis.

The gut microbiota also plays a crucial role in gastrointestinal health, function and symptom onset in IBS. Individuals with IBS typically exhibit a reduction or absence of microbial variety and abundance.<sup>31,32</sup> At the phylum level, people with IBS have an increased Firmicutes to Bacteroidetes ratio, with significant variations in several bacterial families and genera.<sup>33,34</sup> Although a diverse gut microbiota characterizes a 'healthy' gastrointestinal tract, the optimal composition is highly individualized, therefore presenting a challenge to using microbiota profiles as predictive markers in clinical practice.<sup>35</sup>

The complex pathophysiology of IBS involving CNS function, psychological factors, and gut physiology underscores the heterogeneity of the disorder and explains the variable response to treatments. Dietary interventions targeting specific physiological mechanisms represent a promising approach to managing IBS symptoms, with the low FODMAP diet emerging as one of the most evidence-based dietary strategies.

### DIETARY MANAGEMENT OF IBS

Studies have assessed various dietary interventions for IBS management, with the low FODMAP diet emerging as the most efficacious for global symptom improvement in meta-analysis.<sup>2</sup> Historically, exclusion diets aimed to identify food intolerances through strict elimination followed by structured reintroduction. Given that most patients associate their IBS symptoms with food consumption, exclusion diets have high credibility and acceptability. Indeed, dietary exclusion is a commonly adopted self-management strategy in 70%-89% of individuals with IBS, with more severe symptoms correlating with greater food exclusion.<sup>36</sup>

The FODMAP concept specifically targets short and long-chain carbohydrates that are poorly absorbed in the small intestine and rapidly fermented by colonic bacteria. FODMAPs increase small intestinal water content through osmotic effects and colonic gas production through bacterial fermentation,<sup>37</sup> leading to luminal distention that can trigger symptoms in individuals with visceral hypersensitivity. Recent mechanistic studies have shown that while FODMAPs produce similar increases in colonic gas and volume in both IBS patients and healthy controls, only those with IBS experience significant symptoms, highlighting the role of visceral hypersensitivity rather than excessive gas production in symptom generation.<sup>3</sup>

#### *A three-phase approach to the low FODMAP diet*

The low FODMAP diet is implemented through a structured three-phase process, requiring guidance from an experienced dietitian throughout all phases.<sup>38</sup>

#### **Phase 1 FODMAP Restriction**

The initial phase involves restricting all FODMAPs for two to eight weeks to achieve symptom relief.<sup>39,40</sup> During this period, patients eliminate high-FODMAP foods to reduce the osmotic and fermentative effects that may trigger symptoms. Symptom onset occurs within four hours of FODMAP intake,<sup>41</sup> and symptom improvement typically occurs within days of starting the restrictive diet.<sup>42</sup> This phase serves as a diagnostic tool to determine whether FODMAP restriction leads to symptomatic relief, indicating whether to proceed with this dietary approach.

#### **Phase 2 FODMAP Reintroduction**

If symptom improvement occurs during restriction, the second phase systematically reintroduces specific FODMAP groups to identify individual tolerance thresholds. This involves FODMAP "challenges" where patients consume increasing amounts of high-FODMAP foods over one to three days, with washout periods between challenges. Benefits of this phase include increased dietary variety and reduced likelihood of nutritional inadequacy.<sup>40</sup> The reintroduction phase may take up to 10 weeks to complete all FODMAP challenges.

#### **Phase 3 FODMAP Personalization**

The final phase personalizes FODMAP intake based on symptom responses from Phase 2. Foods that did not elicit symptoms can be freely consumed, while those that triggered symptoms are limited to individual tolerance levels.<sup>40</sup> This approach promotes long-term symptom management while maximizing dietary variety. Patients should be encouraged to periodically re-challenge FODMAPs due to potential changes in tolerance over time.

