

Rethinking Irritable Bowel Syndrome: Unraveling Complexity in Modern Gastroenterology

A. Shenbagavel*, J. Boopathirajakumar, M. Bhavithra, T. Praveena, J. Ramganes

Department of Pharmacology, Arulmigu Kalasalingam College of Pharmacy, Anand Nagar, Krishnankoil, Srivilliputhur, Virudhunagar, Tamil Nadu- 626126.

ABSTRACT

Abstract: Irritable bowel syndrome (IBS) is a long-term disorder of gut–brain interaction marked by recurrent abdominal pain together with altered bowel habits, without any detectable structural or biochemical cause. IBS does not shorten life expectancy, yet it markedly reduces physical and psychological well-being and adds to the load on health care systems. The underlying mechanisms are multifactorial: disturbed gut–brain signaling, visceral hypersensitivity, altered motility, a compromised intestinal barrier, low-grade immune activation, microbial dysbiosis, and psychological influences all contribute. Because symptom patterns differ widely between patients, both diagnosis and treatment remain difficult. Care is individualized and draws on dietary and lifestyle changes, symptom-directed drugs, therapies aimed at the microbiota, and psychological interventions. Progress in molecular biology, microbiome science, and personalized medicine has deepened understanding and created new therapeutic opportunities. This review covers epidemiology, pathophysiology, clinical features, diagnostic criteria, and management of IBS, and considers emerging directions, including biomarkers, novel drug targets, microbiome-based treatments, and digital health tools.

Keywords: Irritable bowel syndrome, Gut–brain axis, Gut microbiota, Visceral hypersensitivity, Rome IV criteria, Low-FODMAP diet

INTRODUCTION:

Irritable Bowel Syndrome (IBS) is a functional bowel disorder defined as the presence of chronic abdominal pain with altered bowel habits in the absence of any organic changes [1,2]. DGBI includes many syndromes that present a link between the central nervous system and enteric nervous system [1,2]. IBS belongs to one of the most common disease diagnoses in the gastrointestinal tract that is a significant contributor to the use of health care worldwide [3].

The prevalence of IBS is divergent worldwide, based on the various diagnostic criteria used and different geographical regions. Based on the pooled results, – 5-15% of the population might be affected by this disease [4,5]. Moreover, there is a significant difference in the prevalence of IBS between younger and older age groups (less than 50 years vs. more than 50 years) and between males and females [6,7]. The prevalence of IBS varies by country due to factors such as differences in diet, sociocultural factors, and access to health care [8]. IBS might not be diagnosed

in developing countries, which can result in a higher prevalence in the population [9].

There does not appear to be any increased mortality risk with IBS, but it has a negative impact on the quality of life for those who have it. The symptoms of the disorder include chronic abdominal pain, bloating, diarrhea, constipation, and changes in bowel movements [10,11]. These symptoms can be very disruptive to the activities people engage in and can have a negative impact on mental health [12]. Thus, this condition places a significant burden on society, as patients must visit many doctors and undergo extra testing and treatment [13].

IBS has several etiological factors. The gut-brain axis plays an important role in the development of this syndrome [14]. Changes in motility, visceral hypersensitivity, alteration of intestinal permeability, immune system activation, and alterations in gut microbiota are some factors related to the pathology of the disease [15,16,17]. In addition, environmental

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



stressors and stressful experiences in childhood may influence the pathogenesis of the syndrome [18,19].

As advances in microbiome science have become available, there has been a lot of interest in the involvement of dysbiosis in IBS. There are several differences reported in the scientific literature about the metabolic activity of the intestinal flora and composition of the bacterial flora when compared with healthy controls [20,21]. However, the results vary slightly, and the cause of the effect has not been decided. Similarly, chronic mild inflammation and alterations in the immune response have been proposed as possible causes of PI-IBS [22].

The diagnosis of IBS is based on the Rome IV criteria, which include recurrent abdominal pain associated with defecation and stool changes [23]. In recent times, the strategy of testing for evidence consistent with the diagnosis of disease instead of several exclusion examinations has been promoted, thereby reducing the need for unindicated medical examination [24]. Nevertheless, due to the risk of organic diseases, careful assessment of the patient is needed.

Over the past decade, there have been major changes in the treatment of IBS. Therapy is individualized based on patient complaints and conditions, including dietary therapy, medication, and behavioral treatments [25]. Although great steps have been made in treatment, patients with IBS continue to meet challenges in self-management of their complaints, making it necessary to further investigate the subject.

Finally, IBS is a complex disease that affects a significant proportion of the population and has significant implications for patients' health, calling for its investigation as an important clinical topic. Therefore, this paper reviews the epidemiological, pathophysiological, diagnostic, and treatment-related information on IBS to provide up-to-date and comprehensive information.

2. EPIDEMIOLOGY

IBS is a well-known disease of the digestive tract. Numerous epidemiological studies have proved that the prevalence rate of IBS is high and affects a significant percentage of the world's population. The prevalence rate of IBS is typically 5–15%, but the exact rate can depend on the diagnostic criteria used and the demographics of the population under study [26,27].

