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Gut Microbiota in Obesity: From Dysbiosis and Metabolic Inflammation to Microbiome-Targeted Therapy

Running title: Gut microbiota and obesity

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Abstract

Background: Obesity is a chronic endocrine-metabolic disease characterized by excess adiposity, metabolic inflammation and a high burden of cardiometabolic complications. The gut microbiota has emerged as a biologically plausible determinant of obesity because it regulates energy harvest, gut barrier integrity, immune signaling, bile acid metabolism and appetite-related neuroendocrine pathways.

Methods: A structured literature search was conducted in PubMed/MEDLINE, ScienceDirect and Google Scholar for publications from 2000 to 2024 using English and French terms related to obesity, gut microbiota, dysbiosis, inflammation, probiotics, prebiotics, fecal microbiota transplantation, microbiota-targeted therapy and energy metabolism. Systematic reviews, meta-analyses, randomized trials, observational studies and mechanistic investigations were eligible when they addressed microbiota composition, obesity-related mechanisms or microbiome-based therapeutic strategies.

Results: Seventy-two records were initially identified. After duplicate removal, 40 records were screened and 26 full-text publications were retained for qualitative synthesis. Obesity was frequently associated with reduced microbial richness, altered Firmicutes and Bacteroidetes profiles, enrichment of inflammatory taxa and depletion of potentially beneficial organisms such as Akkermansia muciniphila, Bifidobacterium and Faecalibacterium prausnitzii. The principal mechanisms involve short-chain fatty acid signaling, bile acid transformation, metabolic

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endotoxemia, low-grade inflammation, altered intestinal permeability, adipose-tissue dysfunction and gut-brain axis dysregulation. Dietary strategies, probiotics, prebiotics, next-generation probiotics and fecal microbiota transplantation show therapeutic potential, although clinical efficacy remains heterogeneous.

Conclusion: The gut microbiota is not merely an associated biomarker of obesity but a dynamic metabolic interface that may influence disease expression and therapeutic response. Microbiome-targeted approaches are promising for future precision obesity care, but routine clinical implementation requires standardized, adequately powered and mechanistically informed human trials.

Keywords

gut microbiota; obesity; dysbiosis; short-chain fatty acids; bile acids; probiotics; prebiotics; fecal microbiota transplantation

Abbreviations

BMI, body mass index; FMT, fecal microbiota transplantation; FXR, farnesoid X receptor; GLP-1, glucagon-like peptide-1; GPCR, G-protein-coupled receptor; HDAC, histone deacetylase; LPS, lipopolysaccharide; SCFA, short-chain fatty acid; TGR5, Takeda G-protein-coupled receptor 5; TLR4, Toll-like receptor 4.

Introduction

Obesity is characterized by excessive adipose-tissue accumulation and is commonly defined by a body mass index (BMI) of 30 kg/m2 or higher. It is a major contributor to cardiometabolic morbidity, including type 2 diabetes, hypertension, dyslipidemia, cardiovascular disease, nonalcoholic fatty liver disease and several obesity-associated inflammatory disorders. Although excess energy intake and reduced energy expenditure remain central to obesity pathogenesis, the clinical phenotype of obesity cannot be fully explained by caloric balance alone. Individuals exposed to similar dietary environments may experience markedly different changes in weight, adiposity, insulin sensitivity and inflammatory status, suggesting that additional biological mediators shape the metabolic response to diet and lifestyle interventions.

The gut microbiota, a dense and functionally diverse ecosystem of bacteria, archaea, viruses and fungi inhabiting the gastrointestinal tract, has become a key candidate mediator. The intestinal microbial community contributes to fermentation of otherwise indigestible substrates, short-chain fatty acid production, bile acid transformation, gut-barrier maintenance, immune maturation and neuroendocrine signaling. Its structure is shaped by birth mode, breastfeeding,

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genetics, age, geography, diet, medication exposure, physical activity and metabolic status. When microbial ecology is disturbed, a state of dysbiosis may occur, with potential consequences for energy harvest, adipose-tissue biology, low-grade inflammation and gut-brain signaling [1,2].

