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REVIEW ARTICLE

The role of *Lactobacillus* in combination with *Bifidobacterium* strains in mitigating obesity-related effects: A systematic review of studies in mice and humans

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Abstract

Body mass index (BMI) and waist circumference are regarded as early risk assessment factors for cardiometabolic comorbidities such as obesity, cardiovascular disease, and weight-related cancer. Specifically, obesity is a result of an imbalance of energy intake and expenditure and is usually determined by BMI. According to the Obesity Medicine Association Clinical Practice Statement, the adolescent obesity rate in the United States has drastically increased in the last 30 years affecting more than 20% adolescents. Addressing the rising rate of obesity has provided extensive research that suggests a strong link between gut microbiota phyla and the alleviation of obesity-related challenges. While a balanced lifestyle is the main recommendation to prevent and treat obesity, curative therapy is the goal. Research suggests that the human gut microbiota can help protect from pathogens, enhance the immune system, support digestion and metabolism, control epithelial cell proliferation and differentiation, modify insulin resistance and its secretion, and positively influence brain-gut communication This complex relationship suggests a strong link between gut microbiota and obesity-related effects. Microbiota imbalance is highly recognized as an indicator of a given disease or a poor health status. There are several probiotics that directly support the gut microbiota imbalance on obesity, including *Lactobacillus* (*e.g.*, *Lactobacillus casei, Lactobacillus gasseri, Lactobacillus rhamnosus*, and *Lactobacillus plantarum*) and *Bifidobacterium* (*e.g.*, *Bifidobacterium infantis*, *Bifidobacterium longum*, and *Bifidobacterium breve B3*). In this systematic review, we aim to consolidate existing evidence on the role of gut microbiota in managing obesity-related comorbidities, with a particular focus on the impact of specific probiotics on weight management and metabolic health. The review also provides an overview of the interplay between gut microbiota and obesity-related factors, including energy homeostasis, inflammation, and metabolic regulation.

Keywords: *Lactobacillus*; *Bifidobacterium*; Obesity; Systematic review

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1. Introduction

Obesity is the excessive accumulation of adipose tissue in the body, which can lead to health hazards. It is diagnosed when a person's body mass index (BMI) reaches or exceeds 30. Obesity is one of the most pressing and prevalent issues worldwide, affecting both healthcare systems and the general public. The Fogarty International Center conference on obesity, held at the National Institutes of Health in October 1977, responded to the growing concern over this condition and called for official action.[1] Despite early recognition, obesity remains a chronic disease and a significant health challenge. Over the past 30 years, adolescent obesity rates in the U.S. have tripled, with over 20% of adolescents now classified as obese. Early prevention is crucial, particularly for adolescents with a BMI above the 95th percentile, as they face a higher risk of continuing obesity into adulthood compared to younger children.[2] In addition, overweight adolescents are at an increased risk of long-term morbidity and mortality. Addressing obesity during childhood is the most effective strategy to reduce adult obesity and its associated comorbidities.[3]

To address obesity, treatment strategies should include a balanced diet that maintains gut microbiota stability, as well as a diet enriched with prebiotics and probiotics to prevent or manage the onset of obesity. The use of prebiotics and probiotics is particularly beneficial in cases of sarcopenic obesity or obesity associated with glycemic disorders.[4,5] Shiu *et al.*[5] reported that an improved diet alone enhanced insulin sensitivity in mice. However, no significant additional benefit was observed with probiotic administration. This finding underscores the importance of lifestyle changes, such as reduced calorie intake and increased anaerobic exercise, as foundational steps in treating obesity.

According to the International Scientific Association of Probiotics and Prebiotics (ISAPP), probiotics are live microorganisms that, when consumed in adequate amounts, confer health benefits to the host.[5] Combining probiotics with prebiotics and postbiotics has been shown to enhance sleep quality, alleviate anxiety and stress, and, most notably, mitigate obesity-related effects.[4-6] A growing area of interest in probiotic research focuses on Lactobacillus due to its high efficiency in regulating gut microbiota health. *Lactobacillus* supplementation has demonstrated improvements in gastrointestinal symptoms, inflammatory profiles, and vitamin levels.[7] Notably, the *Lactobacillus plantarum* strain has exhibited anti-obesity effects by modulating gut microbiota, increasing short-chain fatty acid (SCFA) production, and regulating metabolic pathways.[8] Similarly, *Bifidobacterium* has been shown to produce SCFAs, including acetate, propionate, butyrate, and lactate, which modulate gene expression related to adiposity and inflammation.[9] Building on these findings, we conducted a comprehensive analysis of combined probiotic strains to explore their potential as a strategy for mitigating obesity-related effects, including those on metabolic health, gut microbiota composition, and associated comorbidities. This investigation aims to provide a deeper understanding of how specific probiotic combinations may offer therapeutic benefits in managing obesity and its long-term health impacts.

2. Methods

This study was conducted in accordance with PRISMA recommendations.[10] We systematically reviewed the available literature using PubMed, Google Scholar, ClinicalTrials, and EMBASE databases. A comprehensive search was conducted for clinical trials, meta-analyses, and randomized controlled trials evaluating the impact of probiotics on obesity-related effects, covering the period from January 2020 to December 2024. The search was completed in December 2024. Articles from PubMed were screened using EndNote software, while others were identified through database search tools and filters. The search terms used included "obesity," "*Lactobacillus*," "*Bifidobacterium*," "probiotics," and "probiotics and human obesity." All articles were reviewed, and duplicates were manually removed by two researchers. The population of interest included individuals with a BMI over 25, classified as overweight or clinically obese. Limitations of this study included the restriction to English-language articles and limited access to certain publications. Despite these constraints, the study identified a potential solution for obesity management using probiotics through a selection process based on effective treatment outcomes.

