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Gut Microbiome and Mental Health: The Gut–Brain Axis in the Era

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Abstract

The human gut microbiome has emerged as an important component of the bidirectional communication network connecting the gastrointestinal tract and the central nervous system. Growing evidence suggests that alterations in microbial composition and metabolic activity may influence mental health through neural, endocrine, immune, and metabolic pathways. This narrative review examines current evidence concerning the microbiota – gut – brain axis, with particular emphasis on depression and anxiety, microbiome-mediated biological mechanisms, therapeutic interventions, and emerging applications in precision medicine. Relevant literature was identified through a structured PubMed search, prioritizing publications from 2023 to October 2026 alongside foundational studies. The reviewed evidence indicates that microbial metabolites, including short-chain fatty acids, tryptophan-derived compounds, and bile acids, may participate in neuroimmune regulation, intestinal barrier function, and stress-related signaling. Human observational and multi-omics studies have identified microbial and metabolic differences associated with depressive disorders, although findings remain heterogeneous and do not establish universal disease-specific microbial signatures. Probiotics, prebiotics, dietary interventions, and fecal microbiota transplantation have demonstrated varying degrees of therapeutic potential, but clinical findings remain inconsistent. Precision medicine approaches integrating microbial composition, functional pathways, metabolomic profiles, host characteristics, and lifestyle factors may improve patient stratification and intervention selection. However, standardized methods, validated biomarkers, and adequately powered longitudinal trials remain necessary before microbiome-guided mental healthcare can become routine clinical practice.

Keywords: Gut Microbiome, Gut–Brain Axis, Mental Health, Psychobiotics, Precision Medicine

INTRODUCTION

Mental health disorders, particularly major depressive disorder (MDD) and anxiety disorders, represent substantial challenges for modern healthcare systems. Although pharmacological treatments and psychological interventions remain the principal approaches to managing these conditions, considerable variability exists in treatment response, symptom remission, and long-term outcomes. Some patients experience incomplete improvement or adverse effects, while others continue to experience recurrent symptoms despite receiving conventional treatment. These challenges have encouraged researchers to investigate additional biological pathways that may contribute to the development and persistence of mental health disorders. Among the emerging research directions, the relationship between the intestinal microbiome and the central nervous system has attracted considerable scientific attention [1], [2].

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The human gastrointestinal tract contains a complex microbial ecosystem consisting of bacteria, archaea, fungi, viruses, and other microorganisms. Collectively, these microorganisms contribute to digestion, nutrient metabolism, immune regulation, intestinal barrier maintenance, and the production of biologically active metabolites. The term gut microbiota refers to the microorganisms inhabiting the gastrointestinal tract, whereas gut microbiome generally encompasses their genetic material, functional potential, and broader ecological interactions. Increasing evidence indicates that this microbial ecosystem participates in bidirectional communication with the central nervous system through what is commonly described as the microbiota–gut–brain axis [1].

The gut–brain axis represents an interconnected communication network involving neural, endocrine, immune, and metabolic pathways. Communication occurs through the enteric nervous system, vagus nerve, hypothalamic–pituitary–adrenal (HPA) axis, immune mediators, and microbial metabolites. Through these pathways, intestinal microorganisms may influence physiological processes associated with stress regulation, neuroinflammation, neurotransmitter metabolism, and emotional functioning. Conversely, psychological stress, neurological activity, dietary patterns, and neuroendocrine changes can influence gastrointestinal function and microbial composition, demonstrating the bidirectional nature of this relationship [1], [2].

Recent investigations have expanded understanding of the potential relationship between microbial alterations and depressive disorders. Observational studies have identified differences in microbial composition, functional metabolic pathways, and circulating metabolites among individuals with MDD compared with healthy controls. In particular, research has investigated short-chain fatty acid (SCFA) production, tryptophan metabolism, bile acid regulation, and inflammatory pathways as possible biological connections between intestinal microorganisms and mental health [3]–[5].

Importantly, the relationship between the gut microbiome and mental health is not limited to identifying differences in microbial composition. Emerging research increasingly focuses on understanding how microbial functions interact with individual characteristics, including genetic background, dietary intake, medication exposure, metabolic health, and lifestyle. Multi-omics approaches combining microbial sequencing, metabolomics, inflammatory markers, and clinical information are providing opportunities to identify biological patterns that may be more informative than individual microbial taxa. Such developments are particularly relevant to precision medicine, which seeks to improve prevention, diagnosis, and treatment through approaches tailored to individual biological and clinical characteristics [6].

Microbiome-targeted interventions have also become an important area of investigation. Probiotics, prebiotics, synbiotics, dietary modification, and fecal microbiota transplantation (FMT) have been examined for their potential to influence microbial composition and related physiological processes. Although several clinical studies and meta-analyses have reported improvements in depressive and anxiety symptoms following selected interventions, considerable differences remain in study populations, intervention formulations, treatment duration, and outcome measurements [7] – [10]. Consequently, these approaches should currently be considered emerging therapeutic possibilities rather than established replacements for conventional mental healthcare.

Despite growing interest in the gut–brain axis, several important questions remain unresolved. These include the extent to which microbial alterations contribute directly to mental health disorders, the reliability of proposed microbiome-related biomarkers, the mechanisms through which microbial interventions may influence psychological outcomes, and the possibility of identifying individuals who are more likely to benefit from specific interventions.

The present narrative review examines the relationship between the gut microbiome and mental health through the perspective of precision medicine. It primarily focuses on depression and anxiety, considering the biological mechanisms underlying gut – brain communication, human clinical findings, microbiome-targeted interventions, and emerging diagnostic and therapeutic applications. Rather than presenting microbial alterations as established causes of psychiatric disorders, this review critically evaluates the strength and limitations of existing evidence. It further explores how integrated microbiome, metabolomic, clinical, and lifestyle information may contribute to individualized mental healthcare.

The central objective is to establish a translational framework connecting current microbiome research with future personalized approaches to mental health prevention and treatment.

LITERATURE REVIEW

Development of the Microbiota–Gut–Brain Axis Concept

The relationship between gastrointestinal activity and psychological functioning has long been recognized through observations connecting stress, emotional states, and digestive symptoms. However, the identification of the gut microbiome as an active participant in this relationship has substantially expanded the biological understanding of gut–brain communication.

