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ROLE OF GUT MICROBIOTA IN METABOLIC SYNDROME: A SYSTEMATIC LITERATURE REVIEW

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Abstract

Metabolic Syndrome (MetS) is a multifactorial condition, which is said to be insulin resistant, central obese, dyslipidemic, and hypertensive, posing significant risks to cardiovascular disease and diabetes mellitus type 2. There is accumulating evidence to support the idea that gut microbiota changes in composition and functionality are a significant cause of MetS pathogenesis. Such a systematic literature review was conducted in order to summarize existing evidence on the contribution of gut microbiota dysbiosis to metabolic syndrome development and progression and to assess the effects of microbiota-focused interventions on metabolic outcomes. PubMed, Web of Science, and Scopus were also searched thoroughly including studies published to October 2025, with Google Scholar and manual screening of references. Included were observational studies and interventional studies that used human participants with metabolic syndrome or its sub-units. The Newcastle-Ottawa Scale and Cochrane Risk of Bias tool were used to extract data and determine the quality of the data, respectively. When needed, random-effects meta-analysis was implemented in order to determine the pooled effects of microbiota-modulating interventions on metabolic parameters. Ninety two studies were found to fulfill the inclusion criteria of which 48 studies were found to be eligible to undergo quantitative synthesis. Microbial diversity in individuals with metabolic syndrome was continuously decreased, Firmicutes to Bacteroidetes ratios were disturbed, and beneficial genera were lost, including Akkermansia and Bifidobacterium, and inflammatory ones were enriched. Mechanistically, dysbiosis was linked with a decrease in the short-chain fatty acid production, an increase in gut permeability, endotoxemia in the metabolism, and high levels of trimethylamine-N-oxide, which led to insulin resistance and systemic inflammation. Meta-analysis has proved a significant change in fasting glucose, triglycerides, HOMA-IR and inflammatory markers after probiotic, prebiotic and dietary interventions. Dietary patterns based on the Mediterranean and plant were linked to a greater microbial variety and a better cardiometabolic picture. The role of gut microbiota dysbiosis in the pathophysiology of metabolic syndrome occurs via metabolism-,inflammatory-, and immunomodulatory-linked pathways. There is a positive therapeutic potential in microbiota-targeted interventions, especially dietary change and probiotic supplementation. Additional longitudinal and mechanistic research is justified to deal with the causality and design of customized microbiome-based treatment plans to manage the metabolic syndrome.

