Journal of Research High School

Vol. 2026 (9) 721 – 728
ISSN 2688-3651 [online]

The Association Between Gut Microbiota and Depression

Annika Zhang[1] *

[1]Hinsdale Central High School, Hinsdale, IL, USA
*Corresponding Author: annikaszhang@gmail.com

Advisor: Bailey Holt-Gosselin, baileyholtgos@gmail.com

Received October 17, 2025; Revised March 30, 2026; Accepted May 11, 2026

Abstract

280 million people suffer from depression worldwide. Many people who suffer from depression experience digestive problems that are associated with alterations in the gut microbiome, such as less diversity and more harmful species within the gut microbiome. However, there have been mixed findings regarding the link between depression and the gut microbiome, which make it difficult to understand the precise nature of this association. The purpose of this review is to synthesize current knowledge regarding the relationship between gut microbiota and depression. Specifically, this review discusses studies examining the relationship between the gut microbiome and depression in terms of specific taxa (e.g., Bifidobacterium, Lactobacillus), the mechanisms and processes that take place along the microbiota-gut-brain-axis, the role of stress on the gut microbiome and depression, as well as treatment options (e.g., antidepressants, probiotics) for individuals suffering from depression with gut-related symptoms. Finally, this review discusses limitations of current work and recommendations for future research. This review found that there was a large amount of evidence that gut microbiota was related to depression, but additional research is needed to elucidate causal mechanisms. Disentangling the complex relationship between the gut microbiome and depression is critical for enhancing risk identification, tailored interventions, and treatment development.

Keywords: Gut Microbiota, Depression, Stress, Gut-Brain Axis

1. Introduction

According to the World Health Organization (WHO), 280 million people suffer from depression worldwide (Han et al., 2019). In regards to economic burden, the direct costs incurred by individuals with depression in 2018 was 114.3 billion dollars (Greenberg et al., 2021). Representing about 3.8% of the entire population (Han et al., 2019), depression is caused by a combination of biological, psychological, and social factors (Limbana et al., 2020). Symptoms include persistent sadness, fatigue, loss of sleep, appetite, lack of interest in activities, apathy, and feelings of worthlessness (Kennedy, 2008). While little is known about the specific mechanisms underlying the pathogenesis of depression, one of the potential causes and consequences is alterations in the gut microbiome.

The gut microflora is important for the transmission of brain signals, and disruption in these communication pathways may partially contribute to the onset of mental disorders such as depression. The gut microbiome is the ecosystem of microbes that live within the intestines and that interact with each other and their environment in a multitude of processes (Hills et al., 2019). The microbiota include fungi, parasites, bacteria, and viruses (Hills et al., 2019). A person's gut microbiome is unique to them and while it is highly influenced by reproductive and birth processes, other gut microbiota can be introduced to or eliminated from the body via environmental factors (e.g., dietary changes, antibiotic use) (Cleveland Clinic, 2023). Furthermore, gut microbiota are involved in digestive, nervous, and immune system processes (Cleveland Clinic, 2023). While certain gut microflora produce or stimulate neurotransmitters, such as serotonin, bacteria can also poison and damage nerves, leading researchers to explore the relationship between these toxins and depression.

Vol. 2026 (9) 721 – 728
ISSN 2688-3651 [online]

There is currently a well-established association between alterations in gut microbiota composition and depression (Ameer Luqman et al., 2024; Limbana et al., 2020). Despite the well-established link between these variables, the causal mechanism remains unclear. Specifically, it is unclear whether alterations in gut microbiota are a cause or consequence of depression. Noticeably absent from the literature are studies focusing on larger sample sizes and longitudinal studies. Many studies also fail to sufficiently include numerous potentially relevant confounders that may skew results. This review's unique contribution is that it synthesizes findings on the gut microbiota and depression across correlational, mechanistic, and treatment studies, and highlights current gaps in the literature. Specifically, this review discusses the mechanisms underlying the microbiota-gut-brain-axis, the role of stress on the gut microbiome and depression, and treatment options (e.g., antidepressants, probiotics, etc.) for individuals suffering from depression with gut-related symptoms. Finally, this review discusses recommendations for future research. Understanding the complex relationship between the gut microbiome and depression is critical for enhancing risk identification and treatment development.

