Review Article

JHSMR Journal of Health Science and Medical Research

The Role of Probiotics on Depression and Quality of Life in Irritable Bowel Syndrome Patients

Diana Erlita, M.D.[1], Hamzah Shatri, M.D.[1], Achmad Fauzi, M.D.[2], Murdani Abdullah, M.D.[2]

[1]Department of Psychosomatic and Palliative Medicine, Faculty of Medicine, University of Indonesia, Central Jakarta, Jakarta 10430, Indonesia.

[2]Department of Gastroenterohepatology, Faculty of Medicine, University of Indonesia, Central Jakarta, Jakarta 10430, Indonesia.

Received 10 January 2025.● Revised 18 March 2025 ● Accepted 23 April 2025 ● Published online 22 July 2025

Abstract:

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by abdominal pain and/or constipation, often accompanied by altered stool frequency and shape. The gut microbiota, predominantly residing in the distal small and large intestines, comprises approximately 100 trillion microorganisms. Studies have identified a higher prevalence of Firmicutes (e.g., *Lactobacillus*, *Ruminococcus*), *Proteobacteria*, and *Veillonella* in IBS patients, alongside reduced populations of *Lactobacillus* and *Bifidobacterium.* Probiotics haves a role in alleviating IBS symptoms and depressive symptoms. Emerging evidence highlights the potential of probiotics to modulate the brain–gut axis, particularly in IBS patients with coexisting depressive symptoms, in order to alleviate IBS symptoms and depressive symptomps.

Keywords: depression, irritable bowel syndrome, probiotic, quality of life

Contact: Diana Erlita, M.D.
Department of Psychosomatic and Palliative Medicine, Faculty of Medicine, University of Indonesia, Central Jakarta, Jakarta 10430, Indonesia.
E-mail: dianaerlita08@gmail.com

J Health Sci Med Res 2026;44(2):e20251242
doi: 10.31584/jhsmr.20251242
www.jhsmr.org

Introduction

Irritable bowel syndrome (IBS) is a functional disorder of the gastrointestinal system, commonly characterized by alterations in stool frequency and shape of stools, as well as abdominal pain and/or constipation. Although classified as a non-life-threatening condition, this functional impairment significantly diminishes quality of life and contributes to economic losses[1,2].

In Asian countries such as Bangladesh, India, and Malaysia, the prevalence rates of IBS are reported to be 7.7–12.9%, 4.2–7.5%, and 11.0–14.0%, respectively. A study conducted in Indonesia involving 180 adolescents aged 10 to 18 revealed that 32.2% of the participants were diagnosed with IBS. Among these cases, IBS with diarrhea (IBS-D) accounted for 39.7%, IBS with constipation (IBS-C) for 37.9%, and mixed IBS (IBS-M) for 22.4%. According to the Rome IV criteria for the classification of IBS, the prevalence rates are as follows: IBS-D at 28.8%, IBS-C at 37.9%, IBS-M at 17.2%, and unclassified IBS (IBS-U) at 16.1%.[3,4].

Pro-inflammatory bacterial species, including *Enterobacteriaceae*, exhibit a higher prevalence in the microbiota of patients with IBS, whereas the genera *Lactobacillus* and *Bifidobacterium* are found to be less prevalent. Bacteriocins, which are synthesized by certain species within the genera *Lactobacillus* and *Bifidobacterium*, demonstrate a bactericidal effect against pathogens such as *Salmonella* and *Listeria monocytogenes* in vitro. Furthermore, IBS patients show reduced levels of the bacterial species *Bifidobacterium*, *Clostridiales*, *Ruminococcaceae*, and *Erysipelotrichaceae*, all of which are significant producers of short-chain fatty acids (SCFAs)[5].

