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The Role of the Gut-Brain Axis in the Pathogenesis and Treatment of Irritable Bowel Syndrome in Children and Adolescents: A Review of Current Research with Focus on Dietary and Psychoneurogastroenterological Interventions

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ABSTRACT
Background. Irritable bowel syndrome (IBS) is a prevalent disorder of gut-brain interaction (DGBI) affecting 5-20% of children worldwide, with the microbiota-gut-brain axis (MGBA) playing a central pathophysiological role [7, 8, 21].
Aim. This narrative review evaluates MGBA-targeted therapeutic interventions in pediatric IBS.
Materials and methods. A systematic search of PubMed/MEDLINE (2021-2025) following PRISMA guidelines identified 31 eligible studies from 45 initially screened articles.
Results. Pediatric IBS pathophysiology involves intestinal dysmotility, visceral hypersensitivity, dysbiosis, and altered central processing of visceral signals [14, 15, 26]. The low-FODMAP diet has demonstrated efficacy in adults; however, pediatric evidence remains limited to five randomized trials with inconsistent results [25]. Probiotic supplementation with Lactobacillus rhamnosus GG and Limosilactobacillus reuteri DSM 17938 shows strain-specific efficacy [3, 4]. Cognitive-behavioral therapy and gut-directed hypnotherapy effectively target central signal processing [5, 21]. Pharmacological options, including neuromodulators, remain understudied in pediatric populations, with off-label use predominating [2, 12]. Psychological comorbidities, particularly anxiety and depression, significantly influence treatment response [1, 18].
Conclusions. The MGBA represents the primary therapeutic target in pediatric IBS, supporting multimodal approaches, but limitations in pediatric-specific evidence suggest the need for high-quality randomized controlled trials with standardized outcome measures and adequate long-term follow-up [6, 31].

Key words: irritable bowel syndrome; pediatric; microbiota-gut-brain axis; functional abdominal pain; disorders of gut-brain interaction; dietary interventions; probiotics; cognitive-behavioral therapy

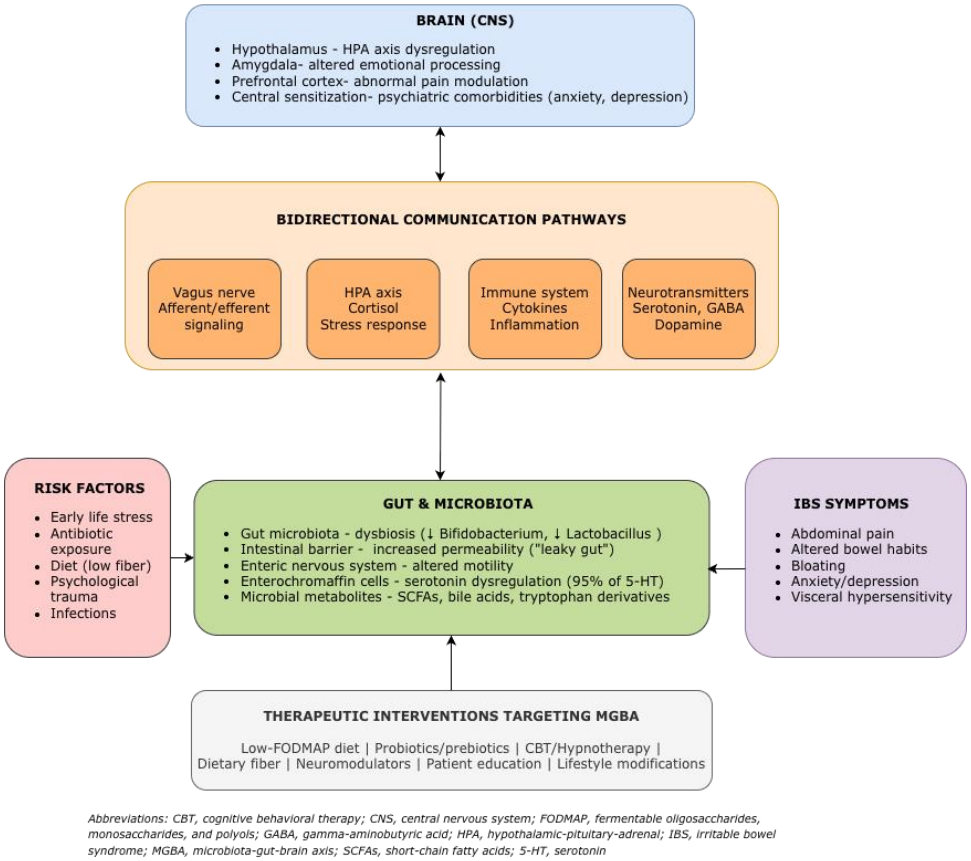
1. Introduction

Irritable bowel syndrome (IBS) is one of the most prevalent functional gastrointestinal disorders in the pediatric population worldwide, affecting approximately 5-20% of children and adolescents [7, 8, 21]. According to the Rome IV classification, pediatric IBS is now categorized within disorders of gut-brain interaction (DGBI), reflecting the bidirectional communication between the gastrointestinal tract and the central nervous system [6, 21]. The condition manifests as recurrent abdominal pain associated with altered bowel habits,

occurring without identifiable organic pathology, and significantly impacts quality of life, school attendance, and family functioning [1, 18].

The pathophysiology of pediatric IBS remains incompletely understood, yet multiple contributing mechanisms have been identified. Key factors include disordered intestinal motility, visceral hypersensitivity, low-grade mucosal inflammation, and alterations in gut microbiome composition [21, 26]. The microbiota-gut-brain axis (MGBA) has emerged as a central conceptual framework integrating these mechanisms. This bidirectional network encompasses the enteric nervous system, autonomic pathways, the hypothalamic-pituitary-adrenal axis, and the intestinal microbiota, all continuously exchanging signals that influence both digestive function and central nervous system activity [14, 21].

