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## NARRATIVE REVIEW

# Exercise therapy in type 2 diabetes mellitus with special emphasis on running: effects on glycemic control, metabolic adaptations, and psychosocial outcomes - *a narrative review*

## HIGHLIGHTS

- ▶ Structured aerobic exercise reduces HbA1c by 0.67–0.89% in adults with type 2 diabetes mellitus.
- ▶ Leisure-time running lowers the risk of incident T2DM by 28% (Aerobics Center Longitudinal Study, n>19,000).

- ▶ Key molecular mechanisms: GLUT4 translocation, AMPK signaling, and PGC-1 $\alpha$ -driven mitochondrial biogenesis.
- ▶ Regular running reduces visceral and hepatic ectopic fat and improves multiple cardiometabolic risk factors.
- ▶ Aerobic training significantly reduces depression and anxiety symptoms and improves quality of life in T2DM.

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## ABSTRACT

**BACKGROUND:** Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease affecting over 500 million adults worldwide and represents one of the most important public-health challenges of the 21st century. Regular physical activity — and structured exercise therapy in particular — is a cornerstone of evidence-based T2DM management.

**AIM:** This narrative review synthesises current evidence on the effects of exercise training on glycemic control and related metabolic, physiological, and psychosocial outcomes in individuals with T2DM, with special emphasis on running as a clinically relevant and globally accessible form of aerobic exercise.

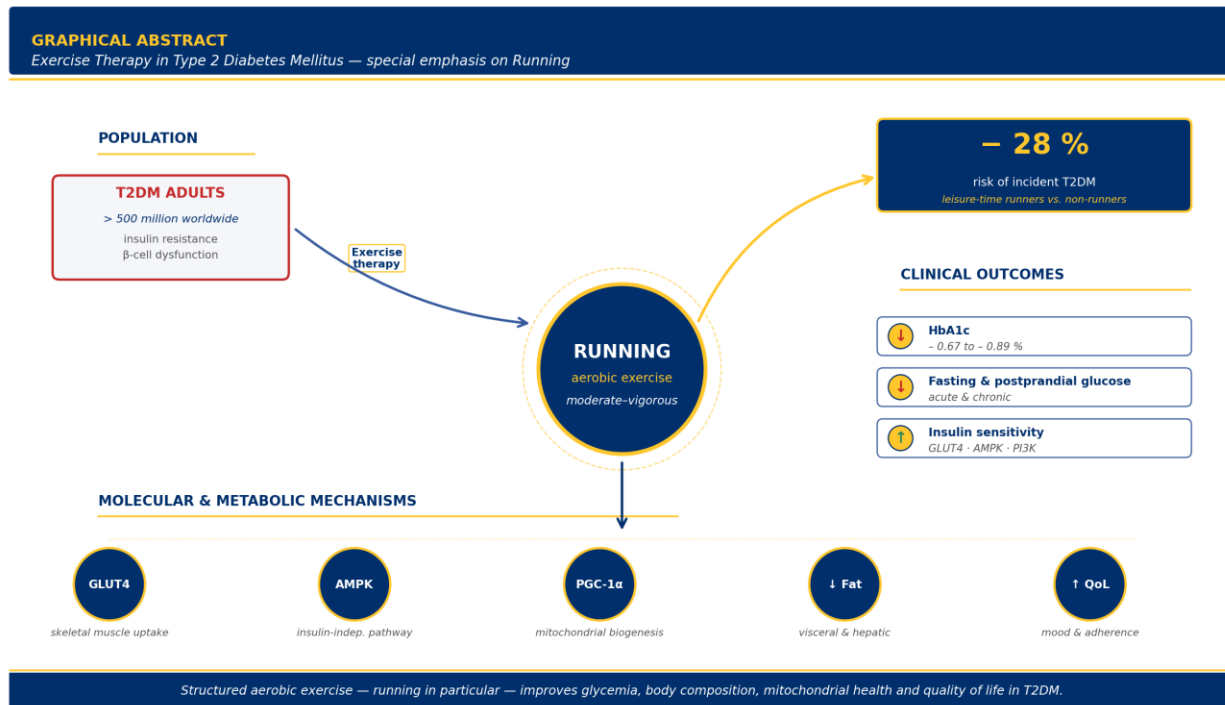
**MATERIALS AND METHODS:** A structured literature search was conducted in PubMed, Scopus, and Google Scholar, encompassing publications from the last decade with particular emphasis on studies published between 2020 and 2026. Meta-analyses, randomised controlled trials, prospective cohort studies, and position statements were included.

