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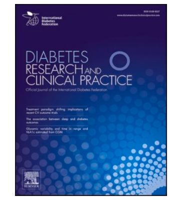

Review

Youth with type 1 diabetes mellitus are more inactive and sedentary than apparently healthy peers: A systematic review and meta-analysis

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ABSTRACT

Aims: To conduct a meta-analysis of differences in physical activity, sedentary behaviour, and physical fitness between children and adolescents with type 1 diabetes and their healthy peers.

Methods: The databases EMBASE, PubMed and SportsDiscus were searched for studies. Pooled effects were calculated using random effects inverse-variance models with the Hartung–Knapp–Sidik–Jonkman adjustment.

Results: Thirty-five studies were included, comprising a total of 4,751 youths (53% girls, 2,452 with type 1 diabetes). Youth with type 1 diabetes were less physically active (Cohen's d = −0.23, 95%CI − 0.42 to −0.04), more sedentary (Cohen's d = 0.33, 95%CI 0.06 to 0.61), and had lower cardiorespiratory fitness (Cohen's d = −0.52, 95%CI − 0.73 to −0.31) than their healthy peers. This corresponds to –12.72 min/day of moderate-to-vigorous physical activity, 63.3 min/day of sedentary time (accelerometry) and –4.07 ml/kg/min of maximum/peak oxygen consumption. In addition, young people with type 1 diabetes were less likely to meet the international physical activity recommendations than their healthy peers (odds ratio = 0.44, 95%CI 0.31 to 0.62).

Conclusions: Keeping in mind the heterogeneity between studies in the design, population and assessment, our findings show that children and adolescents with type 1 diabetes seem to be less active, more sedentary, and have lower cardiorespiratory fitness levels than their healthy peers.

1. Introduction

Type 1 diabetes is a chronic disease caused by the autoimmune destruction of pancreatic beta-cells, leading to a lifelong deficiency of insulin and resulting in increased morbidity, mortality, and reduced quality of life [1]. In addition to insulin therapy, diet, physical activity, and diabetes education also play crucial roles in managing this condition [2]. There is a growing body of evidence supporting the numerous health benefits of physical activity/exercise for patients with type 1 diabetes [3-6]. Meta-analyses of both clinical trials and observational studies in youth have also found significant improvements in glycated haemoglobin (HbA1c) levels associated with physical activity [7,8]. In contrast, sedentary behaviour has been linked to increased HbA1c levels, a higher cardiovascular risk, and an increased risk of all-cause mortality [7,9].

International guidelines recommend that children and adolescents with type 1 diabetes engage in daily moderate to vigorous aerobic physical activity (MVPA) for at least 60 min, in addition to 3 days per week of vigorous exercises and activities that strengthen bones and muscles [2,10]. These recommendations are not different from those for children and adolescents without type 1 diabetes. The International Society for Pediatric and Adolescent Diabetes (ISPAD) states that very few patients with type 1 diabetes meet the recommended levels of physical activity and that they are generally less active and more sedentary than their nondiabetic peers [10].

A number of studies have compared levels of physical activity between youth with and without type 1 diabetes, but their findings are somewhat inconsistent, showing no differences [11,12] or reporting that healthy peers are more active than youth with type 1 diabetes [13,14]. Overall, the findings of these studies are contradictory, and further research is needed to determine the true difference in physical activity levels between youth with and without type 1 diabetes. Additionally, cardiorespiratory fitness (CRF) is widely recognized as a strong and independent marker of cardiovascular health and overall mortality and

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should be routinely assessed in clinical practice, especially in high-risk patients such as those with type 1 diabetes [15]. Studies comparing the levels of CRF in youths with type 1 diabetes and healthy controls have shown contradictory findings [16-19]. Last, other physical fitness variables, such as muscular strength, have rarely been considered, which is a significant gap given the importance of the muscle as an endocrine organ [20-22].

Due to the discrepancies observed in the literature, the primary aim of our study was to determine whether the levels of physical activity, sedentary behaviour, and physical fitness of children and adolescents with type 1 diabetes differ from those of apparently healthy youths using a meta-analytic approach. In the past, Elmesmari et al. [23] conducted a meta-analysis comparing accelerometer-measured physical activity levels and sedentary time between youths with chronic diseases and healthy peers. Their findings showed no difference in MVPA between controls and patients with type 1 diabetes [23]. However, the study only included five studies assessing youths with type 1 diabetes. As a secondary objective, we evaluated whether the duration of the disease, age, and type of measurement (objective vs questionnaire/field test) had an influence on these relationships. Our study will help identify whether these youths could be at higher cardiometabolic risk due to inactivity or lower CRF levels and would therefore benefit from more intensive strategies to improve their physical activity levels and physical fitness.

2. Methodology

This systematic review and meta-analysis was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (Registration number: CRD42022384968). Its accomplishment was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [24] and The Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines [25].

2.1. Eligibility criteria

Studies were required to meet the following PECOS criteria: (1) Population: children and adolescents with a mean age between 3 and 20 years diagnosed with type 1 diabetes and healthy peers; (2) Exposition: disease (i.e., type 1 diabetes); (3) Outcomes: Physical activity (e.g., total, MVPA), sedentary behaviour (e.g., screen time, sitting time), and physical fitness (e.g., cardiorespiratory fitness [CRF], muscular fitness); (4) Comparison: youth with type 1 diabetes compared to apparently healthy peers; and (5) Study design: cross-sectional, longitudinal and case-control studies. Published studies in English and Spanish languages were included, while reports in other languages were excluded. Authors not reporting the outcomes of interest were contacted and included if they provided the required information. No limitation based on the date of publication was done.

2.2. Information sources

Two investigators (NHU and AGH) independently and systematically conducted the search from inception to December 7th, 2022. The sources searched were EMBASE, PubMed, and SportsDiscus. Reference lists of key papers and previous systematic reviews were reviewed, and studies fulfilling the inclusion criteria were included. Google Scholar was used to identify any studies not captured by the above methods.

2.3. Search strategy

The search terms and all combinations used in the search strategy can be found in the Electronic Supplementary Material (ESM Methods 1).

2.4. Selection process

Two authors (NHU and AGH) performed the search of titles and abstracts of interest independently and selected the studies based on the criteria stated above. In case of disagreements, a third author (MI) was consulted.

2.5. Data collection process

The data collection of the selected reports was carried out by two investigators as follows: One author (NHU) extracted the data of interest from every paper, and a second author (AGH) examined the accuracy of the data.

2.6. Data Items (outcomes and other variables)

The following data were extracted (Table 1): (i) Study: authors and year of publication and country where the study was developed; (ii) Participants: sample size in each group (i.e., type 1 diabetes and apparently healthy youth), proportion of girls and boys in each group, age of participants in each group; and (iii) Dependent variables: method of measurement of physical activity (e.g., accelerometry, total physical activity measured by questionnaire, heart rate monitoring, etc.), method of measurement of sedentary behaviour (e.g., accelerometry, self-reported screen time), method of measurement of CRF (e.g., bicycle ergometer or treadmill protocol to exhaustion, 20-m endurance shuttle run test), and method of measurement of muscular fitness (e.g., handgrip, standing long jump). Study authors were contacted in case of any missing information.

2.7. Study quality assessment

Two investigators (NHU and AGH) determined the risk of bias of every article independently. The NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies [26] was used to assess the methodological quality of all studies included. Interrater agreements were calculated for the initial set of ratings, and a third reviewer (MI) was consulted in the event of disagreements.

