Review

Modulating the Gut Microbiome in Obesity: Interventions and Clinical Implications

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Modulating the Gut Microbiome in Obesity: Interventions and Clinical Implications

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Abstract

Background: Obesity arises from complex interactions beyond energy imbalance, with the gut microbiome increasingly recognised as a key modulator of metabolic function in obesity. This narrative review examines microbiome-targeted interventions for obesity prevention and treatment. **Objective**: To synthesise evidence on diet, exercise, biotics (pre/pro/post/synbiotics) and faecal microbiota transplantation (FMT) as modulators of gut microbiota composition and function to improve body composition and metabolic health. **Methods**: A structured literature search of PubMed, Scopus and Web of Science (2015–2026) informed this narrative review, focusing on studies evaluating the role of the gut microbiome in obesity and the impact of microbiome-targeted interventions. Randomised controlled trials, systematic reviews, meta-analyses and key observational and preclinical studies were prioritised. Evidence was synthesised narratively. **Results**: Microbiome-targeted interventions including dietary modification, physical activity and biotic therapies demonstrate modest and variable effects on adiposity but may improve metabolic outcomes through mechanisms involving short-chain fatty acids (SCFA), inflammation and gut barrier function. High-fibre diets (e.g., resistant starch, Mediterranean) consistently enhance SCFA-producing taxa and reduce fat mass. Exercise induces modest microbiome shifts favouring beneficial bacteria such as *Akkermansia* / *Bifidobacterium*. Biotics (*Lactobacillus* / *Bifidobacterium* strains) yield small-moderate reductions in BMI / fat mass with next-generation strains (*A. muciniphila, F. prausnitzii*) showing promise in preclinical / human pilots. Evidence for FMT in obesity remains limited and inconsistent in humans. Mechanisms converge on energy harvesting, barrier integrity, endotoxemia reduction and GLP-1 / bile signalling. **Conclusions**: Microbiome modulation appears to complement lifestyle and therapeutic interventions but translation into clinical practice requires strain-specific, well-designed randomised controlled trials and longitudinal data. Personalised multiomics approaches offer future potential.

Keywords: gut microbiome; obesity; prebiotics; probiotics; synbiotics; postbiotics; short-chain fatty acids; faecal microbiota transplantation; *Akkermansia muciniphila*; body composition

1. Introduction

Obesity has traditionally been viewed as a disorder of energy imbalance, where increase in weight is a consequence of increased calories consumed than burned.[1] This concept however does not explain the considerable variations in fat distribution, insulin sensitivity and long-term weight patterns noted in populations despite similar energy intake and physical activity levels. Recent studies indicate that host metabolism is more complex than calorie balance alone.[2,3] Research shows that the gut microbiome plays a key role in host energy handling by influencing digestion and energy extraction. Obese individuals tend to have less diverse microbiomes and different microbial profiles than lean individuals, with reduced beneficial species and more pro-inflammation-linked

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species. This gut dysbiosis is linked with poor insulin sensitivity, dyslipidaemia and low-grade systemic inflammation regardless of calorie intake.[4–6]