3. Results

A total of 130 records were initially identified, and 123 were screened after duplicate removal. Of these, 74 articles were selected for full-text review and data extraction. The flow of information through the stages of the scoping review is illustrated in the accompanying flowchart (Figure 1).

3.1. Lactobacillus

The growing interest in *L. plantarum* as a probiotic intervention underscores its multifaceted benefits for metabolic and gastrointestinal health. Studies have consistently demonstrated its ability to modulate gut microbiota, enhance SCFA production, and regulate blood glucose levels through mechanisms such as increased insulin sensitivity and improved glucose uptake. Notably, *L. plantarum* NCHBL-004 shows significant alteration in gut microbial diversity at the phylum, family, and genus

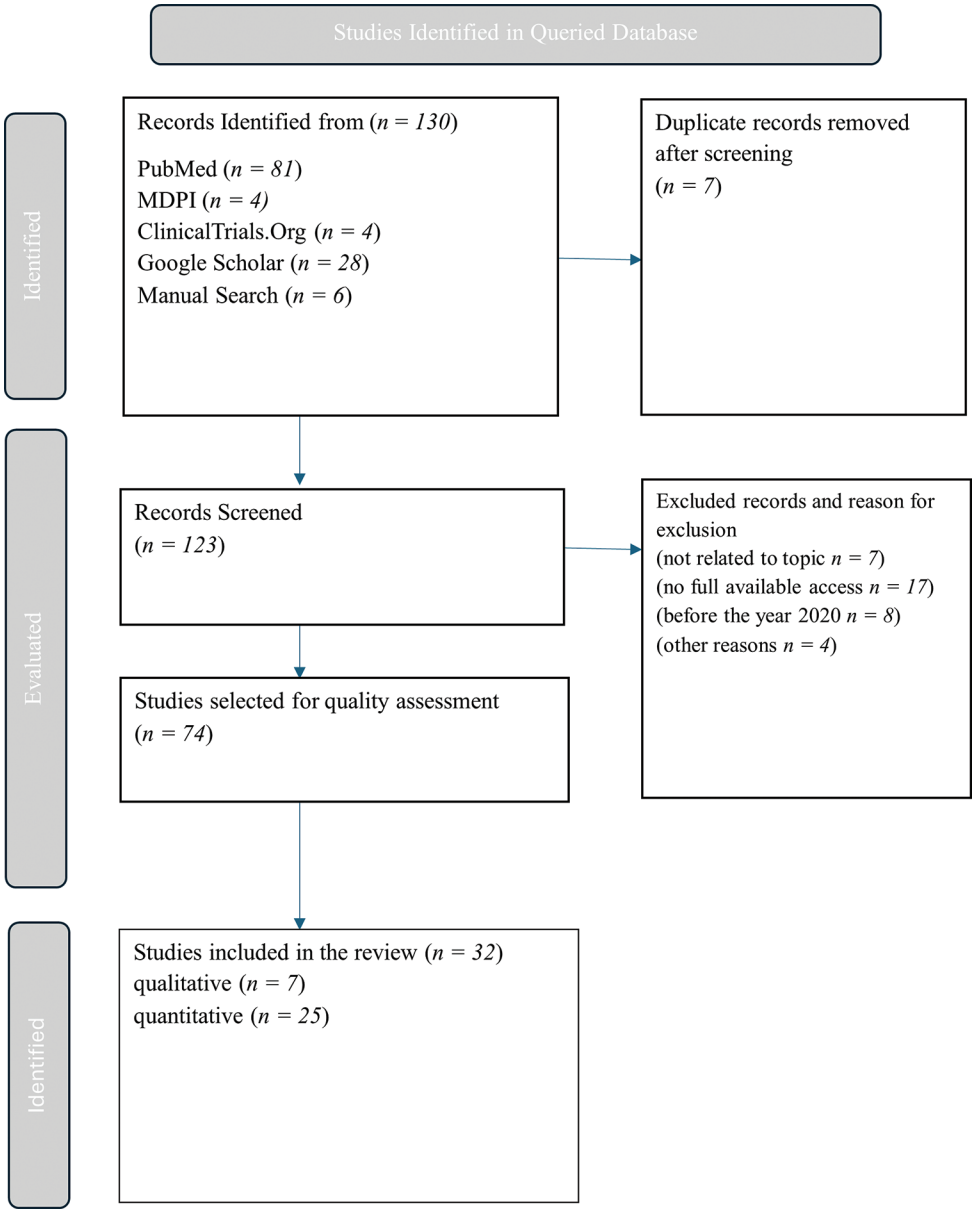

Figure 1. Workflow of the scoping review

levels, with prominent increases in SCFA-producing bacteria.[11] Differences in experimental design, such as strain concentration (*e.g.*, 10^9 CFU/mouse) and diet-induced obesity models, complicate direct comparison.[12] Furthermore, a critical evaluation of methodologies reveals significant variability in gut microbiome analysis, with some studies utilizing Shannon indices to assess alpha diversity, while others employ more robust metrics, such as Bray–Curtis dissimilarity or weighted UniFrac analyses, to examine beta diversity. Despite these methodological disparities, converging evidence consistently supports the role of *L. plantarum* in promoting hepatic health, as demonstrated by reductions in hepatic triglyceride levels and the suppression of lipogenesis-related genes, including *pparg* and *srebp*1. However, much of the existing research is limited to murine models, highlighting the need for human trials to validate these findings and address potential safety concerns.[11]

