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## Protective effects of physical activity against health risks associated with type 1 diabetes: “Health benefits outweigh the risks”

Addisu Dabi Wake

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### Abstract

The magnitude of diabetes mellitus (DM) has increased in recent decades, where the number of cases and the proportion of the disease have been gradually increasing over the past few decades. The chronic complications of DM affect many organ systems and account for the majority of morbidity and mortality associated with the disease. The prevalence of type 1 DM (T1DM) is increasing globally, and it has a very significant burden on countries and at an individual level. T1DM is a chronic illness that requires ongoing medical care and patient self-management to prevent complications. This study aims to discuss the health benefits of physical activity (PA) in T1DM patients. The present review article was performed following a comprehensive literature search. The search was conducted using the following electronic databases: “Cochrane Library”, Web of Science, PubMed, HINARI, EMBASE, Google for grey literature, Scopus, African journals Online, and Google Scholar for articles published up to June 21, 2021. The present review focused on the effects of PA on many outcomes such as blood glucose (BG) control, physical fitness, endothelial function, insulin sensitivity, well-being, the body defense system, blood lipid profile, insulin resistance, cardiovascular diseases (CVDs), insulin requirements, blood pressure (BP), and mortality. It was found that many studies recommended the use of PA for the effective management of T1DM. PA is a component of comprehensive lifestyle modifications, which is a significant approach for the management of T1DM. It provides several health benefits, such as improving BG control, physical fitness, endothelial function, insulin sensitivity, well-being, and the body defense system. Besides this, it reduces the blood lipid profile, insulin resistance, CVDs, insulin requirements, BP, and mortality. Overall, PA has significant and essential protective effects against the health risks associated with T1DM. Even though PA has several health benefits for patients with T1DM, these patients are not well engaged in PA due to barriers such as a fear of exercise-induced hypoglycemia in particular. However, several effective strategies have been identified to control exercise-induced hypoglycemia in these patients. Finally, the present review concludes that PA should be recommended for the management of patients with

T1DM due to its significant health benefits and protective effects against associated health risks. It also provides suggestions for the future direction of research in this field.

**Key Words:** Type 1 diabetes mellitus; Physical activity; Health benefit; Glycemic control; Exercise

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**Core Tip:** Diabetes mellitus (DM) is a group of chronic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The impairment of beta-cell function is an ancient feature of disease pathogenesis, while a significant reduction in beta-cell mass is closely associated with clinical manifestations in type 1 DM and type 2 DM. Physical activity (PA) is good for almost every individual. PA is a significant mediator of glycemic control and prevents pathologies related to increased postprandial glucose. Its significant role in the prevention and management of noncommunicable diseases is extensively understood. PA is widely known to be an effective approach for the prevention and management of numerous chronic diseases.

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## INTRODUCTION

Diabetes mellitus (DM) is a group of chronic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both[1]. The loss of beta-cells ( $\beta$ -cells) is a determinant factor for the development of type 1 DM (T1DM)[2]. In T1DM and type 2 DM (T2DM), the impairment of  $\beta$ -cell function is an early feature of disease pathogenesis, while a significant reduction in  $\beta$ -cell mass is closely associated with clinical manifestations[3]. Reduced functional  $\beta$ -cell mass is the hallmark of both T1DM and T2DM and this triggers absolute or relative insulin insufficiency in both circumstances [4]. T1DM is characterized by an immune-mediated depletion of  $\beta$ -cells that results in a lifelong dependence on exogenous insulin[5-9]. Despite all the efforts made to identify efficient therapeutic methods for T1DM, insulin is the only effective treatment[2].

However, even modest levels of  $\beta$ -cell activity were associated with a reduction in the incidence of retinopathy and nephropathy in T1DM individuals[10]. Even though the factors that predict the occurrence and rapidity of the decrease in  $\beta$ -cell function are still largely unknown, evidence has identified islet cell autoantibodies as predictors. Historical as well as recent clinical experience has underlined the significance of residual insulin production for glycemic control and to avoid end-organ complications[11]. T1DM can arise at any age while a peak in incidence is seen around puberty[12]. Overweight and obesity are highly prevalent among young people and adults with T1DM which is (25%-35%) and (37% to nearly 80%), respectively. Obesity raises the risk of developing T1DM and may lead to an earlier age at diagnosis. Also, obesity may raise the risk of macrovascular disease, retinopathy, and metabolic syndrome among these patients[13]. The chronic hyperglycemia of diabetes is linked to long-term damage, dysfunction, and failure of different organs, particularly the eyes, kidneys, nerves, heart, and blood vessels[1].

Generally, diabetes-related complications can be divided into macrovascular and microvascular complications. Stroke, coronary artery disease, and peripheral arterial disease are included under macrovascular complications and microvascular complications comprise, retinopathy, diabetic nephropathy, and neuropathy[14]. In addition, T1DM is linked with premature cardiovascular disease (CVD)[15]. In T1DM individuals, the absolute and relative risks of CVD remain very high[16]. When women with T1DM are compared to men with T1DM, women have nearly 40% more excess risk of all-cause mortality and twice the excess risk of fatal and nonfatal vascular events[17]. The age at onset and the duration of T1DM seem to be significant determinants of survival and all cardiovascular outcomes. Early onset is associated with up to a 30-fold augmented risk of serious cardiovascular outcomes, with risk levels being 90-fold greater for women with early-onset diabetes, and who die approximately 18 years earlier than nondiabetics[18]. Vascular complications are a significant cause of morbidity and mortality in individuals with T1DM and T2DM[19].

The magnitude of DM has increased in recent decades[20], where the number of cases and the proportion of the disease have been gradually increasing over the past few decades[21]. The incidence of childhood T1DM is significantly increasing globally[22]. It is the epidemic of the century and without effective diagnostic approaches at an early stage, diabetes will continue to increase[23]. The global

estimates for the prevalence of diabetes for 2015 and 2040 were 8.8% and 10.4%, respectively[24]. Whereas it was 8.8% and 9.9% of the world population in 2017 and by 2045, respectively[25].

In recent decades, a significant increase in the proportion of DM has been evidenced in nearly all regions of the world. The increase in the number of subjects with the disease is possibly due to a change in the disease profile in numerous populations around the world and this is primarily because of a larger incidence of diabetes-related complications such as kidney failure and peripheral arterial disease [26]. It is a significant public health problem and is one of the four ranked noncommunicable diseases targeted for action by world leaders[21]. T1DM is associated with an increased risk of CVDs and all-cause mortality in insulin-treated patients with diabetes while the connection between hypoglycemia and cardiovascular consequences and mortality exists over a long period[27]. Whereas, more than the general population, elderly individuals with diabetes have higher all-cause mortality rates[28]. The excess mortality observed in T1DM is almost totally associated with diabetes and its related comorbidities[29].

