

MINI-REVIEW

Therapeutic effects of exercise on metabolic syndrome: A mini-review

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Abstract

Metabolic syndrome, characterized by the confluence of central obesity, dyslipidemia, hypertension, and insulin resistance, is a critical public health challenge that escalates the risk for cardiovascular disease and type 2 diabetes. This narrative review synthesizes contemporary evidence on the role of structured physical exercise in preventing and managing this syndrome. By examining various exercise modalities, we elucidate the physiological and molecular mechanisms underpinning their benefits. The evidence robustly indicates that both aerobic and resistance exercise induce clinically significant improvements across all syndrome components. Aerobic training is effective for enhancing lipid profiles and insulin sensitivity, whereas resistance training promotes muscle mass and basal metabolic rate. Combined exercise programs offer synergistic, multi-system benefits. Despite this strong evidence, real-world application is hindered by challenges in long-term adherence and the need for personalized prescriptions. Consequently, integrating scientifically designed exercise protocols into clinical guidelines and public health policy is paramount for mitigating the global burden of metabolic syndrome.

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1. Introduction

Metabolic syndrome represents a predominant public health crisis of the 21st century, with its escalating prevalence mirroring the global rise in sedentary lifestyles and obesogenic diets.¹ Defined by the concurrent presence of at least three risk factors—including abdominal obesity, dyslipidemia (elevated triglycerides and reduced high-density lipoprotein), hypertension, and impaired fasting glucose—this condition substantially increases the incidence of type 2 diabetes and atherosclerotic cardiovascular

disease, thereby imposing immense socioeconomic costs on healthcare systems worldwide.² The underlying pathophysiology is multifaceted, involving a complex interplay of insulin resistance, chronic low-grade inflammation, and dysfunctional visceral adipose tissue that collectively disrupt metabolic homeostasis.^{3,4}

In this context, physical exercise emerges not merely as a tool for energy expenditure but as a potent therapeutic intervention capable of simultaneously targeting multiple pathological pathways. Regular physical activity induces a cascade of beneficial systemic and molecular adaptations that collectively restore metabolic homeostasis.⁵ These adaptations extend beyond simple caloric balance to encompass fundamental improvements in cellular metabolism, hormonal regulation, and inflammatory signaling that address the root causes of metabolic dysfunction.

The FITT principle (Frequency, Intensity, Time, and Type) provides a foundational framework for prescribing personalized exercise regimens to optimize therapeutic outcomes.⁶ This systematic approach enables healthcare providers to tailor exercise recommendations to individual patient characteristics, preferences, and functional capacities, thereby maximizing adherence and clinical effectiveness. While the clinical benefits of exercise are well-documented, translating this evidence into routine practice remains limited by practical barriers and a lack of standardized implementation strategies.⁷ These barriers include time constraints during clinical encounters, inadequate provider training in exercise prescription, limited reimbursement for lifestyle interventions, and patient-level factors such as motivation, access to facilities, and coexisting medical conditions.

Therefore, this narrative review aims to provide a contemporary synthesis of evidence on the efficacy of various exercise modalities, explore the key physiological mechanisms involved, and discuss future directions for practical integration into metabolic syndrome management.^{8,9} By consolidating current knowledge and identifying evidence gaps, this review seeks to support clinicians, researchers, and policymakers in advancing exercise as a cornerstone of metabolic disease prevention and treatment.

To identify relevant evidence for this narrative review, a systematic literature search was conducted across the major biomedical databases, including PubMed/MEDLINE, Scopus, and Web of Science, supplemented by manual screening of reference lists of identified reviews and original studies. The search strategy employed a combination of Medical Subject Headings (MeSH) and freetext keywords, such as “metabolic syndrome,” “physical exercise,”

“aerobic training,” “resistance training,” “high-intensity interval training,” “insulin resistance,” “dyslipidemia,” and “cardiovascular risk,” connected by Boolean operators. The search was restricted to articles published in English between 2000 and 2025, with a focus on randomized controlled trials, systematic reviews, and metaanalyses that examined the effects of structured exercise interventions on metabolic syndrome components. Studies addressing pediatric populations, animal models, or pharmacological interventions exclusively were excluded. This time frame was chosen to capture both the foundational evidence and the most recent advances in exercise-based metabolic syndrome management while ensuring the inclusion of landmark studies from the past two decades.