2. Methods

PubMed was used to gather the literature for this review. To examine the relationship between gut microbiota and depression, the following key words were used: "gut microbiota", "depression", "gut-brain-axis", "trial". To examine the associations among stress, gut microbiota, and depression, the following key words were used: "stress", "gut microbiota", "depression", "trial". Finally, to examine treatment options for individuals suffering from depression with gut-related symptoms, the following key words were used: "treatment," "gut microbiota", "depression". Additionally, year published was used as a filter, such that only papers published in the last 10 years were examined in order to utilize the most up-to-date research studies. The abstracts of all papers that came up from the search were critically reviewed, and papers were excluded if they did not examine the research question(s) that this review was examining.

3. The Microbiota Gut-Brain (MGB) Axis

The composition of intestinal microbiota impacts cognition via multiple pathways collectively known as the gut-brain axis (Hernández-Cacho et al., 2025; Bosch et al., 2022; Liu et al., 2020). These neural, hormonal, immune, and metabolic pathways include the immune system, tryptophan metabolism, the vagus nerve, and the enteric nervous system (Hernández-Cacho et al., 2025; Cryan et al., 2019; Liu et al., 2020), all of which appear to be involved in the pathophysiology of depression (Chang et al., 2022). Microbial metabolites are part of these pathways and include short-chain fatty acids, branched-chain amino acids, and peptidoglycans (Chang et al., 2022). These microbial metabolites act as signaling molecules, strengthen the blood-brain barrier, and alter neuroinflammation. The gut-brain axis is known to maintain homeostasis (the body's automatic process of maintaining a stable environment), but recent evidence on the role of microbiota on gut-brain function has brought more attention to the gut-brain axis. For instance, one study suggests that Bifidobacterium, ubiquitous inhabitants of the gastrointestinal tract, in particular shapes cognitive function through the gut-brain axis (Yu et al., 2024). Despite this evidence, few studies have sought to examine the causal relationship between microbiota and gut-brain function, but did not observe causal links (Chang et al., 2022). Thus, the specific underlying mechanisms of the gut-brain axis remain unclear (Yu et al., 2024). This indicates the need to conduct large, longitudinal randomized-control studies examining the associations among gut microbiome, depressive symptoms, and interventions (Bosch et al., 2022; Xie et al., 2024; Yang et al., 2023).

The enteric nervous system and the brain hold the most crucial interaction along the gut-brain axis (Hernández-Cacho et al., 2025; Liu et al., 2020; Xie et al., 2024; Yang et al., 2023). They work together to stabilize normal function by communicating through the vagus nerve (vagal activation) (Liu et al., 2020). Enteroendocrine cells are then stimulated to produce neuropeptides and activate nerve pathways; these cells also promote stress responses and hypothalamic-pituitary-adrenal axis development and function, which may influence depressive symptomatology. The production of signaling molecules such as cytokines and metabolites by the microbiota affects both the gut and the brain. Once these molecules travel to the brain, they can also influence the onset of depressive-symptomatology.

Vol. 2026 (9) 721 – 728
ISSN 2688-3651 [online]

Microbial metabolites (e.g., butyrate and acetate) regulate neurotransmitter production, modulate inflammation, and maintain the blood-brain barrier, while other metabolites play a role in the synthesis of serotonin, directly influencing observed depression in individuals (Liu et al., 2020). Furthermore, changes in intestinal permeability by the vagus nerve's anti-inflammatory responses and stress-induced glucocorticoid induction can influence microbial changes: if the gut is more permeable, it is easier for the beneficial bacteria to flow out and for harmful bacteria to get in (Liu et al., 2020). This increased abundance of harmful taxa as a result of activity along the microbiota-gut-brain axis could contribute to the onset of depressive-symptomatology. This is evidenced by the observation that probiotics paired with antidepressants tend to be effective in alleviating depression symptoms by increasing diversity and the abundance of beneficial species within the microbiome. In summary, converging evidence points to the role of the microbiota-gut-brain axis as a biological pathway through which the gut microbiota may contribute to depression symptoms. Additional knowledge on the specific role of the microbiota-gut-brain axis in depression can further the potential for microbiota-related treatment to alleviate depression symptoms.

4. Associations Between the Gut Microbiome and Depression

Changes in the gut microbiome have been observed in individuals with major depressive disorder (Kumar et al., 2023). In fact, the gut microbiota is sometimes known as the "second brain" due to its role in regulating the central nervous system through a plethora of processes (Ameer Luqman et al., 2024). The bidirectional link between the brain and gut has been observed through metabolic, neuroendocrine and neuroimmune pathways in human and animal clinical studies (Averina et al., 2024; Limbana et al., 2020).

