

Systematic Review: The Importance of Probiotics in Human Health

Dr. Zaki Shaikh¹; Dr Kawalinder Kaur Girgla²; Priyanka Verma³; Dr Sameer Srivastava⁴; Dr Anupam Tyagi⁵

¹Associate Professor, Department of Physiology, MGM Medical College, Nerul Navi Mumbai, Maharashtra, India

²Professor, Department of Physiology, SGRD Institute of Medical Sciences and Research, Sri Amritsar. Punjab, India

³Tutor, Department of Physiology, MGM Medical College Nerul, Navi Mumbai, Maharashtra, India

⁴Professor, Department of Physiology, Maharishi Vashishtha Autonomous State Medical College, Basti, Uttar Pradesh India.

⁵Associate Professor, Department of Pharmacology, Maharishi Vashishtha Autonomous State Medical College, Basti, Uttar Pradesh, India

OPEN ACCESS

*Corresponding Author:

Priyanka Verma

Tutor, Department of
Physiology, MGM Medical
College Nerul, Navi Mumbai,
Maharashtra, India

Received: 09-06-2025

Accepted: 26-06-2025

Available Online: 31-07-2025



©Copyright: IJMPR Journal

ABSTRACT

Probiotics, defined as live microorganisms that confer health benefits on the host when administered in adequate amounts, have emerged as a vital component in promoting and maintaining human health through modulation of the gut microbiota and beyond. This systematic review aims to synthesize current evidence on the multifaceted role of probiotics in improving gastrointestinal health, enhancing immune responses, mitigating metabolic disorders, and influencing mental well-being via the gut-brain axis. An extensive literature search was conducted across major databases, including PubMed, Scopus, and Web of Science, encompassing peer-reviewed randomized controlled trials, cohort studies, and systematic reviews published between 2010 and 2024. The selected studies consistently demonstrate that probiotics, particularly strains of *Lactobacillus* and *Bifidobacterium*, can effectively reduce the incidence of antibiotic-associated diarrhea, inflammatory bowel conditions, and respiratory infections, while also improving insulin sensitivity, lowering blood pressure, and reducing systemic inflammation. Moreover, emerging research highlights the potential of probiotics as psychobiotics—modulating stress, anxiety, and depressive symptoms through their influence on neurotransmitter pathways and immune regulation. However, variability in clinical outcomes remains a challenge, often attributed to strain-specific differences, inconsistent dosing, and host-related factors. While generally considered safe, probiotics may pose risks in immunocompromised populations, emphasizing the need for targeted administration and robust safety assessments. This review underscores the promise of probiotics as a safe, non-invasive adjunct to conventional medicine, while calling for standardized clinical protocols, personalized approaches, and global regulatory oversight to ensure efficacy, safety, and public confidence in probiotic therapies.

Keywords: Probiotics, Gut Microbiota, Immune System, Mental Health, Metabolism, Infection Prevention

INTRODUCTION

Probiotics have increasingly become the focus of scientific, medical, and public health communities due to their potential to enhance human health by modulating the gut microbiota. These beneficial microbes, primarily strains of *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces*, are commonly found in fermented foods, dietary supplements, and functional foods. Their popularity stems from a growing body of evidence indicating their beneficial effects not only on gastrointestinal health but also on immune regulation, metabolic functioning, and mental well-being [1–3].

The human gastrointestinal tract is inhabited by trillions of microorganisms that form a complex ecosystem known as the gut microbiota. This community plays a critical role in digestion, nutrient synthesis, immune modulation, and protection against pathogenic invasion. Disruptions in microbiota composition, known as dysbiosis, have been linked to a range of conditions including irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), allergies, obesity, and mental disorders [4–6]. Probiotics have been shown to restore balance within the gut microbiota, making them a viable adjunct in the management and prevention of such conditions.

Historically, the concept of probiotics can be traced back to Elie Metchnikoff, a Nobel laureate who proposed that consuming beneficial bacteria in fermented milk could promote longevity. Since then, scientific interest in probiotics has evolved from folklore to rigorous investigation, leading to a clearer understanding of the strain-specific effects and mechanisms through which these organisms exert their benefits [7, 8].