### EVIDENCE FOR EFFICACY

Meta-analyses show that the low FODMAP diet significantly improves global IBS symptoms, abdominal pain, bloating, and flatulence.<sup>2</sup> The efficacy of the low FODMAP diet depends partly on the comparison condition. Evidence shows a clear advantage over high FODMAP diets,<sup>43</sup> and habitual diets,<sup>44</sup> with mixed results when compared to active controls based on established dietary guidelines.<sup>45,46</sup> Overall, the low FODMAP diet is effective in 50%-80% of individuals with IBS,<sup>2</sup> leading to its inclusion in clinical guidelines for IBS management.

Importantly, studies have found that improvement in IBS symptoms correlates with adherence to the low FODMAP diet, albeit weakly ( $r = -0.26$ ).<sup>47</sup> Recent association analyses from a Swedish randomized control trial (RCT) showed that better adherence to a 4-week low FODMAP diet (lower FODMAP intake) was associated with larger symptom response ( $r = -0.30$ ),<sup>48</sup> further supporting the mechanistic rationale for FODMAP restriction in symptom management.

### CHALLENGES AND LIMITATIONS

Despite its efficacy, the low FODMAP diet presents several important challenges. Adherence difficulties are common, particularly when eating away from home, due to restrictions, cost, and limited food availability.<sup>8,49,50</sup>

Regional dietary considerations are particularly relevant for Asia-Pacific populations. While Western diets

typically include higher amounts of FODMAPs, some countries in the region (such as India and Korea) may have higher FODMAP intake due to dietary pattern preferences like vegetarianism,<sup>51</sup> or culturally relevant foods.<sup>7,9</sup> Compliance with a low FODMAP diet in these regions faces unique challenges related to the availability and identification of suitable food alternatives and their cost.<sup>8</sup> Additionally, herbal medicines and complementary alternatives may be preferred in Asian regions due to their long history of use and acceptability.<sup>51</sup>

Nutritional compromise is a risk, with studies from Western regions reporting lower carbohydrate, energy, and calcium intakes,<sup>52,53</sup> and changes to the colonic microbial profile following the restrictive phase,<sup>42,54-56</sup> especially when multiple dietary strategies are used simultaneously.<sup>57</sup> Psychological impacts include reduced food-related QoL and the potential risk of disordered eating.<sup>58-61</sup> The longer-term effects of a low FODMAP diet are yet to be explored specifically in Asia-Pacific populations.

## CURRENT EVIDENCE FOR PREDICTORS OF RESPONSE TO A LOW FODMAP DIET

Given the heterogeneity in the pathophysiology of IBS, identifying accessible and effective predictors of treatment response is critical to optimizing patient outcomes, improving treatment success and reducing healthcare system burden. Evidence is emerging for predictors of response to FODMAP-modified diets across multiple domains: clinical measures, biological markers, and microbiome profiles. Table 1 summarizes key studies investigating these potential predictors, their findings, and limitations for clinical application.

### PREDICTORS OF RESPONSE

Evidence for predictors of response to the low FODMAP diet has emerged across several domains, each with varying levels of clinical applicability. These can be broadly categorised into: (1) clinical measures, including symptom profiles and psychological assessments that can be readily implemented in practice; (2) biological and biochemical measures, such as breath testing that require specialized equipment; and (3) experimental predictors such as volatile organic compounds (VOCs), microbial measures and metabolites that examine the gut microbial composition and function which, while promising, remain largely experimental. The following sections explore the current evidence within each category, highlighting potential clinical applications and limitations.

#### *Clinical measures*

Clinical measures such as symptom severity and psychological symptoms may have a role in predicting response to a low FODMAP diet. In a randomized crossover trial of a high vs low FODMAP diet, higher symptom severity independently predicted better response, indicating participants with more severe symptoms may benefit most from dietary intervention.<sup>62</sup> This effect likely reflects the greater potential for symptom reduction in those with higher baseline severity.