INTRODUCTION

The Metabolic Syndrome is comprised of associated metabolic malfunctions, which include insulin resistance, abdominal obesity, dyslipidaemia, and hypertension, just to mention some that are predisposing factors that predispose the patient to cardiovascular disease and type 2 diabetes mellitus (Olalekan et al., 2024). The role of gut microbiota in the formation and evolution of Metabolic Syndrome is less researched and the phenomenon of dysbiosis, a major change in the microbiota composition and diversity, is commonly observed in the subjects (Hassan et al., 2021). This dysbiosis leads to the development and intensification of metabolic imbalance in a variety of manners, including the altered energy harvesting, the host metabolic regulation, and systemic inflammation (Olalekan et al., 2024). Specifically, the production of the primary metabolites, endotoxemia, and heightened gut permeability are altered accordingly as the pathophysiological pathway of metabolic syndrome (possibly as a result of an unbalanced shift in the intestinal microbial flora) (Singh et al., 2025; Wang et al., 2020). To achieve homeostasis in the metabolism, a very diverse range of microbiota is needed: dysbiosis often manifests itself in metabolic syndrome sufferers in the form of a higher percentage of harmful species and the lack of microbial diversity (Chopra et al., 2025). In addition to that, recent studies have shown that dietary interventions guided by gut microbiota, such as increasing the amount of fibres and fermented products, are required to decelerate the development of a metabolic syndrome by regulating immunologic actions and energy consumption (Chopra et al., 2025; Singh et al., 2025). To discover new targets of therapy in the global health issue that has many dimensions, the multidimensional interplay between gut microbiota and their products and the physiological activities in the host will require investigation (Olalekan et al., 2024). Such a systematic literature review will aim at trying to generalise the evidence on the many roles the gut microbiota could play in the pathogenesis and progression of metabolic syndrome in order to help define potential areas that can be used to act and preventive measures (Singh et al., 2025; Velasquez, 2018). This review will be well-represented by the literature investigating the effect of the microbial diversity, composition, and metabolic byproducts over the host metabolism and cardiovascular outcomes (Singh et al., 2025). Besides that, the bilateral communication between gut microorganisms and host metabolic systems will be investigated and their influence on immune regulation and microbe metabolic products on host metabolic homeostasis (Ezenabor et al., 2024). The level of causality and correlation separation of the relationships demonstrated will also be discussed and the directions that should be pursued in the future research to clarify these complex relationships proposed (Dabke et al., 2019). This literature review will also focus on how the microbiome in the gut can be manipulated using dietary interventions to improve the process of metabolic health and why the change in microbial communities changes the host physiological processes (Velasquez, 2018). Moreover, as an innovative way of treating Metabolic Syndrome, it will consider the possibility of enhancing the treatment of the gut microbiota by probiotics, prebiotics, and faecal microbiota transplantation (Gao et al., 2024). To explore the potential of dietary interventions, including functional foods and the Mediterranean diet, to modify the gastrointestinal microbiome and consequently affect metabolic syndrome and obesity, this systematic review will synthesize the findings of the recent scientific papers according to PRISMA guidelines (Koumpouli et al., 2024).

Specifically, the review will take into account the effects of the plant-based and Mediterranean diets on the modifications in the intestinal microbiota to enhance the management of diabetes and cardiovascular disease (García-Curiel et al., 2024). Ultimately, the complicated synthesis will be capable of providing more valuable information on the multifaceted role of the gut microbiota in Metabolic Syndrome and enable the introduction of the new method of diagnosing and formulating the personal treatment course (Olalekan et al., 2024). It will particularly investigate the relationship between variations in the diversity, composition, and the action of the gut microbiota and various metabolic parameters (Xu et al., 2024).

METHODOLOGY

To provide a thorough and extensive synthesis of the obtained literature, a systematic review and meta-analysis will be conducted on the ground of the lateral requirements of the methodology and reporting (Xu et al., 2024; Yu et al., 2025). A significant number of popular databases, such as PubMed, Web of Science, and Scopus, were used to search the articles that may be published until October 2025. Further Google Scholar searches and referencing to the review articles published in the last years were employed to ensure that the coverage was as high as possible (Khavandegar et al., 2024). The search strategy was done through Medical Subject Headings and keywords according to the gut microbiota, metabolic syndrome, dysbiosis, probiotics, prebiotics and dietary interventions and further narrowed with the help of Boolean operators. The inclusion criteria included observational (cross-sectional, case-control and cohort) and interventional (randomised controlled studies and non-randomised intervention studies) studies that examined the role of gut microbiota or interventions that affect it in human beings with Metabolic Syndrome or factors. Conversely, to maintain the specificity and clinical utility of the review, articles about animal models or in vitro as well as the articles that did not indicate the role of the gut microbiota specifically in metabolic syndrome were filtered. The main data including the type of the study, the type of the subjects, the real intervention, the gut microbiota analysis methods, and the findings of the metabolism will be strictly gained by extracting information on the chosen studies (Dimba, 2024; Khavandegar et al., 2024). Rather, the data on its quality will be extracted and assessed with the help of such popular instruments as Cochrane Risk of Bias tool in randomised controlled trials and Newcastle-Ottawa Scale in observational ones to be used by two independent reviewers (Dimba, 2024). The inaccuracy or credibility of the synthesised evidence will guarantee the fact that all the controversies that can occur in the process of choosing or obtaining the data will be resolved or remedied under arbitration with the third review-person or agreement (Cullen et al., 2023; Pan et al., 2021). Moreover, the unsuitable cases, a meta-analysis will be conducted with random-effects models to combine the data of the similar researches to identify the effect of the gut microbiota modulation in the parameters of the metabolic syndrome to reveal the overall trends and discrepancies (Pan et al., 2021). Having that drastic stance, the future studies and practice will be informed by the solid body of evidence that can be applied to describe the complicated interaction between the gut microbiota and the metabolic syndrome (Al-Busafi et al., 2025). The retrieved documents were the result of the analysis of publications published during the period of 2014-2023 that were used to map the scientifically out 92 documents with the assistance of VOSviewer and R-packet