2.8. Effect measures

We calculated the standardized mean difference and 95% confidence interval (CI) of each article as the main effect size in the synthesis of results and expressed it as Cohen's d. The effect sizes were categorized as small [Cohen's $d = 0.2$], medium ($d = 0.5$), or large ($d \geq 0.8$) based on these methods.

2.9. Synthesis methods

STATA 17.0 (STATA Corp., College Station, TX, USA) was used to conduct all analyses. A random effects inverse-variance model with the Hartung–Knapp–Sidik–Jonkman adjustment was performed [27]. Heterogeneity across results was calculated using the inconsistency index (I^2), derived from the Cochran Q statistic [28,29].

2.10. Reporting bias assessment

Small-study effects and publication bias were examined using the Luis Furuya-Kanamori index and the Doi plot, respectively [30]. A Luis Furuya-Kanamori index value greater than 1 or less than -1 indicates minor asymmetry, and values greater than 2 or smaller than -2 indicate major asymmetry.

2.11. Additional analysis

Whenever possible, subgroup analyses were performed based on sex,

Table 1
Study characteristics.

First author (year) Country	Sample (n)	Girls (n)	Mean age or range (years)	Diabetes duration (years)	Type of PA/assessment	Type of sedentary behaviour	Physical fitness component	Study quality
Arslanian et al. 1990 [56] USA	T1D: 27 Healthy: 10	T1D: 11 Healthy: 6	T1D: 16.6 Healthy: 14.3	7.7			VO2max	5/14
Austin et al. 1993 [55] USA	T1D: 59 Healthy: 18	T1D: 31 Healthy: 9	T1D: 15.6 Healthy: 14.2	7.6			VO2max	5/14
Baraldi et al. 1992 [54] Italy	T1D: 33 Healthy: 47	T1D: 16 Healthy: 23	T1D: 13.2 Healthy: 12.7	5.0			VO2max	6/14
Bjornstad et al. 2015 [48] USA	T1D: 69 Healthy: 13	NR	T1D: 15.5 Healthy: 15.1	6.3	Total PA/questionnaire		VO2 peak	6/14
Cuenca-García et al. 2012 [18] UK	T1D: 60 Healthy: 37	T1D: 20 Healthy: 17	T1D: 12.5 Healthy: 12.0	NR	MVPA/accelerometer		PWC170	7/14
Czenczek-Lewandowska et al. 2019 [13] Poland	T1D: 215 Healthy: 115	T1D: 119 Healthy: 50	T1D: 12.6 Healthy: 12.0	NR	MVPA/accelerometer	Total sedentary time		8/14
De Lima et al. 2017 [47] Brazil	T1D: 45 Healthy: 119	T1D: 20 Healthy: 51	T1D: 12.4 Healthy: 11.6	6.5	MVPA/accelerometer	Total sedentary time	VO2 max	5/14
Dos Santos Haber et al. 2022 [46] Brazil	T1D: 77 Healthy: 30	NR	T1D: 12.5 Healthy: 12.6	4.4	Total PA/questionnaire			5/14
Elmesmari et al. 2022 [45] UK	T1D: 20 Healthy: 20	T1D: 9 Healthy: 9	T1D: 7.4 Healthy: 7.3	2.12	Total PA/ accelerometer	Total sedentary time		7/14
Fainardi 2011 [12] Italy	T1D: 129 Healthy: 214	T1D: 68 Healthy: 119	T1D: 12.13 Healthy: 12.18	5.6	Total PA/questionnaire	Screen time		6/14
Fintini et al. 2012 [19] Italy	T1D: 35 Healthy: 31	T1D: 20 Healthy: 16	T1D: 10.2 Healthy: 10.6	3.5	Total PA/SenseWear Armband	Total sedentary time	VO2 max	6/14
Gusso et al. 2008 [53] New Zeland	T1D: 12 Healthy: 10	T1D: 12 Healthy: 10	T1D: 15.4 Healthy: 15.1	6.1			VO2 max	3/14
Heyman et al. 2005 [31] France	T1D: 17 Healthy: 18	T1D: 0 Healthy: 0	T1D: 10.5 Healthy: 10.3	NR			PWC170	6/14
Jegdic et al. 2013 [17] Croatia	T1D: 100 Healthy: 100	T1D: 49 Healthy: 51	13.0	NR			6-minutes walk test	5/14
Kaya Mutlu et al. 2015 [40] Turkey	T1D: 47 Healthy: 55	T1D: 26 Healthy: 27	T1D: 9.87 Healthy: 9.56	2.77	Total PA (PAQ-C)			7/14
Kaya Mutlu et al. 2017 [50] Turkey	T1D: 41 Healthy: 38	T1D: 23 Healthy: 18	T1D: 15.3 Healthy: 14.7	2.8	Total PA (PAQ-A)			7/14
Komatsu et al. 2005 [16] Brazil	T1D: 72 Healthy: 46	T1D: 34 Healthy: 20	T1D: 16.0 Healthy: 16.0	4.9			VO2 peak	6/14
Lobelo et al. 2010 [44] USA	T1D: 384 Healthy: 173	T1D: 196 Healthy: 102	10–20	3.8	MVPA 30-min blocks per d/questionnaire	Screen time		7/14
Lukács et al. 2013 [21] Hungary	T1D: 106 Healthy: 130	T1D: 53 Healthy: 69	8–18	5.1	–	–	Eurofit physical fitness test	6/14
Maggio et al 2010 [43] Switzerland	T1D: 48 Healthy: 85	NR	T1D: 10.7 Healthy: 10.1	3.3	Total PA and MVPA/ accelerometer	Total sedentary time	VO2 peak	7/14

(continued on next page)

Table 1 (*continued*)