The increasing disease burden of DM globally is a major public health priority, placing a fluctuating need on the patients, their careers, health systems, and society[30]. Diabetes is one of the leading and rising causes of hospital admission and disability due to other diseases[31]. This high magnitude of the disease has a greater social and financial burden[24]. It imposes a rising economic burden on national health care systems globally[32]. The global costs of DM and its significance are huge and will markedly rise by 2030[33]. Even though the present data found an increase in the magnitude of diabetes, the recent understanding of the international burden of and variation in the disease linked with complications is poor worldwide[26].

Diabetes is a chronic illness that requires ongoing medical care and patient self-management to prevent complications. Diabetes care is complex, requires numerous issues to be addressed, and it is more than glycemic control[34]. T1DM is a chronic disease with severe complications due to its mismanagement. The health professionals should be equipped with suitable evidence based on multiple management approaches to those individuals to support patient-centered care and improve their capacity for problem-solving and self-management[35]. Maintaining the long-term integration of lifestyle changes and medical management is crucial to accomplish good metabolic control in diabetes subjects[14,36].

Self-management participation could lead to clinically associated progress in the behavior and clinical parameters[37] and those individuals who participate in self-management can be considered volunteers in the majority of cases where they have either wanted an intervention or decided to take part[38]. Physical activity (PA) and nutrition are significant components of a healthy lifestyle and treatment of diabetes[39]. The benefit of exercise in T1DM remains a significant component of its treatment[40]. Therefore, the adoption and maintenance of PA are crucial for the management of glycemia and the entire health of individuals with diabetes and prediabetes[41]. Exercise is a cornerstone in the lifestyle of nearly all individuals with T1DM[42]. As the patients may be more agreeable to lifestyle changes, exercise should be encouraged from diagnosis. In addition, to improve patient confidence in managing their diabetes with exercise, standard advice on exercise and diabetes needs to be made available to health professionals and subjects with diabetes[43].

With regard to PA, even though, the term PA and exercise are not synonymous they are often used interchangeably[44,45]. However, the term "PA" should not be mistaken with "exercise", as exercise is a subgroup of PA[46]. Due to this, it is recommended that they should not be used interchangeably[47]. PA can be defined as any bodily movement formed by the skeletal muscles that result in energy expenditure above resting levels[46,48-50]. While exercise is defined as a planned, structured PA typically performed with the intent of improving health and/or fitness[46,48]. The term PA is broadly comprised of exercise and sport, and PA is performed as a part of daily living, occupation, leisure, and active sport[46,48]. Exercise can be classified as aerobic and resistance exercise[51]. Aerobic exercise involves the repeated and continuous movement of huge muscle groups[52]. Anaerobic exercise comprises activities such as walking, cycling, jogging, and swimming. Resistance exercise includes activities such as free weights, weight machines, bodyweight, or elastic resistance bands[51].

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## METHODS

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### **Research questions**

What are the protective effects of physical activity against the health risks associated with T1DM?

### **Study setting**

The present review article includes all studies conducted in various countries globally.

### **Search strategies**

The present review article was carried out using a comprehensive literature search. The search was performed using the following electronic databases: "Cochrane Library", Web of Science, PubMed, HINARI, EMBASE, Google for grey literature, Scopus, African journals Online, and Google Scholar. The

search was conducted using the following search terms; “diabetes mellitus”, “type 1 diabetes”, “T1DM”, “complications”, “insulin-dependent diabetes mellitus”, “IDDM”, “physical activity”, “exercise”, “Glycemic Control”, “Physical Fitness”, “Blood Lipids Profile”, “Endothelial Function”, “Insulin Resistance”, “Insulin Sensitivity”, “Insulin Requirement”, “Cardiovascular Diseases”, “Blood Pressure”, “Well-being”, “Body’s Defense Systems”, “Mortality”, “barriers”, “factors”, “strategy”, and “hypoglycemia”. The Boolean operators; “AND” and “OR” were used to integrate them during the search.

### **Eligibility criteria**

The inclusion criteria for the present review were; Articles on this topic globally, published in the English language, quality articles, and those with outcome variables well defined and measured, and articles published up to June 21, 2021. The exclusion criteria for the present review article were: articles of poor quality and articles in which the outcome variable was not clearly defined and measured.

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## **THE HEALTH BENEFITS OF PHYSICAL ACTIVITY FOR T1DM PATIENTS**

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Overall, PA is good for almost every individual[52]. It provides numerous health benefits mainly for obese individuals[53]. Even among healthy individuals, daily PA is a significant mediator of glycemic control and enhances the prevention of pathologies related to increased postprandial glucose[54]. Its significant role in the prevention and management of noncommunicable diseases is extensively understood[55]. Exercise is largely known as an effective approach for the prevention and management of many chronic diseases[56]. It is essential in the primary and secondary prevention of chronic diseases such as CVD, diabetes, cancer, hypertension, obesity, depression and osteoporosis, and premature death [57]. The effects of exercise also include the management of many metabolic syndromes as well as improved mood and quality of life[58].

Exercise training leads to improved body composition, cardiovascular, and metabolic outcomes in subjects with metabolic syndrome[59]. Moreover, PA helps to decrease all causes of morbidity and improves the quality of life in people of all age groups[60,61]. It also benefits principally older adults by protecting against and ameliorating several diseases, the achievement and maintenance of a healthy body weight, improved mental health and well-being, and musculoskeletal health. The amelioration of disease risk factors, the achievement of peak bone mass, and maintenance of healthy body weight were the benefits of PA in children[62].

Activity may play a protective role due to the consistent relationship between historical PA and the development of complications in insulin-dependent DM (IDDM)[63]. Exercise also has many significant health merits in both T1DM and T2DM subjects[64] and many exercises are supportive in these subjects [65]. The findings from randomized trials support the role of resistance training as an adjunctive mode of management in T1DM patients[66]. Both aerobic and resistance exercises are excellent for patients with T1DM[67]. In addition, regular moderate to vigorous PA was linked with many health benefits in adolescents with T1DM[68]. Exercise decreases the rate of diabetes-related complications in T1DM subjects[69].

Vigorous-intensity PA has a role in metabolic control in T1DM patients[70]. Consistent regular PA can improve metabolic control in these patients[71] and is significant for best physical and psychological development during childhood, and it improved glycemic control, cardiovascular function, blood lipid profiles, and psychological well-being[72]. Consistent PA has a beneficial effect on glycemic control, diabetes-related comorbidities, and cardiovascular risk factors without the risk of adverse events[73]. A summary of the effects of PA on many health outcomes such as blood glucose (BG) control, physical fitness, endothelial function, insulin sensitivity, well-being, body defense system, blood lipid profile, insulin resistance, CVDs, insulin requirements, BP, and mortality is shown in [Figure 1](#).