3.2. *L. plantarum* NCHBL – 004

A study by Jang *et al.*[11] demonstrated that the oral administration of live *L. plantarum* NCHBL-004 attenuates weight gain in mice subjected to a high-fat diet (HFD). Interestingly, heat-killed NCHBL-004 also

exhibited anti-obesity effects comparable to those of its live counterpart. To assess the impact of NCHBL-004 on gut microbiota composition, the researchers performed a detailed analysis, revealing significant alterations at the phylum, family, and genus levels. Oral administration of NCHBL-004 was found to significantly increase SCFA-producing and secondary bile acid (BA)-producing microbes. In contrast, the HFD led to a reduction in SCFA-producing and secondary BA-producing strains, including *Lactobacillus spp*. Notably, NCHBL-004 supplementation effectively counteracted these HFD-induced effects. In addition, NCHBL-004 regulated hepatic lipid metabolism and exerted anti-obesity effects through the activation of glucagon-like peptide-1 (GLP-1). GLP-1 plays a critical role in enhancing insulin secretion for blood glucose control, suppressing appetite, aiding in weight management, and serving as a promising therapeutic tool for obesity and type 2 diabetes management.[11]

3.3. *L. plantarum* FRT10

Cai *et al.*[13] assessed the efficacy of *L. plantarum* FRT10 in mice over an 8-week period. The study included four groups: a control group, an HFD group with no probiotic administration, an HFD group receiving low doses of *L. plantarum*, and an HFD group receiving high doses of *L. plantarum. L. plantarum* FRT10 alleviated HFD-induced lipid accumulation and hepatic steatosis. Furthermore, *L. plantarum* FRT10 reduced triglyceride accumulation, which is directly linked to gene expression affecting lipid metabolism. The *L. plantarum* FRT10 supplementation group showed improvements in gut dysbiosis, a reduction in organ weight (particularly due to decreased visceral adipose tissue), increased mRNA levels of peroxisome proliferator-activated receptors (PPARs), and decreased mRNA expression of sterol regulatory element-binding proteins (SREBPs).[13]

3.4. *L. plantarum* FRT4

Cai *et al.*[14] investigated the effects of *L. plantarum* FRT4 and showed that its administration led to decreases in body weight, weight gain, liver weight (visceral fat), triglyceride levels, and ALT levels while improving gut barrier integrity, attenuating inflammation, and increasing microbial biodiversity in the gut. The study highlights the complex mechanisms within the gut microbiota. *L. plantarum* FRT4 significantly reversed the effects of an HFD on choline, glycerophosphocholine, and phosphorylcholine levels. The group receiving probiotics also exhibited beneficial changes, with increased levels of species such as *Bacteroides*, *Alistipes*, *Intestinimonas*, *Butyricimonas*, *Butyricicoccus*, and *Lactobacillus*, while HFD-induced levels of *Roseburia* and *Blautia* were suppressed following probiotics administration. In addition, an HFD altered the levels of *Akkermansia* and *Odoribacter*, but these levels returned to normal after FRT4 administration, without a significant decrease in phosphatidylcholine levels. The HFD-induced decrease in trimethylammonium cations was further reduced after probiotics treatment. These findings suggest that while *L. plantarum* administration can mitigate several HFD-induced effects, it does not fully reverse all physiological changes. This highlights the need for further research to better understand the specific mechanisms at play within the gut microbiota.[14]

3.5. *L. plantarum* HMRS-6

Zhu *et al.*[15] investigated the effects of *L. plantarum* HMRS-6 (150 μL/day) in a 15-week study involving 30 female ICR mice, divided into three groups: control, HFD, and HFD + probiotic (administered from week 11 to week 13). The results showed that *L. plantarum* HMRS-6 significantly reduced body weight, shifted microbial diversity, lowered blood glucose levels, and improved insulin resistance, with these parameters returning close to control levels by week 15. This study underscores *L. plantarum* HMRS-6 as a promising probiotic for mitigating obesity-related effects.[15]

3.6. *L. plantarum* Dad-13

Rahayu *et al.*[9] demonstrated that administering *L. plantarum* Dad-13 (2×10^9 CFU/gram/sachet) led to significantly decreased body weight (in females), BMI, and *Bacteroidetes* abundance, without significantly affecting SCFA levels, pH, lipid profiles, cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), or the HDL/LDL ratio. The study also observed a decrease in *Firmicutes* abundance, underscoring the relevance of the *Firmicutes*-to-*Bacteroidetes* ratio in obesity-related treatments, as gut microbiota dysbiosis is linked to obesity and its comorbidities.[3] An increase in *Firmicutes* is associated with reduced microbial diversity, a key factor in obesity risk.[9] However, potential bias exists due to a significant reduction in energy intake in both placebo and treatment groups during the final month, which was not accounted for in the statistical analysis.[9]

