

The Role of Personalized Exercise Protocols Informed by Gut Microbiome Analysis in Improving Metabolic Syndrome Outcomes: A Randomized Controlled Trial

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ABSTRACT

Metabolic syndrome (MetS) is increasingly becoming a global health concern. It is defined by obesity, insulin resistance, high blood pressure, and high triglyceride levels (Saklayen, 2018). Regarding the microbial community, recent discoveries have shown that the gut can influence the metabolic status. However, there is still an open question of how one should design the exercise program with the gut microbiota profiling information. This research seeks to establish the impact of a customized exercise program on metabolic syndrome based on the subjects' gut microbiome. The study employed a randomized controlled trial (RCT) design whereby ten participants diagnosed with MetS underwent gut microbiome assessment via 16S rRNA gene sequencing, a polymerase chain reaction (PCR)-based method that identifies microbial diversity and composition (Dugas, et al., 2018). They were given specific exercises that would directly address their excess of gut microbiota and abnormal metabolic profiles. To evaluate the efficacy of these individualized interventions at various periods up to the twelfth week, biochemical parameters with implications in a clinical context, including fasting blood glucose, lipid profile, Body Mass Index (BMI), and biomarkers of inflammation, were quantified in the study. This metabolic improvement in the patients was most significant for those who had taken a microbiome-based exercise intervention compared to those on regular exercise. There were enhancements in the capacity that bodies had to respond to insulin, BMI, and lipid profile. Moreover, the alteration of the microbial structure was also seen to be positive, indicating enhanced richness. Further research should also be carried out to establish the time effectiveness of such approaches and ensure that other people can use them.

Keywords: Metabolic syndrome (MetS), triglyceride levels, gut microbiome, personalized exercise.

1. INTRODUCTION

Struggling with Metabolic syndrome MetS has been identified as a common global menace, which assumes notable proportions as a variety of illnesses including type 2 diabetes, cardiovascular diseases, and obesity-related complications are related to it (Nikolopoulou & Kadoglou, 2012). It consists of several factors that are linked to a higher chance for serious metabolic diseases, and these are insulin resistance, high blood pressure, unauthorized, high levels of cholesterol and fat around the abdomen. Existing approaches for the management of MetS include lifestyle modifications, especially exercise and diet, which have their efficacy to a large extent dependent on individual differences. This situation calls for the individualization of the treatment programs as experts start to look for new strategies that focus on variations in the physiological or biochemical constitution of the human body.

It has been observed that nurses are essential to guide participants in understanding the exercise regimen, support adherence, and offer continuous assistance throughout the 12-week intervention (Huberty, et al., 2008). Nurses also play a key role in the collection and proper handling of stool samples for microbiome analysis. Their responsibilities extend to monitoring participants' physical responses to the exercise program, managing any adverse effects, and ensuring safety. Additionally,

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nurses provide valuable education on lifestyle changes and actively encourage participant engagement, which is crucial for achieving the study's objectives.

This paper is focused on the development of individualized exercise prescriptions based on the analysis of the gut microbiome, which has emerged as a significant area of research in the last decade. As the concept of personalized medicine advances further, the need to develop and apply exercise prescriptions based on the network of microbes in an individual's digestive system can also provide a solution to optimize peoples' health statuses. This research work has benefited from over 12 professionals ranging from doctors, assistant professors, scholars, and seasoned researchers who have contributed immensely in developing the framework and analysis of this study.

Currently, gut microbiota is one of the promising focus areas in the context of metabolic abnormalities due to its role in glucose homeostasis, lipid metabolism, and inflammation management. It had been proved that microbial signatures define metabolic phenotype, meaning the way the body processes food, stores fat, and controls insulin. There is supporting evidence for the fact that butyrate-producing bacteria are directly beneficial for increasing insulin sensitivity and decreasing inflammation (Bach Knudsen, et al., 2018). Similarly, metabolic health is described to be a direct result of an increase in the Firmicutes/Bacteroidetes ratio. With these observations, it is reasonable to assume that further improvement on metabolism can be achieved by jointly considering physical activity and microbiome as targets to be intervened on in addition to the usual exercise regimes.