Randomised trials combining calorie restriction with exercise often improve weight and metabolic health but changes in the gut microbiome diversity and function observed are inconsistent or small. This suggests that the calorie-focused approaches do not fully address the key biological factors driving obesity including the microbe-host interactions.[7,8] The gut microbiome ferments non-digestible carbohydrates into key metabolites, including short-chain fatty acids (acetate, propionate and butyrate) and tryptophan-derived compounds, that regulate host microbiota interactions and metabolic functions through mechanisms such as enhanced caloric extraction, SCFA-mediated control of adiposity and inflammation, bile acid signalling, gut–brain appetite pathways, intestinal barrier dysfunction and immune dysregulation.[9–15] Observational studies consistently demonstrate lower microbial alpha diversity and reduced abundance of SCFA-producing taxa in obese individuals compared with lean controls altering host responsiveness to dietary interventions.[6,16] Recent meta-analyses and systematic reviews indicate that microbiome-targeted interventions (prebiotics, probiotics and synbiotics) can shift microbial composition and improve metabolic parameters in overweight and obese adults, though heterogeneity in study design and outcomes highlight the need for standardised protocols.[17–19] Restoring microbial diversity and function in obese individuals may attenuate inflammation, improve gut barrier integrity and aid in energy balance.[20] This shifts treatment strategy beyond calorie restriction to target gut microbial pathways to improve host metabolic functions.[21–23] With this background, we synthesised evidence from clinical and preclinical studies on microbiome modulating interventions, including dietary patterns, exercise, biotics including next-generation strains and faecal microbiota transplantation and multiomics approaches focused on obesity phenotypes and clinical translation, to evaluate their effects on microbial composition, metabolite production and obesity related outcomes.

Literature Search and Selection

This narrative review was informed by a structured literature search conducted in PubMed, Scopus, Web of Science, and Google Scholar (January 2015–February 2026) using MeSH terms and keywords: ("obesity" OR "overweight") AND ("gut microbiome" OR "gut microbiota") AND ("prebiotic*" OR "probiotic*" OR "synbiotic*" OR "postbiotic*" OR "fecal microbiota transplantation" OR "diet" OR "exercise"). Priority was given to RCTs, meta-analyses, systematic reviews and key observational and preclinical studies reporting microbiome composition, metabolites (SCFAs) or metabolic outcomes (BMI, fat mass, insulin sensitivity) (n=103 included). Evidence was narratively synthesised, and greater emphasis placed on higher-quality evidence. Study design, sample size and consistency of findings were considered while evaluating robustness of findings. The narrative review did not undergo a formal systematic review protocol.

2. Treatment Modalities Targeting the Gut Microbiota for Obesity

Dietary modification, physical activity, microbiota-directed biotics and faecal microbiota transplantation influence gut microbial composition and function through overlapping and distinct mechanisms that converge on host metabolic regulation in obesity. In addition, pharmacological therapies such as GLP-1 receptor agonists and bariatric surgery have also been shown to influence gut microbiome composition and metabolic outcomes, highlighting the broader role of microbiome modulation across obesity treatments. (**Figure 1)**.

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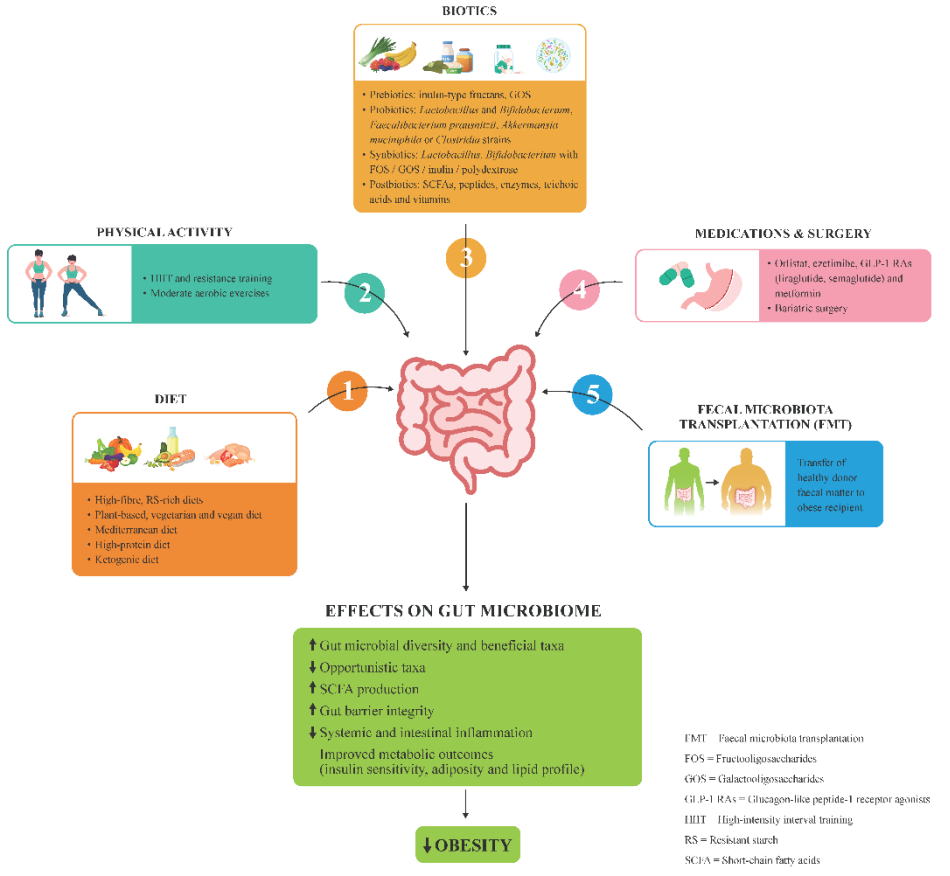

