International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
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+15878858911
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ARTICLE TITLE	IRRITABLE BOWEL SYNDROME - PATHOGENESIS, EPIDEMIOLOGY, TREATMENT
DOI	https://doi.org/10.31435/ijitss.2(50).2026.5401
RECEIVED	12 February 2026
ACCEPTED	01 April 2026
PUBLISHED	15 April 2026
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IRRITABLE BOWEL SYNDROME - PATHOGENESIS, EPIDEMIOLOGY, TREATMENT

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ABSTRACT

Irritable bowel syndrome (IBS) is a common disorder of gut–brain interaction characterized by recurrent abdominal pain and altered bowel habits, including diarrhea, constipation, or mixed patterns. Despite its significant impact on quality of life and healthcare systems, IBS remains underdiagnosed. Diagnosis is based on the Rome IV criteria, which emphasize symptom patterns rather than structural abnormalities. The pathogenesis of IBS is multifactorial and not fully understood, involving low-grade intestinal inflammation, immune activation, alterations in the gut microbiota, and dysregulation of the gut–brain axis, as well as psychological factors such as stress, anxiety, and depression. Epidemiological data show substantial global variation in IBS prevalence, influenced by geographic, methodological, and diagnostic differences. Recent meta-analyses estimate a global prevalence of approximately 14%, with higher rates observed in women and individuals experiencing psychological distress. Post-infectious IBS is also increasingly recognized, with a significantly elevated risk following acute gastroenteritis. Management of IBS requires a multidisciplinary and individualized approach. First-line strategies include patient education, dietary modifications, and stress management. Pharmacological treatments are selected based on the predominant symptom subtype, with options including antibiotics such as rifaximin for IBS-D and laxatives or secretagogues for IBS-C. Increasing attention has been given to microbiota-targeted therapies, including probiotics and fecal microbiota transplantation. Dietary interventions, particularly the low FODMAP diet, have shown effectiveness in reducing global IBS symptoms, although long-term adherence requires careful supervision. Overall, advances in research and treatment strategies offer promising prospects for improving symptom control, patient outcomes, and disease awareness.

KEYWORDS

IBS, Irritable Bowel Syndrome, Gut-Brain

CITATION

Dominika Walczak, Karolina Niewola, Kamil Arciszewski, Natalia Hariasz, Karolina Orda, Jakub Szumiło, Klaudia Kasperska, Mariana Markiv, Michał Słowik, Paweł Stenzel. (2026) Irritable Bowel Syndrome - Pathogenesis, Epidemiology, Treatment. *International Journal of Innovative Technologies in Social Science*. 2(50). doi: 10.31435/ijitss.2(50).2026.5401

Introduction

Irritable bowel syndrome (IBS) is a common and complex disorder of gut-brain interaction (DGBI). It is characterized by recurrent abdominal pain and changes in bowel habits, such as constipation, diarrhea, or a mixture of both. Although IBS significantly affects patients' quality of life and contributes to substantial healthcare costs, it is often underdiagnosed. This overview examines the epidemiology, underlying mechanisms, diagnostic standards, and collaborative management approaches used in treating IBS. [1] Diagnosis is based on a set of clinical signs and symptoms, currently defined by the Rome IV criteria. The underlying mechanisms of IBS are complex and not yet fully clarified, and several hypotheses have been suggested to explain its manifestations, including changes in the intestinal microbiota, psychological factors, and dysfunction of the gut–brain axis. Despite the growing body of data, managing IBS and alleviating its symptoms remains difficult due to the unclear pathogenesis and the many factors affecting bowel function. Treatment is typically organized in stages, with a stepwise approach that prioritizes non-pharmacological interventions at the outset. [2]

Methodology

The literature used in this review was obtained through a narrative search of PubMed and Google Scholar. Publications from 2000 to 2025 were considered. Preference was given to articles focused on irritable bowel syndrome (IBS).

