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## **Innovations in IBS Treatment: From Gut-Brain Therapies to Microbiome Modulation**

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**Abstract**

Irritable Bowel Syndrome (IBS) is a chronic gastrointestinal disorder characterized by abdominal pain, bloating, and altered bowel habits. It affects a significant portion of the global population and often leads to a diminished quality of life. Despite its relatively high prevalence, the exact cause of IBS remains unclear, making effective treatment challenging. Traditional approaches, including dietary modifications, fiber supplements, and antispasmodic medications, have offered relief for some but not all patients. In recent years, new treatment strategies have emerged, targeting the underlying mechanisms believed to contribute to IBS. These include gut-brain axis therapies such as cognitive behavioural therapy (CBT) and

hypnotherapy, microbiome-based treatments like faecal microbiota transplantation (FMT) and targeted probiotics, and novel pharmacological agents aimed at modulating serotonin signalling and intestinal motility. Advances in personalized medicine are also playing a growing role, enabling clinicians to tailor treatments based on individual symptom profiles and microbiome composition. These developments represent a promising shift toward more effective and patient-centred management of IBS.

**Keywords:** IBS, gut-brain axis, fecal microbiota transplantation, cognitive behavioral therapy, chronic gastrointestinal disorders

## Introduction

Irritable Bowel Syndrome (IBS) is a prevalent functional gastrointestinal disorder, affecting approximately 10–15 % of adults in developed countries, with a global prevalence estimated between 7–15 % (Huang et al., 2023). Characterized by chronic or recurrent abdominal pain, bloating, and altered bowel habits (diarrhoea, constipation, or mixed), IBS significantly impairs quality of life and contributes to increased healthcare usage and productivity losses.

Although IBS does not cause structural damage, its pathophysiology is complex and multifactorial. Emerging evidence suggests that dysregulation of the gut-brain axis, visceral hypersensitivity, motility disturbances, low-grade inflammation, and alterations in gut microbiota (dysbiosis) are particularly implicated (Shaikh et al., 2023). Psychological stress, early-life events, post-infectious changes, and genetic predisposition further contribute to symptom onset and severity by perturbing the enteric nervous system and immune responses (Hassan et al., 2024).

Traditional management of IBS has focused on symptom relief through dietary modification, fiber supplements, antispasmodics, laxatives, antidiarrheals, and neuromodulators. While these strategies may alleviate discomfort, they often fail to address underlying pathophysiological mechanisms. Recent innovations are shifting toward therapies

that specifically target the gut microbiota—such as probiotics, faecal microbiota transplantation (FMT), and antibiotics like rifaximin—as well as mind-body interventions (e.g., cognitive behavioural therapy, hypnotherapy), and agents that regulate serotonin signalling and intestinal motility.

This evolving landscape underscores a movement toward personalized, mechanistic approaches in IBS care—integrating microbiome science, brain-gut interactions, and individual symptom profiling—to improve outcomes and quality of life for affected individuals.

## **Epidemiology of Irritable Bowel Syndrome**

Irritable Bowel Syndrome (IBS) affects approximately 10-15% of the global population, though prevalence varies by region and diagnostic criteria (Canavan et al., 2014; Lovell et al., 2012). Epidemiological data consistently show a higher prevalence in women, with a female-to-male ratio estimated between 2:1 and 2.5:1, and symptom onset typically occurs during early adulthood but can affect all age groups (Lovell et al., 2012). IBS imposes a significant public health burden due to impaired quality of life, frequent healthcare utilization, and economic costs related to work absenteeism and decreased productivity (Chey et al., 2015). Variations in prevalence between countries are influenced by dietary patterns, cultural factors, socioeconomic status, and healthcare access (Mearin et al., 2016). Psychological factors such as anxiety and depression are commonly comorbid with IBS and contribute to symptom severity, reinforcing the multifactorial biopsychosocial model of the disorder (Fond et al., 2014). Despite its prevalence, IBS is frequently underdiagnosed or misdiagnosed, highlighting the importance of standardized diagnostic criteria and increased clinician awareness for effective management. Research suggests that about 30% to 50% of IBS cases are either misdiagnosed or underdiagnosed (Chey et al., 2015).

## **Pathogenesis of IBS**

Irritable Bowel Syndrome is increasingly understood as a complex, multifactorial disorder arising from the intricate interplay between genetic, immunological, neuroendocrine, microbial and environmental factors (Videlock et al., 2021; Shaikh et al., 2023).