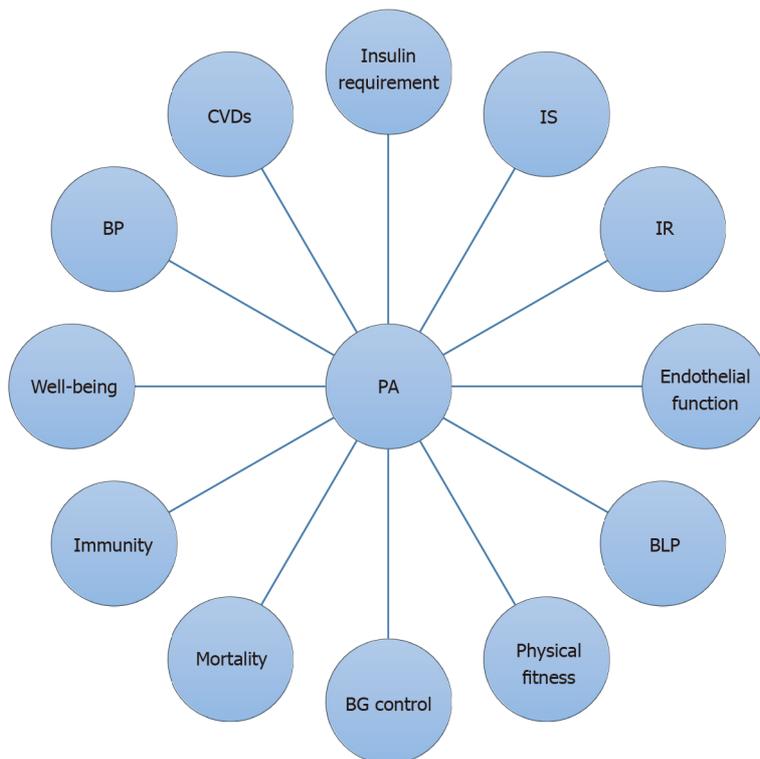
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## **GLYCEMIC CONTROL**

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Discrepancies have been observed in the literature regarding the role of PA in T1DM glycemic control. For instance, in T1DM female individuals, daily physical training for several months did not improve glycemic control[74]. In addition, Yki-Jarvinen *et al*[75] demonstrated that a controlled physical training program in pump-treated T1DM subjects did not change an already near-normal glycemic control. Furthermore, Zinman *et al*[76] found that, although plasma glucose declines acutely with exercise, an augmented caloric intake on exercising days obviates the long-term effect of training on glucose control. Similarly, glycemic control did not significantly improve in pregnant women with T1DM during postprandial walking exercise[77]. Moreover, glycemic control was not found to be associated with long-term PA in T1DM subjects and PA did not negatively affect long-term glycemic control[78].

Several studies have found that PA improved glycemic control in individuals with T1DM[69,71,79-113]. Regular PA can lead to decreased BG level among these patients, it is safe and does not result in



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**Figure 1 The health benefits of physical activity in type 1 diabetes patients.** PA: Physical activity; BG: Blood glucose; BLP: Blood lipid profile; IR: Insulin resistance; IS: Insulin sensitivity; CVDs: Cardiovascular diseases; BP: Blood pressure.

more hypoglycemic episodes[91]. A systematic review showed that PA had a positive impact on glycemic control in children and adolescents with T1DM[97]. Similarly, regular PA enhances BG control in children with T1DM[98]. Prolonged moderate aerobic exercise leads to a consistent decrease in plasma glucose but frequent hypoglycemia can occur when pre-exercise glucose concentrations are < 120 mg/dL in young people with T1DM[100]. Increased leisure-time PA (LTPA) between the ages of 50 and 70 years in the absence of active intervention was also found to be associated with improved glucose in men[101]. Campaign *et al*[71] demonstrated that regular high-intensity PA can improve metabolic control in young children with IDDM. In addition, combined exercise training (endurance training and resistance training) improves glycemic control to a better extent than endurance or resistance training alone, under moderate-intensive training situations with equal training durations [82]. Supervised strength training in T1DM male patients was associated with significant changes in glycemic control[93]. Marrone *et al*[95] found that free-play PA has a crucial role in helping to maintain BG levels in children with T1DM. Furthermore, anaerobic circuit training was found to improve glucose regulation in adolescents with IDDM[96]. Regular participation in moderate to intense PA or sports improves metabolic control in T1DM subjects[103]. High-intensity training (HIT)[105] and resistance training[106] improve plasma glucose in T1DM patients. Generally, an enhanced skeletal muscle, by either an intrinsic mechanism or PA, provides better advantages and benefits in facilitating glucose regulation[86] as peripheral glucose utilization rises during exercise, despite a reduction in circulating insulin levels[85]. During PA, muscle glucose uptake also rises and can reach values that are 30-50 times greater than at rest[87].

PA decreased glycosylated hemoglobin (HbA1c) in T1DM patients[81,89,90,111-113]. This effect is acceptable since the HbA1c level is increased following PA cessation[89]. This shows that the reduction of HbA1c level is a major sign of glycemic control. This is because the amount of glucose that combines with HbA1c is directly proportional to the total amount of glucose within a system. This means, if the BG levels have been high in current weeks, the HbA1c level will also increase. This could be evidence of PA reducing BG level, and was proved by the decrease in this biomarker of glycemic control.

## PHYSICAL FITNESS

Physical fitness is defined as a set of attributes that are either health- or skill-related and the extent to which individuals have these attributes can be measured with specific tests[50]. Evidence shows that patients with T1DM have reduced physical fitness[114]. Furthermore, children with T1DM presenting

with poor glycemic control had lower aerobic fitness compared to those with good glycemic control [115]. In addition, lower cardiorespiratory fitness in children with T1DM is associated with poor glycemic control [116].

However, numerous studies have shown that PA improves physical fitness in individuals with T1DM [92,93,96,97,117,118]. Supervised strength training in male patients was associated with augmented strength [93]. Also, exercise training among adolescents with T1DM leads to improved physical fitness [92]. Even, a training program of 1 h per week for 3 mo was found to improve physical fitness [117]. Anaerobic circuit training improved muscle strength in adolescents with IDDM [96]. Furthermore, a systematic review showed that PA improved physical fitness in children and adolescents with T1DM [97]. Moreover, a randomized trial demonstrated that combined exercise training appeared to improve physical fitness in adolescents with T1DM [118]. Regular PA also improved cardiovascular fitness [71,98,102,107] and increased lean mass in these patients [98].

