Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Review

Benefits of physical activity in children and adolescents with type 1 diabetes: A systematic review

Hélène Absil [a,1], *Lia Baudet* [a,1], *Annie Robert* [b], *Philippe A. Lysy* [a,c,*]

[a] *Unité d'Endocrinologie Pédiatrique, Cliniques universitaires Saint Luc, Belgium*
[b] *Pôle d'Epidémiologie et Biostatistique, Belgium*
[c] *Pôle PEDI, Institut de Recherche Expérimentale et Clinique, UCLouvain, Av. Hippocrate 10, B-1200 Brussels, Belgium*

ARTICLE INFO

Article history:
Received 21 May 2019
Accepted 6 August 2019
Available online 8 August 2019

Keywords:
Type 1 diabetes
Physical activity
Children
Adolescents
Glycemic control
Blood lipid profile
Body composition
Quality of life

ABSTRACT

Aims: We performed a systematic review of clinical trials investigating the health benefits of physical activity in pediatric patients with type 1 diabetes.
Methods: To perform this systematic review, search strategies were created and adapted to four databases. Only randomized controlled trials written in English before 1998 and that answered to the PICOS criteria were included. The PRISMA guidelines were followed to ensure highest scientific rigor within studies.
Results: Seven studies out of 2655 were included in this systematic review according to the inclusion criteria. These studies showed positive gains on global health: blood lipid profile, physical fitness, quality of life and body size and body composition but only one demonstrated a positive effect on glycemic control.
Conclusion: Globally, physical activity exerts a positive impact on metabolic (i.e., decrease in total cholesterol, improvement of physical fitness, etc.) and psychological health in children with type 1 diabetes. Yet variations in study protocols or sample size restrict statistical power to reach the outcome of improving glycemic control in most studies. Here, we address the measured outcomes in individual trials and discuss potential key elements to consider for future clinical trials.

Contents

* Corresponding author at: Avenue Hippocrate 10, B-1200 Brussels, Belgium.
E-mail address: philippe.lysy@uclouvain.be (P.A. Lysy).
[1] These authors contributed equally to this work, and they are thus sharing first authorship.
https://doi.org/10.1016/j.diabres.2019.107810
0168-8227/

1. Introduction

Regular physical activity is well recommended in the management of type 1 and 2 diabetes. The common recommendations are to perform at least 150 min per week (divided in 3 times a week) of moderate-intensity aerobic physical activity or 75 min of vigorous-intensity aerobic physical activity per week or a combination of moderate- and vigorous-intensity activities [1,2]. For children and adolescents with diabetes, the recommendations are to perform at least 60 min per day of moderate- or vigorous-intensity aerobic activity, with vigorous muscle-strengthening and bone-strengthening activities at least 3 days a week [3,5].

Practicing physical activity induces metabolic improvements in terms of insulin sensitivity and glucose intake [1]. The evidence about the benefits of physical activity for type 2 diabetes (T2D) is strong: physical activity reduces levels of HbA_{1C}, triglycerides, blood pressure and insulin resistance [4,5]. It also diminishes the risk of cardiovascular mortality and the progression of disease correlates, such as chronic hyperglycemia and body mass index [6]. However, for type 1 diabetes (T1D), data are conflicting. In this setting, it is generally accepted that physical activity reduces the cardiovascular risk and insulin requirements, and improves the muscular strength and well-being of patients [5,7], yet the literature is unclear about the effects of physical activity on glycemic control. Some findings emphasize that children with T1D should practice at least 3 times a week for more than 12 weeks of combined aerobic and resistance exercise to experience effective reduction of their HbA_{1C} levels [8].

Exercise induces various effects on blood glucose levels according to the duration, intensity and type of exercise [3]. Aerobic exercise decreases blood glucose values [9] by raising the glucose uptake [10] whereas short high-intensity or anaerobic exercise mostly increases blood glucose values [11] by prolonging the insulin action up to 24 h after short intense activities [12]. High intensity exercise (>85% of aerobic capacity) also increases catecholamines (epinephrine and norepinephrine) and growth hormone secretion. These counter-regulatory hormones operate on the liver that will release more glucose after short bouts of exercise [13]. During combined exercise, including low or moderate-intensity physical activity and bouts of vigorous-intensity exercise, glucose values tend to decrease but to a lower extent than during a continuous moderate activity [14]. Those acute bouts of high-intensity physical activity increase the glucose uptake in the liver and in muscles [15].

The main obstacle to physical activity is the fear of hypoglycemia [16]. Indeed, exercise generally reduces blood glucose levels, which induces the need for the patients to adapt their insulin doses and carbohydrate intakes. Unfortunately, the results of these adaptations may be difficult to anticipate and often lead to dysglycemia [17–19]. Therefore, sport practicing in children with T1D is a real challenge. Most of the time, children and adolescents practice spontaneous physical activity and/or team sports. Those types of sports correspond to long moderate-intensity physical activity with short bouts of high-intensity physical activity which lead to a moderate decrease of blood glucose [20]. Children and adolescents must either adapt their carbohydrate intake according to the insulin dose regimen, the duration and timing of physical activity and the type of exercise [21], or adapt their

insulin doses by reducing the insulin levels before and/or during physical activity. The technique of adapting insulin doses may elude the need of extra carbohydrate intake [22], but hypo- or hyperglycemia cannot always be avoided [23].

The aims of this systematic review are to clarify the effect of physical activity on glucose control in children and adolescents with T1D and to assess the health benefits of a regular physical practice in this setting.

2. Material and methods

2.1. Protocol

In our study, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Prisma) Guidelines which consist in a flow diagram and a checklist of 27 items [24].

2.2. Eligibility criteria

We selected articles following the PICOS method. Inclusion criteria were: concerning the target population: patients between 6 and 18 years old with T1D, regardless of the diabetes duration; concerning the intervention: any sort of exercise, fitness or physical activity; concerning the outcomes: any effect of physical activity on the glycemic control estimated using the evaluation of HbA_{1C} levels (first outcome) but also on lipid profile, body composition and size, quality of life (QoL), physical fitness, glycemic control (secondary outcomes); concerning the category of studies: randomized control trials, full-text in English, published between 1998 and 2018.

2.3. Search

We based our research on different search strategies according to the databases. The keywords from the PICOS (Table S1) method associated with Boolean operators allowed us to build the following search strategy: ("diabetes mellitus, type 1" OR "type 1 diabete" OR "type 1 diabetes") AND ("physical activity" OR exercise OR exercises OR sport OR sports OR fitness OR training OR "exercise therapy") AND (child OR children OR adolescent).

We modified this equation to fit in the different databases such as Pubmed, Scopus, SportDiscuss and Cochrane. We limited the results to the past 20 years. Those researches were performed in the course of October 2018. The complete search strategies are detailed in the Table S2. We searched the keywords using the Title/abstract filter.

2.4. Study selection

The research in databases has been made by two examiners and the study selection by the same two reviewers, but independently. Firstly, we deleted the duplicates of the articles. Secondly, we sorted the articles according to the PICOS criteria and the language. Afterwards, we selected the articles if they were randomized controlled trials. The disagreements were discussed between the reviewers until a consensus was found. We also contacted the authors when we could not find the full article. Only one answered and gave us the full article.

2.5. Data collection process

A table was created to synthetize the characteristics of the patients in every study and also to assess the potential effects of physical activity on the outcomes of every study. This step was achieved by two reviewers independently. The data regarding the population are synthetized in Table 1.

2.6. Risk of bias in individual studies

2.6.1. The PEDro scale

We used the PEDro (Physiotherapy Evidence Database) scale to assess the methodological quality of the randomized controlled trials we chose [25]. The scale contains eleven items, but the first item is not accounted for in the total scoring. The first criterion corresponds to the attendance of the eligibility criteria and relates to the external validity. Criteria two to nine estimate the internal validity of the study. The information about the statistical interpretation of the results is provided by the tenth and eleventh criteria. For every other item, points are given only if the criterion is completely satisfied at the first literal reading. The closer the score is to ten, the better the methodological quality.

2.6.2. The Downs and Black checklist

We used the Downs and Black [26] checklist, which is a valid and reliable checklist which provides a score for the methodological quality of the study, and a score for power, internal and external validity. The most recent version of this checklist contains 27 items rated at zero (no or unable to determine) or one (yes) except for the fifth item, coted on two. Items 1–10: reporting, if the information was sufficient to get an unbiased assessment of the findings; 11–13: external validity, if the information is generalizable; 14–20: study bias; 21–26: confounding, bias in the selection of subjects; 27: power, if findings are due to chance. The closer is the score to 28, the better is methodological quality of the study. According to O'Connor et al (2015), it is possible to assign a grade of "excellent" (24 to 28 points), "good" (19–23 points), "fair" (14–18 points) or "poor" (<14 points). The twenty-seventh item has been modified and can now be rated as 0 or 1 [27].