Probiotics are defined as live microorganisms that, when administered in adequate quantities, confer health benefits to the host organism[6,7]. These beneficial microorganisms are commonly found in fermented foods such as kefir and yogurt, which contain a variety of microbial species that may enhance gastrointestinal health. The most frequently utilized probiotic organisms include *Streptococcus thermophilus*, various strains of *Lactobacillus*, *Lactobacillus delbrueckii subsp. bulgaricus*, and strains of *Bifidobacterium*. Empirical studies have demonstrated that probiotics not only improve health but also contribute to improvedimmune responses[8,9].

A randomized clinical study involving adults diagnosed with mild to moderate Major Depressive Disorder (MDD) indicated that the administration of probiotic supplements over an eight-week period resulted in a greater reduction in Beck Depression Inventory (BDI) scores compared to a placebo group; however, the observed difference between the 2 groups did not reach statistical significance[10]. The objective of this study was to evaluate the effects of probiotics on depressive symptoms in individuals suffering from IBS, as well as to assess the influence of probiotics on the quality of life of IBS patients.

Irritable bowel syndrome (IBS)

Periodic abdominal pain in the absence of any identifiable structural or metabolic abnormalities is a significant indicator of IBS. The diagnosis of IBS is currently based on the Rome IV criteria, which stipulate that patients must experience at least one episode of pain per week for a minimum duration of 3 months, accompanied by 2 or more of the following symptoms: a decrease in the frequency of bowel movements (fewer than three times per week), alterations in stool form or consistency, and pain associated with bowel movements[11].

The clinical symptoms of IBS typically include abdominal pain, which is often acute in nature, lasting from several minutes to several hours. This pain is usually localized to one side of the abdomen, specifically in the left or right iliac fossa, and may present as a throbbing sensation. Notably, the discomfort often alleviates following defecation or the passage of gas. As IBS is classified as a functional gastrointestinal disorder, it is essential to

evaluate the symptoms and signs of any physical disorders in patients in order to ascertain the presence of potential organic pathologies, including:[13,14] (1) Palpable abdominal mass or lymphadenopathy. (2) Age over 50 years, no previous history of colon cancer screening. (3) Marked gastrointestinal bleeding. (4) Pain or urge to defecate at night. (5) Unexplained weight loss. (6) Family history of Irritable Bowel Disease (IBD) or colorectal cancer. (7) Change in bowel habits.

A variety of factors may contribute to the development of this disease, including psychological disorders, altered gut motility, food hypersensitivity, genetic predispositions, abnormalities in the gut microbiota, bacterial overgrowth, and disruptions in the brain–gut axis, which encompasses the communication between the gut, microbiota, and central nervous system[12,13].

Despite ongoing research, the etiology of IBS continues to elude definitive explanation. However, a multitude of studies have identified several contributing factors, including visceral hypersensitivity, food intolerances, dysregulation of the brain–gut axis, motility disorders, and post–infectious sequelae. In cases of post–infectious IBS, symptoms typically manifest within one month following an infection, with the most prevalent pathogens being viruses, Giardia, or amoebae[15]. Approximately 30.0% of IBS cases are reported to develop following an infectious episode[11,15].

Depression and quality of life in IBS patients

The Brain–Gut Axis Theory posits that feedback mechanisms within the interaction cycle between the central nervous system (CNS) and the gastrointestinal tract enable the brain to modulate the composition and activity of the gut microbiota. The gastrointestinal tract is a complex organ that is integral to numerous physiological functions, particularly in its interactions with diverse gut bacteria. The vagus nerve, which facilitates bidirectional communication between the CNS and the intestinal wall, extends from the brainstem to the intestine and regulates subconscious activities. Neural signaling pathways from the brain to the digestive tract enhance the motor, sensory, and secretory functions of the digestive system, thereby influencing bacterial–host interactions either directly, through signaling molecules released into the intestinal lumen by immune cells, or indirectly, by altering the permeability of the intestinal wall. These signaling systems—including the immunoendocrinological system, the hypothalamic–pituitary–adrenal (HPA) axis, the autonomic nervous system (both sympathetic and parasympathetic), and the enteric nervous system—facilitate the brain's ability to impact the functional dynamics of gut microbiota within the digestive tract[16].