First author (year) Country	Sample (n)	Girls (n)	Mean age or range (years)	Diabetes duration (years)	Type of PA/assessment	Type of sedentary behaviour	Physical fitness component	Study quality
Marshall et al. 2021 [42] Wales	T1D: 23 Healthy: 17	T1D: 14 Healthy: 6	T1D: 12.1 Healthy: 11.8	5.0	MVPA/accelerometer	Total sedentary time		6/14
Massin et al. 2005 [11] Belgium	T1D: 127 Healthy: 200	T1D: 75 Healthy: 100	3–16	3.9	MPA and VPA/Heart rate monitoring			5/14
Mohammed et al. 2014 [41] Canada	T1D: 66 Healthy: 54	T1D: 31 Healthy: 31	T1D: 16.0 Healthy: 16.3	6.0	Total PA/questionnaire			6/14
Nadeau et al 2010 [52] USA	T1D: 12 Healthy: 12	T1D: 6 Healthy: 6	T1D: 15.6 Healthy: 14.8	7.5			VO2 peak	6/14
Nascimento et al. 2017 [38] Brazil	T1D: 21 Healthy: 16	T1D: 15 Healthy: 8	T1D: 12.7 Healthy: 13.1	4.2	Total PA/questionnaire		VO2max	5/14
Nguyen et al. 2015 [22] Canada	T1D: 16 Healthy: 8	NR	T1D: 14.0 Healthy: 13.6	4.5	MVPA/accelerometer		VO2peak Muscle power Grip strength	5/14
Raile et al. 1999 [37] Germany	T1D: 142 Healthy: 97	NR	6–18	NR	Total PA/questionnaire			4/14
Särnblad et al. 2005 [36] Sweden	T1D: 26 Healthy: 49	T1D: 26 Healthy: 49	T1D: 15.7 Healthy: 15.8	6.2	MVPA/accelerometer	Total sedentary time		7/14
Sundberg et al 2012 [35] Sweden	T1D: 24 Healthy: 26	T1D: 12 Healthy: 14	T1D boys: 4.3 T1D girls: 4.7 Healthy boys: 4.9 Healthy girls: 4.4	Boys: 2.1 Girls: 1.8	Total PA and MVPA/ accelerometer	Total sedentary time		7/14
Thongpaeng et al. 2022 [14] Thailand	T1D: 100 Healthy: 100	T1D: 56 Healthy: 56	T1D: 14.5 Healthy: 14.3	NR	MVPA/questionnaire			5/14
Trigona et al. 2010 [34] Switzerland	T1D: 32 Healthy: 42	T1D: 15 Healthy: 25	T1D: 11.5 Healthy: 10.7	5.1	MVPA/accelerometer	Total sedentary time	VO2max	7/14
Valerio et al. 2007 [33] Italy	T1D: 138 Healthy: 269	T1D: 71 Healthy: 149	T1D: 13.6 Healthy: 12.9	6.1	MVPA/questionnaire			5/14
Van Ryckeghem et al. 2021 [49] Belgium	T1D: 19 Healthy: 19	T1D: 6 Healthy: 5	T1D: 14.8 Healthy: 14.4	9.0	Total PA/questionnaire		VO2peak	5/14
Williams et al. 2011 [51] Australia	T1D: 62 Healthy: 62	T1D: 36 Healthy: 36	T1D: 10.9 Healthy: 10.9	4.3			QCST	5/14
Wu et al. 2021 [32] China	T1D: 48 Healthy: 19	T1D: 30 Healthy: 11	T1D: 14.0 Healthy: 13.6	3.6	Total PA/accelerometer	Total sedentary time	VO2max	7/14

NR: not reported; PA, physical activity; PAQ-A: Physical Activity Questionnaire for Adolescents; PAQ-C: Physical activity questionnaire for older children; PWC170: Physical work capacity (watts) at a heart rate of 170 beats/min; T1D: type 1 diabetes; QCST: Queens College Step Test; VPA: vigorous physical activity.

age (children and adolescents), and type of physical activity (i.e., objective or self-reported). We also quantified mean differences between groups in minutes of moderate-to-vigorous physical activity and sedentary time and in ml/kg/min of VO_2 maximum or peak.

Random-effect meta-regression analyses were used to evaluate the relationship between diabetes duration (years) and mean age and the effect sizes. Additionally, we determined the association between the differences in CRF and differences in physical activity and sedentary behaviour between youths with type 1 diabetes and their healthy peers.

Finally, a sensitivity analysis was performed to assess the robustness of the summary estimates and to determine whether a particular study accounted for the heterogeneity. To examine the effects of each result from each study on the overall findings, the results were analysed with each study deleted from the model once.

3. Results

3.1. Study selection

The systematic search in the different databases resulted in a total of 3,095 articles that were subsequently screened to exclude duplicates (n = 2,205). The 890 remaining papers were screened based on title and abstract, and 60 were retained for detailed evaluation. Thirty-five articles meeting the inclusion criteria were finally included in our analysis and report. Reasons for exclusion of studies can be found in ESM Results 1 in the Electronic Supplementary Material.

3.2. Study characteristics

A total of 4,751 youths, 2,452 with type 1 diabetes and 2,299 apparently healthy controls, were included in the study. The age of the participants ranged from 3 to 20 years. Fifty-three percent of the youths were girls and one study included only boys [31].

A total of 25 studies evaluated physical activity and/or sedentary behaviour, and all of them were included in the analysis [11-14,18,19,22,32-49]. Twelve studies measured physical activity through objective measurements (i.e., accelerometry or heart rate monitoring) [11,13,18,22,32,34-36,42,43,45,47] and the remaining participants completed questionnaires [12,14,19,33,37,38,40,41,44,46,48-50].

Twenty studies reported CRF estimations, all of which were included in the analysis comprising a total of 1,735 youths, 893 with type 1 diabetes [16-19,21,22,31,32,34,38,43,47-49,51-56]. Five studies estimated CRF through field tests [17,18,21,31,51], while 15 measured CRF directly through spirometry during maximal or submaximal tests [16,19,22,32,34,38,43,47-49,52-56]. Only two studies examined muscular strength [21,22]; therefore, the analysis of this fitness component was not possible.

3.3. Quality of individual studies

The average score of the studies included in this report was 5.86, based on the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. Since all studies were observational, none of them fulfilled the criteria 6, 7, 10, 12 and 13. Moreover, given that the exposure of interest was having type 1 diabetes, the 8th criterion was not applicable. Thus, the highest possible grade was 8 out of 14. Taking this into consideration, most of the papers included in our study were considered to have moderate to good methodological quality (ESM Table 1).

3.4. Results of individual studies

All effect sizes (i.e., Cohen’s d) of each study are shown in Figs. 2–5.

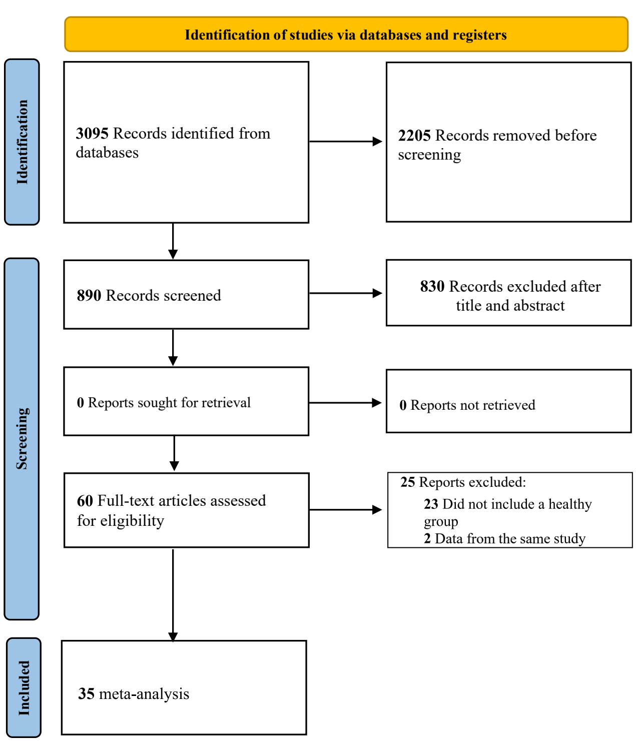

Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.

3.5. Results of synthesis

The results of the meta-analysis showed that, compared with their healthy peers, youth with type 1 diabetes were less physically active (Cohen’s d = −0.23, 95% CI − 0.42 to −0.04, p = 0.020; I^2 = 81.9%; n = 22) (Fig. 2), more sedentary (Cohen’s d = 0.33, 95% CI 0.06 to 0.61, p = 0.014; I^2 = 76.9%; n = 11) (Fig. 3) and had lower CRF (Cohen’s d = −0.52, 95% CI − 0.73 to − 0.31, p < 0.001; I^2 = 65.0%; n = 20) (Fig. 4). In addition, taking international physical activity recommendations into account, young people with type 1 diabetes were less likely to meet them than their healthy peers (odds ratio [OR] = 0.44, 95% CI 0.31 to 0.62, p < 0.001; I^2 = 34.8%; n = 9) (Fig. 5). Unfortunately, we have not been able to analyse the differences in muscular strength and motor agility.