2.7. Summary measures

We calculated differences of the means to measure improvements in the results. These are summarized in the Tables 3–7. We also measured the means of the chronological age, HbA_{1C}, duration of the studies, time of physical activity per week and frequency of training sessions. As we calculated the mean HbA_{1C} levels, we encounter an issue. Indeed, the mean HbA_{1C} of only four of our studies was calculated [28–31] because only the medians of the three other studies were available. Therefore, we used the formula of Luo et al. [32] and Wan et al. [33] to calculate the means of the data in those three studies.

Table 1 – Characteristics of the studies.

Authors (Years) Countries	Method for Recruitment	Sample (intervention/ control)	Gender	Diabetes duration (years)	Age (years)	Outcomes
Roberts et al (2002) *Australia*	Diabetes clinic	n = 24 (12/12)	24 ♀	5.0 ± 3.1	14.0 ± 1.2	Body composition (BMI, body mass, height, skinfolds scores), aerobic capacity, HbA_{1C}
Heyman et al (2007) *France*	Hospital	n = 16 (9/7)	IG: 9♀ CG: 7♀	IG: 6.3 ± 4.4 CG: 8.4 ± 4.5	IG: 15.9 ± 1.5 CG: 16.3 ± 1.2	Body composition, peak O_2 uptake, PWC170, daily insulin requirement, lipid profile (HDL, LDL, TG, cholesterol), QOL, physical activity, HbA_{1C}
Newton et al (2009) *New Zeland*	Hospital outpatient	n = 78 (38/40)	36 ♂; 42♀	NM	14.4 ± 2.4 range (11–18)	Daily steps count, exercises (min/week), HbA_{1C} Systolic/diastolic blood pressure, BMI, SQOL, daily insulin dose, NZPAQ
Salem et al (2010) *Egypt*	University hospital	n = 196 (IG1: 75, IG2: 73 CG: 48)	75♂; 121♀	4.6 ± 1.9 range (3–10)	14.8 ± 2.3	BMI, waist circumference, blood pressure, lipid profile (HDL, LDL, cholesterol, TG), HbA_{1C}, hypoglycemia episodes, dyslipidemia, insulin dosage
D'hooge et al (2010) *Belgium*	Hospital	n = 16 (8/8)	9♀; 7♂	*median* (min–max) IG: 5.4 range (3.4–7.3) CG: 5.3 range (2.9–5.9)	*median* (min–max) IG: 14.1 range (10.1–16.8) CG: 13.2 range (10.1–15.3)	DID, peak VO_2, BMI, body composition, HbA_{1C}, waist circumference, peak power, peak O_2/peak power, 6MWT, 1RM, Functional sit-to-stand test, handgrip strength, muscle fatigue resistance, QoL (SF 36), PWC_{170}
Tunar et al (2012) *Turkey*	Hospital	n = 31 (17/14)	15 ♂; 16 ♀ IG: 11♀; 6♂ CG: 5♀; 9♂	IG: 5.3 ± 4.1 CG: 6.0 ± 4.2	IG: 14.2 ± 2.2 CG: 14.3 ± 1.8	BMI, HbA_{1C}, DID, blood lipids profile (HDL, LDL, TG, cholesterol), peak power, mean power, flexibility, vertical jump
R.Tomar (2014) *Saudi Arabia*	Diabetes clinic	n = 24 (12/12)	IG: 12 ♂ CG: 12 ♂	IG: 4.36 ± 2.4 CG: 4.63 ± 2.06	IG:14.3 ± 1.7 CG:14.3 ± 1.9	HbA_{1C}, lipid profile (HDL, LDL, TG, cholesterol), daily insulin doses

Values are mean ± SD. NM: not mentioned; IG: intervention group; CG: control group; PWC_{170}: predicted work rate at a heart rate of 170; HDL: high density lipoproteins; LDL: low density lipoproteins; TG: triglycerides; BMI: body mass index; HbA_{1C}: hemoglobin A_{1C}; 6MWT: 6-minute walk test; 1 RM: One repetition maximum; QOL: quality of life; SQOL: subjective quality of life; SF 36: The General Health Survey Short Form; DID: daily insulin doses; NZPAQ: higher New Zealand Physical Activity Questionnaire.

Table 2 – Characteristics of the interventions.

Studies (years) Countries	Setting	Adherence to training	Program durations (weeks)	Duration of exercise Frequency	Intervention Type and intensity
Roberts et al (2002) Australia	12 weeks supervised by an experienced trainer 12 weeks unsupervised	100%	24 S:12 U:12	45 min 3x/week	IG: Supervised session: Aerobic and anaerobic exercises (ratio: 7/3) including: running, light training circuits, games and aerobics HR > 160 bpm for 30 min Unsupervised session: Regularly training CG: NS
Heyman et al (2007) France	Supervised (S) sessions at training facility + Unsupervised (U) sessions with specific recommendations at home	100%	24	S: 120 min U: 60 min S: 1x/week U: 1x/week	IG: Supervised session: Combination of aerobic (intermittent workloads) and strength exercises (ratio 2/1) workload 80 to 90% HRR Unsupervised session: Specific recommendations for technique, duration, frequency and ways to avoid common errors workload 80 to 90% HRR CG: Usual exercise and treatment
Newton et al (2009) New Zealand	Home-base with motivational text messaging	95%	12	NM NM	IG: Moderate, vigorous physical activities Goal: 10,000 steps/day + motivational text messaging CG: Usual activities
D'hooge et al (2010) Belgium	Supervised by physiotherapists	100% (total of 38 training sessions, median number of participations: 24 (20–32))	20	70 min 2x/week	IG: Aerobic training: cycling, running, stepping gradually 60 to 75% HR; strength exercises gradually 20 RM to 12 RM CG: Daily normal activities
Tunar et al (2012) Turkey	Supervised by an expert Pilates trainer	100%	12	45 min 3x/week	IG: Pilates training (8 Pilates exercises and stretching exercises) CG: Usual activities
R.Tomar et al (2014) Saudi Arabia	Supervised by qualified personnel at a fitness center	92%	12	60 min 3x/week	IG: Aerobic training cycling and walking Low to moderate intensity (gradually 40 to 70% MHR) cycling (20 min), walking (30 to 40 min) CG: No training, normal life style

NM: not mentionned; IG: intervention group; CG: control group; HR: heart rate; HRR: heart rate reserve; THRR: total heart rate reserve; MHR: maximal heart rate; 1RM: one repetition max; PRE: progressive resistive exercises; Sd: supervised; USd: unsupervised.

Table 3 – Results - Glycemic control.

Studies (years) Countries	Interventions (D: Program duration; T: Time to exercise; F: Frequency; I: intervention)	HbA_{1C} (%)	DID ($IU \cdot kg^{-1} \cdot day^{-1}$)	Frequency of Hypoglycemia
Roberts et al (2002) *Australia*	**D**: 24 weeks (S:12 and U:12) **T**: 45 min **F**: 3x/week I: Aerobic + anaerobic exercises (7/3)	IG, CG: NS IG vs CG: NS	UND	Missing data (disabling for a meaningful comparison)
Heyman et al (2007) *France*	**D**: 24 weeks (24 S or 24 U) **T**: S: 120 min U: 60 min **F**: S: 1x/week U: 1x/week **I:** aerobic + strength exercises (2/1)	IG, CG: NS	IG, CG: NS	UND
Newton et al (2009) *New Zealand*	**D**: 12 weeks (U) **T**: NM **F**: NM I: daily steps (goal: 10,000 steps/day)	IG vs CG: NS (p = 0.2)	IG vs CG: NS (p = 0.6)	UND
Salem et al (2010) *Egypt*	**D**: 24 weeks (S) **T**: 60 min **F**: IG1: 1x/week IG2: 3x/week **I**: aerobic + anaerobic + strength exercises	*mean ± SD (baseline, 6-month program)* CG: NS (p = 0.2) IG1: −0.8 ± 0.3 (p = 0.03)* IG2: −1.1 ± 0.6 (p = 0.01)*	*mean ± SD (baseline, 6-month program)* CG: NS (p = 0.49) IG1: −0.06 ± 0.03 (p = 0.002)* IG2: −0.3 ± 0.1 (p = 0.00)*	*(times/month) (baseline, 6-month program)* IG1/IG2 vs CG: NS (p = 0.888)
D'hooge et al (2010) *Belgium*	**D**: 20 weeks (S) **T**: 70 min **F**: 2x/week **I**: aerobic + strength exercises	CG: NS IG: NS	*median* (min–max) *(baseline* vs *20 weeks)* CG: 1.10 (0.76–1.72) vs 1.16 (0.83–1.79)* IG: 0.96 (0.75–1.70) vs 0.90 (0.79–1.52)*	*median* (min–max) *(times/20 weeks)* IG: 3 (1–6) (for 7/8 children)
Tunar et al (2012) *Turkey*	**D**: 12 weeks (S) **T**: 45 min **F**: 3x/week **I**: aerobic + stretching exercises	IG and CG: NS	IG and CG: NS	UND
R.Tomar et al (2014) *Saudi Arabia*	**D**: 12 weeks (S) **T**: 60 min **F**: 3x/week **I**: aerobic exercises	IG and CG: NS	*Median (range) (baseline, 12-week program)* IG vs CG: 0.00 (-0,2–0,1) vs 0.1 (0.05–0.24) (p = 0.00)*	UND

* : significant change; NM: not mentioned; UND: undetermined; NS: not significant; Sd: supervised; USd: unsupervised; IG: intervention group; CG: control group; HbA_{1C}: hemoglobin A_{1C}; DID: daily insulin doses.

