Acta Scientific NUTRITIONAL HEALTH (ISSN:2582-1423)

Volume 9 Issue 12 December 2025

Research Article

An Umbrella Review (To 30 April 2025) of the Impact of Gut Microbiome on Mental Health

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Received: October 06, 2025

Published: November 14, 2025

Abstract

Mental health conditions affect millions worldwide, disrupting behavioural and cognitive functions. Emerging evidence suggests an association between gut microbiota alterations and the development of these conditions; however, findings remain inconsistent due to methodological limitations and variation in sequencing techniques. Therefore, this umbrella review aims to synthesize and critically evaluate existing systematic reviews and meta-analyses investigating the role of the gut microbiome in mental health. A PubMed search identified systematic reviews and meta-analyses published up to 30 April 2025, focusing on major depressive disorder (MDD), anxiety, autism spectrum disorder (ASD), schizophrenia, bipolar disorder (BD), anorexia nervosa (AN), attention-deficit/hyperactivity disorder (ADHD), and post-traumatic stress disorder (PTSD). Of 150 reviews screened, 31 were included in this umbrella review. Findings were organized into two themes: (a) microbial composition and diversity in mental health conditions, and (b) functional metabolites of the microbiota influencing brain function. Across disorders, alpha diversity findings were relatively inconsistent, except for more reliable differences reported in MDD, ASD, and AN. Beta diversity differences were observed more consistently, particularly in MDD and ASD. At the taxonomic level, reproducible shifts included reductions in butyrate-producing taxa (*Faecalibacterium* and *Coprococcus*) and enrichments of pro-inflammatory taxa (*Eggerthella* and *Escherichia/Shigella*). Alterations in functional metabolites, such as reduced short-chain fatty acids (SCFAs), particularly butyrate, and disruptions in tryptophan metabolism were also highlighted to impair gut barrier integrity and influence neurotransmitter pathways. Hence, current evidence suggests that gut microbiota alterations may play a role in the pathophysiology of several mental health conditions, although inconsistencies and reliance on indirect associations across these reviews limit the strength of findings. Future research with standardized methodologies and mechanistic analyses is needed to clarify gut-brain pathways and strengthen disorder-specific microbial signatures.

Keywords: Mental Health; World Health Organization (WHO); COVID-19

Introduction

Mental health conditions have been on the rise globally, affecting millions of individuals across all age groups. These conditions can significantly disrupt a person's cognition, emotional regulation, and behaviour, and in severe cases, may lead to an increased risk of self-harm. According to the World Health Organization (WHO), an estimated 1 in every 8 people is likely to experience a mental health issue at some point in their lives [1]. Such conditions can influence a person's ability to manage stress, perform daily tasks, and succeed in academic or professional settings. Additionally, they may face challenges in forming and maintaining social relationships. In 2020, the prevalence of anxiety and depressive disorders increased by 26% and 20%, respectively [1]. This significant rise is likely to be contributed to by the COVID-19 pandemic, as many individuals experienced job loss, economic instability, and prolonged periods of social isolation due to quarantine measures. Although pandemic-related restrictions have begun to ease and economic recovery is expected over time, financial burdens and unemployment remain persistent challenges around the world [2]. These challenges may influence poor mental health outcomes, including increased stress, anxiety, and depressive symptoms.

Considering the growing burden of mental health conditions, recent studies have shown a growing interest in the biological factors of these conditions. One research area that has gained much attention is the gut microbiota [2], with many evidence supporting a link between gut microbial composition and various mental health conditions. The gut microbiota is believed to influence brain function and behaviour through the gut-brain axis [2,3] - a bidirectional communication system between the central nervous system (CNS) and the gastrointestinal tract, involving neural, immune responses, endocrine, and metabolic signalling. This microbial system is made up of microorganisms, from bacteria to viruses, which play essential roles in maintaining this communication network [3].

Some studies suggested that the gut microbiota contributes to several physiological and psychological processes, such as stress responses, mood regulation and cognitive performance. They are able to produce and regulate neurotransmitters, including dopamine, serotonin, gamma-aminobutyric acid (GABA), and short-chain fatty acids (SCFAs), which influence mood, cognition, and emotional regulation through their interaction with the CNS [3]. In addition, the gut microbiome affects the hypothalamic-pituitary-adrenal (HPA) axis, which regulates stress responses and plays a contributing factor in developing mood disorders [3]. The gut-brain axis is also mediated through the body's immune responses, including the regulation of cytokine production and inflammatory mediators, which can influence the permeability of the blood-brain barrier [4]. Alterations in gut microbial composition, commonly referred to as gut dysbiosis, occur when beneficial microorganisms are outnumbered by the pathogenic ones. This imbalance may cause disruptions in key physiological processes, including immune function and neurotransmitter synthesis, possibly leading to the onset of various mental health conditions [3,4]. Therefore, the gut microbiome's role in maintaining these signalling pathways may be an important factor in the development and progression of mental health conditions.