3.7. *L. plantarum* pro1 and *Lactobacillus rhamnosus* pro2

Darwish *et al.*[16] evaluated the effects of *L. plantarum* pro1 (MT505334.1) and *L. rhamnosus* pro2 (MT505335.1) individually and in combination on obesity-related kidney dysfunction in 50 mice. The study included five groups: HFD-only group, a regular diet group, and three HFD groups supplemented with pro1, pro2, or their combination from weeks 0 to 8. The combination group showed the

most favorable outcomes, including the highest HDL levels, and the lowest levels of cholesterol, triglycerides, and LDL, along with reduced serum and urinary creatinine levels. Notably, weight gain in the combination group was comparable to the regular diet control group, highlighting its potential in mitigating obesity-related effects.[16]

3.8. *L. plantarum* from fermented barley extract (LFBE)

Gu *et al.*[17] investigated the effects of LFBE on obesity in Sprague–Dawley rats with HFD-induced adipocyte hypertrophy. Over an 8-week period, LFBE supplementation reduced weight gain, fasting blood glucose levels, lipid accumulation, and fatty acid synthesis while maintaining an HFD. Transcriptomic analysis showed that the LFBE inhibited genes responsible for lipid overproduction and promoted mitochondrial biogenesis. Notably, LFBE supplementation transforms white adipose tissue in the groin and epididymis into brown-like adipose tissue, marked by smaller fat droplets and increased mitochondrial density. These findings highlight LFBE's potential in combating obesity-related effects.[17]

3.9. *L. casei* Zhang (LCZ)

He *et al.*[18] evaluated the effects of LCZ, a probiotic derived from koumiss, on mesenteric and perirenal fat in wild-type and GLUT1 villi CKO mice. LCZ administration significantly reduced both fat types in both groups, addressing critical markers of obesity-related complications. Elevated mesenteric fat was associated with systemic inflammation and increased gut permeability, while increased perirenal fat was linked to kidney damage and lipotoxicity. Despite the study's limitation of small sample size ($n = 5$ for GLUT1 villi CKO mice), the findings highlight LCZ's potential benefits for managing obesity and glucose transporter impairments.[18]

3.10. *L. kefiranofaciens*

Kurakawa *et al.*[6] investigated the metabolic effects of an inactive *L. kefiranofaciens* in mice over a 15-week period. The low-dose group (50 mg/kg) showed weight reduction after 12 weeks, while the high-dose group (100 mg/kg) exhibited similar results after 15 weeks. Notably, the low-dose group experienced significant visceral fat reduction, suggesting a dose-dependent relationship between probiotics and metabolic benefits. Both groups demonstrated reductions in insulin resistance, body weight, and the *Firmicutes/Bacteroidetes* ratio, alongside increases in SCFA production and acetate levels. While the findings are limited by the use of mice, this study highlights the potential of inactive *L. kefiranofaciens* strains as postbiotics for future clinical trials.[6]

3.11. *Lactobacillus gasseri* BNR17 and *Lactobacillus fermentum* ABF21069

Jo *et al.*[12] examined the effects of *L. gasseri* BNR17 and *L. fermentum* ABF21069 on obesity and fatty liver in a sucrose-induced obese animal model over 10 weeks. Probiotic supplementation improved β-oxidation, thermogenesis, and lipolysis, while also reducing inflammation, with combination therapy outperforming the individual strains. Key outcomes included reduced body fat, alleviated fatty liver, enhanced exopolysaccharide (EPS) production, and regulation of sugar transport and inflammatory gene expression. BNR17 was more effective in EPS production and visceral fat reduction, while ABF21069 led to better mitigation of liver fat and inflammation.[12]

3.12. *Lactobacillus delbrueckii* subsp. *lactis* CKDB001 (LL)

The study investigated LL for the treatment of metabolic-associated steatotic liver disease (MASLD) in an HFD-induced murine model. LL supplementation reduced body weight, hepatomegaly, fibrosis, and non-alcoholic steatosis scores while improving insulin sensitivity, triglyceride levels, and liver-specific AMPK activation. In addition, it promoted healthier adipocyte hypertrophy through enhanced mitochondrial biogenesis and energy utilization. However, gaps remain in understanding LL's impact on gut microbiota, its long-term effects, and human bioavailability.[11]

Table 1 provides a comprehensive overview of anthropometric parameters, as well as metabolic and inflammatory biomarkers influenced by specific *Lactobacillus* strains. Note that directly related parameters, such as weight and BMI, are included based on study-specific criteria. Consequently, a group listed under 'Decrease of weight' may not appear under 'Decrease of BMI,' even though a direct relationship is understood (Table 1).