**RESULTS:** Evidence consistently demonstrates that structured aerobic exercise produces significant reductions in glycated haemoglobin (HbA1c) and fasting blood glucose. Prospective cohort data show that leisure-time running reduces the risk of incident T2DM by 28%, with dose–response relationships for duration, frequency, distance, and speed. Molecular mechanisms include AMPK-mediated GLUT4 translocation in skeletal muscle, post-translational modifications of insulin-signaling proteins, and PGC-1 $\alpha$ -driven mitochondrial biogenesis. Regular exercise additionally reduces visceral and hepatic ectopic fat, improves multiple cardiometabolic risk factors, and produces clinically relevant psychological benefits including reduced symptoms of depression and anxiety.

**CONCLUSIONS:** Exercise therapy — with running as one of its most accessible and effective forms — provides an advantageous approach to managing all aspects of T2DM. It should be systematically integrated into individualised treatment plans alongside pharmacological and dietary strategies.

**KEYWORDS** type 2 diabetes mellitus; exercise therapy; aerobic exercise; running; glycemic control; insulin sensitivity; glycated hemoglobin; mitochondrial biogenesis.

## GRAPHICAL ABSTRACT



**Figure 1.** Graphical overview of running-based exercise therapy in T2DM — from population and intervention through clinical outcomes (HbA1c, fasting & postprandial glucose, insulin sensitivity) to molecular and metabolic mechanisms (GLUT4, AMPK, PGC-1 $\alpha$ , ectopic fat, quality of life).

## PLAIN LANGUAGE SUMMARY

Type 2 diabetes is a long-term disease in which the body has trouble using sugar (glucose) properly. More than half a billion adults live with it worldwide. This review explains why regular physical activity — and running in particular — is so helpful in managing the disease. The research shows that structured aerobic exercise lowers long-term blood sugar (HbA1c) by about 0.7–0.9 percentage points, a change that can be as powerful as some diabetes medicines. In a large study following over 19,000 adults, people who ran in their free time were about 28% less likely to develop type 2 diabetes than non-runners. Running works because the muscles that carry us forward soak up sugar from the blood more easily, the cells' tiny 'power plants' (mitochondria) become stronger, and dangerous fat around the liver and belly is reduced. On top of that, regular running improves mood, lowers anxiety and depression, and helps people feel more confident about managing their health. For most adults with type 2 diabetes, a well-planned running programme — adjusted to fitness, medications, and joint health — is a safe, affordable, and very effective addition to medicines and a healthy diet.

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## 1. INTRODUCTION

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Type 2 diabetes mellitus (T2DM) is one of the world's leading chronic metabolic diseases. It is characterised by persistently elevated blood glucose levels secondary to progressive insulin resistance and progressive loss of  $\beta$ -cell function [1]. In 2021, more than 500 million adults lived with T2DM and the number is projected to increase substantially over the next decades [1]. The growing global burden of T2DM is associated with numerous comorbidities and increased mortality, leading to a considerable rise in healthcare expenditures and representing a major public-health challenge.

In addition to pharmacotherapy, clinical management of T2DM relies on lifestyle interventions, including dietary modification, weight loss, and regular physical activity. Current evidence-based recommendations highlight lifestyle modifications as essential both for prevention and treatment of T2DM [2]. Beyond complementing pharmacological treatment, regular physical activity has been shown to be an independent therapeutic modality that improves glycemic control, reduces cardiovascular risk, and enhances quality of life in individuals with T2DM [2,3].