Figure 1. Treatment modalities targeting the gut microbiota for obesity.

2.1. Diet as the Primary Gut Microbiome Modulator

Diet is the most potent environmental determinant of gut microbiome composition and function. In longitudinal studies, changes in diet particularly increases in intake of fermentable fibres, resistant starches and diverse plant foods rapidly and reproducibly reshape microbial communities and is associated with reduced risk of chronic diseases including cardiovascular disease, diabetes, obesity and certain cancers [24,25]. Fermentation of dietary fibre by the gut microbiota generates metabolites that regulate gut health, mucosal inflammation and epithelial proliferation.

In contrast, western dietary patterns characterised by high intake of refined carbohydrates, saturated fats and ultra-processed foods combined with low intake of dietary fibre are linked with decrease in microbial diversity and reduction of SCFA-producing taxa and expansion of taxa associated with proinflammation. These microbial shifts are mechanistically linked to increase in the intestinal permeability, metabolic endotoxemia, chronic low-grade inflammation and adverse adipose tissue distribution, which contribute to obesity risk [26–28] In addition, food additives such as emulsifiers, including polysorbates, can alter gut microbiota composition, disrupt intestinal barrier integrity and promote endotoxemia and inflammatory responses, thereby contributing to the development of metabolic disorders, diabetes and obesity. [29–33]

Resistant starch, one of the dietary fibres, is difficult to digest and hence it is digested and fermented by gut bacteria in the large intestine.[34,35] RS supplementation increases butyrate production, mainly produced by *Firmicutes*, which enter the bloodstream and exerts beneficial epigenetic and immunological effects in the body thus making RS a potential treatment strategy to reduce obesity risk. [34,36] In individuals with type 2 diabetes, dietary fibres can modulate the gut microbiome by significantly increasing relative abundance of *Bifidobacterium* causing increase in SCFA production. This improves glycated haemoglobin aiding in weight reduction.[37] Consistent with these findings, a randomised placebo-controlled crossover trial demonstrated that eight weeks

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of RS supplementation, combined with an isoenergetic balanced diet, resulted in significant reductions in body weight and improvements in insulin resistance among individuals with overweight and obesity, effects attributed to microbiota-mediated mechanisms.[38]

A plant-based diet; vegetarian and vegan diet, rich in fruits, vegetables, grains and legumes intake, has been shown to be effective in weight management. These diets are naturally high in dietary fibre and hence promote growth of beneficial bacteria and reduce production of harmful metabolites thus supporting both growth of healthy gut microbiota and reduction in metabolic diseases risks suggesting a promising strategy for clinical practice.[39–41] Mediterranean diet has been known to aid in weight loss and prevent various diseases due to abundance of polyunsaturated fatty acids (PUFAs), dietary fibre, polyphenols, vitamins and trace elements. Healthy changes in gut microbiota were observed in OW/OB people who adopted the Mediterranean diet pattern in comparison to western diet.[27,42–44] An extract of Carob (Legume tree), common in Mediterranean area, has high fibre content, vitamin and minerals and can be a potential therapy for management and prevention of diabetes and obesity. Carob is known to support balanced gut flora and improve glucose metabolism.[45]