Experimental and observational evidence support the involvement of the gut microbiome in mental health. Animal studies, particularly those using germ-free rodents (animals raised in sterile environments without microbiota), have reported disruption of gut microbial composition that marked changes in behaviour, stress responses and cognition [5]. Transferring microbiota from an individual with psychiatric disorders to rodents also induced characteristics of depressive-like behaviours, which are consistent with the individual's condition [6,7]. While these studies provide important insights into the impact of the gut microbiome, human-focused research is essential to determine the relevance of these findings.

In recent years, an increasing number of human studies have investigated the relationship between gut microbiota and mental health by comparing the gut microbial profiles of individuals with mental health conditions to those of healthy controls [6]. Many of these studies reported alterations in alpha diversity (within-sample

microbial richness) and beta diversity (between-sample microbial differences) [6-8], which may suggest disruptions in the balance and structure of microbial communities. Furthermore, a recent systematic review identified shared microbial signatures across several psychiatric disorders [8]. Specifically, consistently depleted levels of *Faecalibacterium* and *Coprococcus*, and enriched levels of *Eggerthella*, were observed in individuals with major depressive disorder (MDD), schizophrenia, anxiety, and bipolar disorder (BD) [8]. This may suggest that these conditions are characterized by a reduction of anti-inflammatory butyrate-producing bacteria, and an enrichment of pro-inflammatory genera [8].

Despite the increasing interest, findings across studies remain inconsistent due to differences in methodology, population demographics and microbial sequencing techniques. Therefore, this umbrella review aims to synthesize and critically evaluate existing systematic reviews and meta-analyses on the impact of the gut microbiome on mental health, with a focus on microbial diversity and composition, as well as functional metabolites that may influence brain function across mental health conditions. These include MDD, anxiety, autism spectrum disorder (ASD), schizophrenia, BD, anorexia nervosa, attention-deficit/hyperactivity disorder (ADHD), and post-traumatic stress disorder (PTSD).

Methods

Search strategy

A PubMed search was conducted on 24th May 2025 for systematic reviews and meta-analyses examining the impact of the gut microbiome on mental health conditions. The following search terms were used: ((depression OR "major depressive disorder") OR (anxiety OR "panic disorder" OR phobia OR Agoraphobia OR "selective mutism" OR "Post-traumatic stress disorder" OR "Obsessive-compulsive disorder" OR Hypochondriasis OR hypochondria) OR "Mixed anxiety-depressive disorder") AND gut AND (microbiome OR microbiota) AND ("systematic review"[tiab] OR meta-analysis[tiab]). The complete search URL is: https://pubmed.ncbi.nlm.nih.gov/?term=((depression+OR+"major+depressive+disorder")+OR+(anxiety+OR+"panic+disorder"+OR+phobia+OR+Agoraphobia+OR+"selective+mutism"+OR+"Post-traumatic+stress+disorder"+OR+"Obsessive-compulsive+disorder"+OR+Hypochondriasis+OR+hypochondria)+OR+"Mixed+anxiety-depressive+disorder")+AND+gut+AND+(microbiome+OR+microbiota)+AND+("systematic+review"[tiab]+OR+meta-analysis[tiab])&filter=dates.1000/1/1-2025/4/30.

Inclusion and exclusion criteria

The following exclusion criteria were applied: (A) articles without access to the full text; (B) articles not written in English language; (C) primary research articles, including original studies, randomized controlled trials, and observational studies; (D) preprint articles; (E) articles that did not include relevant keywords related to mental health conditions, gut, and microbiome or microbiota; (F) articles unrelated to the research topic; and (G) articles focused on interventional studies or treatment-based outcomes. After applying these criteria, the remaining articles were included in this umbrella review. Additionally, some relevant articles were also identified by manually screening the reference lists of eligible reviews. Animal studies will not be included in the main analysis but may be referenced as supplementary background if relevant.

Study selection

Titles and abstracts were screened for relevance, followed by full-text review based on the inclusion and exclusion criteria. Screening and selection were conducted independently, and in cases of uncertainty, final inclusion decisions were made through further full-text evaluation.

Data synthesis

A narrative synthesis approach was used to summarize the findings across the included reviews. Particular attention was given to recurring patterns of microbial diversity, disorder-specific taxonomic alterations, and functional metabolites. Findings were grouped thematically by mental health condition.

Results

A total of 150 articles were initially identified through the PubMed search (Figure 1). After exclusions, 31 articles were included in this umbrella review, comprising 23 systematic reviews and 8 meta-analyses.