Figure 1. Schematic representation of the microbiota-gut-brain axis in pediatric irritable bowel syndrome



Abbreviations: CBT, cognitive behavioral therapy; CNS, central nervous system; FODMAP, fermentable oligosaccharides, monosaccharides, and polyols; GABA, gamma-aminobutyric acid; HPA, hypothalamic-pituitary-adrenal; IBS, irritable bowel syndrome; MGBA, microbiota-gut-brain axis; SCFAs, short-chain fatty acids; 5-HT, serotonin

Figure 1. Schematic representation of the microbiota-gut-brain axis in pediatric irritable bowel syndrome

IBS symptoms arise from altered interactions within this axis, affecting bowel habits, chronic pain perception, and psychiatric comorbidities [14, 26]. Intestinal dysbiosis is present in pediatric IBS cohorts, though no uniform microbial pattern has been consistently established [15]. Psychological comorbidities, particularly anxiety and depression, occur at elevated rates among affected children and substantially influence symptom severity and treatment response [1, 18]. Early-life factors, including mode of delivery, breastfeeding, and antibiotic exposure, further shape the developing MGBA and may contribute to IBS susceptibility [13, 29].

Current therapeutic strategies increasingly target the MGBA at multiple levels. Dietary interventions, particularly low-FODMAP restriction, have gained prominence as first-line approaches, though evidence remains limited to five pediatric randomized controlled trials with inconsistent results [25]. Probiotic supplementation represents another microbiome-

targeted intervention with strain-specific efficacy demonstrated for Lactobacillus rhamnosus GG and Limosilactobacillus reuteri DSM 17938 [3, 4]. Psychological interventions, including cognitive-behavioral therapy and gut-directed hypnotherapy, have shown substantial efficacy by targeting the central processing of visceral signals [5, 21]. Pharmacological management, including the use of neuromodulators, remains largely based on adult evidence, with limited pediatric-specific data available [2, 12, 31].

Despite growing recognition of the MGBA's role in pediatric IBS, comprehensive reviews synthesizing dietary, probiotic, psychoneurogastroenterological, and pharmacological interventions specifically in children remain limited. This is further underscored by the recent publication of the first joint ESPGHAN/NASPGHAN guidelines for pediatric IBS [31].

Research Objective. To evaluate current evidence regarding the pathophysiological role of the microbiota-gut-brain axis in pediatric IBS and to critically appraise therapeutic interventions targeting this axis.

Research Problems. What is the current evidence base for MGBA-targeted interventions in pediatric IBS? Which therapeutic approaches demonstrate sufficient efficacy and safety in children and adolescents? What gaps remain in pediatric-specific evidence?

Research Hypotheses. The MGBA plays a central pathophysiological role in pediatric IBS, and multimodal therapeutic approaches targeting this axis at multiple levels are more effective than single-modality interventions.

2. Materials and methods

2.1. Search Strategy and Information Sources

This narrative review followed the PRISMA 2020 guidelines, tailored for narrative syntheses. A thorough literature search was carried out in the PubMed/MEDLINE database from January 2021 to December 2025. The search strategy used Medical Subject Headings (MeSH) terms and keywords connected with Boolean operators (AND/OR). Terms included: primary: "irritable bowel syndrome" AND ("children" OR "pediatric" OR "adolescents"); axis-related: "gut-brain axis" OR "microbiota-gut-brain axis" OR "brain-gut interaction"; pathophysiology: "gut microbiome" OR "intestinal microbiota" OR "dysbiosis"; therapeutic: "low FODMAP diet" OR "probiotics" OR "psychotherapy" OR "cognitive behavioral therapy" OR "hypnotherapy" OR "neuromodulators" OR "tricyclic antidepressants".

2.2. Eligibility Criteria

Studies qualified for inclusion if they met these conditions:

population - children and adolescents aged 0-18 years with irritable bowel syndrome (IBS) or functional abdominal pain disorders (FAPDs);

diagnosis - IBS per Rome IV criteria, requiring recurrent abdominal pain at least once weekly on average over the prior 3 months, linked to at least two of the following: defecation-related, altered stool frequency, or changed stool form [6, 21];

focus - investigations of the microbiota-gut-brain axis (MGBA), pathophysiology, or treatments in pediatric IBS, including pharmacological interventions and neuromodulators;

design - randomized controlled trials, systematic reviews, meta-analyses, narrative reviews, clinical guidelines, or observational studies;

language - English;

dates - January 2021 to December 2025.

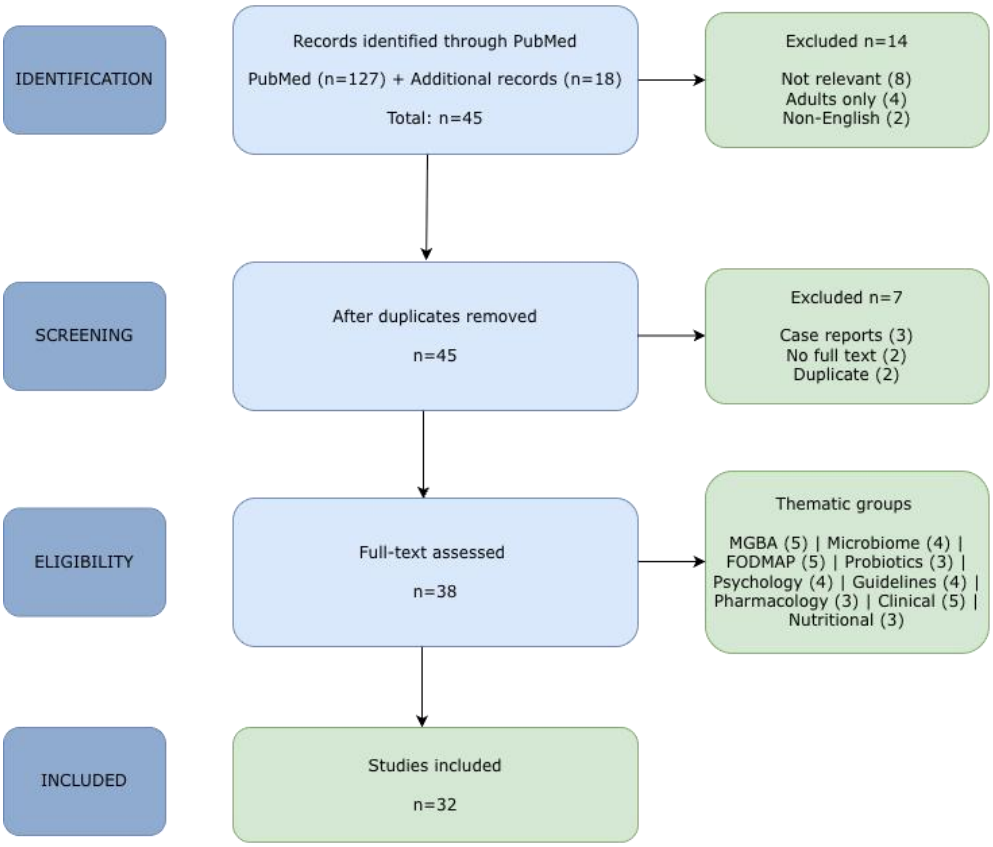
Excluded were studies solely on adults, case reports with fewer than 5 cases, conference abstracts lacking full texts, and studies on organic gastrointestinal conditions without functional disorder links.