The microbiota – gut – brain axis describes a bidirectional system through which intestinal microorganisms interact with gastrointestinal, immune, endocrine, and neurological processes. Research indicates that microbial communities can influence host physiology through the production of metabolites, modification of intestinal permeability, regulation of immune responses, and interaction with neural signaling pathways [1]. The gut microbiome is not a static biological structure. Its composition and functional activity are influenced by multiple factors, including age, dietary patterns, environmental exposures, medication use, physical activity, and metabolic health. These influences contribute to substantial variation between individuals and may partially explain why microbiome findings are not consistently reproduced across different populations.

Recent reviews have increasingly emphasized that microbial functions may be more relevant to mental health than the presence or absence of individual bacterial species. Microorganisms with different taxonomic identities may perform similar metabolic functions, while closely related strains may demonstrate different biological activities [2], [6]. This distinction is important for precision medicine because an individual's microbial composition alone may not adequately represent the biological processes occurring within the intestinal environment.

Neural Communication Between the Gut and Brain

Neural communication is one of the principal mechanisms through which the gut and brain interact. The enteric nervous system regulates gastrointestinal motility, secretion, and sensory activity, while communicating with the central nervous system through autonomic pathways. The vagus nerve provides an important route for transmitting information from the gastrointestinal tract to the brain. Intestinal epithelial cells, enteroendocrine cells, immune cells, and microbial metabolites can influence sensory signaling, which subsequently affects neural circuits involved in stress responses and emotional regulation [1]. Microbial activity may influence the availability of compounds involved in neural signaling, including gamma-aminobutyric acid (GABA), serotonin-related metabolites, and other neuroactive substances. However, the production of a neurotransmitter by intestinal microorganisms does not necessarily mean that the substance directly enters the brain. Many such compounds have limited capacity to cross the blood–brain barrier. Their potential influence may instead occur through peripheral signaling, vagal pathways, immune regulation, or changes in precursor availability. The relationship between the vagus nerve and microbial activity is particularly relevant to stress-related disorders. Alterations in autonomic regulation may influence gastrointestinal functioning, while microbial metabolites may modify sensory and neuroimmune signaling. These processes provide a plausible biological explanation for the association between intestinal microbial activity and emotional functioning, although their specific contribution to human psychiatric disorders requires further investigation [1], [20].

Endocrine Communication and the HPA Axis

The hypothalamic–pituitary–adrenal axis is an essential component of the physiological stress response. Following exposure to stress, the hypothalamus releases corticotropin-releasing hormone, which stimulates the pituitary gland to release adrenocorticotropic hormone. This subsequently promotes cortisol production by the adrenal glands. Although this response is necessary for maintaining physiological stability, prolonged or dysregulated HPA-axis activity has been associated with several conditions involving altered stress regulation and depressive symptoms.

The gut microbiome may interact with this system through microbial metabolites, immune signaling, and regulation of intestinal barrier function. Changes in microbial composition may influence the production of compounds involved in stress-related signaling, while stress hormones can also affect intestinal motility, epithelial function, and microbial ecology [1], [8]. The interaction is therefore bidirectional. Psychological

stress may contribute to changes in gastrointestinal physiology and microbial composition, while microbial activity may influence physiological responses to subsequent stress exposure. Nevertheless, evidence connecting these processes with specific clinical outcomes remains incomplete. Much of the mechanistic understanding comes from experimental models, and direct confirmation of the same pathways in human psychiatric populations remains an important research priority.

Immune Signaling and Neuroinflammation

Immune regulation represents another important mechanism connecting the gut microbiome with mental health. The intestinal microbiota interacts continuously with the host immune system, contributing to immune development, epithelial defense, and inflammatory regulation. The intestinal epithelial barrier helps prevent excessive movement of microorganisms and microbial products into systemic circulation. Disruption of this barrier may increase exposure to bacterial components, including lipopolysaccharide (LPS), which can stimulate inflammatory signaling. Inflammatory mediators, including interleukin-6, tumor necrosis factor-alpha, and other cytokines, have been investigated in relation to depressive disorders. Persistent inflammatory activity may influence neurotransmitter metabolism, neuroendocrine function, and neural processes associated with mood regulation.

Microbial metabolites, particularly butyrate, may contribute to intestinal barrier maintenance and immune regulation. Experimental studies suggest that SCFAs can influence microglial maturation and activity, although the precise mechanisms and clinical implications remain under investigation [1], [8], [20]. It is important to distinguish between the observation of elevated inflammatory markers in some individuals with depression and the proposition that gut-derived inflammation is the primary cause of their psychiatric condition. Inflammation may represent one component of a broader biological phenotype, and its relevance is likely to differ between individuals.

Microbial Metabolites and Neuroactive Pathways

Microbial metabolites provide a particularly important connection between intestinal microbial activity and host physiology. Unlike taxonomic measurements alone, metabolomic analysis can provide information about the functional products generated through microbial and host metabolic processes. Three metabolite groups have received particular attention in gut–brain research: short-chain fatty acids, tryptophan-derived metabolites, and bile acids.

Short-Chain Fatty Acids

Short-chain fatty acids are primarily generated through microbial fermentation of dietary carbohydrates that escape digestion in the upper gastrointestinal tract. The major SCFAs include acetate, propionate, and butyrate. These compounds contribute to intestinal epithelial energy metabolism, barrier integrity, immune regulation, and host metabolic signaling. Butyrate has received particular attention because of its potential anti-inflammatory effects and involvement in epithelial maintenance. SCFAs may also influence neural functioning through interactions with immune pathways, enteroendocrine signaling, and receptors expressed in different host tissues. Experimental evidence suggests that these metabolites may affect processes relevant to neuroinflammation and stress responses [8]. However, their relationship with mental health is not necessarily straightforward. Differences in circulating or fecal SCFA concentrations do not automatically indicate improved or impaired microbial function. Concentrations may be influenced by production, absorption, intestinal transit, and host metabolism.