Experimental and clinical studies have reported differences between obese and non-obese individuals in microbial richness, diversity and specific taxa. However, the direction and magnitude of these associations vary across studies. The Firmicutes/Bacteroidetes ratio has been frequently discussed but is not sufficiently consistent to function as an isolated diagnostic marker. A more clinically useful approach is to consider microbial functional capacity, metabolite production, barrier function and host context. This review was prepared to synthesize the evidence linking gut microbiota to obesity, to clarify the principal mechanistic pathways, and to summarize therapeutic strategies targeting microbiota modulation.

Methods

This work was designed as a structured narrative review informed by systematic search procedures. The literature search covered PubMed/MEDLINE, ScienceDirect and Google Scholar and targeted publications from 2000 to 2024. Search terms were used in French and English and included obesity, gut microbiota, intestinal microbiome, dysbiosis, inflammation, probiotics, prebiotics, fecal microbiota transplantation, microbiota-targeted therapies, energy metabolism, bile acids and short-chain fatty acids. Boolean operators were used to combine obesity-related terms with microbiota-related and intervention-related terms.

The inclusion criteria were systematic reviews, meta-analyses, randomized controlled trials, observational studies and relevant mechanistic experimental studies that addressed the relationship between gut microbiota and obesity, mechanisms linking microbial ecology to obesity, or therapeutic modulation of the microbiota. Publications in English or French were eligible. Studies involving adults, children, adolescents or animal/mechanistic models were considered when they contributed directly to the biological or therapeutic understanding of obesity. Articles with insufficient methodological description, limited relevance to obesity, duplicate records or unavailable full text were excluded.

The search identified 72 records: 38 from ScienceDirect, 30 from PubMed/MEDLINE and 4 from Google Scholar. After duplicate removal, 40 records were screened; 14 records were excluded at screening and 26 full-text publications were assessed for eligibility. No full-text

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publication was excluded after eligibility assessment, resulting in 26 publications retained for qualitative synthesis. The selection process is summarized in Figure 1. Methodological appraisal was adapted to study design: observational studies were interpreted using domains derived from the Newcastle-Ottawa Scale, randomized trials in relation to the Cochrane risk-of-bias framework, and systematic reviews/meta-analyses using reporting and methodological domains derived from PRISMA and AMSTAR 2. Because the evidence base included heterogeneous designs, the appraisal was presented descriptively rather than as a single pooled quality score. Data were extracted on study design, population when available, principal microbial findings, mechanistic or clinical outcomes and relevance to obesity pathophysiology.

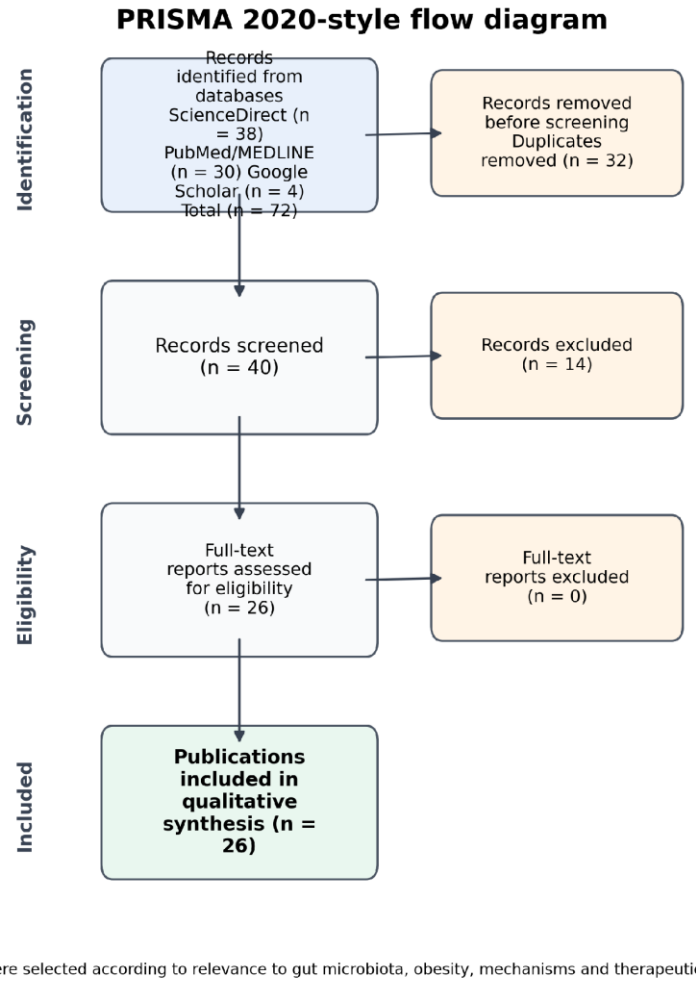

Figure 1. PRISMA 2020-style flow diagram summarizing record identification, duplicate removal, screening, full-text assessment and inclusion in the qualitative synthesis.