2.3. Study Selection and Data Extraction

The preliminary search identified 45 potentially eligible articles. After screening titles and abstracts, removing duplicates, and evaluating full texts, 31 articles were retained. These were selected for their pertinence to the gut-brain axis in pediatric IBS, innovative insights, and

pediatric emphasis. Studies included in the final analysis were verified to focus primarily on pediatric populations; sources addressing adult populations only were excluded, consistent with the stated eligibility criteria.

Figure 2. PRISMA flow diagram of study selection process



PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; IBS, irritable bowel syndrome; MGBA, microbiota-gut-brain axis; FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols

Figure 2. PRISMA flow diagram of study selection process

2.4. Thematic Grouping of Included Studies

Included articles were classified into the following themes:

Pathophysiology of the microbiota-gut-brain axis (n=5): explorations of bidirectional gut-brain signaling mechanisms, encompassing vagus nerve, enteric nervous system, short-chain fatty acids, and neurotransmitter influences [13, 14, 15, 26, 29].

Gut microbiome changes in pediatric IBS (n=4): analyses of dysbiosis profiles, microbial composition, and symptom associations in children [3, 15, 28, 29].

Dietary approaches -- low FODMAP (n=5): trials and reviews examining fermentable oligosaccharide, disaccharide, monosaccharide, and polyol restriction efficacy in pediatric IBS [16, 19, 20, 22, 25].

Probiotics, prebiotics, synbiotics (n=3): evaluations of microbial intervention benefits [3, 4, 28].

Psychological factors and psychosocial therapies (n=4): examinations of anxiety, depression, cognitive behavioral therapy, and hypnotherapy in pediatric IBS [1, 5, 18, 30].

Pharmacological management and neuromodulators (n=3): reviews of pharmacological options including antispasmodics, neuromodulators, and off-label agents in children [2, 12, 31].

Guidelines and diagnostics (n=4): global and national consensus documents and Rome IV implementations for children [6, 21, 31, 10].
Clinical characteristics and comorbidities (n=5): studies on healthcare utilization, eating disorder overlap, sleep disturbances, and patient characteristics [7, 8, 11, 17, 23].
Nutritional approaches beyond FODMAP (n=3): fiber supplementation, herbal medicines, and general nutritional guidance [9, 19, 24].

