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THE ROLE OF GUT MICROBIOTA IN THE DEVELOPMENT OF OBESITY, TYPE 2 DIABETES, AND DEPRESSION - A REVIEW OF CURRENT LITERATURE 2020–2026

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ABSTRACT

Background: The gut microbiota constitutes a complex and functionally active ecosystem that is increasingly recognized as a potential contributor to metabolic, immunological, and neuroendocrine homeostasis. Between 2020 and 2026, research has shifted from taxonomic descriptions toward functional and multi-omic approaches, improving understanding of the potential involvement of the microbiome in chronic metabolic and psychiatric disorders. This review summarizes current evidence on gut dysbiosis in obesity, type 2 diabetes, and depression, and evaluates proposed microbiota-targeted interventions.

Methods:A narrative synthesis was conducted based on a targeted search of PubMed and PubMed Central for studies published between January 2020 and May 2026. After screening more than 100 records, 68 full-text articles were assessed, and 31 publications, including systematic reviews, meta-analyses, and selected primary studies, were included..

Results: Gut dysbiosis, characterized by reduced microbial diversity, depletion of butyrate-producing bacteria, alterations in intestinal barrier function, and metabolic endotoxemia, has been consistently reported in association with obesity, type 2 diabetes, and depression. In obesity and type 2 diabetes, dysbiosis has been linked to chronic low-grade inflammation, altered short-chain fatty acid signaling, and insulin resistance. In depression, proposed mechanisms include gut–brain axis dysregulation, alterations in tryptophan metabolism toward the kynurenine pathway, and neuroinflammatory processes; however, the strength of evidence remains less consistent compared with metabolic disorders. Dietary patterns, particularly Mediterranean- and high-fiber–based diets, appear to be the most consistently supported modifiable factors associated with beneficial microbiota profiles and metabolic outcomes. Microbiota-targeted interventions, including probiotics, prebiotics, synbiotics, and fecal microbiota transplantation, show biological plausibility and early clinical signals, but current evidence remains heterogeneous and not yet definitive.

Conclusions: Current evidence suggests that the gut microbiota may represent one component of a broader immunometabolic and neuroendocrine network potentially involved in the development of obesity, type 2 diabetes, and depression, rather than a primary causal driver. Routine clinical use of microbiota profiling is not currently supported. Nevertheless, microbiota-modulating strategies, particularly dietary interventions, may serve as adjunctive approaches alongside standard care. Further well-designed, standardized, and adequately powered prospective and interventional studies integrating metagenomic and functional data are needed to clarify clinical utility and causality.

KEYWORDS

Gut Microbiota, Dysbiosis, Obesity, Type 2 Diabetes, Depression, Gut–Brain Axis, Short-Chain Fatty Acids, Diet, Probiotics, Psychobiotics

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1. Introduction

The gut microbiota constitutes a complex ecosystem of microorganisms colonizing the human gastrointestinal tract, is increasingly recognized as a potential contributor to the regulation of metabolic, immunological, and neuroendocrine homeostasis (Fan & Pedersen, 2021; Rondinella et al., 2025). Contemporary review studies indicate that the microbiota is not merely a passive component of the internal environment, but rather is considered a functional biological system capable of modulating host metabolism, intestinal barrier integrity, and inflammatory responses (Alqahtani, 2025; Chen et al., 2021; Fan & Pedersen, 2021). Advances in next-generation sequencing, metagenomics, and multi-omics analyses have substantially expanded our understanding of the relationships between gut microbiota composition and the pathogenesis of chronic diseases (Chen et al., 2021; Fan & Pedersen, 2021). Numerous systematic and narrative reviews emphasize the particular role of gut dysbiosis in the development of metabolic disorders, most notably obesity and type 2 diabetes, as well as psychiatric conditions, including depression (Borrego-Ruiz & Borrego, 2025;

Cao et al., 2026; Chong et al., 2025; Clerici et al., 2025; Islam et al., 2023). Concurrently, authors highlight that despite a growing body of clinical and experimental evidence, definitively establishing whether observed microbiota alterations are causally implicated or secondary to the disease process remains challenging in many areas in most human studies (Chong et al., 2025; Fan & Pedersen, 2021; Jiang et al., 2026).

In the pathophysiology of obesity, the gut microbiota may influence energy balance, appetite regulation, lipid metabolism, and the maintenance of chronic low-grade inflammation (Borrego-Ruiz & Borrego, 2025; Islam et al., 2023; Liu et al., 2021). Review studies demonstrate that obesity is frequently accompanied by a reduction in microbial diversity, alterations in taxonomic composition, and increased intestinal barrier permeability, thereby being associated with metabolic endotoxemia and the progression of metabolic disturbances (Cheng et al., 2022; Islam et al., 2023; Liu et al., 2021). The classical hypothesis regarding an altered Firmicutes/Bacteroidetes ratio has not been consistently corroborated across all studied populations; instead, increasing importance is attributed to qualitative and functional changes in the microbiota, including a reduction in bacteria producing short-chain fatty acids with anti-inflammatory properties (Anachad et al., 2023; Borrego-Ruiz & Borrego, 2025; Zhang et al., 2024).

In type 2 diabetes, characteristic deviations in gut microbiota composition have been described, encompassing a reduction in the abundance of taxa with potentially protective functions, such as butyrate-producing bacteria, alongside an increased proportion of bacteria associated with activation of inflammatory responses and impaired intestinal barrier integrity (Chong et al., 2025; Jin et al., 2026; Senesi et al., 2021). Systematic reviews have demonstrated that patients with type 2 diabetes more frequently exhibit reduced microbial diversity, an altered taxonomic profile, and impaired metabolic functions; however, heterogeneity in study designs and study populations constrains the ability to draw unequivocal causal conclusions (Chong et al., 2025; Ruan et al., 2025). Studies focusing on microbiota-targeted interventions suggest that modulation of microbiome composition may influence glycemic parameters and insulin sensitivity, although the quality of available evidence is assessed as moderate to low (Jiang et al., 2026; Qureshi et al., 2025; Ur Rehman et al., 2025).

In recent years, there has also been a significant increase in interest regarding the contribution of gut microbiota to the pathophysiology of depression (Góralczyk-Bińkowska et al., 2022; F. Zhu et al., 2022; Z. Zhu et al., 2025). The gut–brain axis, encompassing neuronal, immunological, endocrine, and metabolic mechanisms, constitutes the basis of bidirectional communication between the microbiota and the central nervous system, and its dysregulation is associated with the development of depressive symptoms (Góralczyk-Bińkowska et al., 2022; F. Zhu et al., 2022; Z. Zhu et al., 2025). Available literature reviews suggest that patients with depression more frequently exhibit reduced abundance of short-chain fatty acid-producing bacteria, an increased proportion of pro-inflammatory taxa, and disruptions in tryptophan and serotonin metabolism, which may predispose to neuroinflammation and dysregulation of neurotransmission (Cao et al., 2026; Clerici et al., 2025; Su & Xia, 2026). Attention is also drawn to the potential role of psychobiotics and dietary interventions as complementary therapeutic strategies, although current clinical evidence remains limited and inconclusive (Clerici et al., 2025; Sá Filho et al., 2026; Z. Zhu et al., 2025).