Psychological comorbidity may affect symptom response to the low FODMAP diet. In IBS-D and IBS-M subtypes, higher scores on the Hospital Anxiety and De-

pression Scale (HADS-D) with respect to depression scores were associated with a poorer symptom response. At the same time, no significant difference was observed with higher or lower anxiety (HADS-A) scores.<sup>63</sup> The bi-directional communication between the brain-gut axis relies on the autonomic nervous system, hypothalamic-pituitary-adrenal (HPA) axis and microbiome.<sup>64</sup> Dysregulation of the HPA axis may have an integral role in perpetuating depression in IBS.<sup>65</sup> Several psychological therapies are efficacious in reducing IBS symptom severity,<sup>66</sup> signifying the overlap between psychological factors and clinical features of IBS. As highlighted by Biesiekierski et al., psychological factors, particularly gastrointestinal-specific anxiety, can significantly influence treatment outcomes in IBS, suggesting their inclusion in predictor models.<sup>26</sup>

#### *Biological and biochemical measures*

Studies have assessed hydrogen breath testing for its potential to be a predictor of response to the low FODMAP diet. Variable testing protocols (Table 1) found that patients showing higher hydrogen production ( $\geq 10$ ppm) typically responded better to the diet. This included baseline (fasting) hydrogen and methane levels being higher in those who subsequently responded to dietary intervention, particularly for bloating symptoms.<sup>67</sup> These findings suggest that greater fermentation capacity may identify patients most likely to benefit from FODMAP restriction.

However, hydrogen breath testing has significant clinical limitations.<sup>68</sup> Results lack consistency across studies,<sup>69</sup> do not reliably correlate with symptom severity,<sup>70</sup> and are complicated by dose-dependent effects with certain sugars.<sup>71</sup> Psychological factors and placebo effects further confound interpretation, suggesting breath testing should be viewed as a supplementary rather than a primary predictor of dietary response.

VOCs have emerged as a promising tool in understanding the pathophysiology and response to dietary management in IBS. Specific VOCs have been identified in 'responders' to a low FODMAP diet,<sup>72</sup> while classifying VOCs as pathogenic or healthy in an IBS population showed that individuals with a 'pathogenic' profile exhibited a significantly greater reduction in IBS-SSS scores.<sup>73</sup> VOCs can be detected through blood, skin, breath, urine and fecal samples, making them less intrusive biomarkers for clinicians to utilize. VOCs are produced through physiological and pathological metabolic processes, including bacterial metabolism of non-digestible food components.<sup>74</sup> This holds clinical relevance to IBS, where microbial, inflammatory and cellular processes within the bowel may be reflected in VOC analysis. However, VOC profiling has not been successfully implemented in practice due to a lack of standardization in sample collection and analysis, reliance on gas chromatography, and limited validation in larger patient samples.<sup>75</sup>

#### *Microbial measures*

Microbiome profiling reveals distinct bacterial signatures between responders and non-responders to the low FODMAP diet, though significant heterogeneity exists in these profiles and analysis methods used. This is particularly evident at the genus level, with *Bacteroides* being

**Table 1.** Evidence summary and clinical applicability of trials utilizing predictors of response to the low FODMAP diet in IBS