Traditional approach for weight loss, a low-fat diet, has been challenged by alternative diets focusing mainly on increasing protein and decreasing carbohydrate intake. In a dietary intervention trial, a calorie-restricted diet high in protein was linked with higher microbial diversity when compared to calorie-restricted normal-protein diet.[46] Ketogenic diet, low on carbohydrate and high in fat diet, showed increase in microbiome diversity and ratio of Bacteroidetes to Firmicutes.[42,47] Further analysis are however needed to evaluate the efficacy and potential risks of ketogenic diet in weight loss across all ages.[47] In a recent study, intermittent fasting - protein pacing significantly increased beneficial gut microbes and circulating metabolites in eight weeks compared to calorie restriction. Protein pacing refers to intake of 4 meals/day evenly paced at 4 hours and each meal consists of 25-50 g of protein. In addition, comparatively greater reductions in weight loss, BMI as well as fat mass were noted with retention of lean mass, possibly attributed to gut microbiome modulation and improved metabolic outcomes.[48] A prebiotic incorporated high protein, low-carbohydrate diet showed *Faecalibacterium* abundance and was associated with comparatively greater decrease in total body fat and visceral adiposity than a low-carbohydrate diet.[49] The SWEET study observed improved maintenance of weight loss and favourable gut microbiota changes among adults with overweight or obesity who replaced sugar-rich products with sweeteners and sweetness enhancers as part of a reduced-sugar diet, without negative cardiometabolic effects.[50] Variability in microbiome and metabolic responses to dietary interventions may be influenced by baseline microbial composition, fibre type and dose, dietary adherence, and host metabolic phenotype, which together determine responsiveness to dietary modulation.

The effects of various dietary patterns on body weight, body composition and related metabolic parameters mediated through gut microbiome modulation are summarised in **Table 1.**

Table 1. Effect of dietary modalities targeting the gut microbiota for weight loss.

Diet	Alteration in Gut microbiota	Effects on the host
High-fibre diet, diets rich in resistant starch [35–37]	Improves gut microbiota structure; acts as a prebiotic and stimulates growth of beneficial bacteria; ↑ *Ruminococcus*, *Agathobacter*,	↓ fat accumulation; ↑ blood glucose regulation and insulin sensitivity; supports weight reduction and lowers risk of metabolic disease.

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	Faecalibacterium, *Bifidobacterium*; ↑ butyrate production; improves gut barrier function; ↓ inflammation	
Plant-based diet, vegetarian and vegan diet [40,41,51]	↑ *Prevotella* abundance and growth of beneficial bacteria; ↑ SCFA production; ↓ pro-inflammatory cytokines.	Promotes positive changes in body weight and body composition; reduces risk of metabolic diseases.
Low-fat vegan diet [39]	↑ *Faecalibacterium prausnitzii*; smaller reduction in *Bacteroides fragilis*.	↓ Body weight, fat mass and visceral fat; ↑ insulin sensitivity.
Mediterranean diet [27,43,44]	↑ gene richness; ↑ fibre-degrading *Faecalibacterium prausnitzii*, *Bacteroides*, *Prevotella* and other SCFA-producing bacteria.	Greater reduction in body weight and BMI compared with other diets; reduction in waist circumference and fat mass; maintains fat-free mass; improves insulin sensitivity and inflammation; decreases cardiovascular risk.
High-protein diet [46,52,53]	↑ *Akkermansia*, *Bifidobacterium*, and *Faecalibacterium*; ↓ *Prevotella* spp.	↓ Fat mass; maintenance of fat-free mass; improved insulin resistance.
Ketogenic diet [42]	↑ *Akkermansia muciniphila* and *Parabacteroides*; variable changes in *E. coli* and *Lactobacillus*; ↓ *Bifidobacterium* and some Proteobacteria.	↓ Glucose levels and BMI with associated ketosis; aids weight loss, visceral fat reduction and appetite control.