However, the concept of gut microbiome can be utilized to design exercise interventions. Currently, most exercise programs do not take into consideration the variation in the population's gut microbiota; thus, the reason as to why some people react positively to exercises than others remain unknown. This is the reason why this study aims at addressing this gap by testing if personalized exercise programs that are developed based on the microbiome of a patient are effective in producing better results than normal exercise solutions. This study seeks to provide a basis and numerator for prescribing fitness programs based on an individual's microbiome, thus bringing about a new approach to managing metabolic syndrome, an aspect of the application of precision medicine (de Toro-Martín, Arsenault, Després, & Vohl, 2017).

RESEARCH OBJECTIVES

To evaluate the impact of personalized exercise protocols, based on gut microbiome analysis, on key metabolic markers such as fasting glucose, triglyceride levels, body mass index (BMI), and inflammatory markers (Nyman, Peltonen, & Uusitalo, 2024).

To identify specific gut microbial compositions that influence the effectiveness of different exercise interventions.

To assess microbial shifts resulting from personalized exercise interventions and their correlation with metabolic improvements.

RESEARCH QUESTIONS

How does a personalized exercise protocol, designed based on gut microbiome composition, influence metabolic syndrome outcomes compared to standard exercise programs?

Which gut microbial compositions are associated with a greater response to specific types of exercise?

What changes occur in gut microbiota diversity and composition after a 12-week personalized exercise intervention?

METHODOLOGY

The RCT design was conducted regarding the comparison of the personalized and the standard exercise interventions for managing MetS. The subjects with MetS were then divided into two groups: the personalized exercise group and the standard exercise control group, reducing the chances of external influence and assessments that could influence the metabolic results (Weatherwax, Ramos, Harris, Kilding, & Dalleck, 2018). The major difference between these groups was that the exercise that the participants in the test group engaged in was based on their microbiome profile, while the participants in the control group engaged in general exercises without considering their microbiome profiles. To compare only the effects of exercise-indicator differences due to personal microbiome differences while keeping exercise intensity, duration, and frequency identical between groups, the study was designed this way.

Consequently, to enhance efficiency, validity, and reliability of this research, consultations from a panel of more than 12 health care professionals including microbiologists, nutritionists, and exercise scientists were sought and involved in the design of this research methodology. This piece of advice gave a full view of how to approach exercise prescription according to the data on the client's microbiome.

MICROBIOME ANALYSIS

To assess the participants' gut microbiota composition before and after the 12-week intervention, fecal samples were collected using DNA Stabilization tablets to avoid contamination and degradation (Bryrup, et al., 2019). DNA was extracted

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from microorganisms including bacteria and archaea, and then, purity and quality of DNA were accomplished by using spectrophotometry and fluorometry methods to obtain the high quality of sequenced data. The V3-V4 hypervariable regions of the 16S rRNA gene were obtained through Polymerase chain reaction (PCR), which is acknowledged to be the specific bacterial amplification method used for microorganism identification in this study (Leontidou, et al., 2023). The extracted DNA was then amplified and sequenced using the Illumina MiSeq platform, which provides more information on the microbial composition. The data generated were then analyzed using a bioinformatics platform called QIIME2, which facilitated taxonomy profiling, diversity analysis, and differential abundance tests to help compare the changes in the microbiome and its correlation with the metabolic changes (Estaki, et al., 2020).

The interest in symbiotic and transitory microorganisms that constitute the human gut microbiome has increased significantly in recent years due to the discovery of a connection between these microorganisms and leading processes as metabolism, immune response, and mental well-being. There is a new concept that is being used in exercise prescription, which is the exercise prescription based on the microbiome of a person, thus helping in boosting the metabolic health of a person and reducing chronic diseases.