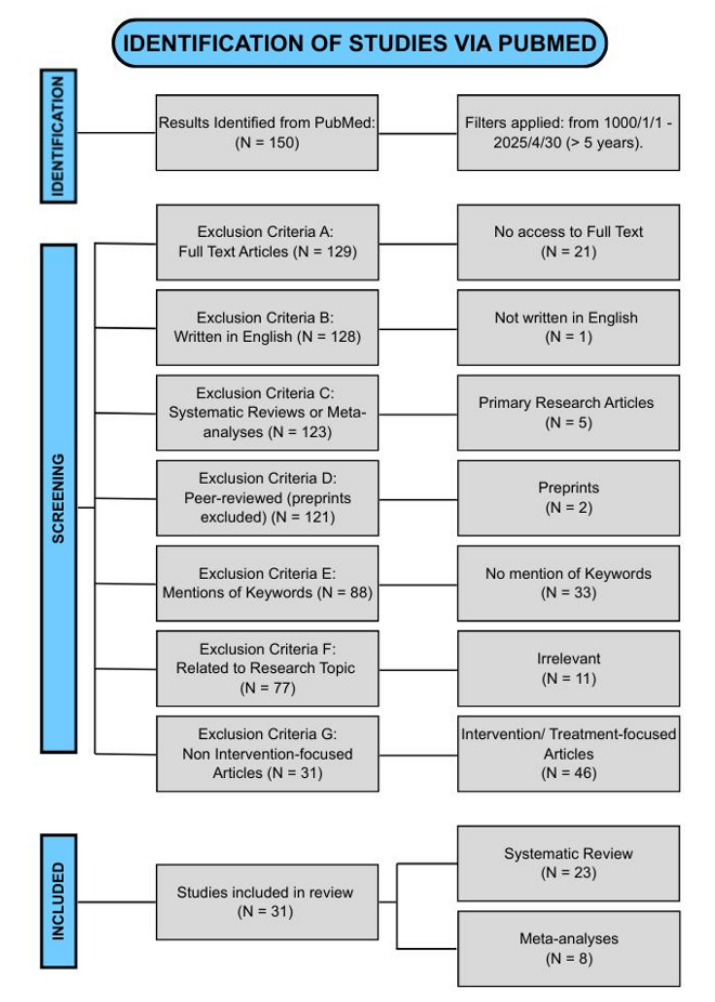

Figure 1: Flow of process through 7 exclusion criteria.

The included reviews were published between 2015 and 2025 and primarily focused on mental health conditions such as MDD, anxiety, ASD, schizophrenia and BD. Most reviews employed 16S rRNA gene sequencing as the primary method for assessing gut microbial composition, although a minority incorporated multiple methodologies. Measures of microbial diversity, both alpha (within-sample) and beta (between-sample), were commonly reported, along with taxonomic profiles at various phylogenetic levels. The findings were categorised into 2 main themes - Theme 1 addresses microbial composition and diversity for each mental health condition, while Theme 2 focuses on functional metabolites. This structure enables a more comprehensive understanding of the gut microbiota's role across various individual conditions (Table 1).

Table 1: Thematic classification of included systematic reviews and meta-analyses.

Theme	Included Articles
Theme 1: Mental Health Conditions with Microbial Composition and Diversity Alterations	
1.1. Depression/ Major Depressive Disorder (MDD)	24 [3,4,6,8–28]
1.2. Anxiety	5 [3,8,9,24,28]
1.3. Autism Spectrum Disorder (ASD)	8 [11,17,18,20,26,28–30]
1.4. Schizophrenia	9 [3,7,8,12,16,18,21,26,28]
1.5. Bipolar Disorder (BD)	7 [3,7,8,12,16,21,31]
1.6. Anorexia Nervosa (AN)	3 [8,17,32]
1.7. Attention-Deficit/Hyperactivity Disorder (ADHD)	4 [10,11,28,29]
1.8. Post-Traumatic Stress Disorder (PTSD)	3 [17,33,34]
Theme 2: Functional Metabolites of Microbiota Influencing Brain Function	8 [3,6,12,13,15,16,30,33]

Theme 1.1: Depression/Major depressive disorder (MDD)

Depression, particularly MDD, was the most frequently investigated condition across the included reviews. A total of 24 reviews examined MDD, either as the primary focus or as part of multi-disorder research. Its contribution to gut-brain axis research [4] reflects its high prevalence, significant impact on quality of life, and links to both physiological and psychological dysfunctions [1]. Across reviews, MDD was consistently explored in the context of its complex aetiology, involving central nervous system signalling, immune-inflammatory pathways, and stress-related hormonal imbalances, all of which have been proposed to be influenced by gut microbial alterations [4,17].