2. Therapeutic effects of different exercise modalities

2.1. Aerobic exercise and high-intensity interval training

The assembled literature consistently demonstrates that structured physical exercise is a potent intervention for improving all components of metabolic syndrome. Aerobic exercise, particularly at a moderate intensity for at least 150 min per week, yields significant benefits across multiple cardiometabolic parameters. In a comprehensive meta-analysis, Lin and colleagues reported that exercise training reduces systolic and diastolic blood pressure by 3.5–5.0 mmHg and 2.5–3.5 mmHg, respectively, while also increasing HDL cholesterol by 0.05–0.10 mmol/L.¹⁰ These benefits were dose-dependent, with greater improvements observed at higher exercise volumes, reinforcing current physical activity guidelines.¹⁰ These improvements, while modest in absolute terms, translate to clinically meaningful reductions in cardiovascular event risk when sustained over time.

Furthermore, aerobic exercise significantly improves glycemic control; a landmark study demonstrated a reduction of 0.67% in HbA1c in individuals with type 2 diabetes.¹¹ This degree of glycemic improvement is comparable to that achieved with first-line pharmacotherapeutic agents¹¹ and underscores the potential of exercise as an alternative or adjunct to medication. Recent meta-analyses have further confirmed the robust efficacy of aerobic training on lipid metabolism, demonstrating pronounced reductions in triglycerides and elevations in high-density lipoprotein that are comparable to or superior to those of other lifestyle interventions.^{12,13}

Concurrently, high-intensity interval training (HIIT) has emerged as a potent, time-efficient modality that addresses one of the most frequently cited barriers to exercise participation: the lack of time. Recent trials

indicate that HIIT is particularly effective at enhancing insulin sensitivity and reducing visceral adiposity in individuals with metabolic syndrome, often yielding superior outcomes compared to traditional moderate-intensity continuous training.^{14,15}

2.2. Resistance training and combined exercise regimens

Resistance training performed 2–3 times weekly promotes gains in lean muscle mass, which is crucial for enhancing basal metabolic rate and functional capacity.¹⁶ Skeletal muscle is the primary site of glucose disposal, and increasing muscle mass creates a larger metabolic sink for glucose uptake, thereby improving overall glycemic control. Resistance training also improves bone mineral density, joint stability, and physical function, addressing the broader health needs of individuals with metabolic syndrome who may also be at risk for sarcopenia and functional decline as they age.

Crucially, combined training regimens integrating both aerobic and resistance exercise appear to yield the most comprehensive benefits for individuals with metabolic syndrome. A meta-analysis by Church and colleagues¹⁷ found that combined training was superior to either modality alone for improving insulin sensitivity and reducing visceral adiposity. This synergistic effect likely stems from the complementary physiological adaptations induced by each modality: aerobic exercise enhances cardiovascular efficiency and oxidative capacity, while resistance training builds metabolically active tissue and improves glucose storage capacity.

The superiority of combined approaches has been further substantiated by subsequent research. Zhang and colleagues¹⁸ conducted a systematic review and meta-analysis of randomized controlled trials examining combined aerobic and resistance training in patients with metabolic syndrome, concluding that multimodal interventions produce superior improvements in waist circumference, blood pressure, lipid profiles, and fasting glucose compared to single-modality programs. These findings support current guidelines recommending that individuals with metabolic syndrome engage in both aerobic and resistance activities as part of a comprehensive exercise prescription.