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Results

The retained literature included systematic reviews, meta-analyses, clinical trials, observational studies, mechanistic animal studies and translational reviews. The main themes were differences in microbiota composition between obese and non-obese subjects; microbial mechanisms influencing host energy homeostasis, inflammation and appetite regulation; and interventions designed to modify microbial ecology. Adult data were more abundant than pediatric data, but pediatric evidence suggests that obesity-related dysbiosis begins early and may be influenced by lifestyle and physical activity [3]. The methodological profile and qualitative contribution of the retained publications are summarized in Table 1.

Table 1. Methodological appraisal and qualitative contribution of the retained publications.

Ref.	Publication	Evidence type / focus	Main contribution	Interpretability considerations
[1]	Zhang et al., 2024	Translational review	Microbiota composition, obesity and type 2 diabetes; overview of microbiota-targeted therapeutic strategies.	High clinical relevance; broad review with heterogeneous source evidence.
[2]	Pinart et al., 2021	Systematic review and meta-analysis	Gut microbiome composition in obese and non-obese persons.	Appropriate for pooled taxonomic trends; heterogeneity limits biomarker conclusions.
[3]	Morgado et al., 2023	Systematic review	Children/adolescents with overweight or obesity and physical activity interventions.	Relevant pediatric synthesis; intervention studies remain heterogeneous.
[4]	Gong et al., 2022	Meta-analysis of existing datasets	Pooled microbiota datasets in obesity.	Useful for recurring taxa; limited by differences in datasets and pipelines.
[5]	Pinto et al., 2021	Narrative review	Dysbiosis and obesity.	Useful background; not designed for quantitative inference.

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Ref.	Publication	Evidence type / focus	Main contribution	Interpretability considerations
[6]	Crovesy et al., 2020	Systematic review	Adult gut microbiota profile in obesity.	Good synthesis of adult taxonomic findings; phylum-level conclusions inconsistent.
[7]	Vallianou et al., 2019	Narrative review	Microbial metabolites and obesity-associated metabolic disorders.	Mechanistically informative; narrative design limits grading of effect size.
[8]	Leonario-Rodriguez and Saavedra, 2022	Narrative review	Microbiota and adipose-tissue modulation.	Relevant for adipose-tissue mechanisms; indirect clinical evidence.
[9]	Joyce and Gahan, 2014	Narrative review	Microbiota and host metabolic health.	Foundational mechanistic review; older but conceptually important.
[10]	Saad et al., 2016	Narrative review	Microbiota, inflammation, obesity and insulin resistance.	Strong mechanistic relevance for endotoxemia and insulin resistance.
[11]	Galmiche and Dechelotte, 2023	Narrative review	Microbiota-gut-brain axis and eating behavior.	Recent mechanistic synthesis; clinical translation remains emerging.
[12]	Breton et al., 2022	Overview review	Dysbiotic bacteria, metabolic mechanisms and next-generation probiotics.	Relevant to therapeutic perspectives; early-stage clinical applicability.
[13]	Schele et al., 2013	Experimental mechanistic study	Leptin sensitivity and obesity-suppressing neuropeptides.	Provides mechanistic evidence; animal model limits direct clinical extrapolation.

