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Associations between Lifestyle Medicine activities and Type 1 Diabetes Mellitus management: a systematical review

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Abstract

According to the Brazilian Society of Diabetes, the prevalence of Type 1 Diabetes Mellitus (T1DM) is increasing; thus, alternative and pharmacological measures are required to manage and control the disease. Many studies discussed lifestyle medicine with Type 2 Diabetes Mellitus (T2DM). However, studies on the pillars of lifestyle medicine with T1DM are limited. The lack of research on the subject prompted the development of this systematic review. We aimed to evaluate the association between lifestyle medicine activities and delay in the clinical manifestations of T1DM. We included randomized and nonrandomized clinical trials and retrospective or prospective longitudinal studies. English, Portuguese and Spanish were screened as accepted languages. Participants could be of any geographic location or sex. Regarding the interventions, we selected diet, exercise, sleep, stress reduction, and smoking cessation as lifestyle medicine practices with a possible association with glycemic control improvement in patients with T1DM. In total, 22,552 publications have been identified; at the end, 28 articles, 11 clinical trials, and 17 cohorts were selected, involving 16.627 patients and 14 countries. Although lifestyle modifications seem to have the potential to alter the course of T1DM in many ways, the evidence available to date is insufficient.

Keywords: Lifestyle medicine, Type 1 Diabetes Mellitus, Diabetes control.

1. Introduction

Type 1 Diabetes Mellitus (T1DM) is a T-cell-mediated disorder of autoimmune etiology characterized by the destruction of insulin-producing pancreatic ß-cells and is one of the most common endocrine pediatric diseases [1]. According to the EURODIAB study, a more significant increase in the incidence of T1DM for the group of children under five years old was observed, predicting the number of new cases in this same age group will double between 2005 and 2020 [2].

Several factors are involved in the pathogenesis of the disease, including diet, Body Mass Index (BMI), virus infections, geography, medication use, population hygiene, sun exposure, and vaccination rates [1,3,4]. However, genetic predisposition is noteworthy, accounting for about 70–75% of the organism's susceptibility to the development of the disease [4]. As in other autoimmune diseases, the pathogenesis of T1DM is correlated with human leukocyte antigens (HLA), the two most involved combinations being HLA DR4-DQ8 and HLA DR3-DQ2. These combinations were found in a sample of children with T1DM, especially those who developed the disease earlier. Furthermore, previous studies have suggested that the presence of anti-islet of Langerhans (ICA), anti-insulin (IAA), or antiglutamic acid decarboxylase (anti-GAD) autoantibodies would be risk predictors of the development of T1DM [1,5].

The pharmacological treatment of T1DM, for more than 50 years, was only regular insulin, NPH, derived from the animal pancreas. Until the late 1970s, other treatments were developed, including blood glucose meters and the use of recombination of genes for the production of regular human insulin. [6]. After the publication of the Diabetes Control and Complications Trial in 1993, the management of glucose monitoring and the adoption of intensive insulin therapy changed, resulting in an improvement in diabetes management [6,7].

Most people with T1DM receive insulin through injections or subcutaneous infusion, usually known as insulin pump therapy. The therapy made through insulin injection is promoted through long-acting basal insulin, used once or twice a day, and fast-acting insulin after meals. There is an inhaled insulin on the market whose duration of action is more similar to the duration of action of physiological insulin but has not been widely used [6].

The World Health Organization Health Glossary defines lifestyle as a "way of living based on identifiable patterns of behavior that are determined by the interaction between an individual's characteristics, social interactions, and living conditions, socioeconomic and environmental conditions” [8]. Unlike conventional medicine, the focus of lifestyle medicine is not on treating chronic diseases but rather on preventing them through the acceptance and adoption of a healthier standard of living [9,10]. This new medical aspect is based on the environment, healthy plant-based diet, exercise, stress control, cessation of smoking, alcohol and illicit drugs, adequate rest, healthy social relationships, and emotional health, among others, with the goal of preventing, treating, and reversing the progression of chronic diseases.

According to the Brazilian Society of Diabetes, the prevalence of T1DM is increasing, thus requiring alternative measures and pharmacological measures for its control. The glycosylated hemoglobin (HbA1c) mean was 9.1% in a cross-sectional, multicenter study conducted in 28 public clinics of the secondary and tertiary care level located in 20 cities in Brazil involving 1774 adults with T1DM between December 2008 and December 2010 [11]. The Brazilian College of Lifestyle Medicine defines lifestyle medicine as an interdisciplinary scientific approach that prioritizes the therapeutic use of lifestyle to control chronic diseases, such as T1DM.