Specifically, studies have shown an increase in Eggertella levels, a decrease in Subdoligranulum and Coprococcus, and low levels of Ruminococcaceae in individuals with depression (each are specific species within the gut microbiome) (Kumar et al., 2023). Another study, utilizing Mendelian Randomization, found that Actinobacteria, Bifidobacterium, and Ruminococcus played a role in preventing the development of depression, while Streptococcaceae led to the development of depression (Chen et al., 2022). Another study found that lower levels of Bifidobacterium and Lactobacillus are often observed in individuals with depression (Aizawa et al., 2016). Additionally, researchers have found that beta-diversity and microbial composition were different between individuals with depression and individuals without depression. However, this study did not find a difference in alpha-diversity between the two groups (Xie et al., 2024). These findings contrast some prior work, which has shown that probiotics are able to help alleviate depressive-symptomatology by increasing alpha-diversity in the gut microbiome and that individuals with depression tend to have lower levels of alpha-diversity (Liu et al., 2020). Despite extant literature showing the relationship between gut microbiota and depression, more research is needed to precisely identify the bidirectional relationships between them (Kumar et al., 2023). Overall, while research has identified notable differences in the gut microbiome composition in individuals with depression, further research is needed to understand the complex, bidirectional relationship between the gut microbiome and depression.

5. Associations Between the Gut Microbiome and Stress

Stress, especially prolonged stress, has been shown to play a role in the pathogenesis of depression alongside several other environmental and behavioral factors. In regards to the gut microbiome, lactobacillus and bifidobacterial species have been observed in animal models to influence depression and stress-related behavior. Stress can lead to several behavioral and cognitive effects that can be protected against and alleviated by depression treatments that target the gut microbiome (Ameer Luqman et al., 2024; Chang et al., 2022). Stress has been shown to reduce hippocampal volume and diminish memory, learning, and cognitive abilities (Capuco et al., 2020). In addition to altering neuronal morphology and neuronal proliferation (Capuco et al., 2020), stress has been observed to influence shifts in the gut microbiome (Bertollo et al., 2025). Specifically, an increase of the family Coriobacteriaceae or phyla Actinobacteria and genera Alistipes and odoribacter of phyla Bacteroidetes. Additionally, gut microbes are able to regulate stress response through the activation of vagal pathways, contributing to hyperactivation of the immune system. Furthermore, cytokine inflammation is typically found in individuals with depression and may be brought on

Vol. 2026 (9) 721 – 728
ISSN 2688-3651 [online]

by microbial-related signals (Chang et al., 2022; Limbana et al., 2020); specifically, gut microbial composition may cause increased sensitivity to stress or resilience to stress (Bastiaanssen et al., 2020). Individuals with depression and who have reported high stress have also been reported to have decreased alpha diversity, lower levels of Lactobacillus, and reduced short chain fatty acid (SCFA) production (Bastiaanssen et al., 2020). This is likely due to the vagal afferent fibres projecting into the nucleus tractus solitarius, brain stem, and forebrain structures (Bertollo et al., 2025), particularly the hypothalamus, that may cause stress to trigger mood changes and the gut microbiota along the hypothalamic-pituitary-adrenal axis (Ameer Luqman et al., 2024).

Stress can lead to lack of sleep and unhealthy diets, which can cause gut leakiness, which is associated with inflammation and immunosenescence. In turn, inflammation can cause dysbiosis of the gut microbiota (Chang et al., 2022). A deterioration in microbial composition and diversity can contribute to the onset of depressive-symptomatology. Therefore, stress' behavioral impacts can lead to depression.

Animal models have been used to examine the impact of stress on the relationship between the gut microbiome and depression. For example, Capuco et al. found that stressed rats exhibit changes in their gut microbiome, specifically decreased Lachnospiraceae and Ruminococcaceae. A decrease in these two taxa is also typically observed in individuals with depression. Tryptophan and metabolism and monoamine concentrations were also impacted by acute stress. Overall, there was a reduction in content and diversity (Limbana et al., 2020). Additionally, stress-induced depressed rodents demonstrated abnormal levels of gut microbial SCFAs and other metabolites associated with depressive-like phenotypes (Chang et al., 2022). When treating depressive symptoms in mice with these SCFAS (e.g., rifaximin and minocycline), the stress-induced depressive-like behaviors were alleviated (Chang et al., 2022). However, more research is needed on probiotics containing SCFA producing bacteria as they are able to inhibit depressive stress along the entire microbiota-gut-brain axis.