There is also geographical variation in the prevalence rates of IBS. Several epidemiological studies have been conducted in North America and some European countries, which have reported significantly higher prevalence rates than those in developing countries. The prevalence of IBS in these areas could be more than 10-20% of the adult population [28]. Slightly lower prevalence rates of IBS are found in several Asian nations while the others are comparable with the U.S. A few Asian nations have slightly lower rates of IBS, while others are similar to the U.S. Currently, the prevalence rate in Asia is estimated to be between 4% and 10%. However, changes in diet and lifestyle [29,30] will lead to a rising prevalence.

Moreover, sex is known to be an important determinant of the prevalence rate of IBS. Several epidemiological studies have shown that the prevalence rate of IBS is higher among women than among men. Almost twice as many women are affected by IBS symptoms [31]. This result may be attributed to the differences in hormonal makeup, gastrointestinal tract motility, and visceral sensation between the sexes [32].

Age is an important epidemiological risk factor for the prevalence of IBS. As a rule, patients most often suffer from IBS when they are young adults and middle-aged. Generally, the highest incidence is seen in individuals aged < 50 years [33]. Although IBS can occur at various ages, it tends to decrease in older patients. This is because age-related changes in the physiology of the GI tract and age-related differences in symptom feeling [34] contribute to this.

Some environmental and lifestyle factors may lead to IBS. Acute gastrointestinal infection due to bacteria, viruses, or parasites [35] is known as one of the most common ways to develop post-infectious IBS, which is severe infectious diarrhea. Individuals with a history of infectious diarrhea are at a higher risk of contracting infectious diarrhea than non-diarrheal individuals.

Moreover, psychological and psychosocial factors play a crucial role in the epidemiology of IBS. Many patients with IBS experience depression, anxiety, and high levels of stress. Depression and stressful situations can cause IBS and worsen patients' symptoms [36]. These conditions also have a negative impact on the brain-gut axis and result in alterations in GI motility and hyperalgesia.

Finally, there is evidence of genetic susceptibility to IBS. For example, family and twin studies have revealed that those with IBS in their family members are more likely to have IBS [37]. Nevertheless, it is not known which factors decide the degree to which genetic and common environmental factors are important to this tendency.

The socioeconomic costs of IBS are high and enormous in terms of healthcare. This leads to a high consultation, diagnosis, and sometimes treatment rate. On the other hand, this disorder seriously affects patients' work ability and productivity, leading to absenteeism. Patients have significant work functioning problems [38,39,40]. In summary, epidemiological studies have proven the significance and high prevalence of IBS.

3. PATHOPHYSIOLOGY OF IRRITABLE BOWEL SYNDROME

Irritable Bowel Syndrome is a complex disorder that cannot be explained by a single cause. Rather, it is the result of multiple physical, psychological, and environmental influences that disrupt normal gastrointestinal functioning.

3.1 Gut–Brain Axis Dysfunction

One important factor in IBS is the disruption of the gut-brain axis. This axis and communication between the central nervous system and enteric nervous system is a two-way street. Altered neural signaling may result in abnormal intestinal motility, secretion, and pain sensation. This axis can be affected by stress and emotional factors, which may worsen gastrointestinal symptoms [41].

3.2 Visceral Hypersensitivity

Patients with IBS tend to be more sensitive to stimuli in the gut or visceral hypersensitivity. Normal functions, such as passing bowels, can cause pain. The increased sensitivity is probably due to sensitized gut receptors and greater pain signals in the brain [42].

3.3 Altered Gastrointestinal Motility

Patients with IBS tend to have abnormalities in gastrointestinal motility. These changes may manifest as “rapid” transit in diarrhea predominate IBS (IBS-D) or “slow” transit in constipation-predominant IBS (IBS-C). These motility problems result from disturbances in smooth muscle activity and enteric nervous system activity [43].

3.4 The Gut Microbiome and Dysbiosis

The gut has a microbiota that is vital for its health. Dysbiosis (or imbalance in the composition of microbes) has been reported in IBS. Altered diversity and activity of gut bacteria may influence gut permeability, immune activation, and sensitivity. However, there is no consistency in the studies, and scientists are working to understand exactly how the microbiota works [44].

3.5 Immune Activation and Low-Grade Inflammation

Some patients with IBS have been seen to have low-grade inflammation and activation of the immune system. Inflammatory substances, immune cells, and cytokines may heighten gut function and result in the occurrence of symptoms. This is particularly significant in post-infective IBS [45].

3.6 Intestinal Barrier Dysfunction

This is another contributing factor known as “leaky gut” This increased permeability allows antigens and bacteria from the gut to meet the immune system, potentially causing inflammation and sensitivity [46].

3.7 Psychological Factors

Anxiety, depression, and chronic stress are all highly associated with IBS. These conditions may affect gastrointestinal function via neuroendocrine pathways, including the hypothalamic–pituitary–adrenal (HPA) axis effects on motility, sensitivity, and immune responses [47].