The LFK index for the Doi plots showed no asymmetry for CRF (Luis Furuya-Kanamori index = 0.33) (ESM Fig. 1), minor asymmetry for total physical activity (Luis Furuya-Kanamori index = −1.61) (ESM Fig. 2) and physical activity recommendations (Luis Furuya-Kanamori index = −0.73) (ESM Fig. 3), and major asymmetry for sedentary behaviour (Luis Furuya-Kanamori index = 2.10) (ESM Fig. 4).

Sensitivity analyses confirmed that findings remained stable after omitting each study at a time for CRF (ESM Fig. 5), physical activity recommendation (ESM Fig. 6) and sedentary behaviour (ESM Fig. 7). Regarding total physical activity, this sensitivity analysis showed that some studies influenced the overall results after its removal (ESM Fig. 8).

Subgroup analysis revealed that total physical activity differences between type 1 diabetes and healthy peers remained significant only for objective measures (Cohen’s d = –0.28, 95% CI –0.53 to –0.03) (Table 2). Regarding sedentary behaviour, differences were large among adolescents (Cohen’s d = 0.86, 95% CI 0.60 to 1.12). Additionally, the total mean sedentary time per day difference assessed with objective tools was 63.3 min/day (95% CI 14.9 min/day to 111.7 min/day). Concerning CRF, differences were slightly stronger in adolescents (Cohen’s d = –0.70, 95% CI –0.90 to –0.49), with a mean difference in VO_2 of –4.07 ml/kg/min (95% CI –6.51 ml/kg/min to –2.97 ml/kg/min).

Meta-regression analyses showed that differences in total physical activity (β = 0.09, 95% CI –0.04 to 0.24; p = 0.179) (ESM Fig. 9), compliance with physical activity recommendations (β = 0.01, 95% CI –0.23 to 0.26; p = 0.922) (ESM Fig. 10), sedentary behaviour (β = 0.05, 95% CI –0.15 to 0.25; p = 0.606) (ESM Fig. 11) and CRF (β = –0.02, 95% CI –0.10 to 0.07; p = 0.950) (ESM Fig. 12) were not associated with diabetes duration. In contrast, CRF (β = –0.09, 95% CI –0.14 to –0.03; p = 0.032) (ESM Fig. 13) was associated with the mean age of the participants but not with total physical activity (β = 0.05, 95% CI –0.01 to 0.11; p = 0.087) (ESM Fig. 14), physical activity recommendations (β = 0.03, 95% CI –0.14 to 0.20; p = 0.759) (ESM Fig. 15) and sedentary behaviour (β = –0.01, 95% CI –0.07 to 0.04; p = 0.602) (ESM Fig. 16).

Finally, differences in CRF were related to differences in sedentary behaviour (β = –1.28, 95% CI –2.37 to –0.20) (ESM Fig. 17) but not with physical activity (β = 0.23, 95% CI –0.14 to 0.60) (ESM Fig. 18).

4. Discussion

Our meta-analysis examined the levels of physical activity, sedentary behaviour and physical fitness in children and adolescents with type 1 diabetes compared to their healthy peers. The results showed that youths with type 1 diabetes were generally less active, more sedentary, and had lower levels of cardiovascular fitness than their peers without the disease. These findings suggest that interventions to increase physical activity, decrease sedentary behaviour, and improve cardiovascular fitness should be prioritized to improve cardiometabolic health in this population.

4.1. Physical activity

Physical activity has been shown to have positive effects on

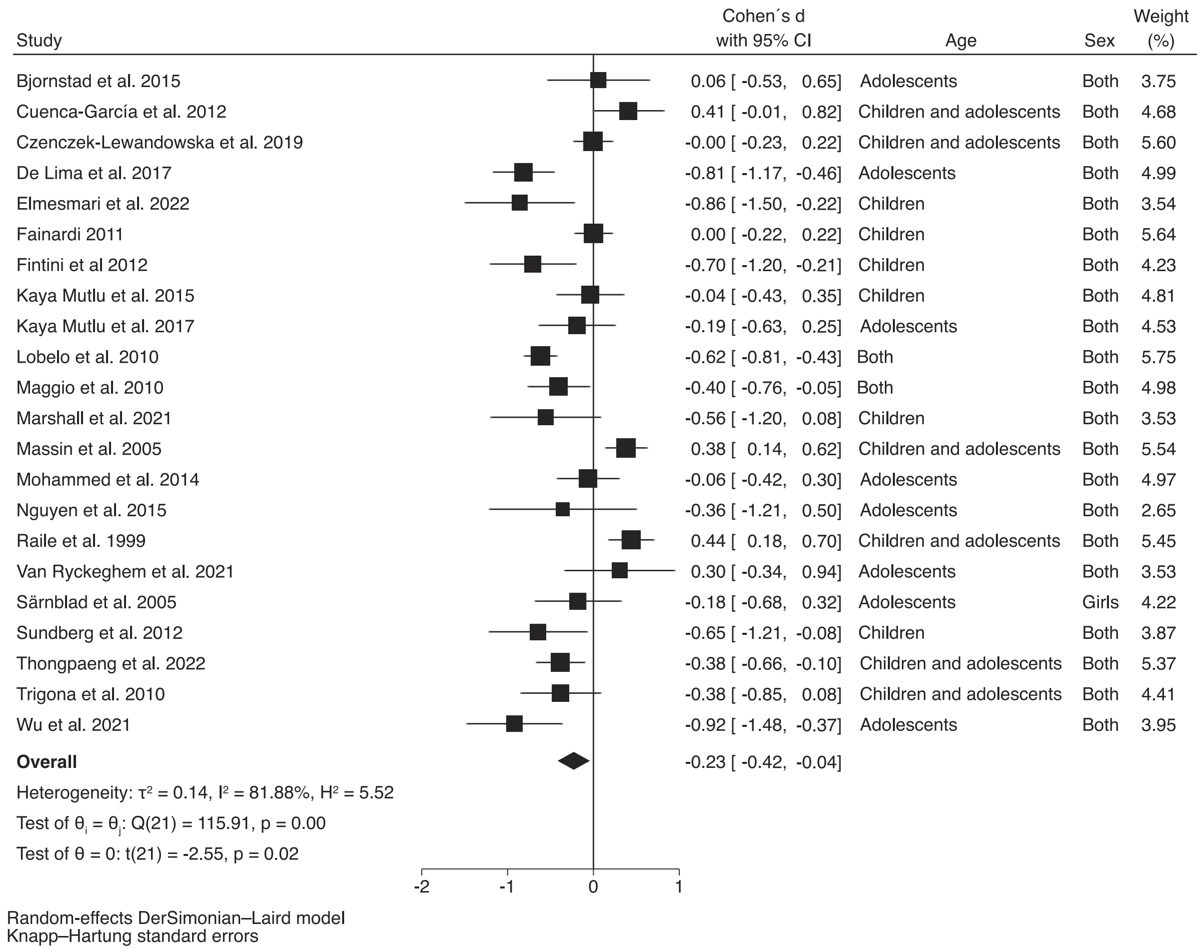

Fig. 2. Forest plot showing the difference in total physical activity between youths with insulin-dependent diabetes mellitus and apparently healthy youths.