Tryptophan Metabolism

Tryptophan is an essential amino acid involved in several metabolic pathways relevant to neurological functioning. It can contribute to serotonin synthesis, kynurenine metabolism, and the production of microbial indole derivatives. The gut microbiome may influence these pathways by modifying tryptophan availability and producing metabolites that interact with intestinal and immune signaling systems. The kynurenine pathway is particularly relevant because its activity can be influenced by inflammatory processes. Alterations in tryptophan metabolism may therefore connect microbial activity, immune regulation, and neurological functioning. Although serotonin is commonly associated with mood regulation, peripheral serotonin produced in the gastrointestinal tract does not directly cross the blood–brain barrier. Consequently, the relationship between gut microbial serotonin-related activity and central serotonergic function should not be interpreted as a simple direct transfer of intestinal serotonin into the brain. Recent reviews have identified amino-acid metabolism and SCFA-related pathways as important areas for further investigation in depression

research [8].

Bile Acid Metabolism

Bile acids are involved in lipid digestion and metabolic regulation. They are also biologically active signaling molecules that interact with host receptors and metabolic pathways. Intestinal microorganisms participate in the transformation of primary bile acids into secondary bile acids. Changes in microbial composition may therefore influence bile acid profiles and related physiological signaling. A 2024 multi-omics investigation identified abnormalities in bile acid metabolism among individuals with MDD and reported associations between microbial characteristics, altered bile acid profiles, and cognitive impairment [5]. These findings suggest that bile acid metabolism may represent an important component of the relationship between intestinal microbial activity and neurological functioning. Nevertheless, further longitudinal and intervention-based studies are necessary to establish the direction and clinical significance of these associations.

METHODOLOGY

Review Design

This study employed a narrative literature review approach to examine the relationship between the gut microbiome and mental health, with particular emphasis on the microbiota–gut–brain axis and its potential applications in precision medicine. A narrative approach was selected because the research question encompasses multiple interconnected biological mechanisms, clinical conditions, intervention strategies, and emerging technological applications. The objective was to integrate findings from different research designs and critically evaluate their relevance to personalized mental healthcare rather than calculate a pooled intervention effect. The review was informed by the principles of transparent narrative-review reporting, including clear identification of the research objective, description of the literature search, appropriate referencing, and critical interpretation of evidence [19].

Literature Search Strategy

PubMed was used as the principal biomedical literature database. The search emphasized publications from January 2023 through October 30, 2026, while earlier foundational studies were considered when necessary to explain established biological mechanisms. The search strategy combined terms relating to the gut microbiome, gut – brain communication, mental health disorders, microbial metabolites, therapeutic interventions, and precision medicine. The principal search expression was:

Literature Selection Criteria

Priority was given to peer-reviewed research articles, randomized controlled trials, observational human studies, systematic reviews, meta-analyses, and authoritative clinical recommendations. Studies were considered particularly relevant when they investigated relationships between microbial composition or function and validated mental-health outcomes, examined biological mechanisms connecting microbial activity with neurological processes, or evaluated microbiome-targeted interventions. Foundational mechanistic studies and established reviews published before 2023 were included selectively to provide biological context. Animal and experimental studies were considered when they provided relevant mechanistic explanations. However, findings from these studies were not treated as equivalent to evidence obtained directly from human clinical populations. Studies with limited relevance to mental health, insufficient methodological information, or outcomes unrelated to the principal review objectives were not prioritized.

Thematic Organization and Evidence Synthesis

The selected literature was organized into five principal themes: biological mechanisms of the microbiota–gut–brain axis, human microbiome findings in depression and anxiety, microbial metabolites and multi-omics research, microbiome-targeted interventions, and applications of precision medicine. The evidence was interpreted qualitatively, considering study design, population characteristics, intervention type, outcome measurements, and methodological limitations. Particular attention was given to distinguishing observational associations from mechanistic evidence and clinical intervention findings. Differences in study

populations, sequencing techniques, medication exposure, dietary patterns, and intervention formulations were considered when interpreting inconsistencies.

The review was not designed as a systematic review or meta-analysis. Accordingly, no PRISMA screening counts or pooled effect estimates were generated by the present authors. The literature selection was purposeful and thematic, and the findings are presented as a critical synthesis of relevant published research.

(("gut microbiome" OR "gut microbiota" OR "microbiota-gut-brain axis" OR "gut-brain axis") AND ("mental health" OR depression OR "major depressive disorder" OR anxiety OR stress OR psychiatric) AND ("precision medicine" OR personalized OR biomarker OR metabolomics OR "multi-omics" OR probiotic OR psychobiotic OR prebiotic OR synbiotic OR diet OR "fecal microbiota transplantation"))

Additional topic-specific searches were used to identify literature concerning:

- Neural and vagal communication between the gut and brain.
- HPA-axis regulation and stress responses.
- Inflammatory pathways and intestinal barrier function.
- Short-chain fatty acids, tryptophan metabolism, and bile acids.
- Human microbiome studies involving depression and anxiety.
- Probiotic, prebiotic, dietary, and FMT interventions.
- Microbiome-based biomarkers and precision medicine.

RESULTS OF THE LITERATURE SYNTHESIS

Gut Microbiome Alterations in Depressive Disorders

Human observational studies have identified differences in intestinal microbial composition between individuals with depressive disorders and healthy comparison groups. However, the findings are not entirely consistent, particularly regarding overall microbial diversity and the relative abundance of major bacterial groups.

A systematic review and meta-analysis by Gao et al. examined 44 studies involving 2,091 individuals with depressive disorders and 2,792 healthy controls [3]. The analysis did not identify significant overall differences in alpha-diversity indices or the relative abundance of Firmicutes and Bacteroidetes. Nevertheless, several bacterial genera demonstrated recurring differences across studies. The review identified reductions in several genera associated with butyrate production, including Faecalibacterium, Coprococcus, and Fusicatenibacter. Other genera, including Eggerthella, Enterococcus, and Flavonifractor, were reported at higher levels in depressive populations. These observations suggest that microbial alterations associated with depression may involve changes in specific microbial communities and their metabolic functions rather than a uniform reduction in overall microbial diversity. An important finding of this review was the influence of medication exposure and dietary habits on microbial composition [3]. This is particularly relevant because individuals with depression may differ considerably in antidepressant use, nutritional intake, physical activity, and gastrointestinal health. Consequently, the identification of a single microbial profile characteristic of depression remains difficult.