Many studies have discussed lifestyle medicine for T2DM. However, studies on lifestyle medicine for T1DM are limited. However, the lack of research on the subject prompted the development of this review.

2. Materials and Methods

This systematic review aimed to evaluate the association between lifestyle medicine activities and delay in the clinical manifestations of T1DM, for which the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) were used [12]. Moreover, the modified Jadad scale and the Newcastle-Ottawa Scale (NOS) were used to assess clinical trials and longitudinal studies, respectively, to rate the methodology and bias of the selected studies.

In this article, we included randomized and nonrandomized clinical trials and retrospective or prospective longitudinal studies. English, Portuguese, and Spanish were screened as accepted languages. The search was not restricted, and participants could be of any geographic location or sex. Other types of studies and those that have not yet been published were excluded.

In terms of interventions, we selected diet, exercise, sleep, stress reduction, and smoking cessation as lifestyle medicine practices with a possible association with glycemic control improvement in patients with T1DM.

The research was performed electronically by accessing the PubMed database. The keywords for the search were as follows: “type 1 diabetes mellitus”, “insulin-dependent diabetes mellitus”, “lifestyle”, “diet”, “nutrition”, “exercise”, “training”, “sports”, “fitness”, “sleep”, “stress”, “smoking”, “alcohol”. Figure 1 illustrates the results of the search. The search was performed on 06/05/21, and the analyses ended on 12/07/21.

The primary analysis of the articles was carried out independently by five authors (L, E, FG, MS, and ML) by reading the titles and abstracts. The studies that met the inclusion criteria were read in their entirety by the same authors, and those that did not present any new evidence to justify their withdrawal were used in this review. Any questions about the inclusion of these articles were discussed between all the authors in search of a consensus.

3. Results

We identified 22,552 publications, and, at the end, 28 articles, 11 clinical trials [13–23], and 17 cohorts [18,24–40] meeting all the inclusion criteria were selected (Figure 1). Seven articles evaluated the association between diet and T1DM (Table 1) [13,19,20,24,34,36,37]. Three articles examined the correlation between smoking and T1DM (Table 1) [25,26,35]. Three articles investigated the relationship between sleep and T1DM (Table 1) [27,28,38]. Seven articles evaluated the associations between exercise and TIDM (Table 2) [14,16–18,33,39,40], and eight articles investigated the associations between stress and T1DM (Table 3) [15,21–23,29–32]. Moreover, most studies analyzed the effectiveness of intervention through HbA1c; one article used glycosylated albumin [18] and another aimed to evaluate the risk of developing T1DM [30].

In total, 16,627 subjects were included in this systematic review. The oldest article was published in 1980 [17], whereas the most recent was published in 2019 [28,35]. The studies took place in several countries: 10 in the USA [16,18,28,29,31,33,35–37,39]; two in Sweden [21,30], Denmark [14,23], UK [13,32], and New Zealand [19,20]; one in India [15], Iran [22], Italy [24], Norway [17], Spain [40], Switzerland [25], Australia [26], France [27], and Germany [38]. Both children and adults were enrolled.

The NOS score obtained the analysis of possible bias in observational studies ranged from 4 to 8. The absence of a control group was the main limiting factor observed. On the other hand, the score obtained on the modified Jadad scale for the analysis of possible bias in clinical trials ranged from 3 to 6. The main limiting factors observed were the absence of a control group and blinding. Table 4 includes the scores for both scales. More information about the included articles will be revealed in the Discussion section.

4. Discussion

Nutrition and T1DM

Three clinical trials were among the articles that evaluated the effectiveness of diet correction in glycemic control [13,19,20]. Krebs et al. [19] conducted a small randomized controlled trial. They found that beyond HbA1c improvement, the low carbohydrate group required less insulin dose. Moreover, Perry and Kinmonth [13,20] performed crossover trials. Perry tested lifestyle practices and found improvement in low-density lipoprotein (LDL) cholesterol and maximal oxygen consumption after the intervention. Kinmonth tested an unrefined diet (low carbohydrate and high fiber), which resulted in better mean 24-hour glucose and mean 24-hour urinary glucose loss in this intervention.

Four cohorts were included, and two of those were controlled [24,34,36,37]. Giacco et al. tested a high-fiber diet; as a result, beyond HbA1c improvement, they found better mean daily plasma glycose and fewer hypoglycemics events [24]. Moreover, Mottalib et al. analyzed multidiscipline weight management in obese adult patients with T1DM, and the result was significant weight loss and less daily insulin dose and utilization of antihypertensive medications among the intervention group, which was not observed in the control group [36]. Balk et al. conducted a large prospective uncontrolled cohort with a 7-year follow-up and found that low vegetable protein and dietary fiber intake is associated with worse glycemic control in type 1 diabetes [34]. Furthermore, Delahanty performed a large prospective uncontrolled cohort with a 5-year follow-up and found that lower carbohydrate intake and higher saturated, monounsaturated, and total fat intakes were associated with higher HbA1c [37].