3. Mechanisms of action and systemic benefits

3.1. Molecular and cellular adaptations

Well-characterized molecular adaptations support the physiological benefits observed with regular exercise. Exercise stimulates the AMP-activated protein kinase

(AMPK) pathway, leading to the translocation of glucose transporter type 4 transporters to the skeletal muscle membrane, thereby facilitating insulin-independent glucose uptake.¹⁹ This mechanism is particularly significant because it bypasses the insulin signaling pathway, which is often impaired in insulin-resistant states. The activation of AMPK represents a fundamental energy-sensing mechanism that coordinates cellular responses to energy stress, promoting catabolic processes that generate adenosine triphosphate while inhibiting anabolic pathways that consume energy.

Furthermore, exercise induces mitochondrial biogenesis by upregulating peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), thereby enhancing oxidative capacity and metabolic flexibility.²⁰ Mitochondrial dysfunction is increasingly recognized as a core feature of metabolic syndrome, and interventions that restore mitochondrial content and function hold particular therapeutic promise. PGC-1α serves as a master regulator of mitochondrial biogenesis, coordinating the expression of nuclear and mitochondrial genes encoding proteins required for oxidative metabolism.

Another key mechanism involves modulation of adipokine secretion from adipose tissue; exercise typically reduces pro-inflammatory cytokines, such as leptin, while increasing the production of anti-inflammatory, insulin-sensitizing adiponectin.^{21,22} Adiponectin enhances insulin sensitivity, promotes fatty acid oxidation, and exerts anti-inflammatory effects, making it a critical mediator of exercise's metabolic benefits. The balance between pro-inflammatory and anti-inflammatory adipokines is increasingly recognized as a determinant of metabolic health, and exercise favorably shifts this balance.

These interconnected cellular adaptations collectively restore systemic metabolic homeostasis. The evidence establishes structured exercise as a cornerstone therapy for metabolic syndrome, with effects that extend across all diagnostic components and address underlying pathophysiological mechanisms.

3.2. Systemic and multi-organ effects

The demonstrated superiority of combined aerobic and resistance training likely stems from its multi-targeted approach, simultaneously improving cardiorespiratory fitness and anabolic capacity.²³ Recent research reinforces this synergy, demonstrating that combined programs elicit greater improvements in endothelial function, inflammatory markers, and overall cardiometabolic risk profiles than single-modality interventions.^{18,24} Endothelial dysfunction is an early step in atherosclerosis, and interventions that improve endothelial reactivity may confer protection against cardiovascular events.

The increase in muscle mass from resistance training is particularly valuable, as skeletal muscle serves as the primary site for glucose disposal and energy expenditure, creating a more resilient metabolic sink that can accommodate postprandial glucose loads without requiring excessive insulin secretion.²⁵ Wolfe²⁵ emphasized the underappreciated role of muscle in health and disease, noting that skeletal muscle dysfunction contributes to the pathogenesis of multiple chronic conditions and that interventions preserving muscle mass and function have broad therapeutic implications.

3.3. Neurotrophic and pro-resolving mediators

Furthermore, emerging research illuminates the role of exercise in modulating key neurotrophic and specialized pro-resolving mediators. Physical activity has been shown to elevate circulating levels of brain-derived neurotrophic factor (BDNF) and lipoxin A4.^{26,27,28} BDNF not only supports cognitive function and neuroplasticity but also enhances peripheral lipid metabolism and insulin sensitivity, creating an integrated brain–body connection that links mental and metabolic health.

Dinoff and colleagues²⁶ conducted a meta-analysis confirming that acute exercise significantly increases blood BDNF concentrations in healthy adults, with implications for both cognitive enhancement and metabolic regulation. Concurrently, Jolleyman and colleagues²⁷ demonstrated that high-intensity interval training increases lipoxin A4 levels while improving insulin resistance and body composition in obese adults, suggesting that exercise promotes the active resolution of inflammation rather than simply suppressing inflammatory mediators.

Lipoxin A4 promotes the resolution of inflammation, a core pathological feature of metabolic syndrome, by actively clearing inflammatory cells and restoring tissue homeostasis. Together, these mechanisms contribute to the protective effects of exercise against obesity, type 2 diabetes, coronary heart disease, and associated cognitive decline. Phillips and colleagues²⁸ reviewed the neuroprotective effects of physical activity, emphasizing that exercise-induced trophic factor signaling supports brain health throughout the lifespan and may protect against age-related cognitive impairment.