Multi-Omics Evidence and Metabolic Disturbances

Recent multi-omics investigations have expanded the understanding of microbiome-related differences in MDD by combining microbial sequencing with metabolic measurements. Xie et al. conducted an integrated investigation involving 99 patients with MDD and 50 healthy controls [4]. Their analysis combined 16S rRNA sequencing, metagenomic sequencing, and plasma metabolomics. The researchers identified structural and functional alterations in the gut microbiota, including increased Enterococcus abundance and changes in several microbial metabolic pathways. Plasma metabolomic analysis also identified differences in amino acids, bile acids, sphingolipids, and cholesterol-related metabolites. This investigation is important because it demonstrates that depression-associated microbial changes may occur alongside broader metabolic disturbances. It also highlights the limitations of relying exclusively on bacterial

abundance when investigating complex psychiatric conditions.

Further evidence is provided by Jia et al., who investigated microbial and metabolic characteristics in individuals with MDD and examined their relationship with cognitive impairment [5]. Their research included serum metabolomic profiling of 104 patients with MDD and 77 healthy controls, with additional fecal metagenomic analysis and validation in an independent cohort. The study identified abnormalities in bile acid metabolism and associations between microbial characteristics, bile acid-related metabolic pathways, and cognitive dysfunction. These findings suggest that microbiome-related metabolic disturbances may be relevant not only to mood symptoms but also to specific cognitive characteristics associated with depression.

More recently, Zhao et al. examined microbiota–metabolome interactions in first-episode depression using fecal and serum metabolomic analyses [6]. Their investigation included an initial cohort of 186 participants and three additional validation cohorts. The researchers identified alterations involving microbial species, metabolic pathways, and circulating metabolites. A model based on 34 serum metabolites achieved area-under-the-curve values of approximately 0.82 and 0.80 in test and validation datasets, respectively [6]. These findings provide promising evidence for metabolite-based biomarker development. However, the reported predictive performance should not be interpreted as proof that the model is ready for clinical diagnosis. Further independent validation, comparison with conventional clinical assessments, and evaluation across diverse populations are necessary. Overall, the multi-omics literature indicates that functional microbial activity and host metabolic responses may offer more informative biological signatures than isolated taxonomic measurements.

The Gut Microbiome and Anxiety-Related Symptoms

Although depression currently has a comparatively developed microbiome research literature, anxiety has also become an important area of investigation. Anxiety disorders involve complex interactions among stress regulation, autonomic functioning, inflammatory responses, and emotional processing. These physiological processes overlap with several mechanisms through which intestinal microorganisms may influence host functioning. The gut microbiome may contribute to anxiety-related processes through modulation of the HPA axis, vagal signaling, intestinal barrier function, and microbial metabolite production [1], [2]. Nevertheless, evidence linking particular microbial taxa to anxiety disorders remains inconsistent. Differences in diagnostic definitions, symptom severity, medication exposure, and study populations make direct comparisons difficult.

A further complication is the frequent coexistence of anxiety and depressive symptoms. Some intervention studies examine both outcomes simultaneously, making it difficult to determine whether observed improvements are associated with a specific psychiatric condition or broader changes in psychological well-being. The intervention literature provides some encouraging findings. A systematic review and meta-analysis by Asad et al. examined 23 randomized controlled trials involving 1,401 participants with clinically diagnosed psychiatric conditions [9]. The analysis identified significant reductions in depressive and anxiety symptoms associated with probiotic interventions, although substantial heterogeneity was observed. A broader meta-analysis by Zhang et al. included 72 randomized controlled trials investigating probiotics, prebiotics, and synbiotics [10]. The pooled analysis reported improvements in depression and anxiety scores compared with control conditions. However, the included studies involved heterogeneous populations, including individuals with diagnosed psychiatric conditions, chronic illnesses, and psychological symptoms in otherwise healthy populations. These findings support further investigation of the microbiome–anxiety relationship but do not establish a universal microbial signature or demonstrate that microbiome interventions are effective for all anxiety disorders.

Evidence from Microbiome-Targeted Interventions

Microbiome-targeted interventions represent an important translational application of gut–brain research. The principal approaches include probiotics, prebiotics, synbiotics, dietary modification, and fecal microbiota transplantation. Probiotics are live microorganisms that, when administered in adequate amounts, provide a health benefit to the host. Psychobiotics refer more specifically to microorganisms or microbial-related interventions investigated for their potential effects on psychological functioning.

Probiotics and Psychobiotics

Probiotic interventions have received considerable attention because certain bacterial strains may

influence intestinal barrier function, microbial metabolism, immune responses, and neuroactive signaling. However, probiotic effects are strain-specific. Different microorganisms may have different metabolic properties, and results obtained using one formulation cannot automatically be generalized to another. Walden et al. investigated a multistrain probiotic intervention in 70 healthy adults using a randomized, double-blind, placebo-controlled design [11]. Participants receiving the probiotic reported improvements in several mood and anxiety questionnaire scores. The study also identified changes in plasma serotonin measurements.

However, the participants were healthy adults rather than patients diagnosed with MDD or anxiety disorders. The findings therefore provide preliminary evidence of possible psychological effects but do not establish clinical effectiveness in psychiatric populations. Strodl et al. conducted a randomized, double-blind controlled trial involving 120 adults diagnosed with MDD [12]. The intervention combined probiotics with magnesium orotate and coenzyme Q10. The study reported improvements in selected depressive and anxiety outcomes during the treatment period. Nevertheless, because the intervention contained multiple components, the individual contribution of probiotics could not be isolated. A 2026 randomized, placebo-controlled study by Moschonis et al. investigated a probiotic blend in adults with subthreshold depression [13]. The study examined psychological outcomes alongside inflammatory, immune, and stress-related biomarkers. Although some biomarker changes were observed, the findings did not establish a consistent between-group improvement in the principal psychological symptom outcomes.

These individual trials demonstrate why probiotic research should be interpreted according to population characteristics, intervention composition, and the clinical significance of measured outcomes. A systematic review and meta-analysis by Asad et al. reported that probiotics were associated with a reduction in depression symptoms (standardized mean difference [SMD] = −0.96; 95% confidence interval [CI]: −1.31 to −0.61) and anxiety symptoms (SMD = −0.59; 95% CI: −0.98 to −0.19) in clinically diagnosed populations [9]. The authors also reported substantial heterogeneity, indicating that intervention characteristics and study design influenced the findings.