In the United States, IBS affects approximately 10.0–15.0% of the population and is associated with a significant deterioration in health–related quality of life. The overall symptom burden experienced by individuals with IBS correlates with a notable decline in their quality of life. A comprehensive review indicated that IBS patients scored significantly lower across all domains of the Short Form 36 (SF–36) compared to control subjects[18,19].

SF–36 is a widely utilized instrument for evaluating quality of life. It encompasses 8 domains: physical functioning, role limitations due to physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health. These domains are further categorized into mental and physical components. Numerous studies have indicated that individuals with IBS experience a quality of life impairment that is either greater than or comparable to that of patients suffering from other chronic conditions. Furthermore, IBS patients exhibit less impairment in their quality of life across several SF–36 dimensions, including physical pain, social functioning, and mental health[18,19].
Microbiota and the Gut–Brain Axis.

The gastrointestinal tract in the human body constitutes one of the largest interfaces, measuring approximately 250–400 m^2, between the host and various stimuli and antigens. Throughout an individual's lifetime, the human digestive system processes approximately 60 tons of food, alongside a diverse array of environmental microbes that can significantly undermine gut integrity. The term "gut microbiota" refers to the collective community of bacteria, archaea, and eukaryotes residing within the gastrointestinal system. Over millennia, these microorganisms have co-evolved with their host, resulting in a complex and mutually beneficial relationship[20].

Each individual establishes a unique microbiota following birth, influenced by various factors such as age, breastfeeding, mode of delivery, antibiotic administration, and dietary intake. These microorganisms play a crucial role in maintaining physiological homeostasis by facilitating digestion, regulating energy balance, synthesizing SCFAs, producing vitamins, defending against pathogenic microbes, and modulating the immune system[21].

With a total genome (microbiome) more than 100 times that of the human body and at least 1014 bacteria weighing roughly one kilogram, the human gastrointestinal system is home to the most numerous and varied microbial population. The most prevalent phyla of bacteria in the human gut are *Firmicutes* and *Bacteroidetes*, which account for over 70.0–75.0% of the 200 species of bacteria that are found there. *Actinobacteria*, *Proteobacteria*, and *Verrucomicrobia* are the next most prevalent phyla. *Ruminococcus*, *Eubacterium*, *Bacteroides*, *Clostridium*, *Faecalibacterium*, *Peptidococcus*, *Peptidostreptococcus*, and *Bifidobacterium* are the most prevalent genera[22].

The relationship between the host and the gut microbiota is governed by a complex and mutualistic symbiosis that takes place within the gastrointestinal tract. Various factors influence these ongoing interactions, which may result in the disruption of the microbial community's structure. Dysbiosis, characterized by disturbances in the composition of the microbiota, has been associated with IBS and other chronic immunological disorders affecting the gut immune system[23].

Alterations in gastrointestinal motility, mucosal inflammation, dysbiosis (variations in the gut microbiota), and the involvement of the central nervous system, particularly the gut-brain axis, are among the factors associated with IBS. Inflammation and immunological changes induced by dysbiosis affect the gastrointestinal barrier and enhance intestinal permeability. This disruption may influence the brain-gut nociceptive system and gastrointestinal homeostasis, resulting in visceral hypersensitivity and increased pain perception in individuals with IBS[24].

Imbalance of the gut flora can lead to dysbiosis. Dysbiosis is the process of loss or overgrowth in an organism, lowering microbial diversity and gene mutations. Dysbiosis may contribute to the pathogenesis of IBS. The disturbances in the gut microbiome lead to inflammatory changes that trigger oxidative stress, increase intestinal permeability, and allow for the translocation of bacteria across the mucosal surface, which leads to increased visceral hypersensitivity in IBS patients. Pain symptoms in IBS patients are related to a reduction in cortisol secretions[24].