3.8 Post-Infectious Mechanisms

Acute gastrointestinal infections may trigger IBS. This type of IBS has continual symptoms after the infection has passed. This is due to several mechanisms, such as persistent immune activation, alteration of microbiota, and an increase in gut permeability [48].

4. CLINICAL FEATURES AND SUBTYPES OF IRRITABLE BOWEL SYNDROME

Irritable Bowel Syndrome (IBS) is characterized by a combination of persistent gastrointestinal symptoms that vary in severity and occurrence depending on the individual. The clinical picture of IBS varies, and proper classification is important for diagnosis and management.

4.1 MAIN CLINICAL SYMPTOMS

The main symptom of IBS is recurrent abdominal pain associated with bowel movements or changes in bowel patterns. The pain is crampy, intermittent, or persistent and is usually relieved upon defecation. In addition to pain, patients may experience bloating, a sensation of fullness in the abdomen, and overproduction of gas [49].

Another important symptom is a change in bowel habits. These may involve diarrhea, constipation, or other alternating patterns of diarrhea and constipation, depending on the IBS type. Stool is usually irregular, may be loose or hard, and the patient may feel urgency, straining, or that the bowel movement is incomplete [50].

4.2 IBS Subtypes

There are four IBS subtypes, depending on the consistency of the stool, as decided by the Bristol Stool Form Scale:

- **IBS-C (constipation-predominant):** hard or lumpy stools with infrequent bowel movements.
- **IBS-D (diarrhea-predominant):** loose or watery stools with more frequent bowel movements.
- **IBS-M (mixed):** a mixture of hard and loose stools.
- **IBS-U (unclassified):** symptoms that do not fit any of the above subtypes [51].

(Table 1) summarizes the Rome IV diagnostic criteria. Recognizing the subtype helps in choosing treatment and planning clinical care.

Table 1: Rome iv Diagnostic Criteria for IBS

Criteria	Description
Recurrent abdominal pain	On average at least 1 day/week in the last 3 months
Associated with defecation	Pain related to bowel movements

Criteria	Description
Change in stool frequency	Increased or decreased frequency
Change in stool form	Altered stool appearance

Note: Diagnosis requires recurrent abdominal pain together with two or more of the other three criteria; the criteria should be fulfilled for the last 3 months, with symptom onset at least 6 months before diagnosis [51].

4.3 Other Gastrointestinal Symptoms

Patients with IBS may also have other bowel symptoms, such as urgency, mucus in the stool, and incomplete bowel emptying. These symptoms can change over time and may be caused by diet, stress, or hormonal changes [52].

4.4 Extra-Intestinal Symptoms

Many patients also have symptoms outside the bowel, including fatigue, headache, disturbed sleep, and urinary complaints (Table 2). Such symptoms show that IBS is more than a digestive disorder and has systemic and neurological dimensions [53].

Table 2: Extra-Intestinal Manifestations Associated with IBS

System affected	Common manifestations
Nervous system	Headache, fatigue
Psychological	Anxiety, depression
Urinary system	Frequent urination
Musculoskeletal	Muscle pain, back pain
Sleep	Sleep disturbances

4.5 Psychological Conditions

Psychological problems, such as anxiety, depression, and somatization disorders, are also common among patients with IBS. These conditions can affect symptom severity, treatment efficacy, and overall quality of life [54].

4.6 Red Flags

Although IBS is functional, some features call for investigation to rule out serious organic disease. These alarm features include:

- Unintentional weight loss
- Bleeding
- Anemia

- Onset after age 50
- History of colon or rectal polyps

Any of these features call for further diagnostic testing [55].

4.7 Impact on Quality of Life

IBS has a significant impact on the patient's daily life. Continuing symptoms may result in reduced productivity, social limitations, and emotional effects. Patients often struggle to follow their normal routines because of variable patterns of symptoms [56].

5. MANAGEMENT OF IRRITABLE BOWEL SYNDROME

A variety of techniques are used to treat IBS with the goals of reducing symptoms, enhancing quality of life, and addressing long-term care. Treatment strategies are tailored according to the kind and intensity of symptoms met because symptoms can differ greatly across individuals.

5.1 Lifestyle and Dietary Changes

Changing one's lifestyle is the cornerstone of managing IBS. Patients must develop regular eating habits, drink plenty of water, and exercise. Dietary changes are important, and the low FODMAP diet is especially helpful since it restricts the consumption of fermentable oligosaccharides, disaccharides, and monosaccharides (FODMAPs), which can cause problems like bloating and diarrhoea (Table 3) [57].

Table 3: Examples of Foods to Limit and Lower-Fodmap Alternatives

Foods to limit	Lower-FODMAP alternatives
Milk products	Lactose-free milk
Apples, pears	Banana, orange
Wheat products	Rice, oats, wheat-free (gluten-free) products
Onion, garlic	Garlic-infused oil, green tops of spring onion

Increasing fiber intake-especially soluble kinds like psyllium-may be beneficial for those with constipation-predominant IBS, but caution should be used because insoluble fiber can occasionally worsen symptoms [58].