Author, year, country	Study design	Predictor and measurement	Intervention
Clinical predictors			
Algera et al. (2022) Sweden, <sup>62</sup>	Randomized crossover trial; n=56, Rome IV	Symptom severity (IBS-SSS); >50 point decrease in IBS-SSS deemed ‘responder’	23g vs. 4g FODMAPs/day for 7 days
Colomier et al. (2022) Sweden, <sup>85</sup>	Secondary analysis of RCT; n=77, Rome III	Anxiety and depression (HADS); Gastrointestinal Symptom Rating Scale (GSRS)	4-week low FODMAP diet or generalized dietary advice
O’Connor et al. (2024) Ireland, <sup>63</sup>	Prospective cohort study; n=448, Rome IV IBS-D or IBS-M	Anxiety and depression (HADS); Symptom severity (IBS-SSS)	12-week generalized dietary advice; if no symptom response, then 6-week low FODMAP diet followed by 12-week reintroduction
Author, year, country	Results and limitations	Clinical applicability*	
Clinical predictors			
Algera et al. (2022) Sweden, <sup>62</sup>	Severity of gastrointestinal symptoms independently predicted response after adjusting for anxiety. Limited by subjective measure which does not distinguish between symptom types.	★★★	Easy to assess with simple questionnaires in clinical practice without specialized equipment
Colomier et al. (2022) Sweden, <sup>85</sup>	More severe psychological distress significantly predicted worse response to bloating (Time x HADS $\beta = 0.08 \pm 0.04$ p = 0.03). Limited by small sample size and not statistically powered.	★★★	HADS is accessible and readily available without specialized training
O’Connor et al. (2024) Ireland, <sup>63</sup>	Participants with HADS-D score >8 significantly less likely to achieve primary endpoint compared to score <8 (43.8% vs 64%, p<.01). No significant difference for HADS-A scores. Results may be influenced by participants providing socially desirable responses.	★★★	HADS is accessible and requires minimal training; results confirm previous study findings, <sup>85</sup>

FBT: fructose breath test; FODMAP: fermentable oligosaccharide, disaccharide, monosaccharide and polyol; FS: fecal supernatant; GSRS-IBS: gastrointestinal symptom rating scale irritable bowel syndrome; IBS-D: irritable bowel syndrome diarrhoea subtype; IBS-M: irritable bowel syndrome mixed subtype; IBS-C: irritable bowel syndrome constipation subtype; IBS-SSS: irritable bowel syndrome symptom severity score; HADS: hospital anxiety and depression scale; NCT: nutrient challenge test; RCT: randomized controlled trial; VOC: volatile organic compound.

Clinical Applicability Rating: ★★★ = readily available in typical clinical settings, straightforward interpretation; ★★ = requires some specialized equipment but feasible in many settings; ★ = requires advanced laboratory techniques, significant expertise, or faces substantial implementation barriers.

**Table 1.** Evidence summary and clinical applicability of trials utilizing predictors of response to the low FODMAP diet in IBS (cont.)

Author, year, country	Study design	Predictor and measurement	Intervention
<i>Biochemical predictors</i>			
Melchior et al. (2020) France, <sup>69</sup>	Prospective controlled trial; n=88, Rome III	Fructose breath test (FBT); IBS-SSS	2-week low fructose diet
Schindler et al. (2021) Belgium, <sup>86</sup>	Retrospective analysis; n=110, Rome III or IV	Hydrogen breath test during nutrient challenge test (NCT); IBS-SSS	3–4-week low FODMAP diet following 30g lactulose NCT
Somvanapanich et al. (2023) Thailand, <sup>67</sup>	Uncontrolled intervention; n =38, functional GI disorder	Spot breath test (hydrogen, methane); 30% decrease in bloating = response	4-week low FODMAP diet
Ghoshal et al. (2024), India, <sup>87</sup>	Prospective case-control; n=40, (20 IBS, 20 healthy)	Hydrogen breath test; IBS-SSS	12-week low FODMAP diet following a high/low FODMAP meal test

Author, year, country	Results and limitations	Clinical applicability*
<i>Biochemical predictors</i>		
Melchior et al. (2020) France, <sup>69</sup>	64.9% of patients with positive FBT and 72.1% with negative FBT reported improvement ( <i>p</i> = 0.32). Limited by high false positive rate and fructose dose not representing typical food intake.	★★ Specialized equipment required; interpretation straightforward but evidence inconsistent across studies
Schindler et al. (2021) Belgium, <sup>86</sup>	Patients with greater hydrogen increases during proximal intestinal transit had significantly better response, with a reduction of 66 points in IBS-SSS per 10-ppm hydrogen increase ( <i>p</i> =0.045). Nutrient challenge test is time-consuming and not validated in larger samples.	★★ Specialized equipment required; interpretation relatively standard; findings mostly consistent with other studies
Somvanapanich et al. (2023) Thailand, <sup>67</sup>	Baseline gas levels higher in responder's vs non-responders (hydrogen 9.5 vs 4.5, methane 3 vs 1.5). Limited by lack of control over pre-breath test meal composition.	★★ Specialized equipment required; breath test interpretation relatively standardized
Ghoshal et al. (2024), India, <sup>87</sup>	Positive breath test associated with sensitivity of 78.6%, specificity of 66.6% in predicting response. Limited by small, underpowered sample.	★★ Specialized equipment required; interpretation straightforward