Bifidobacterium longum 35624 provides relief to the cardinal symptoms of IBS and the visceral symptoms, but does not improve quality of life or depression. Another Bifidobacterium longum strains, Bifidobacterium longum 1714, has shown improvements in stress responses or psychological symptoms. Multistrains of Bifidobacterium longum 35624 and Bifidobacterium longum-1714 decreases the psychological and visceral symptoms in moderate to severe IBS patients. The IBS-SSS component-score, such as abdominal pain severity, abdominal pain frequency, abdominal distension severity, and bowel habit satisfaction, is also significantly decreased[30]. *Lactobacillus acidophilus*

has a role in alleviating gastrointestinal symptoms, such as bloating, and improving the quality of life in IBS patients[37].

Lactobacillus and *Bifidobacterium* populations were significantly decreased in IBS microbiota, but pro-inflammatory bacterial species, including *Enterobacteriaceae,* were more prevalent. *Bacteriocins*, which have bactericidal properties against pathogens like *Salmonella* and *Listeria monocytogenes* in vitro, are produced by specific species within the genera *Lactobacillus* and *Bifidobacterium*. IBS patients have decreased levels of the species *Bifidobacterium*, *Clostridiales*, *Ruminococcaceae*, and *Erysipelotrichaceae*, which are important producers of SCFAs[5].

The role of probiotics on serotonin levels in IBS

Probiotics are live bacteria that provide the body with health benefits when provided in sufficient quantities[6,7]. Probiotics are found in kefir, yogurt, and a number of other fermented foods. There are many microorganisms in each of them that may help to enhance gut health. *Streptococcus thermophilus*, *Lactobacillus* strains, *Lactobacillus delbrueckii subsp. Bulgaricus*, and *Bifidobacterium* strains are the most often utilized organisms. According to studies, they enhance immunological and anti-inflammatory responses as well as gastrointestinal health[8,9].

5-Hydroxytryptamine (5-HT), another name for serotonin, is a neurotransmitter and hormone that is present in platelets; it is essential for both the central nervous system (CNS) and the peripheral nervous system. Although the gastrointestinal tract contains 90.0% of the body's serotonin and the central nervous system has 10.0%, this neurotransmitter is well known for playing a major role in the emergence of a number of neurological conditions. Serotonin has a significant impact on both gastrointestinal and brain function. About 90.0% of the body's serotonin is stored in the gastrointestinal system by a unique kind of cell called an enterochromaffin cell, which serves as an endocrine cell. Enterochromaffin cells are essential for neurotransmission and serotonin release because they release serotonin in response to a variety of chemical stimuli. Therefore, enterochromaffin cell activity plays a part in influencing gut function and its link to the central nervous system, as well as significantly regulating serotonin levels in the gut[25].

Serotonin (5-HT) is a neurotransmitter and a substance involved in paracrine signaling in the gastrointestinal tract. The initiation of peristalsis, secretory, vasodilation, vagal, and nociceptive responses is caused by the release of 5-HT from enterochromaffin cells (EC). Intestinal and extraintestinal symptoms may be brought on by altered 5-HT signaling, a characteristic of IBS[25].

One short-term method of altering the gut microbiota is to consume isolated bacteria, like those found in probiotic supplements. There is a type of probiotics based on pigment production: the colorizing probiotics; that produce pigment, and the non colorizing probiotics, that do not produce pigment. An example of a colorizing probiotic is *Luitebacter sahni sp.*; examples of non colorizing probiotics is *Lactobacillus spp* and *Bifidobacterium spp*[39]. Numerous studies have demonstrated the beneficial effects of oral bacteria on host physiological processes in both humans and animal models [25]. The fact that the gut microbiota of both humans and animals with IBS is altered in comparable ways, both quantitatively and qualitatively, supports the use of probiotics as one of the strategies to alleviate symptoms. Restoring a healthy microbiome is believed to help treat or even cure IBS. The use of Bifidobacteria and Lactobacilli is thought to be the simplest and most effective way to accomplish this goal and restore the natural composition of the microbiota[26].