5.2 Medications

Pharmaceuticals for IBS are customized to address the symptoms shown:

- Whole grain meals (such as whole grain bread, crackers, and cereals) and secretagogues such as linaclotide and lubiprostone are suggested for IBS with constipation (IBS-C).
- Antidiarrheal medications such as loperamide and bile acid sequestrants may be useful for IBS with diarrhea (IBS-D).

Antispasmodics (such as hyoscine or dicyclomine) or modest dosages of antidepressants (like SSRIs or tricyclic antidepressants, or TCAs) may be used as analgesics to reduce pain and cramping. These drugs aid in controlling intestinal sensitivity and function, both of which are essential for treating IBS symptoms [59,60].

5.3 Microbiota-Targeted Therapies

IBS is linked to the gut microbiome, according to recent studies. Scientists and medical professionals are researching therapies that affect the gut microbiota, such as probiotics, prebiotics, and some antibiotics. Probiotics might be brought into equilibrium into the gut microbiotics. Bloating and decreased stomach discomfort might result from this equilibrium. For those with IBS D, rifaximin, a specific antibiotic that does not enter the body, has shown promise [61].

5.4 Psychological Therapies

Psychological techniques can be quite beneficial for those who suffer from stress or mental health problems. Relaxation treatments, gut-directed hypnosis, and cognitive behavioral therapy (CBT) have all been shown to be effective in reducing the severity of symptoms and enhancing general wellbeing. These techniques make advantage of the gut-brain link to lessen the severity of symptoms [62].

5.5 Innovative and Emerging Treatments

Exciting new therapeutic possibilities have appeared recently:

- Serotonin receptor modulators like alosetron and tegaserod.
- Fecal microbiota transplantation (FMT) as a microbiome-based therapy.

- Molecule targeting to address inflammation and gut permeability.

Although these emerging treatments show potential, further clinical validation is needed before they can be widely implemented in practice [63,64].

5.6 Patient Education and Multidisciplinary Care

To effectively manage IBS, patient education and reassurance are vital. Patients' expectations can be matched by informing them that it is a benign condition and encouraging them to be more compliant with treatment. It is often important to involve a team approach including a gastroenterologist, dietitian and mental health professional to get the most positive result [65,66].

6. FUTURE DIRECTIONS IN IRRITABLE BOWEL SYNDROME

The causes of IBS are multiple and still make the condition difficult to treat. Although the mechanisms and management of this process are now better understood, there are gaps to be filled. Research is now underway in personalized medicine, improved diagnostics and targeted therapies to further improve patient outcomes.

6.1 Personalized Medicine Approaches

A workable avenue of research in IBS is personalized medicine. Since IBS is unique to everyone, genetic, microbiome and clinical profiles-based treatments could increase effectiveness. Advances in genomics, metabolomics and proteomics may enable physicians to tailor treatment to the individual patient [67].

6.2 Microbiome-Based Innovations

The gut microbiota continues to be a significant area of study. Future studies focus on defining a microbial profile associated with each type of IBS and the development of specific microbiome-based therapies, including the development of new probiotics as well as strategies to alter microbiome. There is also a need for protocols of fecal microbiota transplantation (FMT) to be standardized prior to broad application [68].

6.3 Biomarker Development

Currently, the diagnosis of IBS is primarily based on symptoms. If reliable biomarkers could be used, it would enhance the accuracy of the diagnosis and

reduce the number of long exclusion tests. Current studies are aimed at the development of novel markers of inflammation, gut barrier permeability, and microbial metabolites that may help in early diagnosis and subtyping [69].

6.4 Advances in Gut–Brain Axis Research

There's new evidence that suggests the gut-brain connection is involved in the underlying processes of IBS. Future research will probably focus on neural pathways, neurotransmitters and central mechanisms associated with symptom feeling. This study could result in new treatments that affect pathways involved in stress and neural signaling [70].

6.5 Novel Pharmacological Targets

Researchers are looking into new medications that can target serotonin receptors, ion channels, immune pathways, and intestinal permeability. These treatments are designed to offer more symptom control in fewer side effects than what's currently available [71].

6.6 Digital Health and Artificial Intelligence

Artificial intelligence and health technology give new opportunities to IBS management. Symptom monitoring for IBS, identification of triggers for IBS and personalizing treatment regimens for IBS can be eased using mobile health applications, wearable devices and AI based models [72].

6.7 The Need for Long-Term and Multidisciplinary Research

Future research on IBS must focus on long-term effects, and it should be conducted using a multidisciplinary approach involving gastroenterology, psychology, nutrition, and microbiology. To better understand how IBS functions and to provide patients with better therapy, collaborative research will be essential [73].