Similarly, Zhang et al. reported pooled reductions in depression (SMD = −0.53; 95% CI: −0.67 to −0.39) and anxiety (SMD = −0.44; 95% CI: −0.59 to −0.28) across 72 randomized controlled trials [10]. Although these results are encouraging, the two meta-analyses should not be interpreted as independent confirmation of the same treatment effect because their study populations and included trials may overlap. The evidence therefore supports continued investigation of probiotics as potential adjunctive interventions rather than their use as substitutes for established psychiatric treatments.

Prebiotics and Synbiotics

Prebiotics are substrates selectively utilized by host microorganisms that confer a health benefit. They may include specific dietary fibers and other compounds capable of influencing microbial fermentation and metabolic activity. Synbiotics combine live microorganisms with substrates intended to support beneficial microbial activity. Their potential relevance to mental health is associated with their ability to modify intestinal microbial ecology and influence the production of metabolites such as SCFAs.

However, evidence concerning their effectiveness in psychiatric populations remains less established than the broader probiotic literature. Asad et al. reported that prebiotics did not demonstrate a statistically significant effect on depressive symptoms in the clinically diagnosed populations included in their meta-analysis [9]. The broader analysis by Zhang et al. identified potential benefits of prebiotic and synbiotic interventions for psychological outcomes, but the authors emphasized the substantial heterogeneity and limitations of the available trials [10]. Differences in the type of prebiotic substrate, dose, dietary background, baseline microbial composition, and intervention duration may contribute to inconsistent outcomes. Future studies should investigate whether baseline microbial characteristics can identify individuals who are more likely to respond to specific prebiotic or synbiotic formulations.

Dietary Interventions and Microbial Regulation

Diet is one of the most important modifiable influences on gut microbial composition and function. Dietary fiber, fermented foods, plant-derived compounds, fats, and protein sources can influence microbial ecology and metabolite production. Dietary patterns rich in diverse plant foods may support microbial fermentation and SCFA production, whereas diets characterized by low fiber intake and high consumption of highly processed foods may contribute to less favorable metabolic and inflammatory profiles. However, the

relationship between dietary modification and mental health involves several pathways beyond the microbiome, including nutrient availability, metabolic regulation, cardiovascular health, and inflammatory processes.

Magzal et al. examined a personalized dietary intervention based on Mediterranean dietary principles among community-dwelling older adults [14]. The six-month intervention was associated with improvements in depressive symptoms and quality of life, together with changes in microbial diversity and metabolite profiles. The study also identified associations between dietary nutrient intake, microbiome characteristics, and mental-health measurements. Nevertheless, the observed relationships do not independently establish that microbiome changes mediated the psychological improvements. Further evidence comes from the PREDIDEP randomized trial analysis reported by Cabrera-Suárez et al. [15]. The study evaluated a Mediterranean diet intervention enriched with extra virgin olive oil among individuals with previous depressive episodes.

After two years, the intervention did not demonstrate a significant difference in the primary outcome of depression recurrence. However, improvements in subsyndromal depressive symptoms were observed at selected follow-up periods. These findings suggest that dietary interventions may contribute to mental-health management, although their effects should be evaluated independently of assumptions about microbiome mediation. A major opportunity for future research is to combine personalized nutrition with microbiome and metabolomic profiling to identify dietary approaches that are better suited to individual biological characteristics.

Fecal Microbiota Transplantation

Fecal microbiota transplantation involves transferring intestinal microbial communities from a screened donor into a recipient to modify the recipient's microbial ecosystem. FMT has attracted attention because it provides a more direct approach to altering microbial community composition than conventional dietary or probiotic interventions. Green et al. conducted a pilot randomized controlled trial investigating FMT in adults with moderate-to-severe MDD [16]. The study primarily examined feasibility, acceptability, and safety. Although the intervention demonstrated that FMT could be administered within a controlled research setting, the small sample size was insufficient to establish therapeutic efficacy. More recent evidence is provided by Li et al., who conducted a randomized, double-blind, placebo-controlled trial investigating FMT as an adjunct to escitalopram treatment in patients with MDD [17]. The study found no statistically significant difference in remission rates between the intervention and placebo groups at eight weeks. However, the FMT group demonstrated greater reductions in Hamilton Depression Rating Scale scores at selected treatment time points.

Multi-omics analyses also identified donor microbial engraftment and changes in bile acid profiles and inflammatory pathways. These findings are important because they provide clinical evidence connecting microbiome modification with metabolic and inflammatory changes during antidepressant treatment. Nevertheless, the absence of a significant difference in remission rates and the limited number of clinical trials prevent conclusions about routine therapeutic effectiveness. FMT also requires careful consideration of donor screening, infectious risks, long-term safety, and standardized administration procedures. It should therefore remain an investigational approach for psychiatric conditions.

Table 1. Representative Studies Investigating the Gut Microbiome and Mental Health

Study	Design and Population	Principal Findings	Main Limitation
Gao et al. [3]	Systematic review and meta-analysis; 44 studies	Identified recurring microbial differences in depressive disorders, particularly involving butyrate-associated genera	High between-study heterogeneity
Xie et al. [4]	Multi-omics observational study; 99 MDD patients and 50 controls	Identified microbial, functional, and circulating metabolic differences	Observational design
Jia et al. [5]	Multi-omics study with validation cohorts	Identified associations between bile acid metabolism, microbial characteristics, and cognitive impairment	Causal pathways remain uncertain
Magzal et al. [14]	Personalized dietary intervention; older adults	Reported improvements in depressive symptoms and changes in microbial and metabolic profiles	Limited ability to establish microbiome mediation
Asad et al. [9]	Meta-analysis of 23 RCTs;	Reported improvements in depression and	Heterogeneous

	1,401 participants	anxiety with probiotic interventions	interventions and study populations
Zhang et al. [10]	Meta-analysis of 72 RCTs	Reported improvements in depression and anxiety following microbiome-targeted interventions	Mixed populations and methodological heterogeneity
Li et al. [17]	Randomized, double-blind, placebo-controlled FMT trial	Reported selected symptom improvements and microbial-metabolic changes	No significant difference in remission rates

The studies in Table 1 collectively demonstrate that the evidence base has expanded from identifying differences in microbial composition to investigating functional pathways, circulating metabolites, and clinical intervention outcomes. However, the findings also reveal substantial variation in study design and clinical applicability. These differences are important when considering the development of microbiome-informed mental healthcare.