Obesity, type 2 diabetes, and depression frequently co-occur, and their shared pathological substrate may encompass chronic low-grade inflammation, impaired intestinal barrier integrity, aberrant production and signaling of bacterial metabolites including short-chain fatty acids, bile acids, and tryptophan derivatives as well as disrupted communication within the gut–brain axis (Anachad et al., 2023; Borrego-Ruiz & Borrego, 2025; Clerici et al., 2025). In this context, the gut microbiota is regarded not only as a potential biomarker of metabolic and psychiatric disorders, but also as a promising target for therapeutic interventions encompassing dietary modification, probiotic therapy, prebiotic therapy, synbiotics, and other strategies aimed at restoring eubiosis (Jiang et al., 2026; Luo et al., 2026; Masi et al., 2026). Despite promising results from preclinical studies and preliminary clinical trials, further high-quality methodological research is warranted to unequivocally evaluate the efficacy and safety of such interventions (Jiang et al., 2026; Qureshi et al., 2025; Ur Rehman et al., 2025).

The aim of the present review is to summarize the current state of knowledge regarding the role of gut microbiota in the development of obesity, type 2 diabetes, and depression, with particular emphasis on pathophysiological mechanisms, interrelationships between these disease entities, and potential diagnostic and therapeutic implications, based on literature published between 2020 and 2026 (Chong et al., 2025; Islam et al., 2023; Z. Zhu et al., 2025).

2. Characteristics of the Gut Microbiota

2.1. Composition of the Gut Microbiota

The human gut microbiota constitutes a complex and dynamic ecosystem of microorganisms colonizing the gastrointestinal tract, whose qualitative and quantitative composition is subject to genetic, environmental, and behavioral influences (Borrego-Ruiz & Borrego, 2025; Fan & Pedersen, 2021). Under physiological conditions, the dominant bacterial phyla are Firmicutes and Bacteroidetes, while Actinobacteria and Proteobacteria are typically present in lower proportions, although their biological and clinical significance for the maintenance of intestinal eubiosis is considerable (Islam et al., 2023; Liu et al., 2021). The phylum Firmicutes encompasses numerous anaerobic bacteria involved in the fermentation of indigestible polysaccharides and the production of short-chain fatty acids, including butyrate, which plays a pivotal role in maintaining intestinal barrier integrity and colonocyte function (Anachad et al., 2023; Borrego-Ruiz & Borrego, 2025). Bacteroidetes, represented predominantly by the genera *Bacteroides* and *Prevotella*, are characterized by high enzymatic activity in the degradation of dietary components, and their proportion within the microbiota is closely associated with the host's dietary pattern (Fan & Pedersen, 2021; Ross et al., 2024). Actinobacteria are represented primarily by the genus *Bifidobacterium*, regarded as one of the most important groups of commensal bacteria with potential protective properties, linked to oligosaccharide metabolism, modulation of immune responses, and support of mucosal barrier homeostasis (Fan & Pedersen, 2021; Fu et al., 2022). Conversely, an increased proportion of Proteobacteria, encompassing numerous Gram-negative bacteria, is frequently interpreted as a marker of dysbiosis, increased intestinal barrier permeability, and ongoing inflammatory processes (Cheng et al., 2022; Islam et al., 2023). Current literature emphasizes that overall microbial diversity and the presence of specific taxa with anti-inflammatory and metabolite-producing properties may be of greater clinical relevance than the Firmicutes/Bacteroidetes ratio per se (Chong et al., 2025; Zhang et al., 2024). In this context, the gut microbiota profile should be considered not only in taxonomic but also in functional terms, as it is the metabolic and immunomodulatory potential of the microbiome that may most decisively determine its clinical significance (Fan & Pedersen, 2021; Jin et al., 2026).

2.2. Functions of the Gut Microbiota

The gut microbiota fulfills multidirectional metabolic, immunological, and neuroregulatory functions, constituting an essential component of systemic homeostasis (Y. Chen et al., 2021; Fan & Pedersen, 2021). One of its fundamental roles is the fermentation of indigestible dietary components, primarily dietary fiber, leading to the production of short-chain fatty acids, including acetate, propionate, and butyrate (Anachad et al., 2023; Fu et al., 2022). These metabolites exert pleiotropic effects: they serve as an energy source for enterocytes, influence the secretion of intestinal hormones, modulate lipid and carbohydrate metabolism, and are thought to participate in the regulation of insulin sensitivity (Anachad et al., 2023; Borrego-Ruiz & Borrego, 2025). Equally important is the role of the microbiota in shaping immune responses. Commensal bacteria participate in immune system maturation, maintenance of immunological tolerance, and regulation of the balance between pro-inflammatory and anti-inflammatory mechanisms within the intestinal mucosa (Y. Chen et al., 2021; Islam et al., 2023). SCFA production, particularly of butyrate, has been suggested to support intestinal barrier integrity through effects on the expression of tight junction proteins and epithelial cell metabolism, whereas disruptions in microbiota composition may lead to increased intestinal permeability, translocation of bacterial antigens, and activation of chronic low-grade inflammation (Anachad et al., 2023; Chong et al., 2025).

The gut microbiota may additionally exert a significant influence on nervous system function, participating in the regulation of the gut–brain axis via neuronal, immunological, hormonal, and metabolic pathways (Góralczyk-Bińkowska et al., 2022; F. Zhu et al., 2022). It has been demonstrated that microbiota-derived metabolites, including SCFAs and compounds generated through tryptophan metabolic pathways, can modulate neurotransmission, hypothalamic–pituitary–adrenal axis function, microglial cell activity, and neuroinflammatory processes (Cao et al., 2026; Clerici et al., 2025; Z. Zhu et al., 2025). The gut microbiota should therefore be regarded as a key regulator not only of metabolic and immunological processes, but also of neuropsychiatric function (Góralczyk-Bińkowska et al., 2022; Sá Filho et al., 2026).