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Ref.	Publication	Evidence type / focus	Main contribution	Interpretability considerations
[14]	Lecerf, 2011	Narrative review	Prebiotics, intestinal flora, inflammation and obesity.	Useful background; older evidence base.
[15]	Kasubuchi et al., 2015	Narrative review	SCFAs and host metabolic regulation.	Mechanistically central; not obesity-specific clinical evidence.
[16]	Wei et al., 2020	Mechanistic/translational study	Bile acid-gut microbiota axis in obesity susceptibility.	Strong mechanistic value; requires human validation.
[17]	Seganfredo et al., 2017	Systematic review	Weight-loss interventions and gut microbiota changes.	Useful intervention synthesis; heterogeneity in diets and bariatric procedures.
[18]	Caputo et al., 2023	Systematic review of randomized trials	Dietary obesity management targeting the microbiota.	Clinically relevant but heterogeneous intervention designs.
[19]	Ejtahed et al., 2019	Systematic review	Herbal products and microbiota modulation in obesity.	Promising but variable products and endpoints.
[20]	Tome-Castro et al., 2021	Systematic review	Probiotics in overweight and obesity.	Useful clinical synthesis; strain-, dose- and duration-specific effects.
[21]	Mazloom et al., 2019	Narrative review	Probiotic anti-obesity mechanisms.	Mechanistic summary; clinical efficacy remains uncertain.
[22]	Mazier et al., 2021	Preclinical biotherapy study	Christensenella minuta as a potential biotherapy.	Promising next-generation probiotic candidate; preclinical stage.
[23]	Zhang et al., 2019	Systematic review	FMT in obesity and metabolic syndrome.	Proof-of-concept; short-term and inconsistent

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Ref.	Publication	Evidence type / focus	Main contribution	Interpretability considerations
				metabolic outcomes.
[24]	Vazquez-Marroquin et al., 2023	Systematic review/meta-analysis of RCTs	Microbiome therapies and waist circumference in type 2 diabetes.	Higher clinical relevance; population primarily type 2 diabetes.
[25]	Kootte et al., 2012	Narrative review	Manipulating gut microbiota in obesity and type 2 diabetes.	Foundational therapeutic perspective; older evidence base.
[26]	Lee et al., 2019	Narrative review	FMT as a potential approach to alter obesity.	Conceptual therapeutic perspective; investigational outside standard indications.

This table translates and standardizes the original quality-assessment table. A single numerical score was avoided because the retained evidence includes systematic reviews, meta-analyses, narrative reviews, experimental studies and translational investigations. FMT, fecal microbiota transplantation; SCFA, short-chain fatty acid.

Microbiota composition in obesity

Across reviews and meta-analyses, obesity was commonly associated with reduced microbial diversity and richness, although the exact taxonomic signature differed among studies [2,4]. Several reports described increased Firmicutes and reduced Bacteroidetes in obese individuals, while others found inconsistent or even opposite patterns. This confirms that broad phylum-level ratios should be interpreted cautiously [5,6]. More informative signals may include depletion of butyrate-producing bacteria, lower abundance of Akkermansia muciniphila or Faecalibacterium prausnitzii, and enrichment of Proteobacteria or other taxa associated with inflammatory tone [6,7].

Pediatric and adolescent studies add important nuance. A systematic review of children and adolescents reported reduced Bacteroidetes, Bifidobacterium and alpha diversity among obese subjects, with increased Proteobacteria and Lactobacillus. Physical activity interventions appeared to improve microbial diversity and beneficial bacterial abundance in some groups [3]. These findings suggest that microbiota-related obesity risk may be shaped by early-life and lifestyle factors, but substantial interindividual variation limits simple generalization.

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The main findings supporting an association between gut microbiota and obesity are summarized in Table 2.

Table 2. Main findings supporting an association between gut microbiota and obesity.

Study	Year	Design / population	Main findings
Zhang et al. [1]	2024	Translational review	Alterations in gut microbiota composition and diversity are linked to obesity. Dominant phyla include Firmicutes and Bacteroidetes, whereas Proteobacteria, Actinobacteria, Fusobacteria and Verrucomicrobia are generally less abundant. Bariatric surgery can remodel the microbiota and is associated with durable weight loss and metabolic improvement.
Pinart et al. [2]	2021	Systematic review and meta-analysis; adults with obesity	Obesity was associated with lower gut microbial diversity. Firmicutes were reported as more abundant, while Bacteroidetes were slightly lower, although not consistently significant.
Morgado et al. [3]	2023	Systematic review; children and adolescents with overweight/obesity	Obesity was associated with lower overall diversity, reduced Bacteroidetes and Bifidobacterium, and higher Proteobacteria and Lactobacillus. Physical activity interventions may improve diversity and beneficial bacteria in some pediatric groups.
Gong et al. [4]	2022	Meta-analysis of adult obesity datasets	Lower Chao1 richness and evenness indices were reported in obesity, with a higher Bacteroidetes/Firmicutes ratio in some datasets and reductions in Lachnoclostridium, Faecalitalea, Christensenellaceae_R-7_group, Akkermansia, Alistipes and Butyricimonas.
Pinto et al. [5]	2021	Narrative review	A recurrent pattern of increased Firmicutes and decreased Bacteroidetes was described, although this phylum-level ratio is not sufficiently consistent to serve as a diagnostic marker.
Crovesy et al. [6]	2020	Systematic review; adults with obesity	Many studies reported a higher Firmicutes/Bacteroidetes ratio, increased Firmicutes, Fusobacteria, Proteobacteria, Mollicutes and Lactobacillus reuteri, and lower Verrucomicrobia, Akkermansia muciniphila, Faecalibacterium prausnitzii,