Among the different forms of exercise used to manage T2DM, aerobic exercise has been shown to be the most effective. Systematic reviews and meta-analyses demonstrate that aerobic exercise significantly improves glycemic control, increases insulin sensitivity, and improves body composition [4,5,6]. Accordingly, the American Diabetes Association position statement recommends that individuals with T2DM engage in regular moderate-to-vigorous aerobic exercise as part of their treatment plan [3].

Running is one of the most popular forms of aerobic exercise worldwide. Because it can be performed across a wide range of fitness levels and requires no specific or expensive equipment, it is considered one of the most accessible exercise modalities. In addition, by recruiting large muscle groups throughout the body and improving insulin sensitivity through GLUT4 translocation, running is also one of the most effective ways to promote glucose homeostasis. The long-term effects of running have been well documented in epidemiological studies. The Aerobics Center Longitudinal Study, which followed over 19,000 adults, demonstrated that regular leisure-time running was associated with a 28% reduction in incident T2DM compared with non-runners, with consistent dose–response relationships for weekly running time, distance, frequency, and speed [10]. Despite this clear advantage, few systematic reviews or meta-analyses have specifically examined running as an individual modality in T2DM populations.

The goal of this narrative review is to evaluate the current evidence on the effects of exercise therapy on glycemic control and related outcomes in adults with T2DM, with special emphasis on running as a representative and clinically relevant aerobic modality. The review additionally explores the molecular and physiological mechanisms underlying these effects, changes in body composition and ectopic fat distribution, cardiometabolic risk modification, and psychosocial outcomes associated with regular physical activity.

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## 2. METHODOLOGY

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This narrative review follows standard methodology for narrative literature reviews. The focus was on integrating the latest research evidence regarding how aerobic activity and running affect glycemic control and related physiological, metabolic, and psychological outcomes in adults with T2DM.

The literature search was conducted in multiple electronic databases, including PubMed/MEDLINE, Scopus, and Google Scholar. It was generally limited to peer-reviewed articles published during the last decade (2015–2026), with particular emphasis on articles published from 2020 onwards to reflect the most recent body of evidence. Older articles providing foundational mechanistic or clinical information were included when necessary.

Search terms were combined as follows: “Type 2 Diabetes Mellitus”, “Aerobic Exercise”, “Running”, “Jogging”, “Glycemic Control”, “HbA1c”, “Insulin Sensitivity”, “GLUT4”, “Mitochondrial Biogenesis”, “Body Composition”, “Ectopic Fat”, “Psychological Outcomes / Quality of Life”, and “Exercise Training”. Boolean operators AND/OR were used to refine searches. Manual searches were additionally performed on reference lists of all retrieved studies.

Articles included in this review had to meet the following inclusion criteria: published in English; focused on adults ( $\geq 18$  years); addressing a population with established T2DM or at risk for T2DM; and presenting data on at least one of the following: glycemic control, insulin sensitivity, mitochondrial function, body composition, cardiometabolic risk factors, or psychological well-being. Eligible study designs included systematic reviews, meta-analyses, RCTs, prospective cohort studies, and position statements from major scientific societies. Articles focusing exclusively on type 1 diabetes, abstract-only publications, and articles lacking sufficient methodological detail were excluded.

Because of the narrative structure of this review, a formal risk-of-bias assessment and statistical synthesis of results were not performed. Instead, a qualitative synthesis of key findings is provided, grouped thematically according to the categories described in the Results section. High-quality systematic reviews and meta-analyses were prioritised, with individual RCTs included when synthesis-level evidence was lacking.

### 3. AIM

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This review aims to provide an evaluation of the current scientific literature on the effect of exercise therapy on glycemic control and related metabolic, physiological, and psychological outcomes in adults with T2DM, with particular focus on running as a specific and globally accessible form of aerobic exercise.