FBT: fructose breath test; FODMAP: fermentable oligosaccharide, disaccharide, monosaccharide and polyol; FS: fecal supernatant; GSRS-IBS: gastrointestinal symptom rating scale irritable bowel syndrome; IBS-D: irritable bowel syndrome diarrhoea subtype; IBS-M: irritable bowel syndrome mixed subtype; IBS-C: irritable bowel syndrome constipation subtype; IBS-SSS: irritable bowel syndrome symptom severity score; HADS: hospital anxiety and depression scale; NCT: nutrient challenge test; RCT: randomized controlled trial; VOC: volatile organic compound.

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**Table 1.** Evidence summary and clinical applicability of trials utilizing predictors of response to the low FODMAP diet in IBS (cont.)

Author, year, country	Study design	Predictor and measurement	Intervention
<i>Microbial predictors</i>			
Bennet et al. (2018), Sweden, <sup>78</sup>	Secondary analysis of RCT; n=61, Rome III	Faecal bacterial profiles using GA-map Dysbiosis test; IBS-SSS	4-week low FODMAP diet or traditional dietary advice
Valeur et al. (2018), Norway, <sup>76</sup>	Prospective intervention; n=61, Rome III	Microbiota composition and dysbiosis; IBS-SSS (50-point reduction)	4-week low FODMAP diet
Valdez-Palomares et al (2021), Mexico, <sup>88</sup>	Prospective intervention; n=32, Rome III	Microbiota composition; VAS for symptom severity	4-week low FODMAP diet
Zhang et al. (2021), China, <sup>77</sup>	Parallel-group RCT; n=108, Rome IV IBS-D	Microbiota; IBS-SSS	3-week low FODMAP diet or traditional dietary advice
Author, year, country	Results and limitations	Clinical applicability*	
<i>Microbial predictors</i>			
Bennet et al. (2018), Sweden, <sup>78</sup>	Several bacterial species, including <i>Acinetobacter</i> , <i>Bacteroides stercoris</i> and others were more abundant in non-responders. Limited by small sample size when subtyped by bowel pattern.	★ Advanced laboratory equipment and specialized training needed; evidence inconsistent; significant barriers to implementation	
Valeur et al. (2018), Norway, <sup>76</sup>	Responders had higher levels of <i>Bacteroides fragilis</i> , <i>Acinetobacter</i> , <i>Ruminicoccus</i> and others. Limited by small sample size affecting generalisability.	★ Advanced equipment and expertise required; evidence inconsistent; significant barriers to implementation	
Valdez-Palomares et al (2021), Mexico, <sup>88</sup>	Three amplicon sequence variants in <i>Prevotella 9</i> (26.4-fold enrichment) and <i>Veillonella</i> were significantly more abundant in responders. Limited by small sample.	★ Advanced laboratory techniques required; expertise needed; significant barriers to implementation	
Zhang et al. (2021), China, <sup>77</sup>	Fermentation index 'A' positively associated with response in the low FODMAP diet group. Higher abundance of <i>Bacteroides</i> at baseline observed in responders ( $p<0.01$ ). Limited application for IBS-C and IBS-M.	★ Advanced laboratory equipment required; significant barriers to implementation	

FBT: fructose breath test; FODMAP: fermentable oligosaccharide, disaccharide, monosaccharide and polyol; FS: fecal supernatant; GSRS-IBS: gastrointestinal symptom rating scale irritable bowel syndrome; IBS-D: irritable bowel syndrome diarrhoea subtype; IBS-M: irritable bowel syndrome mixed subtype; IBS-C: irritable bowel syndrome constipation subtype; IBS-SSS: irritable bowel syndrome symptom severity score; HADS: hospital anxiety and depression scale; NCT: nutrient challenge test; RCT: randomized controlled trial; VOC: volatile organic compound.