BMI: body mass index; FAO: fatty acid oxidation; GLP-1: glucagon-like peptide-1; SCFAs: short-chain fatty acids; WC: waist circumference.

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2.2. Physical Activity as a Microbial Modifier

Physical exercise along with dietary changes have been associated with reduced obesity and cardiovascular risks. Athletes exhibit richer alpha diversity than obese individuals probably due to positive influence of physical activity and healthy diet. Recent studies, though limited in humans, have observed a close association between physical activity and gut microbiota underscoring the potential of exercise to modulate gut microbiota composition in obesity and metabolic diseases. Studies have noted that changes in the composition of the gut microbiota in obese gut varied with type of exercise. High-intensity interval training (HIIT) and resistance training in non-dieting OW/OB postmenopausal women reduced abdominal and visceral fat mass partly associated with exercise-induced modulation of faecal microbiota; changes in beta, but not alpha diversity were noted.[54] Exercise induced changes in beta diversity with decreased heterogeneity when vigorous activity was followed in OW/OB individuals.[55] Exercise increased butyrate-producing bacteria independent of diet and there was a higher abundance of Firmicutes genus (*Ruminococcaceae* or *Fecalibacteria*) noted.[56] Six weeks of moderate-to-high intensity aerobic exercise were beneficial in modulating gut microbiota diversity; it increased *Bifidobacteriaceae*, *Bacteroides* and *Akkermansia* abundance and decreased *Proteobacteria* in OB individuals.[57] Aerobic training at moderate intensity was also beneficial in previously sedentary healthy individuals with significant changes in variations of *Clostridiales* and *Streptococcus* noted.[58] Further studies need to investigate role of aerobic training in OW/OB individuals. Another study on IF and HIIT in adult OB women noted no changes in gut microbiota composition but suggested that exercise may play a modulatory role in acetate production.[59] Resistance training for six weeks showed mixed effects on gut microbiome in OW/OB young adults; it increased *Roseburia* abundance with minor shifts in microbial pathways, however no significant shifts in the microbial diversity was noted.[60] Exercise may modulate profile of gut microbiota by reducing endotoxemia and impairing inflammatory signalling pathway.[57,61,62] Though physical activity drives a subtle positive shift towards a healthier microbiome in OW/OB individuals, the exercise intensity, type, duration or volume still remains unclear due to lack of more qualitative and quantitative studies in humans. Inconsistent findings across studies may be attributed to differences in exercise modality, intensity, duration and participant characteristics as well as the relatively modest and potentially transient effects of physical activity on gut microbiome composition.

2.3. Microbiota-Targeted Therapeutics

Modulation of the gut microbiome through biotic supplementation represents a targeted approach to influence host metabolic pathways relevant to obesity. The effects of prebiotics, probiotics, synbiotics and postbiotics on host metabolic outcomes and commonly used biotic formulations are summarised in **Table 2**.

Table 2. Effects of biotics on host health.

Biotics for weight loss	**Benefits on host**	**Commonly used biotics**
Prebiotics [19,63–66]	Reduced BW, BMI, WC and fat mass; improved glucose and lipid metabolism and glycaemic control; anti-inflammatory	Inulin-type fructans (FOS, inulin, and oligofructose) or GOS.