IBS symptoms can be lessened by some bacteria; some strains of this species have been demonstrated to be able to disrupt a number of intestinal processes linked to the onset of IBS. *Lactobacillus paracasei* NCC2461 reversed

alterations in intestinal permeability and sensitivity brought on by stress, and it stopped antibiotic-induced visceral hyperalgesia in mice[26]. Higher gut serotonin transporter (SERT) concentrations are linked to probiotic strains such as *Lacticaseibacillus rhamnosus* and *Limosilactobacillus reuteri*. Probiotics may help reduce IBS to some extent, but the precise mechanism is unclear[25]. *Lactobacillus paracasei* HA-196 and *Bifidobacterium longum* R0175 have been demonstrated to reduce the gastrointestinal and psychological symptoms of IBS in adults[38].

Considering that intestinal secretion and motility are caused by enteric 5-HT. When compared to the controls, IBS patients with high 5-HT typically had lower SERT messenger ribonucleic acid (mRNA). SERT may be a novel therapeutic target for IBS and plays a significant role in the pathophysiology of the condition. Numerous elements, such as growth hormones, microRNAs, immunology, inflammation, and gene polymorphisms, might influence SERT. *B. longum* and *L. acidophilus* supernatants may raise intestinal epithelial cell expression of SERT[27].

A connection exists between the systemic neurotransmitter serotonin, neurons, and the bacteria in the stomach mucosa. Probiotics may therefore assist in maintaining the equilibrium of the serotonin system and prevent certain pathophysiologically linked disorders by altering the gut flora. All things considered, there is strong evidence that probiotics can alter gut-derived 5-HT and impact 5-HT-mediated gut function, which may have therapeutic implications[27].

Probiotics, depression, and quality of life

Preclinical studies in animal models have found that probiotics downregulate the HPA axis (thought to be overactive in depression), promote gamma-aminobutyric acid (GABA) biosynthesis (known to be reduced in depressed patients), and increase serotonin levels by increasing the production of tryptophan, a precursor of serotonin[28]. In a study, *Bifidobacterium infantis* 35624 was associated with significant improvements in composite scores for abdominal pain/discomfort, bloating/distention, and/or difficulty defecating compared with placebo [29]. In another study, stress response was suggested as a major factor of IBS symptoms. The multistrain *Bifidobacterium longum strain 1714* and *35642* reduce symptoms in IBS patients and attenuate stress responses in healthy people [30]. IBS symptoms were lessened by *Bifidobacterium longum* strain 35624, whereas strain 1714 decreased cortisol and stress. The 2 strains worked together to improve sleep quality and lessen anxiety and depression[30].

Stress is an exacerbator of IBS symptoms, and anxiety and depression are common comorbidities. IBS patients who report psychological distress have more severe gastrointestinal and non-gastrointestinal symptoms, fatigue, gastrointestinal-specific anxiety, and lower quality of life and response disorders. Additionally, antidepressants and psychological interventions have been shown to be effective in reducing IBS symptoms[30]. Analysis of the mood/depression scale of IBS patients in studies of healthy subjects showed relatively high reported scores, suggesting that the study population, although not formally diagnosed with depression, was indeed likely to be depressed[28].

Regular probiotic use reduced psychological stress levels, particularly depression ratings, in IBS patients. After 6 weeks of taking multispecies probiotic pills or probiotic yogurt, mental health biomarkers improved. Those who first felt down felt better after consuming probiotic yogurt. Patients with major depressive disorders showed improved scores on the BDI after taking probiotics for 8 weeks[29]. Within 5 to 6 months of treatment, a probiotic mixture containing *Lactobacillus rhamnosusGG, L.rhamnosus LC705, Bifidobacterium breve Bb99/B.animalis spp. lactis Bb12, and propionibacterium freudenreichii spp. Shermanii JS* was effective in lowering IBS symptoms, while probiotic mixtures containing *L. reuteri* capsules had no discernible

impact[31]. Another study found a greater improvement in some gastrointestinal symptoms in 3 months in the placebo group, but after 6 months there was no significant difference between the groups in improved gastrointestinal symptoms [31].