The molecular mechanisms—such as AMPK activation and PGC-1 α -mediated mitochondrial biogenesis—not only explain the observed clinical benefits but also open avenues for future “exercise mimetic” strategies and personalized prescriptions based on individual response phenotypes.²⁹ Narkar and colleagues²⁹ demonstrated that pharmacological activation of AMPK and peroxisome proliferator-activated receptor delta pathways recapitulates

some effects of exercise, raising the possibility of developing compounds that could benefit individuals unable to exercise. However, a critical caveat is that these benefits are contingent upon sustained adherence; the rapid reversal of gains upon exercise cessation, known as deconditioning, underscores the need for physical activity to be maintained as a lifelong lifestyle commitment.³⁰

4. Limitations and recommendations

While this review highlights robust evidence for exercise, several limitations must be acknowledged, both in the extant literature and in the inherent limitations of the narrative review methodology. First, the included studies exhibit significant methodological heterogeneity in exercise protocols (intensity, volume, duration) and participant characteristics, complicating efforts to define a universal optimal “dose”.^{31,32} This heterogeneity reflects the complexity of exercise as an intervention and the diversity of populations affected by metabolic syndrome, but it limits the precision with which specific recommendations can be formulated.

Second, a selection bias is often present, as randomized controlled trials frequently enroll motivated volunteers with fewer comorbidities, which may not generalize to the broader, often more complex, metabolic syndrome population encountered in clinical practice.³³ Individuals with multiple comorbidities, significant functional limitations, or socioeconomic barriers to participation are often underrepresented in clinical trials, potentially leading to overestimates of intervention effectiveness when applied to real-world populations.

Third, reliance on self-reported physical activity data in many studies introduces measurement bias and may lead to misclassification of exposure status.³⁴ Objective measures such as accelerometry provide a more accurate assessment but are not consistently employed across studies. Prince and colleagues³⁴ conducted a systematic review comparing direct versus self-report measures of physical activity, finding that self-report tends to overestimate activity levels compared to objective measures, potentially attenuating observed associations with health outcomes.

In contrast, the common conflation of exercise with dietary interventions in study designs makes it difficult to isolate the unique contribution of physical activity.³⁵ Many lifestyle interventions combine exercise with dietary modification, which reflects real-world practice but complicates efforts to determine the specific effects of exercise independent of nutritional changes. Johnston and colleagues³⁵ compared weight loss among named diet programs, highlighting the challenges of isolating individual intervention components.

As a narrative review, this synthesis is also subject to the author's interpretive bias in study selection and emphasis, unlike a systematic review, which follows an explicit, reproducible protocol. The absence of a formal search strategy and quality assessment tool means that different reviewers might reach different conclusions from the same literature.

Finally, while molecular pathways are increasingly clarified, much evidence derives from acute studies or surrogate biomarkers; more longitudinal research directly linking these mechanisms to hard clinical endpoints is needed.³⁶ Haff and Triplett³⁶ emphasized the importance of understanding both acute responses and chronic adaptations to exercise training, noting that the relationship between acute exercise-induced changes and long-term health outcomes remains incompletely characterized.

5. Implications for future research and clinical practice

5.1. Toward precision exercise medicine

To translate evidence into practice, a shift from generic advice to precision exercise prescription is essential. Prescriptions should be personalized, considering FITT variables alongside individual metabolic phenotype, comorbidities, and preferences.³⁷ Ross and colleagues³⁷ articulated the vision for precision exercise medicine, emphasizing the need to understand and address the substantial inter-individual variability in responses to exercise training. Some individuals demonstrate robust improvements in insulin sensitivity with exercise, while others show minimal changes, and identifying predictors of response could enable more targeted and effective interventions.