2.3. Factors Influencing the Gut Microbiota

The composition and metabolic activity of the gut microbiota are subject to dynamic modulation by numerous environmental and lifestyle factors, endowing this ecosystem with considerable plasticity while simultaneously rendering it susceptible to the development of dysbiosis (Clerici et al., 2025; Fan & Pedersen, 2021). Diet remains the most potent modulator of the microbiome. A dietary pattern rich in fiber, plant-based foods, and minimally processed products promotes increased microbial diversity and SCFA production, whereas a Western diet abundant in saturated fats, simple sugars, and ultra-processed foods promotes dysbiosis and metabolic disturbances (Fu et al., 2022; Rondinella et al., 2025; Ross et al., 2024). Antibiotics represent a significant disruptor of microbiota homeostasis, which particularly upon repeated or broad-spectrum exposure may lead to a sustained decline in taxonomic diversity, loss of commensal bacteria, and a relative increase in opportunistic microorganisms (Y. Chen et al., 2021; Fan & Pedersen, 2021). The clinical relevance of these changes is considerable, as long-term microbiota disruption may predispose to the development of both metabolic diseases and disorders associated with the gut–brain axis (Cao et al., 2026; Chong et al., 2025).

The microbiota is also affected by psychosocial stress, which, through activation of the hypothalamic–pituitary–adrenal axis, alterations in glucocorticoid secretion, and modulation of immune responses, may disrupt microbiome composition and intestinal barrier integrity (Góralczyk-Bińkowska et al., 2022; F. Zhu et al., 2022). In contrast, regular physical activity is associated with a more favorable microbiota profile, greater bacterial diversity, and more beneficial microbial metabolism, particularly when accompanied by a health-promoting dietary pattern (Borrego-Ruiz & Borrego, 2025; Zhou et al., 2026). Age also carries significant relevance, as the gut microbiota undergoes substantial changes throughout the lifespan. In older individuals, a decline in diversity, shifts in the proportions of dominant bacterial phyla, and increased susceptibility to eubiosis-destabilizing factors; such as comorbidities, polypharmacy, and dietary changes are frequently observed (Fan & Pedersen, 2021; Tavassol et al., 2026). In elderly individuals with obesity, these changes may further amplify adverse immunometabolic processes, underscoring the importance of incorporating age as a key variable in gut microbiota research (Tavassol et al., 2026).

3. Gut Microbiota and Obesity

3.1. Gut Dysbiosis in Obesity

The gut microbiota of individuals with obesity is characterized by reduced diversity and disrupted taxonomic composition compared to normal-weight individuals (Borrego-Ruiz & Borrego, 2025; X. Chen et al., 2026; Islam et al., 2023). Clinical studies have demonstrated that patients with excess body weight exhibit a distinct microbiological profile, encompassing alterations in the prevalence of short-chain fatty acid-producing taxa and an increase in the abundance of potentially pro-inflammatory bacteria (Borrego-Ruiz & Borrego, 2025; Liu et al., 2021). Numerous studies have analyzed the proportions of dominant bacterial phyla, particularly Firmicutes and Bacteroidetes; however, the direction of observed changes is not fully consistent across populations and study cohorts, suggesting that the qualitative and functional characteristics of dysbiosis carry greater clinical relevance than the Firmicutes/Bacteroidetes ratio per se (Borrego-Ruiz & Borrego, 2025; Islam et al., 2023). Current reviews emphasize the role of reduced microbial diversity, depletion of butyrate-producing taxa, and an increased proportion of Gram-negative bacteria as characteristic features of the microbiota profile in obesity (Borrego-Ruiz & Borrego, 2025; Islam et al., 2023). Obesity-associated dysbiosis is also linked to increased intestinal barrier permeability, impairment of epithelial tight junctions, and facilitated translocation of bacterial cell wall components such as lipopolysaccharide (LPS) into the systemic circulation (Islam et al., 2023; Sasidharan Pillai et al., 2024). This phenomenon promotes the development of metabolic endotoxemia and systemic low-grade inflammation, constituting one of the key links between local intestinal dysfunction and the metabolic disturbances observed in individuals with obesity (Borrego-Ruiz & Borrego, 2025; Raczkowska et al., 2024).

3.2. Metabolic Mechanisms

One of the most important mechanisms linking gut dysbiosis to obesity is chronic low-grade inflammation, developing as a consequence of increased intestinal barrier permeability and immune activation by bacterial molecular patterns, including LPS (Borrego-Ruiz & Borrego, 2025; Islam et al., 2023). The translocation of LPS into the circulation leads to metabolic endotoxemia, activation of TLR4 receptors, augmented production of pro-inflammatory cytokines, and the development of insulin resistance, thereby promoting adipose tissue dysfunction and disturbances in carbohydrate and lipid metabolism (Raczkowska et al., 2024; Sasidharan Pillai et al., 2024). Gut microbiota composition also influences the production of short-

chain fatty acids including butyrate, acetate, and propionate which are thought to modulate tissue insulin sensitivity, lipogenesis, intestinal barrier integrity, and both local and systemic inflammatory responses (Anachad et al., 2023; Fu et al., 2022; Raczkowska et al., 2024). Disruptions in SCFA production, resulting from depletion of fiber-fermenting bacteria, may predispose to the development of insulin resistance, increased adipose tissue mass, and deterioration of the metabolic parameters characteristic of obesity (Anachad et al., 2023; Islam et al., 2023).

The gut microbiota also exerts influence on appetite regulation and energy balance through its effects on the gut–brain axis (Arellano-García et al., 2026; Borrego-Ruiz & Borrego, 2025). SCFAs and other bacterial metabolites modulate the secretion of intestinal hormones such as GLP-1 and PYY, as well as signaling via the vagus nerve and G protein-coupled receptors, thereby influencing satiety, dietary preferences, and feeding behavior (Arellano-García et al., 2026; Masi et al., 2026). Reviews addressing the gut–brain axis in obesity indicate that dysbiosis may promote dysregulation of appetite control, leading to increased energy intake and the perpetuation of a positive energy balance (Arellano-García et al., 2026; Islam et al., 2023).

3.3. Therapeutic Approaches

The growing body of evidence regarding the role of gut microbiota in the pathogenesis of obesity has been reflected in the development of therapeutic concepts aimed at modulating microbiota composition and function, among which dietary intervention is of primary importance (Luo et al., 2026; Ross et al., 2024). A diet rich in dietary fiber, plant-based foods, and fermented products, combined with restriction of ultra-processed foods, promotes increased microbial diversity, enhanced SCFA production, and improved intestinal barrier integrity, translating into favorable changes in metabolic parameters in individuals with obesity (Fu et al., 2022; Islam et al., 2023; Rondinella et al., 2025).

Dietary interventions may be complemented by probiotics and prebiotics. Selected probiotic strains, administered alone or in combination with prebiotics (synbiotics), have demonstrated potential in improving insulin sensitivity, reducing body weight or waist circumference, and modulating inflammatory markers; however, results are heterogeneous and the quality of available evidence is assessed as moderate (Islam et al., 2023; Luo et al., 2026). Prebiotics, through the selective stimulation of beneficial bacterial growth, contribute to increased SCFA production and improvement of metabolic parameters, as documented in studies involving overweight and obese individuals (Anachad et al., 2023; Fu et al., 2022).