Table 1. Study characteristics

No.	Author(s), Year	Country	Study Type	Population	Main Focus	Key Findings
A. PATHOPHYSIOLOGY OF THE MICROBIOTA-GUT-BRAIN AXIS (n=5)						
1	Margolis K et al., 2021	USA	Review	Both	MGBA mechanisms – motility to mood	Bidirectional gut-CNS communication; serotonin key in both GI and brain function
2	Tang H et al., 2021	China	Narrative review	Both	GBA pathophysiology in IBS	HPA axis dysregulation and altered gut permeability contribute to IBS symptoms
3	Marano G et al., 2025	Italy	Review	Pediatric	Pediatric MGBA and neuropsychiatric development	Early microbiome disruption affects neurodevelopment; microbiome-targeted interventions promising
4	Zhou G et al., 2023	China	Review	Both	Early life adverse exposures in IBS	Childhood trauma and stress alter MGBA development, increasing IBS risk
5	Willits A et al., 2021	USA	Original research	Pediatric	Gene expression in pediatric RAP	Pain-specific gene expression profile identified in children with recurrent abdominal pain
B. GUT MICROBIOME IN PEDIATRIC IBS (n=4)						
6	McHarg A et al., 2022	Australia	Review	Pediatric	Gut microbiome in pediatric IBS	Dysbiosis in pediatric IBS; no uniform pattern; potential therapeutic target
7	Zhao Y et al., 2024	China	Review	Both	Microbiome and IBS therapeutics	Microbiome modulation through diet, probiotics, and FMT shows promise
8	Bosi A et al., 2025	Italy	Original research	Animal model	Antibiotic-induced dysbiosis in juvenile mice	Sex-dependent effects of dysbiosis; Lactobacillus rhamnosus GG protective
9	Zhou G et al., 2023	China	Review	Both	Early life adverse exposures	Childhood exposures program MGBA; opportunities for early intervention
C. LOW-FODMAP DIET (n=5)						
10	Stróżyk A et al., 2021	Poland	Systematic review	Pediatric	Low-FODMAP in pediatric FAPD	Only 5 RCTs; inconsistent results; insufficient evidence in children
11	Rhys-Jones D et al., 2022	Australia	Review	Pediatric	FODMAP diet in pediatric setting	Practical guidance for FODMAP implementation; dietitian involvement essential
12	Raja S et al., 2025	USA	Original research	Pediatric	Low-FODMAP efficacy in pediatric DGBI	Limited but emerging evidence for low-FODMAP in children with DGBI
13	Morariu I et al., 2023	Romania	Narrative review	Both	Low-FODMAP in children and adults	Effective in both populations; reintroduction phase crucial
14	Jasiuk I et al., 2024	Poland	Literature review	Both	Current knowledge on IBS treatment	Comprehensive overview including dietary management; gut-brain axis central to IBS
D. PROBIOTICS, PREBIOTICS, AND FIBER (n=3)						
15	Capozza M et al., 2022	Italy	Narrative review	Pediatric	Probiotics in pediatric FGIDs	Strain-specific effects; LGG and L. reuteri most studied in children
16	Salvatore S et al., 2023	Italy	Practical guide	Pediatric	Dietary fibers in pediatric GI disorders	Fiber supplementation beneficial; type and dose must be individualized
17	Hojsak I et al., 2022	Croatia	Review	Pediatric	Dietary fiber benefits in children	Adequate fiber intake supports gut health; specific recommendations for pediatric IBS
E. PSYCHOLOGICAL ASPECTS AND INTERVENTIONS (n=4)						
18	Pop D et al., 2025	Romania	Narrative review	Pediatric	Anxiety and depression in pediatric IBS	High comorbidity; bidirectional relationship requires integrated treatment
19	Al-Beltagi M et al., 2025	Egypt	Review	Pediatric	Psychosocial dimensions of pediatric FGIDs	Family dynamics, school stress, coping strategies influence symptom severity
20	Chakraborty P et al., 2023	USA	Review	Pediatric	Non-pharmacologic treatment of pediatric FAP	CBT, hypnotherapy, yoga effective; multimodal approach recommended; 96% use complementary therapy
21	Zia J et al., 2022	USA	Systematic review	Both	Risk factors for AP-related DGBI	Psychological factors, early life events, family history as key risk factors
F. PHARMACOLOGICAL MANAGEMENT AND NEUROMODULATORS (n=3)						
22	Alyasi A et al., 2023	Saudi Arabia	Review	Pediatric	Pharmacological management of pediatric IBS	Limited evidence; antispasmodics and neuromodulators (TCAs) commonly used off-label
23	Lebowitz JC et al., 2026	USA	Review	Pediatric	Management strategies for pediatric IBS	Comprehensive review including neuromodulators, linaclotide, PENFS; biopsychosocial approach
24	Groen J et al., 2025	International	Clinical guidelines	Pediatric	ESPGHAN/NASPGHAN guidelines pediatric IBS	First joint international guidelines; stepwise algorithm; shared decision-making model
G. GUIDELINES AND DIAGNOSTICS (n=4)						
25	Di Nardo G et al., 2024	Italy	Clinical guidelines	Pediatric	Italian guidelines for pediatric IBS	Comprehensive recommendations based on Rome IV; positive diagnostic approach
26	Rexwinkel R et al., 2022	Netherlands	Therapeutic guide	Pediatric	Pediatric IBS and FAP-NOS treatment	Practical recommendations for psychological and behavioral interventions
27	Huang K et al., 2023	China	Review	Both	IBS epidemiology, pathophysiology and treatment	Comprehensive overview including epidemiology, overlap disorders, and management
28	Kim H, 2022	South Korea	Original research	Pediatric	Sleep quality in pediatric FAP	Poor sleep associated with increased symptom severity; bidirectional relationship
H. CLINICAL CHARACTERISTICS AND COMORBIDITIES (n=5)						
29	Ganzevoort I et al., 2025	Netherlands	Original research	Pediatric	DGBI: primary care vs hospital	Differences in severity and comorbidity profiles between care settings
30	Hogervorst E et al., 2024	Netherlands	Original research	Pediatric	IBS in children in primary care	Prevalence and characteristics of pediatric IBS in primary care
31	Murray H et al., 2021	USA	Original research	Both	DGBI in eating disorders	High prevalence of IBS symptoms in eating disorders including ARFID
32	Rurgo S et al., 2024	Italy	Original research	Pediatric	DGBI and anorexia nervosa	High prevalence of Rome IV-defined DGBI in pediatric anorexia nervosa
I. NUTRITIONAL APPROACHES BEYOND FODMAP (n=3)						
33	Pop D et al., 2023	Romania	Narrative review	Pediatric	Fibers, herbs, spices in pediatric IBS	Peppermint oil and specific fibers show promise; limited pediatric evidence
34	Salvatore S et al., 2023	Italy	Practical guide	Pediatric	Dietary fibers in pediatric GI disorders	Fiber supplementation; type and dose must be individualized
35	Hojsak I et al., 2022	Croatia	Review	Pediatric	Dietary fiber benefits for children	Adequate fiber intake supports gut health in children with IBS

Abbreviations: AP, abdominal pain; ARFID, avoidant/restrictive food intake disorder; CBT, cognitive behavioral therapy; CNS, central nervous system; DGBI, disorders of gut-brain interaction; FAP, functional abdominal pain; FAPD, functional abdominal pain disorders; FGIDs, functional gastrointestinal disorders; FMT, fecal microbiota transplantation; FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; GBA, gut-brain axis; GI, gastrointestinal; HPA, hypothalamic-pituitary-adrenal; IBS, irritable bowel syndrome; LGG, Lactobacillus rhamnosus GG; MGBA, microbiota-gut-brain axis; RAP, recurrent abdominal pain; RCT, randomized controlled trial; TCAs, tricyclic antidepressants.

Table 1. Study characteristics

2.5. Quality Assessment

The methodological quality of randomized controlled trials was evaluated using the Cochrane Risk of Bias 2 (RoB 2) tool [25]. Systematic reviews underwent AMSTAR-2 appraisal [25, 30]. Narrative reviews and guidelines were assessed for PRISMA compliance and AGREE II standards, respectively [6, 31].

2.6. Data collection and analysis

2.6.1. Statistical analysis.

As this work constitutes a narrative review, no primary data were collected, and no statistical analyses were performed. Included studies were synthesized thematically, with findings organized according to predefined thematic categories reflecting the pathophysiology and treatment of pediatric IBS through the lens of the microbiota-gut-brain axis.

2.6.2. AI.

During the preparation of this manuscript, AI-assisted language tools were used solely to improve the clarity, readability, and consistency of the academic English. All substantive decisions regarding the scope of the review, selection of sources, interpretation of findings, and formulation of conclusions were made exclusively by the authors, who take full responsibility for the intellectual content of this publication.

3. Discussion

3.1. Synthesis of Principal Findings

This narrative review analyzed 31 publications from 2021 to 2025, examining the microbiota-gut-brain axis (MGBA) in pediatric irritable bowel syndrome pathogenesis and treatment. Three major thematic domains emerged: pathophysiological mechanisms of bidirectional gut-brain communication; dietary modification strategies, with emphasis on fermentable carbohydrate restriction; and emerging therapeutic approaches, including probiotics, psychological interventions, and pharmacological agents.