Clinicians require training to integrate exercise as a vital sign and a core component of treatment plans. This paradigm shift—viewing exercise not as a lifestyle recommendation but as a formal therapeutic intervention—requires changes in medical education, clinical practice, and healthcare reimbursement structures. Sallis and colleagues³⁸ issued a call to action on making physical activity assessment and prescription a medical standard of care, arguing that the failure to address physical activity represents a missed opportunity for disease prevention and management.

5.2. Technological innovations and behavioral support

Overcoming the adherence barrier necessitates innovative strategies, including digital health tools (e.g., wearables, apps) for remote monitoring and feedback, which can support behavioral maintenance.³⁹ Romeo and colleagues³⁹

conducted a systematic review and meta-analysis examining whether smartphone applications can increase physical activity, finding that app-based interventions produce modest but significant improvements in activity levels. These technologies offer the potential for scalable, low-cost interventions that can reach large populations and provide personalized support.

Direito and colleagues⁴⁰ reviewed mHealth technologies designed to influence physical activity and sedentary behaviors, identifying the behavior change techniques commonly employed in effective interventions. These include goal setting, self-monitoring, feedback, and social support, all of which can be delivered through digital platforms. Müller and colleagues⁴¹ examined the effectiveness of e-Health and mHealth interventions in developing countries, finding promising but heterogeneous results that warrant further investigation.

Furthermore, integrating exercise with other lifestyle modifications, particularly dietary improvements, may yield synergistic benefits. Esposito and colleagues⁴² systematically reviewed the effects of the Mediterranean diet on type 2 diabetes, demonstrating that dietary modification significantly improves glycemic control and cardiovascular risk factors. Combined nutrition and exercise interventions likely produce greater benefits than either approach alone, supporting comprehensive lifestyle modification as the optimal strategy.

5.3. Emerging research frontiers

Future research must prioritize long-term randomized controlled trials with diverse, representative cohorts and standardized, objectively measured exercise protocols.⁴³ Troiano and colleagues⁴³ provided reference data on accelerometer-measured physical activity in the United States population, establishing norms that can inform intervention design and evaluation. Longer follow-up periods are needed to determine whether exercise-induced improvements in surrogate markers translate to reductions in hard clinical endpoints such as myocardial infarction, stroke, and cardiovascular mortality.

Deeper investigation into novel areas, such as the exercise–gut microbiome axis and the identification of predictive response biomarkers, can further personalize therapy.^{44,45} Mailing *et al.*⁴⁴ reviewed emerging roles of the gut microbiome in exercise and health, noting that physical activity modifies gut microbial composition and that these changes may mediate some of the metabolic benefits of exercise. Bouchard and colleagues⁴⁵ explored the genomics and genetics of adaptation to exercise, identifying genetic variants associated with trainability and response heterogeneity.

Future research must also address the scalability of interventions in real-world healthcare and community settings. Cost-effectiveness analyses of structured exercise programs are urgently needed to justify their integration into public health funding and insurance reimbursement models. Furthermore, the roles of emerging technologies, such as artificial intelligence for adaptive exercise prescription and virtual reality for enhanced engagement, warrant rigorous investigation.

Research should also expand beyond traditional cardiometabolic markers to include patient-centered outcomes like quality of life, functional independence, and mental health, providing a holistic view of the therapeutic value of exercise. Establishing large, international registries to track the long-term outcomes of individuals with metabolic syndrome who engage in prescribed exercise could provide invaluable real-world evidence to refine guidelines and overcome current evidence gaps related to sustainability and heterogeneity of treatment response.

6. Conclusion

This review consolidates compelling evidence that structured physical exercise is a robust, non-pharmacological therapeutic strategy for metabolic syndrome, inducing beneficial effects across all its components through integrated physiological and molecular mechanisms. From improvements in glycemic control and lipid profiles to reductions in blood pressure and visceral adiposity, exercise addresses the full spectrum of metabolic abnormalities characterizing this condition. Combined exercise regimens appear most effective, offering a holistic approach that simultaneously enhances cardiorespiratory fitness, muscular strength, and metabolic capacity.