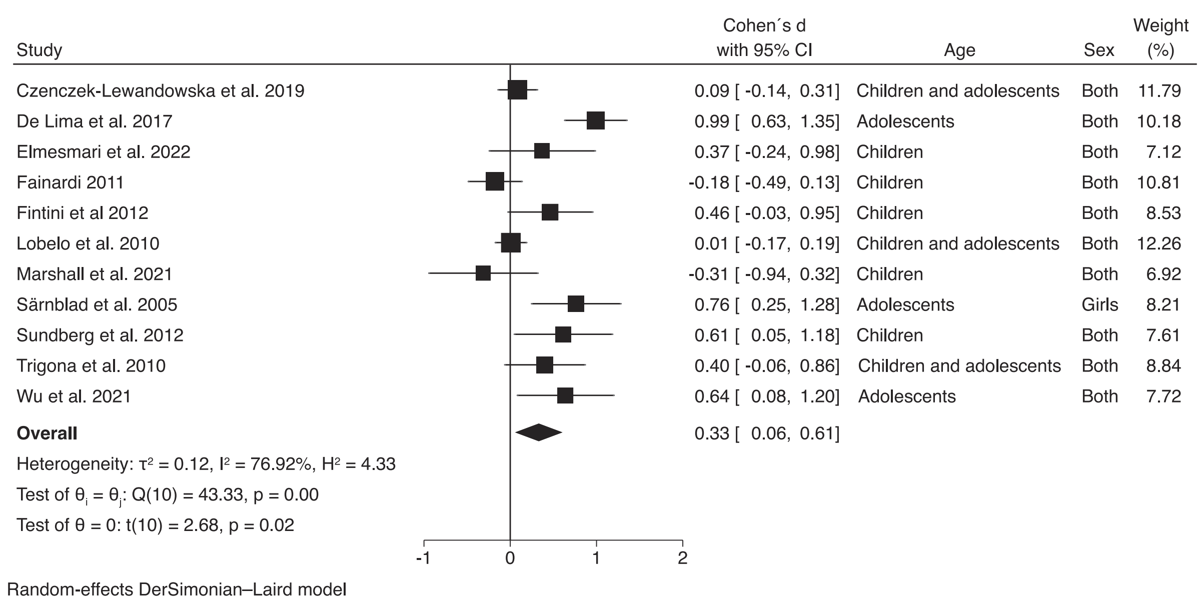

Fig. 3. Forest plot showing the difference in sedentary behaviour between youths with insulin-dependent diabetes mellitus and apparently healthy youths.

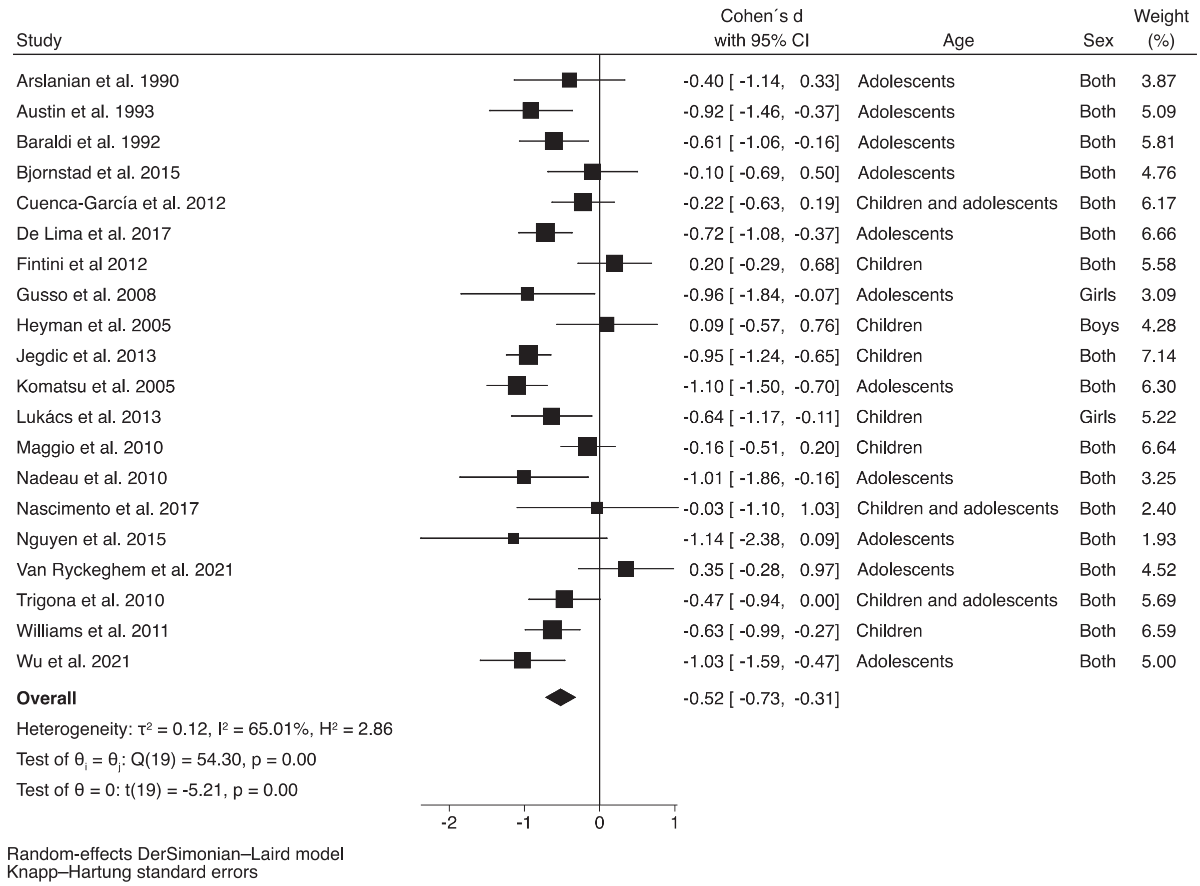

Fig. 4. Forest plot showing the difference in cardiorespiratory fitness between youths with insulin-dependent diabetes mellitus and apparently healthy youths.