Table 4 – Results – Blood lipid profile.

Studies (years) Countries	Interventions (D: Program duration; T: Time to exercise; F: Frequency; I: intervention)	Lipid profiles	
Roberts et al (2002) *Australia*	**D**: 24 weeks (S:12 and U:12) **T**: 45 min **F**: 3x/week **I**: Aerobic + anaerobic exercise (7/3)	UND	
Heyman et al (2007) *France*	**D**: 24 weeks (24 S or 24 U) **T**: S: 120 min U: 60 min **F**: S: 1x/week U: 1x/week **I:** aerobic + strength exercises (2/1)	Plasma total Cholesterol (mmol/L) IG, CG: NS Plasma TG (mmol/L) IG, CG: NS Plasma LDL (mmol/L) IG, CG: NS Plasma HDL (mmol/L) IG, CG: NS	Serum Leptin (ng/mL) IG, CG: NS Serum adiponectin (μg/mL) IG, CG: NS Serum lipoprotein (g/L) IG, CG: NS Apolipoproteins (A-1 ratio) IG: Significant decrease −13.7 ± 13.9%* after 6-month program (in all but one girl of the intervention group) CG: NS
Newton et al (2009) *New Zealand*	**D**: 12 weeks (U) **T**: NM **F**: NM **I**: daily steps (goal: 10,000 steps/day)	UND	
Salem et al (2010) *Egypt*	**D**: 24 weeks (S) **T**: 60 min **F**: IG1: 1x/week IG2: 3x/week **I**: aerobic + anaerobic + strength exercises	HDL (mg/dL) *mean ± SD (baseline, 6-month program)* CG: NS (p = 0.22) IG1: + 9.8 ± 0.3 (p = 0.01)* IG2: + 12.6 ± 1.6 (p = 0.00)* LDL (mg/dL) *mean ± SD (baseline, 6-month program)* CG: NS (p = 0.45) IG1: −12 ± 4.4 (p = 0.01)* IG2: −29.5 ± 7 (p = 0.001)*	TG (mg/dL) *mean ± SD (baseline, 6-month program)* CG: NS (p = 0,49) IG1: −12.3 ± 4.3 (p = 0.00)* IG2: −40.4 ± 6.4 (p = 0.00)* Total cholesterol (mg/dL) *mean ± SD (baseline, 6-month program)* CG: NS (p = 0.49) IG1: −18.4 ± 11.4 (p = 0.01)* IG2: −51.4 ± 0.7 (p = 0.00)*

Table 4 – (Continued)

Studies (years) Countries	Interventions (D: Program duration; T: Time to exercise; F: Frequency; I: intervention)	Lipid profiles	
D'hooge et al (2010) *Belgium*	**D**: 20 weeks (S) **T**: 70 min **F**: 2x/week **I**: aerobic + strength exercises	UND	
Tunar et al (2012) *Turkey*	**D**: 12 weeks (S) **T**: 45 min **F**: 3x/week **I**: aerobic + stretching exercises	HDL (mg/dL) *mean ± SD (baseline, 12-week program)* CG: + 6 ± 4.3 (p = 0.046)* LDL (mg/dL) IG and CG: NS	TG (mg/dL) IG and CG: NS Total cholesterol (mg/dL) IG and CG: NS
R.Tomar et al (2014) *Saudi Arabia*	**D**: 12 weeks (S) **T**: 60 min **F**: 3x/week **I**: aerobic exercises	HDL (mg/dL) IG and CG: NS LDL (mg/dL) IG and CG: NS	TG (mg/dL) IG and CG: NS Total cholesterol (mg/dL) *Median (range) (baseline, 12-week program)* CG vs IG: −11.5 (-44–6) vs 2 (-44–29) (p = 0.035)* IG: 172 (132–234) vs 160 (120–217) (p = 0.033)*

* : significant change; NM: not mentioned; UND: undetermined; NS: not significant; IG: intervention group; CG: control group; Sd: supervised; USd: unsupervised; HDL: high density lipoproteins; LDL: low density lipoproteins; TG: triglycerides.

Table 5 – Results – Quality of life.

Studies (years) Countries	Interventions (D: Program duration; T: Time to exercise; F: Frequency; I: intervention)	QoL	
Roberts et al (2002) *Australia*	**D**: 24 weeks (S:12 and U:12) **T**: 45 min **F**: 3x/week **I**: Aerobic + anaerobic exercise (7/3)	UND	
Heyman et al (2007) *France*	**D**: 24 weeks (24 S or 24 U) **T**: S: 120 min U: 60 min **F**: S: 1x/week U: 1x/week **I**: aerobic + strength exercises (2/1)	Quality of life (DQOL) IG: −14.6 ± 5.5%* CG: NS	
Newton et al (2009) *New Zealand*	**D**: 12 weeks (U) **T**: NM **F**: NM **I**: daily steps (goal: 10,000 steps/day)	Quality of life (SQOL) IG vs CG: NS (p = 0,06) trend toward a decrease	
Salem et al (2010) *Egypt*	**D**: 24 weeks (S) **T**: 60 min **F**: IG1: 1x/week IG2: 3x/week **I**: aerobic + anaerobic + strength exercises	UND	
D'hooge et al (2010) *Belgium*	**D**: 20 weeks (S) **T**: 70 min **F**: 2x/week **I**: aerobic + strength exercises	QoL (SF-36) Role emotional IG: 66.6 (0–100) vs 90 (66.6–100) General health IG: 50 (38–90) vs 60 (20–95)	Vitality IG: 60 (35–90) vs 65 (25–90) All NS but important increase
Tunar et al (2012) *Turkey*	**D**: 12 weeks (S) **T**: 45 min **F**: 3x/week **I**: aerobic + stretching exercises	UND	
R.Tomar et al (2014) *Saudi Arabia*	**D**: 12 weeks (S) **T**: 60 min **F**: 3x/week **I**: aerobic exercises	UND	

* : significant change; NM: not mentioned; UND: undetermined; NS: not significant; IG: intervention group; CG: control group; Sd: supervised; USd: unsupervised; QOL: quality of life; SQOL: subjective quality of life; SF 36: The General Health Survey Short Form; NZPAQ: higher New Zealand Physical Activity Questionnaire.

Table 6 – Results – Physical fitness.

Studies (years) Countries	Interventions (D: Program duration; T: Time to exercise; F: Frequency; I: intervention)	Physical Fitness
Roberts et al (2002) *Australia*	**D**: 24 weeks (S:12 and U:12) **T**: 45 min **F**: 3x/week **I**: Aerobic + anaerobic exercise (7/3)	Aerobics capacity ($W \cdot kg^{-1}$) CG: stable after 24 weeks IG: +17%* *(baseline, 12 weeks)* return to pre-training level *(baseline,24 weeks)*
Heyman et al (2007) *France*	**D**: 24 weeks (24 S or 24 U) **T**: S: 120 min U: 60 min **F**: S: 1x/week U: 1x/week **I:** aerobic + strength exercises (2/1)	PWC_{170} ($W \cdot kg^{-1}$) IG: + 7.9 ± 8.3%* CG: NS
Newton et al (2009) *New Zealand*	**D**: 12 weeks (U) **T**: NM **F**: NM **I**: daily steps (goal: 10,000 steps/day)	Daily steps count [interquartile range] IG vs CG: NS + 819 [-916 to 2,554](P = 0.4) Exercises (min/week) IG vs CG: NS (p = 0.9) SBP (mm Hg) IG vs CG: NS (p = 0.7) DBP (mm Hg) IG vs CG: NS (p = 0.7)
Salem et al (2010) *Egypt*	**D**: 24 weeks (S) **T**: 60 min **F**: IG1: 1x/week IG2: 3x/week **I**: aerobic + anaerobic + strength exercises	SBP (mmHg) CG, IG1, IG2: NS DBP (mmHg) *mean ± SD (baseline, 6-month program)* IG2: −6.8 ± 2.1(p = 0.04)* CG, IG1: NS