Supplementing with multi-strain probiotics proved more advantageous than mono-strain procbiotics. After 6 weeks of treatment, the probiotic formulation i3.1, which contains *Lactobacillus plantarum* and *Pediococcus acidilactici*, enhanced the quality of life for IBS patients who experienced diarrhea[32]. After 12 weeks of therapy, *lactobacillus* also raised serum serotonin levels in IBS-D, while IBS-M showed no discernible change. Mucus secretion, intestinal motility, and bowel movement patterns are all regulated by elevated serotonin[33].

In addition to reducing abdominal pain and improving stool consistency, probiotics and antispasmodics greatly enhanced the quality of life for IBS patients[34]. IBS patients' quality of life was enhanced by symbiotic mixes, which also considerably decreased flatus complaints and lengthened intestinal transit time in the rectosigmoid[35]. *Bifidobacterium, Lactobacillus*, and *Streptococcus salivarius* probiotics alleviated flatus symptoms. For 8 weeks, taking probiotics including *Lactobacillus* and *Bifidobacterium* together reduced symptoms and enhanced quality of life. Long-term probiotic use decreased IBS symptoms and enhanced gut microbial balance. In IBS-D, probiotics had a 48.0% response rate compared to a 12.0% placebo[36].

Conflict of interest

The authors declare that they have no conflicts of interest.

Conclusion

The administration of probiotics demonstrates promising potential in modulating serotonin levels, a critical neurotransmitter involved in the gut-brain axis, particularly for patients with IBS. Evidence suggests that specific strains, such as *Lactobacillus* and *Bifidobacterium*, can positively influence serotonin transporter expression, thereby impacting intestinal motility and overall gut function. Furthermore, by highlighting the dual roles of probiotics in gastrointestinal and mental health, probiotics may alleviate IBS symptoms and depression. However, several study findings remain inconclusive due to their variability and limitations,, such as; differences in probiotic strains, dosages, treatment durations, diverse evaluation methods, and limited sample sizes. Further standardized and controlled research is needed to draw definitive conclusions.

References

1. Lacy BE, Mearin F, Chang L, Chey WD, Lembo AJ, Simren M, et al. Bowel disorders. Gastroenterology. 2016;150:1393-1407.
2. Kopczynska M, Mokros L, Pietras T, Malecka-Panas E. Quality of life and depression in patients with irritable bowel syndrome. Prz Gastroenterol 2018;13:102–8.
3. Gwee KA, Ghoshal UC, Chen M. Irritable bowel syndrome in Asia: pathogenesis, natural history, epidemiology, and management. J Gastroenterol Hepatol 2018;33:99-110.
4. Rahman MM, Mahadeva S, Ghoshal UC. Epidemiological and clinical perspectives on irritable bowel syndrome in India, Bangladesh and Malaysia: A review. World J Gastroenterol 2017;23:6788-6801.
5. Rodiño-Janeiro, Vicario M, Alonso-Cotoner C, Pascua-García R, Santos J, Bruno K. A Review of Microbiota and Irritable Bowel Syndrome: Future in Therapies. Adv Ther 2018;35:289–310.
6. Trindade IA, Melchior C, Törnblom H, Simrén M. Quality of life in irritable bowel syndrome: Exploring mediating factors through structural equation modelling. J Psychosom Res 2022;159.
7. Chen M, Ruan G, Chen L, Ying S, Li G, Xu F, et al. Neurotransmitter and intestinal interactions: focus on the microbiota-gut-brain axis in irritable bowel syndrome. Front Endocrinol (Lausanne) 2022;13:817100.
8. Satish Kumar L, Pugalenthi LS, Ahmad M, Reddy S, Barkhane Z, Elmadi J. Probiotics in irritable bowel syndrome: a review of their therapeutic role. Cureus 2022;14:e24240
9. Kok CR, Hutkins R. Yogurt and other fermented foods as sources of health-promoting bacteria. Nutr Rev 2018;76:4–15.