Stress influences mood and behavior through vagal and immune pathways. While prolonged stress can contribute to depression by impacting brain structure, it can also impact microbial composition. Specifically, stress can contribute to decreased microbial diversity, lower SCFA production, and changes in the abundance of specific taxa (e.g., reduced Lactobacillus, Ruminococcaceae, Lachnospiraceae); these microbial changes are often observed in individuals with depression. More human studies that verify the findings from animal models are needed. Additionally, there is also incomplete knowledge on the role specific metabolites (e.g., SCFAs) play on the onset of depression. More clinical trials are needed to better understand probiotics and SCFA-producing bacteria for developing treatment options. Collectively, evidence suggests that stress can contribute to depression by altering gut microbial composition and function and engaging in neural and immune pathways that may enhance vulnerability to depression symptoms.

6. Treatments

Current knowledge of the causes of depression is incomplete and existing treatments are ineffective for about half to two-thirds of patients (Harbi, 2021). There are a number of treatments for individuals with depression that target the gut microbiome (Table 1). Antidepressants have long been the first-line treatment option for depression due to its ability to modulate neurotransmission, and have been found to interact with the gut microbiome. Specifically, some antidepressants have been observed to have antimicrobial effects, including Selective Serotonin Reuptake Inhibitors (SSRIs), while others, such as tricyclic antidepressants, alter the microbial composition; tricyclic antidepressants increase the abundance of Clostridium leptum, while SSRIs and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) increase the abundance of Eubacterium ramulus (Liu et al., 2023). Overall, the gut microbiome's composition may be used to predict the effectiveness of antidepressants on treating depression. An association between the enrichment of certain bacteria (e.g., Faecalibacterium, Roseburia and Agathobacter relative to Lachnoclostridium) and alleviating depression symptoms has been observed. An individual's gut microbiome composition may influence the body's response to antidepressants by altering their behavior and impact on the body. These impacts can be beneficial or adverse due to a change in toxicity, bioavailability, and bioactivity (Liu et al., 2023).

Certain antidepressants, such as tricyclic and tetracyclic antidepressants, are able to inhibit acid sphingomyelinase activity and then reduce ceramide production in hippocampal tissue, proving to be a target for depression intervention. However, the discovery of the impact that gut microbiome composition has on cognition creates a new opportunity for

Vol. 2026 (9) 721 – 728
ISSN 2688-3651 [online]

providing new treatment options for depression; Bifidobacterium is a potential treatment target.

Resistance to antidepressant treatment is also associated with gut microbial composition depending on the abundance of various taxa and bacteria. When examining the impact of antidepressants on the gut microbiome, Hernandez-Cacho et al. did not observe a significant difference in antidepressant treatment between those who took antidepressants versus those who did not in differentially abundant taxa. Despite this, Hernandez-Cacho et al. state that depression-related gut microbiota changes may not be altered by pharmacological treatment (Hernández-Cacho et al., 2025). More research is needed on how a person's gut microbiome influences their response to antidepressants because the mechanisms underlying the interactions between current depression treatments and the gut microbiome are far more complex than what is currently known. Furthermore, treatment options overall lack substantial research and knowledge in order to properly treat depression.

A review compiling the use of targeting the gut microbiome for treating depression outlines a handful of potential targets and strategies for depression treatment. When considering treatments, it is important to keep in mind that the bacteria of the gut microbiome are the source of several neurotransmitters and neuroactive compounds, such as serotonin, dopamine, norepinephrine, gamma-aminobutyric acid, glutamate, as well as many others. Glutamate has increasingly been observed for its role in causing depression (Averina et al., 2024). Therefore, it has become a new therapeutic target for treating depression. Additionally, the review outlines the role that miRNAs play in the long-term changes associated with the pathogenesis and potentially the treatment of depression. As a result, miRNAs have also become a therapeutic target for depression treatment. Because miRNAs have been seen to influence the onset of depression symptoms when they are dysregulated, antidepressants that reverse those changes should be the most successful. More research is needed to determine the cause of an individual's depression and finding the specific treatment, in this case targeting miRNA, to properly treat the individual without making a shot in the dark with antidepressants.