Contemporary understanding positions pediatric IBS within the category of disorders of gut-brain interaction (DGBI), as defined by Rome IV criteria [6, 21]. The pathophysiology remains incompletely understood, yet multiple factors have been implicated, including disordered gut motility, visceral hypersensitivity, and dysbiosis of the intestinal microbiome [21, 26, 32]. The scientific conceptualization has evolved substantially -- what was previously considered a motility abnormality is now primarily recognized as a complex biopsychosocial condition involving neural, microbial, immunological, and psychological components [10, 14].

3.2. Pathophysiological Mechanisms: The Gut-Brain Connection

The neurobiology of IBS involves intricate bidirectional communication between the gastrointestinal tract and the central nervous system. IBS symptoms arise from altered brain-gut-microbiome interactions affecting bowel habits, chronic abdominal pain, and psychiatric comorbidities, with distinct functional and structural brain signatures observed in affected patients, including alterations in sensory, emotional arousal, and prefrontal cortical regions [14, 26].

These pathophysiological mechanisms involve the gut connectome and enteric nervous system interacting with central processing of visceral signals [26]. The bidirectional nature of this communication is critical -- gastrointestinal symptoms may precede psychological distress in some patients, while in others, anxiety and depression appear first [18, 30]. Shared neurobiological pathways connecting gastrointestinal dysfunction, psychological distress, and central sensitization support the need for integrated screening and management approaches in clinical practice [14, 18].

Pediatric implications of the MGBA are particularly relevant given that early brain development is shaped by microbiome transmission, mode of birth, gestational length, breastfeeding, and antibiotic exposure [13]. This developmental perspective is especially

important for understanding the origins of pediatric IBS and potential prevention strategies [13, 29].
Physical activity represents an additional modulator of the gut-brain axis, with evidence suggesting that exercise can antagonize psychological stress through microbial-gut-brain interactions, with practical implications for lifestyle recommendations in pediatric IBS management [5, 12].

3.3. The Gut Microbiome in Pediatric IBS

Intestinal dysbiosis has been demonstrated in pediatric IBS cohorts, though no uniform microbial pattern has been identified [15]. This imbalance leads to functional dysbiosis, with altered gas and metabolite production interacting with the intestinal wall to cause symptoms [15, 28]. Gut microbiota composition influences treatment response, and the interaction between dietary components and intestinal microbiota, particularly with FODMAPs, has drawn increasing attention as these compounds are fermented by dysbiotic microbial populations [28].
Early life adverse exposures can program the MGBA and influence disease susceptibility, suggesting opportunities for early intervention and prevention [29]. Sex-dependent differences in enteric neuromuscular function following antibiotic-induced dysbiosis, and the restorative potential of Lactobacillus rhamnosus GG, provide mechanistic insights into probiotic action at the gut level [3].

3.4. Dietary Interventions: Low-FODMAP Diet Evidence

The low-FODMAP diet has demonstrated benefit in reducing gastrointestinal symptoms in IBS, though the majority of evidence derives from adult populations [16, 22].

Table 2. Dietary interventions in pediatric irritable bowel syndrome

Intervention	Mechanism of Action	Evidence in Pediatric IBS	Clinical Recommendations	Limitations	Ref.
Low-FODMAP diet	Reduces fermentable carbohydrates → ↓ gas production, ↓ osmotic load, ↓ visceral distension; modulates gut microbiota composition	Only 5 pediatric RCTs with inconsistent results; insufficient evidence to definitively support in children; emerging data from recent studies	3-phase approach: elimination (2–6 weeks) → reintroduction → personalization; requires dietitian supervision; not recommended as universal first-line by ESPGHAN/NASPGHAN	Risk of nutritional deficiencies; may reduce beneficial Bifidobacteria; risk of disordered eating; limited long-term pediatric data	[10, 11, 12, 13, 24, 31]
Dietary fiber (soluble)	Soluble fiber → ↑ SCFA production, ↑ beneficial bacteria, improved stool consistency; prebiotic effect on gut microbiota	Soluble fiber (psyllium, PHGG) shows benefit in pediatric IBS-C; moderate quality evidence; insoluble fiber may worsen bloating	Prefer soluble fiber (psyllium, partially hydrolyzed guar gum); gradual introduction; adequate hydration; individualize based on IBS subtype	Insoluble fiber may exacerbate symptoms in IBS-D; bloating common initially; pediatric RCTs limited	[16, 17, 24]
Herbal medicines (peppermint oil)	Peppermint oil → smooth muscle relaxation via calcium channel blockade, ↓ visceral hypersensitivity	Peppermint oil: moderate evidence for pain reduction in children; enteric-coated capsules preferred	Enteric-coated peppermint oil capsules for children >8 years; consider as adjunct therapy; monitor for reflux/heartburn	Limited pediatric RCTs; dosing not standardized; potential drug interactions; quality control variable	[19]
General dietary modifications	Regular eating patterns → normalized gastrocolic reflex; trigger avoidance → ↓ symptom provocation; ↓ ultra-processed foods → improved microbiota	Expert consensus and guidelines support as first-line approach; limited RCT evidence but clinically accepted	Food diary to identify triggers; regular meal timing; adequate hydration; limit caffeine, spicy and fatty foods; family-based approach	Highly individualized; risk of unnecessary restrictions; requires education and support	[13, 24, 26]
Elimination diets (lactose-free, gluten-free)	Lactose-free → ↓ fermentation in lactase deficiency; Gluten-free → may benefit subset with non-celiac gluten sensitivity	Lactose elimination: benefit only if documented lactose malabsorption; Gluten-free: insufficient evidence in pediatric IBS without celiac disease	Test for lactose malabsorption before elimination; gluten-free diet not routinely recommended; avoid empirical long-term restrictions	Risk of unnecessary dietary restrictions; nutritional concerns; psychological impact on child; may delay proper diagnosis	[13, 24]

Abbreviations: ESPGHAN, European Society for Paediatric Gastroenterology, Hepatology and Nutrition; FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; IBS, irritable bowel syndrome; IBS-C, IBS with constipation; IBS-D, IBS with diarrhea; NASPGHAN, North American Society for Pediatric Gastroenterology, Hepatology and Nutrition; PHGG, partially hydrolyzed guar gum; RCT, randomized controlled trial; SCFA, short-chain fatty acids.