3.13. Combined effects of *Lactobacillus* and *Bifidobacterium*

The combined effects of *Lactobacillus* and *Bifidobacterium* probiotics have garnered significant attention in recent research for their potential to improve metabolic health, particularly in the context of obesity and its comorbidities. These two genera of probiotics work synergistically to modulate the gut microbiota, enhance the production of SCFAs like butyrate, acetate, and propionate, and improve gut diversity. *Lactobacillus* strains, such as *L. plantarum*, and *Bifidobacterium* species, such as *Bifidobacterium lactis*, have demonstrated the ability to reduce body weight, lower BMI, and alleviate fat accumulation, particularly in visceral

Table 1. Effects of various *Lactobacillus* strains on health parameters and related studies

Effect	*Lactobacillus* strains	References
Decrease of BMI	*L. kefiranofaciens, L. plantarum* Dad-13	7, 10
Decrease of weight	*L. plantarum FRT4, L. plantarum Pro1 (MT505334.1),* LFBE*, L. casei Zhang, L. plantarum NCHBL–004, L. Gasseri BNR17 + L. Fermentum ABF21069, L. Kefiranofaciens, L. plantarum Dad–13, L. plantarum HMRS–6*	7, 10, 12, 13, 15, 16, 17, 18, 19
Decrease of visceral fat	*L. kefiranofaciens, L. plantarum FRT10,* LFBE*, L. plantarum FRT4, L. Gasseri BNR17 + L. Fermentum ABF21069, L. casei Zhang, L. plantarum HMRS-6*	7,13,14,15,16,18,19
Decrease of blood glucose level	LFBE*, L. Kefiranofaciens, L. plantarum HMRS-6*	7,16,18
Decrease of serum uric acid	*L. Kefiranofaciens, L. plantarum HMRS-6*	7,16
Favorable lipid profile	*L. plantarum FRT10,* LFBE*, L. plantarum FRT4, L. plantarum & L. rhamnosus, L. plantarum NCHBL–004*	12,14,17,18
Increase of short-chain fatty acids	*L. plantarum NCHBL–004, L. Kefiranofaciens*	7,12
Increase in gut microbiota diversity	*L. plantarum FRT10, L. plantarum FRT4, L. casei Zhang, L. plantarum NCHBL–004, L. Kefiranofaciens, L. plantarum HMRS-6*	7,12,14-16,19
Increase of epithelial barrier integrity	*L. plantarum FRT4, L. Kefiranofaciens*	7,15

Abbreviations: BMI: Body mass index; LFBE: *L. plantarum* from fermented barley extract, BMI: Body mass index; *L. kefiranofaciens: Lactobacillus kefiranofaciens; L. plantarum: Lactobacillus plantarum; L. casei: Lactobacillus casei; L. gasseri: Lactobacillus gasseri; L. Fermentum: Lactobacillus Fermentum.*

fat. In addition, their combined use has shown promising effects on glycemic control, reducing insulin resistance, and improving lipid profiles. This dual approach not only helps restore the balance of beneficial gut bacteria but also appears to mitigate the inflammatory and metabolic disruptions associated with obesity. However, despite these positive outcomes, further research is needed to understand the optimal dosages, long-term effects, and potential safety concerns in human trials, as well as the impact of individual variations in gut microbiota composition.

Othman *et al.*[4] compared the effects of probiotics (*Bifidobacterium longum*, *Lactobacillus helveticus*, *Lactococcus lactis*, and *Streptococcus thermophilus*), a prebiotic diet (30 g carob beans/day), and a low-carbohydrate diet in 45 obese patients over the course of 1 month. The probiotic group showed reductions in weight, BMI, waist circumference, fat mass, depression, and fasting glucose, with improved grip strength. Both the probiotic and prebiotic-receiving groups showed improved lean mass and physical performance, with the probiotic group showing a smaller reduction in serum uric acid (SUA), a key factor in obesity-related insulin resistance, hypertension, and cardiovascular risk.[4,19]

Lactobacillus synthesizes an enzyme that degrades uric acid, a valuable trait in obesity treatment.[19] *Bifidobacterium* produces SCFAs such as acetate, propionate, butyrate, and lactate, which regulate genes associated with fat storage and inflammation.[9] Consequently, combinations of these probiotics have been explored for managing obesity-related effects. Combining *Lactobacillus* and *Bifidobacterium* strains adds complexity to the gut microbiome mechanisms.[20] Kaczmarczyk *et al.*[20] studied a combination of nine strains, including *Bifidobacterium bifidum* W23, *B. lactis* W51/W52, Lactobacillus *acidophilus* W37, and others. In this trial involving 36 post-menopausal women in Poland, two groups received either a low-dose probiotic (LDP, 2.5×10^9 CFU/day) or a high-dose probiotic (HPD, 1×10^{10} CFU/day).

The LDP group experienced a functional change in *Erysipelotrichia* bacteria, which synergized with the probiotics to promote weight and BMI reduction. Interestingly, the HPD group showed no such bacterial shift but still achieved weight and BMI loss. Both groups demonstrated favorable outcomes for obese post-menopausal women, with no significant differences between the doses. These findings suggest that probiotic effectiveness may depend on the pre-existing gut microbiota.[20] A randomized open-label clinical trial in Hong Kong by Lauw *et al.*[21] assessed a synbiotic supplement containing *B. lactis* HN019, *L. acidophilus* NCFM, and PDX on anthropometric indices, obesity-related markers, and gut microbiota in overweight and obese Chinese participants. Synbiotic supplementation alone showed no significant effects on body composition or metabolic biomarkers. However, when combined with increased fruit and vegetable intake, synbiotics led to notable improvements in body weight, BMI, body fat mass, and cardiovascular risk factors, with a clinically significant 5% weight loss. In addition, fasting glucose, insulin resistance, and HOMA-IR (Homeostatic Model Assessment for Insulin Resistance) also improved.