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## BLOOD LIPIDS PROFILE

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A study found that youths with T1DM have abnormal lipid levels and atherogenic changes in lipoprotein composition, even after a relatively short disease duration, and glycemic control is a significant mediator of these abnormalities [119]. In normal-weight T1DM youths, mainly females had more atherogenic low-density lipoprotein-cholesterol (LDL-C) and high-density lipoprotein-cholesterol (HDL-C) distributions which are associated with lower insulin sensitivity [120]. Dyslipidemia is significantly more frequent in children and adolescents with T1DM compared to non-diabetic peers whilst high LDL-C and low HDL-C were the most frequent type of dyslipidemia in the dyslipidemic group [121]. Similarly, dyslipidemia is frequently found in T1DM and appears to be associated with glycemic control. It is a major risk factor for coronary heart disease, and one of the most significant and frequent complications with a high premature mortality and morbidity rate [122]. In addition, apolipoprotein B is consistently associated with an increased risk of mortality in T1DM due to all causes as well as in cardiac disease and ischemic heart disease [123].

Several studies have proved that PA decreases the blood lipids profile in individuals with T1DM [69,74,80,93,98,101-103,110,111,124-128]. Laaksonen *et al* [125] found that endurance training improved the lipid profile in physically active T1DM men. Anaerobic circuit training also improved the lipid profile in adolescents with IDDM [96]. Similarly, regular PA improved the blood lipid profile and reduced body adiposity in children with T1DM [98]. In addition, there is a linear dose-response relationship between augmented PA and loss of abdominal fat in T1DM [91]. Regular exercise had beneficial effects on body fat content and the lipoprotein profile in subjects with T1DM by decreasing high plasma lipoprotein(a) concentrations [128]. Similarly, PA improved the lipoprotein profile in T1DM patients [102]. Increased PA in children with T1DM is related to a lower lipoprotein level [80]. Daily training for a number of months in T1DM females had a significant effect on the HDL3-C subfraction but led to minor changes in serum lipoprotein profiles [74]. Austin *et al* [127] demonstrated that the state of physical fitness was significantly correlated to lipid levels and lipoprotein(a) in adolescents with IDDM, where higher physical fitness levels decreased lipid levels. Total cholesterol (TC) levels significantly declined after an exercise intervention [124]. Consistent supervised strength training among male patients with T1DM was associated with a reduced TC level [93]. A systematic review also showed that PA reduced the TC level in children and adolescents with T1DM [97]. In addition, physical training in IDDM leads to reduced TC levels [126]. Yki-Jarvinen *et al* [75] found that a controlled physical training program in pump-treated diabetic patients increased the HDL-C to TC ratio in T1DM subjects. Postprandial walking exercise in pregnant women with T1DM was associated with significantly lower fasting plasma triglyceride levels in an intensive perinatal diabetes program [77]. Regular moderate to intense PA or sports participation improved the lipid profile in T1DM subjects [103]. Also, augmented LTPA between the ages of 50 and 70 years in the absence of active intervention was associated with improved lipid metabolism in men [101].

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## ENDOTHELIAL FUNCTION

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Evidence shows that endothelial dysfunction is common in adolescents with T1DM [129] and it is a predictor of CVDs in these patients [130]. Studies have found that PA improves endothelial function in individuals with T1DM [110,131,132]. Anaerobic exercise training can improve endothelial function in different vascular beds in individuals with long-standing T1DM who are at substantial risk of diabetic angiopathy [131]. However, regular exercise training involving the lower extremities did not improve endothelial function in the micro- and macro-circulation of the non-exercised upper extremity in T1DM individuals [132].

## INSULIN RESISTANCE

T1DM subjects are insulin resistant compared with nondiabetic subjects[133], and insulin resistance in the liver and skeletal muscle was found to be a significant characteristic in T1DM[134,135]. Youths with T1DM have adipose, hepatic, and peripheral insulin resistance[136]. This insulin resistance is an independent risk factor for the development of macro-and microvascular complications and may also contribute to the development of the disease[137]. Insulin resistance could also impact the length of the honeymoon period, diabetic control and patterns of growth during puberty, insulin requirements and BG control at any time, the birth weight of infants born to diabetic mothers, lipid metabolism, hypertension, rates of progression to insulin dependence and eventually contribute to excess mortality [138].

Insulin resistance is linked with a greater atherogenic lipoprotein cholesterol distribution in all men and women with T1DM[139]. Gender differences in insulin resistance-associated fat distribution may clarify why T1DM increases coronary calcification in women more than in men[140]. Greater insulin resistance was found in a group of premenopausal women with T1DM compared with nondiabetic subjects which was not related to abdominal adiposity, lipids, or androgens[141].

Studies have shown that PA improves insulin resistance in patients with T1DM[142,143]. For instance, aerobic exercise decreases waist circumference which is related to a tendency for raised HDL-C levels, and this may indicate a decrease in visceral fat with an improvement in insulin resistance[143]. This finding is also supported by the trial conducted by Dotzert *et al*[144] where aerobic exercise training was found to improve insulin resistance in insulin-resistant T1DM rats. The capacity of exercise to increase insulin-stimulated glucose uptake *in vivo* was decreased in subjects with insulin-resistant T1DM compared with normal individuals, and this could have been due to either separate or common defects in exercise- and insulin-stimulated pathways[142]. In  $\beta$ -cell transplanted recipients, endurance training may be helpful and preventive by counteracting graft dysfunction, alleviating the side effects of immunosuppressive drugs, and conserving insulin independence after islet transplantation[145].

## INSULIN SENSITIVITY

T1DM adolescents have significantly reduced insulin sensitivity compared with nondiabetic adolescents [146]. Several studies have verified that PA improves insulin sensitivity in patients with T1DM[39,75,83, 84,92,98,101,126,147,148]. Augmented LTPA levels were associated with raised insulin sensitivity[84, 101]. Regular PA enhanced insulin sensitivity in children with T1DM[98]. Also, a controlled physical training program in pump-treated T1DM subjects improved body sensitivity to insulin[75]. Exercise training in adolescents with T1DM can lead to improved insulin sensitivity[92]. Physical training in IDDM also leads to raised peripheral insulin sensitivity[126]. Regular moderate-intensity PA can improve insulin sensitivity in T1DM individuals[39]. The findings from the trial, where exercise led to improved insulin sensitivity and responsiveness by different mechanisms in rats[149] also supports these studies.

## INSULIN REQUIREMENT

PA also decreases insulin requirements in subjects with T1DM[75,84,128]. A controlled physical training program in pump-treated T1DM subjects decreased insulin requirements[75]. In addition, male patients with T1DM appeared to use less insulin when they were physically active[84]. Furthermore, regular exercise[128] and combined exercise training (aerobic and resistance) appears to lower daily insulin requirements in patients with T1DM[118]. Similarly, a study showed that exercise can improve insulin requirements in T1DM rats[150].