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Study	Year	Design / population	Main findings
			Bacteroidetes, Methanobrevibacter smithii, Lactobacillus plantarum and L. paracasei.
Vallianou et al. [7]	2019	Narrative review	Reduced richness and diversity are frequently reported in obesity, but the exact microbial signature remains debated.
Leonario-Rodriguez and Saavedra [8]	2022	Narrative review	The gut microbiome may influence adipose-tissue dysfunction, a key component in obesity pathogenesis.
Joyce and Gahan [9]	2014	Narrative review	Microbial taxa and metabolites may contribute to host metabolic health. Species-level signals such as Akkermansia muciniphila and bile-tolerant taxa should be interpreted as context-dependent markers or modulators rather than isolated causes.
Saad et al. [10]	2016	Narrative review	Dysbiosis, increased intestinal permeability and endotoxin exposure provide a mechanistic bridge between gut microbiota, inflammation, obesity and insulin resistance.

The table was translated from the original manuscript and harmonized with the corrected reference numbering. The Firmicutes/Bacteroidetes ratio is presented as a historical and hypothesis-generating marker rather than a validated diagnostic biomarker.

Mechanistic pathways

Microbiota and adipose-tissue dysfunction. The gut microbiota may influence obesity not only by modifying intestinal nutrient extraction but also by regulating adipose-tissue inflammation, macrophage activation and metabolic signaling [8]. Dysbiosis can promote barrier dysfunction and translocation of microbial products, thereby activating innate immune pathways and favoring insulin resistance [9,10]. In parallel, the gut-brain axis may influence appetite, hedonic eating and satiety signaling, particularly through interactions between microbial metabolites, enteroendocrine cells and neural pathways [11-13].

The principal mechanisms identified in the literature are summarized in Figure 2 and Table 3. Short-chain fatty acids, generated through fermentation of nondigestible carbohydrates, interact with G-protein-coupled receptors and histone deacetylase pathways, thereby influencing glucose metabolism, insulin sensitivity, appetite-related hormones, intestinal barrier function and immune regulation [14,15]. Their role is complex: they can provide additional energy to the host, but they also support epithelial integrity and anti-inflammatory signaling. Bile acid metabolism

is another important pathway. Gut bacteria transform primary bile acids into secondary bile acids that regulate farnesoid X receptor and TGR5 signaling, influencing glucose homeostasis, lipid metabolism, thermogenesis and enteroendocrine secretion [16].

Low-grade inflammation is a central link between dysbiosis and obesity. Lipopolysaccharide from Gram-negative bacteria can cross a compromised intestinal barrier, particularly in the context of high-fat diets, and activate Toll-like receptor 4/CD14 signaling, nuclear factor-kappa B pathways and pro-inflammatory cytokine production. This metabolic endotoxemia contributes to insulin resistance and adipose-tissue dysfunction [10]. Conversely, strategies that increase microbial diversity, strengthen tight junctions or promote beneficial metabolite production may reduce inflammatory tone.