Table 2. Dietary interventions in pediatric irritable bowel syndrome

Pediatric-specific evidence remains critically limited, with only five randomized controlled trials conducted in children with functional abdominal pain disorders yielding inconsistent results, and current evidence is insufficient to definitively support this approach in the pediatric population [25]. Recent pediatric data confirm limited but emerging evidence for the low-FODMAP diet in children with disorders of gut-brain interaction [20, 25]. The recent ESPGHAN/NASPGHAN guidelines do not recommend the low-FODMAP diet or any other restrictive diet as part of their standard treatment algorithm for children [31].
Practical application of the low-FODMAP diet in pediatric settings requires structured implementation across three phases -- restriction, rechallenge, and personalization -- under dietitian guidance [22]. Concerns regarding nutritional adequacy and negative impacts on gut

microbiota diversity with prolonged restriction are particularly relevant in children, where deficiencies in macro and micronutrients may impact adequate growth [22, 24]. The overlap between restrictive dietary interventions and disordered eating behaviors is an additional concern in this age group [17, 23].

3.5. Fiber and Nutritional Approaches

Fiber modification may benefit some pediatric IBS patients while potentially worsening symptoms in others, depending on fiber type and individual tolerance [9, 24]. Selecting the appropriate fiber type is therefore essential in clinical practice. Peppermint oil has shown promise in symptom management in children with IBS and represents a safe and accessible option [19]. The broader nutritional context of functional gastrointestinal disorders, including IBS, underscores the importance of individualized dietary counseling rather than universal restrictive approaches [12, 24].

3.6. Probiotics and Microbiome Modulation

Probiotic effects in IBS are mediated through multiple mechanisms, including modulation of the microbiota, alterations in gut barrier function, reduced visceral hypersensitivity, and communication between the microbiota and the gut-brain axis [4, 28]. A critical principle emerging from the available evidence is that probiotic effects are strain-specific and cannot be generalized across preparations [4].

Table 3. Probiotic strains used in the treatment of irritable bowel syndrome in children

Probiotic strain	Mechanism of action	Clinical effects	Dosage	Evidence level	Ref.
Lactobacillus rhamnosus GG (LGG)	Modulation of gut microbiota; enhancement of intestinal barrier function; reduction of visceral hypersensitivity; anti-inflammatory effects; sex-dependent restorative effects after dysbiosis	Reduction of abdominal pain frequency and intensity; improvement in stool consistency	10^9–10^{10} CFU/day for 4–8 weeks	Moderate (RCTs in children)	[3, 15]
Limosilactobacillus reuteri DSM 17938	Modulation of gut motility; reduction of intestinal inflammation; influence on gut-brain signaling via MGBA	Decrease in abdominal pain episodes; improved quality of life in pediatric populations	10^8 CFU/day for 4 weeks	Moderate (RCTs in children)	[15]
Bifidobacterium lactis	Enhancement of gut barrier integrity; modulation of immune response; SCFA production	Improvement in bloating and abdominal discomfort; normalization of bowel habits	10^9 CFU/day for 4–6 weeks	Low to moderate	[15]
VSL.#3 (multi-strain formulation)	Synergistic effects of multiple strains; restoration of microbial diversity; anti-inflammatory cytokine modulation	Reduction in overall IBS symptom severity; improvement in abdominal pain and bloating	1–2 sachets/day (450 billion CFU/sachet) for 6–8 weeks	Moderate (limited pediatric data)	[15]
Saccharomyces boulardii	Competitive inhibition of pathogens; enhancement of secretory IgA; trophic effects on enterocytes	Reduction in diarrhea-predominant symptoms; improvement in stool frequency	250–500 mg/day for 4 weeks	Low to moderate	[15]
Bifidobacterium infantis 35624	Normalization of IL-10/IL-12 ratio; reduction of systemic inflammation; modulation of gut-brain axis	Improvement in global IBS symptoms; reduction in abdominal pain and bloating	10^8 CFU/day for 4–8 weeks	Moderate (mainly adult data)	[15]

Abbreviations: CFU, colony-forming units; IBS, irritable bowel syndrome; MGBA, microbiota-gut-brain axis; RCT, randomized controlled trial; SCFA, short-chain fatty acids; IL, interleukin; IgA, immunoglobulin A.

Table 3. Probiotic strains used in the treatment of irritable bowel syndrome in children

Among pediatric populations, the strongest evidence exists for Lactobacillus rhamnosus GG and Limosilactobacillus reuteri DSM 17938, though optimal strains, dosages, and treatment durations remain to be defined by future high-quality trials [3, 4].

3.7. Psychological Dimensions and Comorbidities

Psychological comorbidities, particularly anxiety and depression, are highly prevalent in pediatric IBS and function as significant moderators of both symptom persistence and treatment response [1, 18]. The bidirectional nature of this relationship means that gastrointestinal symptoms can precede or exacerbate psychological distress, and vice versa, creating self-reinforcing cycles that require integrated therapeutic approaches [1, 18]. Psychological stress, sleep disturbances, and early adverse experiences are among the most consistently identified risk factors for abdominal pain-related DGBI in children [11, 30].

The overlap between DGBI and eating disorders, including avoidant/restrictive food intake disorder, is clinically significant and highlights the importance of screening for eating pathology when implementing restrictive dietary interventions in pediatric patients [17, 23].

3.8. Non-Pharmacological Treatment Approaches

Non-pharmacological approaches remain the cornerstone of pediatric IBS management, with 96% of patients with functional pain disorders reporting use of at least one complementary therapy [5]. Cognitive-behavioral therapy and gut-directed hypnotherapy represent the most evidence-based psychological interventions, addressing the central component of the brain-gut axis through cognitive restructuring, relaxation techniques, and symptom-focused suggestions [5, 21]. These approaches have demonstrated sustained efficacy in pediatric populations, with benefits reported up to five years following gut-directed hypnotherapy [12, 21].

3.9. Pharmacological Management

Pharmacological management of pediatric IBS remains an area of significant clinical challenge, with evidence for most medications limited and largely extrapolated from adult studies [2, 12]. Commonly used agents include antispasmodics, peppermint oil, and osmotic laxatives, though pediatric-specific randomized controlled trials are scarce [2, 12, 31, 32].