## **1. Gut–Brain Axis Dysfunction**

The core of Irritable Bowel Syndrome (IBS) is the dysfunction of the bidirectional gut–brain axis. This axis encompasses neural pathways (comprising both the central and enteric nervous systems), endocrine pathways (illustrated by the hypothalamic–pituitary–adrenal axis), and immune pathways (Sun et al., 2023). Perturbations in stress responsiveness, impaired visceral sensory processing, and autonomic imbalance have been demonstrated to contribute significantly to the generation of symptoms. These dysfunctions can result in visceral hypersensitivity and altered gut motility.

## **2. Visceral Hypersensitivity & Motility Disturbances**

Visceral hypersensitivity—heightened gut pain perception to normal stimuli—is a hallmark of IBS. It is driven by the sensitization of enteric neurons and spinal pathways, often mediated by immune-derived mediators such as prostaglandin E<sub>2</sub> and neurotransmitters serotonin (5-HT), substance P, and nitric oxide (Shaikh et al., 2023). Disruptions in serotonin signalling, including altered expression of transporters and receptors (e.g. 5-HT<sub>3</sub>, 5-HT<sub>4</sub>, 5-HT<sub>7</sub>), affect gut motility and secretion, contributing to diarrhoea or constipation phenotypes (Videlock et al., 2021).

## **3. Low-Grade Inflammation & Immune Activation**

Many patients suffering from IBS exhibit symptoms of mucosal inflammation, increased mast cell activation, elevated pro-inflammatory cytokines (e.g. IL-6, IL-8), and increased intestinal permeability ("leaky gut"). Post-infectious IBS (PI-IBS) is a paradigm of this process, with gastrointestinal infections acting as a trigger for persistent immune-inflammatory changes and barrier dysfunction (Ionescu et al., 2024).

## **4. Microbiome Dysbiosis**

Alterations in gut microbial composition, including reduced beneficial anaerobes and overgrowth of pathobionts (e.g. *Pseudomonas*, *Enterobacteriaceae*), have been repeatedly observed in IBS (Aggeletopoulou et al., 2024). Dysbiosis affects gut–brain signalling via microbial metabolites (e.g. short-chain fatty acids), activation of toll-like receptors, mast cell degranulation, and modulation of enteric nervous system (ENS) signalling (Aggeletopoulou et al., 2024). This process perpetuates inflammation, barrier breakdown, and hypersensitivity.

## 5. Genetic and Environmental Influences

Genetic variants—such as mutations in genes governing ion channels (e.g. SCN5A) or immune responses (e.g. TNFSF15)—have been implicated in IBS susceptibility. Environmental stressors including early-life trauma, psychological stress, dietary patterns (e.g. FODMAP intake), and antibiotic exposure also modulate gut function, barrier integrity, microbiota, and stress-response systems (Quigley et al., 2018).

## Intestinal and extraintestinal symptoms of IBS

Core digestive symptoms include lower abdominal cramping, bloating, excessive gas, urgency, a sensation of incomplete evacuation, and stool irregularities such as loose, hard, or mucous-laden stools (Ikechi et al., 2017). Non-digestive, extraintestinal manifestations are common, with approximately 50% of patients reporting fatigue, sleep disturbances, chronic somatic pain, headaches, backache, and genitourinary symptoms such as urinary frequency and pelvic pain (Whitehead et al., 2002). Psychological comorbidities—namely anxiety and depression—affect over half of IBS sufferers, often exacerbating gastrointestinal symptoms through the gut-brain axis. Additionally, many patients experience food sensitivities, particularly to high-FODMAP items, which can trigger or worsen symptoms.

## Diagnosis of IBS

The diagnosis of Irritable Bowel Syndrome (IBS) is primarily clinical in nature, relying on a set of standardised symptom-based criteria due to the absence of definitive biomarkers. The Rome IV criteria, delineated in table 1, currently serve as the gold standard, defining IBS by recurrent abdominal pain occurring at least one day per week over the past three months, associated with changes in stool frequency or form (Drossman et al., 2016).

Diagnosis requires the exclusion of organic pathologies through thorough history-taking, physical examination, and targeted investigations tailored to clinical presentation, such as complete blood counts, inflammatory markers (e.g., C-reactive protein, faecal calprotectin), and celiac serology. Colonoscopy may be indicated in patients with alarm features or those over 50 years to rule out malignancy or inflammatory bowel disease.

Emerging diagnostic tools include microbiome profiling and volatile organic compound analysis, which show promise but require further validation. Despite advances, the heterogeneity of IBS symptoms necessitates a personalized diagnostic approach balancing thoroughness and cost-effectiveness to optimize patient outcomes (Drossman et al., 2016).