DISCUSSION

Integrating Biological Evidence with Precision Medicine

The findings of this review indicate that the microbiota – gut – brain axis represents a biologically important area of mental-health research. Neural communication, immune regulation, endocrine responses, and microbial metabolism provide interconnected mechanisms through which intestinal microbial activity may influence neurological and psychological functioning [1], [2]. Nevertheless, the relationship between microbial alterations and psychiatric disorders is complex. Current evidence does not support the existence of a single microbial composition that consistently identifies all individuals with depression or anxiety.

Instead, the findings suggest that mental-health-related microbial differences may be expressed through combinations of taxonomic changes, functional metabolic pathways, inflammatory characteristics, and host-specific biological responses. This observation has important implications for precision medicine. Traditional microbiome studies frequently investigate whether particular microorganisms are more or less abundant in individuals with a specific condition. Although such comparisons provide useful information, they may not adequately represent the functional activity of the microbial community. For example, two individuals may have different microbial compositions but similar capacities for producing particular metabolites. Conversely, individuals with similar microbial profiles may demonstrate different metabolic activities because of differences in diet, medication exposure, or host physiology. Consequently, precision microbiome research should increasingly integrate microbial composition with functional and host-related measurements.

A Multidimensional Framework for Personalized Mental Healthcare

The evidence reviewed in this study supports a conceptual framework in which microbiome-related information is integrated with clinical, metabolic, inflammatory, and lifestyle characteristics.

The proposed framework consists of six interconnected components.

Microbial composition and diversity: Metagenomic and sequencing approaches can identify microbial communities and their relative abundance. These measurements may help characterize individual microbial profiles, although taxonomic information alone is unlikely to provide sufficient clinical discrimination.

Microbial functional characteristics: Functional pathways associated with SCFA production, amino-acid metabolism, inflammatory processes, and bile acid transformation may provide additional information about microbial activity.

Host metabolic profile: Circulating and fecal metabolites may help characterize interactions between microbial activity and host metabolism. Bile acids, amino acids, indole derivatives, and SCFAs are potential candidates for further investigation.

Immune and neuroendocrine characteristics: Inflammatory markers and selected stress-related measurements may contribute to identifying biological subgroups with different physiological characteristics.

Clinical and lifestyle characteristics: Psychiatric diagnosis, symptom severity, gastrointestinal symptoms, medication history, dietary intake, physical activity, sleep, and metabolic health should be

considered alongside microbiome measurements. Integrated prediction and intervention selection: Machine-learning and multi-omics approaches may eventually combine these information sources to identify patient subgroups and evaluate potential intervention responses.

Table 2. Proposed Precision-Medicine Framework for Microbiome-Informed Mental Healthcare

Precision Component	Candidate Measurements	Potential Application	Current Evidence Status
Microbial composition	Microbial species, strains, community diversity	Biological characterization and patient stratification	Emerging; inconsistent disease-specific signatures
Microbial function	SCFA pathways, tryptophan metabolism, bile acid transformation	Functional endotyping	Promising research area
Metabolomic profile	Amino acids, bile acids, indoles, SCFAs	Biomarker discovery and response prediction	Early clinical evidence
Immune phenotype	CRP, IL-6, TNF- α and related markers	Identification of inflammatory characteristics	Investigational and nonspecific
Neuroendocrine phenotype	Cortisol and HPA-axis measurements	Stress-related biological characterization	Mechanistically plausible
Clinical phenotype	Diagnosis, symptom severity, gastrointestinal symptoms, medication history	Clinical classification and treatment planning	Established clinical information
Lifestyle phenotype	Dietary patterns, sleep, exercise, BMI	Personalized prevention and dietary intervention	Important modifiable factors
Integrated analytics	Multi-omics and machine-learning models	Predictive stratification and individualized intervention selection	Research-stage application

This framework is conceptual rather than a validated clinical algorithm. Its purpose is to demonstrate how different biological and clinical information sources could be integrated into future research and healthcare applications.

Microbiome-Based Biomarkers and Diagnostic Potential

The development of microbiome-related biomarkers represents one of the most promising applications of precision medicine in psychiatry. Current diagnostic approaches for depression and anxiety rely primarily on clinical assessments, symptom reports, and established diagnostic criteria. Although these approaches remain essential, they do not directly characterize the biological heterogeneity that may exist between individuals with similar clinical presentations.

Microbiome and metabolomic measurements may eventually contribute additional biological information. The multi-omics investigation by Xie et al. demonstrated that microbial and circulating metabolic changes can be examined simultaneously in patients with MDD [4]. Similarly, Jia et al. identified relationships between microbial characteristics, bile acid metabolism, and cognitive impairment [5]. The findings reported by Zhao et al. provide further support for metabolite-based classification approaches [6]. Their machine-learning model demonstrated encouraging discrimination between depression and control groups in test and validation datasets.

However, several issues must be addressed before such approaches can be applied clinically. First, a biomarker must demonstrate reproducibility across independent populations. Microbial composition varies substantially according to geographical location, dietary patterns, medication exposure, age, and environmental conditions. Second, the predictive value of microbiome-related biomarkers must be compared with established clinical assessments. A biomarker that distinguishes patients from healthy controls does not necessarily improve diagnosis, prognosis, or treatment selection in real clinical settings.

Third, longitudinal studies are necessary to determine whether microbial and metabolic measurements change consistently with disease progression, symptom remission, or treatment response. Therefore, microbiome-based biomarkers should currently be considered exploratory research tools rather than established diagnostic tests.

Personalized Nutrition and Psychobiotic Interventions

Personalized nutrition represents a particularly promising direction because dietary patterns influence both microbial composition and host metabolism. The dietary intervention reported by Magzal et al.

demonstrated that individualized nutritional recommendations can be associated with changes in depressive symptoms and microbial characteristics among older adults [14]. However, the findings from dietary studies must be interpreted carefully because improvements in mental health may result from multiple nutritional and metabolic pathways rather than microbiome modification alone.

Future research should investigate whether baseline microbial characteristics can help predict individual responses to particular dietary interventions. A similar principle applies to psychobiotic interventions. Current probiotic studies frequently use different bacterial strains, doses, combinations, and treatment durations. These differences make it difficult to determine which formulations may be most effective for particular patient populations. Precision psychobiotic research therefore emphasizes the importance of identifying specific microbial strains and establishing their biological mechanisms before recommending them for particular clinical conditions [7].