Smoking Habits and T1DM

Despite the large body of evidence against smoking, the prevalence in patients with diabetes remains high. Smoking is associated with an increase in macrovascular and microvascular complications in people with the disease. The risk of diabetic nephropathy, retinopathy, and neuropathy, for example, is probably attributed to the combination of metabolic effects, inflammation, and endothelial dysfunction caused by tobacco, and this association is very common in patients with diabetes, especially those with T1DM [41].

Kar et al. defined two groups in their meta-analysis: smokers versus nonsmokers and smokers versus ex-smokers [42]. The first group had 47.41% of participants with T1DM, while the second had only 3%, the rest being patients with T2DM. With the analysis of HbA1c levels as one of the outcomes of smoking, a significant reduction in nonsmokers was identified in the first group, with an average of 0.61%. However, this difference was associated with significant factors, such as the age of participants and the time of smoking. In the second group, the difference was smaller, about 0.10%, with no statistically significant difference in this group.

In another study, Chaturvedi et al. found that smokers had worse glycemic control than nonsmokers, as well as a greater number of ketoacidosis episodes [43]. They concluded that compared to nonsmokers, ex-smokers had worse glycemic control and a higher risk of hypoglycemic episodes. Furthermore, other studies (Boren e Nagrebetsky [44,45]) suggested that smoking cessation strategies did not significantly influence the improvement of HbA1c levels and, consequently, the glycemic control of individuals.

Three cohorts were selected that evaluated the impact of smoking habits on glycemic control [25,35,43]. They were all controlled studies. Braffett et al. found that smoking habits also increase the risk of developing retinopathy and nephropathy [35]. Gerber et al. also found a correlation between smoking and microvascular and macrovascular complications [25].

Sleep Quality and T1DM

There is strong evidence that sleep disturbances affect glucose metabolism and insulin resistance. The relationship between sleep and T2DM is widely studied, and it is well known that these patients have a high prevalence of obstructive sleep apnea (OSA), resulting in poor glycemic control. On the other hand, little is known about the impact of T1DM on glycemic control, making research into this topic extremely vital.

In their meta-analysis, Reutrakul et al. analyzed studies that compared the individuals' sleep time with their respective HbA1c values [46]. According to four studies, adults who slept for more than 6 hours had better results in HbA1c levels than those who slept for less than 6 hours. Moreover, patients with optimal glycemic control (HbA1c <7%) reported sleeping an average of 17.3 minutes longer than those with poorer glycemic control (HbA1c ≥7%). However, in this same meta-analysis, it was discovered that in four cohorts of children, no significant difference was observed in glycemic levels between groups with long and short sleep duration.

Barone et al. observed a positive relationship between sleep quality and blood glucose variability in individuals with T1DM, indicating that individuals who experience variations in their blood glucose may have difficulty sleeping [47]. Therefore, no relationship was found between sleep duration and glycemic control. In their meta-analysis, Gu et al. revealed a close correlation between OSA and the development of peripheral neuropathy in patients with T1D [48].

Three cohorts were also selected from the articles that evaluated the impact of sleep quality on glycemic control [27,28,38]. Only Larcher et al. performed a controlled analysis [27]. They found that social jet lag (the time difference between the midpoint of sleep on workdays and free days) >49 min is associated with higher triglyceride levels. Social jet lag was also related to poor HbA1c control and insulin requirement in Frye et al.'s study and Von Schnurbein et al.'s study, respectively [28,38].

Physical Activity and T1DM

The American Diabetes Association (ADA) recommends that people with diabetes mellitus perform at least 150 minutes of moderate-intensity aerobic physical activity or 75 minutes of high-intensity aerobic physical exercise per week [49]. Evidence indicates, over the years, that individuals with T1DM are at least twice as likely to develop cardiovascular disease as those who do not have the disease [50]. This is due to the fact that people with diabetes have risk factors for cardiovascular diseases, such as endothelial dysfunction, which can manifest in childhood and preadolescence [51]. Thus, young people with T1DM are advised to engage in regular physical activity, in conjunction with adequate insulin use and dietary adjustments [52]. In their meta-analysis, Quirk et al. suggested that constant physical activity can provide a range of health benefits for children and young people with T1DM [53]. Such findings are clinically significant in delaying the premature onset of complications, cardiovascular disease, and physical disability [53,54].