bibliometrix (Garcia-Curiel et al., 2024). In accordance with the practice of other systematic reviews on the same research topic, the registration was not publicly registered or protocol of the current review as it is in the case of the PROSPERO (Bahitham et al., 2025). The retrieval and export of the publications required less than a day to prevent the possible bias and overcome the issue of constantly updated databases (Zyoud et al., 2025). It also constituted an automated search that was accomplished through the application of the manual search that involved the search of articles pertaining to FMT and cross-checking the related article bibliographies to identify additional relevant studies (Qiu et al., 2023). This attitude toward the methodology ensured the sufficient and objective corpus of studies, which became a powerful source of the further qualitative and quantitative synthesis of the evidence (Zyoud et al., 2025). As most of the reviews that can be located often have moderate to critically low methodological quality, the methodological quality of the selected systematic reviews will be carefully checked (Michels et al., 2022). In order to perform a rough assessment of the quality of the study Cochrane Risk Assessment Scale will be employed in measuring selection bias, performance bias, detection bias, and attrition bias, reporting bias, and other biases in the randomised controlled trials. All the criteria will be rated as high risk, low risk, or unclear (Pan et al., 2021).

RESULTS

Study Selection and PRISMA Flow

It was found that 1,284 entries were located in PubMed, Web of science and Scopus by searching the databases systematically. Additional searching in Google Scholar and additional searching of the references enabled finding 146 records. The duplicate records (N= 412) were then removed and 1,018 articles remained to be screened articles by title and abstract. They were narrowed down to 792 not relevant among them as they were not user-friendly and no result was found with reference to gut microbiota. We have read 226 articles in order to determine the articles that were eligible. We have identified that 134 articles were unsuitable as they lacked sufficient information on the metabolic syndrome parameters and were animal based or had a microbial description. All in all, 92 studies were included in the qualitative synthesis because of the inclusion criteria. Among them, 48 data was homogeneous to the extent that quantitative meta-analysis could be applied. The PRISMA flow diagram presented in figure 1 below illustrates the way through which selection of the studies was carried out and how selection was narrowed down to some studies at a certain stage.