Regarding microbial diversity compared to healthy controls, the findings are mixed. Among the 24 included reviews, 18 assessed alpha diversity and 17 assessed beta diversity. For alpha diversity, 10 reviews found no or nonsignificant differences [4,6,8,12,13,15,19,23-25], 3 identified significant alterations [3,16,27], and the remaining reported inconsistent findings [9,11,14,21] or unreported results [22]. This suggests that overall richness and evenness of gut species are not consistently affected. By contrast, beta diversity showed clearer patterns, with 10 reviews observed significant differences in microbial composition [3,4,6,11,12,14-16,25,27], 4 found no or nonsignificant changes [8,19,22,24], and 3 reported inconsistent outcomes [9,13,21]. At the taxonomic level,several consistent patterns were observed. Reduced abundances were most frequently reported for *Faecalibacterium* [6,8,12-15,19,20], *Coprococcus* [4,8,12,13,15,22,25,26], and *Ruminococcus* [6,12,13,16,19,20]. In contrast,increased abundances were noted for *Eggerthella* [4,8,9,12,14,15,19,25,26], *Enterococcus* [3,8,12,15], *Actinobacteria* [13,14,18,19], *Streptococcus* [4,12,20], *Enterobacteriaceae* (eg. *Escherichia/Shigella*) [9,27], *Klebsiella* [6,20], and *Desulfovibrio* [25].

Theme 1.2: Anxiety

A total of 5 reviews focused on anxiety, although most did not specify subtypes such as generalized anxiety disorder, panic disorder, or phobias. Anxiety was often studied alongside depression as part of the common affective disorders [3,8,9,24,28]. Across these reviews, anxiety was associated with high prevalence, symptom overlap with depression, and increased stress reactivity, all of which were suggested to be influenced by gut microbial activity [5,35].

In terms of microbial diversity, 3 reviews reported differences in alpha diversity [3,24,28], 1 reported no or nonsignificant differences [9], and 1 found inconsistent results [8]. Similarly, for beta

diversity, 3 reviews identified differences [3,8,24], while 1 found no or nonsignificant differences [8]. At the taxonomic level, anxiety was associated with both reductions in beneficial taxa and increases in pro-inflammatory taxa. Consistent decreases were reported for *Faecalibacterium* [3,8,9] and *Coprococcus* [8,9], while increases were noted for *Enterobacteriaceae* (eg. *Escherichia / Shigella*) and *Eggerthella* [8,9], mirroring the patterns observed in MDD.

Theme 1.3: Autism spectrum disorder (ASD)

ASD was examined in 8 reviews, often in combination with other psychiatric disorders such as depression, anxiety, schizophrenia, and ADHD. Across these reviews, ASD was consistently highlighted due to its early onset, lifelong course, and frequent co-occurrence with gastrointestinal symptoms, which have been associated with the gut-brain axis [17]. Several reviews also highlighted the potential role of gut microbiota as a mediator of neurodevelopmental outcomes through bidirectional neural pathways, immune responses and metabolic functions [17,18,20,29]. In addition, microbial imbalances were linked to behavioural, sensory, and cognitive symptoms commonly observed in ASD [29].

In terms of microbial diversity, evidence remains limited. Of the 8 reviews, only 2 reported findings on alpha and beta diversity [11,17], with both indicating differences in microbial diversity across these measures. At the taxonomic levels, findings were more consistent for both pro-inflammatory taxa and anti-inflammatory taxa. Decreases were commonly observed in *Bifidobacterium* [11,17,18,20,26,30] and *Prevotella* [18,26], both are considered beneficial taxa. In contrast, Increases were more frequently reported for *Clostridium* [17,18,26,29,30], *Desulfovibrio* [17,20,30], *Bacteroides* [11,26,29], and *Sutterella* [11,20].

Theme 1.4: Schizophrenia

A total of 9 reviews investigated schizophrenia in relation to gut microbiota. As a severe and chronic psychiatric disorder, schizophrenia has gained interest in microbiome research due to growing evidence implicating immune system dysregulation in its pathogenesis [18]. Across reviews, schizophrenia was frequently discussed in the context of its complex neurobiological profile, characterised by neuroinflammation, oxidative stress, and disrupted neurotransmission, all of which have been proposed to be modulated by the gut microbiota [16,18]. Several reviews also highlighted the potential role of the gut-brain axis in regulating these processes through immune and inflammatory pathways, suggesting that microbial imbalances may contribute to the onset or progression of schizophrenia [18].