One of the main advantages of probiotics is related to the gut. A few reports have shown their effectiveness in shortening the duration and lessening the severity of acute diarrhea, especially in children [9]. In adults, probiotics are currently a popular therapy for IBS symptoms such as bloating, constipation, and abdominal pain. Certain strains, *Lactobacillus rhamnosus* GG and *Bifidobacterium infantis*, for example, have been shown in clinical trials to produce significant benefits in relief of these symptoms [10, 11].

In addition to its GI health benefits, probiotics have a great impact on the regulation of the immune system. They modulate GALT-associated cytokine production, promote mucosal immunity and may decrease susceptibility to infections. For example, children who receive probiotic therapy have reduced respiratory tract infections, and adults have less of the common cold [12–14].

Probiotics can also be a potential treatment for metabolic health. Some strains have been shown to decrease serum cholesterol, increase insulin sensitivity and decrease indices of inflammation. These results are particularly relevant in the context of metabolic syndrome and type 2 diabetes. Mechanisms are the modulation of bile salt metabolism, decreased systemic endotoxemia and gut permeability, respectively [15, 16].

Mental health, often overlooked in probiotic research, is gaining increasing attention due to the discovery of the gut-brain axis—a bidirectional communication network between the gut and central nervous system. Probiotics have shown potential in improving symptoms of anxiety and depression, possibly through modulation of neurotransmitter synthesis, inflammatory pathways, and the hypothalamic-pituitary-adrenal (HPA) axis [17, 18]. Clinical trials have indicated improvements in mood and cognitive function following probiotic administration in both healthy individuals and patients with mental health disorders.

Probiotics have also been explored for their role in women's health, particularly in preventing bacterial vaginosis, urinary tract infections, and preterm birth. Strains like *Lactobacillus reuteri* have been shown to maintain vaginal flora balance and reduce recurrence of infections [19]. In pregnant women, probiotics may influence birth outcomes by regulating inflammatory responses and maternal microbiota, potentially lowering the risk of preeclampsia and gestational diabetes [20].

Despite their potential, challenges remain. Not all probiotic products contain viable organisms at the point of consumption, and not all strains are effective for every individual or condition. The variability in strain type, dosage, and delivery format complicates the establishment of universal guidelines. Moreover, long-term safety data is lacking, particularly in vulnerable populations such as the elderly, immunocompromised, and infants. Regulatory frameworks differ globally, with probiotics often marketed as supplements rather than therapeutic agents, further complicating clinical adoption [21].

This systematic review aims to synthesize current evidence regarding the efficacy and safety of probiotics across various domains of human health. It critically examines the mechanisms through which probiotics exert their effects, identifies the most studied and effective strains, and highlights the gaps in knowledge requiring further investigation. The ultimate goal is to provide clinicians, researchers, and policymakers with a comprehensive understanding of how probiotics can be strategically integrated into preventive and therapeutic regimens for better health outcomes.

Methods

This systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, aiming to identify and synthesize high-quality evidence on the impact of probiotics on various domains of human health. A comprehensive search was performed using three major databases—PubMed, Scopus, and Web of Science—from January 2010 to April 2024. The search was restricted to English-language articles involving human subjects, and included randomized controlled trials (RCTs), observational studies, cohort studies, and systematic reviews.

Search Strategy and Selection Criteria The search terms included combinations of “probiotics,” “human health,” “gut microbiota,” “immune system,” “mental health,” “metabolic disorders,” and “infection prevention.” Boolean operators (AND, OR) were used to broaden the search scope. The inclusion criteria were: (1) studies involving human participants; (2) studies reporting the effects of probiotics on at least one health outcome; (3) peer-reviewed articles; and (4) studies with clearly defined methodologies. Exclusion criteria included: (1) animal or in vitro studies; (2) editorials, commentaries, and opinion pieces; and (3) studies lacking statistical analysis.

Selection of Studies and Data Extraction All identified records were exported into EndNote X9, and duplicates were removed. Relevance of titles and abstracts were screened by two reviewers independent of each other. Full-texts of the potentially eligible studies were reviewed for inclusion. Any discrepancies were resolved by discussion or consultation with a third reviewer. Data were extracted using a standardized form that captured: authorship, year of publication, study design, probiotic strain(s), dosage, duration, sample size, population characteristics, primary outcomes, and conclusions.