Discussion

Epidemiology

The prevalence of irritable bowel syndrome (IBS) differs substantially across countries and regions. A review conducted by the Rome Foundation working group in 2017 reported that prevalence rates ranged from 1.1% in France and Iran to as high as 35.5% in Mexico, while rates across Asian countries also showed considerable variation. These discrepancies may be partly explained by differences in diagnostic criteria and research methods used in earlier studies, as well as variations in geography, cultural factors, and population characteristics. Because of these inconsistencies and the heterogeneity of the available studies, accurately estimating the worldwide prevalence of IBS remains difficult. For this reason, recent discussions of IBS epidemiology often focus on trends observed within specific continents or regions. [3] The Rome Foundation Global Epidemiological Study [4], which applied the Rome IV criteria in 33 countries, found that prevalence rates in Europe and the United States were similar, whereas slightly lower rates were reported in Asia and Australia. Among the countries surveyed via internet-based studies, Egypt showed the highest prevalence. Additional research conducted in recent years has reported prevalence rates of 5.2% in Gibraltar (Rome IV criteria), 5.9% in Hangzhou, China (Rome III criteria), and 6.98% in Latin America (Rome IV criteria). Population-based surveys in the United States, Canada, and the United Kingdom also demonstrated that prevalence estimates based on the Rome III criteria are roughly twice as high as those obtained using the Rome IV criteria. Overall, some of the highest prevalence rates have been reported in Africa, while rates based on Rome IV criteria appear comparable between Europe and the United States. However, large variations remain between Europe and Asia, particularly in Asian populations studied using online questionnaires. Historically, many studies suggested that IBS occurs more frequently in women. In contrast, research from several Asian countries indicates that the condition affects men and women at similar rates. Higher prevalence has also been observed among individuals with higher education levels, greater socioeconomic status, students, and younger populations, while prevalence tends to decrease with age. Given the substantial regional differences observed in existing research, estimating a single pooled global prevalence of IBS is considered impractical, and future studies are encouraged to focus on regional patterns. [5], [6], [7], [8], [9]