## CARDIOVASCULAR DISEASES

Normal weight adolescents with T1DM have impaired autonomic function and augmented energy expenditure and fat oxidation compared to individuals without diabetes who have similar levels of fitness and PA[151]. T1DM adolescents had significantly reduced peak oxygen consumption (VO<sub>2</sub>peak), and peak work rate compared with nondiabetics. They also had decreased vascular reactivity, diastolic dysfunction, and left ventricular hypertrophy[146]. Maximal workload and oxygen uptake were markedly diminished in chronically hyperglycemic IDDM subjects and physiologically significant cardiopulmonary dysfunction developed in asymptomatic patients with long-standing disease[152]. Insulin resistance in T1DM may contribute to the augmented CVD burden[120]. In T1DM, heart rate variability and arterial wall stiffness are linked to each other where the autonomic nervous system could be a connection between diabetes and vascular disease[153]. In African Americans with T1DM, high

plasma interferon-inducible protein 10 was found to be an independent predictor of incident CVD[154].

Studies have confirmed that PA decreases the risk of CVDs in T1DM patients[39,80,91,104,110,112,124,127,128,143,155-159]. Increased PA in children with T1DM has a beneficial effect on the CV risk profile[80]. There is a linear dose-response relationship between augmented PA and a decrease in lipid-related CV risk factors, with a preferential rise in the HDL3-C subfraction in patients with T1DM[91]. Exercise also improves diabetic complications such as subclinical autonomic neuropathy and CVD risk in children with T1DM[124]. Higher physical fitness levels due to exercise decrease lipid levels and this, in turn, may reduce the risk of CVD[127]. In addition, regular exercise may decrease CV risk in T1DM patients by decreasing high plasma lipoprotein Lp(a) concentrations[128]. Aerobic exercise decreases waist circumference which is related to a tendency for raised HDL-C levels, and this may indicate a decrease in visceral fat with an improvement in insulin resistance which could have an influence on reducing CV risk in these patients[143]. An inverse association was found between PA and the incidence of CVD in women with T1DM[155]. Also, high frequency and high-intensity exercise may decrease the risk of CVD in individuals with T1DM[156]. Regular moderate-intensity PA can decrease the risk of CVD in T1DM individuals[39]. Furthermore, PA has the potential to delay CVD in T1DM as it reduces the risk of CVD[104,112,157]. Integrated with diet, it can also influence lipid-related CV risk factors independent of changes in insulin treatment[158]. T1DM subjects who are physically more active have a lower overall risk of CV events than their sedentary counterparts[159]. Moreover, the study showed that aerobic circuit training was found to improve cardiorespiratory endurance[96] and regular PA improved vascular health in those subjects[160].

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## BLOOD PRESSURE

PA also improved blood pressure (BP) in patients with T1DM[80,91,102,124,128]. A study showed that regular exercise was found to have beneficial effects on BP in these patients[128]. Increased PA in children with T1DM leads to improved diastolic BP (DBP)[80]. A linear dose-response relationship between increased regular PA and decreased BP in patients with T1DM was also found[91]. DBP and heart failure were significantly correlated with lower TC levels which were lowered by performing exercise[124]. In addition, adolescents with T1DM have been associated with reduced stroke volume during exercise[161]. T1DM adolescent girls showed decreased sympathetic activity, although this was possibly compensated by higher adrenomedullary responsiveness or sensitivity, and did not affect their heart rate adaptation to exercise[162].

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## WELL-BEING

Studies have also found that PA improves the well-being of individuals with T1DM[39,69,97,98,118]. A systematic review showed that PA improved the well-being and psychological health of children and adolescents with T1DM[97]. Regular PA enhanced psychosocial well-being in children with T1DM[98]. A randomized trial demonstrated that combined exercise training (aerobic and resistance) appeared to lead to better well-being in adolescents with T1DM[118]. Also, regular moderate-intensity PA can improve the psychological well-being of these individuals[39]. Furthermore, Brazeau *et al*[163] demonstrated an association between greater PA and a better body mass index, body composition, and more favorable health status in individuals with T1DM similar to individuals without diabetes.

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## BODY'S DEFENSE SYSTEMS

T1DM individuals have higher levels of free radicals and may, as a result, be at augmented risk of developing complications related to T1DM[164]. PA has been found to protect against protein denaturation[165]. Aerobic training improves oxidative stress in individuals with diabetes[110]. Acute exercise is an immune system adjuvant that improves defense activity and metabolic health. In addition, there is a clear inverse relationship between moderate exercise training and illness risk[166]. Farinha *et al*[9] demonstrated that exercise training improves the body's defense systems and metabolic health in T1DM patients and induces numerous benefits by decreasing inflammation and improving antioxidant defenses.

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## MORTALITY

Mortality rates in the past decade continue to be much larger in individuals with T1DM than in those without diabetes despite advances in inpatient care[167]. The risk of death rises with less favorable

glycemic status and impaired carbohydrate metabolism contributes to mortality from any cause[168]. The mortality rate due to ischemic cardiac disease is greater in T1DM patients compared with the general population[169]. In these patients, the presence of metabolic syndrome is frequent, and it is linked with an augmented incidence of chronic complications and mortality[170]. Macrovascular and microvascular disease are the main causes of mortality in T1DM[130]. In addition, physical inactivity has been found to contribute to a substantial number of deaths in those with DM[171]. A significantly increased mortality risk due to diabetes was associated with decreased health-related quality of life in subjects who reported no LTPA[172].

Many studies have shown that PA decreases mortality in subjects with T1DM[93,143,155,172-175]. Supervised strength training in men with T1DM was related with no morbidity[93]. An inverse association was found between PA and all-cause mortality in both genders with T1DM[155]. Participating in LTPA may be linked with improved survival in patients with diabetes[172]. Furthermore, exercise is associated with a lower risk of premature all-cause mortality such as CVD and chronic kidney disease in patients with T1DM[173], and PA has been found to decrease CV mortality in these subjects[143,174]. Moreover, PA offers a beneficial effect in terms of long life in IDDM patients [175]. In African Americans with T1DM, low plasma stromal-derived factor-1 was found to be an independent predictor of mortality[154].

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## THE BARRIERS TO PHYSICAL ACTIVITY PRACTICE IN T1DM PATIENTS

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Even though several literature reports have supported the utilization of PA for individuals with T1DM, most of the patients did not engage in regular exercise due to various obstacles. For instance, the fear of exercise-induced hypoglycemia is the strongest barrier to regular PA in adults with T1DM[39,176-180]. Although technological advances have permitted exercisers with diabetes to progress toward more successful management of their BG levels during various types of PA, technology is still far from fully avoiding the fear of hypoglycemia in T1DM subjects[176]. Glucoregulatory failure may cause hypoglycemia in IDDM individuals during and after exercise. This could be due to hypoglycemic episodes which blunt the glucoregulatory response to subsequent exercise while exercise blunts the glucoregulatory response to subsequent insulin excess[181]. Even though regular PA was found to improve glycemic control, its frequency is a major factor affecting the control of glycemia without raising the risk of severe hypoglycemia in pediatric patients with T1DM[94]. This may be supported by a study, where low levels of LTPA were associated with poor glycemic control in T1DM women[84].