In addition to antidepressant medications, other treatments for depression and the gut microbiome include probiotic supplementation. Studies indicate that probiotic supplementation is associated with the reduction of depressive symptoms (He et al., 2023). In a randomized controlled trial, Schaub et al. used high-dose probiotics as an add-on treatment for depression in order to test the potential mediating impacts that probiotics have been shown to have with antidepressants on depression since they are less effective when used alone. Probiotic-treated individuals showed a stronger improvement in depressive-symptomatology than the control group, and exhibited changes in the gut microbiota composition following probiotic treatment. Specifically, healthy bacterial diversity was maintained while there was an increased presence of beneficial species (Schaub et al., 2022). This suggests that probiotic treatment targets both the brain and the gut that results in a reduction in depression symptoms. Therefore, the gut microbiome's diversity and presence of beneficial species likely play some role in reducing the onset of depression symptoms. In another study, antimicrobial minocycline had similar effects, as it altered both the gut microbiota composition and depressive symptoms (Liu et al., 2020). This study, along with other research (Schmidtner et al., 2019, Husain et al., 2017, Dean et al., 2017), suggests that minocycline may be used alongside antidepressants. With this information, it is clear that probiotic treatments that increase alpha-diversity and increase the concentration of beneficial species within the gut microbiome are an up-and-coming treatment for depression when paired with antidepressants. However, perhaps there is a possibility that probiotic treatments may be sufficient on their own without antidepressant medication use. Therefore, more research is needed on whether the successful alleviation of depressive symptomatology is due to a combination of antidepressant and probiotic efforts, or either alone. Additionally, more large-scale randomized controlled trials are needed to test the effectiveness, administration, and dosage of probiotics to treat individuals with depression.

Most studies examining treatments that affect the gut microbiome and depression have been conducted in adult samples. However, a recent study investigated the association between the gut microbiome, depression, and SSRI treatment in adolescents (Thapa et al., 2021). Interestingly, SSRI treatment did not alter the gut microbiome nor depressive symptoms in this adolescent sample. This was potentially due to the study's small sample size which may have led to type II error. Additionally, this may be due to the lack of inclusion of potential confounding variables, and participants coming from outpatient settings, not receiving medication treatment/a lower severity of depression, the anatomy of adolescents and their microbiome requiring more time for alterations, a lack of metagenomic approaches,

Vol. 2026 (9) 721 – 728
ISSN 2688-3651 [online]

or a lack of substantial information on participant's diets preceding their visits. The handful of possible causes for the lack of differentiation between the two sample groups seems to be significant enough to potentially sway the results in this unexpected direction (Thapa et al., 2021). However, if it is not the case that these factors altered the outcome of the study, then the difference found between adult and adolescent groups raises questions: why is it that the relationship between the gut microbiome and depression is less pronounced in adolescents as opposed to adults? It is possible that the difference in microbial composition accounts for this disparity. Specifically, adolescents tend to have a higher abundance of certain species than adults (Carson et al., 2023). Because this was the first known study to assess the relationship between the gut microbiome and depression in adolescents, there is more research needed in adolescent and younger groups to properly analyze and understand the association between the two variables. In summary, findings highlight promising results for various treatments that target the gut microbiome–including antidepressants and probiotics–in alleviating depression symptoms. However, more research is needed to fully understand interactions between the gut microbiome and these treatments for depression.

Table 1. Table of Treatments.

Treatment	Examples	Mechanism	Effect on Gut Microbiome
Antidepressant	Selective Serotonin Reuptake Inhibitors (SSRIs) (e.g., fluoxetine)	Inhibits the reuptake of serotonin	Reduce diversity, bioaccumulation, altered composition/abundance of various species
Probiotics	Bifidobacterium, Lactobacillus	gut microbiota modulation, inflammation reduction, and influence neurotransmitter production and regulation	Increase abundance of beneficial species, SCFA production, increase diversity
Antibiotics	Antimicrobial minocycline	Reduce inflammatory pathways and gut-brain axis modulation	Increased gut permeability, reduced microbial diversity, SCFA production, modulate neurotransmitters