## 4. RESULTS

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### 4.1. Effects on Glycemic Control (HbA1c and Blood Glucose)

Glycated haemoglobin (HbA1c) is one of the principal indicators of long-term blood glucose control in T2DM, and reducing HbA1c is a major therapeutic objective. A landmark meta-analysis by Umpierre et al. showed that structured exercise therapy was significantly more effective than general physical-activity advice in lowering HbA1c in patients with T2DM [4]. Structured exercise overall produced a mean HbA1c reduction of 0.67%; structured aerobic exercise alone produced a 0.73% reduction; and structured programmes exceeding 150 minutes per week were associated with reductions of up to 0.89%. Reductions of this magnitude are clinically meaningful, as even small absolute decreases in HbA1c translate into substantial reductions in the risk of microvascular and macrovascular complications [4,11]. A narrative review by Yanai et al. similarly concluded that adequate prescription of both aerobic and resistance exercises is needed to optimise glycemic control [11].

More recent evidence further supports these findings. A systematic review and meta-analysis by Gallardo-Gómez et al. evaluated the optimal dose and type of physical activity for improving glucose levels in T2DM and concluded that intensity and total aerobic exercise volume were both important determinants of HbA1c reduction, with greater intensity yielding better glycemic outcomes [5]. As a moderate-to-vigorous aerobic activity, running appears particularly effective.

Garcia et al. performed a network meta-analysis comparing different exercise and physical-activity counselling strategies for HbA1c reduction in T2DM [6]. Using data from numerous RCTs, they showed that structured aerobic training programmes produced clinically significant decreases in HbA1c independent of

patient age, baseline HbA1c, or diabetes duration, and that supervised structured exercise outperformed unsupervised advice [6].

Aerobic exercise also lowers fasting and postprandial blood glucose. Activities such as running reduce blood glucose acutely through insulin-independent increases in skeletal-muscle glucose uptake, a particularly important effect in the presence of insulin resistance [4,5]. Chronic aerobic training augments this acute response and improves basal insulin sensitivity, leading to a more stable glycemic profile over time [5]. Epidemiologically, Wang et al. analysed 19,347 adults from the Aerobics Center Longitudinal Study and showed that leisure-time running was associated with a 28% reduction in T2DM risk (HR = 0.72; 95% CI: 0.62–0.84), independent of other aerobic activity, with dose–response relationships across weekly duration, distance, frequency, and speed; the fastest and longest runners experienced the greatest risk reductions (HR 0.57–0.58) [10].

#### 4.2. Insulin Sensitivity and Glucose Uptake in Skeletal Muscle

The glucose-lowering effects of running are mediated, in large part, by molecular mechanisms located in skeletal muscle. Skeletal muscle takes up substantial amounts of glucose during and after aerobic exercise through translocation of glucose transporter type 4 (GLUT4) to the plasma membrane via both insulin-dependent and insulin-independent pathways [8]. Stocks and Zierath provide a comprehensive mechanistic account of how exercise-induced post-translational modifications — such as phosphorylation and acetylation of key signalling proteins — activate GLUT4 translocation and enhance metabolic flexibility in T2DM [8].

A central role in exercise-induced glucose uptake belongs to the AMP-activated protein kinase (AMPK) signalling pathway. Activated under high energy demand, AMPK promotes glucose uptake independently of insulin [8,12]. In T2DM, where insulin signalling is impaired by chronic hyperinsulinaemia, this alternative AMPK-mediated pathway represents a particularly valuable therapeutic target.

Zierath et al. described the short- and long-term skeletal-muscle adaptations to repeated aerobic activity, including increased mitochondrial biogenesis, improved lipid oxidation, and upregulated expression of insulin-signalling components such as IRS-1 and PI3K, all of which contribute to durable improvements in insulin sensitivity [12]. Although each session produces transient improvements, these accumulate over time to yield lasting structural and functional changes in muscle.

Pan et al. conducted a mesh meta-analysis of nine different exercise modalities for improving insulin sensitivity in patients with diabetes; aerobic exercise was consistently ranked among the most effective forms [13]. Modalities characterised by higher metabolic demand and longer muscle engagement — features that running shares — produced the greatest improvements in insulin responsiveness [13].