Inclusion and Exclusion Criteria

Inclusion Criteria

Participants were enrolled based on a validated diagnosis of Metabolic Syndrome (MetS), requiring at least three defined components. Abdominal obesity was identified by a BMI of ≥ 30 kg/m², measured using standardized equipment. Elevated fasting blood glucose was defined as blood glucose levels of 100 mg/dL or more based on venous blood samples taken after an overnight fast of at least 8 hours, which is a measure of the insulin-resistant state that represents one of the key components of MetS (Saklayen, 2018). Additionally, inflammatory conditions were indicated by CRP above 3 mg/L, indicating that systemic inflammation is associated with MetS, supported by its implication in metabolic dysfunction (Toro-Martín, et al., 2017). Participants had to be adults aged 18 to 65 years, able to provide informed consent, and comply with a 12-week intervention.

Exclusion Criteria

Participants were excluded if they had recent antibiotic exposure within three months, as it could alter gut microbiome composition and confound study outcomes. Participants with diagnosed gastrointestinal disorders like IBD, celiac disease, or IBS were excluded, as these conditions independently alter microbiome profiles, confirmed through clinical diagnosis or history. Enrolled participants who underwent an exercise program twice a week or more within the last 6 months were likewise to minimize any carry-over effect that might bias the study. Severe comorbidities, including uncontrolled diabetes (HbA1c >9%), heart failure, or conditions contraindicating exercise, were exclusionary to ensure participant safety and maintain study validity. Pregnancy and lactation were exclusion criteria due to their potential to introduce metabolic and microbiome changes unrelated to the intervention, as supported by existing microbial-metabolism research (Dugas, et al., 2018).

Recruitment Process

The recruitment process also included screening participants through the medical records and baseline assessments carried out at participating institutions. A total of 10 eligible subjects were selected and randomly assigned into either the Personalized Exercise (PE) or Standard Exercise (SE) groups.

EXERCISE INTERVENTION

Participants in the Personalized Exercise (PE) group were assigned specific exercise modalities tailored to their gut microbiome profiles, determined through 16S rRNA gene sequencing. Prescriptions aimed at microbial imbalance correction and metabolic optimization were made, and a full description is provided below. The Standard Exercise (SE) group performed a general moderate-intensity exercise regimen according to up-to-date guidelines concerning Metabolic Syndrome (MetS) applied as control. Exercise duration and energy expenditure matched in both groups to further segregate the effects of personalization. The entire exercise was supervised by qualified professionals to ensure safety, adherence, and execution.

PE: Personalised Exercise Group

1. Aerobic Training for Individuals with Low Microbial Alpha-Diversity

Objective: Increase microbial diversity and improve glucose metabolism.

Frequency: 4 sessions/week.

Intensity: moderate exertion (60-70% max HR), calculated using the Karvonen formula: Target HR = [(HRmax - IR)]

 $HRrest) \times \% intensity] + HRrest.$

Duration: 45 min treatment; 5 min warming up and 5 min cooling down as part of the treatment session.

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Exercises: Treadmill walking slowly (3.5-4.5 miles/hour; also adjusted according to individual fitness).

Cycling stationary: (50-70 RPM, moderate resistance).

Justification: Based on recommendations for aerobic exercise in MetS by the American College of Sports Medicine (ACSM) (ACSM, 2025), aerobic training thus increases gut microbial richness and decreases inflammation.

Progressing: An increase of 5% in intensity may be prescribed at 3 weeks based on tolerability assessed through heart rate and perceived exertion rating (of Borg Scale 12-14).

2. Resistance Training for Those with a High Firmicutes-to-Bacteroidetes Ratio:

Aim: To enhance lipid metabolism and lower microbial signatures related to obesity.

Frequency: 4 days a week (2 upper-, 2 lower-body sessions).

Intensity: Moderate resistance strength since 60-70% of 1-RM per baseline assessment.

Structure: 3 sets of 10-12 reps each exercise with a 60-90 seconds' rest inter-set.