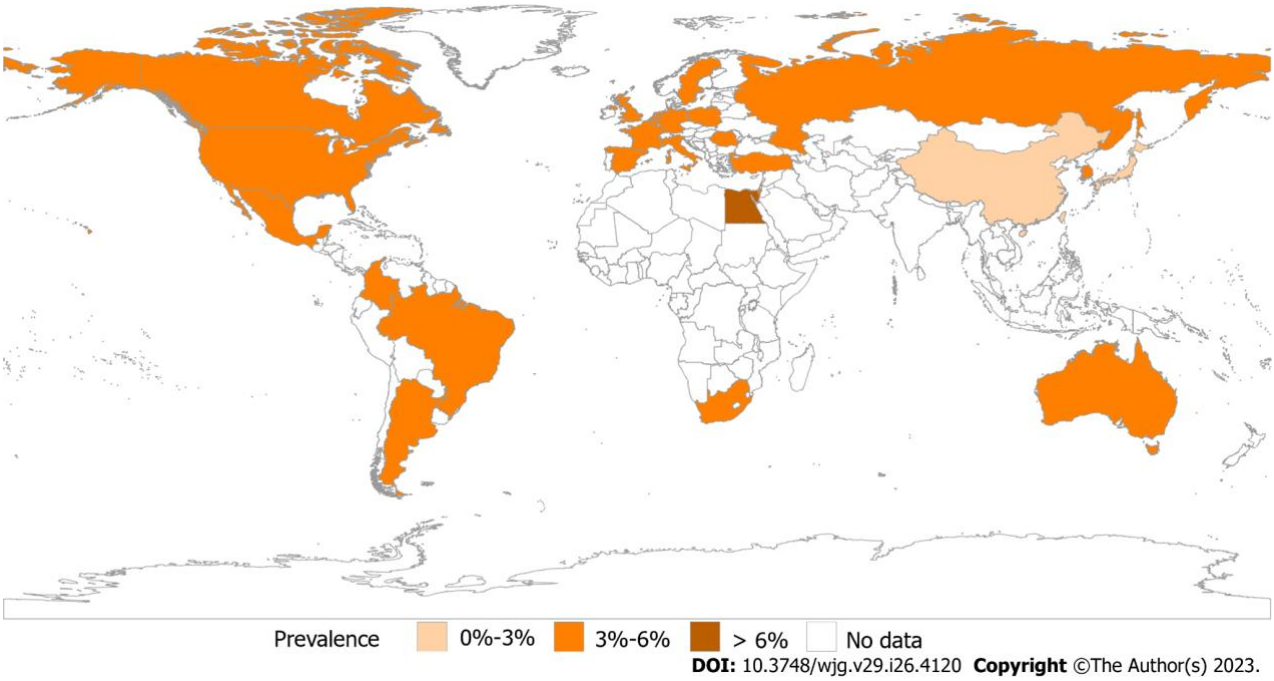

Fig. 1. *Prevalence of irritable bowel syndrome by Rome IV.*
[Huang KY, Wang FY, Lv M, Ma XX, Tang XD, Lv L. Irritable bowel syndrome: Epidemiology, overlap disorders, pathophysiology and treatment. World J Gastroenterol 2023; 29(26): 4120-4135 [PMID: 37475846 DOI: 10.3748/wjg.v29.i26.4120]

Another meta-analysis focusing which used databases like PubMed and Cochrane Libraryon IBS studies from 2006 to June 2024 explored the global prevalence of IBS, considering diagnostic criteria, subtypes, sampling methods, geographical variations, and risk factors. Eligibility criteria included studies on individuals aged ≥18, based on Rome III/IV criteria, using random or convenience sampling. Data on IBS prevalence, subtypes, and sampling methods were extracted, and statistical analysis was performed using Open MetaAnalyst and the review manager. The study reviewed 96 articles on IBS prevalence using Rome III and IV criteria across 52 countries, revealing a global prevalence of 14.1%. The results indicated that women were more likely to have IBS (odds ratio [OR] 1.49). Psychological factors were also significantly more common among IBS patients, including stress (OR 2.47), anxiety (OR 2.93), and depression (OR 2.24)This meta-analysis demonstrates that IBS prevalence varies depending on geographic region and IBS subtype, and it highlights the important role of psychological factors in the development of the disorder. It also shows that prevalence estimates can be influenced by the sampling methods used and by whether the Rome III or Rome IV diagnostic criteria are applied. These findings emphasize the importance of a multidisciplinary approach to treatment and have important implications for the clinical management of IBS. [10] Disorders of gut-brain interaction may also arise after acute gastroenteritis. In 20224 a systematic review and meta-analysis was conducted to determine prevalence of postinfection IBS (PI-IBS) after acute gastroenteritis. In total, 47 studies (28 170 subjects) were eligible. The overall prevalence of post-infectious irritable bowel syndrome (PI-IBS) was 14.5%. Long-term follow-up exceeding five years showed that IBS symptoms persisted in 39.8% of affected individuals after the initial diagnosis. People who had experienced acute gastroenteritis had significantly higher odds of developing IBS compared with those who had not been exposed (OR 4.3). Among infectious causes, PI-IBS was most frequently linked to parasitic infections, with a prevalence of 30.1%, although this finding was based on only two studies. Bacterial infections were associated with a prevalence of 18.3%, while viral infections accounted for 10.7%. In the studies that reported specific pathogens, Campylobacter infection was associated with the highest prevalence of PI-IBS (20.7%). Meanwhile, infections involving Proteobacteria and SARS-CoV-2 were associated with the greatest likelihood of developing PI-IBS (both OR 5.4). [11]

Roman criteria

Table 1. Rome IV diagnostic criteria

Recurrent abdominal pain on average at least 1 d/wk in the last 3 mo, associated with 2 or more of the following criteria
1. Related to defecation
2. Associated with a change in the frequency of stool
3. Associated with a change in the form (appearance) of stool
These criteria should be fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis. Adapted with permission from Bowel Disorders. *Gastroenterology* 2016;150: 1393–407. ©2016 AGA Institute. Published by Elsevier. All rights reserved.

ACG Clinical Guideline: Management of Irritable Bowel Syndrome
Official journal of the American College of Gastroenterology ACG116(1):17-44, January 2021.