CONCLUSION

IBS is a challenging illness that significantly affects both the healthcare system and sufferers' quality of life. Changes in brain-gut connections, motility in the stomach and intestines, sensitivity in the gut activation of the system, and an imbalance in gut flora are some of the mechanisms associated with IBS. Even though we now know a lot about IBS, diagnosing and treating the condition can be challenging due to its

many manifestations. Many people report that their IBS symptoms improve with current treatments, which include dietary recommendations, medications, therapy, and lifestyle modifications tailored to everyone's symptoms. However, many people still experience IBS symptoms, showing the need for better and more targeted treatments. In recent years, new discoveries about gut bacteria, quantifiable symptoms, and customized treatments have opened exciting possibilities to change how IBS is treated by improving diagnosis and creating new ways to help. A patient-centered approach that integrates knowledge from biology, brain science, and technology.

ACKNOWLEDGMENT

The authors are thankful to their institution and library for providing access to the literature and resources used in the preparation of this review article. This review received no specific funding.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest associated with this research work.

REFERENCES

1. Drossman DA, Hasler WL. Rome IV—functional GI disorders: disorders of gut-brain interaction. *Gastroenterology*. 2016 May 1;150(6):1257-61.
2. Black CJ, Drossman DA, Talley NJ, Ruddy J, Ford AC. Functional gastrointestinal disorders: advances in understanding and management. *The Lancet*. 2020 Nov 21;396(10263):1664-74.
3. Canavan C, West J, Card T. The epidemiology of irritable bowel syndrome. *Clinical epidemiology*. 2014 Feb 4:71-80.
4. Oka P, Parr H, Barberio B, Black CJ, Savarino EV, Ford AC. Global prevalence of irritable bowel syndrome according to Rome III or IV criteria: a systematic review and meta-analysis. *The lancet Gastroenterology & hepatology*. 2020 Oct 1;5(10):908-17.
5. Sperber AD, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, Whitehead WE, Dumitrascu DL, Fang X, Fukudo S, Kellow J. Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome Foundation Global Study. *Gastroenterology*. 2021 Jan 1;160(1):99-114.
6. Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clinical gastroenterology and hepatology*. 2012 Jul 1;10(7):712-21.
7. Kim YS, Kim N. Sex-gender differences in irritable bowel syndrome. *Journal of neurogastroenterology and motility*. 2018 Oct 1;24(4):544.
8. Palsson OS, Whitehead WE, Van Tilburg MA, Chang L, Chey W, Crowell MD, Keefer L, Lembo AJ, Parkman HP, Rao SS, Sperber A. Rome IV diagnostic questionnaires and tables for investigators and clinicians. *Gastroenterology*. 2016 Feb 13: S0016-5085.
9. Gwee KA, Gonlachanvit S, Ghoshal UC, Chua AS, Miwa H, Wu J, Bak YT, Lee OY, Lu CL, Park H, Chen M. Second Asian consensus on irritable bowel syndrome. *Journal of neurogastroenterology and motility*. 2019 Jul 30;25(3):343.
10. Gralnek IM, Hays RD, Kilbourne A, Naliboff B, Mayer EA. The impact of irritable bowel syndrome on health-related quality of life. *Gastroenterology*. 2000 Sep 1;119(3):654-60.
11. El-Serag HB, Olden K, Bjorkman D. Health-related quality of life among persons with irritable bowel syndrome: a systematic review. *Alimentary pharmacology & therapeutics*. 2002 Jun;16(6):1171-85.
12. Buono JL, Carson RT, Flores NM. Health-related quality of life, work productivity, and indirect costs among patients with irritable bowel syndrome with diarrhea. *Health and quality of life outcomes*. 2017 Jan;15(1):35.
13. Peery AF, Crockett SD, Murphy CC, Lund JL, Dellon ES, Williams JL, Jensen ET, Shaheen NJ, Barritt AS, Lieber SR, Kochar B. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: update 2018. *Gastroenterology*. 2019 Jan 1;156(1):254-72.