Table 6 – (Continued)

Studies (years) Countries	Interventions (D: Program duration; T: Time to exercise; F: Frequency; I: intervention)	Physical Fitness	
D'hooge et al (2010) *Belgium*	**D**: 20 weeks (S) **T**: 70 min **F**: 2x/week **I**: aerobic + strength exercises	Peak V_{O2} (mL/min) CG, IG: NS Peak power (W) CG, IG: NS Peak heart rate (per min) CG, IG: NS Distance of the 6MWT (m) *median* (min–max) *(baseline* vs *20 weeks)* CG: NS IG: 545(410–670) vs 603 (406–667) ($p < 0.05$)* Number of completed stands of the functional sit-to-stand test (no/30 s) *median* (min–max) *(baseline-20 weeks)* CG: NS IG: 17 (13–29) vs 21 (9–27) ($p < 0.05$)* Hand grip strength (kg) CG, IG: NS	Muscle fatigue resistance (sec) *median* (min–max) *(baseline-20 weeks)* CG: NS IG: 21 (9–39) vs 36 (15–48) ($p < 0.05$)* PWC_{170} (mL/min) *median* (min–max) *(baseline-20 weeks)* CG: NS IG: 13.4 (12.3–16.9) vs 11.3 (10.9–14.3) ($p < 0.05$)* Strength lower limb (kg) *median* (min–max) *(baseline-20 weeks)* CG: NS IG: 31.5 (15.4–61.3) vs 38.8 (18.3–68.2) ($p < 0.05$)* Strength upper limb (kg) *median* (min–max) *(baseline-20 weeks)* CG: NS IG: 47.4 (22.6–86.7) vs 81.7 (46.6–134.8) ($p < 0.05$)*
Tunar et al (2012) *Turkey*	**D**: 12 weeks (S) **T**: 45 min **F**: 3x/week **I**: aerobic + stretching exercises	Peak power (W) *mean ± SD (baseline, 12-week program)* IG: + 18.4 ± 9.7 ($p = 0.02$)* Mean power (W) *mean ± SD (baseline, 12-week program)* IG: +3.3 ± 2.9 ($p = 0.000$)* Flexibility (cm) *mean ± SD (baseline, 12-week program)* IG: + 8 ± 0 ($p = 0.000$)* Vertical jump (cm) *mean ± SD (baseline, 12-week program)* IG: + 3.5 ± 0.2 ($p = 0.003$)*	
R.Tomar et al (2014) *Saudi Arabia*	**D**: 12 weeks (S) **T**: 60 min **F**: 3x/week **I**: aerobic exercises	UND	

* : significant change; NM: not mentioned; UND: undetermined; NS: not significant; IG: intervention group; CG: control group; Sd: supervised; USd: unsupervised; 6MWT: 6-minute walk test; 1 RM: One repetition; PWC 170: predicted work rate at a heart rate of 170; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 7 – Results – Body size and body composition.

Studies (Years) Countries	Interventions (D: Program Duration; T: Time to Exercise; F: Frequency; I: Intervention)	Body Size	Body Composition
Roberts et al (2002) *Australia*	**D**: 24 weeks (S:12 and U:12) **T**: 45 min **F**: 3x/week **I**: Aerobic + anaerobic exercises (7/3)	BMI (kg/m^2) Stable in all groups after 12 weeks Body mass (kg) Stable in all groups after 12 weeks Height (cm) *mean ± SD (baseline, 12 weeks)* *(baseline, 24 weeks)* IG: +0.8 ± 0.1* +1.8 ± 0.2* CG: +1.1 ± 0.1* +1.6 ± 0* Skinfold scores (mm) Stable in all groups after 12 weeks	UND
Heyman et al (2007) *France*	**D**: 24 weeks (24 S or 24 U) **T**: S: 120 min U: 60 min **F**: S: 1x/week U: 1x/week **I:** aerobic + strength exercises (2/1)	Height (cm) *mean ± SD (baseline, 6-months program)* IG: + 0.9 ± 0.87 ($p < 0.001$)* CG: + 1.23 ± 0.31 ($p < 0.001$)* Weight (kg) *mean ± SD (baseline, 6-months program)* IG: + 2.42 ± 2.52 ($p < 0.001$)* CG: + 2.64 ± 2.23 ($p < 0.001$)*	FM (kg) CG: NS (tended to increase significantly) ($p = 0.08$)) FFM (kg) IG: significant increase ($p < 0.005$)* (in all but one girl of the intervention group) CG: NS
Newton et al (2009) *New Zealand*	**D**: 12 weeks (U) **T**: NM **F**: NM **I**: daily steps (goal: 10,000 steps/day)	BMI (kg/m^2) IG vs CG: NS (P = 0.9)	UND

Table 7 – (Continued)

Studies (Years) Countries	Interventions (D: Program Duration; T: Time to Exercise; F: Frequency; I: Intervention)	Body Size	Body Composition
Salem et al (2010) *Egypt*	**D**: 24 weeks (S) **T**: 60 min **F**: IG1: 1x/week IG2: 3x/week **I**: aerobic + anaerobic + strength exercises	Weight (kg) *mean ± SD (baseline, 6-month program)* CG: +10.7 ± 3.7 (p = 0.03)* IG1: −19.6 ± 4.8 (p = 0;001)* IG2: −30.9 ± 6.3 (p = 0.000)* BMI *(SDS)* *mean ± SD (baseline, 6-month program)* CG: NS (p = 0.78) IG1: −0.09 ± 0.4 (p = 0.05)* IG2: −0.19 ± 0.1 (p = 0.001)* Waist circumference (cm) *mean ± SD (baseline, 6-month program)* CG: NS (p = 0,66) IG1: − 4.7 ± 0.9 (p = 0.02)* IG2: − 8.2 ± 2.5 (P = 0.0)*	UND
D'hooge et al (2010) *Belgium*	**D**: 20 weeks (S) **T**: 70 min **F**: 2x/week **I**: aerobic + strength exercises	BMI (kg/m^2) CG, IG: NS Length (cm) CG, IG: NS	Weight (kg) CG, IG: NS Waist circumference (cm) CG, IG: NS	FM (kg) CG, IG: NS FFM (kg) CG, IG: NS
Tunar et al (2012) *Turkey*	**D**: 12 weeks (S) **T**: 45 min **F**: 3x/week **I**: aerobic + stretching exercises	BMI SDS (kg/m^2) IG vs CG: NS		UND
R. Tomar et al (2014) *Saudi Arabia*	**D**: 12 weeks (S) **T**: 60 min **F**: 3x/week **I**: aerobic exercises	UND		UND

* : significant change; NM: not mentioned; UND: undetermined; NS: not significant; Sd: supervised; USd: unsupervised; IG: intervention group; CG: control group; BMI: body mass index; FM: fat mass; FFM: fat-free mass; SDS: standard deviation score.

3. Results

3.1. Study selection

The search strategy identified 2655 articles from the different databases such as Pubmed (n = 884), Scopus (n = 1290), SportDiscuss (n = 178) and the Cochrane Library (n = 303). The Zotero program was used to remove duplicates (n = 1054). Afterwards, the title and abstract of 1601 articles were screened. From this analysis, 1389 articles did not correspond to the PICOS criteria and 19 articles were either not written in English or the full text was not available. Only 186 articles were assessed for the primary eligibility criteria. Subsequently, non-randomized studies, pilot studies, meta-analyses and systematic reviews were excluded. From the analysis, seven studies were included in this systematic review. The details of our analysis procedure are resumed in the PRISMA flow diagram in Fig. 1.

3.2. Risk of bias within studies

The details of the PEDro scores of all studies are summarized in Table S3. Those scores were manually assessed by two reviewers, separately. In this review, the methodological quality of the studies is rated between six and eight points on the PEDro scale, which qualifies them as of high methodological quality. The median score of our selected studies is seven points. As only randomized control trials have been chosen, the second criterion (random allocation) is fulfilled in every study. Moreover, the first (eligibility criteria), fourth (similar groups at baseline), eighth (measures of at least one key outcome were obtained for more than 85% of the subjects), ninth (intention to treat), tenth (results of between-group statistical comparisons) and eleventh criteria (point measures and measures of variability) are also fulfilled in every study. The fifth (blinded subjects) and sixth (blinded therapists) criteria were not met in any of the studies because of the nature of the therapy.