#### 4.3. Mitochondrial Adaptations and Metabolic Health

Mitochondrial dysfunction is increasingly recognised as a primary defect associated with skeletal-muscle insulin resistance in T2DM. This defect manifests as reduced oxidative capacity, impaired fatty-acid oxidation, and accumulation of lipid intermediates that disrupt insulin signalling [9]. Aerobic exercise stimulates mitochondrial biogenesis, providing a direct mechanism to counteract this dysfunction.

The principal molecular pathway driving exercise-induced mitochondrial biogenesis is centred on peroxisome proliferator-activated receptor-gamma coactivator 1-alpha (PGC-1 $\alpha$ ) [9]. PGC-1 $\alpha$  is activated by multiple upstream signals generated during aerobic exercise, including AMPK activation, increased intracellular calcium, and reactive oxygen species. Once active, PGC-1 $\alpha$  drives transcription of nuclear-encoded mitochondrial genes and stimulates TFAM expression, thereby increasing both mitochondrial number and enzymatic activity [9].

A systematic review and meta-analysis by Abrego-Guandique et al. confirmed that aerobic exercise consistently increases mitochondrial density and activity in skeletal muscle, with a clear dose–response relationship driven by exercise intensity and duration [9].

Improvements in glucose and lipid oxidation, reductions in intramuscular lipids, and enhanced metabolic flexibility — all factors that improve insulin sensitivity and glucose regulation — stem not only from mitochondrial biogenesis (production of new mitochondria) but also from mitophagy (selective degradation of defective mitochondria) and balanced mitochondrial fission and fusion [9].

Together, these adaptations help cells maintain high energy production while limiting mitochondrial damage. Because chronic hyperglycaemia and lipid overload — typical features of T2DM — cause considerable oxidative stress and mitochondrial impairment, exercise-induced mitochondrial adaptations can provide both preventive and therapeutic benefits [9].

#### **4.4. Body Composition, Ectopic Fat, and Cardiometabolic Risk**

Obesity and unhealthy body composition are tightly linked to the development of T2DM, particularly when fat accumulates centrally around the abdomen. Visceral adiposity drives insulin resistance through increased circulating free fatty acids, altered adipokine secretion, and chronic low-grade systemic inflammation [14]. Because running expends large amounts of energy compared with many other forms of physical activity, it can meaningfully reduce total and regional body fat, making it a useful intervention for managing body composition in T2DM.

Ectopic fat — lipid deposition at metabolically unfavourable sites such as the liver, visceral depot, skeletal muscle, and pericardial space — has been identified as an important factor in impaired glucose uptake in T2DM. A systematic review and meta-analysis by Sabag et al. demonstrated that structured exercise produced significant reductions in both hepatic fat and visceral adipose tissue in individuals with T2DM [14].

Meta-analyses by Al-Mhanna et al. have shown that combining aerobic and resistance training in overweight, obese, or T2DM populations improves several important health outcomes simultaneously, including HbA1c, blood pressure, systemic inflammation, cardiorespiratory fitness, and overall well-being [15]. Combined training appears to deliver added benefits beyond either modality alone, supporting current guidelines that recommend multimodal training in T2DM [15].

A further meta-analysis by Al-Mhanna et al. evaluated the impact of adding resistance training to ongoing aerobic training on body composition, lipid metabolism, and functional capacity in T2DM with overweight/obesity. The combined intervention reduced total body-fat percentage, waist circumference, and LDL-C, while increasing lean body mass [16]. These findings highlight the versatility of aerobic-based exercise in addressing the multifactorial risk profile of T2DM when complemented by resistance training.

The Look AHEAD (Action for Health in Diabetes) trial provided long-term evidence that an intensive lifestyle intervention including structured aerobic activity produces sustained cardiometabolic benefits in adults with T2DM [17]. At 4 years, participants assigned to the intensive lifestyle arm showed greater reductions in BMI, HbA1c, systolic and diastolic blood pressure, and improvements in lipid profile compared with the diabetes support and education control group [17]. These results confirm that exercise-related metabolic benefits can be sustained over years given adequate support for adherence [17].