Findings on microbial diversity were mixed. For alpha diversity, 2 reviews reported significant differences compared with healthy controls [7,16], 2 reported no or nonsignificant differences [12,21], and 1 noted inconsistencies across included studies [8]. However, results for beta diversity were more consistent, with 5 reviews observing significant differences in microbial community structures between individuals with schizophrenia and controls [7,8,12,16,21]. The remaining reviews did not report on diversity measures. At the taxonomic levels, findings are more consistent across the included reviews. Decreases in beneficial taxa were more frequently reported for *Faecalibacterium* [8,12,21,28] and *Coprococcus* [8,12,26]. Similarly, several reviews also reported increases in pro-inflammatory taxa, including *Lactobacillus* [7,8,12,18], *Eggerthella* [8,12,18], *Megasphaera* [12,18,26], *Escherichia/Shigella* [8,12] and *Clostridium* [18,26].

Theme 1.5: Bipolar disorder (BD)

BD was examined in 7 reviews, often studied alongside depression or schizophrenia. Reviews consistently described BD as a condition characterised by alternating episodes of mania and depression [31]. Emerging evidence across the reviews linked BD to processes such as inflammation, oxidative stress, and disruptions in neuroendocrine signalling [7,16,31]. These processes suggested a potential role for the gut-brain axis in the onset or progression of BD [31].

For microbial diversity, only 6 reviews reported findings, but the results were mixed. For alpha diversity, 1 review observed significant differences compared with healthy controls [3], 3 found no or nonsignificant differences [7,8,12], and 2 reported inconsistent

results [21,31]. Similarly, for beta diversity, 3 reviews identified significant differences [7,8,21], while 1 found no or nonsignificant changes [8]. The remaining 2 reviews that addressed alpha diversity did not report on beta diversity [3,31]. At the taxonomic levels, findings were more consistent. Several studies have found beneficial taxa decreases in *Faecalibacterium* [7,8,12,21,31], *Coprococcus* [8,12], *Roseburia* and *Ruminococcus* [12]. However, increases in pro-inflammatory taxa were also observed for *Lactobacillus* and *Eggerthella* [8,12,31], *Flavonifractor* [12,31], *Enterococcus* [8,12], as well as *Clostridium* [31], *Escherichia/Shigella* [8,31], and *Megasphaera* [12].

Theme 1.6: Anorexia nervosa (AN)

AN was included in 3 reviews. Despite having the lowest prevalence, AN is associated with the highest mortality rate among psychiatric disorders [32,36]. Reviews noted frequent comorbidity with depression, anxiety, and personality disorders. Emerging evidence linked reduced dietary intake, severe weight loss, and psychological stress to the development of intestinal dysbiosis [36]. On the other hand, dysbiosis was reported to disrupt the communication between the gut microbiota, immune system, and neuroendocrine pathways, potentially contributing to the onset or persistence of AN [36].

For alpha diversity, all 3 reviews reported significant differences between individuals with AN and healthy controls [8,17,32], which suggests consistency across available evidence. For beta diversity, 2 reviews reported significant differences [17,32] while 1 found no or nonsignificant differences [8]. At the taxonomic level, findings were relatively consistent. Decreases in beneficial taxa were commonly observed for *Faecalibacterium* [8,17,32] and *Roseburia* [17,32], while increases were also reported for pro-inflammatory taxa such as *Enterobacteriaceae* and *Alistipes* [17,32], as well as *Methanobrevibacter* [8].

Theme 1.7: Attention-deficit/hyperactivity disorder (ADHD)

ADHD was examined in 4 reviews, particularly in those exploring neurodevelopmental or neuropsychiatric conditions related to gut microbiota. It is characterized by inattention, impulsivity, and hyperactivity [10]. Several reviews linked ADHD to the gut-brain axis mechanisms influencing behavioural and cognitive outcomes [10,29]. In addition, some suggested alterations in microbial composition and evidence of neuroinflammation was observed in individuals with ADHD [10,11,29].

Of the 4 reviews, only 1 reported on microbial diversity [11]. For alpha diversity, findings were inconsistent, while beta diversity showed significant differences between ADHD and healthy controls. At the taxonomic level, the findings are relatively consistent. Decreases in beneficial taxa were reported for *Bifidobacterium* [11,29], *Faecalibacterium* [11], and *Roseburia* [28], whereas increases were observed for pro-inflammatory taxa such as *Escherichia/Shigella* [10] and *Actinobacteria* [11].

Theme 1.8: Post-traumatic stress disorder (PTSD)

PTSD was examined in 3 reviews, reflecting emerging interest in its association with chronic stress, dysregulated cortisol levels, and immune-inflammatory responses [33]. Several reviews link PTSD to gastrointestinal disorders, highlighting the relevance of the gut-brain axis. Some reviews suggested that gut dysbiosis may increase the risk of developing PTSD following traumatic experiences [33,34], with particular emphasis on the role of the HPA axis as a stress-response pathway influenced by the gut microbiota [17,33,34,37]. Although current evidence is limited, alterations in microbial composition were suggested to contribute to the development of PTSD.