Adolescents with T1DM who participate in moderate-intensity exercise in the afternoon have augmented glucose needs at the time of and shortly after the completion of exercise. In addition, the reduced counter-regulatory responses to hypoglycemia post-exercise may lead to a higher risk of hypoglycemia overnight[182]. Antecedent hypoglycemia induces acute counter-regulatory failure both during subsequent hypoglycemia and moderate exercise in T1DM. This acute state of counter-regulatory impairment may be one cause of exercise-associated hypoglycemia in these individuals[183]. Anaerobic exercise usually causes BG concentration to reduce quickly, whereas anaerobic exercise may cause it to increase, making glycemic control challenging for patients with T1DM[184]. Prolonged exercise could lead to hypoglycemia even in normal male individuals[185]. Even though the risk of exercise-induced hypoglycemia is a great challenge for these patients, the glycemic response to exercise depends upon several factors concerning the patient him/herself such as therapy, glycemic control, training level, and the characteristics of the exercise performed[186].

Also, evidence shows that there are sex-related differences in exercise responses that might affect BG levels during exercise in patients with T1D[187,188]. Marked sexual dimorphism occurs in the pattern of counter-regulatory responses to moderate, prolonged euglycemic exercise in subjects with T1DM. Despite decreased plasma levels of epinephrine, norepinephrine, and growth hormone, T1DM women have a higher lipolytic response, which probably reflects greater tissue sensitivity to one of these hormones during exercise[188]. When compared with men, women with T1DM are more resistant to the blunting effects of antecedent hypoglycemia on neuroendocrine and metabolic responses to subsequent moderate exercise[189].

A study showed that patients with T1DM have a variable glycemic response to prolonged aerobic exercise, and this variability is partially explained by their pre-exercise BG levels[190]. High-intensity interval training (HIIT) has been found to improve anaerobic capacity without a detrimental decrease in BG in these patients[191]. However, another study showed that HIIT in fasting individuals with T1D produces a large and consistent hyperglycemic response instantly post-exercise[192]. Also, Fahey *et al* [193] demonstrated that a sprint as short as 10 s can raise plasma glucose levels in nondiabetic and T1DM subjects, with this increase resulting from a transient decrease in glucose rate of disappearance (Rd) rather than from a disproportionate rise in glucose rate of appearance (Ra) relative to glucose Rd as reported with intense aerobic exercise. Furthermore, other identified barriers were lack of time and work-related factors, access to facilities, lack of motivation, embarrassment and body image, weather, and having low levels of knowledge about managing diabetes and its complications in relation to exercise as the main barriers to perform exercise[194].

## THE STRATEGY TO CONTROL PHYSICAL ACTIVITY INDUCED HYPOGLYCEMIA IN T1DM

The effective management of T1DM desires a multidisciplinary combined method to develop individualized programs, attention to all factors that may influence the result, and the expectations of those with T1DM should be paramount in the strategy adopted by the diabetes care team[195]. It is essential to know that both hypoglycemia and hyperglycemia can arise during exercise; however, strategies are available to deal with these challenges[64]. In T1DM, due to the potential risk of hypoglycemia, the patients must be carefully educated about the consequences of PA on their BG levels and the modifications of diet and insulin therapy before starting exercise sessions[196].

It is supportive for subjects to monitor their BG levels before, during, and after exercise, to avoid T1DM complications and to identify when changes in insulin or food intake are essential. In particular, individuals who experience late or nocturnal hypoglycemia should have a snack after exercise and/or before going to sleep[197]. It is suggested that the personalized exercise carbohydrate requirement estimation system can be used for the management of exercise-related glycemic imbalances in T1DM [198]. In individuals with T1DM being treated with intensive insulin therapy containing the basal-bolus (NPH-human regular) insulin regimen, walking after meals improves glycemic control[199]. Also, performing resistance exercise before aerobic exercise improves glycemic stability throughout exercise and decreases the duration and severity of post-exercise hypoglycemia in subjects with T1DM[200]. Performing a morning resistance exercise session after an overnight fast and omission of pre-exercise rapid-acting insulin does not induce acute post-exercise hypoglycemia or increase the marker of muscle damage in T1DM patients[201]. In addition, morning exercise reduces the risk of late-onset hypoglycemia compared with afternoon exercise and improves BG control the following day[109]. Eating low glycemic index food with a decreased rapid-acting insulin dose following evening exercise avoids postprandial hyperglycemia and inflammation and provides hypoglycemia protection for nearly 8 h post-exercise[202]. Ingested carbohydrates before moderate-intensity exercise with added repeated sprints is not significantly detrimental to glycemic management in overnight fasted people with T1DM under basal insulin conditions[203]. Also, a qualitative study among athletes with T1DM showed that peer mentoring and mobile apps could potentially support the management of glycemic control in athletes[204]. In athletes with T1DM, while the reductions in glucose level during continuous moderate-intensity exercise and combined (continuous moderate-intensity and intermittent high-intensity) exercise are analogous, the latter form of exercise protects against nocturnal hypoglycemia which indicates that continuous moderate-intensity exercise is linked with a raised risk of nocturnal hypoglycemia in these patients[205].

Furthermore, a larger insulin basal rate decrease and supplemental carbohydrates during exercise may be essential to avoid hypoglycemia[206]. In addition, a combination of ideal glycemic control, empirical adjustments of insulin administration at the time of exercise, and ingestion of carbohydrate supplements tailored to the type, intensity, and duration of an exercise also help to prevent hypoglycemia[207]. Exercise has a role in insulin pump therapy and improves metabolic control in patients with T1DM[208]. A reduction in the basal rate during fasting exercise in continuous subcutaneous insulin infusion-treated individuals seems to be a reasonable step in the maintenance of near-normoglycemia in individuals in whom this occurs[209].

However, reducing the basal insulin infusion rate by 80% up to 40 min pre-exercise onset was found to be insufficient to decrease exercise-induced hypoglycemia[210]. In children, even discontinuing basal insulin during exercise is an effective approach for reducing hypoglycemia in children with T1DM, but the risk of hyperglycemia is increased[211]. Another approach is short-time hypoxia together with graded exercise, which increases cardiorespiratory adaptation to exercise and permits more effective control of glucose homeostasis in T1DM[88]. Combining exercise with hypoxia may permit more effective short-term glycemic control in these patients[212]. Besides, home-HIT appears to provide a strategy to decrease the fear of hypoglycemia, while simultaneously eliminating other identified barriers in individuals with T1DM from performing exercise such as being time-efficient, no travel time or costs related to gym memberships, and providing them with the chance to exercise in their chosen environment, decreasing embarrassment experienced by some when exercising in public[213].