10. Akkasheh G, Kashani-Poor Z, Tajabadi-Ebrahimi M, Jafari P, Akbari H, Taghizadeh M, et al. Clinical and metabolic response to probiotic administration in patients with major depressive disorder: a randomized, double-blind, placebo-controlled trial. Nutrition 2016;32:315–20.
11. Mudyanadzo TA, Hauzaree C, Yerokhina O, Architha NN, Ashqar HM. Irritable bowel syndrome and depression: a shared pathogenesis. Cureus 2018;10:e3178.
12. Holtmann GJ, Ford AC, Talley NJ. Pathophysiology of irritable bowel syndrome. Lancet Gastroenterol Hepatol 2016;1:133–46.
13. Lacy BE, Pimentel M, Brenner DM, Chey WD, Keefer LA, Long MD, et al. Acg clinical guideline: management of irritable bowel syndrome. Am J Gastroenterol 2021;116:17–44.
14. Radovanovic-Dinic B, Tesic-Rajkovic S, Grgov S, Petrovic G, Zivkovic V. Irritable bowel syndrome – from etiopathogenesis to therapy. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2018;162:1–9.
15. Rahman MM, Mahadeva S, Ghoshal UC. Epidemiological and clinical perspectives on irritable bowel syndrome in India, Bangladesh and Malaysia: a review. World J Gastroenterol 2017;23:6788–801.
16. Isaiah S, Loots DT, Solomons R, van der Kuip M, Tutu Van Furth AM, Mason S. Overview of brain-to-gut axis exposed to chronic cns bacterial infection(s) and a predictive urinary metabolic profile of a brain infected by mycobacterium tuberculosis. Front Neurosci 2020;14:296.
17. Kim KN, Yao Y, Ju SY. Heart rate variability and inflammatory bowel disease in humans: a systematic review and meta-analysis. Medicine (United States) 2020;99:E23430.
18. Trindade IA, Melchior C, Törnblom H, Simrén M. Quality of life in irritable bowel syndrome: exploring mediating factors through structural equation modelling. J Psychosom Res 2022;159.
19. Pinto-Sanchez MI, Hall GB, Ghajar K, Nardelli A, Bolino C, Lau JT, et al. Probiotic bifidobacterium longum ncc3001 reduces depression scores and alters brain activity: a pilot study in patients with irritable bowel syndrome. Gastroenterology 2017;153:448–59.
20. Thursby E, Juge N. Introduction to the human gut microbiota. Biochem J 2017;474:1823–36.
21. Al-Assal K, Martinez AC, Torrinhas RS, Cardinelli C, Waitzberg D. Gut microbiota and obesity. Clin Nutr Exp 2018;20:60–4.
22. Sirisinha S. The potential impact of gut microbiota on your health:Current status and future challenges. Asian Pac J Allergy Immunol 2016;34:249–64.
23. Lopetuso LR, Petito V, Graziani C, Schiavoni E, Paroni Sterbini F, Poscia A, et al. Gut microbiota in health, diverticular disease, irritable bowel syndrome, and inflammatory bowel diseases: time for microbial marker of gastrointestinal disorders. Dig Dis 2018;36:56–65.
24. Shaikh SD, Sun N, Canakis A, Park WY, Weber HC. Shaikh SD, et al. Irritable bowel syndrome and the gut microbiome: a comprehensive review. J Clin Med 2023;12:2558.
25. Akram N, Faisal Z, Irfan R, Shah YA, Batool SA, Zahid T, et al. Exploring the serotonin-probiotics-gut health axis: A review of current evidence and potential mechanisms. Food Sci Nutr 2023;12:694–706.
26. Principi N, Cozzali R, Farinelli E, Brusaferro A, Esposito S. Gut dysbiosis and irritable bowel syndrome: The potential role of probiotics. J Infect 2018;76:111–20.
27. Cao YN, Feng LJ, Wang BM, Jiang K, Li S, Xu X, et al. Lactobacillus acidophilus and Bifidobacterium longum supernatants upregulate the serotonin transporter expression in intestinal epithelial cells. Saudi J Gastroenterol 2018;24:59–66.
28. Ng QX, Peters C, Ho CYX, Lim DY, Yeo WS. A meta-analysis of the use of probiotics to alleviate depressive symptoms. J Affect Disord 2018;228:13–9.
29. Huang R, Wang K, Hu J. Effect of probiotics on depression: a systematic review and meta-analysis of randomized controlled trials. Nutrients 2016;8:483.
30. Groeger D, Murphy EF, Tan HTT, Larsen IS, O'Neill I, Quigley EMM. Interactions between symptoms and psychological status in irritable bowel syndrome: an exploratory study of the impact of a probiotic combination. Neurogastroenterol Motil 2023;35:e14477.
31. Begtrup LM, De Muckadell OBS, Kjeldsen J, Christensen RD, Jarbol DE. Long-term treatment with probiotics in primary care patients with irritable bowel syndrome- a randomised, double-blind, placebo controlled trial. Scand J Gastroenterol 2013;48:1127–35.
32. Lorenzo-Zúñiga V, Llop E, Suárez C, Álvarez B, Abreu L, Espadaler J, et al. I.31, a new combination of probiotics, improves irritable bowel syndrome-related quality of life. World J Gastroenterol 2014;:8709–16.