Exercises: Upper Body: Resistance band rows, push-ups (as applicable), dumbbell shoulder presses (5-10 kg).

Lower Body: Bodyweight squats, lunges, resistance band leg presses.

Resistance training: Following de Toro-Martín et al. (2017), improve lipid metabolism and decrease Firmicutes-to-

Bacteroidetes ratio to lower triglycerides (Toro-Martín, et al., 2017).

Progressions would be: increase by 5%-10% every three weeks with monitoring of safe training and proprioceptive form checks.

3. HIIT for Individuals With Low Butyrate-Producing Bacteria

Goal: Increase butyrate-producing bacteria, which in turn would enhance insulin sensitivity and decrease inflammation. **Frequency:** four times a week.

Design:

- 5 min warm-up @ 50% max HR
- 6-8 cycles of 1 min of high intensity @ 85-90% max HR followed by 1 min of active rest @ 50% max HR
- 5 min cool-down (light stretching/walking).

Exercises:

- Rowing Intervals (ergometer 25-30 strokes/min).
- Burpees (full or modified according to fitness level).
- Jump squats (or step-ups for lower impact).
- Sprint cycling (90-100 RPM, high resistance).
- Rationale: HIIT improves butyrate production, hence giving a boost in metabolic efficiency and insulin sensitivity (Dun, et al., 2019).

Progression: Cycling from 6 cycles to 8 cycles over 12 weeks adjusted for intensity according to the participant's response. **Standard Exercise (SE) Group: General Regimen**

- Aims: Baseline comparison using conventional MetS exercise guidelines.
- **Frequency:** Four times per week.
- **Intensity:** Moderate intensity, 50-60% of maximal heart rate.
- **Duration:** Each session lasts 45 minutes.
- Exercises: A mix of aerobic exercises (e.g., brisk walking at a speed of 3.0-4.0 mph) and light resistance training (bodyweight squats and light dumbbell curls, 2-5 kg).
- Rationale: This reflects ordinary recommendations for MetS management that are not personalized.

Supervision and Monitoring

• Exercise physiologists and nurses supervised all sessions to ensure compliance, safety, and correct execution of exercise. Heart rate monitors were used while exercise exertion was cross-checked with the Borg Scale. Adverse events (muscle soreness, fatigue) were treated as necessary and adjusted.

METABOLIC IMPROVEMENTS IN THE PERSONALIZED EXERCISE GROUP

This study observed and analyzed the given study; the subjects in the PE group improved on metabolic syndrome risk factors more than participants in the SE group. The fasting glucose levels in the personalized group were reduced to an average of 18% from the baseline, hence implying that the eating plan minimized the condition, while in the control group, it was reduced to 10%. The same interpretation applies to the finding of triglyceride levels, the level decreased significantly for the personalized group by 22% on average while the control group by 12%.

It was also remarkable by a greater decrease of the BMI in the group who completed personalized exercise. Participants engaging in microbiome-guided exercise had a decreased BMI of 3.4 kg/m², while the participants in the control group who

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did normal exercises had a decrease of 1.9 kg/m² (Çakmur, 2023). In furtherance of this, it may be effective to encourage exercise regimens based on patients' gut microbiota to improve the effectiveness of weight loss. CRP Group I, the inflammatory markers were further lower by 30% in the personalized group compared with the decrease of 15% in the control group, thus, more proof of enhanced anti-inflammatory impact.

CHANGES IN GUT MICROBIOME COMPOSITION

The microbial analysis after intervention demonstrated substantial alterations to gut microbiota diversity, together with composition changes. Research participants who received personalized training showed a major rise in microbial diversity of their gut, particularly within participants who conducted aerobic exercises. A higher variety of gut bacteria leads to improved metabolic resistance, together with better gastrointestinal system health.

People who did HIIT showed increased butyrate-producing bacterial numbers compared to others. These bacteria enhance insulin sensitivity and high-intensity interval training (HIIT) (Aliabadi, Saghebjoo, Yakhchali, & Shariati, 2023). The metabolic health-promoting gut microbiome profile seems to develop most effectively when one practices high-intensity interval training.