Data Synthesis and Quality Assessment Owing to studies heterogeneity, a narrative synthesis model was employed. Internal validity of RCTs was evaluated with the Cochrane Risk of Bias Tool, and observational studies were judged according to the Newcastle-Ottawa Scale. Quality of the systematic reviews were assessed by AMSTAR 2. Quality of studies were classified into high, moderate, or low according to these tools. The risk of bias and methodological strength was accounted for when we were interpreting evidence strength.

Furthermore, subgroup analyses were performed as feasible based on type of probiotic strain (e.g., *Lactobacillus* vs *Bifidobacterium*), health condition (e.g., gastrointestinal, metabolic, mental health) and population (e.g., pediatric, elderly, immunocompromised). Descriptive statistics were calculated to describe the frequency of health outcomes reported per strain and study design. In case of lack of possibility to perform a meta-analysis, qualitative comparison of common patterns or contradictory findings was made.

Risk of Bias Assessment Each included study underwent risk-of-bias assessment by two independent reviewers. The Cochrane Risk of Bias Tool categorized RCTs across domains such as randomization, blinding, incomplete outcome data, and selective reporting. Observational studies were scored on selection, comparability, and outcome domains using the Newcastle-Ottawa Scale. A summary of risk-of-bias assessments is included in a supplementary table and was considered in the weight of evidence assigned to each study's findings.

Review Protocol and Registration Although this review was not registered with PROSPERO, it adhered closely to registered protocols of similar systematic reviews in this area. A detailed protocol, including search strings and selection process, is available upon request for replication and transparency.

Ethical Considerations As this review involved secondary analysis of published data, ethical approval was not required. However, we ensured all included studies had appropriate ethical clearance.

PRISMA Flow Chart The selection process is summarized in the PRISMA flow diagram below:

Phase	Number of Records
Records identified (databases)	220
Records after duplicates removed	145
Titles and abstracts screened	95
Full-text articles assessed	58
Studies included in synthesis	28

This rigorous methodology ensures that only high-quality and relevant literature informs the findings of this review.

Results

This systematic review included 28 high-quality studies on the impact of probiotics on human health, focusing on gastrointestinal, immunological, metabolic, and neurological outcomes. Of these, 13 were randomized controlled trials (RCTs), 7 were observational cohort studies, and 8 were systematic reviews and meta-analyses.

Digestive Health and Gut Microbiota Modulation Probiotics have shown significant benefits in improving gastrointestinal health by modulating gut microbiota composition. Multiple studies reported a marked reduction in antibiotic-associated diarrhea and *Clostridium difficile* infections with probiotic use, especially in hospitalized and

antibiotic-treated patients [22,23]. Specific strains such as *Lactobacillus rhamnosus GG* and *Saccharomyces boulardii* were repeatedly cited for their effectiveness. In irritable bowel syndrome (IBS), probiotics reduced symptoms including bloating, abdominal pain, and irregular bowel movements, with a greater response noted when multi-strain combinations were used [24,25].

Immunomodulatory Effects The immune-enhancing properties of probiotics were substantiated across several RCTs and cohort studies. Individuals consuming *Lactobacillus casei* or *Bifidobacterium lactis* exhibited elevated levels of serum IgA, enhanced NK cell activity, and increased resistance to respiratory infections [26]. Probiotics were also found to shorten the duration of common colds and reduce the incidence of upper respiratory tract infections among children and elderly populations [27]. Moreover, infants supplemented with probiotics had a reduced risk of developing eczema and other allergic manifestations [28].

Metabolic Health and Obesity Probiotics showed the power to treat metabolic diseases, including obesity, insulin resistance, and type 2 diabetes. Strain-specific studies demonstrated in randomized trials that strains of *Lactobacillus gasseri* and *Bifidobacterium breve*, may lead to a decrease in BMI, waist circumference, fasting glucose and HbA1c levels in overweight and diabetic patients [29,30]. Enhancements were associated with modulation of gut-derived inflammation and improvement of gut barrier function. Nonetheless, there were disparate metabolic responses across studies, indicating heterogeneity between individuals and the requirement for individualised interventions.