More advanced therapeutic concepts include the application of fecal microbiota transplantation (FMT) to restore a favorable microbiological profile in patients with obesity and metabolic syndrome (Borrego-Ruiz & Borrego, 2025; Sasidharan Pillai et al., 2024). Available studies indicate that FMT from lean donors may transiently improve insulin sensitivity and selected metabolic parameters; however, the effects are variable, depending in part on the recipient's diet and baseline microbiota composition, and the long-term efficacy and safety of this approach remain insufficiently characterized (Luo et al., 2026; Sasidharan Pillai et al., 2024). Current reviews emphasize that despite promising preclinical and early clinical findings, microbiota-targeted interventions, including FMT, require further evaluation in well-designed randomized controlled trials (Islam et al., 2023; Luo et al., 2026; Masi et al., 2026).

4. Gut Microbiota and Type 2 Diabetes

4.1. The Relationship Between Dysbiosis and Insulin Resistance

Patients with type 2 diabetes have been reported to exhibit characteristic features of gut dysbiosis, encompassing reduced microbial diversity, an altered taxonomic profile, and shifts in the proportions of taxa with potentially protective or pro-inflammatory properties, which have been associated with increased insulin resistance (Crudele et al., 2023; He et al., 2026). Studies have documented a reduction in the abundance of butyrate-producing bacteria alongside an increased proportion of taxa associated with activation of inflammatory responses, correlating with impaired glycemic parameters, greater severity of insulin resistance, and concomitant visceral obesity (He et al., 2026; Senesi et al., 2021). Mendelian randomization analyses suggest potential causal association between specific bacterial taxa and the risk of type 2 diabetes and its subtypes, strengthening the hypothesis that dysbiosis is associated with insulin resistance and may contribute to the development of insulin resistance and glycemic disturbances (Jin et al., 2026; Ruan et al., 2025). It has been demonstrated that alterations in the abundance of particular gut bacterial genera may significantly influence the risk of developing specific T2D phenotypes, indicating the existence of complex, phenotypically distinct interactions between the microbiota and glucose metabolism (He et al., 2026; Jin et al., 2026). It is further noted that the influence of individual taxa may differ across metabolic phenotypes of type 2 diabetes, underscoring the importance of an individualized approach when assessing the role of the microbiota in insulin resistance (He et al., 2026; Jin et al., 2026).

4.2. Pathophysiological Mechanisms: Inflammation, Bacterial Metabolites, and Intestinal Barrier Dysfunction

Chronic low-grade inflammation plays an important role in the pathophysiology of type 2 diabetes, developing in part as a consequence of gut dysbiosis and increased exposure to bacterial cell wall components such as LPS, which activate the innate immune response (Crudele et al., 2023; Senesi et al., 2021). Impaired intestinal barrier integrity, observed in a subset of patients with type 2 diabetes and concomitant obesity, facilitates LPS translocation into the systemic circulation, leading to metabolic endotoxemia and is associated with exacerbation of insulin resistance in adipose tissue and skeletal muscle, and deterioration of pancreatic β-cell function (Raczkowska et al., 2024; Sasidharan Pillai et al., 2024). Bacterial metabolites, in particular SCFAs and secondary bile acids, modulate G protein-coupled receptor signaling, FXR/TGR5 receptor activity, insulin sensitivity, and lipid profiles, thereby influencing glucose homeostasis and cardiovascular risk (Crudele et al., 2023; Raczkowska et al., 2024). Dysbiosis-related disruption of the gut–liver and gut–brain axes may alter the secretion of incretin hormones such as GLP-1, affect appetite regulation, fat storage, and circadian metabolic rhythms, thereby promoting the progression of insulin resistance and the perpetuation of glycemic disturbances (He et al., 2026; Sasidharan Pillai et al., 2024). It is also noteworthy that the microbiota influences the metabolism of antidiabetic medications, most notably metformin, which may interact bidirectionally with the gut microbiota (Crudele et al., 2023; Kumar et al., 2026). Evidence indicates that metformin may in turn modify microbiota composition, while specific microbiome characteristics may determine treatment efficacy and tolerability, raising the prospect of utilizing microbiota profiling as a biomarker of therapeutic response (Kumar et al., 2026).

4.3. Potential Treatment Strategies: Mediterranean Diet, Probiotic Therapy, and Lifestyle Modification

An improved understanding of the role of gut microbiota in the pathophysiology of type 2 diabetes has provided the rationale for therapeutic strategies targeting microbiome modulation as an adjunct to standard pharmacological treatment and conventional lifestyle modification (Crudele et al., 2023; Raczkowska et al., 2024). Among dietary interventions, particular importance is attributed to nutritional patterns characterized by high intake of fiber, plant-based foods, and healthy fats, with a low degree of food processing such as the Mediterranean diet which promote increased microbial diversity, SCFA production, and improvements in insulin sensitivity and glycemic control (Fu et al., 2022; Ross et al., 2024). Attention has also been drawn to the role of specific food products and bioactive compounds that modulate microbiota composition and may attenuate metabolic disturbances, including fermented dairy products and plant-derived extracts (Gómez-García et al., 2025; Yang et al., 2026). Studies have observed that regular consumption of yogurt and selected plant-based extracts is associated with favorable changes in the microbiota profile and improvement in selected metabolic risk indicators (Gómez-García et al., 2025; Yang et al., 2026).

Research on microbiota-targeted interventions suggests that probiotic therapy employing selected bacterial strains with beneficial effects on metabolism and inflammatory status alongside prebiotics, which act as selective growth substrates for beneficial microorganisms, may lead to improvements in glycemic parameters, lipid profiles, and inflammatory markers in patients with type 2 diabetes, although the quality of available evidence varies (Crudele et al., 2023; Raczkowska et al., 2024). Current reviews emphasize the need for standardization of strains, dosages, and treatment duration to enable the formulation of unambiguous clinical recommendations (Crudele et al., 2023). Comprehensive lifestyle modification encompassing dietary changes, weight reduction, and increased physical activity remains an integral component of the therapeutic approach, as its favorable effects on gut microbiota composition, inflammatory status, and insulin sensitivity may substantially support glycemic control and reduce cardiovascular risk in patients with type 2 diabetes (Ross et al., 2024; Senesi et al., 2021).