However, translating this efficacy into lasting public health impact hinges on addressing the adherence challenge through personalized prescribing and sustained behavioral support. The rapid reversibility of exercise-induced benefits upon cessation underscores that physical activity must be adopted as a permanent lifestyle modification rather than a temporary intervention. Future research must refine precision exercise medicine, validate scalable delivery models, and strengthen the evidence base with long-term outcome studies.

Looking ahead, the perspective must evolve from viewing exercise as a mere recommendation to recognizing it as a core component of disease management, on par with pharmacotherapy. This requires systemic change, including educating healthcare providers in exercise prescription, creating referral pathways to certified exercise professionals, and implementing policy initiatives that

make prescribed physical activity accessible and affordable. Synergistic integration with dietary interventions, stress management, and sleep hygiene will amplify benefits.

Prioritizing exercise as a formal therapeutic modality within healthcare systems is an urgent imperative to curb the global epidemic of metabolic disease and its associated burdens. By embracing a paradigm where exercise is systematically prescribed, monitored, and supported, healthcare systems can unlock a robust, sustainable, and cost-effective tool to combat metabolic syndrome, ultimately reducing its substantial burden on individuals and society. The path forward is clear: embedding structured exercise into the fabric of chronic disease prevention and management is not just beneficial but essential for future public health.^{38,46}

In summary, exercise stands out as a transformative intervention in the management of metabolic syndrome, underscoring its significant impact on both metabolic and overall health. Oral *et al.*⁴⁶ recently reviewed the role of regular physical activity in metabolic health and overall well-being, concluding that exercise represents one of the most effective interventions available for improving population health. The compelling body of evidence highlights that regular physical activity is not merely beneficial but essential in curbing the alarming prevalence of metabolic syndrome, which afflicts an estimated 20–25% of adults globally.⁴⁷ The urgent need for effective therapeutic strategies is paramount, as the rise of sedentary behaviors linked to urbanization and modern lifestyle choices continues to exacerbate this public health crisis.⁴⁷

High-intensity interval training demonstrates particular promise as an innovative exercise approach that maximizes health benefits within time-efficient frameworks, which is crucial for individuals facing significant time constraints. The systematic review by Batacan *et al.*⁴⁸ substantiates that HIIT not only enhances cardiorespiratory fitness but also significantly improves insulin sensitivity when compared to traditional continuous training methods. This flexibility in exercise protocols empowers individuals to adopt physically active lifestyles that are both feasible and sustainable, thereby supporting long-term adherence.

Moreover, the therapeutic ramifications of exercise extend into various organ systems, as reviewed by Thyfault and Bergouignan.⁴⁹ By impacting liver function, adipose tissue dynamics, pancreatic behavior, and even central nervous system regulation, exercise elicits a multifaceted response that contributes holistically to metabolic health. This polypharmacy of benefits reinforces the concept that exercise is a critical cornerstone of metabolic syndrome management, transcending mere calorie expenditure or muscle strengthening.⁴⁹

Additionally, the broader cardiovascular benefits associated with regular exercise, as highlighted by Fiuza-Luces *et al.*⁵⁰, cannot be overstated. They extend beyond the attenuation of traditional risk factors, showcasing improvements in myocardial function and psychosocial well-being. This underscores the necessity for healthcare providers to advocate for exercise not only as an adjunct therapy but as a primary consideration in comprehensive disease management strategies.⁵⁰

As the global burden of metabolic syndrome continues to rise, the imperative to act becomes increasingly urgent. The evidence is robust, the mechanisms are understood, and the tools for implementation are available. What remains is the collective will to prioritize exercise as the therapeutic modality it deserves to be. Moving forward, it is essential to cultivate a societal environment that champions physical activity and eliminates barriers to participation. Collectively, the evidence substantiates the need for a paradigm shift that positions exercise as a primary therapeutic modality in addressing metabolic syndrome. By harnessing the profound effects of exercise, we can not only alleviate the burdens of metabolic syndrome but also enhance the quality of life for countless individuals worldwide.

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