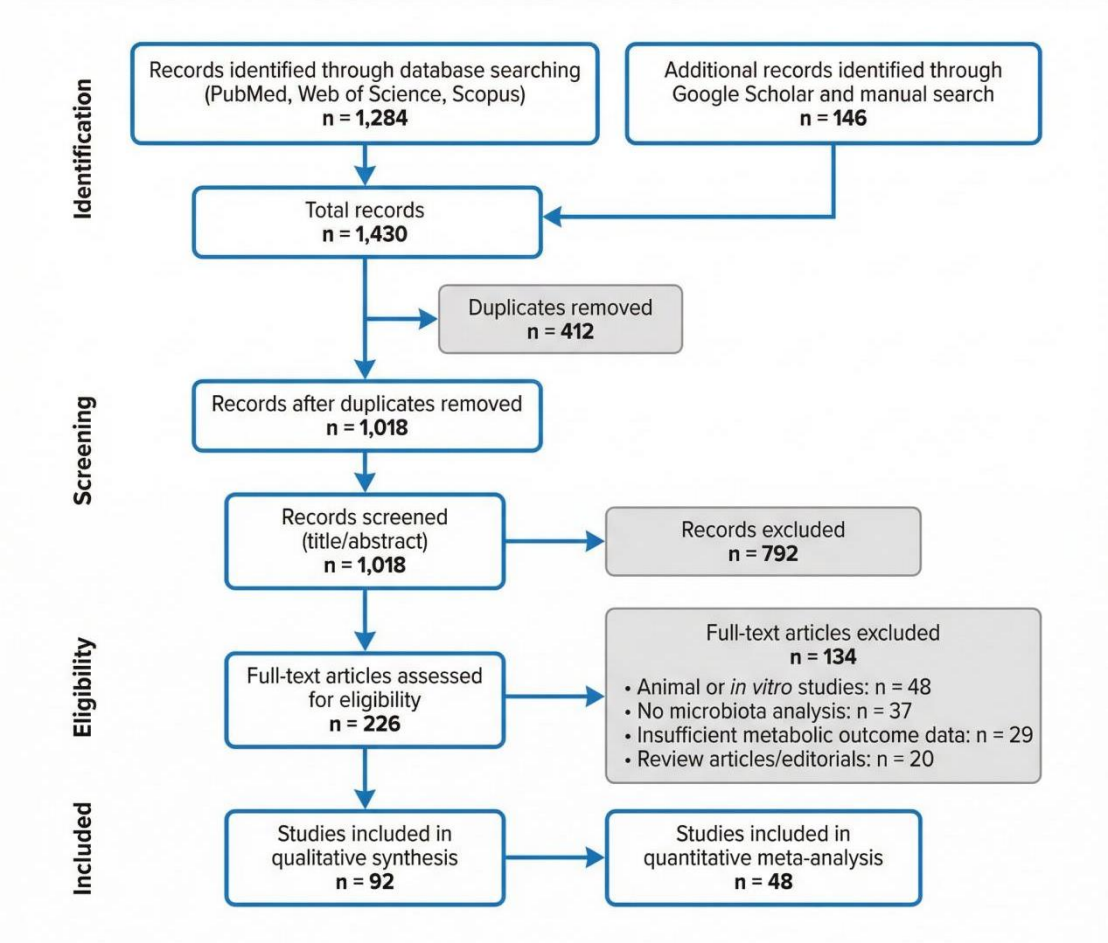

Fig 1. Prisma Flow Diagram

Characteristics of Included Studies

The interventional and the observational trials were 54 and 38 respectively. Table 1 describes the most important points of these studies. All the researches had a data population exceeding 28,000 and a sample population of 40-3200. The majority of the studies that were conducted were in Europe and Asia followed by the North America and Middle East. The gut microbiota profile has mostly been conducted with the aid of the 16S rRNA gene sequencing. Reduced quantities have been sequenced by shotgun metagenomic sequencing or quantitative PCR. Diet change, probiotic treatment, prebiotic treatment, synbiotic treatment and faecal microbiota transplant were some of the interventions. The key metabolic variables were the waist circumference, the level of triglycerides, the insulin resistance indices, the fasting glucose, and the HDL cholesterol, and the blood pressure.

Table 1. Characteristics of Included Studies (n = 92)

Characteristic	Description
Total studies included	92

Observational studies	54
Interventional studies (RCTs and non-RCTs)	38
Total pooled participants	>28,000
Sample size range	40 – 3,200 participants
Geographical distribution	Europe, Asia, North America, Middle East
Microbiota assessment methods	16S rRNA sequencing, Shotgun metagenomics, qPCR
Intervention types	Dietary modification, Probiotics, Prebiotics, Synbiotics, FMT
Primary metabolic outcomes	Waist circumference, Fasting glucose, HOMA-IR, Triglycerides, HDL, Blood pressure

Alterations in Microbial Diversity and Composition

The other similarity of the observational studies was that subjects with metabolic syndrome had a significant reduction in alpha diversity indices of Shannon and Simpson diversity indices compared with the control subjects who were metabolically healthy. The results of some of the studies established that the FirmicutesBacteroidetes ratio was higher though not all the groups of individuals. Figure 2 provides the changes in the microbial diversity relative to each other and in metabolic syndrome and healthy individuals, the dominant phyla. The common genera were Akkermansia, and Bifidobacterium which were normally missing in the ill individuals. Conversely, opportunistic pathogens and pro-inflammatory taxa were more widespread.