For alpha diversity, findings were inconsistent. 2 reviews reported mixed or contradictory results across their included studies [31,33], while 1 review did not specifically address alpha diversity [17]. Similarly, for beta diversity, results were also inconsistent. 1 review reported significant differences between PTSD and healthy controls [17], another 1 found no or nonsignificant differences [34], and 1 did not address beta diversity in their review [33]. At the taxonomic level, findings were somewhat more consistent. De-

creases in beneficial taxa such as *Ruminococcaceae* [31] and *Verrucomicrobiota* [17,31] were observed across included reviews. However, increases in pro-inflammatory taxa, including *Enterococcus*, *Olsenella*, *Catenibacterium*, and *Escherichia / Shigella* were reported in only 1 review [31].

Theme 2: Functional metabolites of microbiota influencing brain function

Reviews frequently reported that alterations in gut microbiota composition were accompanied by differences in microbial metabolites, which may mediate effects on brain function. The most consistently examined metabolites included SCFAs and tryptophan metabolites.

Reduced short-chain fatty acids (SCFA), particularly butyrate, were consistently reported across 6 reviews on several mental health conditions [3,6,12,13,15,16]. These reductions were associated with lower abundances of key butyrate-producing taxa, most notably *Faecalibacterium*, *Coprococcus*, and *Roseburia*. A decrease in the production of SCFAs could lead to impairments in the gut barrier permeability and altered host metabolic and immune function [6,12,33].

Three reviews reported on tryptophan metabolism, reporting differences compared with healthy controls [6,12,31]. 1 review suggested that increased levels of inflammatory cytokines may affect brain functions, shifting tryptophan from serotonin synthesis toward neurotoxic kynurenine metabolites [6]. In schizophrenia, an increased kynurenine-to-tryptophan ratio was observed, suggesting enhanced activity of the kynurenine pathway [12]. Another review also reported altered KEGG orthologies (KOs) that could affect the normal functioning of the tryptophan pathway [31]. This shift may contribute to neuroinflammation and disrupted neurotransmitter balance.

The evidence on neurotransmitter-related metabolites was limited across the included reviews. Direct analyses of neurotransmitter levels were not reported; however, several reviews highlighted that abnormalities in the kynurenine pathway may contribute to the production of neurotoxic metabolites associated with mental health conditions [12]. In addition, gut microbiota were noted to produce precursors to neurotransmitters such as gamma-aminobutyric acid (GABA), dopamine, serotonin, and norepinephrine, suggesting a potential role in regulating brain function [6]. Some reviews also referenced prior evidence that reduced SCFA levels may influence neurotransmitter regulation [6]. These associations were discussed based on previous literature rather than new evidence within the included reviews.

Discussion

This umbrella review synthesized evidence from systematic reviews and meta-analyses on the impact of the gut microbiome in mental health conditions, incorporating findings on microbial diversity and composition, as well as functional metabolites. Findings were categorized into 2 main themes: microbial diversity and taxonomic profiles for each mental health condition, and functional metabolites potentially influencing brain function. Overall, there are consistent alterations in beta diversity across most mental conditions, while alpha diversity findings were mixed. There is also a consistent pattern in the taxonomic profiles, with reductions in butyrate-producing taxa, such as *Faecalibacterium* and *Coprococcus*, and enrichments in pro-inflammatory taxa such as *Eggerthella* and *Escherichia/Shigella*. Functional metabolites, particularly SCFAs and tryptophan metabolites, were also highlighted as potential mediators of gut-brain communication and neurotransmitter regulation, although direct evidence was limited. The following sections discuss mental health conditions, critically evaluating associations with the gut microbiome, while also reflecting on methodological strengths and limitations of existing reviews to guide future research directions.

Conditions with larger evidence

Among the conditions with a larger evidence base; MDD, schizophrenia, BD, and ASD; were the most extensively studied, allowing for stronger synthesis compared with the conditions supported by fewer reviews. Across these mental health conditions, micro-

bial diversity findings were noted for recurring patterns, such as alpha diversity results were largely inconsistent or nonsignificant (except MDD and ASD), whereas beta diversity differences were reported more consistently. This suggests that changes in microbial community structure, rather than within-sample richness or evenness, may be a more reliable feature across these conditions.