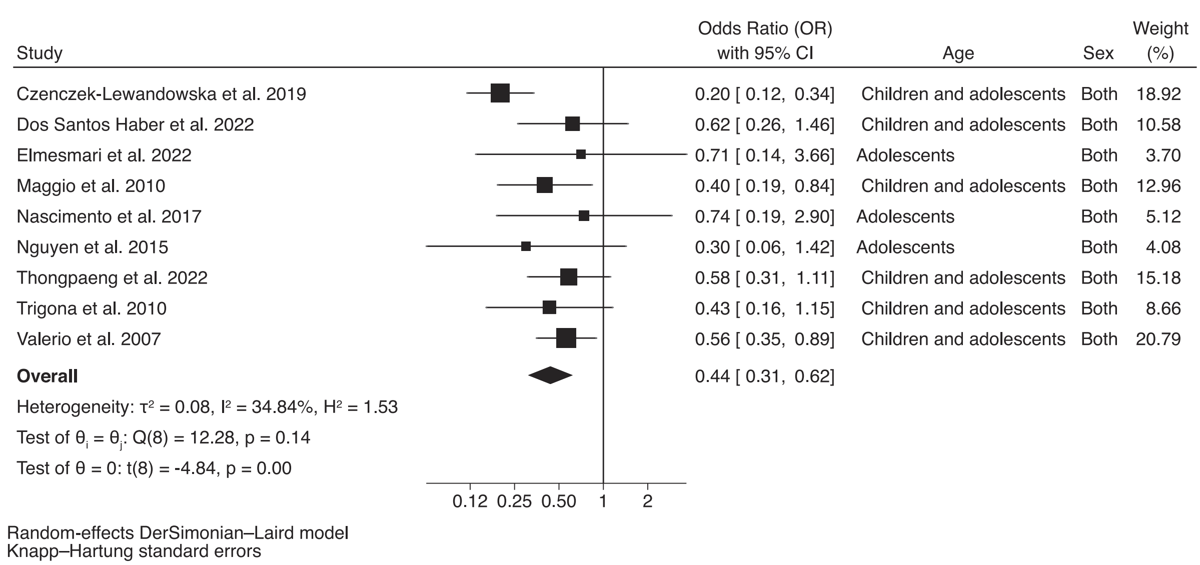

Fig. 5. Forest plot showing the difference in physical activity recommendations between youths with insulin-dependent diabetes mellitus and apparently healthy youths.

cardiometabolic health in children and adolescents with type 1 diabetes [7,57] and therefore should be highly encouraged. Unfortunately, our results indicate that these individuals are less active than their peers without diabetes and are less likely to meet international physical activity recommendations. Despite a low risk of publication bias indicated by the LFK index, the sensitivity analysis revealed that certain studies [19,32,35,44,45,47] greatly influenced the results for total physical activity, and therefore, our findings should be interpreted with caution. Additionally, the difference between groups was not consistently observed after performing subgroup analysis, except for objective measures (i.e., device measures). Further studies may be needed to identify which group is less active. Furthermore, the differences between

Table 2
Differences between groups according to subgroup analysis.

	n	Cohen's d or Mean Difference	95% CI	p	I^2
Total physical activity					
Children	5	−0.12	−0.47 to 0.23	0.257	76.3
Adolescents	10	−0.18	−0.51 to 0.15	0.278	73.4
Subjective	10	−0.16	−0.53 to 0.22	0.415	93.1
Objective (device measure)	16	−0.28	−0.53 to −0.03	0.029	77.9
MVPA (min/day)	7	*−12.72*	*−26.64 to 1.21*	0.073	92.4
Physical activity recommendation					
Adolescents	4	*0.55*	*0.23 to 1.31*	0.178	0
Sedentary behaviour					
Children	6	0.10	−0.18 to 0.39	0.469	57.6
Adolescents	3	0.86	0.60 to 1.12	<0.001	0
Subjective	4	−0.05	−0.19 to 0.09	0.460	0
Objective (device measure)	7	0.44	0.11 to 0.78	0.009	69.1
Total sedentary time (min/day)	6	*63.3*	*14.9 to 111.7*	<0.001	66.8
Cardiorespiratory fitness					
Children	7	−0.38	−0.72 to −0.05	0.026	76.6
Adolescents	16	−0.70	−0.90 to −0.49	<0.001	40.7
VO_2 maximum or peak (ml/kg/min)	20	*−4.07*	*−6.51 to −2.97*	<0.001	63.6

Italics show Mean Difference values. MVPA, moderate-to-vigorous physical activity.

youth with and without type 1 diabetes in terms of meeting physical activity recommendations are not related to the duration of the disease and decrease with age, similar to the general population [58,59].

Our study highlights the need for strategies to increase physical activity levels in children and adolescents with type 1 diabetes to take advantage of its health benefits. However, barriers to physical activity and strategies to overcome them have not been well studied in this population, despite the importance of physical activity. Fear of hypoglycemia or of loss of diabetes control have been identified as main barriers to physical activity among youth with type 1 diabetes, but recent studies suggest that these fears may be less of a barrier than previously thought, possibly due to the use of new technologies in glucose management and monitoring [60-62]. Identifying and addressing these barriers is crucial to increase physical activity levels in this population. Additionally, although multimedia interventions and community-based approaches have shown promise [63,64], it is important for all healthcare professionals involved in the management of youth with type 1 diabetes to routinely and actively encourage physical activity and address any barriers that patients may face.

4.2. *Physical fitness*

Physical fitness is considered an important health marker in childhood and adolescence, and its various components have been linked to a variety of health outcomes [65]. Similar to physical activity and sedentary behavior, our meta-analysis found a significant difference in CRF between children and adolescents with type 1 diabetes and their healthy peers, regardless of the duration of the disease. Specifically, individuals with type 1 diabetes had 4.07 ml/kg/min lower $VO_{2max/peak}$ than their healthy peers, which corresponds to more than 1 metabolic equivalent of task difference (i.e., 1 MET = 3.5 ml/kg/min). In addition, the subgroup analysis showed that this difference remained significant in both children and adolescents, with the difference being greater among adolescents. Furthermore, a positive association with the mean age of the participants was observed, indicating that the difference between those with type 1 diabetes and their healthy peers increases as youth age.

Our results are reliable, as confirmed by the sensitivity analysis and the absence of asymmetry in the Doi plots. As mentioned above, the importance of CRF is supported by epidemiological and clinical data that have identified CRF as a strong cardiovascular health and prognostic marker, stronger than traditional cardiovascular risk factors such as hypertension, dyslipidemia or type 2 diabetes [15,66]. CRF is linked to lower cardiovascular and all-cause mortality in patients with type 1 diabetes, and an inverse dose–response association has been found in the healthy population [67,68]. In healthy youths, boys and girls below the optimal fitness threshold have 5.7 and 3.6 greater risk of having CVD, respectively [69]. It is worth considering that the differences found in CRF were only associated with differences in sedentary behaviour, not with physical activity. This finding suggests that sedentary behaviour may negatively impact CRF independently of physical activity levels, as previously suggested [70]. This association may be explained by a reduction in muscle contraction, leading to changes in muscle metabolism and mitochondrial dysfunction [71,72]. On the other hand, lower fitness levels among individuals with type 1 diabetes seem to be explained by other factors than physical activity or sedentary behaviour. Chang et al [73] conducted a scoping review to assess the effects of exercise on CRF in youth with T1D and found four studies, of which only two reported an improvement in CRF. Altered aerobic muscle capacity has been described in children with poor glycemic control compared to those with better control, irrespective of PA levels [22]. In accordance to this, a systematic review and meta-analysis found a decrease of −0.94 ml/Kg/min in VO2max per 1% increase in HbA1c levels [74]. Moreover, insulin deprivation has shown to reduce mitochondrial ATP production and transcription of oxidative phosphorylation genes in type 1 diabetic patients [75]. Other factors include lower capillary density in skeletal muscle and abnormalities in muscular structure and fibre distribution or mechanisms involving lower oxidative capacity and mitochondrial dysfunction [76,77]. These mechanisms might explain the lack of association between PA and CRF found in our study.