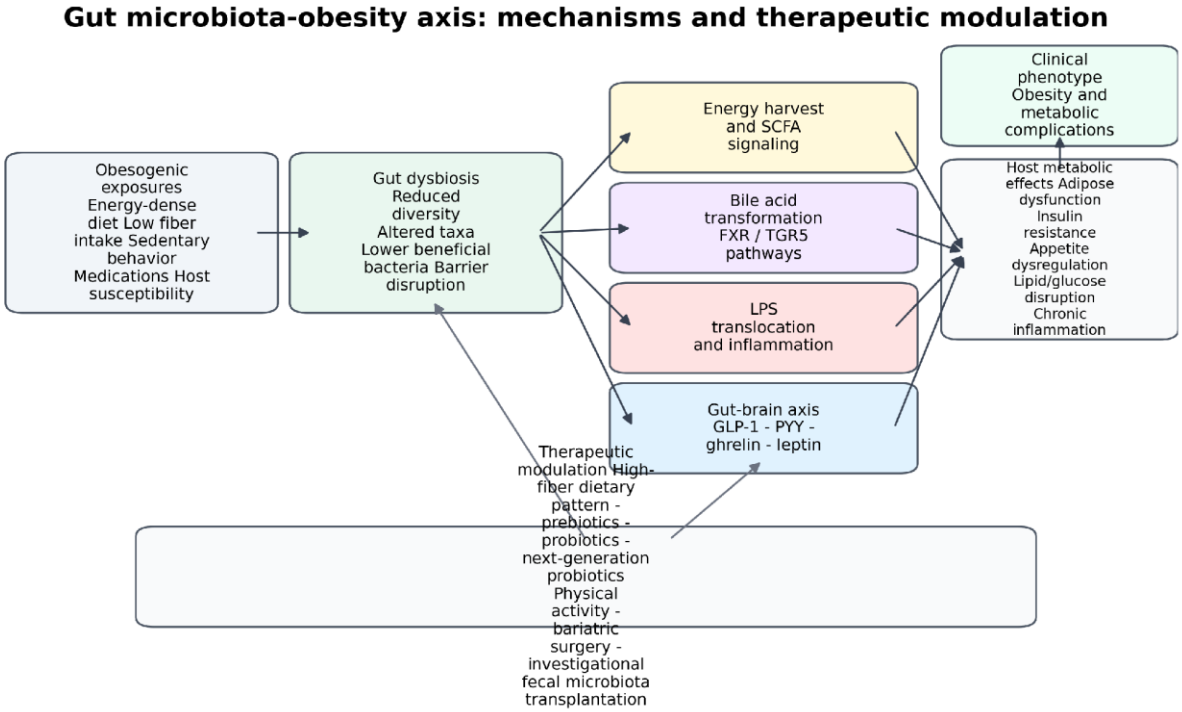

Figure 2. Conceptual framework of microbiota-mediated pathways linking obesogenic exposures, gut dysbiosis, microbial metabolites and host metabolic effects, with potential therapeutic modulation.

Table 3. Main microbiota-related pathophysiological mechanisms involved in obesity.

Study	Year	Mechanistic domain	Main findings
Galmiche and Dechelotte [11]	2023	Microbiota-gut-brain axis	Peripheral signals include appetite-regulating peptides such as ghrelin and GLP-1, SCFAs and bacterial components, supporting a role for microbial signaling in eating behavior and satiety.

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Study	Year	Mechanistic domain	Main findings
Breton et al. [12]	2022	Energy homeostasis, inflammation and fat deposition	Dysbiotic gut bacteria may influence host energy homeostasis, inflammation and fat deposition through bacterial metabolites such as SCFAs and bacterial components such as LPS.
Leonario-Rodriguez and Saavedra [8]	2022	Adipose-tissue dysfunction and barrier integrity	Relevant pathways include dysbiosis-related effects on SCFAs, claudins, macrophage activation and oligosaccharide-mediated signaling.
Lecerf [14]	2011	Fermentation, GLP-1 and endotoxemia	Colonic fermentation of indigestible fibers contributes to intestinal energy retention and modulates GLP-1 production. LPS may increase endocannabinoid tone, lipogenesis and inflammatory cytokine production through TLR4/CD14 signaling.
Schele et al. [13]	2013	Leptin sensitivity and neuropeptides	Gut microbiota reduced expression of anti-obesity neuropeptides such as proglucagon and brain-derived neurotrophic factor and was associated with increased Socs-3 expression, supporting microbiota-related modulation of leptin sensitivity in experimental models.
Wei et al. [16]	2020	Bile acid-gut microbiota axis	In diet-induced obese mice, non-12-OH bile acids such as UDCA, CDCA and LCA were reduced and linked to altered microbiota and lower Clostridium scindens. UDCA supplementation attenuated diet-induced obesity in the experimental model.
Joyce and Gahan [9]	2014	Microbial metabolites and immune function	Microbial metabolites, including SCFAs and other microbial-derived mediators, may affect satiety, intestinal permeability and immune function.
Kasubuchi et al. [15]	2015	SCFA signaling	SCFAs act as signaling molecules through G-protein-coupled receptors and as epigenetic regulators through HDAC inhibition, influencing insulin sensitivity, energy expenditure and inflammatory responses.
Saad et al. [10]	2016	Metabolic endotoxemia and insulin resistance	LPS can induce chronic low-grade inflammation. TLR4 activation contributes to insulin resistance, and altered circulating SCFA levels may participate in reduced

Study	Year	Mechanistic domain	Main findings
			insulin sensitivity and obesity-related metabolic impairment.