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	effects; reduced serum C-reactive protein and ghrelin.	
Probiotics [18,66–80]	Reduced BMI, BW, WC and waist-to-hip ratio; reduced fat mass, percent body fat and abdominal subcutaneous fat; reduced total cholesterol, LDL-C, serum glucose and HbA1c and increased HDL-C; reduced food intake and positively influenced appetite-regulating hormones such as leptin and adiponectin.	*Lactobacillus* species including *L. gasseri*, *L. rhamnosus*, *L. plantarum*, *L. curvatus* and/or *Bifidobacterium* species ; next-generation probiotics such as *Faecalibacterium prausnitzii*, *Akkermansia muciniphila* or *Clostridia* strains.
Synbiotics [18,70,74,79,81]	Reduced BMI, BW, WC and waist-to-hip ratio; reduced fat mass, percent body fat and visceral fat; improved lipid profile and inflammatory markers; reduced food intake and positively affected leptin and adiponectin.	Probiotic-prebiotic mixtures combining *Lactobacillus* and *Bifidobacterium* with FOS, GOS, inulin or polydextrose.
Postbiotics [79,82–84]	May reduce food intake and appetite by regulating hormones such as GLP-1 and PYY; positive effects on obesity have been noted in animal studies.	SCFAs, peptides, enzymes, teichoic acids and vitamins; commonly used postbiotic types include paraprobiotics and FIF.

BMI: Body mass index; BW: Body weight; FIF: Fermented infant formula; FOS: Fructo-oligosaccharides; GLP-1: Glucagon-like peptide-1; GOS: Galacto-oligosaccharides; HbA1c: Haemoglobin A1c; HDL-C: High-density lipoprotein-cholesterol; LDL-C: Low-density lipoprotein-cholesterol; PYY: Peptide YY; WC: Waist circumference.

2.3.1. Prebiotics

Prebiotic refers to substrates that are utilised by host microorganisms to confer a health benefit. Most prebiotic interventions increased the abundance of *Actinobacteria* and *Bifidobacterium*, regarded as beneficial microbiota, which could promote the SCFA levels and maintain gut health. [66] Prebiotics decreased HbA1c and fasting glucose.[67] In contrast, studies investigating the use of prebiotics in obesity have reported mixed results.[19]

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2.3.2. Probiotics

Probiotics are live microorganisms that are administered in specific dosage for specific duration to exert certain host health benefits. Several studies have shown beneficial effects of probiotic supplementation in treating obesity [70]. Some probiotic strains are shown to be more effective in reducing BMI and hip circumference [68], with *Lactobacillus* and *Bifidobacterium* species being more effective against obesity [69,70]. Probiotic interventions were mostly effective in increasing *Lactobacillus* abundance and reducing body weight and fat.[66]

The effects of probiotics were dose- and duration-dependent.[67,71,74] In addition, probiotics improved glucose and lipid profiles [67,71]. Probiotic supplementation within dairy matrices could have anti-obesity effects by lowering lipid concentrations and reducing anthropometric parameters.[75]

In OW/OB postmenopausal women, probiotics regulated glucose metabolism and inflammatory processes, although effects were mild, suggesting their utility as a complementary treatment.[54] Probiotics also reduced lipid profile and inflammatory markers in OW/OB children.[77] and reduced fasting blood glucose, BMI and inflammatory markers in OW/OB adolescents.[78]

Probiotics promote tight junction integrity, reducing intestinal permeability and preventing endotoxemia and LPS-induced inflammation, which leads to increased insulin sensitivity and satiety. Increased leptin in adipose tissue and increased GLP-1 and PYY in the intestine contribute to reduced food intake and enhanced satiety. More research is needed to identify optimal species or strains, dosages, duration and delivery methods for obesity management [72]

The mechanistic links between specific probiotic strains, microbial metabolites and host metabolic pathways are detailed in **Table 3.**

Table 3. Gut microbiota-related biotics in obesity: proposed mechanisms and reported outcomes.