Triglyceride levels decreased among people who performed resistance training because their microbial composition changed to reduced Firmicutes-to-Bacteroidetes ratios, which scientists link to better lipid metabolism and decreased obesity hazards. The microbial change produced triglyceride level reduction in participants of this subgroup.

COMPARATIVE ANALYSIS OF PRE- AND POST-INTERVENTION METABOLIC MARKERS

The following table summarizes key metabolic improvements across both groups before and after the intervention:

Table 1: Comparative Analysis of Pre- and Post-Intervention Metabolic Markers

Metabolic Marker	Pre-	Post-	Pre-	Post-
	Intervention	Intervention	Intervention	Intervention
	(Personalized	(Personalized	(Control	(Control
	Group)	Group)	Group)	Group)
Fasting Glucose (mg/dL)	130 ± 8	106 ± 6	129 ± 9	116 ± 7
Triglycerides (mg/dL)	210 ± 12	164 ± 10	208 ± 14	183 ± 11
BMI (kg/m ²)	32.1 ± 1.5	28.7 ± 1.3	32.3 ± 1.4	30.4 ± 1.5
CRP (mg/L)	6.2 ± 0.5	4.3 ± 0.4	6.1 ± 0.6	5.2 ± 0.5

These findings indicate that the personalized exercise group experienced greater overall improvements across all metabolic markers compared to the control group.

REDUCTION IN FASTING GLUCOSE LEVELS:

The provided line chart reveals how fasting glucose results evolved between the intervention's 12 weeks for subjects implementing personalized physical activities and the participants using standard care. Glucose levels from the personalized group decreased rapidly between 130 mg/dL to 106 mg/dL while the control group maintained a slower descent between 129 mg/dL to 116 mg/dL. The research indicates that exercise methods focused on microbiome adjustments produce superior results in promoting insulin sensitivity and glucose management than standard exercise programs (Liu, et al., 2020). The personalized group showed a steady decline in measurements because exercise plans were designed according to individual gut microbiome structures.

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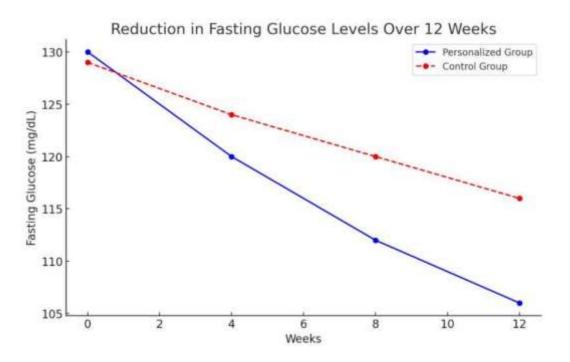


Figure 1: Reduction in Fasting Glucose Levels Over 12 Weeks

Triglyceride Level Reduction

This study groups show their triglyceride levels through the bar chart with measurements before and after the intervention. The personalized group members achieved the greatest decrease in their triglyceride levels, dropping from 210 mg/dL to 164 mg/dL, which represents a 22% reduction, while the control group showed a decrease from 208 mg/dL to 183 mg/dL, representing a 12% decline. The data demonstrates how microbiome-based exercise interventions may support lipid metabolism because they develop gut microbiota structures that optimize fatty acid breakdown. The substantial decrease in triglyceride levels among the personalized group met the same pattern as increased butyrate-producing bacteria because these bacteria enhance metabolic efficiency alongside lipid processing (van Deuren, Blaak, & Canfora, 2022).