The recent ESPGHAN/NASPGHAN guidelines provide the first joint international framework for pharmacological decision-making in pediatric IBS, incorporating recommendations on laxatives, antispasmodics, probiotics, and neuromodulators within a shared decision-making model [31]. Central neuromodulators, particularly low-dose tricyclic antidepressants such as amitriptyline, are among the most commonly used pharmacological agents in pediatric IBS refractory to first-line interventions [2, 12]. These agents act on receptors along the gut-brain axis, modulating visceral hypersensitivity and central pain processing, and may additionally address comorbid anxiety and depression [2, 12]. However, their use in children requires careful consideration of the safety profile, including the black box warning for increased suicidal ideation and potential for cardiac effects, and should be preceded by baseline electrocardiographic assessment [12]. Cyproheptadine, a first-generation antihistamine with serotonin antagonist properties, represents another commonly used agent in pediatric DGBI with a favorable side effect profile [2, 12].

The use of neuromodulators in pediatric IBS remains largely off-label, reflecting the broader scarcity of pediatric-specific pharmacological trials. This constitutes a critical gap in the evidence base and a priority area for future research [2, 12, 31].

3.10. Clinical Characteristics and Healthcare Utilization

IBS in children presents across both primary and hospital care settings, with differences in symptom severity and comorbidity profiles between these contexts [7, 8]. Children managed in hospital settings tend to present with more severe symptoms and a higher burden of psychological comorbidities compared to those managed in primary care [7]. Pain-specific gene expression profiles identified in pediatric recurrent abdominal pain suggest potential future biomarkers for diagnosis and prediction of treatment response [27].

3.11. Guidelines and Therapeutic Frameworks

The publication of the ESPGHAN/NASPGHAN joint guidelines in 2025 represents a landmark development in pediatric IBS management, providing the first collaborative international framework with a proposed treatment algorithm for children aged 4-18 years [31]. These guidelines emphasize a biopsychosocial approach, shared decision-making, and stepwise therapeutic progression, and should be considered the primary reference framework for clinical practice [31]. The Italian guidelines for pediatric IBS similarly emphasize positive diagnostic approaches, patient education regarding gut-brain connections, and stepwise therapeutic algorithms [6].

3.12. Identified Knowledge Gaps

Several critical gaps emerged from this review:

1. Insufficient pediatric-specific randomized controlled trials: most IBS treatment evidence derives from adult studies, with pediatric trials often small and methodologically heterogeneous [4, 25].
2. Limited long-term follow-up data: most studies report outcomes at 4-12 weeks, providing minimal information about sustained efficacy and safety [25].
3. Heterogeneous outcome measures: studies employ varying definitions of treatment success and different pain assessment instruments, complicating evidence synthesis [21].
4. Sparse mechanistic pediatric research: while adult studies have characterized microbiota alterations and brain connectivity patterns, comparable pediatric data remain limited [14, 15].
5. Absence of validated biomarkers: no biological indicators exist for diagnosing pediatric IBS or predicting treatment response [27].
6. Nutritional safety concerns with restrictive diets: the low-FODMAP diet may impact nutritional adequacy and promote disordered eating in vulnerable children [17, 22].
7. Limited pharmacological evidence: the evidence base for neuromodulators and other pharmacological agents in pediatric IBS remains critically underdeveloped, with most use based on adult data or clinical experience [2, 12, 31].

3.13. Controversies and Unresolved Questions

The optimal duration and implementation of FODMAP restriction in children remains unclear. While short-term elimination of 2-6 weeks appears beneficial in some patients, concerns exist regarding nutritional deficiencies and negative impacts on gut microbiota diversity with prolonged restriction [19, 25]. The low-FODMAP diet requires structured dietitian-guided implementation and is not recommended as a universal first-line intervention by current international guidelines [31].

The role of probiotics, while supported by evidence, faces ongoing challenges in strain selection, dosing, and duration. Effects are strain-specific and cannot be generalized across preparations, and the optimal probiotic regimen for pediatric IBS has yet to be established [3, 4].

Psychological interventions, despite strong evidence, encounter practical implementation challenges. Cognitive-behavioral therapy and hypnotherapy require trained specialists who may be unavailable in all healthcare settings, and digital delivery models are emerging as a potential solution to improve accessibility [5, 12].

Pharmacological management of pediatric IBS raises several unresolved controversies. The use of neuromodulators, including tricyclic antidepressants and selective serotonin reuptake inhibitors, remains largely off-label in children, with limited evidence from pediatric-specific trials [2, 12]. The risk-benefit balance of these agents must be carefully considered in individual patients, particularly regarding the black box warning for suicidal ideation and potential cardiac effects of tricyclic antidepressants [12]. The role of newer pharmacological agents approved for adult IBS, such as linaclotide and rifaximin, in pediatric populations remains to be established through dedicated trials [12, 31].

3.14. Clinical Implications and Authors' Proposed Therapeutic Model

Based on synthesized evidence from the included studies and current international guidelines, the authors propose the following stepwise therapeutic model for pediatric IBS. This represents the authors' interpretation of the available evidence and should not be construed as formal clinical guidelines [6, 12, 21, 31].