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**Table 1.** Evidence summary and clinical applicability of trials utilizing predictors of response to the low FODMAP diet in IBS (cont.)

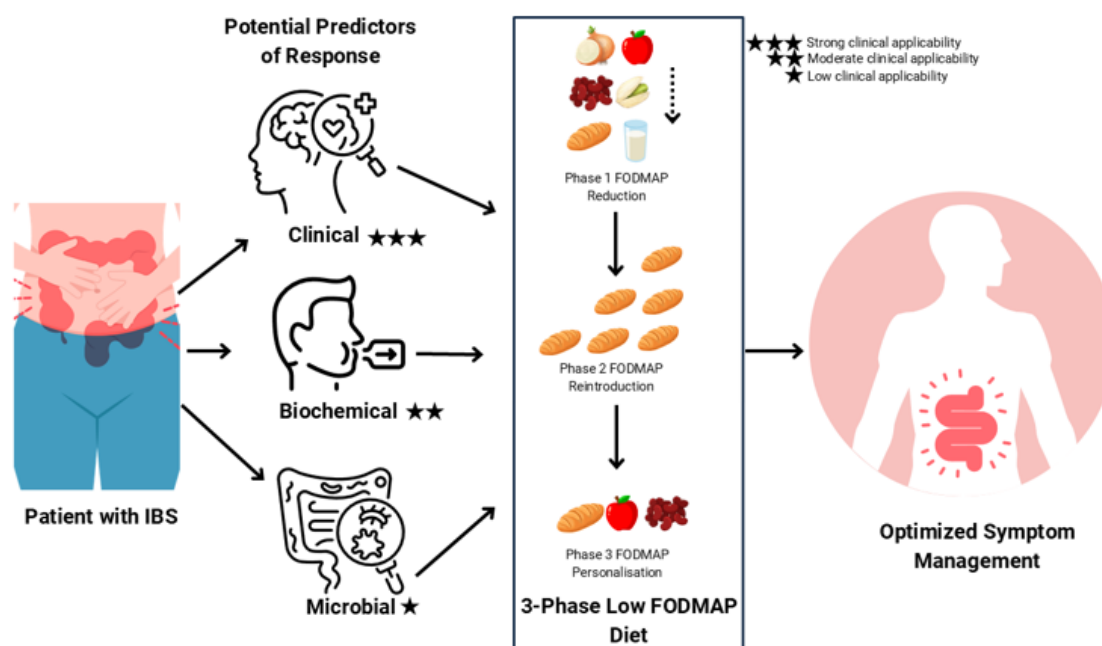
Author, year, country	Study design	Predictor and measurement	Intervention
<i>Microbial predictors</i>			
Vervier et al. (2022), United Kingdom, <sup>79</sup>	Prospective case-control; n=21, Rome IV IBS-D/M	Microbiota composition; IBS-SSS	4-week low FODMAP diet followed by 12-week reintroduction
Tuck et al. (2022), Canada, <sup>81</sup>	Prospective randomized cross-over trial; n=25, Rome IV	Neuroactive metabolites; IBS-SSS	High vs low FODMAP diet (3 weeks each)
Colomier et al (2022), Sweden, <sup>85</sup>	Secondary analysis of RCT; n=77, Rome III	Dysbiosis score (GA-map); GSRS-IBS	4-week low FODMAP diet or traditional dietary advice
Conley et al. (2024), United Kingdom, <sup>73</sup>	Secondary analysis of case-control; n=56, Rome IV IBS-D/M	Volatile organic compounds (VOCs) in stool; IBS-SSS	4-week low FODMAP diet