7. Limitations

There are a number of limitations in the field of examining the links between the gut microbiota and depression. For example, most studies had small sample sizes. It is difficult to fully synthesize current knowledge regarding the influence the gut microbiome has on the pathogenesis of depression because studies often exhibit mixed results, possibly partly due to the limited sample sizes. Additionally, there is a lack of studies that focus on examining a causal relationship between the two variables. Specifically, longitudinal and Mendelian randomization studies should be focused on in order for the relationship to be better elucidated. Little is known about the mechanisms underlying the onset of depression in individuals; having this knowledge would allow researchers to potentially connect the mechanisms and processes that contribute to the pathogenesis of depression to microbial activity. Additionally, understanding the role of the brain-gut axis is also important to examine. Finally, there are several potentially relevant covariates that many studies are unable to fully account for (e.g., lifestyle factors like smoking, alcohol use, exercise, etc.). Together, these limitations may contribute to the inconsistent findings surrounding the relationship between the gut microbiome and depression.

8. Future Directions

Future directions should focus on increasing the number of longitudinal studies to determine the relationship between the gut microbiome and depression, as well as determining the success of probiotics and microbiome-targeting treatments. Specifically, more longitudinal studies that elucidate causal mechanisms underlying gut microbiome and depression are needed(e.g., utilize Mendelian randomization). Additionally, more research utilizing large sample sizes is necessary to better understand the extent to which there is an existing association between gut microbiome and depression. More research is also needed to determine specific taxa to target when intervening depression through the gut microbiome. More research is also needed on the role of prebiotics in treating depression

Vol. 2026 (9) 721 – 728
ISSN 2688-3651 [online]

in a similar manner to that of probiotics. There is also a lack of studies focusing on youth samples. Understanding the relationship between the gut microbiome and depression can greatly assist when considering treatment options.

9. Conclusions

This review summarized current knowledge regarding the association between the gut microbiome and depression. While there is a well-established association between the two variables, additional research is needed to determine causality to inform depression treatment development. When considering treatments, it is known that probiotics and treatments that target the gut microbiome can help to relieve depressive-symptomatology when paired with antidepressants (in comparison to antidepressant treatment on its own). Given the scale at which depression affects the global population, understanding the role of the gut microbiome in the pathogenesis of depression is a critical step for potentially improving the life of millions.

References

Aizawa, E., et al. (2016). Possible association of Bifidobacterium and Lactobacillus in the gut microbiota of patients with major depressive disorder. *Journal of Affective Disorders*, *202*, 254–257. https://doi.org/10.1016/j.jad.2016.05.038

Al-harbi, K. S. (2021). Treatment-resistant depression: therapeutic trends, challenges, and future directions. *Patient Preference and Adherence*, *6*(6), 369. https://doi.org/10.2147/ppa.s29716

Averina, O. V., et al. (2024). Human Gut Microbiota for Diagnosis and Treatment of Depression. *International Journal of Molecular Sciences*, *25*(11), 5782–5782. https://doi.org/10.3390/ijms25115782

Bastiaanssen, T. F. S., et al. (2020). Gutted! Unraveling the Role of the Microbiome in Major Depressive Disorder. *Harvard Review of Psychiatry*, *28*(1), 26–39. https://doi.org/10.1097/hrp.0000000000000243

Bertollo, A. G., et al. (2025). Hypothalamus-pituitary-adrenal and gut-brain axes in biological interaction pathway of the depression. *Frontiers in Neuroscience*, *19*. https://doi.org/10.3389/fnins.2025.1541075

Bosch, J. A., et al. (2022). The gut microbiota and depressive symptoms across ethnic groups. *Nature Communications*, *13*(1), 7129. https://doi.org/10.1038/s41467-022-34504-1

Capuco, A., et al. (2020). Current Perspectives on Gut Microbiome Dysbiosis and Depression. *Advances in Therapy*, *37*(4), 1328–1346. https://doi.org/10.1007/s12325-020-01272-7

Carson, M. D., Westwater, C., & Novince, C. M. (2023). Adolescence and the Microbiome. *American Journal of Pathology*, *193*(12), 1900–1909. https://doi.org/10.1016/j.ajpath.2023.07.004

Chang, L., Wei, Y., & Hashimoto, K. (2022). Brain–gut–microbiota axis in depression: A historical overview and future directions. *Brain Research Bulletin*, *182*, 44–56. https://doi.org/10.1016/j.brainresbull.2022.02.004

Chen, M., et al. (2022). Gut microbiota and major depressive disorder: A bidirectional Mendelian randomization. *Journal of Affective Disorders*, *316*, 187–193. https://doi.org/10.1016/j.jad.2022.08.012