The Downs and Black score was also used to assess the methodological quality of the selected studies. The scores vary between 17 and 23 points. The median score is 21. All studies are thus qualified as fair (14–18) or good (19–23) in terms of methodological quality. The details of each underscore are summarized in Table S4.

3.3. Study characteristics

The description of the seven retrieved studies and the characteristics of the interventions are synthesized in Table 2. In total, 385 patients below 18 years of age, among which were 228 girls and 157 boys, were included in this systematic review. Only six drop-outs were reported from the studies. In the analyzed clinical studies, the sample size varied from 16 to 196 patients and mean age ranged from 13.2 to 16.3 years (14.58 ± 2.17 years). All patients were recruited in hospitals or in diabetes clinics. Every study was composed of an intervention group and a control group, except one [29] which included two intervention groups and one control group.

At baseline, the mean HbA_{1C} levels of the patients were 8.8 ± 1.7% (73 mmol/mol). This mean HbA_{1C} was based on the values of only four studies The mean of all studies but one [34] is 8.1 ± 1.5% (69 mmol/mol) using the Luo et al. (2018)'s formula. The data were missing for one study [34]. The range of HbA_{1C} levels was from 8.0 to 10.4% (64 to 90 mmol/mol). The mean diabetes duration varied from 4.5 ± 2.2 to 7.4 ± 4.4 years. The disease duration was missing in one study only [35].

Regarding the type of exercise, four studies combined aerobic and anaerobic physical activities [28,29,34,36] and three studies evaluated only aerobic exercise [30,31,35]. The aerobic activities corresponded to walking and running outside or on a treadmill, stepping, and cycling, while the anaerobic ones consisted in strengthening exercises, circuit and interval training, workloads and balance exercises. Workload varied between low-to-moderate intensity [30] to moderate-to-vigorous intensity physical activity. In some studies, the charge of exercises increased along the studies [28–30,35,36].

The total duration of the studies ranged from 12 to 24 weeks (18.3 ± 6.0). In four studies, the training sessions were supervised by educators or physiotherapists [29–31,36]. In another study, sessions were at first supervised by professionals for 12 weeks, then the patients were invited to maintain their physical activity unsupervised for twelve additional weeks [34]. Newton et al. added motivational text messaging to their protocol [35]. The study of Heyman et al. consisted in two supervised hours and one unsupervised hour of weekly exercise [28].

In average, patients practiced 144.3 ± 43.0 min of physical activity per week during the programs, in a range from 60 [29] to 180 min [28,30]. The frequency of exercise sessions fluctuated from one to three (2.4 ± 0.8) times a week. For one study [35], those observations could not be performed because of the program protocol consisting in an daily goal to achieve.

3.4. Results of individual studies

The primary outcome evaluated in this systematic review was the glycated hemoglobin (HbA_{1C}) levels, as a representative value of glycemic control. This outcome was measured in all of the seven studies. All studies but one [34] reported daily insulin doses, whereas BMI was mentioned in six studies [28,29,31,34–36] and blood lipid profile in five studies [28–31,36].

Furthermore, five studies [28,31,34–36] analyzed resistance to exercise, via the measurement of the aerobic capacity, peak power, peak oxygen, 6MWT (6 min walking test), PWC170 (physical work capacity), number of total daily steps, handgrip strength and 1RM (one repetition maximum).

Three studies evaluated the QoL of children and adolescents with T1D using three different questionnaires: SF36, Com-QOL and DQOL [28,35,36]. Newton et al. used the SQOL, the subjective part of the Comprehensive Quality of Life Scale (ComQol-S5); this questionnaire includes two components: life satisfaction and affect [37]. In their study, the scores at the SQOL at baseline were lower than the normative range for the same age patients yet without significant difference

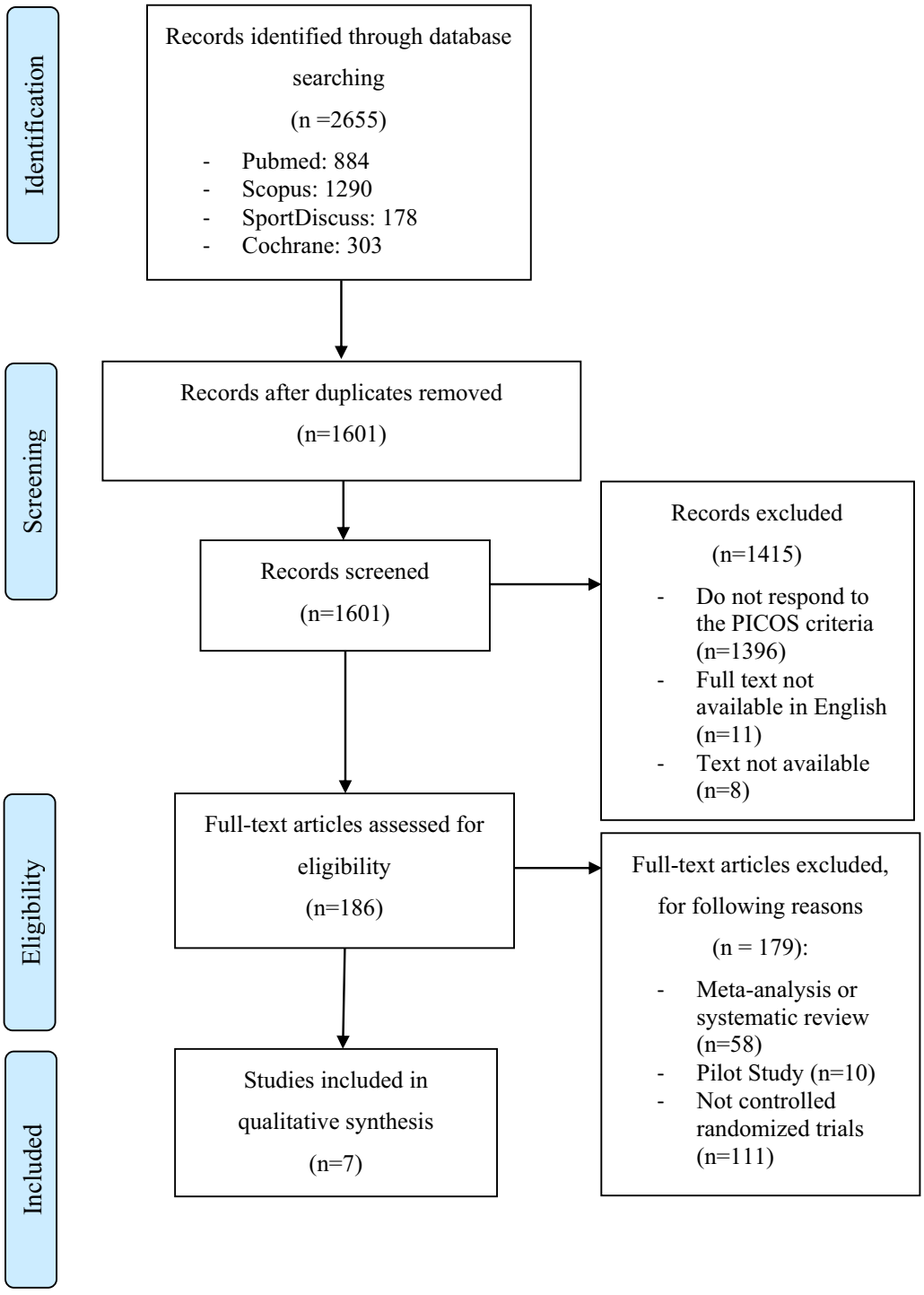

Fig. 1 – PRISMA 2009 flow diagram.

before and after the program. The General Health Survey Short Form (SF36) was used by D'hooge et al. [36] who adapted the Dutch version to the recruited patients. This scale analyzes the physical and social functioning, role physical and emotional, mental functioning, pain, vitality, general health and change in health. There were important increases in role emotional, general health and vitality, yet not reaching significance [38]. Heyman et al. used the Daily Quality of Life (DQOL) questionnaire that includes items gathered in four groups: impact of diabetes, worries about diabetes, satisfaction in life and health perception [39]. These authors found a significant decrease of the DQOL score, indicating a higher QoL [40], in the "satisfaction with diabetes" subgroup after the entire program. Results are summarized in Tables 3–7.

3.5. *Risk of bias across studies: level of scientific evidence*

As enunciated in the eligibility criteria, only randomized controlled trials were included in this systematic review. These studies are associated to a quality of scientific evidence of

level two according to the guidelines of Oxford Centre for Evidence-Based Medicine.