5. The Gut–brain Axis and Depression

5.1. The Gut–Brain Axis: Vagus Nerve, Cytokines, and Neurotransmitters

The gut–brain axis constitutes a complex, bidirectional communication system between the gastrointestinal tract and the central nervous system, encompassing neuronal, hormonal, immunological, and metabolic pathways (Cryan et al., 2020; Doroszkiewicz et al., 2021; Góralczyk-Bińkowska et al., 2022). The vagus nerve plays a central role in the neuronal component of this axis, conducting afferent signals from the intestine to limbic and subcortical structures, as well as efferent signals influencing gastrointestinal motility and secretion; modulation of its activity has been shown to alter the severity of depressive behaviors in experimental animal models (Góralczyk-Bińkowska et al., 2022; Lei et al., 2026). Pro-inflammatory cytokines, produced in response to dysbiosis and impaired intestinal barrier integrity, play an important role in gut–brain axis communication and may modify hypothalamic–pituitary–adrenal axis activity, affect neuroplasticity, and predispose to the development of depressive symptoms (Cao et al., 2026; Góralczyk-Bińkowska et al., 2022). The gut microbiota additionally influences tryptophan metabolism, serotonin and GABA synthesis, the production of other neurotransmitters, and SCFA generation; metabolites that indirectly modulate central nervous system function and mood regulation (Cao et al., 2026; Clerici et al., 2025; Zheng et al., 2026). Reviews emphasize that disruption of this complex signaling network may give rise to neuroinflammatory and neuroendocrine changes that predispose to the development of depression (Góralczyk-Bińkowska et al., 2022; Zheng et al., 2026).

5.2. Gut Microbiota and Depression: Dysbiosis, Inflammation, and Serotonin

Available review literature indicates that patients with depression more frequently exhibit features of gut dysbiosis, including reduced microbial diversity, an altered proportion of SCFA-producing taxa, and an increased representation of bacteria with potentially pro-inflammatory properties (Cao et al., 2026; Clerici et al., 2025; Góralczyk-Bińkowska et al., 2022). These changes are associated with augmented low-grade inflammation, increased intestinal barrier permeability, and activation of the stress response axis, which may promote neuroinflammation and impaired neuroplasticity in brain structures responsible for mood regulation (Cao et al., 2026; Góralczyk-Bińkowska et al., 2022). Particular importance is attributed to disturbances in tryptophan metabolism and the serotonergic pathway. Dysbiosis may influence tryptophan metabolism, potentially affecting serotonergic and kynurenine pathways, and has been associated with low mood and cognitive dysfunction (Clerici et al., 2025; Zheng et al., 2026). Experimental studies have further demonstrated that transfer of microbiota from individuals with depression to germ-free mice has been shown in experimental animal models to induce depression-like behaviors and alterations in energy metabolism, providing additional evidence for the involvement of the microbiota in the pathogenesis of depression and its relationship with metabolic disturbances (Beswick et al., 2025; Lei et al., 2026).

5.3. Psychobiotics and Emerging Therapeutic Directions: Probiotics, Diet, and Future Treatment Prospects

A growing understanding of the role of the gut–brain axis in the pathophysiology of depression has given rise to the concept of psychobiotics, probiotics and other microbiota-targeted interventions with the potential to modulate mood and cognitive function (Clerici et al., 2025; Sá Filho et al., 2026). Literature reviews indicate that selected bacterial strains, including SCFA producers and modulators of inflammatory status, may attenuate depressive symptoms; however, results from available clinical trials remain inconclusive, and optimal strains, dosages, and treatment duration are subjects of ongoing investigation (Cao et al., 2026; Sá Filho et al., 2026).

Diet also plays an important role as a potential therapeutic strategy. Dietary patterns rich in fiber, plant-based foods, and minimally processed products promote eubiosis maintenance, enhanced SCFA production, and favorable effects on tryptophan metabolism and stress axis function (Clerici et al., 2025; Ross et al., 2024). It is emphasized that dietary interventions may constitute a meaningful adjunct to pharmacotherapy, exerting effects on both the microbiota and the metabolic and clinical dimensions of depression (Clerici et al., 2025).

Among future treatment prospects, individualized approaches based on microbiota profiling are under consideration, combining dietary and probiotic interventions with potential fecal microbiota transplantation as a complement to standard pharmacotherapy; however, further high-quality methodological research is required to evaluate the efficacy and safety of such strategies in patients with depression (Beswick et al., 2025; Halabitska et al., 2024; Zheng et al., 2026).

A schematic representation of the role of the gut microbiota as a shared pathophysiological nexus linking obesity, type 2 diabetes, and depression is presented in **Figure 1.**

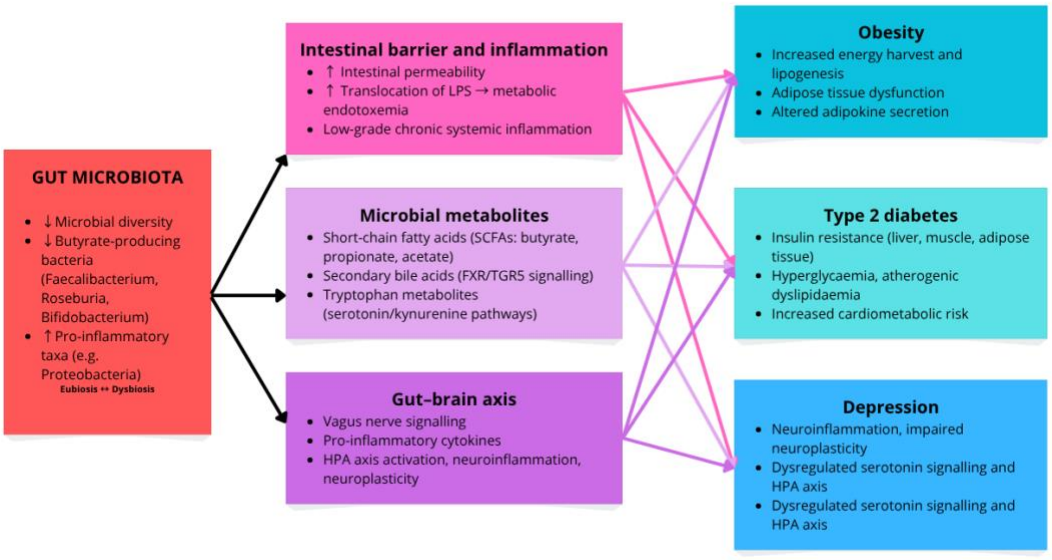

Fig. 1. *Schematic representation of the role of gut dysbiosis as a shared pathophysiological nexus in the development of obesity, type 2 diabetes and depression.*