14. Mayer EA, Tillisch K, Gupta A. Gut/brain axis and the microbiota. *The Journal of clinical investigation*. 2015 Mar 2;125 (3):926-38.
15. Camilleri M. Peripheral mechanisms in irritable bowel syndrome. *New England Journal of Medicine*. 2012 Oct 25;367 (17):1626-35.
16. Enck P, Qasim Aziz GB, Farmer AD, Fukudo S, Emeran A. Mayer⁵, Beate Niesler⁶, Eamonn MM Quigley⁷, Mirjana Rajilic-Stojanovic⁸, Michael Schemann⁹, Juliane Schwille-Kiuntke¹, Magnus Simren¹⁰, Stephan Zipfel¹¹ and Robin C. Spiller¹¹ Abstract| irritable bowel syndrome (IBS) is a functional gastrointestinal disease with a high population.
17. Barbara G, Cremon C, Carini G, Bellacosa L, Zecchi L, De Giorgio R, Corinaldesi R, Stanghellini V. The immune system in irritable bowel syndrome. *Journal of neurogastroenterology and motility*. 2011 Oct 31;17 (4):349.
18. Fond G, Loundou A, Hamdani N, Boukouaci W, Dargel A, Oliveira J, Roger M, Tamouza R, Leboyer M, Boyer L. Anxiety and depression comorbidities in irritable bowel syndrome (IBS): a systematic review and meta-analysis. *European archives of psychiatry and clinical neuroscience*. 2014 Dec;264 (8):651-60.
19. Bradford K, Shih W, Videlock EJ, Presson AP, Naliboff BD, Mayer EA, Chang L. Association between early adverse life events and irritable bowel syndrome. *Clinical gastroenterology and hepatology*. 2012 Apr 1;10 (4):385-90.
20. Pittayanon R, Lau JT, Yuan Y, Leontiadis GI, Tse F, Surette M, Moayyedi P. Gut microbiota in patients with irritable bowel syndrome—a systematic review. *Gastroenterology*. 2019 Jul 1;157 (1):97-108.
21. Jeffery IB, O'toole PW, Öhman L, Claesson MJ, Deane J, Quigley EM, Simrén M. An irritable bowel syndrome subtype defined by species-specific alterations in faecal microbiota. *Gut*. 2012 Jul;61 (7):997-1006.
22. Thabane M, Marshall JK. Post-infectious irritable bowel syndrome. *World journal of gastroenterology: WJG*. 2009 Aug 7;15 (29):3591.
23. Lacy BE, Mearin F, Chang L, Chey WD, Lembo AJ, Simren M, Spiller R. Bowel disorders. *Gastroenterology*. 2016 May 1;150 (6):1393-407.
24. Lacy BE, Ford AC, Talley NJ. Quality of care and the irritable bowel syndrome: is now the time to set standards?. *Official journal of the American College of Gastroenterology| ACG*. 2018 Feb 1;113 (2):167-9.
25. Chey WD, Kurlander J, Eswaran S. Irritable bowel syndrome: a clinical review. *Jama*. 2015 Mar 3;313 (9):949-58.
26. Gwee KA, Bak YT, Ghoshal UC, Gonlachanvit S, Lee OY, Fock KM, Chua AS, Lu CL, Goh KL, Kositchaiwat C, Makharia G. Asian consensus on irritable bowel syndrome. *Journal of gastroenterology and hepatology*. 2010 Jul;25 (7):1189-205.
27. Quigley EM, Abdel-Hamid H, Barbara G, Bhatia SJ, Boeckxstaens G, De Giorgio R, Delvaux M, Drossman DA, Foxx-Orenstein AE, Guarner F, Gwee KA. A global perspective on irritable bowel syndrome: a consensus statement of the World Gastroenterology Organisation Summit Task Force on irritable bowel syndrome. *Journal of clinical gastroenterology*. 2012 May 1;46 (5):356-66.
28. Adeyemo MA, Spiegel BM, Chang L. Meta-analysis: do irritable bowel syndrome symptoms vary between men and women?. *Alimentary pharmacology & therapeutics*. 2010 Sep;32 (6):738-55.
29. El-Salhy M. Recent developments in the pathophysiology of irritable bowel syndrome. *World journal of gastroenterology: WJG*. 2015 Jul 7;21 (25):7621.
30. Thabane M, Kottachchi DT, Marshall JK. Systematic review and meta-analysis: the incidence and prognosis of post-infectious irritable bowel syndrome. *Alimentary pharmacology & therapeutics*. 2007 Aug;26 (4):535-44.
31. Saito YA, Petersen GM, Larson JJ, Atkinson EJ, Fridley BL, De Andrade M, Locke III GR, Zimmerman JM, Almazar-Elder AE, Talley NJ. Familial aggregation of irritable bowel syndrome: a family case-control study. *The American journal of gastroenterology*. 2010 Mar 16;105 (4):833.
32. Lacy BE, Patel NK. Rome criteria and a diagnostic approach to irritable bowel syndrome. *Journal of clinical medicine*. 2017 Oct 26;6 (11):99.