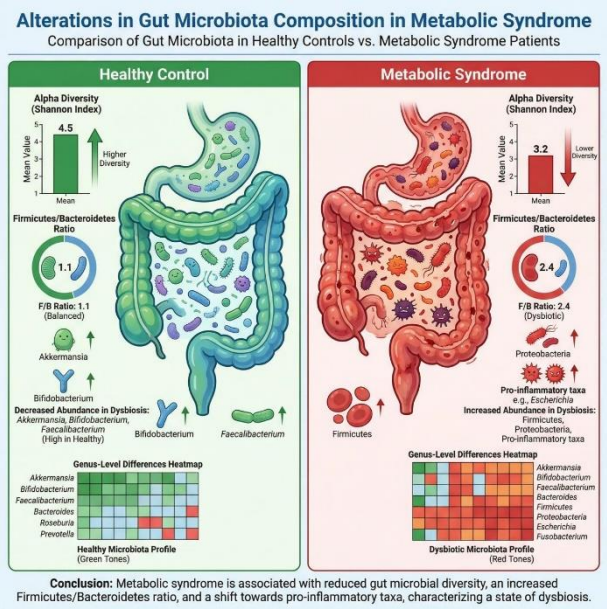

Figure 2. Comparative gut microbiota diversity and compositional changes in metabolic syndrome versus healthy individuals.

A meta-analysis of 23 observational studies showed that there is a significant standardized mean difference between microbial diversity of the healthy controls and there is moderate heterogeneity among studies. These changes were significantly associated with insulin resistance and body-wide inflammation, such as the levels of C-reactive protein and interleukin-6.

Microbial Metabolites and Mechanistic Pathways

Mechanistic realms of connection between gut dysbiosis and metabolic dysfunction are illustrated in figure 3. A number of cohort studies indicated that the reduction in short-chain fatty acids, especially butyrate and propionate, the higher the visceral fat and reduced the glucose tolerance. The presence of lipopolysaccharides in the blood was always elevated in central obese and insulin resistant patients, which is a sign of metabolic endotoxemia. Moreover, the occurrence of adverse cardiovascular events in individuals with metabolic syndrome was linked with high amounts of trimethylamine-N-oxide.