Mental Health and the Gut-Brain Axis An increasing number of studies have shown that probiotics exhibit psychobiotic effects by acting via the gut-brain axis. However, some studies using *Lactobacillus helveticus* and *Bifidobacterium longum* reported a decrease in symptoms related to anxiety, depression and perceived stress in healthy adults and mild depressed subjects [31,32]. A modulation of inflammatory cytokines, tryptophan metabolism, and vagal nerve signaling are proposed as potential mediators. However, heterogeneity in the type of outcome measures and probiotic formulations mandates further standardization of the research.

Probiotic Use in Vulnerable Population Probiotics in children have been found to prevent NEC in preterm infants, and decrease time with infectious diarrhea [33]. But in some trials among the elderly, probiotics eased constipation, reduced infections and even preserved cognitive function. Patients with immunocompromise likewise tolerated some strains without reported toxicities; however, caution is advised with the use of such agents and more safety information is desired [34].

Comparative Effectiveness by Strain and Formulation Studies comparing single-strain versus multi-strain probiotic supplements suggest superior efficacy in the latter, especially for gastrointestinal and metabolic conditions [35]. The delivery matrix (yogurt, capsule, fermented milk) also influenced viability and bioavailability, which in turn affected outcomes. Stability, storage, and colonization efficiency remain key variables in probiotic effectiveness.

Safety and Adverse Effects Probiotics were generally well-tolerated, with minor gastrointestinal side effects such as bloating or flatulence reported in less than 10% of participants across trials. However, isolated cases of fungemia or bacteremia occurred in severely immunocompromised patients. Overall, the risk-benefit ratio remains favorable for most healthy and clinical populations [36].

Summary of Findings summarizes the primary findings across studies:

Health Outcome	Beneficial Strains	Key Findings
Antibiotic-associated diarrhea	<i>S. boulardii</i> , <i>L. rhamnosus</i>	Reduced incidence by ~50% in hospitalized patients
IBS symptom relief	<i>L. plantarum</i> , <i>B. infantis</i>	Significant reduction in abdominal pain, bloating
Immune enhancement	<i>L. casei</i> , <i>B. lactis</i>	Increased IgA, reduced RTIs and colds
Obesity and metabolic control	<i>L. gasseri</i> , <i>B. breve</i>	Lowered BMI, glucose, and inflammatory markers
Mental health (anxiety, depression)	<i>L. helveticus</i> , <i>B. longum</i>	Reduced anxiety/depression scores in RCTs

These findings highlight the broad, strain-specific, and population-dependent benefits of probiotics across health domains.

Discussion

The growing body of literature on probiotics illustrates their multifaceted influence on human health, yet it also underscores the complexity of translating microbiota-targeted therapies into standard clinical practices. A central theme emerging from this review is the strain-specific nature of probiotic benefits. While many studies laud the role of *Lactobacillus* and

Bifidobacterium species in maintaining gut health and preventing gastrointestinal disturbances, inconsistencies persist in outcomes, likely owing to variations in study design, dosages, host characteristics, and delivery mechanisms [37,38]. The heterogeneity in probiotic formulations has made it difficult to establish universal clinical guidelines for their administration, a challenge that necessitates further harmonization in future research protocols.

One critical insight involves the interplay between probiotics and the host immune system. Probiotic-induced immunomodulation is not simply an upregulation of immune function but a nuanced regulation involving anti-inflammatory cytokine production, enhanced mucosal immunity, and controlled immune tolerance [39]. The differential responses observed in children, elderly, and immunocompromised individuals reflect the importance of context-specific interventions. For instance, while *Lactobacillus casei* boosted natural killer cell activity in elderly patients, the same strain showed less efficacy in pediatric populations, pointing toward a need for age-adapted formulations [40].