Technology such as continuous glucose monitoring (CGM) is a strategy to control hypoglycemia during exercise in T1DM, and it allows individuals to see the trends in glycemic fluctuations when exercising and in the subsequent night to deal pre-emptively with hypoglycemic risks and treat hypoglycemic episodes in a timely way[214]. Using CGM during exercise may avoid exercise-induced hypoglycemia, but usual BG control should be carried out during intensive exercise[215]. High-intensity exercise leads to delayed nocturnal hypoglycemia and CGM is a useful approach in T1DM subjects who undergo an exercise program[216].

Using CGM trends and carbohydrate intake based on standard exercise carbohydrate intake guidelines to facilitate exercise in children with T1DM is effective as both were found to minimize hypoglycemia and maintained euglycemia during exercise in young children with T1DM[217]. In addition to this, real-time continuous glucose monitoring (RT-CGM) can be recommended as an extra tool that offers T1DM adolescents a rapid reaction to decrease glycemic variability within a short time [218]. Besides, RT-CGM with a carbohydrate intake algorithm may avoid hypoglycemia and maintain euglycemia during exercise, mainly if the subject consumes carbohydrates when trend arrows alert

them to a drop in glycemia[219].

Furthermore, closed-loop insulin delivery also offers an effective means to decrease the risk of nocturnal hypoglycemia while increasing the percentage of time spent in the target range, irrespective of activity level during mid-afternoon. This could benefit these patients even if it is limited to the overnight period[220]. The hybrid closed-loop systems are another approach that help to avoid hypoglycemia, relying on accurate carbohydrate ratios and carbohydrate counting, and the algorithm that was tested against moderate exercise and an over-reading glucose sensor performed well in terms of hypoglycemia prevention[221]. Moreover, a study demonstrated that the heart rate-enhanced artificial pancreas system improved protection against hypoglycemia during exercise in T1DM[222]. Several studies have shown different strategies that could be integrated with exercise as a means of glycemic control in individuals with T1DM (Table 1)[223-240].

## PHYSICAL ACTIVITY RECOMMENDATIONS FOR T1DM PATIENTS

It is essential to balance the risks of insulin-induced hypoglycemia with the risks related to poorly controlled diabetes and poor physical fitness in individuals with T1DM[241]. Considering the risk-benefit ratio, several studies have recommended PA in patients with T1DM[9,71,79,92,97,113,124,158,191,207,214,231,242-248]. Regular PA should be a routine aim in these subjects, for various health and fitness reasons. However, considerable challenges remain for these patients, and their healthcare team, in the management of exercise and sports[244]. Exercise is highly recommended for patients with T1DM as it has several beneficial health effects, with the prevention of long-term cardiovascular complications being dominant[207,214].

With regard to exercise, regular moderate-to-vigorous exercise should become a central part of the management of subjects with T1DM, in the absence of contraindications and accompanied by all desirable educational support for optimal diabetes management[245]. Children with IDDM can be engaged in regular vigorous PA (with minimal risks)[71] and regular exercise[124]. A combined exercise of strength training (ST) and HIIT for at least 2 mo, 3 times per week, will provide many health benefits for T1DM subjects[9].

Another study showed that HIIT sessions reduced glycemia to a greater degree than ST or ST+HIIT sessions over 10 wk in real-life situations. Because of this, T1DM individuals who develop severe exercise-associated hypoglycemia and/or present pre-exercise capillary glucose levels close to 5.5 mmol/L are recommended to carry out ST or HIIT after ST as the preferred option[247]. Resistance exercise was also found to have several benefits and should be recommended as a significant activity for health and well-being in these individuals, although caution with regard to BG levels will always be essential while performing resistance exercise[231]. However, HIIT may be the chosen training approach for some individuals with T1DM as it has been found to improve anaerobic capacity without a detrimental decrease in BG in these patients[191]. For T1DM patients using ultra-long-acting insulin, both aerobic high-intensity interval exercise and moderate continuous exercise can be safely performed [67].

In addition, high-intensity exercise does not raise the risk of early post-exercise hypoglycemia in patients with T1DM[249]. High-intensity bouts linked with high-intensity exercise result in a more rapid and higher increase in endogenous glucose production during exercise than moderate-intensity exercise alone. During early recovery from exercise, glucose use reduces following high-intensity exercise, while leftovers raised after moderate-intensity exercise despite the performance of more whole work[250]. In pediatric patients with T1DM, the frequency of regular PA was the main factor that affected the control of BG without raising the risk of severe hypoglycemia and this is why it is recommended in these patients[94].

Moreover, for subjects with T1DM, the emphasis must be on adjusting the therapeutic regimen to allow safe participation in all forms of PA consistent with an individual's desires and goals. Eventually, all subjects with diabetes should have the chance to benefit from the valuable effects of PA[248]. Daily PA should be recommended in these patients as part of their management[113] and could be used as an adjunct in glycemic control[92]. Diet and PA can influence glycemic control in IDDM independent of changes in insulin treatment[158].

Besides exogenous insulin therapy and CGM, exercise is recommended in adults with T1DM to improve the entire health of individuals[79]. However, to perform regular PA, the patient and those who supervise them should be aware of disease-specific recommendations and contraindications[242]. Evidence recommends that even individuals with ketonemia may engage in intensive physical training, provided this is part of a program including adequate insulin dosage, dietary advice, and close supervision with multiple daily BG measurements[246]. Evidence suggests that it is significant to consider the needs of the wider support network, as well as the child's or adolescent's concerns and preferences, during the development of new or existing strategies and programs to promote PA in children and adolescents with T1DM[251]. Finally, during PA, the parameters such as supervision, duration, frequency of sessions, protocols with mixed PA may positively affect the metabolic outcome of patients with T1DM[97].