4.3. *Sedentary behaviour*

Our study also found that children and adolescents with type 1 diabetes were more sedentary than their healthy peers. The subgroup analysis showed that this difference remained significant among adolescents but not in children and that those with type 1 diabetes spent more than one hour more in sedentary behaviours than those without diabetes, specifically 63.3 min per day. However, it should be noted that our results should be interpreted with caution due to the risk of publication bias indicated by the LKF index, and more studies using a standardized methodology are needed to confirm these findings. The fact that youth with type 1 diabetes seem to be more sedentary than their peers is a cause for concern, as this behaviour is related to increased HbA1c levels [7], which further increase the cardiovascular risk of individuals with type 1 diabetes. Therefore, the American Diabetes Association recommends limiting sedentary behaviour as much as possible and breaking these periods every 30 min as strategies that may improve glycaemic control [78]. A stronger focus on reducing sedentary behaviour and strategies to reduce time spent in these activities among youths with type 1 diabetes is strongly recommended to address this issue.

In conclusion, keeping in mind the heterogeneity between studies in the design, population and outcome assessment, our findings show that children and adolescents with type 1 diabetes seem to be less active, more sedentary, and have lower cardiorespiratory fitness levels than their healthy peers. Our findings suggest that this specific population may be at increased risk for cardiovascular diseases, as these parameters have been consistently linked to cardiometabolic health. Thus, our study emphasizes the need for comprehensive approaches to increase physical activity levels, decrease sedentary time and improve fitness levels in these youths to lower their cardiovascular risk and improve their overall health.

4.4. Strengths and limitations

To our knowledge, this is the first study assessing the differences in physical activity levels, sedentary time, and CRF between children and adolescents with type 1 diabetes and their healthy peers through a meta-analytic approach. This summarizes the data collected thus far, allowing us to answer our question while taking into account the heterogeneity of the numerous studies in this field. However, some limitations should be considered. First, no causality can be inferred due to the cross-sectional and observational nature of all included studies. Second, we found a significant risk of publication bias and heterogeneity in the sedentary time analysis, as well as high heterogeneity in the studies included in the physical activity analysis; therefore, these findings should be interpreted with caution. Third, the language limitation to papers in English and Spanish and the search in only three databases may have contributed to selection bias. Fourth, the estimation of physical activity levels by questionnaire and CRF by field tests may have overestimated these parameters, which could have confounded our results. Fifth, analysis of other fitness components, such as strength and motor agility, was not possible due to a lack of studies addressing these parameters. Finally, some of the studies included in the analysis were quite old and may not represent the current status of the physical activity level in type 1 diabetes; e.g., some guidelines concerning physical activity in type 1 diabetes [2,10] were published in recent years, making physical activity safer, and the usage of continuous glucose monitoring is much wider, also making physical activity easier and safer [79].

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2023.110697.

References

[1] McCarthy M, Yan J, Jared MC, You E, Ilkowitz J, Gallagher MP, et al. Cardiovascular health in emerging adults with type 1 diabetes. Eur J Cardiovasc Nurs 2022;21:213–9. https://doi.org/10.1093/eurjcn/zvab062.

[2] American Diabetes Association. 14. Children and Adolescents: Standards of Medical Care in Diabetes—2022. Diabetes Care 2022;45:S208–31. https://doi.org/10.2337/dc22-S014.

[3] Quirk H, Blake H, Tennyson R, Randell TL, Glazebrook C. Physical activity interventions in children and young people with Type 1 diabetes mellitus: A systematic review with meta-analysis. Diabet Med 2014;31:1163–73. https://doi.org/10.1111/dme.12531.

[4] Ostman C, Jewiss D, King N, Smart NA. Clinical outcomes to exercise training in type 1 diabetes: A systematic review and meta-analysis. Diabetes Res Clin Pract 2018;139:380–91. https://doi.org/10.1016/j.diabres.2017.11.036.

[5] Wu N, Bredin SSD, Guan Y, Dickinson K, Kim DD, Chua Z, 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;8:1–26. https://doi.org/10.3390/jcm8020253.

[6] Herbst, Antje; Kordonouri, Olga; Schwab, Karl O; Schmidt, Frank; Holl R. 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.

[7] Huerta-Uribe N, Ramírez-Vélez R, Izquierdo M, García-Hermoso A. Association between physical activity, sedentary behavior and physical fitness and glycated hemoglobin in youth with type 1 diabetes: a systematic review and meta-analysis. Sport Med 2023; 53:111–123. https://doi.org/10.1007/s40279-022-01741-9.

[8] Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, et al. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. Diabetes Care 2016;39:2065–79. https://doi.org/10.2337/dc16-1728.

[9] Patterson R, McNamara E, Tainio M, de Sá TH, Smith AD, Sharp SJ, et al. Sedentary behaviour and risk of all-cause, cardiovascular and cancer mortality, and incident type 2 diabetes: a systematic review and dose response meta-analysis. Eur J Epidemiol 2018;33:811–29. https://doi.org/10.1007/s10654-018-0380-1.

[10] Adolfsson P, Taplin CE, Zaharieva DP, Pemberton J, Davis EA, Riddell MC, et al. ISPAD clinical practice consensus guidelines 2022: Exercise in children and adolescents with diabetes. Pediatr Diabetes 2022;23:1341–72. https://doi.org/10.1111/pedi.13452.

[11] Massin MM, Lebrethon MC, Rocour D, Gérard P, Bourguignon JP. Patterns of physical activity determined by heart rate monitoring among diabetic children. Arch Dis Child 2005;90:1223–6. https://doi.org/10.1136/adc.2005.075283.

[12] Fainardi V, Scarabello C, Cangelosi A, Fanciullo L, Mastrorilli C, Giannini C, et al. Physical activity and sedentary lifestyle in children with type 1 diabetes: a multicentre Italian study. Acta Biomed 2011;82:124–31.

[13] Czenczek-Lewandowska E, Leszczak J, Baran J, Weres A, Wyszyńska J, Lewandowski B, et al. Levels of physical activity in children and adolescents with type 1 diabetes in relation to the healthy comparators and to the method of insulin therapy used. Int J Environ Res Public Health 2019;16:1–17. https://doi.org/10.3390/ijerph16183498.

[14] Thongpaeng S, Sorncharoen P, Preechasuk L, Santiprabhob J. Dietary intake and physical activity of Thai children and adolescents with type 1 diabetes mellitus. Nutrients 2022;14:1–12. https://doi.org/10.3390/nu14235169.

[15] Ross R, Blair SN, Arena R, Church TS, Després JP, Franklin BA, et al. Importance of Assessing Cardiorespiratory Fitness in Clinical Practice: A Case for Fitness as a Clinical Vital Sign: A Scientific Statement from the American Heart Association. Circulation 2016;134:e653–99. https://doi.org/10.1161/CIR.0000000000000461.

[16] Komatsu WR, Lima Gabbay MA, Castro ML, Saraiva GL, Chacra AR, de Barros L, et al. Aerobic exercise capacity in normal adolescents and those with type 1 diabetes mellitus. Pediatr Diabetes 2005;6:145–9. https://doi.org/10.1111/j.1399-543X.2005.00120.x.

[17] Jegdic V, Roncevic Z, Skrabic V. Physical fitness in children with type 1 diabetes measured with six-minute walk test. Int J Endocrinol 2013;2013. https://doi.org/10.1155/2013/190454.

[18] Cuenca-García M, Jago R, Shield JPH, Burren CP. How does physical activity and fitness influence glycaemic control in young people with Type1 diabetes? Diabet Med 2012;29:369–76. https://doi.org/10.1111/j.1464-5491.2012.03740.x.

[19] Fintini D, Di Giacinto B, Brufani C, Cafiero G, Patera PI, Turchetta A, et al. Impaired energy expenditure despite normal cardiovascular capacity in children with type 1 diabetes. Horm Res Paediatr 2012;78:1–7. https://doi.org/10.1159/000339465.