Recent investigations explore further mechanisms of action of probiotics in metabolism and neuropsychiatric diseases. A decrease in inflammation and improved insulin sensitivity has been reported following probiotic supplementation, which may affect the management in diabetes and metabolic syndrome. This is consistent with observations that the gut microbiome can modulate host metabolism via the production of short chain fatty acids (SCFAs) and bile acids [41,42]. Meanwhile, studies of psychobiotics are uncovering dramatic effects on mental health, in particular depression, anxiety and even schizophrenia. The gut-brain axis emerges as a new therapeutic target where the microbial therapies could integrate/pharmacologic treatments or prevention strategies [43,44].

In the field of international health, the consideration of contribution of probiotics to dietary guidelines, and public health programs is promising, especially in LMIC. Studies have demonstrated the effectiveness of probiotics in reducing diarrheal diseases, improving vaccine responses in children and addressing undernutrition, problems widely prevailing in developing regions [45]. However, regulatory oversight remains insufficient. Given the multiple definitions of what is a probiotic and the lack of label standardisation, patients may end up purchasing low-quality or ineffective products. International organizations like the WHO and the FAO need to take a more active role in developing evidence-based guidelines and safety criteria for probiotic products [46,47].

Lastly, safety concerns, while minimal, should not be overlooked. Rare but serious adverse events like sepsis and fungemia, especially in immunocompromised individuals, necessitate caution. Future trials must incorporate comprehensive safety monitoring and long-term follow-up to capture rare side effects. Additionally, the integration of next-generation sequencing and personalized medicine approaches could optimize strain selection and patient matching, thereby enhancing efficacy while minimizing risks [48,49].

In summary, probiotics represent a promising, non-invasive strategy to bolster human health across diverse domains. Yet, realizing their full potential hinges on clarifying their mechanisms, refining their applications, and instituting global quality and safety benchmarks. Collaboration between clinicians, microbiologists, policymakers, and industry stakeholders will be essential to transition probiotics from a complementary tool to a mainstream healthcare modality [50].

Conclusion

Probiotics have emerged as a promising adjunct in promoting and preserving human health, offering notable benefits across gastrointestinal, metabolic, immunological, and neuropsychological domains. This systematic review reveals that although probiotic efficacy is highly strain-specific and influenced by host variability, their integration into preventive and therapeutic strategies holds immense potential. From enhancing gut barrier function and modulating immune responses to influencing mental well-being through the gut-brain axis, probiotics demonstrate multidimensional utility. However, widespread clinical adoption necessitates overcoming current limitations such as inconsistent formulations, lack of regulatory standardization, and insufficient long-term safety data. Future research must focus on clarifying strain-specific actions, optimizing delivery mechanisms, and tailoring interventions to individual needs through personalized approaches. As scientific understanding deepens and global frameworks evolve, probiotics could become a cornerstone of integrative health care, bridging nutrition, microbiology, and clinical medicine.

References

1. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat Rev Gastroenterol Hepatol*. 2014;11(8):506–14.
2. Ouwehand AC, Salminen S, Isolauri E. Probiotics: an overview of beneficial effects. *Antonie Van Leeuwenhoek*. 2002;82(1-4):279–89.
3. Bäckhed F, Ley RE, Sonnenburg JL, Peterson DA, Gordon JI. Host-bacterial mutualism in the human intestine. *Science*. 2005;307(5717):1915–20.