4. Discussion

In this systematic review, we aimed to identify the benefits of physical activity on several health aspects in children and adolescents with T1D. The primary outcome was the HbA_{1C} levels which is a fair indicator of glycemic control. The secondary outcomes were the blood lipid profile, physical fitness, QoL, body composition and daily insulin doses.

All the studies included in this systematic review were graded a PEDro score higher than six points with a median score of seven points. As such, they qualify as being of high methodological quality. The fifth and sixth criteria were not filled in because the treatments could not be blinded. This creates an intrinsic risk of bias because patients do not benefit from the effects of a placebo. The median score for the Downs and Black scale was 21 points across the chosen studies, which qualify them as having a good methodological quality. Therefore, we may easily compare these studies in terms of methodological quality. Yet the studies protocols were heterogeneous. Some studies lasted for 12 weeks [30,31,35] while others proceeded for six [36] or twelve more weeks [28,29,34]. Number of exercises sessions varied between one to three times weekly and patients practiced from 60 to 180 min of physical activity per week. Four studies combined aerobic and anaerobic training. [28,29,34,36] and the three others only included aerobic exercise. [30,31,35] Four studies included supervised training sessions [29–31,36], two other studies comprised supervised sessions and non-supervised training [28,34] and one study is a compound of motivational text messages without supervision [35].

Also, the populations of patients in the studies were heterogeneous. The sample sizes varied from 16 to 196 patients. The age of the patients was almost similar, the mean age varied between 13.2 and 16.3 years old. At baseline, the mean HbA_{1C} was 8.1 ± 1.5% (65 mmol/mol) and varied between 8.0 and 10.4% (64 mmol/mol).

4.1. *Glycemic control*

All studies from our review evaluated HbA_{1C} levels but only one found significant improvements in this outcome [29]. In this trial, patients combined aerobic and anaerobic training and the exercise sessions were supervised. In a similar study, Aouadi et al. enrolled 33 adolescents with T1D including eleven patients who practiced supervised aerobic exercise four times a week for 24 weeks; these authors found a significant improvement of HbA_{1C} levels in the trained group [41]. Salem et al. [29] showed that improvements in HbA_{1C} were correlated with the frequency of physical activity because the group who practiced three times a week had the highest reduction of HbA_{1C} levels. This is corroborated by the study of Herbst et al. [42] who analyzed the levels of HbA_{1C} in relation with the frequency of physical activity in 19,143 patients with T1D aged 3–20 years. These authors found that patients who trained the most frequently had the lowest HbA_{1C} levels [42].

However, in their systematic review, Kennedy and colleagues could not find evidence for a benefit of exercise on HbA_{1C} levels in pediatric and adult patients with T1D [43]. Contrarily, after the analysis of 24 randomized and non-randomized controlled studies (adult and pediatric patients), Wu et al. observed a reduction of HbA_{1C} levels of −0.45% with a 95% CI of −0.73 to −0.17 [44]. These inconsistent findings, in terms of the influence of exercise on HbA_{1C} levels, reflect the heterogeneity of clinical trials gathered for analyses, at the level of both inclusion criteria and study protocols.

It is important to notice that the outcome "glycemic control" is difficult to analyze as it reflects several aspects of glucose homeostasis. Since the development of continuous glucose monitoring (CGM), it appears that glycemic variability overcome HbA_{1C} in its capacity to reflect disease control and risk of complications [45–47]. Other parameters as the frequency of nocturnal hypoglycemia and of hyperglycemia consecutive to hypoglycemia should be taken into account in the evaluation of diabetes control during and after exercise [48,49].

No episode of severe hypoglycemia was reported in any of the seven studies of our review. Either this was not analyzed or it could reflect the fact that exercise sessions were planned, so that the participants could adapt their insulin doses and food intake according to the ongoing physical activity. The fear of hypoglycemia may also have influenced glycemic control in the studies [28,30,31,34–36]. Indeed, since patients did not follow any specific diet, they might have decreased their insulin doses or have ingested more carbohydrates than usual to avoid hypoglycemias [16,44]. Tomar et al. [30] also noted that patients were not supervised after the exercise sessions for their food intake or the way they managed their diabetes at home. This aspect of diabetes care was not mentioned in any of the study protocols.

Both Salem et al. [29] and D'hooge et al. [36] noticed a significant reduction of daily insulin doses in intervention groups, at the end of the trial. This is probably the consequence of insulin dose adaptation to avoid hypoglycemia during and/or after exercises. Another hypothesis is that physical activity improves insulin sensitivity in trained muscles [50,51] so that the insulin needs may be quite lowered. These findings are in agreement with another study held by Moniotte et al. [52] who identified an average reduction of 29 to 42% in daily insulin doses (per kg body weight). Moreover, the meta-analysis of Wu et al. (2019) also showed a reduction (mean: −0.88 IU per kg body weight per day) in insulin requirements induced by exercise after a mean period of 18 weeks [44].

There are only few recommendations regarding the adaptation of insulin doses or of carbohydrates intake in the context of physical activity. The team of Riddell found that glucose levels should be comprised between 5.0 and 9.0 mmol/L in order to ensure the best performance and security for children with T1D. These authors suggested that small amount of carbohydrates (8–20 g) are sufficient to prevent episodes of hypoglycemia when insulin boluses have been adapted before the exercise session [53]. Also, recent data suggest that patients should ingest carbohydrates in prevention to hypoglycemia when glucose levels are still within normal ranges [53,54].

4.2. Blood lipid profile

Blood lipid profile is an adequate marker of cardiovascular risk factors which must be monitored in patients with T1D. Indeed, diabetic patients have to take care of this aspect because of their higher risk of developing macro- or microvascular disease [7,55].

Salem et al. (2010) observed significant improvements in blood lipid levels after the 24-weeks program in the two intervention groups of their study. They correlated the levels of improvements of the lipidograms with the frequency of exercise sessions. These findings are in agreement with those of Aouadi et al. [41]. According to these latter authors, a minimum of three months-long programs with four one-hour sessions per week or of six months-long programs with at least two one-hour sessions per week is necessary to detect an improvement in patients' blood lipid profile [41]. This is corroborated by the study by Tomar et al. [30] where patients practiced three hours a week for three months and experienced a marginal improvement in total cholesterol levels only; a mild increase in HDL and a mild decrease in LDL were also noticed. This suggests that the study setting might have been sufficient to induce a decrease in total cholesterol but not enough to provoke significant benefits in the other components of the blood lipid profile. Those findings are in line with the ones of the systematic reviews by Aljawarneh et al. [56] and Wu et al. [44], in which the authors concluded that improvements in blood lipid profile are proportional with physical activity levels.

In their investigations, Heyman et al. [28] only observed a significant reduction in the apolipoprotein B:A ratio, though they noticed mild trends in blood lipids levels. According to this study's program duration and frequency, we could have expected better outcomes, yet the study cohort was composed by 16 adolescent girls with T1D among which five were overweight and three obese, while eight girls suffered from dyslipidemia at baseline, which may have negatively influenced the evolution of blood lipid profiles [57]. Concordantly, Herbst et al. studied cardiovascular risk factors in adolescents with T1D and observed that girls had higher total cholesterol, HDL, LDL and TG levels than boys at same age [58].

4.3. Quality of life

While the overall literature supports a positive effect of physical activity on well-being in children [59], studies with children [60] or young adults [61] with T1D could not find a positive correlation between exercise and QoL. In 2013, a study on 106 children and adolescents observed a positive correlation ($r = 0.208$) between health-related QoL and VO2-max, suggesting the benefits of exercise in these children. Still, when these authors submitted QoL to physical activity levels, they did not observe a similar correlation, suggesting the presence of multiple variables associated to diabetes management during exercise (e.g., insulin dose adaptation, sugar intake, increase of glucose self-monitoring).

However, significant effects have been observed between physical activity and well-being in adults with T1D [62]. Edmunds et al. [60] explain this difference by the hypothesis that children mostly practice physical activity by spontaneous short and intense bouts of exercise although adults prefer planned continuous physical activity. Barriers encountered for spontaneous exercise in children with T1D may partially explain why this activity may be more worrisome at this age. Evaluation of QoL within a clinical study protocol is influenced by other factors as well (e.g., duration of the study protocol, stability of diabetes control, psychological situation of the patients), which is emphasized by the fact that two other studies [28,36] with planned exercise sessions were discrepant in their findings regarding this parameter.

4.4. Physical fitness

D'hooge et al. [36], Heyman et al. [28] and Roberts et al. [34] studied the aerobic capacity by using the PWC_{170} and the Aerobic Power Index submaximal test. They all found significant effects in the intervention groups. Roberts et al. [34] detected an increase while using the Aerobic Power Index submaximal test after 12 supervised weeks but returned to baseline rates after the 12 unsupervised weeks.