#### **4.5. Psychological Outcomes, Quality of Life, and Adherence**

The psychosocial aspects of T2DM management are often underestimated clinically but represent key drivers of long-term treatment success. Individuals with T2DM experience depression and anxiety at significantly higher rates than the general population, and their coexistence is associated with poorer glycemic control, lower treatment adherence, and worse overall health status [18,19]. A systematic review and meta-analysis by

Tang et al. evaluated high-frequency, short-session exercise interventions in T2DM and demonstrated significant, clinically meaningful reductions in both depression and anxiety symptoms in RCTs [18]. The authors suggested that exercise frequency may be a key factor in maintaining these psychological benefits [18].

He et al. analysed how aerobic training affects overall clinical outcomes in individuals with T2DM and comorbid mental health conditions [19]. Aerobic training improved both metabolic measures and mental health, suggesting a bidirectional relationship between physical and mental health in this population. Improvements in depressive and anxiety symptoms may, in turn, support better self-care, medication adherence, and dietary behaviour, creating a positive feedback loop that promotes long-term disease management [19].

Cardiorespiratory fitness is consistently associated with greater exercise self-efficacy and improved quality of life across the adult lifespan, as shown in the systematic review by Medrano-Ureña et al. [20]. Because low exercise self-efficacy is a common barrier to regular activity in T2DM, improving fitness may establish a reinforcing cycle of motivation and adherence.

## 5. DISCUSSION

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The evidence reviewed here demonstrates that structured aerobic exercise produces substantial benefits for managing T2DM. Consistent findings from RCTs and network meta-analyses confirm that structured aerobic exercise significantly reduces both HbA1c and fasting blood glucose [4,5,6]. These reductions are not trivial: HbA1c decreases of 0.5–1.0% reported across multiple high-quality interventions are comparable to the glycemic efficacy of several oral antidiabetic medications [4,5], and higher-intensity activity yields larger glycemic improvements [5].

Beyond glycemic control, robust mechanistic explanations for these improvements have emerged. Skeletal muscle increases glucose uptake through enhanced GLUT4 translocation via both insulin-dependent and insulin-independent pathways, with substantial augmentation by AMPK activation [8,12]. Post-translational modifications of insulin-signalling components during and after exercise enhance cellular responsiveness to insulin in a durable manner [8]. Chronic exercise further increases mitochondrial biogenesis through PGC-1 $\alpha$ , raising mitochondrial density, oxidative capacity, and lipid-handling capacity within skeletal muscle [9]. Together, these molecular adaptations translate into sustained improvements in glycaemia.

The broader cardiometabolic consequences of structured aerobic exercise are equally important in T2DM, which is itself a systemic metabolic disorder characterised by high cardiovascular risk [1,2]. Aerobic training simultaneously addresses multiple components of this risk profile: it reduces visceral and hepatic ectopic fat [14]; improves lipid profile and lowers blood pressure [15,16]; enhances cardiorespiratory function; and reduces systemic inflammation [15]. Long-term Look AHEAD data confirm that these benefits can be sustained over years within comprehensive lifestyle programmes [17].

The psychological dimension of exercise therapy in T2DM warrants particular attention. Higher prevalence of depression and anxiety in T2DM is linked to worse glycemic control and lower adherence [18,19]. Structured aerobic exercise produces statistically significant reductions in both, with frequency emerging as an important determinant of long-term mental-health benefits [18]. Improved cardiorespiratory fitness is consistently associated with greater exercise self-efficacy and better quality of life [20], potentially creating a self-reinforcing cycle of continued engagement.

Running is particularly well-positioned to activate these pathways because of its capacity for sustained high energy expenditure and recruitment of large muscle mass. Several limitations must, however, be

acknowledged. Most studies have examined aerobic exercise broadly without isolating running as a specific modality; although physiological responses to running are generally consistent with other aerobic modalities, few running-specific intervention studies have been conducted in T2DM populations. Furthermore, while supervised and standardised protocols are typical in clinical trials, real-world running behaviour varies substantially in intensity, frequency, duration, and environment, which may limit the direct generalisability of trial results.