The Rome IV criteria, derived by consensus from a multinational group of experts in the field of disorders of gut-brain interaction, can be used to diagnose IBS for both clinical and research purposes. Patients with IBS should report symptoms of abdominal pain at least once weekly (on average) in association with a change in stool frequency, a change in stool form, and/or relief or worsening of abdominal pain related to defecation (Table 1). Although bloating is a commonly reported symptom, its presence is not mandatory to accurately diagnose IBS. [12]

Pathogenesis

The exact cause of IBS remains unknown, however, there are several factors which have been identified as contributing to its pathophysiology. The intestinal mucosa forms a key component of the complex enteric immune system and contains a wide range of immune cells. Exposure to dietary components, bacteria, parasites, and viruses can sensitize this system and trigger inflammatory responses. Compared with healthy individuals, patients with typical symptoms of IBS have been found to exhibit a higher number of immune cells in the lamina propria of the colonic mucosa and significantly lower concentrations of oleoylethanolamide—an endogenous PPAR-α agonist and fatty acid amide known for its anti-inflammatory effects. These findings point toward the presence of chronic, low-grade microscopic inflammation. [13] [14] [15] T- and B-type lymphocytes located in the mucosa are also important elements of the gastrointestinal adaptive immune system. Analyses of colonic biopsies from IBS patients have shown both an increased number and heightened activation of T cells, which aligns with the hypothesis that low-grade immune activation contributes to the disease process. Similar signs of immune activation have been observed in duodenal biopsy samples. Additionally, blood analyses from IBS patients revealed an activated immune profile, characterized by a higher proportion of CD4+ and CD8+ T cells expressing the gut-homing integrin β7. Altogether, these observations indicate enhanced immune activity within the gut in individuals with IBS. [16] [17] [18] Both mucosal inflammation and psychological disturbances are considered important factors in the development of irritable bowel syndrome (IBS). Research in adults with IBS has also identified links between inflammatory cells—particularly mast cells and eosinophils—and symptoms of depression. Studies have shown that patients with IBS have higher densities of mast cells, eosinophils, and TH17 cells in the descending and rectosigmoid regions of the colon compared with healthy individuals. Among IBS patients, a greater number of mast cells in the rectosigmoid colon has been associated with reports of pain relief following defecation. Additionally, increased eosinophil presence in this region has been linked to higher levels of anxiety, and eosinophil density has been found to correlate with depression scores. In the descending colon, the densities of both eosinophils and mast cells were also positively correlated with depression severity. Overall, these findings suggest that mucosal inflammation—particularly involving mast cells and eosinophils—is related not only to symptom patterns such as pain relief after defecation, but also to psychological symptoms including anxiety and depression in young individuals with IBS. [19] [20]

The brain–gut–microbiota axis is a two-way communication network through which intestinal microorganisms interact with the central nervous system (CNS), while the CNS simultaneously influences gut function. Although the exact mechanisms underlying this communication are not yet fully clarified, they involve multiple pathways, including neural, endocrine, immune, and metabolic signaling. [21][22][23] [24][25] A variety of factors can influence the functioning of the microbiome–gut–brain axis, such as diet, genetic background, medications, environmental conditions, physical activity, cognitive and behavioral patterns, stress, social interactions, and fear.