6. The Role of Diet in Microbiota Modulation

6.1. The Mediterranean Diet

The Mediterranean diet, characterized by high consumption of vegetables, fruits, legumes, whole grains, olive oil, and nuts, along with moderate intake of fish and fermented products, is among the most extensively studied dietary patterns and has been associated with beneficial effects on gut microbiota composition and metabolic disease risk (Borrego-Ruiz & Borrego, 2025; Ross et al., 2024). Reviews addressing diet–microbiome interactions indicate that dietary patterns approximating the Mediterranean diet promote increased microbial diversity, a higher proportion of short-chain fatty acid-producing bacteria, and the presence of taxa with anti-inflammatory properties, such as *Faecalibacterium prausnitzii* and *Bifidobacterium* (Fu et al., 2022; Ross et al., 2024). It is emphasized that through its high content of fiber, polyphenols, and unsaturated fatty acids, the Mediterranean diet modulates not only the composition but also the functional capacity of the microbiota, translating into improved metabolic parameters, attenuation of chronic low-grade inflammation, and a favorable cardiovascular profile (Islam et al., 2023; Ross et al., 2024; Senesi et al., 2021). Studies examining the relationships between dietary quality, degree of food processing, and microbiota composition have demonstrated that dietary patterns consistent with the Mediterranean diet correlate with a more favorable bacterial profile and a lower risk of obesity, type 2 diabetes, and mood disorders (Clerici et al., 2025; Rondinella et al., 2025; Ross et al., 2024).

6.2. High-Fat Diet

The antithesis of the Mediterranean diet is the Western diet, abundant in saturated fats, simple sugars, red and highly processed meats, salt, and ultra-processed foods, while simultaneously deficient in dietary fiber and plant-derived components (Rondinella et al., 2025; Ross et al., 2024). Reviews examining the impact of diet on gut microbiota indicate that prolonged adherence to a high-fat, highly processed dietary pattern has been associated with reduced microbial diversity, a decline in the abundance of beneficial taxa such as *Akkermansia muciniphila* and *Faecalibacterium prausnitzii*, and an increased proportion of bacteria with pro-inflammatory potential, including Proteobacteria (Borrego-Ruiz & Borrego, 2025; Islam et al., 2023; Rondinella et al., 2025). Ultra-processed foods, characterized by low fiber content and high concentrations of technological additives such as emulsifiers, artificial sweeteners, and preservatives, may promote dysbiosis, increased intestinal barrier permeability, and chronic low-grade inflammation, which have been associated

with a higher risk of obesity, type 2 diabetes, and other metabolic disorders (Islam et al., 2023; Rondinella et al., 2025). Studies in the context of obesity and its metabolic complications have demonstrated that a high-fat diet induces shifts in the microbiota profile that promote the development of metabolic endotoxemia, insulin resistance, and dyslipidemia (Islam et al., 2023; Luo et al., 2026; Moon et al., 2026). In this context, restricting the consumption of ultra-processed foods and saturated fats should be considered an important component of strategies aimed at restoring intestinal eubiosis and improving metabolic parameters (Islam et al., 2023; Rondinella et al., 2025; Ross et al., 2024).

6.3. Dietary Fiber and SCFAs

Dietary fiber is one of the key modulators of the gut microbiota, and its consumption is closely linked to short-chain fatty acid production and has been associated with a broad range of beneficial metabolic effects(Fu et al., 2022; Ross et al., 2024). Reviews indicate that various fiber fractions including soluble and fermentable polysaccharides undergo fermentation by intestinal bacteria, yielding acetate, propionate, and butyrate, which serve as energy substrates for colonocytes, regulators of gene expression, and signaling mediators influencing glucose and lipid metabolism (Anachad et al., 2023; Fu et al., 2022). SCFAs modulate the secretion of intestinal hormones such as GLP-1 and PYY, influence insulin sensitivity, thermogenesis, and lipogenesis, and reinforce intestinal barrier integrity by upregulating the expression of tight junction proteins effects of particular relevance for the prevention of metabolic endotoxemia and chronic low-grade inflammation (Anachad et al., 2023; Borrego-Ruiz & Borrego, 2025; Islam et al., 2023). Reviews addressing obesity and type 2 diabetes have highlighted that inadequate fiber intake and the resultant decline in SCFA production contribute to the development of dysbiosis, insulin resistance, and glycemic disturbances (Anachad et al., 2023; Chong et al., 2025; Fu et al., 2022).

Interventional studies employing high-fiber diets and fiber supplementation indicate that increasing fermentable fiber intake leads to an expansion of SCFA-producing bacteria including *Bifidobacterium*, *Anaerostipes*, and *Faecalibacterium* and to improvements in selected metabolic parameters (Fu et al., 2022; Luo et al., 2026; Zhou et al., 2026). For these reasons, interventions aimed at increasing fiber intake through both dietary modification and prebiotic supplementation are currently regarded as one of the cornerstone elements of microbiota-targeting strategies in the prevention and treatment of obesity, type 2 diabetes, and potentially mood disorders (Clerici et al., 2025; Fu et al., 2022; Ross et al., 2024). The main dietary patterns and their effects on microbiota composition and bacterial metabolite production are summarized in **Table 1.** A comparative overview of dysbiosis features, pathophysiological mechanisms, and microbiota-targeted interventions across the three conditions is presented in **Table 2.**

Table 1. Diet and gut microbiota- major dietary patterns and their effects.

Dietary pattern / intervention	Effects on microbiota composition	Effects on bacterial metabolites (SCFAs, bile acids)	Main metabolic / clinical effects
Mediterranean diet	↑ diversity; ↑ butyrate-producing bacteria (*Faecalibacterium*, *Bifidobacterium*); ↓ pro-inflammatory taxa	↑ SCFA production; favorable modulation of bile acid profile	Improved lipid profile, glycemia, and cardiovascular parameters; reduction of inflammation
High-fat diet	↓ diversity; ↓ beneficial bacteria (e.g. *Akkermansia*, *Faecalibacterium*); ↑ Proteobacteria and pro-inflammatory taxa	↓ production of "beneficial" SCFAs; disrupted bile acid metabolism; ↑ LPS	Increased intestinal permeability, metabolic endotoxemia, insulin resistance, exacerbation of obesity and T2D risk
High-fiber diet / plant-rich diet	↑ fiber-fermenting bacteria (*Bifidobacterium*, *Faecalibacterium*, *Anaerostipes*); ↑ diversity	Marked ↑ SCFA production (butyrate, propionate, acetate); favorable modulation of bile acids	Improved insulin sensitivity, reduced glycemia, weight loss or BMI stabilization, decreased inflammatory markers

Dietary pattern / intervention	Effects on microbiota composition	Effects on bacterial metabolites (SCFAs, bile acids)	Main metabolic / clinical effects
High ultra-processed food (UPF) intake	↓ diversity; ↑ pro-inflammatory taxa; potential additive-related changes (emulsifiers, sweeteners)	↓ beneficial SCFAs; possible increase in metabolites promoting inflammation and intestinal barrier dysfunction	Higher risk of obesity, T2D, and metabolic disorders; possible associations with depression
Specific foods / ingredients (e.g. yogurt, *Opuntia ficus-indica* extract)	Increase in specific beneficial taxa, including lactose- or plant fiber-fermenting bacteria; modulation of microbiota profile toward eubiosis	↑ SCFA production; changes in lipid and glucose metabolism depending on intervention	Improvement in selected metabolic risk indicators (e.g. waist circumference, lipid profile, inflammatory markers)

Table 2. Gut microbiota in obesity, type 2 diabetes, and depression shared features and differences.