This approach may eventually support the development of interventions selected according to individual microbial and metabolic characteristics. Nevertheless, such strategies require more rigorous clinical testing. The available evidence does not currently justify routine microbiome testing to select commercial probiotic products for patients with depression or anxiety.

Challenges in Clinical Translation

Despite growing scientific interest, several challenges continue to limit the translation of gut – brain research into clinical practice.

Methodological Heterogeneity

Studies use different sequencing technologies, sample-processing procedures, microbial classification methods, and statistical approaches. Differences in sample collection, storage, and laboratory protocols may influence the findings. Standardization is therefore necessary to improve reproducibility and allow meaningful comparisons between research populations.

Confounding Variables

Microbial composition is influenced by multiple factors, including diet, age, sex, body mass index, medication use, gastrointestinal health, physical activity, sleep, and geographical environment. Psychiatric populations may also differ in antidepressant exposure and the severity or duration of symptoms. Failure to adequately account for these factors can lead to incorrect interpretations of microbial associations.

Limited Longitudinal Evidence

Many studies use cross-sectional designs, making it difficult to determine whether microbial alterations precede psychiatric symptoms, develop as a consequence of illness, or reflect shared environmental and physiological influences. Longitudinal investigations are necessary to clarify these relationships.

Intervention Variability

Probiotic and prebiotic studies differ considerably in microbial strains, formulations, dosage, treatment duration, and participant characteristics. The same intervention may not produce similar outcomes across different populations. Consequently, intervention-specific findings should not be generalized to all probiotic or prebiotic products.

Biomarker Validation

Although multi-omics and machine-learning studies have identified promising biological signatures, most remain at the research stage. Clinical implementation requires independent validation, standardized measurements, reproducible prediction performance, and evidence that biomarker-guided decisions improve patient outcomes.

Safety and Ethical Considerations

FMT and other intensive microbiome-modifying approaches require careful evaluation of infectious risks, donor selection, treatment standardization, and long-term safety. Microbiome-based precision healthcare also raises questions regarding patient privacy, data protection, accessibility, and the potential cost of advanced diagnostic testing.

Future Research Priorities

Future research should move beyond the identification of general microbial differences and focus on

establishing clinically meaningful relationships between microbial function and mental-health outcomes.

First, large prospective cohort studies should investigate the temporal relationship between microbiome characteristics and the development of depression and anxiety. Repeated microbial and metabolic measurements may help distinguish persistent biological characteristics from temporary changes associated with diet, medication, or illness. Second, clinical intervention trials should incorporate standardized microbial and metabolomic measurements alongside validated psychiatric outcome assessments. Such studies should determine whether biological changes occur before, alongside, or independently of improvements in psychological symptoms. Third, future research should examine whether individuals with different baseline biological characteristics respond differently to specific probiotic strains, dietary interventions, or other microbiome-targeted treatments.

Fourth, integrated multi-omics approaches should be developed using sufficiently large and diverse populations. Predictive models should be validated across independent cohorts and compared with conventional clinical assessment methods. Fifth, clinical studies should improve reporting of intervention composition, dosage, treatment duration, adherence, adverse events, and long-term outcomes. Finally, future clinical recommendations should distinguish between interventions supported by replicated clinical evidence and those that remain experimental.

The 2026 CANMAT task force recommendations represent an important development in this direction [18]. The recommendations cautiously position probiotics as potential third-line adjunctive interventions for adults with MDD, while identifying insufficient evidence to recommend routine use of prebiotics, synbiotics, or FMT. The subsequent 2026 FMT randomized trial provides additional clinical information, but its findings do not yet establish a clear improvement in remission rates [17]. Together, these developments demonstrate the importance of connecting emerging biological discoveries with appropriately cautious clinical recommendations.

Limitations of the Present Review

The present review has several limitations. First, it employed a narrative rather than systematic review design. Although a structured PubMed search strategy was used, the literature selection was thematic and purposeful rather than exhaustive. Therefore, the possibility of selection bias cannot be completely excluded. Second, the review prioritized publications from 2023 through October 2026, with selected earlier studies included to explain foundational biological mechanisms. Relevant research published in other databases or outside the selected literature may not have been fully represented. Third, considerable methodological heterogeneity exists across the included literature. Differences in microbial sequencing, diagnostic criteria, study populations, intervention formulations, and outcome measurements limit direct comparisons. Fourth, much of the mechanistic evidence remains dependent on experimental and preclinical research. Although these findings provide important biological explanations, they cannot automatically be generalized to human psychiatric populations. Finally, the emerging nature of microbiome-based precision medicine means that many proposed biomarkers and individualized intervention strategies have not yet undergone sufficient independent clinical validation. Despite these limitations, the review provides an integrated assessment of current evidence and identifies important opportunities for future translational research.

CONCLUSION

The gut microbiome has emerged as an important component of the biological systems involved in communication between the gastrointestinal tract and the central nervous system. Evidence suggests that microbial composition and metabolic activity may influence mental health through neural signaling, immune regulation, HPA-axis activity, and the production of biologically active metabolites. Human studies have identified microbial and metabolic differences associated with depressive disorders, particularly involving short-chain fatty acid production, amino-acid metabolism, bile acid regulation, and inflammatory pathways. Probiotics, dietary modification, prebiotics, synbiotics, and fecal microbiota transplantation have demonstrated varying degrees of therapeutic potential. However, the available evidence remains heterogeneous and does not support the routine use of microbiome-targeted interventions as replacements for established psychiatric treatments. The principal opportunity for future research lies in integrating microbiome composition, functional metabolic pathways, host biological characteristics, and lifestyle

information through precision-medicine approaches. Such integration may eventually improve patient stratification, biomarker development, and the selection of individualized interventions.

Nevertheless, clinical translation requires standardized research methodologies, validated biomarkers, adequately powered longitudinal studies, and clinical trials demonstrating that microbiome-informed treatment decisions improve patient outcomes. Ultimately, the microbiota–gut–brain axis offers a promising direction for understanding the biological complexity of mental health disorders. Its greatest potential may lie not in identifying a universal microbial signature of depression or anxiety, but in understanding the individual biological differences that influence disease vulnerability and treatment response.

REFERENCES

[1] J. F. Cryan et al., "The microbiota-gut-brain axis," *Physiological Reviews*, vol. 99, no. 4, pp. 1877–2013, 2019, doi: 10.1152/physrev.00018.2018.