D'hooge et al. [36] also noticed significant improvements in other components of physical activity. They observed an improvement in the VO_2/power ratio which means that children who practiced physical activity used less oxygen for the same work and that their muscles worked more efficiently. Al Kahlifah et al. found that physical activity is inversely correlated with cardiovascular disease risks [44,63].

Children and adolescents with T1D may suffer from early cardiovascular complications, especially when suffering from poor glycemic control. Ozdemir et al. [64] suggested that children with T1D are likely to suffer from ventricle dysfunction, proportionally to blood glucose levels; these children might be at risk for premature heart failure [64,65]. It is therefore important to monitor the cardiac function to detect any abnormality in children and adolescents with T1D [64].

In our systematic review, the studies that controlled heart functions evaluated systolic and diastolic blood pressure at a resting state [29,35]. No significant difference was found, except in the study by Salem et al. [29] for the second intervention group (with three sessions of exercise per week), in the levels of pre-exercise diastolic blood pressure. It may thus be interesting to monitor cardiovascular tolerance of children with diabetes at rest and during physical activity.

4.5. Body size and body composition

All studies but one [30] analyzed anthropometric measures of the patients. Heyman et al. [28] and Roberts et al. [34] noticed a significant increase in the mean height of the patients after the 24 weeks, reflecting a mere consequence of their growth.

Heyman et al. [28] and Salem et al. [29] both observed a significant increase in total weight, as observed elsewhere [56,57,66,67]. This may be due either to the growth given that FFM and FM increased significantly, or to muscle gain. Salem et al. [29] observed a reduction of waist circumference in their intervention groups which may suggest that the significant increase in BMI they observed was not related to a gain of FM.

4.6. *Limitations*

During this systematic review, some limitations may have arisen. We only included randomized controlled trials to target study with the highest methodological quality and available evidence. However, we might have missed other important information in non-randomized controlled trials. Our strategy of trial selection allowed us to include only seven studies published during the past twenty years. Those studies are highly heterogeneous regarding the duration of intervention, the frequency of sessions, the characteristics and number of participants, the type of physical activity and the measured outcomes. This heterogeneity influenced the quality of conclusions we could draw during our review process. To overcome these hurdles, the PRISMA checklist was used to ensure the highest scientific rigor inside the evaluated studies.

5. Conclusion

One study out of the seven of our review revealed a positive effect of physical activity on glycemic control. The protocol of this study consisted of a 24-week supervised program which combined aerobic and anaerobic exercises, while the other studies only lasted for less than 24 weeks or contained unsupervised programs. Three studies highlighted some improvements in blood lipid profile, which is beneficial for these patients regarding cardiovascular risk factors. Improvements in QoL were detected in two studies, but only one with significant results, which may reflect the challenge to properly manage insulin doses and glucose control during physical activity.

In our review, most of the positive metabolic effects and even the improvement of well-being were observed in studies where exercise sessions were supervised, when lasting for at least 24 weeks and when conducted at least two times a week. Also, most significant results were noticed in protocols where aerobic and anaerobic physical activities were combined. We may conclude that these parameters (i.e., supervision, duration, frequency of sessions, protocols with mixed physical activity) may positively influence the metabolic outcome of studies in children with T1D.

For future researches, it would be indicated to evaluate exercise protocols lasting more than 24 weeks, with a high supervised sessions frequency (at least two or three times a week) of a minimum of one hour per training. Several aspects of glucose control should be recorded during and after exercise sessions: occurrence of daily and nocturnal episodes of hypoglycemia and hyperglycemia, amount of sugar intake during hypoglycemia, total of daily insulin dose, of insulin adaptations and participation to other activities implicating physical activity. If used, a notebook may also help to log carbohydrate content of meals and extra food intake. Patients' insulin sensitivity indexes and physical fitness levels may be recorded before the start of the program. Also, key outcomes to measure are HbA_{1C}, daily insulin doses, number of episodes of daytime and nocturnal hypoglycemia, reactional hyperglycemia, glycemic variability, QoL, blood lipid profile and cardiovascular risk factors. Monitoring cardiac function is also necessary to uncover any heart dysfunction to prevent cardiovascular events. Those analyses should preferably be performed at rest and during exercise.

It should also be beneficial to individualize the training program to each patient and to establish personal goals. Therefore, supervisors could use new real-life settings, like smart-watches, specific applications, web-based programs, to empower patients in their own health care program and/or to foster unsupervised physical activity. It is also important for children to have fun and to be exposed to various levels and sources of training to ensure a good participation rate.

Acknowledgements

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors declare no conflict of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.107810.

REFERENCES

[1] Global report on diabetes. World Health Organization; 2016.
[2] American Diabetes Association. 4. Lifestyle management: standards of medical care in diabetes—2018. Diabetes Care 41; 2018. p. S38–S50.
[3] Adolfsson P et al. ISPAD Clinical practice consensus guidelines 2018: exercise in children and adolescents with diabetes. Pediatr Diabetes 2018;19:205–26.
[4] Snowling NJ, Hopkins WG. Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients: a meta-analysis. Diabetes Care 2006;29:2518–27.
[5] Colberg SR et al. Physical activity/exercise and diabetes: a position statement of the American diabetes association. Diabetes Care 2016;39:2065–79.
[6] Powell KE et al. The scientific foundation for the physical activity guidelines for Americans, 2nd Edition. J. Phys. Act. Health 2019;16:1–11.
[7] Chimen M et al. What are the health benefits of physical activity in type 1 diabetes mellitus? A literature review. Diabetologia 2012;55:542–51.
[8] MacMillan F et al. A systematic review of physical activity and sedentary behavior intervention studies in youth with type 1 diabetes: study characteristics, intervention design, and efficacy: physical activity and type 1 diabetes. Pediatr Diabetes 2014;15:175–89.
[9] The Diabetes Research in Children Network (DirecNet) Study Group. The Effects of Aerobic Exercise on Glucose and Counterregulatory Hormone Concentrations in Children With Type 1 Diabetes. Diabetes Care 2006;29:20–5.
[10] Magkos F, Tsekouras Y, Kavouras SA, Mittendorfer B, Sidossis LS. Improved insulin sensitivity after a single bout of exercise