Gut microbiota analysis revealed a decrease in *Megamonas* and an increase in *Parabacteroides*, which were linked to changes in body composition. Limitations of the study included the absence of a placebo group, a small sample size, short duration, and a lack of measurements for fecal SCFAs and serum zonulin. Further research is needed to explore the role of *Parabacteroides*, its effects on type 2 diabetes, and its long-term benefits in larger, more diverse populations.[21] In the study conducted by Michael *et al.*,[22] the combination of *L. acidophilus* CUL60 and CUL21, *L. plantarum* CUL66, *B. bifidum* CUL20, and *Bifidobacterium animalis* subsp. *lactis* CUL34 resulted in clinically significant weight reduction in 40% of overweight adults in the treatment group, with 70% achieving at least a 3% weight loss over 9 months.[22] A weight loss of 5% or more, linked to improvements in glycemic index and plasma lipid levels, highlights the study's promising results. The study involved 70 overweight Bulgarian adults (BMI 25 – 29.9), with half receiving 50 billion CFU/day for 9 months. Notably, the placebo group showed no significant difference in weight loss during the first 6 months but experienced weight gain between months 6 and 9, possibly due to holiday-related factors. Meanwhile, the treatment group sustained favorable outcomes, showing statistically significant effects during the latter period. This underscores the potential of the probiotic combination as a therapeutic agent for obesity-related metabolic disorders.[22]

A 24-week study by Kanazawa *et al.*[23] assessed the effects of a symbiotic comprising *Lacticaseibacillus paracasei* strain Shirota (LcS), *Bifidobacterium breve* strain Yakult (BbrY), and galactooligosaccharides (GOS) in obese patients with type 2 diabetes mellitus. The study included a control group and a synbiotic group, with data collected at baseline, 12 weeks, and 24 weeks. Key findings showed a significant increase in *Bifidobacteriaceae*, particularly *Bifidobacterium adolescentis* and *Bifidobacterium pseudocatenulatum*, as well as elevated fecal acetic, butyric, and lactic acid levels in the synbiotic group at 24 weeks. Decreases were observed in bacterial families such as *Bacteroidaceae, Marinifilaceae, Fusobacteriaceae*, and *Monoglobaceae*. However, no significant differences were noted in inflammatory markers or glycemic control (HbA1c) between the groups. The study highlighted research gaps, including the lack of evidence on synbiotics' effects on gut barrier function, plasma inflammatory markers (*e.g.*, tumor necrosis factor-alpha [TNF-α]), and bacterial translocation to the blood. Future research should explore these aspects to better understand the impact of synbiotics on metabolic and immune responses in patients with type 2 diabetes mellitus.[23] Banach *et al.*[24] conducted a 12-week study involving 54 obese participants, who were divided into subgroups matched for height, age, and BMI. The intervention consisted of a hypocaloric diet supplemented with yogurt containing *L. acidophilus* LA-5 and *B. lactis* BB-12. The results showed no significant differences in weight reduction or anthropometric measures (*e.g.*, BMI, waist circumference, visceral adipose tissue) between the probiotic and control groups, consistent with findings from similar prior studies.[24]

Potential benefits on lipid profiles, insulin sensitivity, and immune responses were noted, although variability in results may be attributed to differences in probiotic strain survivability, yogurt manufacturing conditions, and participant adherence. Limitations of the study included a small sample size (particularly among males), a short study duration, and uncertainties regarding adherence to yogurt consumption and the viability of live probiotics due to transport and storage conditions. Future research should focus on longer study durations, larger and more diverse populations, and controlled conditions. In addition, it is crucial to investigate probiotic survivability and functionality within the gastrointestinal environment.[24]

A study by Khan *et al.*[25] investigated the effects of a dairy-based multi-strain probiotic community (MSPC) on obesity-related gut microbiota using an *in vitro* CoMiniGut intestinal model. The MSPC consists of 19 lactic acid bacteria strains including *Lactobacillus* and *Bifidobacterium* strains. The study showed that MSPC reduced harmful bacteria in lean samples and increased beneficial ones in obese samples, improving microbial diversity. The findings suggest MSPC's potential for addressing obesity-related gut dysbiosis, though further research is needed.[25]

Table 2 summarizes the effects of various *Lactobacillus* strains on parameters including BMI, weight, visceral fat, blood glucose, SUA, lipid profiles, SCFAs, gut microbiota diversity, and epithelial barrier integrity, highlighting the strain-specific impacts on metabolic and inflammatory biomarkers.

4. Discussion

Each study included in this review examines various parameters to assess the effectiveness of probiotics in addressing obesity and its related metabolic disorders. These parameters commonly include BMI, waist circumference, visceral adiposity (with some studies also evaluating hepatic fat to assess the risk of hepatosteatosis), body weight, fasting blood glucose levels, SUA, SCFAs, and gut dysbiosis.