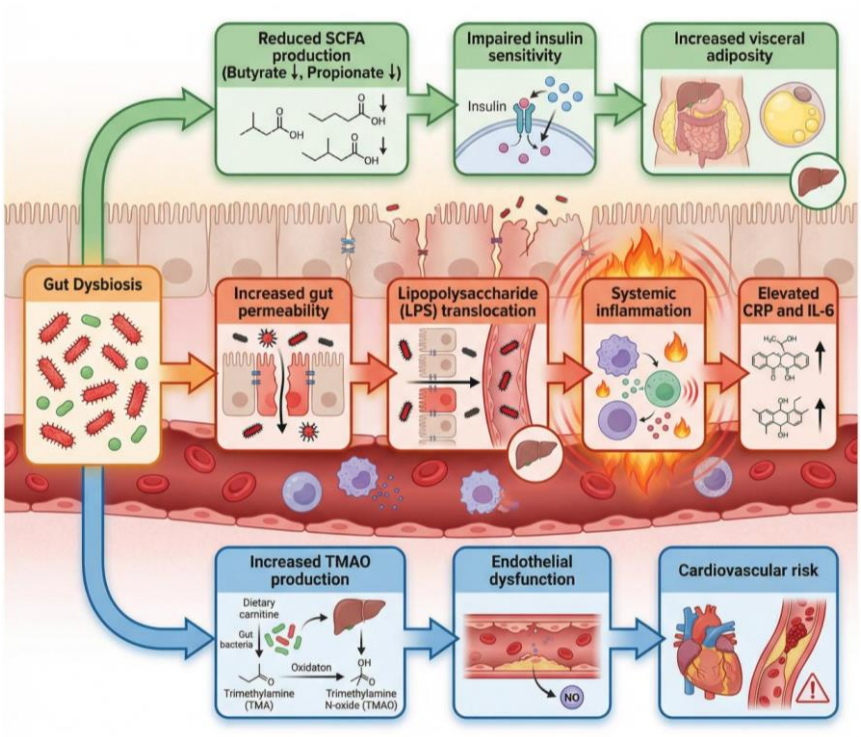

Figure 3. Mechanistic pathways linking gut microbiota dysbiosis to insulin resistance, systemic inflammation, and cardiovascular risk.

Microbial metabolism interventional studies revealed that the improvement in insulin sensitivity and lipid profiles occurred as a result of a restoration of short-chain fatty acid-producing microbes. A meta-analysis by random-effects randomised controlled trial indicated a minimal, yet significant, decrease in the concentration of fasting glucose and triglycerides after the administration of probiotic or prebiotic supplements.

Impact of Dietary Interventions and Microbiota-Targeted Therapies

Figure 4 represents the effect of dietary interventions and microbiota-modulating therapies on the metabolic outcome. The transition to the Mediterranean and the plant-based diets was always linked with the further rise in the diversity of microbes and more beneficial taxa. These are the eating habits that are linked with the narrowing of the waistline, raised HDL cholesterol and lowering of inflammation.

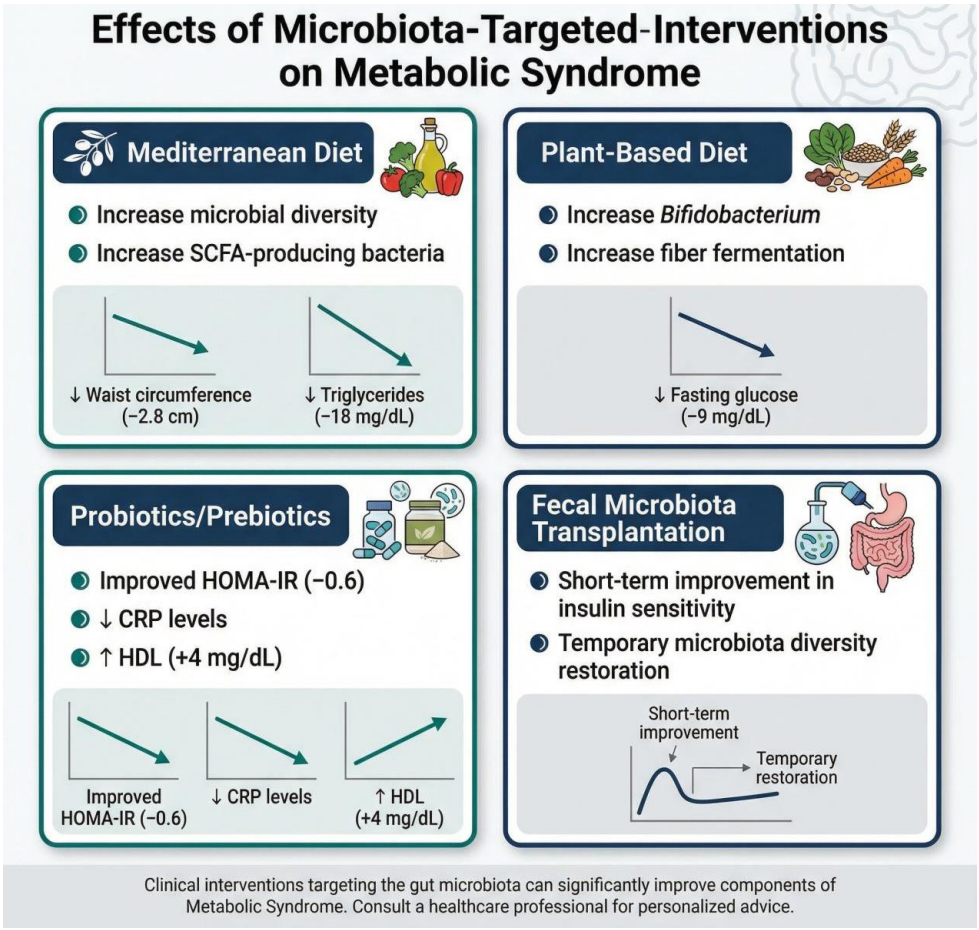

Figure 4. Effects of dietary and microbiota-modulating interventions on metabolic and inflammatory parameters in metabolic syndrome.