Although the benefits are well supported, F Sundberg et al., in their case-control study, demonstrated that children under 7 years old with T1DM are less physically active than healthy ones, raising the need for health promotion based on regular physical activity [54]. When considering the importance of lifestyle and physical exercise throughout the life of the individual with T1DM, health education is one of the most important strategies to be applied, which should cover not only the patients involved but also the family members, advising them about the healthy lifestyle associated with possible glycemic control [55].

To date, there is solid evidence that exercise improves fitness, insulin resistance, and macrovascular risk in people with T1DM [56]. However, the results of studies on exercise and glycemic control are conflicting for patients with T1DM, in contrast to the evidence already supported by the demonstrable benefits of glycemic control in DM2 [56,57]. Kennedy et al. concluded in their meta-analysis that although benefits of glycemic control associated with physical exercise in patients with T1DM were not detected, other benefits were already consolidated, including macrovascular risk reduction, mortality, and improved well-being [56–59]. Therefore, constant exercise should continue to play an important role in T1DM management and its glycemic benefits are more consistently investigated [59].

Among the articles that evaluate the effectiveness of physical activity in glycemic control, four were randomized controlled clinical trials [14,16–18]. In these studies, the activity, intensity, and time of practice vary, but they all significantly improved the HbA1c levels after the intervention. Three of the selected articles were cohorts, and one was an uncontrolled study. A positive association was found between physical activity and better HbA1c levels in all four studies.

Psychiatric Disorders Management and T1DM

We selected four clinical trials and four cohorts among the articles that evaluate the relationship between stress management and glycemic control. In the trials, group therapy and dialogue were performed and glycose improvement was observed [15,21–23]. Amsberg et al. and Saghaei et al. also observed a reduction in anxiety and depression [15,21]. The four cohorts were not controlled [29–32]. Special attention should be given to the ABIS study [30], which was the only included article that assessed the risk of developing T1DM as the outcome. Exposure to stressful life events in children was the risk factor studied, and a significant association was found.

As evidenced in Nagaraja et al.'s study, stress is responsible for inducing organic adaptations that contribute to the pathophysiology of various diseases in modern society [60]. According to data from the American Institute of Stress (AIS), 90% of health problems are stress-related [61].

Emotional stress is one of those factors that contribute to deterioration without glycemic control. In addition to being related to problems in dietary compliance, physical activity level, and control of insulin use [62], it also triggers hormonal responses with cortisol that directly affect diabetes.

Anxiety, depression, and stress symptoms are prevalent in young people with T1DM,. which have been associated with higher levels of HbA1c. The prevalent relationship between diabetes and concomitant psychiatric disorders is complex and bidirectional; both influence each other, thus providing a poor prognosis. Thus, there is an increasing demand for treatment for this clinical condition [63].

In their review of randomized controlled trials, Yang et al. demonstrated that lifestyle modifications based on cognitive behavioral therapy (CBT) effectively improve glycemic control and psychiatric symptoms in patients with T1DM [64]. Yoga is a vital nondrug therapy that should be included in this treatment, and it encompasses exercises such as meditation, breath control, and muscle relaxation. The constant practice of yoga maintains the balance in controlling various organ systems, thus improving stress, anxiety, and quality of life. These factors influence blood glucose control, consequently improving diabetes symptoms. Therefore, more studies on these nondrug therapies and their relationship with T1DM are warranted [65–67].

Limitations

This systematic review has some limitations. Although we have separated the different associations between lifestyle medicine and T1DM, the articles discussing each aspect show significant differences in factors such as design, number and age of participants, and outcomes. We could not include themes of interest such as sitting time, consumption of whole foods, and consumption of alcohol since no article using those risk factors met our inclusion criteria.

5. Conclusion

We collected some interesting data in this systematic review. Low-carbohydrate and high-fiber diets are associated with better glycemic control. Higher HbA1c level among smoking patients and patients was correlated with insufficient sleep or social jet lag. Moreover, lower HbA1c levels were observed in patients engaged in exercise programs or stress management therapies.

Although lifestyle modifications seem to alter the course of T1DM in many ways, the evidence available to date is incomplete. Most of the available studies analyzed the role of physical activity, nutrition, and smoking in the course of T1DM; however, many questions remain unanswered (such as whether there is a relationship between specific diets and glycemic control). Other aspects of lifestyle medicine are still rarely studied. Better study design, a well-defined control group, and blinding are essential requirements for better answers. Thus, studies that primarily assess the efficacy of lifestyle interventions in the course of T1DM are warranted.