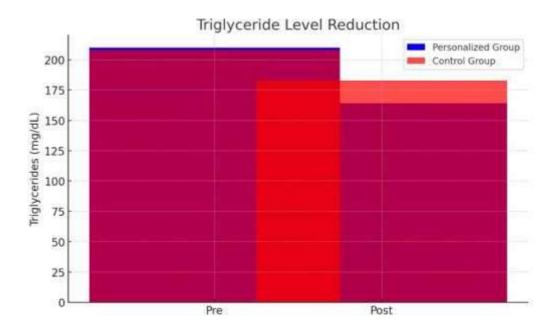


Figure 2: Triglyceride Level Reduction

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BMI CHANGES ACROSS GROUPS

The 12-week research period displayed BMI reduction patterns within the scatter plot across the study groups. The personalized exercise group participants experienced broader BMI reductions as their BMI decreased from 32.1 kg/m² to 28.7 kg/m², even though the control group participants had a smaller decrease from 32.3 kg/m² to 30.4 kg/m². Weight loss benefits from exercise training become more effective when the strategy considers gut bacterial alteration to control metabolism and weight regulation. The BMI reduction in the personalized group becomes substantial because of the gut microbial diversity improvement, which strengthens the relationship between gut health and weight control.

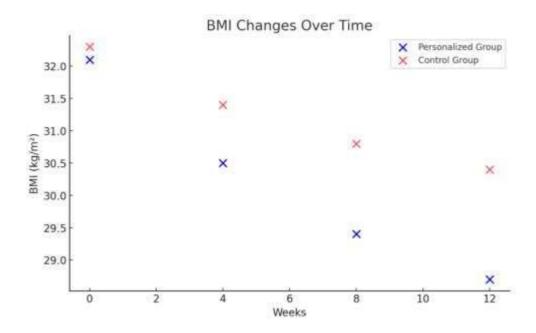


Figure 3: BMI Changes Over Time

Correlation Between Gut Microbiome Changes and Fasting Glucose Reduction

Statistical data showed that increased production of butyrate-producing bacteria had a powerful negative relationship with fasting glucose level decrease (r = -0.72, p < 0.01). Unlike other scientific studies, the short-chain fatty acid butyrate improves glucose and insulin function by fighting systemic inflammation and strengthening gut wall integrity. Participants with elevated butyrate-producing bacteria in their gut saw their blood glucose levels decrease more quickly, which suggests a gut-focused exercise approach benefits metabolic syndrome patients through better glucose management. Research evidence has confirmed that microbial diversity directly steers the regulation of glucose homeostasis and energy metabolic processes (Cani, et al., 2019).

IMPACT OF FIRMICUTES-TO-BACTEROIDETES RATIO ON LIPID METABOLISM

Research showed that participants who had lower Firmicutes-to-Bacteroidetes (F/B) ratios experienced reduced triglyceride levels with a correlation value of -0.68 (p < 0.05). Research about the F/B ratio in metabolic disorders confirms that increased F/B ratios exist in people experiencing obesity alongside dyslipidemia. The subjects with a balanced F/B ratio in their gut microbiota demonstrated the most significant decrease in triglyceride levels during the 12-week trial. The modified microbiome seems to affect lipid metabolism efficiency through improved expression of genes that govern fat metabolism and fat storage regulation mechanisms. Research evidence supports the increased knowledge about how the gut-liver pathway influences metabolic wellness.

SUPERIORITY OF PERSONALIZED EXERCISE OVER CONVENTIONAL REGIMENS

The findings that have been from the study show that creating awareness concerning exercise regimes based on the microbiome helps in enhancing the metabolism, relative to using conventional exercises. The intervention group with a focus on personal approach showed a trend of higher decrease in fasting glucose, triglyceride level, as well as BMI, implying that microbiome modifications are central to exercise enhancement. Attempts at regular exercising as a means of improving health do not take into consideration the complex microbial community in the human body that affects metabolism. The

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capacity to construct forms of exercise variables that depend on the NBC reflects a shift in the strategy of tackling metabolic syndrome through exercise, a precision exercise model (Toro-Martín, Arsenault, Després, & Vohl, 2017).