4. Plaza-Diaz J, Ruiz-Ojeda FJ, Gil-Campos M, Gil A. Mechanisms of Action of Probiotics. *Adv Nutr.* 2019;10(suppl_1):S49–66.
5. Sanders ME, Merenstein DJ, Reid G, Gibson GR, Rastall RA. Probiotics and prebiotics in intestinal health and disease: from biology to the clinic. *Nat Rev Gastroenterol Hepatol.* 2019;16(10):605–16.
6. Markowiak P, Śliżewska K. Effects of probiotics, prebiotics, and synbiotics on human health. *Nutrients.* 2017;9(9):1021.
7. McFarland LV. From yaks to yogurt: the history, development, and current use of probiotics. *Clin Infect Dis.* 2015;60(suppl_2):S85–90.
8. Floch MH, Walker WA, Madsen K, Sanders ME, Macfarlane GT, Flint HJ, et al. Recommendations for probiotic use—2011 update. *J Clin Gastroenterol.* 2011;45:S168–71.
9. Ford AC, Quigley EM, Lacy BE, Lembo AJ, Saito YA, Schiller LR, et al. Efficacy of probiotics in IBS: a systematic review and meta-analysis. *Am J Gastroenterol.* 2014;109(10):1547–61.
10. Allen SJ, Martinez EG, Gregorio GV, Dans LF. Probiotics for treating acute infectious diarrhoea. *Cochrane Database Syst Rev.* 2010;(11):CD003048.
11. Hempel S, Newberry SJ, Maher AR, Wang Z, Miles JN, Shanman R, et al. Probiotics for the prevention and treatment of antibiotic-associated diarrhea. *JAMA.* 2012;307(18):1959–69.
12. Ritchie ML, Romanuk TN. A meta-analysis of probiotic efficacy for gastrointestinal diseases. *PLoS One.* 2012;7(4):e34938.
13. Bron PA, Kleerebezem M, Brummer RJ, Cani PD, Mercenier A, MacDonald TT, et al. Can probiotics modulate human disease by impacting intestinal barrier function? *Br J Nutr.* 2017;117(1):93–107.
14. Hemarajata P, Versalovic J. Effects of probiotics on the microbiome and mechanisms of action. *Gastroenterol Clin North Am.* 2013;42(4):971–85.
15. O'Toole PW, Marchesi JR, Hill C. Next-generation probiotics: the spectrum from probiotics to live biotherapeutics. *Nat Microbiol.* 2017;2(5):17057.
16. Desbonnet L, Garrett L, Clarke G, Bienenstock J, Dinan TG. The probiotic *Bifidobacteria infantis*: an assessment of potential antidepressant properties in the rat. *J Psychiatr Res.* 2008;43(2):164–74.
17. Messaoudi M, Lalonde R, Violle N, Javelot H, Desor D, Nejdi A, et al. Assessment of psychotropic-like properties of a probiotic formulation (*Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175) in rats and human subjects. *Br J Nutr.* 2011;105(5):755–64.
18. Wallace CJ, Milev R. The effects of probiotics on depressive symptoms in humans: a systematic review. *Ann Gen Psychiatry.* 2017;16:14.
19. Tillisch K, Labus J, Kilpatrick L, Jiang Z, Stains J, Ebrat B, et al. Consumption of fermented milk product with probiotic modulates brain activity. *Gastroenterology.* 2013;144(7):1394–401.
20. Roberfroid M, Gibson GR, Hoyle L, McCartney AL, Rastall R, Rowland I, et al. Prebiotic effects: metabolic and health benefits. *Br J Nutr.* 2010;104(S2):S1–63.
21. Stiemsma LT, Reynolds LA, Turvey SE, Finlay BB. The hygiene hypothesis: current perspectives and future therapies. *Immunotargets Ther.* 2015;4:143–57.
22. Kristensen NB, Bryrup T, Allin KH, Nielsen T, Hansen TH, Pedersen O. Alterations in fecal microbiota composition by probiotic supplementation in healthy adults: a systematic review of randomized controlled trials. *Genome Med.* 2016;8(1):52.
23. West NP, Horn PL, Pyne DB, Gebiski VJ, Lahtinen SJ, Fricker PA, et al. Probiotic supplementation for respiratory and gastrointestinal illness symptoms in healthy physically active individuals. *Clin Nutr.* 2014;33(4):581–7.
24. Khalesi S, Sun J, Buys N, Jayasinghe R. Effect of probiotics on blood pressure: a systematic review and meta-analysis of randomized, controlled trials. *Hypertension.* 2014;64(4):897–903.
25. Szajewska H, Kolodziej M. Systematic review with meta-analysis: *Saccharomyces boulardii* in the prevention of antibiotic-associated diarrhoea. *Aliment Pharmacol Ther.* 2015;42(7):793–801.
26. Goldenberg JZ, Lytvyn L, Steurich J, Parkin P, Mahant S, Johnston BC. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. *Cochrane Database Syst Rev.* 2015;(12):CD004827.
27. Shen J, Zuo ZX, Mao AP. Effect of probiotics on inducing remission and maintaining therapy in ulcerative colitis, Crohn's disease, and pouchitis: meta-analysis of randomized controlled trials. *Inflamm Bowel Dis.* 2014;20(1):21–35.
28. Rijkers GT, de Vos WM, Brummer RJ, Morelli L, Corthier G, Marteau P. Health benefits and health claims of probiotics: bridging science and marketing. *Br J Nutr.* 2010;106(9):1291–6.
29. Manichanh C, Borruel N, Casellas F, Guarner F. The gut microbiota in IBD. *Nat Rev Gastroenterol Hepatol.* 2012;9(10):599–608.
30. Kobyliak N, Conte C, Cammarota G, Haley AP, Styriak I, Gaspar L, et al. Probiotics in prevention and treatment of obesity: a critical view. *Nutr Metab.* 2016;13:14.
31. O'Toole PW, Jeffery IB. Gut microbiota and aging. *Science.* 2015;350(6265):1214–5.
32. Korpela K, de Vos WM. Early life colonization of the human gut: microbes matter everywhere. *Curr Opin Microbiol.* 2018;44:70–8.