In the taxonomic profiles, MDD, schizophrenia, and BD displayed overlapping microbial signatures. The most reproducible findings included reductions in butyrate-producing taxa (*Faecalibacterium*, *Coprococcus*, and *Ruminococcus*) and enrichments in pro-inflammatory taxa (*Eggerthella*, *Escherichia / Shigella*, *Clostridium*, and *Megasphaera*). These shifts are biologically plausible given their associations with reduced SCFA production [6,8], impaired gut barrier function, and increased systemic inflammation, processes implicated in brain function and psychiatric pathophysiology [4,8]. However, beyond these taxa, reproducibility was limited. For instance, *Roseburia* was reported as increased in some reviews but decreased in others, while *Oscillibacter* also showed conflicting directionality. Such inconsistencies highlight the need for standardized methodologies and larger, well-characterized cohorts to clarify the direction of these associations. Methodological heterogeneity in sampling and sequencing, as well as diagnostic variability (eg. reliance on self-report vs. clinical assessment in MDD or inclusion of psychosis alongside schizophrenia), further weakens confidence in disorder-specific microbial signatures.

In schizophrenia, in addition to these compositional shifts, 1 review reported alterations in tryptophan metabolism, suggesting possible involvement of the kynurenine pathway in neuroinflammation and neurotransmitter disruption [12]. BD findings also aligned with the general mood disorder profile, with 1 review noting a potential role for increased abundance of *Lactobacillus* in influencing tryptophan metabolism [31], though evidence remains too limited to establish disorder-specific mechanisms.

In contrast, ASD presented a more distinctive microbial profile compared to mood and psychotic disorders. Consistent findings included reductions in beneficial taxa such as *Bifidobacterium* and *Prevotella*, alongside enrichments in pro-inflammatory taxa such as *Clostridium*, *Sutterella*, *Bacteroides*, and *Desulfovibrio*. 1 review further suggested that these pro-inflammatory shifts may promote intestinal inflammation, contributing to elevated lipopolysaccharide (LPS) and peripheral IL-6 levels, a cytokine with neuromodulatory effects [30]. However, findings were inconsistent for other taxa, such as *Coprococcus* and *Faecalibacterium,* which limits reproducibility in disorder-specific associations.

Taken together, MDD, schizophrenia, and BD share overlapping microbial alterations characterized by reduced SCFA-producing taxa and increased pro-inflammatory taxa, suggesting potential common gut-mediated pathways in mood and psychotic disorders. ASD demonstrates more distinct microbial alterations, though conclusions remain constrained by the small number of reviews reporting microbial diversity.

Conditions with limited evidence

Among the conditions supported by fewer reviews, anxiety, AN, ADHD, and PTSD present weaker and less reproducible evidence compared with MDD, schizophrenia, BD, and ASD. Across these disorders, microbial diversity findings were inconsistent overall, although some patterns were noted. In anxiety and AN, beta diversity differences were more consistently observed than alpha diversity changes, suggesting possible alterations in microbial community composition rather than richness alone. In ADHD and PTSD, diversity findings were limited and inconclusive due to the small number of supporting reviews.

In the taxonomic profiles, anxiety shared overlapping microbial shifts with MDD, including reductions in butyrate-producing taxa (*Faecalibacterium* and *Coprococcus*) and enrichments in pro-inflammatory taxa (*Enterobacteriaceae* and *Eggerthella*), although beyond these taxa, the results were inconsistent. AN showed more distinctive features, with consistent reductions in alpha diversity, alongside reductions in SCFA-producing taxa (*Faecalibacterium* and *Roseburia*) and enrichment of pro-inflammatory taxa (*Enterobacteriaceae*, *Alistipes* and *Methanobrevibacter*). The latter has been proposed as a disorder-specific marker of AN, though it was

not identified across other reviews [8]. In ADHD, current findings suggested reductions in *Faecalibacterium, Bifidobacterium*, and *Roseburia*, and enrichments in *Escherichia/Shigella* and *Actinobacteria*, pointing toward microbial alterations broadly similar to those observed in mood disorders. PTSD evidence was the weakest, with few reproducible taxonomic patterns; isolated reports reported reductions in *Ruminococcaceae* and *Verrucomicrobiota*, alongside enrichment of pro-inflammatory taxa (*Enterococcus, Olsenella, Catenibacterium*, and *Escherichia/Shigella*).

Taken together, these disorders with smaller evidence bases show some overlap with microbial alterations seen in mood disorders, particularly reductions in SCFA-producing taxa and enrichment in pro-inflammatory groups. However, methodological heterogeneity, small numbers of included reviews, and disorder-specific confounders such as dietary restriction in AN [17], pediatric cohorts in ADHD, and comorbidities in PTSD [34], limit the reliability of these associations. Consequently, while the current findings suggest possible microbial pathways, stronger evidence is needed before disorder-specific microbial signatures can be established.