33. Sarkawi M, Raja Ali RA, Abdul Wahab N, Abdul Rathi ND, Mokhtar NM. A randomized, double-blinded, placebo-controlled clinical trial on Lactobacillus-containing cultured milk drink as adjuvant therapy for depression in irritable bowel syndrome. Sci Rep 2024;14:9478.
34. Barraza-Ortiz DA, Pérez-López N, Medina-López VM, Minero-Alfaro JI, Zamarripa-Dorsey F, Fernández-Martínez NDC, et al. Combination of a probiotic and an antispasmodic increases quality of life and reduces symptoms in patients with irritable bowel syndrome: a pilot study. Dig Dis 2021;39:294-300.
35. Cappello C, Tremolaterra F, Pascariello A, Ciacci C, Iovino P. A randomised clinical trial (RCT) of a symbiotic mixture in patients with irritable bowel syndrome (IBS): effects on symptoms, colonic transit and quality of life. Int J Colorectal Dis 2013;28:349–58.
36. Shavakhi A, Minakari M, Farzamnia S, Peykar M, Taghipour G, Tayebi A, et al. The effects of multi-strain probiotic compound on symptoms and quality-of-life in patients with irritable bowel syndrome: a randomized placebo-controlled trial. Adv Biomed Res 2014;3:140.
37. Mullish BH, Michael DR, Dabcheva M, Webberley TS, Coates N, John DA, et al. A double-blind, randomized, placebo-controlled study assessing the impact of probiotic supplementation on the symptoms of irritable bowel syndrome in females. Neurogastroenterol Motil 2024;36:e14751.
38. Lewis ED, Antony JM, Crowley DC, Piano A, Bhardwaj R, Tompkins TA. Efficacy of *Lactobacillus paracasei* HA-196 and *Bifidobacterium longum* R0175 in alleviating symptoms of irritable bowel syndrome (IBS): a randomized, placebo-controlled study. Nutrients 2020;12:1159.
39. Jaiswal G, Rana R, Nayak PK, Chouhan R, Gandhi SG, Patel HK, et al, A novel yellow-pigmented probiotic bacterium from rice seed microbiome. Curr Microbiol 2024;81:424.