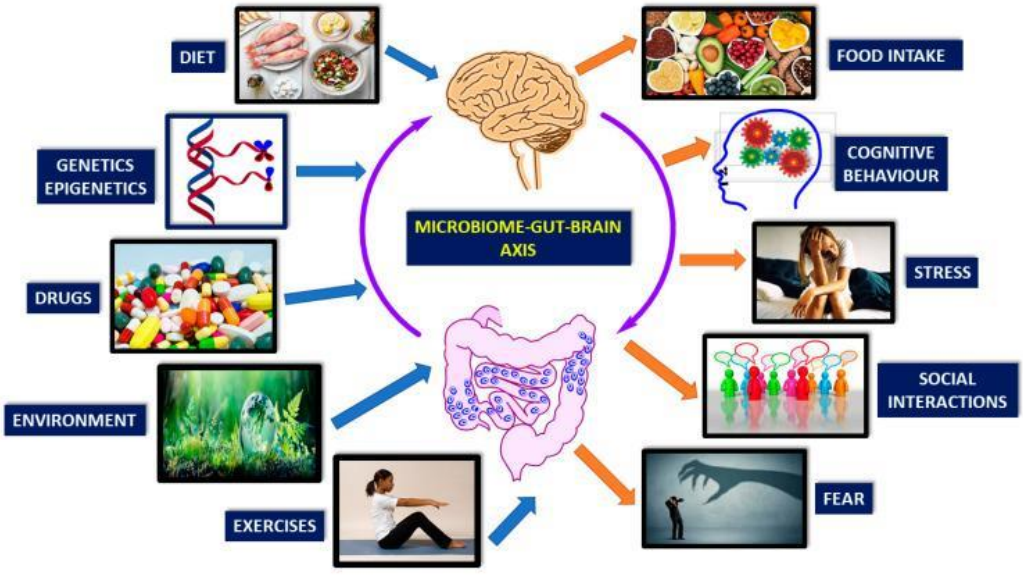

Fig. 2. *Microbiome - gut brain axis*

Karakan T, Ozkul C, Küpeli Akkol E, Bilici S, Sobarzo-Sánchez E, Capasso R. Gut-Brain-Microbiota Axis: Antibiotics and Functional Gastrointestinal Disorders. Nutrients. 2021 Jan 27;13(2):389. doi: 10.3390/nu13020389. PMID: 33513791; PMCID: PMC7910879.

Furthermore, intestinal microorganisms can synthesize many of the neurotransmitters that are also present in the human brain. Although these signaling molecules mainly exert their effects locally within the gut by regulating the enteric nervous system, substantial evidence suggests that gut microbes are also able to affect the central nervous system through several different pathways. [26] Gut microbiota play a vital role in the pathogenesis of functional gastrointestinal disorder. Gut microbiota and brain interactions are important factors for prevention and therapy. Further clinical studies are required for understanding the true effect of gut microbiota on disease progression in humans. While antibiotics are essential treatment strategies in most conditions, the long-lasting effects on host microbiome and immune functions, especially during early life should be interpreted with caution. [27]

Treatment

Over the past decade, the range of treatments available for IBS has expanded, and clinicians are no longer restricted to prescribing only fiber supplements and antispasmodics. While all individuals with IBS experience abdominal pain and irregular bowel habits, treatment needs to be individualized and should focus on the predominant symptom. [28] A solid, supportive relationship between physician and patient is crucial, along with education, dietary advice, and stress management. If patients do not respond to these measures, treatment may be expanded to include non-pharmacological interventions and/or pharmacotherapy.The choice of therapy should target the dominant symptom, and a specific follow-up point should be set to evaluate effectiveness and modify the dose if needed. For patients with IBS-D, therapeutic options primarily include antibiotics such as rifaximin, peripheral opioid receptor agonists, mixed opioid agonist–antagonists, bile acid sequestrants, and serotonin 5-hydroxytryptamine type 3 receptor antagonists. In comparison, bulk-forming agents and osmotic laxatives are typically used as first-line treatments for IBS-C, while drugs like lubiprostone and linaclotide are more often reserved for cases that do not respond well to initial therapy. At the same time, the gut microbiota has attracted growing interest, as it may be altered through interventions such as probiotics, prebiotics, synbiotics, and fecal microbiota transplantation. [29] [30]

Rifaximin is an antibiotic that is not absorbed into the bloodstream and has been approved by the US FDA for the treatment of patients with IBS-D. Its use is based on the concept that some people with IBS-D have an imbalanced gut microbiota. Two large, identically structured double-blind trials showed that rifaximin had a statistically significant benefit compared to placebo, based on a US FDA interim endpoint. In the month after a short, two-week course of treatment, 40.8% of patients reported improvement in both abdominal pain and stool consistency, compared to 31.7% in the placebo group ($P < 0.001$) when the results of both of both trials were combined. [31]