is curvilinearly related to exercise energy expenditure. Clin Sci 2008;114:59–64.
[11] Riddell MC, Perkins BA. Type 1 diabetes and vigorous exercise: applications of exercise physiology to patient management. Can J Diabetes 2006;30:63–71.
[12] Gillen JB et al. Acute high-intensity interval exercise reduces the postprandial glucose response and prevalence of hyperglycaemia in patients with type 2 diabetes. Diabetes Obes Metab 2012;14:575–7.
[13] Yardley JE, Sigal RJ, Perkins BA, Riddell MC, Kenny GP. Resistance exercise in type 1 diabetes. Can J Diabetes 2013;37:420–6.
[14] Guelfi KJ, Ratnam N, Smythe GA, Jones TW, Fournier PA. Effect of intermittent high-intensity compared with continuous moderate exercise on glucose production and utilization in individuals with type 1 diabetes. Am J Physiol Endocrinol Metab 2007;292:E865–70.
[15] Roberts CK, Hevener AL, Barnard RJ. Metabolic syndrome and insulin resistance: underlying causes and modification by exercise training. In: Terjung R, editor. Comprehensive physiology. John Wiley & Sons, Inc.; 2013.
[16] Martyn-Nemeth P et al. Fear of hypoglycemia: influence on glycemic variability and self-management behavior in young adults with type 1 diabetes. J Diabetes Complicat 2017;31:735–41.
[17] Brazeau A-S, Rabasa-Lhoret R, Strychar I, Mircescu H. Barriers to physical activity among patients with type 1 diabetes. Diabetes Care 2008;31:2108–9.
[18] Kennedy A, Narendran P, Andrews RC, Daley A, Greenfield SM. Attitudes and barriers to exercise in adults with a recent diagnosis of type 1 diabetes: a qualitative study of participants in the Exercise for Type 1 Diabetes (EXTOD) study. BMJ Open 2018;8 e017813.
[19] Nadella S, Indyk JA, Kamboj MK. Management of diabetes mellitus in children and adolescents: engaging in physical activity. Transl Pediatr 2017;6:215–24.
[20] Guelfi KJ, Jones TW, Fournier PA. The decline in blood glucose levels is less with intermittent high-intensity compared with moderate exercise in individuals with type 1 diabetes. Diabetes Care 2005;28:1289–94.
[21] Colberg SR, Laan R, Dassau E, Kerr D. Physical activity and type 1 diabetes: time for a rewire?. J Diabetes Sci Technol 2015;10.
[22] Campbell MD et al. Insulin therapy and dietary adjustments to normalize glycemia and prevent nocturnal hypoglycemia after evening exercise in type 1 diabetes: a randomized controlled trial. BMJ Open Diabetes Res. Care 2015;3 e000085.
[23] Tsalikian E et al. Prevention of hypoglycemia during exercise in children with type 1 diabetes by suspending basal insulin. Diabetes Care 2006;29:2200–4.
[24] Liberati A et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 2015;30.
[25] Verhagen AP, Boers M, Bouter LM, Knipschild PG. The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. J Clin Epidemiol 1999;8.
[26] Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 1998;1979–52:377–84.
[27] O'Connor SR et al. Failure of a numerical quality assessment scale to identify potential risk of bias in a systematic review: a comparison study. BMC Res Notes 2015;8.
[28] Heyman E et al. Exercise training and cardiovascular risk factors in type 1 diabetic adolescent girls. Pediatr Exerc Sci 2007;19:408–19.
[29] Salem MA, AboElAsrar MA, Elbarbary NS, ElHilaly RA, Refaat YM. Is exercise a therapeutic tool for improvement of cardiovascular risk factors in adolescents with type 1 diabetes mellitus? A randomised controlled trial. Diabetol Metab Syndr 2010;2:47.
[30] Tomar R, Hamdan M, Al-Qahtani MH. Effect of low to moderate intensity walking and cycling on glycaemic and metabolic control in type 1 diabetes mellitus adolescent males: a randomized controlled trial. Isokinet Exerc Sci 2014;22:237–43.
[31] Tunar M et al. The effects of Pilates on metabolic control and physical performance in adolescents with type 1 diabetes mellitus. J Diabetes Complicat 2012;26:348–51.
[32] Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. Stat Methods Med Res 2018;27:1785–805.
[33] Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Method 2014;14.
[34] Roberts L, Jones TW, Fournier PA. Exercise training and glycemic control in adolescents with poorly controlled type 1 diabetes mellitus. J Pediatr Endocrinol Metab JPEM 2002;15:621–7.
[35] Newton KH, Wiltshire EJ, Elley CR. Pedometers and text messaging to increase physical activity: randomized controlled trial of adolescents with type 1 diabetes. Diabetes Care 2009;32:813–5.
[36] D'hooge R et al. Influence of combined aerobic and resistance training on metabolic control, cardiovascular fitness and quality of life in adolescents with type 1 diabetes: a randomized controlled trial. Clin Rehabil 2011;25:349–59.
[37] Petito F, Cummins RA. Quality of life in adolescence: the role of perceived control, parenting style, and social support. Behav Change 2000;17:196–207.
[38] Ware Jr John E, Sherbourne CD. The MOS 36-Item short-form health survey (SF-36): I. Conceptual framework and Item selection. Med Care 1992;30:473–83.
[39] The DCCT Research Group. Reliability and validity of a diabetes quality-of-life measure for the diabetes control and complications trial (DCCT). Diabetes Care 1988;11:725–32.
[40] Burroughs TE, Desikan R, Waterman BM, Gilin D, McGill J. Development and validation of the diabetes quality of life brief clinical inventory. Diabetes Spectr 2004;17:41–9.
[41] Aouadi R et al. Aerobic training programs and glycemic control in diabetic children in relation to exercise frequency. J Sports Med Phys Fitness 2011;51:393–400.
[42] Herbst A, Bachran R, Kapellen T, Holl RW. Effects of regular physical activity on control of glycemia in pediatric patients with type 1 diabetes mellitus. Arch Pediatr Adolesc Med 2006;160:573–7.
[43] Kennedy A et al. Does exercise improve glycaemic control in type 1 diabetes? A systematic review and meta-analysis. PLoS ONE 2013;8 e58861.
[44] Wu N et al. Cardiovascular health benefits of exercise training in persons living with type 1 diabetes: a systematic review and meta-analysis. J Clin Med 2019;8:253.
[45] Chehregosha H, Khamseh ME, Malek M, Hosseinpanah F, Ismail-Beigi F. A view beyond HbA1c: role of continuous glucose monitoring. Diabetes Ther 2019. https://doi.org/10.1007/s13300-019-0619-1.
[46] Heinemann L et al. Real-time continuous glucose monitoring in adults with type 1 diabetes and impaired hypoglycaemia awareness or severe hypoglycaemia treated with multiple

daily insulin injections (HypoDE): a multicentre, randomised controlled trial. Lancet 2018;391:1367–77.
[47] Kovatchev BP. Metrics for glycaemic control — from HbA1c to continuous glucose monitoring. Nat Rev Endocrinol 2017;13:425–36.
[48] Patton SR et al. Use of continuous glucose monitoring in young children with type 1 diabetes: implications for behavioral research. Pediatr Diabetes 2011;12:18–24.
[49] Thomakos P et al. Avoiding hypoglycemia: the use of insulin pump combined with continuous glucose monitor in type 1 diabetes crossing a Rocky Gorge. QJM Mon J Assoc Physicians 2018;111:629–33.
[50] Goodyear LJ, Kahn BB. Exercise, glucose transport, and insulin sensitivity. Annu Rev Med 1998;49:235–61.
[51] Kristiansen S, Gade J, Wojtaszewski JFP, Kiens B, Richter EA. Glucose uptake is increased in trained vs. untrained muscle during heavy exercise. J Appl Physiol 2000;89:1151–8.
[52] Moniotte S, Owen M, Barrea T, Robert A, Lysy PA. Outcomes of algorithm-based modifications of insulinotherapy during exercise in MDI vs insulin pump-treated children with type 1 diabetes: results from the. Pediatr Diabetes 2017;18:925–33.
[53] Riddell MC, Milliken J. Preventing exercise-induced hypoglycemia in type 1 diabetes using real-time continuous glucose monitoring and a new carbohydrate intake algorithm: an observational field study. Diabetes Technol Ther 2011;13:819–25.
[54] Shetty VB et al. Effect of exercise intensity on glucose requirements to maintain euglycemia during exercise in type 1 diabetes. J Clin Endocrinol Metab 2016;101:972–80.
[55] Snell-Bergeon JK, Nadeau K. Cardiovascular disease risk in young people with type 1 diabetes. J Cardiovasc Transl Res 2012;5:446–62.
[56] Aljawarneh YM, Wardell DW, Wood GL, Rozmus CL. A systematic review of physical activity and exercise on physiological and biochemical outcomes in children and adolescents with type 1 diabetes. J Nurs Scholarsh 2019;51:337–45.
[57] Heyman E et al. Metabolic dysfunction in late-puberty adolescent girls with type 1 diabetes: relationship to physical activity and dietary intakes. Diabetes Metab 2012;38:337–42.
[58] Herbst A, Kordonouri O, Schwab KO, Schmidt F, Holl RW. Impact of physical activity on cardiovascular risk factors in children with type 1 diabetes: a multicenter study of 23,251 patients. Diabetes Care 2007;30:2098–100.
[59] Department of Health. At least five a week: Evidence on the impact of physical activity and its relationship to health: (591412009-001); 2004. http://doi.org/10.1037/e591412009-001.
[60] Edmunds S, Roche D, Stratton G, Wallymahmed K, Glenn SM. Physical activity and psychological well-being in children with Type 1 diabetes. Psychol Health Med 2007;12:353–63.
[61] Häyrinen M, Tarkka IM. Physical activity does not inevitably improve quality of life in young adults with type 1 diabetes. Diabetes Res Clin Pract 2016;121:99–101.
[62] Stewart AL et al. Long-term functioning and well-being outcomes associated with physical activity and exercise in patients with chronic conditions in the medical outcomes study. J Clin Epidemiol 1994;47:719–30.
[63] Al Khalifah RA et al. Association of aerobic fitness level with exercise-induced hypoglycaemia in Type 1 diabetes. Diabet Med J Br Diabet Assoc 2016;33:1686–90.
[64] Ozdemir O, Koksoy AY, Bulus AD, Andiran N, Yagli E. The effects of type 1 diabetes mellitus on cardiac functions in children: evaluation by conventional and tissue Doppler echocardiography. J Pediatr Endocrinol Metab 2016;29.
[65] Hensel KO et al. Subclinical alterations of cardiac mechanics present early in the course of pediatric type 1 diabetes mellitus: a prospective blinded speckle tracking stress echocardiography study. J Diabetes Res 2016;2016:2583747.
[66] Mohammed J et al. Assessment of habitual physical activity in adolescents with type 1 diabetes. Can J Diabetes 2014;38:250–5.
[67] Parthasarathy L, Chiplonkar S, Khadilkar V, Khadilkar A. Association Between Metabolic Control and Lipid Parameters in Indian Children with Type 1 Diabetes. Indian Pediatr 2016;53:39–41.