Disease	Main features of dysbiosis	Proposed pathophysiological mechanisms	Typical microbiota-targeted interventions	Level and nature of evidence
Obesity	Reduced diversity; ↓ butyrate-producing bacteria (*Faecalibacterium*, *Roseburia*); ↑ pro-inflammatory bacteria (including Proteobacteria); altered Firmicutes/Bacteroidetes ratio (inconsistent across populations)	Increased intestinal barrier permeability; metabolic endotoxemia (LPS); chronic low-grade inflammation; impaired SCFA production; modification of intestinal hormones (GLP-1, PYY) and appetite regulation	Mediterranean and high-fiber diet; restriction of ultra-processed foods; probiotics, prebiotics, synbiotics; early-stage FMT studies	Predominantly narrative and systematic reviews and meta-analyses; numerous observational and interventional studies; limited methodological standardization
Type 2 diabetes	Reduced diversity; ↓ butyrate-producing bacteria; ↑ pro-inflammatory taxa; altered functional microbiota profile	Chronic low-grade inflammation; metabolic endotoxemia; impaired SCFA signaling; altered bile acid metabolism (FXR/TGR5); insulin resistance in adipose tissue, skeletal muscle, and liver; modification of metformin response	Dietary modification (Mediterranean and high-fiber patterns); probiotics, prebiotics; microbiota-targeted interventions (including FMT- under investigation); optimization of pharmacotherapy accounting for microbiota effects	Systematic reviews and Mendelian randomization analyses suggesting possible causal relationships; growing number of RCTs and interventional studies, still methodologically heterogeneous
Depression	Reduced diversity; ↓ SCFA-producing bacteria; ↑ pro-inflammatory taxa; disrupted metabolite profile (tryptophan, serotonin, bile acids)	Gut–brain axis dysregulation; HPA axis activation; neuroinflammation and impaired neuroplasticity; disrupted tryptophan metabolism (shift toward the kynurenine pathway at the expense of serotonin synthesis); effects on mood and cognitive function	Psychobiotics (selected probiotic strains), prebiotics; dietary interventions (health-promoting, high-fiber diet); FMT - conceptually proposed, at a very early stage of investigation	Narrative and scoping reviews; moderate number of clinical trials, often underpowered; robust experimental data (animal models, microbiota transfer studies); limited clinical validation

7. Methods

This narrative review was based on a targeted literature search conducted in PubMed and PubMed Central (PMC), focused on the role of gut microbiota in the pathogenesis of obesity, type 2 diabetes, and depression, and on the influence of diet on microbiome modulation. The search was conducted in 2026 and covered publications from January 2020 to May 2026. Search terms included "gut microbiota," "obesity," "type 2 diabetes mellitus," "depression," "gut–brain axis," "diet," "Mediterranean diet," "high-fat diet," "short-chain fatty acids," "probiotics," "prebiotics," and "psychobiotics," combined using AND/OR operators.

Studies were selected based on their scientific relevance, methodological quality, and contribution to understanding the mechanisms linking gut dysbiosis to metabolic and psychiatric disorders. Of the over 100 records initially screened by title and abstract, 68 were assessed in full text. 46 publications were ultimately included, comprising narrative and systematic reviews, meta-analyses, and selected primary studies.

Where sources conflicted, preference was given to more recent publications, systematic reviews, and studies incorporating clinical or functional data. Exclusion criteria included case reports and articles not available in English. In the initial phase, two authors (FW and WW) conducted a screening of titles and abstracts. Subsequently, they assessed full-text articles to confirm their alignment with the specified inclusion criteria. In case of uncertainty, a supervising author, JG, was consulted to reach a consensus.

This review was conducted as a narrative synthesis and does not constitute a fully systematic review of all available literature.

8. Limitations

Despite a growing body of evidence linking gut microbiota to obesity, type 2 diabetes, and depression, several methodological limitations make it difficult to draw firm clinical or causal conclusions (Borrego-Ruiz & Borrego, 2025; Chong et al., 2025).

A major challenge is the lack of methodological consistency across studies. Differences in sample collection and storage, sequencing techniques (16S rRNA vs. shotgun metagenomics), and bioinformatic pipelines limit the comparability of results and make replication difficult (Borrego-Ruiz & Borrego, 2025; Islam et al., 2023). The absence of standardized protocols for patient selection, dietary control before sampling, and reporting of key clinical variables, such as age, BMI, medications, and comorbidities, further complicates interpretation and increases the risk of confounding (Borrego-Ruiz & Borrego, 2025; Chong et al., 2025).

Many studies are also limited by small sample sizes and cross-sectional designs, which reduce statistical power and make it hard to account for confounding variables (Borrego-Ruiz & Borrego, 2025; Chong et al., 2025). Population heterogeneity in diet, genetics, and lifestyle means findings from one cohort may not generalize to others (X. Chen et al., 2026; Islam et al., 2023).

Another limitation is the predominant focus on taxonomic composition rather than microbiota function. Data from metabolomics, metatranscriptomics, and proteomics remain scarce, even though the metabolic activity of the microbiota including SCFA production, tryptophan metabolism, and bile acid modification likely drives most of its clinical relevance (Anachad et al., 2023; Fan & Pedersen, 2021).

Perhaps most importantly, establishing causality remains difficult. Most available data are observational, leaving open the question of whether dysbiosis drives disease or is simply a consequence of it (Borrego-Ruiz & Borrego, 2025; Cao et al., 2026). Interventional studies with probiotics, prebiotics, dietary changes, or FMT show promising but often modest and inconsistent effects (Jiang et al., 2026; Luo et al., 2026). Mendelian randomization analyses provide some causal support for links between specific taxa and type 2 diabetes risk, but require further validation (Jin et al., 2026; Ruan et al., 2025). Animal models offer mechanistic insights, yet their clinical translatability is limited (Beswick et al., 2025; Lei et al., 2026).

Confounding by diet and medication use is also a persistent issue. Many interventions lack adequate dietary control, and drugs such as metformin, antibiotics, proton pump inhibitors, and statins independently affect the microbiota, potentially obscuring true intervention effects (Kumar et al., 2026; Ross et al., 2024).