[2] S.-H. Lee, C. Han, and C. Shin, "IUPHAR review: Microbiota-gut-brain axis and its role in neuropsychiatric disorders," *Pharmacological Research*, vol. 216, Art. no. 107749, 2025, doi: 10.1016/j.phrs.2025.107749.

[3] M. Gao, J. Wang, P. Liu, H. Tu, R. Zhang, Y. Zhang, N. Sun, and K. Zhang, "Gut microbiota composition in depressive disorder: A systematic review, meta-analysis, and meta-regression," *Translational Psychiatry,* vol. 13, Art. no. 379, 2023, doi: 10.1038/s41398-023-02670-5.

[4] Z. Xie et al., "Integrated multi-omics analysis reveals gut microbiota dysbiosis and systemic disturbance in major depressive disorder," *Psychiatry Research*, vol. 334, Art. no. 115804, 2024, doi: 10.1016/j.psychres.2024.115804.

[5] M. Jia et al., "Gut microbiota dysbiosis promotes cognitive impairment via bile acid metabolism in major depressive disorder," *Translational Psychiatry*, vol. 14, Art. no. 503, 2024, doi: 10.1038/s41398-024-03211-4.

[6] L. Liu et al., "The emerging role of the gut microbiome in depression: Implications for precision medicine," *Molecular Psychiatry*, vol. 30, no. 12, pp. 5901–5913, 2025, doi: 10.1038/s41380-025-03191-x.

[7] R. F. Slykerman et al., "Precision psychobiotics for gut-brain axis health: Advancing the discovery pipelines to deliver mechanistic pathways and proven health efficacy," *Microbial Biotechnology*, vol. 18, no. 1, Art. no. e70079, 2025, doi: 10.1111/1751-7915.70079.

[8] M. Chen, Q. Lyu, L. Huang, Y. Lou, and L. Wang, "Gut-brain axis and depression: Focus on the amino acid and short-chain fatty acid metabolism," *Behavioural Pharmacology*, vol. 36, no. 7, pp. 439–453, 2025, doi: 10.1097/FBP.0000000000000851.

[9] A. Asad, M. Kirk, S. Zhu, X. Dong, and M. Gao, "Effects of prebiotics and probiotics on symptoms of depression and anxiety in clinically diagnosed samples: Systematic review and meta-analysis of randomized controlled trials," *Nutrition Reviews*, vol. 83, no. 7, pp. e1504–e1520, 2025, doi: 10.1093/nutrit/nuae177.

[10] J. Zhang, L. Zhu, Q. Meng, Z. Wang, and H. Zhu, "The efficacy of probiotics, prebiotics, and synbiotics on anxiety, depression, and sleep: A systematic review and meta-analysis of randomized controlled trials," *BMC Psychiatry*, vol. 25, Art. no. 1199, 2025, doi: 10.1186/s12888-025-07644-z.

[11] K. E. Walden, J. M. Moon, A. M. Hagele, L. E. Allen, C. J. Gaige, J. M. Krieger, R. Jäger, P. W. Mumford, M. Pane, and C. M. Kerksick, "A randomized controlled trial to examine the impact of a multi-strain probiotic on self-reported indicators of depression, anxiety, mood, and associated biomarkers," *Frontiers in Nutrition*, vol. 10, Art. no. 1219313, 2023, doi: 10.3389/fnut.2023.1219313.

[12] E. Strodl, M. Bambling, S. Parnam, G. Ritchie, S. Cramb, and L. Vitetta, "Probiotics and magnesium orotate for the treatment of major depressive disorder: A randomised double blind controlled trial," *Scientific Reports*, vol. 14, Art. no. 20841, 2024, doi: 10.1038/s41598-024-71093-z.

[13] G. Moschonis et al., "Evaluation of a probiotic blend on psychosocial health and biomarkers of inflammatory, immune and stress response in adults with subthreshold depression: A double-blind, randomised, placebo-controlled trial," *British Journal of Nutrition*, vol. 135, no. 5, pp. 481–495, 2026, doi: 10.1017/S0007114524001703.

[14] F. Magzal, S. Turroni, M. Fabbrini, M. Barone, A. Vitman Schorr, A. Ofran, and S. Tamir, "A personalized diet intervention improves depression symptoms and changes microbiota and metabolite profiles among community-dwelling older adults," *Frontiers in Nutrition*, vol. 10, Art. no. 1234549, 2023, doi: 10.3389/fnut.2023.1234549.

[15] B. M. Cabrera-Suárez et al., "Mediterranean diet-based intervention to improve depressive symptoms: Analysis of the PREDIDEP randomized trial," *Nutritional Neuroscience,* vol. 27, no. 9, pp. 951–961, 2024, doi: 10.1080/1028415X.2023.2283290.

[16] J. E. Green et al., “Feasibility, acceptability, and safety of faecal microbiota transplantation in the treatment of major depressive disorder: A pilot randomized controlled trial,” *The Canadian Journal of Psychiatry,* vol. 68, no. 5, pp. 315–326, 2023, doi: 10.1177/07067437221150508.

[17] J. Li et al., “Adjunctive fecal microbiota transplantation for major depressive disorder: A randomized, double-blind, placebo-controlled trial,” *Cell Host & Microbe*, vol. 34, no. 7, pp. 1367–1382.e7, 2026, doi: 10.1016/j.chom.2026.05.017.

[18] A. Bahji et al., “The Canadian Network for Mood and Anxiety Treatments Task Force recommendations for the use of probiotics, prebiotics, synbiotics, and fecal microbiota transplants in adults with major depressive disorder,” *The Canadian Journal of Psychiatry*, vol. 71, no. 5, pp. 346–358, 2026, doi: 10.1177/07067437251394363.

[19] C. Baethge, S. Goldbeck-Wood, and S. Mertens, “SANRA—a scale for the quality assessment of narrative review articles,” *Research Integrity and Peer Review*, vol. 4, Art. no. 5, 2019, doi: 10.1186/s41073-019-0064-8.

[20] C. Long-Smith, K. J. O'Riordan, G. Clarke, C. Stanton, T. G. Dinan, and J. F. Cryan, “Microbiota-gut-brain axis: New therapeutic opportunities,” *Annual Review of Pharmacology and Toxicology*, vol. 60, pp. 477–502, 2020, doi: 10.1146/annurev-pharmtox-010919-023628.