Abbreviations: CDCA, chenodeoxycholic acid; GLP-1, glucagon-like peptide-1; GPCR, G-protein-coupled receptor; HDAC, histone deacetylase; LCA, lithocholic acid; LPS, lipopolysaccharide; SCFA, short-chain fatty acid; TLR4, Toll-like receptor 4; UDCA, ursodeoxycholic acid.

Therapeutic modulation of microbiota

Several approaches have been evaluated, including dietary change, prebiotics, probiotics, next-generation probiotics and fecal microbiota transplantation. Weight-loss interventions, exercise and bariatric surgery can remodel the microbiota, but effects may differ according to baseline microbial ecology, degree of caloric restriction and host metabolic state [17]. Diet-based microbiota interventions and herbal-product strategies are promising but remain heterogeneous in design, outcomes and durability [18,19]. The main therapeutic findings are summarized in Table 4.

Probiotic trials show heterogeneous outcomes. Some systematic reviews report reductions in BMI, body weight, visceral adiposity, waist circumference or waist-to-hip ratio, but effects depend on strain, dose, duration, background diet and host phenotype [20,21,24]. Candidate next-generation probiotics, including Christensenella minuta and Akkermansia muciniphila-related strategies, are mechanistically promising because they may influence weight gain, microbial diversity, metabolic markers and gut-barrier function [12,22]. However, these approaches remain insufficiently standardized for routine obesity treatment.

Fecal microbiota transplantation provides proof-of-concept that microbial transfer can influence metabolic phenotype. Evidence suggests short-term improvement in insulin sensitivity or glycemic parameters in some patients with obesity or metabolic syndrome, whereas effects on BMI, lipids and long-term outcomes are inconsistent [23,25,26]. Donor selection, route of administration, baseline recipient microbiota, diet after transplantation and durability of engraftment are major determinants that require further study.

Table 4. Potential microbiota-targeted therapies in obesity and metabolic disease.

Study	Year	Methodology / intervention	Main findings
Mazier et al. [22]	2021	Preclinical diet-induced obesity model; SHIME	Christensenella minuta DSM33407 showed anti-obesity effects in experimental models, limiting weight

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Study	Year	Methodology / intervention	Main findings
		human gut simulator; metagenomic sequencing	gain, improving metabolic markers, increasing microbial diversity, restoring the Firmicutes/Bacteroidetes balance and strengthening intestinal barrier markers.
Seganfredo et al. [17]	2017	Systematic review of weight-loss interventions	Restrictive diets and bariatric surgery can modify microbiota diversity and composition. Prebiotics may help restore a healthier gut microbiome and may reduce body fat in some settings.
Zhang et al. [23]	2019	Systematic review of FMT in obesity and metabolic syndrome	FMT showed short-term, non-durable improvements in insulin sensitivity and HbA1c in some patients, with no consistent improvement in BMI, lipids or long-term metabolic outcomes.
Vazquez-Marroquin et al. [24]	2023	Systematic review and meta-analysis of randomized trials in type 2 diabetes	Microbiome therapies, particularly probiotics, significantly reduced waist circumference, HbA1c, fasting glucose and insulin resistance. Prebiotics and synbiotics showed more variable effects.
Tome-Castro et al. [20]	2021	Systematic review of probiotics in overweight/obesity	Probiotics were associated with reductions in BMI, weight, visceral fat and waist-to-hip ratio in a subset of trials. Only a minority of trials directly assessed microbiota changes.
Vallianou et al. [7]	2019	Narrative review	Microbial metabolites such as butyrate may have favorable metabolic effects and could support prevention or treatment strategies for obesity-related metabolic disorders.
Caputo et al. [18]	2023	Systematic review of randomized dietary trials in adults with obesity	Dietary interventions improved weight, metabolic and inflammatory outcomes in some trials. The Prevotella/Bacteroides ratio emerged as a potential indicator of diet-response heterogeneity.
Ejtahed et al. [19]	2019	Systematic review of herbal and dietary products	Non-digestible carbohydrates promoted beneficial bacteria such as Bifidobacterium and Faecalibacterium prausnitzii, but weight loss was not systematic. Polyphenol-rich products