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Conflict of Interest

None

Author Contributions

L, E, FG, MS, ML, F, and D conceived the idea. L, E, FG, MS, ML, and D wrote the manuscript. L, E, FG, MS, and ML critically reviewed the content. L, F, and D carefully reviewed the final manuscript. All authors approved the final manuscript and submission.

Abbreviations:

T1DM: Type 1 Diabetes Mellitus; BMI: Body Mass Index; HLA: human leukocyte antigens; ICA: anti-islet of Langerhans; (IAA): anti-insulin; anti-GAD: antiglutamic acid decarboxylase; HbA1c: glycosylated hemoglobin; LDL: low-density lipoprotein; ADA: American Diabetes Association; T2DM: Type 2 Diabetes Mellitus; OSA: obstructive sleep apnea; AIS: American Institute of Stress; CBT: cognitive behavioral therapy.

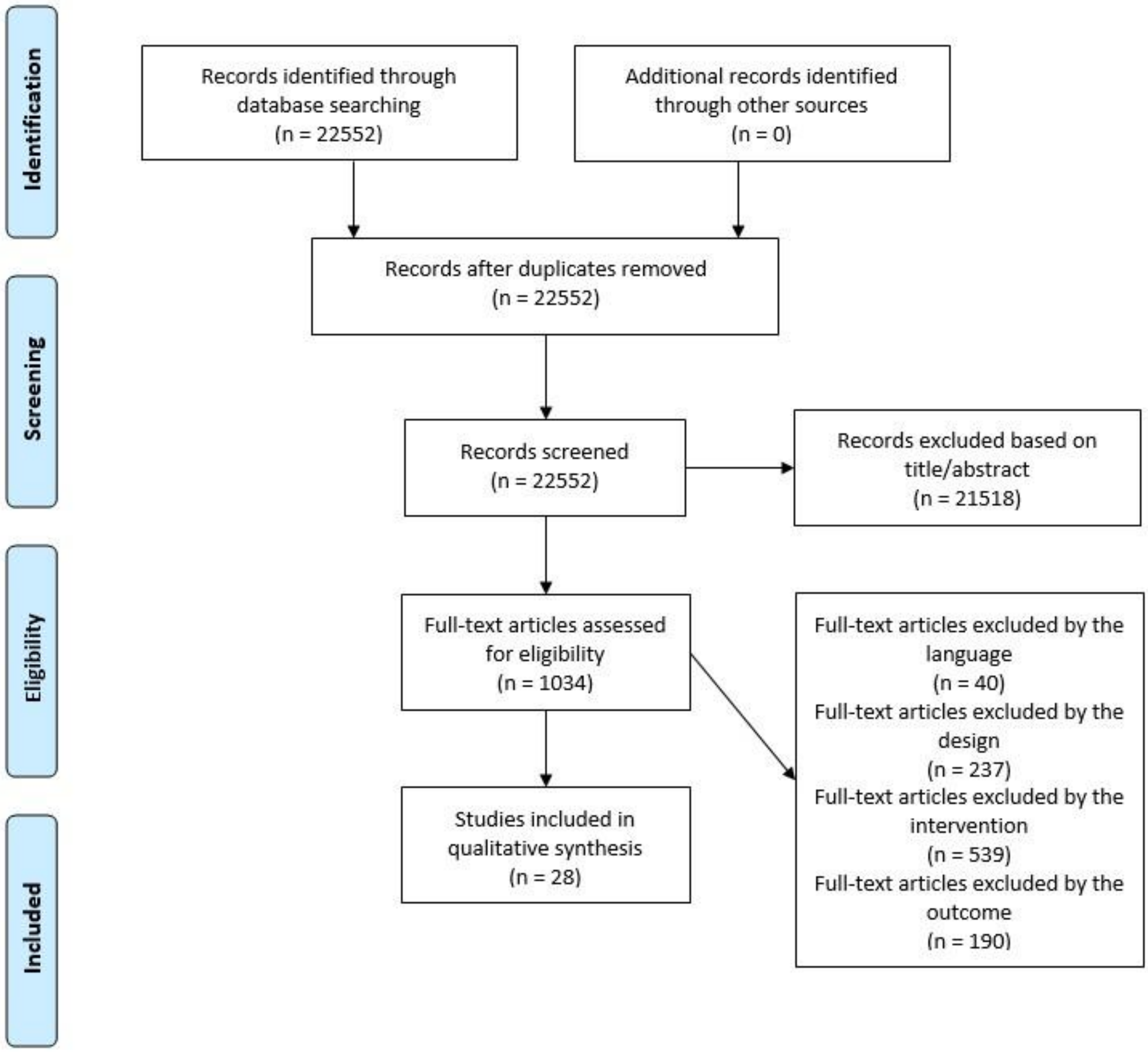

Figure 1. PRISMA flow diagram.