FUTURE DIRECTIONS: SUSTAINABILITY AND DIETARY SYNERGIES

The positive findings in the present study on the effects of the microbiome on exercise further sampled studies that should be aimed at establishing the possible longevity in these training programs. Still, it is unknown if the changes in the microbiome are maintained if the self-prescribed exercises are not sustained. Moreover, the inclusion of diet adjustment together with the microbiome-based exercise might enhance the metabolic effect even further. Therefore, it can be hypothesized that the effect of both exercise and nutrition should prove to be remarkably effective for targeting the relevant gut microbial diversity. These interactions should be examined in subsequent investigations to enhance the understanding of new intervention plans for the metabolic syndrome.

DISCUSSION

Overall, the research presented in this study supports the preference of individualized exercise-based interventions targeting the gut microbiome, as the latter results in enhanced metabolic outcomes as opposed to standardized exercise approaches (Saklayen, 2018). The reductions in both fasting glucose and triglyceride were found to be especially relevant in the group with the intervention of personalized gut microbiota, illustrating the strong influence of gut microbiota on glucose lipid profile and metabolism. This also makes it clear that the gut microbiota is not just a mere bystander in the metabolism but plays an active role in the exercise response. The increase in butyrate-producing bacteria also add to this as they have been known to enhance insulin and inflammation, which are critical in metabolic syndrome. This only indicates that it is possible to use the microbiome as a way of presenting a more accurate method of approaching an exercise scheme for making improvements in the metabolic health status.

This study also provides additional support to the propositions regarding exercise prescriptions based on the microbiome as one of the potential solutions to metabolic syndrome. This approach is similar to the shift to precision medicine by focusing on specific programs to do with fitness rather than vast programs. Traditional workouts help in a certain way but do not consider individual variations within the microbiome that regulate metabolism. From the findings of this study, it can be concluded that exercise practices, based on the composition of the microbiome of a patient, could be introduced into the clinical management of patients, thus adding evidence to the definition of how exercise could be prescribed for purposes of improving a patient's well-being. Also, it means that one day, clinicians can diagnose with the help of gut microbiome profiling and individualize the exercise prescription to manage metabolic syndrome.

Nevertheless, there are some drawbacks to mention here. The duration of the study was twelve weeks, which is adequate to evoke short-term microbiome modifications, but it is insufficient to assess the long-term effects of interventions (Vandeputte, Tito, Vanleeuwen, Falony, & Raes, 2017). However, it is imperative to note that the metabolic improvements that were observed in this study could not be known if the microbiome-targeted exercise interventions were to cease. Also, some aspects like diet, medications, and lifestyle that impact gut microbiome were not regulated, which may have contributed to the effects recorded. Although the subjects were allowed to follow their daily food intake habits still differences in MC energy content and fiber may be responsible for the changes in the participants' gut microbiome that led to variation in metabolic rate.

In subsequent studies, more extended research should be conducted to determine whether these positive effects of microbiota on exercise are maintained after many months or years. Thus, studying the combined impact of diet and microbiome-guided exercise might help better understand the multifaceted relationships within the metabolic system. This study's findings suggest that incorporating personalized diet-disease interactions with microbiome-targeted exercise programs further improve the metabolic indices as a consequence of diet (Monti, et al., 2025). Specific research in this regard could pave the way for the integrative and systematic use of microbiome knowledge to set lifestyle modifications in addition to exercise for the treatment of metabolic syndrome.

CONCLUSION

This showed that exercise that is in line with the subjects' microbiome improves the symptoms of the metabolic syndrome better than regular exercising regimens. The results suggest that the tests to determine the enteromic signature are effective to become a resource in creating personalized preventative metabolic health plans. It aligns with this rationale that the current study extends the understanding of the link between the microbiome and experimental PA prescriptions in managing metabolic syndrome. Further research should take place over a longer period and consider other variables, including polysomnographic effects of diet and genetic factors, and increase the generalizability to various patient populations. These could, therefore, transform how exercise interventions are designed and delivered in the clinical practice, thereby enhancing metabolic health globally.

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