Cleveland Clinic. (2023, August 18). *Gut Microbiome*. Cleveland Clinic. https://my.clevelandclinic.org/health/body/25201-gut-microbiome

Cryan, J. F., et al. (2019). The Microbiota-Gut-Brain Axis. *Physiological Reviews*, *99*(4), 1877–2013. https://doi.org/10.1152/physrev.00018.2018

Greenberg, P. E., et al. (2021). The Economic Burden of Adults with Major Depressive Disorder in the United States (2010 and 2018). *PharmacoEconomics*, *39*(6), 653–665. https://doi.org/10.1007/s40273-021-01019-4

Vol. 2026 (9) 721 – 728
ISSN 2688-3651 [online]

Han, K.-M., et al. (2019). Chronic medical conditions and metabolic syndrome as risk factors for incidence of major depressive disorder: A longitudinal study based on 4.7 million adults in South Korea. *Journal of Affective Disorders*, *257*, 486–494. https://doi.org/10.1016/j.jad.2019.07.003

He, J., et al. (2023). Effect of probiotic supplementation on cognition and depressive symptoms in patients with depression: A systematic review and meta-analysis. *Medicine*, *102*(47), e36005–e36005. https://doi.org/10.1097/md.0000000000036005

Hernández-Cacho, A., et al. (2025). Multi-omics approach identifies gut microbiota variations associated with depression. *Npj Biofilms and Microbiomes*, *11*(1). https://doi.org/10.1038/s41522-025-00707-9

Hills, R. D., et al. (2019). Gut Microbiome: Profound Implications for Diet and Disease. *Nutrients*, *11*(7), 1613. https://doi.org/10.3390/nu11071613

Kennedy, S. H. (2008). Core symptoms of major depressive disorder: relevance to diagnosis and treatment. *Dialogues in Clinical Neuroscience*, *10*(3), 271–277. https://doi.org/10.31887/dcns.2008.10.3/shkennedy

Kumar, A., et al. (2023). Gut Microbiota in Anxiety and Depression: Unveiling the Relationships and Management Options. *Pharmaceuticals*, *16*(4), 565–565. https://doi.org/10.3390/ph16040565

Limbana, T., Khan, F., & Eskander, N. (2020). Gut Microbiome and Depression: How Microbes Affect the Way We Think. *Cureus*, *12*(8). https://doi.org/10.7759/cureus.9966

Liu, L., et al. (2023). Gut microbiota and its metabolites in depression: from pathogenesis to treatment. *EBioMedicine*, *90*(90), 104527. https://doi.org/10.1016/j.ebiom.2023.104527

Liu, R. T., et al. (2020). Reductions in anti-inflammatory gut bacteria are associated with depression in a sample of young adults. *Brain, Behavior, and Immunity*, *88*, 308–324. https://doi.org/10.1016/j.bbi.2020.03.026

Luqman, A., et al. (2024). Mood and microbes: a comprehensive review of intestinal microbiota's impact on depression. *Frontiers in Psychiatry*, *15*. https://doi.org/10.3389/fpsyt.2024.1295766

Schaub, A.-C., et al. (2022). Clinical, gut microbial and neural effects of a probiotic add-on therapy in depressed patients: a randomized controlled trial. *Translational Psychiatry*, *12*(1), 1–10. https://doi.org/10.1038/s41398-022-01977-z

Thapa, S., et al. (2021). Gut microbiome in adolescent depression. *Junuuuuuunal of Affective Disorders*, *292*, 500–507. https://doi.org/10.1016/j.jad.2021.05.107

Xie, Z., et al. (2024). Integrated multi-omics analysis reveals gut microbiota dysbiosis and systemic disturbance in major depressive disorder. *Psychiatry Research*, *334*, 115804. https://doi.org/10.1016/j.psychres.2024.115804

Yang, Y., et al. (2023). The Association between Gut Microbiota and Depression in the Japanese Population. *Microorganisms*, *11*(9), 2286–2286. https://doi.org/10.3390/microorganisms11092286

Yu, T., et al. (2024). Dissecting the association between gut microbiota, body mass index and specific depressive symptoms: a mediation Mendelian randomisation study. *General Psychiatry*, *37*(4), e101412–e101412. https://doi.org/10.1136/gpsych-2023-101412