A major practical challenge is the relatively high drop-out rate from running interventions [3,20], which can be explained by several clinically relevant barriers: musculoskeletal injury risk, especially with high-impact weight-bearing activity; hypoglycaemic episodes in patients on insulin or insulin secretagogues; and motivational barriers [3]. Clinicians and exercise professionals prescribing running for T2DM patients must therefore consider baseline fitness, musculoskeletal comorbidities, medication, and individual preferences to design programmes that are safe and sustainable.

Future research should compare running directly with other aerobic modalities in T2DM using standardised protocols, characterise dose–response relationships between running parameters and glycaemic outcomes, assess long-term adherence, and integrate digital health tools and evidence-based behaviour-change strategies. Such research will be essential to translate findings into routine clinical and public-health practice.

## 6. CONCLUSIONS

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Exercise therapy is an effective, evidence-based intervention for the management of T2DM. The available evidence supports the capacity of structured aerobic exercise to improve glycemic control through clinically significant reductions in HbA1c and fasting blood glucose, mediated by well-characterised molecular mechanisms including enhanced insulin sensitivity, GLUT4 translocation, and PGC-1 $\alpha$ -driven mitochondrial biogenesis. In addition to improving glycaemia, exercise programmes favourably affect body composition, reduce ectopic fat deposition, lower multiple cardiometabolic risk factors, and provide meaningful psychosocial benefits including reduced symptoms of anxiety and depression. Running is one of the most accessible forms of aerobic exercise worldwide, physiologically effective and suitable for many individuals. Its capacity to engage metabolic pathways at moderate-to-vigorous intensities makes it particularly useful for prevention and provides proof of concept for incorporation into individualised exercise prescriptions. Clinicians and fitness professionals are encouraged to integrate structured running programmes into T2DM treatment plans — with appropriate attention to safety, individual patient characteristics, and alignment with pharmacological and dietary strategies.

## 7. DISCLOSURE

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### 7.1. Author Contributions

Conceptualization: Maciej Szczupaj, Jakub Rudnicki, Katarzyna Latalska, Marta Krzyżanowska; Methodology: Maciej Błaszczyk, Katarzyna Latalska; Investigation: Wiktoria Leja, Andżelika Pastuszek, Konrad Borkowski, Marta Krzyżanowska; Validation / Check: Andżelika Pastuszek, Konrad Borkowski; Writing — rough preparation: Maciej Szczupaj, Katarzyna Latalska; Writing — review & editing: all authors; Resources: Maciej Błaszczyk, Julia Zjawiony; Project Administration: Maciej Błaszczyk, Zeeshan Zulfiqar; Data Curation: Wiktoria Leja, Andżelika Pastuszek, Jakub Rudnicki. All authors have read and agreed to the published version of the manuscript.

## 7.2. Funding

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## 7.3. Institutional Review Board Statement

Not applicable — this is a narrative literature review and does not involve human or animal subjects.

## 7.4. Informed Consent Statement

Not applicable.

## 7.5. Conflict of Interest

The authors declare no conflict of interest.

## 7.6. Data Availability Statement

No new data were created or analysed in this study. All findings reported are based on publicly available literature retrieved from PubMed, Scopus, and Google Scholar. Data sharing is therefore not applicable to this article. All cited articles are available through their respective publishers via the DOI links provided.

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*Mapped to the CRediT (Contributor Roles Taxonomy, NISO Z39.104-2022):*

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- **Methodology:** MB, KL
- **Investigation:** WL, AP, KB, MK
- **Validation:** AP, KB
- **Formal analysis:** MS, KL
- **Resources:** MB, JZ
- **Data curation:** WL, AP, JR
- **Writing – original draft:** MS, KL
- **Writing – review & editing:** MS, MB, KL, WL, AP, KB, JR, JZ, ZZ, MK
- **Visualization:** MS, MB
- **Supervision:** MS, KL
- **Project administration:** MB, ZZ

## Declaration of the use of generative AI and AI-assisted technologies in the writing process

In preparing this work, the authors used ChatGPT for the purpose of improving language and readability, text formatting and verifying bibliographic styles. After using this tool, the authors have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

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