Lack of evidence on functional microbial metabolites

Among the included reviews, alterations in gut microbiota were frequently accompanied by changes in microbial metabolites, which may influence brain function. The most consistently examined metabolites were SCFAs and tryptophan metabolites. Reduced SCFAs, particularly butyrate, were repeatedly linked to lower abundances of key SCFA-producing taxa, such as *Faecalibacterium, Coprococcus*, and *Roseburia*, and may contribute to impaired gut barrier integrity, altered immune function, and neuroinflammation [3,6,12,13,15,16,33]. However, most of these findings were reported in MDD, BD, and schizophrenia, with limited or no direct evidence for other mental conditions. Moreover, most evidence was indirect: only a minority of reviews incorporated metagenomic or metabolomic analyses alongside microbiota profiling, meaning that SCFA reductions were often inferred from taxonomic changes rather than direct measurements.

Alterations in tryptophan metabolism were also reported, including shifts toward neurotoxic kynurenine metabolites due to inflammation, and changes in KOs affecting the tryptophan pathway, supporting a potential mechanism for disrupted neurotransmitter balance, particularly in schizophrenia [6,12,31]. Given the small number of reviews addressing tryptophan metabolism, the evidence base remains weak, and the directionality of associations is unclear.

Evidence on neurotransmitter-related metabolites was even more limited. While gut microbiota has been noted to produce precursors of GABA, dopamine, serotonin, and norepinephrine [6,12], no review has provided direct metabolomic evidence in psychiatric populations. Instead, these associations were drawn from previous reviews. Some reviews even hypothesized that alterations in microbial metabolites, such as SCFAs and tryptophan metabolites, may influence gut-brain communication pathways, including the HPA axis and immune regulation [34,37]. Although such hypotheses align with the broader literature on microbial contributions to neural signalling, they remain theoretical within the current evidence base.

Overall, the findings suggest potential microbiome-driven mechanisms, but the lack of direct metabolomic evidence and reliance on inferred associations from taxonomic shifts underscore a major gap in this review.

Strengths and Limitations

This umbrella review has several strengths. First, it provides a comprehensive synthesis of systematic reviews and meta-analyses published between 2015 and 2025, covering a broad range of mental health conditions, including MDD, anxiety, ASD, schizophrenia, BD, AN, ADHD, and PTSD. By combining findings on microbial diversity, taxonomic composition, and functional metabolites, this review offers a more holistic understanding of the potential role of the gut microbiome in mental health. Second, this review has a comparative perspective, which highlights taxonomic patterns that

appear consistent across disorders, such as reductions in butyrate-producing taxa (eg. *Faecalibacterium* and *Coprococcus*) and enrichments in pro-inflammatory taxa (eg. *Eggerthella* and *Escherichia/Shigella*). At the same time, disorder-specific alterations observed in ASD or AN were identified, offering a more interesting insight into condition-related differences. Finally, this review critically evaluated all findings, considering the consistency, reproducibility, and methodological limitations of the included evidence, distinguishing between direct and indirect findings.

Despite these strengths, several limitations were also noted in these findings. First, heterogeneity in diagnostic criteria may have influenced findings, as some reviews relied on validated clinical assessments while others included studies using self-reported symptom scales, which may increase the risk of misclassification. Second, methodological variability, such as differences in sequencing platforms and microbial profiling techniques, may have contributed to inconsistencies in microbial diversity and taxonomic patterns. Third, there are significant evidence gaps. Few reviews directly examined microbial metabolites, and neurotransmitter-related pathways were largely based on previous literature rather than supported by direct analyses. Certain conditions, such as PTSD and ADHD, were underrepresented, limiting the generalizability of findings across the full spectrum of mental health conditions. Finally, some systematic reviews overlapped, raising the potential for duplicate findings, such as the depletion of *Faecalibacterium* was repeatedly reported across reviews.

Conclusion

In conclusion, this umbrella review highlights the potential role of the gut microbiome in mental health conditions, drawing on evidence from recent systematic reviews and meta-analyses. Although recurring taxonomic patterns were observed, many findings were inconsistent or repeatedly reported across reviews, limiting confidence in their specificity. However, these shifts align with reductions in SCFAs, which may contribute to impaired gut barrier integrity, disrupted immune regulation, and neuroinflammation. Such processes may be linked to the development and progression of psychiatric symptoms. Future research should address these gaps by conducting well-powered, disorder-specific studies with standardized diagnostic criteria and microbial assessment methods. Analysis of functional metabolites is needed to clarify the association between gut microbiota and brain function.

Supplementary Materials

Supplementary materials can be downloaded from https://bit.ly/GutMicro_MH.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgements

The authors wish to thank the institute, Management Development Institute of Singapore, for its support towards this work. The cost of publication fees was borne by the authors.

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