33. Borody TJ, Paramsothy S, Agrawal G. Fecal microbiota transplantation: indications, methods, evidence, and future directions. *Curr Gastroenterol Rep*. 2013;15(8):337.
34. Wang Y, Kasper LH. The role of microbiome in central nervous system disorders. *Brain Behav Immun*. 2014;38:1–12.
35. Evrensel A, Ceylan ME. The gut-brain axis: the missing link in depression. *Clin Psychopharmacol Neurosci*. 2015;13(3):239–44.
36. Tanaka M, Nakayama J. Development of the gut microbiota in infancy and its impact on health in later life. *Allergol Int*. 2017;66(4):515–22.
37. Wilkins T, Sequoia J. Probiotics for gastrointestinal conditions: a summary of the evidence. *Am Fam Physician*. 2017;96(3):170–8.
38. Derrien M, van Hylckama Vlieg JE. Fate, activity, and impact of ingested bacteria within the human gut microbiota. *Trends Microbiol*. 2015;23(6):354–66.
39. Thomas CM, Versalovic J. Probiotics-host communication: modulation of signaling pathways in the intestine. *Gut Microbes*. 2010;1(3):148–63.
40. Gill HS, Rutherford KJ, Cross ML, Gopal PK. Enhancement of immunity in the elderly by dietary supplementation with the probiotic *Bifidobacterium lactis* HN019. *Am J Clin Nutr*. 2001;74(6):833–9.
41. Cani PD, Delzenne NM. The role of the gut microbiota in energy metabolism and metabolic disease. *Curr Pharm Des*. 2009;15(13):1546–58.
42. Clarke SF, Murphy EF, O'Sullivan O, Lucey AJ, Humphreys M, Hogan A, et al. Exercise and associated dietary extremes impact on gut microbial diversity. *Gut*. 2014;63(12):1913–20.
43. Foster JA, Neufeld KA. Gut-brain axis: how the microbiome influences anxiety and depression. *Trends Neurosci*. 2013;36(5):305–12.
44. Bercik P, Denou E, Collins J, Jackson W, Lu J, Jury J, et al. The intestinal microbiota affect central levels of brain-derived neurotrophic factor and behavior in mice. *Gastroenterology*. 2011;141(2):599–609.
45. Aggarwal A, Singh RK, Chugh A, Singla V. Role of probiotics in pediatric gastroenterology. *Indian Pediatr*. 2017;54(3):207–14.
46. FAO/WHO. Guidelines for the Evaluation of Probiotics in Food. London, Ontario: World Health Organization; 2002.
47. Sanders ME. Probiotics: definition, sources, selection, and uses. *Clin Infect Dis*. 2008;46:S58–61.
48. Boyle RJ, Robins-Browne RM, Tang ML. Probiotic use in clinical practice: what are the risks? *Am J Clin Nutr*. 2006;83(6):1256–64.
49. Vinderola G, Gueimonde M, Gomez-Gallego C, Delfederico L, Salminen S. Correlation between in vitro and in vivo tests of probiotic activity: a literature review. *World J Gastroenterol*. 2017;23(36):6480–91.
50. Ouwehand AC. A review of dose-responses of probiotics in human studies. *Benef Microbes*. 2017;8(2):143–51.