Figure 3. Authors proposed stepwise therapeutic model for IBS in children

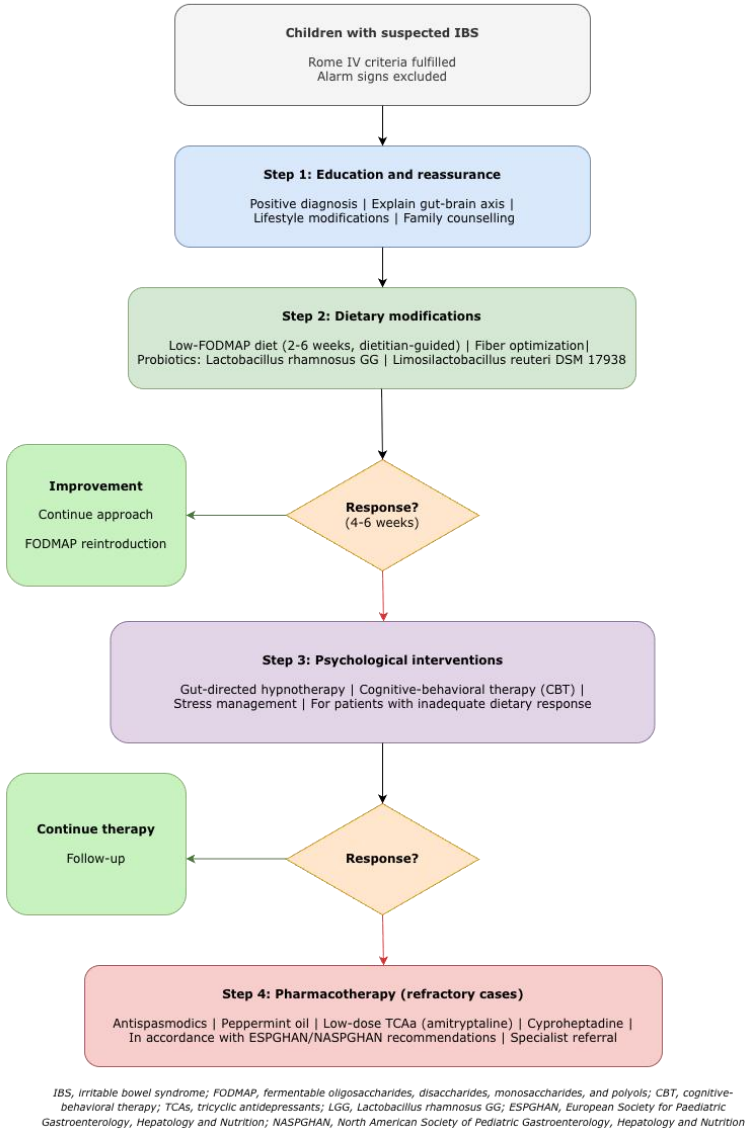


Figure 3. Authors' proposed stepwise therapeutic model for IBS in children

Step 1: Education and reassurance -- establishing a positive diagnosis, explaining gut-brain axis concepts to patients and families, and building a therapeutic alliance through clear communication [1, 6, 12].

Step 2: Dietary modifications -- supervised FODMAP restriction of 2-6 weeks with dietitian guidance where indicated, fiber optimization, and consideration of specific probiotic strains with established pediatric evidence [4, 22, 24, 25].

Step 3: Psychological interventions -- particularly gut-directed hypnotherapy or cognitive-behavioral therapy, for patients with inadequate response to dietary and microbiome-targeted approaches, or where psychological comorbidities are prominent [5, 12, 21].

Step 4: Pharmacological management -- reserved for refractory cases, including peppermint oil, cyproheptadine, or low-dose tricyclic antidepressants, in accordance with current ESPGHAN/NASPGHAN recommendations and with careful consideration of individual risk-benefit profiles [2, 12, 31].

3.15. Future Research Directions

Future investigations should prioritize large, multicenter randomized controlled trials specifically designed for pediatric populations with standardized outcome measures [21, 25]. Studies examining gut microbiome using metagenomic approaches may identify microbial

signatures predictive of treatment response [15, 28]. Research into developmental origins of IBS, including early-life MGBA programming, may reveal prevention opportunities [13, 29]. Dedicated pharmacological trials evaluating neuromodulators and newer agents in children are urgently needed to establish an evidence base independent of adult extrapolation [2, 12, 31].

3.16. Strengths and Limitations

This review comprehensively covered recent literature from 2021 to 2025, integrated multiple therapeutic domains including pharmacological management, and focused specifically on pediatric populations. The inclusion of the most recent ESPGHAN/NASPGHAN guidelines [31] and updated evidence on neuromodulators addresses gaps identified in prior reviews. However, as a narrative review, the methodology is less rigorous than a systematic review with meta-analysis. Language restrictions to English may have excluded relevant studies, and the rapidly evolving field may have led to newer evidence emerging since our search.

4. Conclusions

This review demonstrates that the microbiota-gut-brain axis (MGBA) plays a central role in the pathophysiology of pediatric irritable bowel syndrome, integrating intestinal dysfunction, microbial alterations, and central nervous system processing into a unified conceptual framework [14, 21]. Contemporary evidence supports reclassifying pediatric IBS as a disorder of gut-brain interaction (DGBI), reflecting the bidirectional communication between the gastrointestinal tract and the brain [6, 21].

Therapeutic interventions targeting the MGBA show promise at multiple levels. The low-FODMAP diet demonstrates benefit in reducing IBS symptoms, although pediatric-specific evidence remains limited to only five randomized controlled trials with inconsistent results [25]. Probiotic supplementation with specific strains, particularly Lactobacillus rhamnosus GG and Limosilactobacillus reuteri DSM 17938, provides an evidence-based microbiome-targeted approach, though effects cannot be generalized across preparations [3, 4]. Psychological interventions, including cognitive-behavioral therapy and gut-directed hypnotherapy, effectively address the central component of the brain-gut axis and demonstrate substantial efficacy in pediatric populations [5, 21]. Pharmacological management, including the use of neuromodulators such as low-dose tricyclic antidepressants, represents an additional therapeutic option in refractory cases, though evidence remains largely extrapolated from adult populations and most use in children remains off-label [2, 12, 31].

However, significant knowledge gaps persist. High-quality, pediatric-specific randomized controlled trials with standardized outcome measures and adequate long-term follow-up are urgently needed [25]. Validated biomarkers for diagnosis and prediction of treatment response remain absent, limiting personalized therapeutic approaches [27]. The optimal implementation of dietary restrictions in children requires further investigation, particularly regarding nutritional safety and the potential to promote disordered eating behaviors [17, 22].

Based on current evidence, a multimodal therapeutic approach combining patient education, dietary modifications, psychological interventions, and selective pharmacotherapy appears most appropriate for pediatric IBS management [6, 31]. Further studies with larger pediatric cohorts, standardized Rome IV diagnostic criteria, and comprehensive assessment of MGBA-targeted interventions are warranted to establish definitive evidence-based guidelines specific to children and adolescents.

Disclosure

Author Contribution

For full transparency, all submitted manuscripts must include an Author Contribution Statement specifying the work of each author.
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During the preparation of this work, the authors used AI-assisted language tools for the purpose of improving the clarity, readability, and consistency of the academic English. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the substantive content of the publication.

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