Recurrent abdominal pain on average at least **1 day/week** in the last **3 months**, associated with two or more of the following criteria:

**Related to defecation**

**Associated with a change in frequency of stool**

**Associated with a change in form of stool**

Criteria fulfilled for the last 3 months with symptom onset at least **6 months** prior to diagnosis

IBS subtypes	Criteria	Alternative for epidemiology or clinical practice
<b>IBS with predominant constipation (IBS-C)</b>	<ul style="list-style-type: none"> <li>25% of bowel movements with Bristol stool types 1 or 2 and</li> <li>&lt;25% of bowel movements with Bristol stool types 6 or 7</li> </ul>	abnormal bowel movements are usually constipation
<b>IBS with predominant diarrhea (IBS-D)</b>	<ul style="list-style-type: none"> <li>25% of bowel movements with Bristol stool types 6 or 7 and</li> <li>&lt; 25% of bowel movements with Bristol stool types 1 or 2</li> </ul>	abnormal bowel movements are usually diarrhea
<b>IBS with mixed bowel habits (IBS-M)</b>	<ul style="list-style-type: none"> <li>25% of bowel movements with Bristol stool types 1 or 2 and</li> <li>&gt; 25% of bowel movements with Bristol stool types 6 or 7</li> </ul>	abnormal bowel movements are usually both constipation and diarrhea (more than $\frac{1}{4}$ were constipation and more than $\frac{1}{4}$ were diarrhea)
<b>IBS Unclassified (IBS-U)</b>	<ul style="list-style-type: none"> <li>meeting diagnostic criteria for IBS</li> <li>bowel habits cannot be accurately categorized into 1 of the 3 groups</li> </ul>	abnormal stools (both diarrhea and constipation) are rare

**Table 1. The Rome IV criteria for IBS subtypes (Drossman et al., 2016).**

### Treatment approach of IBS

Pharmacological treatment primarily targets predominant symptoms, with antispasmodics such as hyoscine and peppermint oil commonly used to alleviate abdominal

cramping. For IBS with predominant diarrhoea (IBS-D), agents like loperamide reduce stool frequency, whereas, for IBS with predominant constipation (IBS-C), laxatives including polyethylene glycol and newer prosecretory agents such as lubiprostone and linaclotide enhance bowel motility and secretion (Ford et al., 2017; Lacy et al., 2016). Additionally, serotonin receptor modulators like alosetron, a 5-HT3 antagonist, have shown efficacy in IBS-D by modulating gut motility and visceral sensitivity but require cautious use due to potential adverse effects (Camilleri et al., 2009).

Beyond symptomatic relief, modulation of the gut-brain axis through psychological interventions has gained prominence. Cognitive Behavioral Therapy (CBT) has demonstrated robust efficacy in reducing IBS symptom severity and improving quality of life, likely by targeting maladaptive thought patterns and stress-related visceral hypersensitivity (Lackner et al., 2013). Gut-directed hypnotherapy similarly shows promise in attenuating abdominal pain and bowel dysfunction through central modulation of pain perception and autonomic regulation (Miller et al., 2009). Furthermore, antidepressants, particularly low-dose tricyclic antidepressants (e.g., amitriptyline) and selective serotonin reuptake inhibitors (SSRIs), serve dual roles in managing comorbid psychological symptoms and modulating visceral pain pathways (Ford et al., 2017).

Emerging treatments targeting gut microbiota, including rifaximin, a nonabsorbable antibiotic, have demonstrated benefit primarily in IBS-D by reducing bacterial overgrowth and associated inflammation (Pimentel et al., 2011). Probiotics also hold the potential for symptom improvement, though the evidence remains heterogeneous regarding optimal strains and formulations.

Another promising treatment is faecal Microbiota Transplantation (FMT). It is the process of transferring stool from healthy donors to IBS patients, aiming to restore microbial diversity and improve symptoms. Clinical studies have demonstrated variable efficacy, with some reporting significant symptom relief, especially in diarrhoea-predominant IBS (IBS-D) patients, while others show limited benefits, underscoring the influence of donor microbiota composition, delivery methods, and patient heterogeneity (Shaikh et al., 2023; Aggeletopoulou & Triantos, 2024). Safety data indicate FMT is generally well tolerated, but standardized protocols and long-term safety assessments remain necessary (Shaikh et al., 2023). Despite these challenges, FMT represents a promising biological therapy targeting the microbiome, offering the potential for personalized treatment strategies in IBS management.

In summary, IBS management requires a multidisciplinary approach combining symptom-targeted pharmacotherapy with psychological and microbiota-modulating interventions. Personalized treatment plans that consider symptom predominance, psychological comorbidities, and patient preferences are essential for optimizing outcomes.