BMI, which is calculated as the ratio of weight to height (kg/m^2), is commonly used as an indicator of risk for cardiometabolic diseases like obesity.[1,20] Obesity is associated with comorbidities such as cardiovascular

Table 2. Comparison of parameters and *Lactobacillus* strains

Parameters	Strain	Sample	Reference
Decreased BMI	*L. kefiranofaciens*	Mice	7
	L. plantarum Dad-13	Overweight humans	10
Decreased weight	*L. plantarum* FRT4	Mice	14
	L. plantarum pro1	Mice	17
	LFBE	Rats	18
	L. casei *Zhang*	Mice	19
	L. plantarum NCHBL-004	Mice	12
	L. gasseri BNR17 + *L. Fermentum* ABF21069	Mice	13
	L. kefiranofaciens	Mice	7
	L. plantarum Dad-13	Overweight women	10
	L. plantarum HMRS-6	Mice	16
Decreased visceral fat	*L. plantarum* FRT4	Mice	15
	LFBE	Rats	18
	L. casei Zhang	Mice	19
	L. kefiranofaciens	Mice	7
	L. plantarum HMRS-6	Mice	16
Decreased blood glucose level	LFBE	Rats	18
	L. kefiranofaciens	Mice	7
	L. plantarum HMRS-6	Mice	16
Decreased SUA	*L. kefiranofaciens*	Mice	7
	L. plantarum HMRS-6	Mice	16
Favorable lipid profile	*L. plantarum* FRT10	Mice	14
	L. plantarum FRT4	Mice	15
	L. Plantarum pro1	Mice	17
	LFBE	Rats	18
	L. plantarum NCHBL-004	Mice	12
Increased SCFAs	*L. plantarum NCHBL-004*	Mice	12
	L. Kefiranofaciens	Mice	7
Increased gut microbiota diversity	*L. plantarum* FRT10	Mice	14
	L. plantarum FRT4	Mice	15
	L. casei Zhang	Mice	19
	L. Plantarum NCHBL-004	Mice	12
	L. kefiranofaciens	Mice	7
	L. plantarum HMRS-6	Mice	16
Increased epithelial barrier integrity	*L. plantarum* FRT4	Mice	15
	L. kefiranofaciens	Mice	7

Abbreviations: BMI: Body mass index; LFBE: *Lactobacillus plantarum* from fermented barley extract; SCFAs: Short-chain fatty acids; SUA: Serum uric acid; *L. kefiranofaciens: Lactobacillus kefiranofaciens; L. plantarum: Lactobacillus plantarum; L. casei: Lactobacillus casei; L. gasseri: Lactobacillus gasseri; L. Fermentum: Lactobacillus Fermentum.*

disease, diabetes, weight-related cancers, and hepatic steatosis, all of which often arise from metabolic disorders linked to the accumulation of adipose tissue.[19,26] According to the World Health Organization,[1] adults with a BMI between 25 and 29.9 are classified as overweight, while those with a BMI of 30 or higher are considered obese.[1] However, the BMI scale has limitations, as it only measures weight relative to height and cannot be relied upon as the

sole indicator of metabolic diseases.[1] Other important factors to consider include waist circumference and visceral fat area (VFA).[1,19] Increased waist circumference, resulting from excess adipose tissue, is positively associated with weight-related cancers, including colon, post-menopausal breast, endometrial, and pancreatic cancers.[26] VFA, which measures adipose tissue around internal organs, is a critical indicator, as its accumulation is linked to obesity-related metabolic disorders. In contrast, subcutaneous adipose tissue does not show a significant positive relationship with these disorders and is not considered a major risk factor.[19] Excess adipose tissue accumulation found on the liver leads to hepatic steatosis and is measured in studies involving mice.[6,13,14,17,18]

The relationship between SUA and VFA is intriguing but not yet fully understood. An increase in VFA is often accompanied by a rise in SUA, potentially as a mediating response. Since elevated VFA is linked to hypertension, cardiovascular disease, and diabetes, SUA has emerged as a biomarker for these risks due to its apparent positive correlation. *Lactobacillus* probiotics, which synthesize enzymes that degrade SUA, may help mitigate its effects and reduce VFA. Similarly, *Bifidobacterium* probiotics have been shown to decrease both VFA and SUA, leading to favorable outcomes. Consequently, combinations of these probiotics are commonly used to support metabolic health in patients.[19] However, a challenge remains in identifying the specific probiotic strains that are most effective for a broad population.[6,19] The domino effect observed in many studies suggests that the addition of *Lactobacillus* and/or *Bifidobacterium* increases the abundance of the phylum *Bacteroidetes* (Bacteroidata), which in turn enhances gut biodiversity and promotes the production of SCFAs.[6,11,13] SCFAs – specifically butyrate, propionate, and acetate – help mitigate the harmful effects of accumulated visceral adipose tissue on the liver. Acetate, in particular, binds to SCFA receptors, which may lead to the downregulation of lipogenic genes. This simplified mechanism offers insight into the positive effects of probiotics, with speculation that these processes could help reduce insulin resistance. As a result, SCFAs are increasingly being measured as a key parameter in obesity treatment.[6]

As mentioned previously, an increase in the phylum *Bacteroidetes* is associated with positive effects, alongside a decrease in *Firmicutes*. The relationship between these two phyla plays a crucial role in dysbiosis, which refers to an imbalance of species within the gut microbiota. Dysbiosis, often characterized by the *Firmicutes*/*Bacteroidetes* ratio, has been used as a parameter to assess the diversity of species in the gut, particularly in the context of obesity and metabolic health.[9,13,18]

A reduction in BMI and weight was observed in a study using a combination of 9 strains, namely *B. bifidum* W23, *B. lactis* W51, *B. lactis* W52, *L. acidophilus* W37, *Levilactobacillus brevis* W63, *Lacticaseibacillus casei* W56, *Ligilactobacillus salivarius* W24, *L. lactis* W19, and *L. lactis* W58.[20] A significant reduction in weight, BMI, waist circumference, fasting glucose, fasting insulin HOMA-IR in a study using *B. longum* BB536, *L. rhamnosus* HN001 for 26 measured breast cancer survivors. However, the small sample size of this study may affect the quality of analysis concluded.[27]