33. Camilleri M, Lasch K, Zhou W. Irritable bowel syndrome: methods, mechanisms, and pathophysiology. The confluence of increased permeability, inflammation, and pain in irritable bowel syndrome. *American Journal of Physiology-Gastrointestinal and Liver Physiology*. 2012 Oct 1;303 (7):G775-85.
34. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology*. 2006 Apr 1;130 (5):1480-91.
35. Whitehead WE, Palsson O, Jones KR. Systematic review of the comorbidity of irritable bowel syndrome with other disorders: what are the causes and implications?. *Gastroenterology*. 2002 Apr 1;122 (4):1140-56.
36. Vanner SJ, Depew WT, Paterson WG, DaCosta LR, Groll AG, Simon JB, Djurfeldt M. Predictive value of the Rome criteria for diagnosing the irritable bowel syndrome. *The American journal of gastroenterology*. 1999 Oct 1;94 (10):2912-7.
37. Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology*. 2014 Jan 1;146 (1):67-75.
38. Moayyedi P, Quigley EM, Lacy BE, Lembo AJ, Saito YA, Schiller LR, Soffer EE, Spiegel BM, Ford AC. The effect of fiber supplementation on irritable bowel syndrome: a systematic review and meta-analysis. *Official journal of the American College of Gastroenterology| ACG*. 2014 Sep 1;109 (9):1367-74.
39. Ford AC, Moayyedi P, Chey WD, Harris LA, Lacy BE, Saito YA, Quigley EM. American College of Gastroenterology monograph on management of irritable bowel syndrome. *Official journal of the American College of Gastroenterology| ACG*. 2018 Jun 1;113:1-8.
40. Lacy BE, Pimentel M, Brenner DM, Chey WD, Keefer LA, Long MD, Moshiree B. ACG clinical guideline: management of irritable bowel syndrome. *American Journal of Gastroenterology*. 2021 Jan;116 (1):17-44.
41. Pimentel M, Lembo A, Chey WD, Zakko S, Ringel Y, Yu J, Mareya SM, Shaw AL, Bortey E, Forbes WP. Rifaximin therapy for patients with irritable bowel syndrome without constipation. *New england journal of medicine*. 2011 Jan 6;364 (1):22-32.
42. Lazaraki G, Chatzimavroudis G, Katsinelos P. Recent advances in pharmacological treatment of irritable bowel syndrome. *World Journal of Gastroenterology: WJG*. 2014 Jul 21;20 (27):8867.
43. El-Salhy M, Hatlebakk JG, Gilja OH, Bråthen Kristoffersen A, Hausken T. Efficacy of faecal microbiota transplantation for patients with irritable bowel syndrome in a randomised, double-blind, placebo-controlled study. *Gut*. 2020 May;69 (5):859-67.
44. Drossman DA. Functional gastrointestinal disorders: history, pathophysiology, clinical features, and Rome IV. *Gastroenterology*. 2016 May 1;150 (6):1262-79.
45. Black CJ, Ford AC. Irritable bowel syndrome: a spotlight on future research needs. *The lancet Gastroenterology & hepatology*. 2021 Jun 1;6 (6):419-22.
46. Simrén M, Tack J. New treatments and therapeutic targets for IBS and other functional bowel disorders. *Nature Reviews Gastroenterology & Hepatology*. 2018 Oct;15 (10):589-605.
47. Mayer EA. Gut feelings: the emerging biology of gut-brain communication. *Nature reviews neuroscience*. 2011 Aug;12 (8):453-66.
48. Camilleri M, Ford AC. Pharmacotherapy for irritable bowel syndrome. *Journal of Clinical Medicine*. 2017 Oct 27;6 (11):101.
49. Ghoshal UC, Sachdeva S, Pratap N, Karyampudi A, Mustafa U, Abraham P, Bhatt CB, Chakravartty K, Chaudhuri S, Goyal O, Makharia GK. Indian consensus statements on irritable bowel syndrome in adults: A guideline by the Indian Neurogastroenterology and Motility Association and jointly supported by the Indian Society of Gastroenterology. *Indian Journal of Gastroenterology*. 2023 Apr;42 (2):249-73.
50. Camilleri M, Boeckxstaens G. Irritable bowel syndrome: treatment based on pathophysiology and biomarkers. *Gut*. 2023 Mar;72 (3):590-9.
51. Huang KY, Wang FY, Lv M, Ma XX, Tang XD, Lv L. Irritable bowel syndrome: Epidemiology,