Author, year, country	Results and limitations	Clinical applicability*
<i>Microbial predictors</i>		
Vervier et al. (2022), United Kingdom, <sup>79</sup>	Participants with 'pathogenic' microbiome had more pronounced symptom response (IBS-SSS change of 194 vs 114, $p=0.02$ ). Limited by small sample size.	★ Advanced laboratory equipment required; significant barriers to implementation
Tuck et al. (2022), Canada, <sup>81</sup>	Faecal supernatant from responders showed reduced nociceptive afferent neuron excitability after the low FODMAP diet. Complex methodology with advanced equipment required.	★ Complex methodology and advanced equipment needed; results yet to be reproduced; significant barriers to implementation
Colomier et al (2022), Sweden, <sup>85</sup>	Lower dysbiosis index score associated with better response to both diets. Limited by small, underpowered sample.	★ Advanced laboratory equipment required; significant barriers to implementation
Conley et al. (2024), United Kingdom, <sup>73</sup>	IBS patients with 'pathological' VOC profile had significantly greater symptom improvement (56.9% vs 38.6% reduction in IBS-SSS, $p<0.05$ ). Limited sample size with 33% attrition during follow-up.	★ Advanced laboratory equipment needed; requires significant expertise; promising but preliminary evidence

FBT: fructose breath test; FODMAP: fermentable oligosaccharide, disaccharide, monosaccharide and polyol; FS: fecal supernatant; GSRS-IBS: gastrointestinal symptom rating scale irritable bowel syndrome; IBS-D: irritable bowel syndrome diarrhoea subtype; IBS-M: irritable bowel syndrome mixed subtype; IBS-C: irritable bowel syndrome constipation subtype; IBS-SSS: irritable bowel syndrome symptom severity score; HADS: hospital anxiety and depression scale; NCT: nutrient challenge test; RCT: randomized controlled trial; VOC: volatile organic compound.

Clinical Applicability Rating: ★★ = readily available in typical clinical settings, straightforward interpretation; ★★ = requires some specialized equipment but feasible in many settings; ★ = requires advanced laboratory techniques, significant expertise, or faces substantial implementation barriers.





Graphical abstract.

more abundant in responders,<sup>76,77</sup> yet also more abundant in non-responders,<sup>78</sup> despite the *Bacteroidetes* phylum being more depleted in some IBS participants, which was associated with a more marked symptom response.<sup>79</sup> Similar to VOCs, the lack of standardization across studies has led to a limited reproducibility of results in IBS participants.

Moreover, acute changes in dietary intake, environmental exposures, stress, medications, geographical location and habitual diet can influence the abundance of certain bacteria and functionality of the gut microbiota.<sup>80</sup> Nonetheless, gut microbiome testing may be relevant in the future. However, its application is currently limited in clinical practice. Other novel techniques have demonstrated that a reduction in FODMAP intake may modulate the production of luminal mediators influencing pain response to the diet, suggesting an additional factor that may predict response.<sup>81</sup>

While these studies provide valuable insights into potential predictors of response to the low FODMAP diet, significant heterogeneity in methodologies, outcome measures, and populations studied limits their immediate clinical application. The following section outlines the key gaps in current research that must be addressed to develop reliable predictors of response for routine clinical use.

### CURRENT GAPS IN PREDICTORS OF RESPONSE TO THE LOW FODMAP DIET

Despite the promising research, critical gaps remain in predicting response to the low FODMAP diet. Four key limitations must be addressed:

First, existing predictors lack validation in diverse, real-world populations and healthcare settings, particularly in the Asia-Pacific region where dietary patterns differ significantly from Western populations. The unique food cultures and dietary compositions in this region may influence both FODMAP intake patterns and responses to

dietary modification, yet most studies have been conducted in Western populations.