Probiotics	**Prebiotics**	**Postbiotics**	**Proposed pathway**	**Reported outcome**
Lactobacillus (*rhamnosus*, *gasseri*, *plantarum*, *paracasei*, *curvatus*) [85–87]	Inulin, FOS	SCFAs (acetate, propionate)	↑ AMPK/PPARs (FAO); ↑ GLP-1 signalling; microbiota modulation	↓ body weight and fat mass; ↑ insulin sensitivity
Bifidobacterium (*animalis/lactis*) [88]	GOS	SCFAs (acetate)	↑ barrier function; ↓ endotoxemia; ↑ lipolysis/FAO	↓ inflammation and adiposity
Akkermansia muciniphila (live/pasteurised,	Mucin, inulin	Propionate, indoles	↑ barrier function; ↓ endotoxemia; ↓ inflammation;	↓ metabolic endotoxemia and obesity risk

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e.g., AKM Lab-01) [89–91]			↑ GLP-1 signalling; ↑ bile acid metabolism	
Bifidobacterium longum APC1472/BB536 (synbiotic) [92,93]	Resistant starch, FOS	SCFAs, lactate	↓ appetite and ghrelin; ↑ homeostasis; ↓ fat accumulation	↓ food intake and fat storage
Faecalibacterium prausnitzii [94,95]	Inulin, resistant starch	Butyrate	↑ barrier function; ↑ IL-10/Tregs; ↓ lipid accumulation; ↑ FAO	↓ obesity, inflammation, and insulin resistance
Clostridium butyricum [96]	Resistant starch, FOS	Butyrate	↑ barrier function; ↓ endotoxemia; ↓ inflammation; ↑AMPK/PPARα/FAO	↓ body weight and fat mass; ↓ hepatic steatosis; ↑ insulin sensitivity

AMPK: AMP-activated protein kinase; FAO: fatty acid oxidation; FOS = fructo-oligosaccharides; GLP-1: glucagon-like peptide-1; GOS = galacto-oligosaccharides; PPARα: peroxisome proliferator-activated receptor alpha; PPARs: peroxisome proliferator-activated receptors; SCFAs: short-chain fatty acids; Tregs: regulatory T cells.

2.3.3. Synbiotics

Synbiotics, a mixture of both probiotics and prebiotics, serve to further enhance the beneficial effects of probiotics. Probiotic or synbiotic supplementation significantly reduced anthropometric indices such as BMI, birth weight, waist circumference and waist-to-hip ratio in healthy, overweight and obese individuals with or without associated metabolic disorders compared to control groups. [18,67–70]

Body composition studies demonstrated significant reductions in fat mass and percent body fat, with no difference in fat-free mass or lean body mass compared to controls.[18] These effects were observed when probiotics or synbiotics were consumed either naturally through food or as supplements.[18] Synbiotic supplementation significantly improved lipid profiles, obesity indices such as body weight and waist circumference and inflammatory markers [81] Probiotic or synbiotic supplementation also had positive effects on appetite-regulating hormones such as leptin and adiponectin [74]

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2.3.4. Postbiotics

Postbiotics are biological components produced by probiotics that exert beneficial effects on the host. In animal studies, postbiotics showed positive anti-obesity effects, while human clinical trials observed improvements in body composition and anthropometric indices that may help prevent cardiometabolic diseases in individuals with obesity. Postbiotics were shown to reduce adipogenesis and increase energy expenditure. [18,66–80,82]

2.3.5. Next-Generation Probiotics

Although *Bifidobacterium* and *Lactobacillus* strains remain the most commonly used probiotics, next-generation probiotics such as *Faecalibacterium prausnitzii*, *Akkermansia muciniphila* and selected *Clostridia* strains have demonstrated promising results in preclinical and emerging clinical studies (**Table 3**).

The heterogeneity in outcomes observed with biotic interventions likely reflects strain-specific effects, variations in dosage and duration, differences in delivery matrices, and host-related factors such as baseline microbiota composition and metabolic status.