Table 1. Description of the articles that evaluated associations between diet and T1DM, smoking and TIDM, and sleep and T1DM.

Study ID	Desing	Nos/ Jaded score	N (I vs C)	Age (I vs C)	Gender Male (I vs C)	Aims	Result
Larcher, S.	Cohort	8	Social jetlag ≤49min (n= 41) vs Social jetlag >49min (n= 39)	Social jetlag ≤49min (mean= 44 (30–51)) vs Social jetlag >49min (mean=38 (25–47))	Social jetlag ≤49min (49%) vs Social jetlag >49min (59)	To evaluate which specific sleep behavior might be related to glycemic control	Social jetlag >49min were significantly associated with higher HbA1c (p<0.05)
Von Schnurbein, J.	Cohort	4	N = 191	Mean = 16.5 (1.8)	48%	The association between poor sleep habits and glycemic control in adolescents with type 1 diabetes	Poor sleep habits were significantly associated with higher HbA1c (p<0.05)
Frye, S. S.	Cohort	4	N = 111	Mean = 13.59 ± 2.11 years	52%	To investigate the mediating role of diabetes management in the relations between sleep duration and glycemic control in a sample of youth with T1DM	Less sleep was significantly associated with worse management and glycemic control and HbA1c (p<0.05)
Krebs, J. D.	Clinical Trial	5	Standard carbohydrate group (n = 5) vs Carbohydrate restricted group (n = 5)	Standard carbohydrate group (mean = 44.8 (8.3)) vs Carbohydrate restricted group (mean = 44.5 (10.4))	Standard carbohydrate group (60%) vs Carbohydrate restricted group (80%)	To test the feasibility of a low carbohydrate diet compared with a standard diet on glycaemic control, glucose variability, total daily insulin dose, and quality of life in a group of participants with T1DM	Glycaemic control as measured by HbA1c improved and total daily insulin use reduced in the low carbohydrate group (p<0.05)
Mottalib, A.	Cohort	7	I (n = 68) vs C (n = 68)	I (mean = 43.3 (11)) vs C (mean = 42 (12))	I (n = 38%) vs C (n = 38%)	To evaluate the effect of a 12-week multidisciplinary weight management intervention on body weight, glycemic control in comparison to standard diabetes care	Glycemic control improved in the intervention group compared to baseline (HbA1c p<0.01) with no change in the control group
Perry, T. L.	Cross-over Clinical trial	6	Group 1 (n = 31) vs Group 2 (n = 30)	Group 1 (n = 41.5 ± 11.6) vs Group 2 (n = 42.8 ± 12.6)	Group 1 (48%) vs Group 2 (66%)	To quantify the effects of an intensive diet and exercise programme on glycaemic control and cardiovascular risk factors	A significant (p<0.05) decrease in HbA1c levels was observed in both groups between recruitment and randomisation
Blak, S. N.	Cohort	4	N = 1659	Mean = 32.5 ± 9.8	52%	To investigate the longitudinal relation between dietary and lifestyle variables and HbA1c levels in T1DM	Lower intake of total dietary fibre, soluble and insoluble fibre and higher intake of animal protein were significantly associated with higher HbA1c (p<0.03)
Kinmonth A. L.	Cross-over Clinical Trial	6	Group 1 (n = 5) vs Group 2 (n = 5)	Group 1 (mean = 11.3-17.0) vs Group 2 (mean = 11.3-17.0)	Group 1 (60%) vs Group 2 (60%)	To investigate the effect on blood glucose and the acceptability to families of substituting naturally available high-fibre whole foods for the traditional low-fibre foods in the diets of diabetic children	Glycaemic control was significantly better on the unrefined diet (p< 0.01)
Delahanty, L. M.	Cohort	4	N = 532	Mean = 27.3 ± 7	48%	To examine the association of diet composition with subsequent Hb A1c concentrations in intensively treated participants with T1DM	Higher insulin dose, lower carbohydrate intake, and higher saturated, monounsaturated, and total fat intakes were associated with higher Hb A1c concentrations at year 5 (p<0.05)
Giacco, R.	Cohort	5	High Fiber (n = 53) vs Low Fiber (n = 47)	High Fiber (mean = 29.5 ± 11.0) vs Low Fiber (mean = 26.2 ± 7.9)	High Fiber (41%) vs Low Fiber (34%)	To evaluate the feasibility in the long term (6 months) of an high fiber diet and the efficacy of such a diet in relation to blood glucose control and rate of hypoglycemic events	The high fiber diet improved the blood glucose daily profile and significantly reduced the mean daily blood glucose concentration (p<0.05)
Brafett, B. H.	Cohort	5	Never Smoker (n = 926) vs Former Smorker (n = 221) and Current Smoker (n = 294)	Never Smoker (mean = 25.2) vs Former Smoker (mean = 30.4) and Current Smoker (mean = 29.1)	Never Smoker (51%) vs Former Smorker (52%) and Current Smoker (56%)	Long-term associations of smoking on glycemic control and diabetes-related complications	HbA1c levels were significantly higher for ever smokers compared with never smokers (p<0.01)
Gerber P. A.	Cohort	7	Non-Smokers (n = 603) vs Smokers (n = 160)	Non-Smokers (mean = 36.1 - 14.2) vs Smokers (mean = 35.1 - 12.8)	Non-Smokers (52%) vs Smokers (71%)	Metabolic control assessed by HbA1c measurements and presence of diabetes related complications associated with smoking	HbA1c levels remained significantly higher (p<0.001) among the smokers group until year 5 of follow-up
Smythe, K.	Cohort	7	HbA1c >7.0% (n = 80) vs HbA1c ≤7.0% (n = 23)	HbA1c >7.0% (mean = 36.9 (14.6)) vs HbA1c ≤7.0% (mean = 33.8 (13.4))	Not available	Identify the factors that are associated with better glycaemic control	Current or previous smoking were significantly associated with HbA1c >7.0%(p<0.05)
Larcher, S.	Cohort	8	Social jetlag ≤49min (n= 41) vs Social jetlag >49min (n= 39)	Social jetlag ≤49min (mean= 44 (30–51)) vs Social jetlag >49min (mean=38 (25–47))	Social jetlag ≤49min (49%) vs Social jetlag >49min (59)	To evaluate which specific sleep behavior might be related to glycemic control	Social jetlag >49min were significantly associated with higher HbA1c (p<0.05)
Von Schnurbein, J.	Cohort	4	N = 191	Mean = 16.5 (1.8)	48%	The association between poor sleep habits and glycemic control in adolescents with type 1 diabetes	Poor sleep habits were significantly associated with higher HbA1c (p<0.05)
Frye, S. S.	Cohort	4	N = 111	Mean = 13.59 ± 2.11 years	52%	To investigate the mediating role of diabetes management in the relations between sleep duration and glycemic control in a sample of youth with T1DM	Less sleep was significantly associated with worse management and glycemic control and HbA1c (p<0.05)