Second, current research focuses almost exclusively on predicting initial response (Phase 1), with virtually no data on predictors of successful reintroduction (Phase 2) or long-term management (Phase 3), which is the ultimate goal of dietary intervention. Identifying factors that predict successful food reintroduction and long-term diet personalization could significantly improve the clinical utility of the low FODMAP diet.

Third, proposed biological and microbial markers require specialized equipment and expertise unavailable in many clinical settings, limiting their practical utility. While breath hydrogen testing is more accessible than VOC analysis or microbiome profiling, all these methods face challenges in standardization, interpretation, and resource requirements.

Finally, few studies have attempted to develop integrated prediction models combining multiple factors (clinical, psychological, and biological) that could more accurately identify likely responders. Given the heterogeneous nature of IBS, a multifaceted approach to prediction may be necessary.

### FUTURE DIRECTIONS

Identifying reliable predictors for low FODMAP response would allow clinicians to target this resource-intensive intervention to patients most likely to benefit, improving both clinical outcomes and healthcare efficiency. Addressing these gaps requires several approaches:

Validating current biological and microbial data requires access to substantial and diverse patient numbers and funding for the analysis of participant samples. Wu et al.'s findings on brain responses to FODMAPs suggest that neuroimaging might eventually contribute to predicting treatment response, though practical implementation remains challenging.<sup>3</sup> Meanwhile, Biesiekierski et al.'s work on the paradox between exclusion and exposure

treatments highlights the need to incorporate psychological assessments into prediction models.<sup>26</sup>

A more immediately feasible strategy may be leveraging questionnaire-based data, which can be used to characterize patients and tailor management plans accordingly. Symptom-based scores, including severity and predominant symptom type (bloating, pain or bowel motions) may offer quick and accurate insight into whether dietary restriction is needed. Moreover, given the substantial overlap with psychological symptoms in IBS,<sup>23</sup> further exploration of psychological symptom severity may be useful to determine whether dietary intervention is likely to be effective, or if other management options are likely to be more efficacious.<sup>82</sup>

The heterogeneous, multi-factorial nature of this condition demands an individualized approach to dietary management that accounts for both physiological and psychological factors. Future research should focus on:

1. Developing and validating simple clinical tools that combine symptom profiles with psychological assessment
2. Conducting prospective studies examining predictors of success across all three phases of the diet
3. Investigating regional variations in diet response, particularly in Asia-Pacific populations
4. Integrating findings from physiological and psychological research to create comprehensive prediction models
5. Exploring the potential for stratified treatment approaches that match patients to the most appropriate intervention based on predictor profiles

By addressing these research priorities, we can move toward a more personalized approach to dietary management in IBS that optimizes outcomes while minimizing unnecessary dietary restriction.

## CONCLUSION

The low FODMAP diet remains a cornerstone in IBS management, yet implementation challenges and variable response rates highlight the need for reliable predictors of treatment success. Current evidence suggests readily available clinical measures—including symptom severity, psychological profiles, and predominant symptom patterns—hold the most immediate clinical promise. While biological markers and microbiome analysis offer potential for precision nutrition, their utility is currently limited by methodological heterogeneity and accessibility barriers.

A multimodal approach combining clinical, psychological, and biological markers may provide the most comprehensive predictive model, particularly relevant for Asia-Pacific populations with unique dietary patterns. Implementing such predictive tools would optimize resource allocation, improve outcomes, and minimize unnecessary dietary restriction. This personalized approach aligns with our understanding of IBS as a heterogeneous disorder requiring individualized management strategies addressing the complex interplay of physiological, psychological, and nutritional factors.

## CONFLICT OF INTEREST AND FUNDING DISCLOSURE

All authors declare nil conflicts of interest.

JRB is supported by an Australian National Health and Medical Research Council Emerging Leadership Fellowship (APP2025943).

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