**Table 1 Summary of studies on exercise intervention in type 1 diabetes mellitus patients to improve glycemic control**

Ref.	Year	Intervention	Findings
Sonnenberg <i>et al</i> [223]	1990	CSII during exercise	Hypoglycemia could only be avoided when the premeal insulin bolus was decreased by 50% and discontinuation of the basal insulin infusion during exercise
Rabasa-Lhoret <i>et al</i> [224]	2001	Premeal insulin dose reductions for post-prandial exercises	Minimized risk of hypoglycemia during postprandial exercises of different intensities and different durations by a suitable decrease in premeal insulin lispro
Dubé <i>et al</i> [225]	2005	Glucose supplement during exercise in subjects using N-lispro	For 60 min of late post-prandial exercise followed by 60 min of recovery, an estimated 40 g of a liquid glucose supplement, ingested 15 min before exercise was good for BG control
Diabetes Research in Children Network (DirecNet) Study Group <i>et al</i> [211]	2006	Suspension of basal insulin during exercise	Basal insulin suspension decreases hypoglycemia from 43% to 16% in individuals, but hyperglycemia 45 min after exercise was more frequent
Bussau <i>et al</i> [226]	2006	Ten-second sprint after moderate-intensity exercise	This avoided early post-moderate intensity exercise hypoglycemia
Bussau <i>et al</i> [227]	2007	Ten-second sprint before moderate-intensity exercise	Prevented hypoglycemia during early recovery from moderate-intensity exercise
West <i>et al</i> [228]	2010	Reductions in pre-exercise rapid-acting insulin by 75%, 50%, or 25%	A 75% reduction in pre-exercise insulin resulted in the greatest preservation of BG, and a decreased dietary intake, for 24 h after running
Taplin <i>et al</i> [229]	2010	20% reduction of basal rate overnight  2.5 mg bedtime dose of oral terbutaline	Was safe and effective in preventing nocturnal hypoglycemia  Effective at avoiding hypoglycemia, but linked with hyperglycemia
Riddell <i>et al</i> [219]	2011	RT-CGM and carbohydrate intake algorithm (8-20 g), depending on the concentration of glucose at the time of RT-CGM alert and rates of change in glycemia	The coupled carbohydrate intake algorithm with RT-CGM avoided hypoglycemia and maintained euglycemia during exercise
Garg <i>et al</i> [230]	2012	An automatic suspension of insulin delivery when BG ≤ 70 mg/dL during or after exercise	This significantly decreased the duration and severity of induced hypoglycemia without causing rebound hyperglycemia
Yardley <i>et al</i> [200]	2012	Resistance exercise before aerobic exercise	Performing resistance first improved glycemic stability throughout the exercise and decreased the duration and severity of post-exercise hypoglycemia
Yardley <i>et al</i> [231]	2013	Resistance vs aerobic exercise	Resistance caused a less initial decline in BG but prolonged decreases in post-exercise glycemia than aerobic exercise
Campbell <i>et al</i> [232]	2013	Pre- and post-exercise rapid-acting insulin reductions	25% pre-exercise and 50% post-exercise rapid-acting insulin dose preserved glycemia and protected patients against early-onset hypoglycemia (8 h)
Schiavon <i>et al</i> [233]	2013	In silico optimization of basal insulin infusion rate during exercise	A decrease in basal insulin by 50% starting 90 min before exercise and by 30% during exercise is safe and effective for glucose control
Danne <i>et al</i> [234]	2014	PLGM (suspension of insulin delivery based on predicted sensor glucose values)	PLGM may decrease the severity of hypoglycemia above that already established for algorithms that use a threshold-based suspension
Campbell <i>et al</i> [235]	2015	Combined basal-bolus insulin dose reduction and carbohydrate feeding strategy following exercise	Reducing basal-bolus insulin by 20% (80%) protected from nocturnal hypoglycemia for 24 h post-exercise
Cherubini <i>et al</i> [236]	2019	PLGM system during exercise	Effective for avoiding hypoglycemia during and after exercise, regardless of the thresholds of PLGM used
Moser <i>et al</i> [237]	2019	Oral administration of carbohydrates during moderate-intensity exercise	Pre-exercise BG levels determine the amount of orally administered carbohydrates during exercise to maintain euglycemia
Zaharieva <i>et al</i> [238]	2019	Basal rate reductions set 90 min pre-exercise vs pump suspension at exercise onset	50%-80% Basal rate reductions set 90 min pre-exercise improved BG control and reduced hypoglycemia risk during exercise better than pump suspension at exercise onset
Moser <i>et al</i> [239]	2019	Reduction in insulin degludec dose (75% IDeg dose vs 100% IDeg dose)	Reducing the usual IDeg dose by 25% led to more time spent in euglycemia with small effects on time spent in hypo- and hyperglycemia

Zaharieva <i>et al</i> [240]	2020	Insulin pump connected (pump on) <i>vs</i> pump disconnected (pump off) during high-intensity exercise	No significant differences in BG concentrations during 40 min of intermittent high-intensity exercise
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CSII: Continuous subcutaneous insulin infusion; BG: Blood glucose; RT-CGM: Real-time continuous glucose monitoring; PLGM: Predictive low glucose management.

## CONCLUSION

As T1DM is rising globally, PA is recommended as evidence shows that PA can control the burden of disease. The benefit of PA in T1DM is a significant component in its management. It is recognized as having beneficial effects and is key to a healthy lifestyle as well as the management of T1DM. PA can be considered an efficient and inexpensive non-pharmacologic tool for the management of T1DM in addition to insulin therapy. It has significant health benefits such as improves BG control, physical fitness, endothelial function, insulin sensitivity, well-being, and the body defense system. In addition, it reduces the blood lipid profile, insulin resistance, CVDs, insulin requirements, BP, and mortality associated with T1DM.

Overall, ideal glucose control is of principal significance in T1DM including during PA. Previously, it is challenging to prevent the hazards associated with PA in these individuals. Hypoglycemia and fear of hypoglycemia are the greatest challenges in T1DM individuals engaging in PA and can limit suitable glycemic control in these patients. However, a better understanding of energy metabolism and homeostasis has made it possible for individuals with diabetes to take part in exercise. In addition, several strategies have been identified to make PA more suitable for T1DM individuals. In particular, improvements in glucose monitoring technology and the availability of other interventional approaches during PA have further contributed to the feasibility of exercise programs for these subjects. There are also strategies for preventing exercise-induced hypoglycemia during and after exercise.

The present review may help health professionals to encourage PA as part of the management of individuals with T1DM. It is also recommended that PA can be performed carefully with reference to diabetes guidelines. Therefore, health professionals in clinical practice should inform and encourage patients with T1DM to manage exercise-induced hypoglycemia. Furthermore, in-depth knowledge of factors such as gender, therapy, glycemic control, training level and characteristics of the exercise performed will allow the development of individualized strategies to minimize the risk of hypoglycemia as the glycemic response to exercise depends upon these factors.

Moreover, health professionals should distinguish between hyperglycemia induced by HIIT and the concern of hypoglycemia-related to less intense forms of exercise during patient counseling for T1DM. Also, this should be clearly set out in practice guidelines. Patients and health professionals should be aware of the degree and duration of post-HIIT hyperglycemia and the potential benefit of an insulin correction bolus. Support for patients on how better to control their BG after exercise could encourage these patients to be less fearful of exercise-induced hypoglycemia and participate in regular PA. Clear-cut quantitative approaches to prevent exercise-induced hypoglycemia are desired to allow patients to engage in regular PA and enjoy its beneficial aspects. It is essential to consider the potential alterations in exercise responses that may occur in T1DM and not to judge this activity as harmful, but these alterations can reduce its full beneficial health effects. Lastly, the present review also provides suggestions for the future direction of research on the types of exercise, duration, and intensity recommended for T1DM patients, considering the individual's factors that could be detrimental to the response that occurs during and after exercise.

## FOOTNOTES

**Author contributions:** The author made substantial contributions to conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the article and making critical revisions related to important intellectual content of the manuscript; and final approval of the version of the article to be published.

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