Table 2. Description of the articles that evaluated associations between exercise and T1DM.

Study ID	Desing	Nos/ Jaded score	N (I vs C)	Age (I vs C)	Gender Male (I vs C)	Aims	Result
Bak, J. f.	Clinical Trial	3	IDDM patients (n = 7) vs Normal subjects (n = 7)	IDDM patients (mean = 27.9 ± 7.1) vs Normal subjects (mean = 28.0 ± 6.3)	IDDM patients (57%) vs Normal subjects (57%)	To compare insulin action in skeletal muscle tissue from IDDM patients and normal healthy subjects. The diabetic patients were reexamined after physical training for 6 weeks	Six weeks of moderate physical training induced a significantly improvement in HbAic levels (p<0.05) and a 10% decrease in daily insulin requirements in the IDDM patients
Campaigne B. N.	Clinical Trial	4	Experimental (n = 9) vs Control (n = 10)	Experimental (mean = 9.0 ± 0.47) vs Control (mean = 8,5 ± 0.57)	Not available	To determine the effects of a regular physical activity program on metabolic control and cardiovascular fitness in children aged 5-11 yr with IDDM	HbA1c was significantly (p<0.05) lower in the experimental group after the 12 wk of study when compared with the control group
Dahl-Jorgensen, K.	Clinical Trial	3	Training (n = 14) vs Control (n = 8)	Training (mean = 9 ± 15) vs Control (mean = 9 ± 13)	Not available	To evaluate the effect of exercise on diabetic control	In the training group the HbA1c, values significantly decreased during the exercise period (p<0.001). In the control group values did not change significantly (p=0.20)
Michaliszyn, S. F.	Cohort	4	N = 109	Mean = 15.3 ± 1.9 yr	55%	To determine associations between amounts of activity at various intensities and changes in known CV risk factors	Times spent in light, moderate, and moderate and vigorous physical activity were associated with decreases in total cholesterol, LDL-c, triglycerides, and A1C (p<0.05)
Martinez-Ramonde, T.	Cohort	6	Active group (n = 8) vs Sedentary group (n = 11)	Active group (mean = 21.9 ± 4.2 8) vs Sedentary group (mean = 23.3 ± 2.2)	Active group (62%) vs Sedentary group (63%)	To evaluate the influence of physical activity at the moment of onset of IDDM	The more active group debuted with and maintained significantly lower HbA1c levels and insulin requirements compared to the more sedentary group (p<0.05)
Nansel, T. R.	Cohort	8	I (n = 40) vs C (n = 41)	I (mean = 13.6 ± 1.9) vs C (n =13.9 ± 1.6)	I (42%) vs C (46%)	To assess the social-cognitive, behavioral, and physiological outcomes of a self-management intervention for youth with type 1 diabetes	At both short-term and 1-year follow-up the HbA1c were significantly better in the intervention group (p<0.05)
Stratton, R.	Clinical Trial	5	Supervised exercise (n = 8) vs Control (n = 8)	Supervised exercise (mean = 15.1 ± 1.2) vs Control (mean = 15.5 ± 0.9)	Supervised exercise (50%) vs Control (50%)	To evaluate parallel responses in glycemic control to an 8-wk program of supervised, moderate exercise aimed at improving cardiorespiratory fitness	Significant decline in glycosylated serum albumin for the supervised-exercise group (p<0.01), with no significant change for the control group