Michael *et al.*[22] found that the probiotic combination Lab4P, consisting of *L. acidophilus* CUL60, *L. acidophilus* CUL21, *L. plantarum* CUL66, *B. bifidum* CUL20, and *B. animalis* subsp. *lactis* CUL34, significantly reduced body weight, waist and hip circumference, and blood pressure in overweight Bulgarian adults. This suggests Lab4P's potential as an effective probiotic for managing obesity and related metabolic risks.[22] The microbial diversity increase as the *Firmicutes*/*Bacteroidetes* ratio decrease in both low-dose and high-dose probiotic groups in the study by Tremblay *et al.*[28] using the following combination: *L. helveticus* R0052, *L. rhamnosus* R0011, *L. casei* R0215, *Pediococcus acidilactici* R1001, *B. breve* R0070, *B. longum* ssp. *longum* BB536, *L. plantarum* R1012, and *L. lactis ssp. lactis* R1058. Since this study focused on the adverse effects and safety of high-dose probiotic administration, the other factors measured are not relevant to this paper.[28] A study showed that yogurt containing *L. acidophilus* LA-5 and *B. lactis* BB-12 did not significantly reduced body weight, BMI, or waist circumference in obese individuals on a hypocaloric diet. Despite the absence of improvements in anthropometric parameters, the study suggested potential benefits for lipid profiles and insulin sensitivity. The lack of effectiveness may be due to probiotic strain survivability and participant adherence.[24]

5. Limitations

This systematic review provides valuable insights but has limitations and unresolved key issues that must be acknowledged. Addressing the challenges outlined below through standardized methodologies and larger, well-controlled studies is essential for improving the reliability and applicability of the findings.

Study heterogeneity. The variability in sample populations, methodologies, and intervention designs makes direct comparisons challenging. As discussed by Glasziou and Sanders,[29] differences in study protocols can lead to inconsistencies in reported outcomes. This heterogeneity ultimately limits the generalizability of the findings.

Human vs. animal models. Jucker[30] discussed how physiological differences between humans and animals hinder the direct translation of results. As a result, animal models may not fully replicate human disease mechanisms. This discrepancy impacts the applicability of findings to clinical practice.

Small sample sizes and short follow-ups. Many studies have been reported to have a limited number of participants and brief follow-up periods. These constraints reduce statistical power and the reliability of conclusions. Therefore, longer and larger studies are needed to generate stronger evidence.[31]

Variability in probiotic strains and dosages. Differences in probiotic types, dosages, and study conditions impact study outcomes. In addition, inconsistent protocols make it difficult to determine the most effective formulations. Therefore, standardization is essential for improved reproducibility.[32]

Publication bias and confounding factors. Bias in research can arise from selective reporting and publication bias, where studies with positive results are more likely to be published, leading to an overestimation of treatment effects.

In addition, uncontrolled variables such as diet, lifestyle, and genetics can significantly influence study outcomes. For instance, genetic predispositions can affect eating behaviors, which in turn impact health-related research findings.[33] These factors underscore the importance of rigorous study design and comprehensive data analysis to ensure reliable and valid conclusions.

6. Key unresolved issues and future direction

The following key unresolved issues require deeper investigation in future research: the long-term effects of probiotics on obesity; optimal strain combinations and dosages for maximum efficacy; a mechanistic understanding of how probiotics influence obesity and related metabolic pathways; the role of diet, lifestyle, and host genetics in modulating probiotic effects; and inconsistencies between animal and human study outcomes.

To address these challenges, the following research directions should be prioritized:

- Conducting long-term clinical trials to evaluate the sustained effects of probiotics on obesity and metabolic health.
- Establishing standardized probiotic strains and dosages to ensure consistency and reproducibility across studies.
- Utilizing multi-omics approaches (*e.g.*, metagenomics, metabolomics, transcriptomics) to uncover the underlying mechanisms of probiotic action.
- Bridging the gap between animal and human research through translational studies that enhance clinical relevance.
- Developing personalized probiotic therapies that account for individual gut microbiome variations and host responses.
- Integrating diet and lifestyle factors into probiotic intervention strategies to maximize their effectiveness.

Future research efforts focused on these areas will enhance our understanding of probiotics and their role in metabolic health, ultimately improving clinical applications

7. Conclusion

This systematic review emphasizes the growing body of evidence supporting the potential of probiotics, particularly those from the genera *Lactobacillus* and *Bifidobacterium*, as promising therapeutic agents for managing obesity and its associated comorbidities. The studies included in this review demonstrated significant effects of probiotics on gut microbiota modulation, enhanced production of SCFAs, improved glycemic control, and reductions in body weight, BMI, and fat mass. Specific strains, such as *L. plantarum* NCHBL-004 and combinations of *Lactobacillus* with *Bifidobacterium*, have shown notable benefits in weight loss and metabolic health, as well as improvements in gut microbiota diversity. However, the interpretation of these promising results is limited by several factors, including variations in study designs, reliance on animal models, and small sample sizes in human trials. The interaction between probiotic dosage, pre-existing gut microbiota composition, and individual responses further highlights the need for personalized approaches to probiotic treatment.

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Conflict of interest

The authors declare that there are no conflicts of interest.

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Availability of data

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