2.4. Faecal Microbiota Transplantation

Faecal microbiota transplantation (FMT) was initially developed for treatment of infections especially recurrent *C. difficile* infections. Following its success in treating *C. difficile* infections, recently FMT has been studied to address non-infectious diseases such as metabolic diseases and obesity. FMT which involves transfer of healthy donor faecal material to the recipient is proposed to restore gut microbiota balance in the recipient.[97] While FMT provides important mechanistic insights into microbiome–host interactions, its clinical applicability in obesity remains uncertain.

Evidence from animal studies suggests that FMT may be beneficial in preventing obesity and associated metabolic diseases. Germ-free mice colonised with microbiota from obese humans developed obesity while those receiving microbiota from lean donors continued to remain lean supporting a causal role of the gut microbiome in obesity development.[98,99] However, translation of these findings to humans has been inconsistent, highlighting key differences between controlled experimental models and complex human metabolic environments. Human studies on effects of FMT on obesity are very limited and report mixed findings. Observed benefits are generally modest, variable across studies and often transient, with limited evidence supporting sustained weight loss or long-term metabolic improvements. A RCT on obese adolescents observed no weight loss post FMT, however a reduction in abdominal adiposity was reported. [98,99] Human FMT studies examining its benefits on metabolic syndromes also report variable outcomes, with some reporting metabolic improvements while others demonstrating no clear clinical benefit despite sustained alterations in gut microbiota composition.[100] In another study, preliminary data revealed that FMT may be beneficial in preventing metabolic syndrome in individuals with obesity.[101] Outcomes may also be influenced by donor characteristics and variability in microbiota engraftment, which can affect the reproducibility and durability of responses. A 4-year followup study in obese adolescents treated with a single FMT noted reductions in waist circumference and total body fat as well as improvements in metabolic parameters compared to the placebo group.[102] Animal studies have also noted an alteration in dopamine and serotonin after FMT and similar effect was observed in obese humans with metabolic syndrome possibly mediated through alterations in plasma metabolites, composition and involvement of the GBA.[103] Overall, while FMT remains a valuable research tool, current evidence does not support its routine clinical use for obesity, and further studies are needed to optimise donor selection, engraftment and long-term efficacy.

3. Future Directions & Research Gaps

Despite growing evidence that diet, physical activity, microbiota-targeted biotics and FMT can influence gut microbiome composition in obesity, important research gaps persist. Human studies of

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dietary and physical activity interventions are heterogeneous and largely short-term with inconsistent findings and limited clarity on dose-response relationships or the optimal dietary patterns, fibre types and exercise modality, intensity, duration and volume required for sustained microbiome-mediated metabolic benefits [7,8,55–61,67]. While prebiotics, probiotics and synbiotics generally show favourable effects on body weight and metabolic outcomes, their clinical translation is constrained by population heterogeneity, strain specificity, variability in formulation and dosing and limited long-term safety data, particularly in immunocompromised populations [17,80,105,106]. Evidence for FMT in obesity is strong in animal models but limited and inconsistent in humans highlighting the need for larger, well-designed longitudinal trials [98]. Across interventions, mechanistic human studies, stratified obesity phenotyping and longitudinal multiomics approaches are required to support the development of safe and personalised microbiome-based therapies.

4. Conclusion

Microbiome-targeted interventions for obesity appear to enhance metabolic responses and treatment efficacy through modulation of microbial energy extraction, inflammation, gut barrier function and metabolic signalling potentially contributing to inter-individual variability in obesity and the limited long-term success of calorie restriction. High-fibre diets are among the most effective in reshaping the gut microbiome, with exercise providing complementary benefits on microbial diversity and SCFA production. Probiotics and synbiotics complement lifestyle and pharmacological therapies, while next-generation biotics including *Akkermansia muciniphila*, *Faecalibacterium prausnitzii* and select Clostridia together with postbiotic SCFAs show promise in targeting adiposity, insulin resistance and metabolic inflammation. Future advances will rely on well-designed clinical trials and multiomics-driven precision approaches to personalise microbiota-targeted interventions alongside standard obesity treatments.

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