Table 3. Description of the articles that evaluated associations between stress and T1DM.

Study ID	Desing	Nos/ Jaded score	N (I vs C)	Age (I vs C)	Gender Male (I vs C)	Aims	Result
Amsberg, S. A.	Clinical Trial	6	I (n = 36) vs C (n = 38)	I (mean = 11.7; 23–65) vs C (mean = 12.9; 19–64)	I (55%) vs C (42%)	To examine the impact of the 48 weeks structured and expanded CBTbased intervention in poorly controlled adult T1DM	At 8 weeks and further on up to 48 weeks, a significant difference ($p<0.05$) was shown between the intervention group and the control group
Attari, A.	Clinical Trial	5	I (n = 30) vs C (n = 30)	I (mean = 19.7 ± 3.29) vs C (mean = 20.8 ± 4.52)	Not available	In this study, it has been tried to investigate the effect of stress management training on glycemic control in type 1 diabetic patient	HbA1 levels decreased significantly in study group ($p<0.001$) but not in the control group
Due-Christensen, M.	Clinical Trial	3	Not controlled	Not controlled	Not controlled	To investigate the benefits of diabetes dialogua meetings on diabetes distress and glucose control in T1DM people	HbA1c showed a small but significant decrease ($p<0.0001$) by one year
Helgeson, V. S.	Cohort	4	Not controlled	Not controlled	Not controlled	To determine the relation of stressful life events to metabolic control	Stressful life events predicted changes in metabolic control over time ($p<0.05$), such that more life events were associated with declines in metabolic control (Higher HbA1c) over time
Nygren, M.	Cohort	4	Not controlled	Not controlled	Not controlled	To evaluate if increased risk of type 1 diabetes in children is associated with previous experience of serious life events and in children whose parents reported higher levels of parenting stress	Both SLEs including death and illness experienced by the child and SLEs including death, illness and accidents experienced by the parent were associated with a higher risk of diagnosis ($p=0.017$)
Hood, K. K.	Cohort	4	Not available	Not available	Not available	The aim of this article is to report 1-year outcomes of the STePS program for adolescents with T1D who participated in this multisite RCT	Diabetes distress was correlated with depressive symptoms, diabetes management, and A1C level (p<0..001)
Lloyd, S. A.	Cohort	4	Not controlled	Not controlled	Not controlled	To examine the relationship between stressful life events and alterations in glycemic control in adults with diabetes	Subjects whose control deteriorated over time or who remained in poor glycemic control were significantly more likely to report severe personal stressors in the month before HbA1c measurement, compared with subjects whose control remained fair or whose control improved ($p=0.000$)
Saghaei, M.	Clinical Trial	5	I (n = 25) vs C (n = 25)	I (mean = 9.27 ± 2.56) vs C (mean = 9.12 ± 1.86)	I (28%) vs C (36%)	To evaluate the effectiveness of stress management through cognitive-behavioral therapy in controlling the blood glucose of children with type 1 diabetes mellitus	Measurements of HbA1c level significantly decreased in the children received the diabetes management intervention from their educated mothers ($P = 0.002$) Moreover, the amount of HbA1c in the children received the parental intervention sessions was gnificantly lower than the control group