Finally, high inter-individual variability makes it difficult to identify universal microbiota-based biomarkers, pointing toward the need for personalized diagnostic and therapeutic approaches (Borrego-Ruiz & Borrego, 2025; Luo et al., 2026).

Moving forward, well-designed multicenter cohort studies and adequately powered randomized trials using standardized protocols and integrating both taxonomic and functional data will be essential to translate microbiota research into reliable clinical applications (Borrego-Ruiz & Borrego, 2025; Chong et al., 2025; Jiang et al., 2026).

9. Clinical Implications and Future Research Directions

Growing evidence suggests that the gut microbiota may in the future serve both as a biomarker of metabolic and psychiatric risk and as a therapeutic target in patients with obesity, type 2 diabetes, and depression (Jiang et al., 2026; Luo et al., 2026; Sá Filho et al., 2026). In clinical practice, particular value may lie in identifying microbiota profiles associated with insulin resistance, chronic low-grade inflammation, gut–brain axis dysfunction, and variable responses to dietary and pharmacological treatment (Jiang et al., 2026; Luo et al., 2026). The current evidence does not yet support the routine use of gut microbiota analysis as a standalone diagnostic or therapeutic tool, but does support the development of adjunctive strategies including dietary interventions, prebiotics, probiotics, synbiotics, and more personalized treatment models alongside standard care (Jiang et al., 2026; Luo et al., 2026; Sá Filho et al., 2026).

In the context of depression, psychobiotics have attracted particular interest; however, current reviews note that while some probiotic strains have shown beneficial effects on depressive symptoms, the quality of evidence remains inconsistent, and the efficacy of prebiotics and synbiotics in this setting requires further confirmation (Sá Filho et al., 2026).

Looking ahead, large multicenter prospective studies and adequately powered randomized trials are needed, using standardized protocols for sample collection, bioinformatic analysis, and clinical endpoint assessment (Jiang et al., 2026; Luo et al., 2026). Integration of metagenomic data with metabolomics, metatranscriptomics, and clinical outcomes will be particularly important, as it may enable the identification of functional microbiota signatures with predictive and therapeutic relevance (Jiang et al., 2026). Parallel research is also needed to evaluate the long-term safety of microbiota-targeted therapies, the durability of their effects, and their role within integrated, personalized management of metabolic and depressive disorders (Luo et al., 2026).

10. Discussion

The literature reviewed here suggests that the gut microbiota may represent a shared pathophysiological link between obesity, type 2 diabetes, and depression, though the strength and consistency of evidence varies across these conditions. For obesity and type 2 diabetes, the available data are more coherent, consistently pointing to associations between dysbiosis and chronic low-grade inflammation, impaired intestinal barrier integrity, metabolic endotoxemia, and abnormal bacterial metabolite production particularly SCFAs. In the context of depression, the relationship appears biologically plausible but remains more complex and less firmly established clinically, reflecting greater disease heterogeneity, the influence of psychosocial factors, and a relative scarcity of high-quality interventional data.

Notably, many of the mechanisms discussed are shared across all three conditions. These include dysbiosis characterized by depletion of butyrate-producing bacteria, increased intestinal permeability, immune activation by bacterial molecular patterns, and disrupted metabolic and neuroendocrine signaling. Viewed from this angle, the gut microbiota emerges not as a disease-specific factor, but as part of a broader immunometabolic network in which disrupted intestinal homeostasis may simultaneously affect glucose metabolism, energy balance, and gut–brain axis function.

A key finding of this review is the importance of diet as one of the most significant modifiable determinants of microbiota composition and function. Data from studies on the Mediterranean diet, high fiber intake, and restriction of ultra-processed foods suggest that dietary interventions can favorably influence both microbiota profile and metabolic parameters, and indirectly mental health. Diet therefore appears to be the safest and most clinically well-supported tool for microbiota modulation, particularly compared to more advanced and still experimental strategies such as fecal microbiota transplantation.

At the same time, despite the growing body of evidence linking gut microbiota to metabolic disease and depression, the current state of knowledge does not yet support the routine incorporation of microbiota analysis into clinical practice as a standalone diagnostic or predictive tool. This reflects the considerable heterogeneity across studies, lack of standardization in microbiome analytical methods, limited cross-population comparability, and the difficulty of establishing clear causal relationships. Mendelian randomization analyses and functional studies integrating metagenomic, metabolomic, and clinical data are promising in this regard, but still require validation in larger, well-characterized cohorts.

At this stage, the most reasonable approach is to regard the gut microbiota as an important component of a complex pathophysiological model rather than a single autonomous causal factor. This framing helps explain the frequent co-occurrence of obesity, type 2 diabetes, and depression, and highlights the value of an

interdisciplinary therapeutic approach encompassing dietary modification, physical activity, metabolic treatment, and mental health support. Looking ahead, developing standardized models for microbiota assessment, identifying functional biomarkers, and determining which microbiota-targeted interventions yield durable and clinically meaningful benefits will be among the most important priorities for the field. However, due to the predominance of observational and experimental studies, causality cannot be firmly established for most microbiota–disease associations

11. Conclusions

This literature review indicates that the gut microbiota is increasingly recognized as a potential contributor to the pathophysiology of obesity, type 2 diabetes, and depression, and may represent one of several elements linking metabolic, immunological, and neuroendocrine disturbances. Particular importance is attributed to gut dysbiosis, impaired intestinal barrier integrity, chronic low-grade inflammation, and abnormal production of bacterial metabolites, especially short-chain fatty acids. Available evidence suggests that microbiota disruption may affect both energy and glucose homeostasis and gut–brain axis function, positioning the microbiome as a potential shared pathogenetic link between metabolic diseases and depressive disorders.

At the same time, the current state of knowledge does not yet allow for unequivocal causal conclusions, nor does it support the routine use of microbiota analysis as a standalone diagnostic or therapeutic tool in clinical practice. Among the microbiota-modulating strategies discussed, dietary interventions, particularly diets rich in fiber, plant-based foods, and minimally processed products, have the most well-established practical relevance, as they promote eubiosis and improve metabolic parameters. Probiotics, prebiotics, synbiotics, and other microbiota-targeted interventions remain a promising area of research, but their efficacy and safety require further confirmation in methodologically rigorous studies.

In light of current evidence, the gut microbiota should be regarded as an important component of a complex pathophysiological network rather than an isolated causal factor. Further progress in this field will require standardization of research methods, integration of metagenomic and functional data, and large prospective interventional trials capable of establishing the true clinical value of microbiota-targeted therapies in the prevention and treatment of obesity, type 2 diabetes, and depression.

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