Table 2. Treatment for irritable bowel syndrome

Pharmacotherapy for diarrhea	
Peripheral opioid agonist	Loperamide (2–4 mg/d up to 16 mg/d)
Bile acid sequestrants	• Cholestyramine (9 g twice or thrice daily) • Colestipol (2 g once or twice daily) • Colesevelam (625 mg once or twice daily)
5-HT3 receptor antagonists	• Alosetron (0.5–1 mg twice daily) • Ondansetron (4–8 mg thrice daily) • Ramosetron (5 mg once daily)
Mixed opioid agonists/antagonists	Eluxadoline (100 mg twice daily)
Antibiotics	Rifaximin (550 mg thrice daily for 14 d)
Pharmacotherapy for constipation	
Soluble fiber	Psyllium (up to 30 g/d in divided doses)
Laxatives	Polyethylene glycol (17–34 g/d)
Type 2 chloride-channel activator	Lubiprostone (8 μg twice daily)
Guanylate cyclase-C agonist	Linaclotide (290 μg once daily)
Pharmacotherapy for abdominal pain	
Antispasmodics	• Dicycylomine (10–20 mg once daily) • Otilonium (40–80 mg twice or thrice daily) • Mebeverine (135 mg thrice daily) • Peppermint oil (250–750 mg, twice or thrice daily)
Peripheral opioid agonists	Trimebutine (150 mg twice or thrice daily)
Tricyclic antidepressants	• Desipramine (25–100 mg/d) • Amitriptyline (10–50 mg/d)
Selective serotonin reuptake inhibitors	• Paroxetine (10–40 mg/d) • Sertraline (25–100 mg/d)
Nonpharmacological treatment	
Lifestyle interventions	• Dietary modifications • Physical activity • Stress reduction
Microbiome manipulation	• Probiotics, prebiotics, and synbiotics • Fecal microbiota transplantation
Complementary and alternative medicine	• Relaxation training • Hypnotherapy • Cognitive-behavioral therapy • Acupuncture

Bonetto S, Fagoonee S, Battaglia E, et al. Recent advances in the treatment of irritable bowel syndrome. Pol Arch Intern Med. 2021; 131: 709-715. doi:10.20452/pamw.16067

FOODMAP

The elimination of fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) from the diet has rapidly become a widely used approach for treating patients with IBS. These carbohydrates promote increased water secretion in the gastrointestinal tract and enhanced fermentation in the colon, producing short-chain fatty acids and gases. This fermentation process is linked to the development of common IBS symptoms, including bloating, abdominal discomfort, and changes in bowel habits. The combined effects of increased luminal fluid due to osmotic activity and gas production lead to intestinal distension, which may intensify sensations of bloating and abdominal pain [32][33][34]. A recent meta-analysis [35] identified seven randomized controlled trials (RCTs) involving 397 patients with IBS, comparing the low FODMAP diet to various alternative approaches. The findings showed that the low FODMAP was associated with a significant reduction in global IBS symptoms compared with the different comparators (risk

ratio 0.69; 95% CI 0.54–0.88, I^2 = 25%). However, in the three studies that directly compared the low FODMAP diet with another dietary intervention, the results suggested a non-significant trend in its favor (RR 0.82; 95% CI 0.66–1.02). In general, the low FODMAP diet appears to be safe and not associated with serious adverse events, although prolonged restriction may increase the risk of micronutrient deficiencies. Therefore, it is essential that healthcare providers clearly guide patients through all three stages of the diet: the first stage is replacing high-FODMAP foods with low-FODMAP alternatives, then gradually reintroducing foods while monitoring symptoms, and finally tailoring the diet to avoid foods that trigger symptoms. [36]

Conclusions

Irritable bowel syndrome (IBS) is a significant problem nowadays, one that directly affects patients' daily lives and can lead to serious health consequences. The prevalence of IBS is significantly underestimated, due to both changing diagnostic criteria between Rome III and Rome IV, and the low public awareness of the condition. In many countries, there is still insufficient discussion of IBS, which also has implications for its epidemiology data. Modern lifestyles, along with the increasing prevalence of mental health issues, contribute to a higher risk of developing IBS. Overall, IBS appears to affect a substantial proportion of the population, with some studies suggesting a global prevalence of around 14%, and higher susceptibility observed in women, younger individuals, and those with psychological comorbidities. The pathogenesis of IBS is complex and multifactorial, involving low-grade intestinal inflammation, immune system activation, alterations in gut microbiota, and dysregulation of the brain–gut axis. The role of psychological factors such as stress, anxiety, and depression in IBS development and the severity of the symptoms also plays a significant role. Treatment should require a more individualized and multidisciplinary approach. integrating dietary modifications, psychological support, and pharmacological interventions when necessary. In recent years, the number of studies of IBS has grown, which lead to the emergence of new therapies for patients, offering hope for a significant improvement in patients' quality of life, as well as greater awareness and a broader understanding of the condition in the future.

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