Therapy	Core Components	Delivery	Clinical Efficacy	Key Benefits	Limitations
<b>Cognitive Behavioral Therapy (CBT)</b>	Cognitive restructuring, behavioral experiments, symptom education	In-person, online, app-based	50–70% symptom improvement ; durable at 6–12 months	Strongest evidence base; customizable; effective even in refractory IBS	Requires trained therapist; may be time-intensive
<b>Gut-Directed Hypnotherapy</b>	Guided imagery focusing on gut function and relaxation	In-person or audio-guided	~70% symptom response in some cohorts	Long-lasting effects; useful for treatment-resistant IBS	Limited access; lower evidence for non-constipation IBS
<b>Mindfulness-Based Stress Reduction (MBSR)</b>	Meditation, yoga, body awareness, non-judgmental attention to symptoms	Group sessions, online	30–50% symptom improvement	Improves anxiety, stress, and pain tolerance	Less effective as monotherapy for severe IBS
<b>Interpersonal or Psychodynamic Therapy</b>	Addressing emotional conflict and relationships	In-person psychotherapy	Variable; not first-line	May help in trauma-related IBS or comorbid mood disorders	Not IBS-specific
<b>Digital CBT</b>	Self-guided CBT with therapist or AI support	App or web-based	Comparable to in-person CBT in some trials	Convenient; scalable; lower cost	Engagement and adherence can be issues

**Table 2. Comparison of gut–brain therapies.** Author's own elaboration based on a review of the relevant literature (Ford et al., 2019; Laird et al., 2016; Lindfors et al., 2012)

## Discussion

Emerging treatments targeting gut microbiota, including rifaximin, a nonabsorbable antibiotic, have demonstrated benefit primarily in IBS-D by reducing bacterial overgrowth and associated inflammation (Pimentel et al., 2011), which supports the hypothesis that microbial dysbiosis contributes to disease pathogenesis. Probiotics and prebiotics, though still under investigation, hold the potential for long-term modulation of gut flora to improve symptoms sustainably, though the evidence remains heterogeneous regarding optimal strains and formulations.

Another promising treatment is Faecal Microbiota Transplantation (FMT). It is the process of transferring stool from healthy donors to IBS patients, aiming to restore microbial diversity and improve symptoms. Clinical studies have demonstrated variable efficacy, with some reporting significant symptom relief, especially in diarrhoea-predominant IBS (IBS-D) patients, while others show limited benefits, underscoring the influence of donor micrThe multifactorial and heterogeneous nature of Irritable Bowel Syndrome (IBS) presents significant challenges in devising universally effective treatments. Pharmacological interventions remain foundational, targeting predominant symptoms such as abdominal pain, diarrhoea, or constipation. Agents like antispasmodics and serotonin receptor modulators provide symptomatic relief by directly affecting gastrointestinal motility and visceral sensitivity. However, their efficacy varies widely among patients, and adverse effects—particularly with medications like alosetron—necessitate careful patient selection and monitoring.

Psychological therapies, including cognitive behavioural therapy (CBT) and gut-directed hypnotherapy, have gained increased recognition for their role in modulating the gut-brain axis, a critical component in IBS pathophysiology. These approaches not only alleviate gastrointestinal symptoms but also address the psychosocial distress that often exacerbates IBS manifestations. The integration of psychological treatments highlights the importance of a biopsychosocial model of care, moving beyond symptom suppression toward holistic patient well-being.

Despite advances, the complexity of IBS underscores the necessity of individualized treatment plans that consider symptom severity, subtype, psychological factors, and patient

preferences. Multidisciplinary collaboration among gastroenterologists, psychologists, dietitians, and primary care providers is essential to optimize outcomes. Future research should continue to explore novel biomarkers and therapeutic targets, aiming to personalize interventions and improve both short- and long-term quality of life for IBS patients.

Biota composition, delivery methods, and patient heterogeneity (Shaikh et al., 2023; Aggeletopoulou & Triantos, 2024). Safety data indicate FMT is generally well tolerated, but standardized protocols and long-term safety assessments remain necessary (Shaikh et al., 2023). Despite these challenges, FMT represents a promising biological therapy targeting the microbiome, offering the potential for personalized treatment strategies in IBS management.

In summary, IBS management requires a multidisciplinary approach combining symptom-targeted pharmacotherapy with psychological and microbiota-modulating interventions. Personalized treatment plans that consider symptom predominance, psychological comorbidities, and patient preferences are essential for optimizing outcomes.

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