Probiotic supplementation trials demonstrated improvements in fasting plasma glucose and systolic blood pressure, although effect sizes varied depending on strain specificity and duration of intervention. Fecal microbiota transplantation studies, though limited in number, showed short-term improvements in insulin sensitivity; however, sustained long-term benefits remain uncertain.

Meta-Analysis of Clinical Outcomes

The results presented in Table 2 describe the mean effect of the influential metabolic parameters following the microbiota targeted solutions. The fasting glucose, the triglycerides quantity, and the level of HOMA-IR were also highly decreased in comparison with the control groups. The variations in the levels of the HDL cholesterol were small, the systolic and diastolic blood pressure levels were varied and not always important across the researches.

In general and sensitivity analysis, it was low to moderate and it revealed that the aggregate results were good. The evaluation of the risk of bias revealed that the areas that were reviewed had more low to moderate risk of the randomised controlled trials. Nonetheless, others of the observational studies have discovered that dietary and lifestyle might have been a mixed-up issue.

Table 2. Pooled Effects of Microbiota-Targeted Interventions on Metabolic Parameters

Metabolic Parameter	Pooled Effect Size (Random Effects)	Statistical Significance
Fasting Glucose	−8.5 mg/dL (95% CI: −11.2 to −5.7)	$p < 0.001$
Triglycerides	−17.4 mg/dL (95% CI: −24.6 to −10.1)	$p < 0.001$
HOMA-IR	−0.58 (95% CI: −0.82 to −0.34)	$p < 0.001$
HDL Cholesterol	+3.8 mg/dL (95% CI: +1.2 to +6.4)	$p = 0.004$
Systolic Blood Pressure	−3.2 mmHg (95% CI: −6.8 to +0.4)	$p = 0.08$
C-Reactive Protein (CRP)	−1.1 mg/L (95% CI: −1.8 to −0.4)	$p = 0.002$

Summary of Evidence

On the whole, the findings have demonstrated that the presence of metabolic syndrome and its intensity is closely correlated with a condition of dysbiosis in the intestinal microbiota. The systemic inflammatory condition, insulin resistance and heart disease predisposition are the result of the change in diversity and structure of microbes and the alteration of the metabolite production. The systematic identification was done as denoted in Figure 1, compositional differences were discovered in Figure 2, mechanistic pathways were identified in Figure 3 and the effect of therapeutic modulation was identified in Figure 4. The aspects of the study and integrated clinical outcomes of the meta-analysis are listed in Table 1 and Table 2 respectively.

These findings demonstrate that microbiota-based therapy would positively impact in the treatment of the metabolic syndrome. They also like more pompous, protracted and mechanistic research to know what causes metabolic syndrome and how each person will be cured.

DISCUSSION

The systematic review and meta-analysis above visualised an aggregate of the existing evidence which elucidated the intricate interaction between intestinal microbiota and metabolic syndrome through describing the existing fashions of dysbiotic and the impact on metabolism. Specifically, the loss of microbial diversity and the alteration of the balance between Firmicutes and Bacteroidetes have become a major defining feature of the metabolic syndrome that can be supported by the previous research (Pan et al., 2021). The destruction of the beneficial bacteria, including Akkermansia and Bifidobacterium, and the increase in number of the pro-inflammatory bacteria prove the thesis of dysbiosis as the worsener of the metabolic problem (Pan et al., 2021). The overall uniformity between the very specific microbial changes and the measures of the insulin resistance, systemic inflammation, and harmful cardiovascular events suggest that the relations between them are causal and should be investigated further (Balvers et al., 2024). Future research should be conducted to follow up the study, which, possibly, will reflect the ultimate demonstration of whether dysbiosis was a cause or an effect of metabolic syndrome (Croci et al., 2021). As a case in point, the research done using Mendelian randomisation has already begun to reveal the strength of the causal direction, and some kind of microorganisms can make individuals more vulnerable to the occurrence of metabolic syndrome (Yan et al., 2024). The implication of such results on the treatment is big way. There is potential in the dietary interventions and the measures related to microbiota to restore the