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Study	Year	Methodology / intervention	Main findings
			may increase Akkermansia muciniphila and support weight modulation.
Mazloom et al. [21]	2019	Narrative review of probiotic mechanisms	Combined probiotic strains may influence fat absorption and excretion, gut hormone signaling, barrier restoration and SCFA production, but clinical efficacy remains strain-specific and heterogeneous.

Abbreviations: BMI, body mass index; FMT, fecal microbiota transplantation; HbA1c, glycated hemoglobin; HOMA-IR, homeostatic model assessment of insulin resistance; SHIME, simulator of the human intestinal microbial ecosystem.

Discussion

This review supports the concept that obesity is associated with a dysbiotic microbial phenotype, but it also emphasizes that no single microbial signature consistently defines obesity across all populations. Broad taxonomic patterns, such as Firmicutes and Bacteroidetes shifts, are useful for hypothesis generation but are insufficient for clinical decision-making. The clinically relevant question is not only which organisms are present, but what metabolic functions they perform, how they interact with the host, and whether they can be modified to improve outcomes.

The strongest mechanistic evidence converges on four interrelated domains: microbial energy harvest and short-chain fatty acid signaling; bile acid transformation; gut barrier integrity and endotoxemia; and neuroendocrine regulation of appetite and satiety. These pathways provide a plausible explanation for interindividual variability in response to dietary interventions. Two individuals consuming similar diets may differ in fermentative capacity, bile acid pool composition, mucosal permeability, inflammatory tone and incretin secretion. Such differences may influence weight loss, glycemic control, lipid metabolism and appetite regulation.

From a clinical standpoint, microbiota modulation should currently be viewed as an adjunctive rather than a stand-alone obesity treatment. Dietary patterns rich in fiber, plant-derived bioactive compounds and minimally processed foods remain the safest and most physiologically grounded way to support a diverse microbial ecosystem. Probiotics, prebiotics and synbiotics may provide additional benefit in selected patients, but standardized strain-specific recommendations cannot yet be made for obesity management. Fecal microbiota transplantation should remain investigational for obesity and metabolic syndrome outside approved indications and controlled research settings.

Several limitations of the evidence should be acknowledged. First, sequencing methods, sample-processing protocols and bioinformatic pipelines differ widely, reducing comparability among studies. Second, obesity is heterogeneous and influenced by diet, medications, geography, ethnicity, age, sex, endocrine status and comorbidities. Third, many human trials are small and short-term, and few simultaneously measure microbial function, metabolomics and clinically meaningful endpoints. Fourth, fecal microbiota may not fully represent mucosal microbial communities. Finally, causality remains difficult to establish in observational studies because diet, adiposity and microbiota influence each other bidirectionally.

Future studies should prioritize standardized prospective designs, deep phenotyping, repeated microbiome sampling and multi-omics integration. Clinically useful biomarkers will probably combine microbial taxa, gene content, metabolite profiles and host variables rather than rely on a single ratio or organism. In endocrinology and nutritional practice, microbiota-informed obesity care may eventually support personalized diet selection, prediction of response to lifestyle interventions and rational use of prebiotics or probiotics, but this requires validation in large, diverse and clinically representative cohorts.

Conclusion

Gut microbiota is a biologically plausible and clinically relevant contributor to obesity pathophysiology. It affects energy harvest, short-chain fatty acid production, bile acid signaling, barrier function, low-grade inflammation, appetite regulation and metabolic homeostasis. Current evidence supports microbiota modulation as a promising therapeutic axis, particularly through dietary strategies, prebiotics, probiotics and selected investigational microbial therapies. Nevertheless, substantial heterogeneity prevents routine microbiota-guided obesity treatment at present. Robust clinical trials with standardized methodology and mechanistic endpoints are required to translate microbiome science into personalized obesity management.

Statements

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Data Availability Statement: All data supporting this review are derived from published articles cited in the reference list.

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