- overlap disorders, pathophysiology and treatment. *World Journal of Gastroenterology*. 2023 Jul 14;29 (26):4120.
52. Wang XJ, Thakur E, Shapiro J. Non-pharmaceutical treatments for irritable bowel syndrome. *bmj*. 2024 Dec 16;387.
53. Hanna-Jairala I, Drossman DA. Central neuro-modulators in irritable bowel syndrome: why, how, and when. *The American journal of gastroenterology*. 2024 Apr 9;119 (7):1272.
54. Travers P, Lacy BE, Cangemi DJ. Irritable bowel syndrome—less irritable, or better treatments?. *Current Opinion in Gastroenterology*. 2024 Jan 1;40 (1):27-33.
55. Goodoory VC, Khasawneh M, Black CJ, Quigley EM, Moayyedi P, Ford AC. Efficacy of probiotics in irritable bowel syndrome: systematic review and meta-analysis. *Gastroenterology*. 2023 Nov 1;165 (5):1206-18.
56. Axelsson E, Kern D, Hedman-Lagerlöf E, Lindfors P, Palmgren J, Hesser H, Andersson E, Johansson R, Olén O, Bonnert M, Lalouni M. Psychological treatments for irritable bowel syndrome: a comprehensive systematic review and meta-analysis. *Cognitive behaviour therapy*. 2023 Nov 2;52 (6):565-84.
57. Halkjær SI, Lo B, Cold F, Christensen AH, Holster S, König J, Brummer RJ, Aroniadis OC, Lahtinen P, Holvoet T, Gluud LL. Fecal microbiota transplantation for the treatment of irritable bowel syndrome: a systematic review and meta-analysis. *World Journal of Gastroenterology*. 2023 May 28;29 (20):3185.
58. Wu Y, Li Y, Zheng Q, Li L. The efficacy of probiotics, prebiotics, synbiotics, and fecal microbiota transplantation in irritable bowel syndrome: a systematic review and network meta-analysis. *Nutrients*. 2024 Jul 2;16 (13):2114.
59. Ng QX, Yau CE, Yaow CY, Chong RI, Chong NZ, Teoh SE, Lim YL, Soh AY, Ng WK, Thumboo J. What has longitudinal ‘omics’ studies taught us about irritable bowel syndrome? A systematic review. *Metabolites*. 2023 Mar 28;13 (4):484.
60. Haghbin H, Hasan F, Gangwani MK, Zakirkhodjaev N, Lee-Smith W, Beran A, Kamal F, Hart B, Aziz M. Efficacy of dietary interventions for irritable bowel syndrome: a systematic review and network meta-analysis. *Journal of Clinical Medicine*. 2024 Dec 11;13 (24):7531.
61. Zhang J, Yu P, Xu Y, Lu XY, Xu Y, Hang J, Zhang Y. Efficacy and safety of a low-FODMAP diet in combination with a gluten-free diet for adult irritable bowel syndrome: a systematic review and meta-analysis. *Digestive diseases and sciences*. 2024 Nov;69 (11):4124-32.
62. Porcari S, Ingrosso MR, Maida M, Eusebi LH, Black C, Gasbarrini A, Cammarota G, Ford AC, Ianiro G. Prevalence of irritable bowel syndrome and functional dyspepsia after acute gastroenteritis: systematic review and meta-analysis. *Gut*. 2024 Sep;73 (9):1431-40.
63. Schäfer A, Stangl S, Parisi S, Bauer N, Roll J, Loeffler C, Gagyor I, Haas K, Heuschmann PU, Langhorst J, Keil T. Systematic review with meta-analysis: Stress-management interventions for patients with irritable bowel syndrome. *Stress and Health*. 2023 Oct;39 (4):694-707.
64. So D, Loughman A, Staudacher HM. Effects of a low FODMAP diet on the colonic microbiome in irritable bowel syndrome: a systematic review with meta-analysis. *The American journal of clinical nutrition*. 2022 Oct;116 (4):943-52.
65. Le Morvan de Sequeira C, Kaeber M, Cekin SE, Enck P, Mack I. The effect of probiotics on quality of life, depression and anxiety in patients with irritable bowel syndrome: a systematic review and meta-analysis. *Journal of Clinical Medicine*. 2021 Aug 8;10 (16):3497.
66. Simpson CA, Mu A, Haslam N, Schwartz OS, Simmons JG. Feeling down? A systematic review of the gut microbiota in anxiety/depression and irritable bowel syndrome. *Journal of affective disorders*. 2020 Apr 1;266:429-46.
67. Wang L, Alammari N, Singh R, Nanavati J, Song Y, Chaudhary R, Mullin GE. Gut microbial dysbiosis in the irritable bowel syndrome: a systematic review and meta-analysis of case-control studies. *Journal of the Academy of Nutrition and Dietetics*. 2020 Apr 1;120 (4):565-86.
68. Ni Y, Qian L, Siliceo SL, Long X, Nychas E, Liu Y, Ismaiah MJ, Leung H, Zhang L, Gao Q, Wu Q. Resistant starch decreases intrahepatic triglycerides in patients with NAFLD via gut

- microbiome alterations. *Cell Metabolism*. 2023 Sep 5;35 (9):1530-47.
69. Veraza DI, Calderon G, Jansson-Knodell C, Aljaras R, Foster ED, Xu H, Biruete A, Shin A. A systematic review and meta-analysis of diet and nutrient intake in adults with irritable bowel syndrome. *Neurogastroenterology & Motility*. 2024 Jan;36 (1):e14698.
 70. Shams M, Ahmed J, Umar A, Rehman A, Sohail K, Javed B, Mustafa R, Payal FN, Shehryar A, Khan M. Dietary interventions in irritable bowel syndrome: A systematic review of clinical outcomes, microbiota changes, and inflammatory markers. *Cureus*. 2024 Sep 30;16 (9).
 71. Black CJ, Ford AC. Personalisation of therapy in irritable bowel syndrome: a hypothesis. *The Lancet Gastroenterology & Hepatology*. 2024 Dec 1;9 (12):1162-76.
 72. Nasser Y, Shin A, Ford AC, Camilleri M, Black CJ. Pathophysiology of irritable bowel syndrome. *The Lancet Gastroenterology & Hepatology*. 2026 Jul 16.
 73. Butt MF, Reghefaoui MH, Benedict AS, Reghefaoui M, Al-Jabir H, Shaikh A, Vojtekova K, Moran GW, Corsetti M, Aziz Q. Irritable bowel syndrome in inflammatory bowel disease: an evidence-based practical review. *Journal of Clinical Medicine*. 2025 Dec 24;15 (1):116.

HOW TO CITE: A. Shenbagavel, J. Boopathirajakumar, M. Bhavithra, T. Praveena, J. Ramganes, Rethinking Irritable Bowel Syndrome: Unraveling Complexity in Modern Gastroenterology, *Int. J. Sci. R. Tech.*, 2026, 3 (10), 742-752. <https://doi.org/10.5281/zenodo.23315022>