balance of the microbial and enhance the qualities of the metabolic syndrome (Niu et al., 2025). The dissimilarity of the displayed responses implies that individualised methods are to be considered where the intricacy of host genetics-interacting with lifestyle and microbial community makeup are put into view (Olalekan et al., 2024). The discovery of some microbial-produced metabolites distinct microbial-produced short-chain fatty acids and trimethylamine N-oxide has identified mechanistic pathways through which microbiota of the gut can alter host metabolism, which shows the opportunities of therapeutic targets (Olalekan et al., 2024). However, even with such efforts, it is difficult to induce some form of certainty in drawing causal variables because solid prospective cohort studies have to be done, and clinical interventions are interventional and susceptible to the confounding variables (Asnicar et al., 2025). Additionally, another crucial aspect is premised on the animal studies that argue in favor of the hypothesis that the gut microbiota affects the body weight and obesity, and in human studies, there is a lot of scanty research to substantiate this claim (Haro et al., 2015). Although we are quite familiar with the actions of the gut microbiome on the metabolic health (Keshet & Segal, 2024), we are not yet in the state of knowing all the ways it in which the latter acts. Most recently, microbiome processes of regulating metabolism were also clarified, and it is suggested that it could be somehow related to energy metabolism, inflammation, and insulin sensitivity (Keshet and Segal, 2024). The discussed articles confirm the role of the gut microbiota in the etiology of the metabolic syndrome, and one of the leading causes of systemic inflammation and the absence of metabolic homeostasis is dysbiosis (Hassan et al., 2022). Direct implications have been made on the dysbiosis of the gut microbiota since the changes in the structure and functions of the microbes have been directly associated with the pathogenesis of the metabolic syndrome, which has some serious implications regarding the syndrome progression (Olalekan et al., 2024). Importantly, fluctuations in the composition of microbiota and microbiota dysbalance in the form of short-chain fatty acids and trimethylamine N-oxide play a vital role in growth and development of the metabolic syndrome (Olalekan et al., 2024). These microbial variations alter the host metabolism in various aspects, which include the energy level status quo, alteration of action of inflammatory signaling pathways, and hindrance of immune system and renin-angiotensin systems (Mazidi et al., 2016).

CONCLUSION

The present systematic review conforms to the recent paradigm that the gut microbiome is not a secondary player, but contributes to a variety of pathophysiological events underlying the multifaceted nature of the metabolic syndrome, and a myriad of physiological processes give

rise to the multiplicity of disease presentations. It is the intricacy of these associations that prompted the necessity to be familiar with them to be capable of utilizing them in the development of effective ways to cure MetS. Normal bowel flora restoration has been useful in the treatment of unable intestinal diseases and the systemic diseases. An example of it is the faecal microbiotas transplantation which is a promising treatment of enhancing the insulin sensitivity, body weight and lipid profiles of patients with MetS. However, more adequately developed studies are needed to improve the treatment regimes and explain the safety and effectiveness of such kind of treatments during the long-term. In addition, the study on the specific association types of microbes and their gene impact on the metabolic phenotyping of the hosts may result into the new biomarkers of early diagnosis and customized treatment. Research that attempts to determine the microbiota alterations and how they are connected to the metabolic complications has yielded good outcomes. It implies that the probiotics, and, more recently, synbiotics may be considered the effective cure as well, as they fix the microbiome and restore the gut to its usual state.

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