[20] Legård GE, Pedersen BK. Muscle as an endocrine organ. Muscle Exerc Physiol 2018:285–307. https://doi.org/10.1016/B978-0-12-814593-7.00013-X.

[21] Lukács A, Mayer K, Juhász E, Varga B, Fodor B, Barkai L. Reduced physical fitness in children and adolescents with type 1 diabetes. Pediatr Diabetes 2012;13:426–31. https://doi.org/10.1111/j.1399-5448.2012.00848.x.

[22] Nguyen T, Obeid J, Walker RG, Krause MP, Hawke TJ, Mcassey K, et al. Fitness and physical activity in youth with type 1 diabetes mellitus in good or poor glycemic control. Pediatr Diabetes 2015;16:48–57. https://doi.org/10.1111/pedi.12117.

[23] Elmesmari R, Reilly JJ, Martin A, Paton JY. Accelerometer measured levels of moderate-to-vigorous intensity physical activity and sedentary time in children and adolescents with chronic disease: a systematic review and meta-analysis. PLoS One 2017;12:1–20. https://doi.org/10.1371/journal.pone.0179429.

[24] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. statement: An updated guideline for reporting systematic reviews. BMJ 2020;2021:372. https://doi.org/10.1136/bmj.n71.

[25] Brooke BS, Schwartz TA, Pawlik TM. MOOSE reporting guidelines for meta-analyses of observational studies. JAMA Surg 2021;156:787. https://doi.org/10.1001/jamasurg.2021.0522.

[26] National Heart, Lung and Blood Institute. Quality assessment tool for observational cohort and cross-sectional studies. Available at: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools [accessed 25.03.2023].

[27] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88. https://doi.org/10.1016/0197-2456(86)90046-2.

[28] Higgins, Julian P T; Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539–58.

[29] Higgins, Julian PT; Thompson, Simon G; Deeks, Jonathan J; Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60. https://doi.org/10.1136/bmj.327.7414.557.

[30] Furuya-Kanamori, Luis; Barendregt, Jan J; Doi SAR. A new improved graphical and quantitative method for detecting bias in meta-analysis. Int J Evid Based Healthc 2018;16:195–203.

[31] Heyman E, Briard D, Gratas-Delamarche A, Delamarche P, De Kerdanet M. Normal physical working capacity in prepubertal children with type 1 diabetes compared with healthy controls. Acta Paediatr Int J Paediatr 2005;94:1389–94. https://doi.org/10.1080/08035250510040232.

[32] Wu N, Bredin SSD, Jamnik VK, Koehle MS, Guan Y, Shellington EM, et al. Association between physical activity level and cardiovascular risk factors in adolescents living with type 1 diabetes mellitus: a cross-sectional study. Cardiovasc Diabetol 2021;20:1–11. https://doi.org/10.1186/s12933-021-01255-0.

[33] Valerio G, Spagnuolo MI, Lombardi F, Spadaro R, Siano M, Franzese A. Physical activity and sports participation in children and adolescents with type 1 diabetes mellitus. Nutr Metab Cardiovasc Dis 2007;17:376–82. https://doi.org/10.1016/j.numecd.2005.10.012.

[34] Trigona B, Aggoun Y, Maggio A, Martin XE, Marchand LM, Beghetti M, et al. Preclinical noninvasive markers of atherosclerosis in children and adolescents with type 1 diabetes are influenced by physical activity. J Pediatr 2010;157:533–9. https://doi.org/10.1016/j.jpeds.2010.04.023.

[35] Sundberg F, Forsander G, Fasth A, Ekelund U. Children younger than 7 years with type 1 diabetes are less physically active than healthy controls. Acta Paediatr Int J Paediatr 2012;101:1164–9. https://doi.org/10.1111/j.1651-2227.2012.02803.x.

[36] Särnbladn S, Ekelund U, Åman J. Physical activity and energy intake in adolescent girls with Type 1 diabetes. Diabet Med 2005;22:893–9. https://doi.org/10.1111/j.1464-5491.2005.01544.x.

[37] Raile K, Kapellen T, Schweiger A, Hunkert F, Nietzschmann U, Dost A, et al. Physical activity and competitive sports in children and adolescents with type 1 diabetes. Diabetes Care 1999;22:1904–5. https://doi.org/10.2337/diacare.22.11.1904.

[38] Nascimento MS, Espindola CF, Do Prado C, Amarins MB, Potenza AL, Pacheco L, et al. Type 1 diabetes does not impair the physical capacity of non-sedentary adolescents. Diabetol Metab Syndr 2017;9:1–7. https://doi.org/10.1186/s13098-017-0300-7.

[39] Mutlu EK, Mutlu C, Taskiran H, Ozgen IT. Relationship between physical activity level and depression, anxiety, quality of life, self-esteem, and Hba1C in adolescents with Type 1 diabetes mellitus. Turkish J Physiother Rehabil Rehabil 2017;28:38–46.

[40] Mutlu EK, Mutlu C, Taskiran H, Ozgen IT. Association of physical activity level with depression, anxiety, and quality of life in children with type 1 diabetes mellitus. J Pediatr Endocrinol Metab 2015;28:1273–8. https://doi.org/10.1515/jpem-2015-0082.

[41] Mohammed J, Deda L, Clarson CL, Stein RI, Cuerden MS, Mahmud FH. Assessment of habitual physical activity in adolescents with type 1 diabetes. Can J Diabetes 2014;38:250–5. https://doi.org/10.1016/j.jcjd.2014.05.010.

[42] Marshall ZA, Mackintosh KA, Lewis MJ, Ellins EA, McNarry MA. Association of physical activity metrics with indicators of cardiovascular function and control in children with and without type 1 diabetes. Pediatr Diabetes 2021;22:320–8. https://doi.org/10.1111/pedi.13159.

[43] Maggio ABR, Hofer MF, Martin XE, Marchand LM, Beghetti M, Farpour-Lambert NJ. Reduced physical activity level and cardiorespiratory fitness in children with chronic diseases. Eur J Pediatr 2010;169:1187–93. https://doi.org/10.1007/s00431-010-1199-2.

[44] Lobelo F, Liese AD, Liu J, Mayer-Davis EJ, D'Agostino RB, Pate RR, et al. Physical activity and electronic media use in the search for diabetes in youth case-control study. Pediatrics 2010;125: e1364–e1371. https://doi.org/10.1542/peds.2009-1598.

[45] Elmesmari RA, Reilly JJ, Paton JY. 24-Hour Movement Behaviors in Children with Chronic Disease and Their Healthy Peers: A Case-Control Study. Int J Environ Res Public Health 2022:19. https://doi.org/10.3390/ijerph19052912.

[46] dos Santos Haber JF, Chagas EFB, Barbalho SM, Sgarbi JA, Haber RSDA, de Labio RW, et al. Level of physical activity and gene expression of IL-10 and TNF-α in children and adolescents with Type 1 diabetes. J Diabetes Complications 2022:36. https://doi.org/10.1016/j.jdiacomp.2021.108104.

[47] de Lima VA, Mascarenhas LPG, Decimo JP, de Souza WC, Monteiro ALS, Lahart I, et al. Physical activity levels of adolescents with type 1 diabetes. Hum Kinet 2017;28:588–95.

[48] Bjornstad P, Cree-Green M, Baumgartner A, Maahs DM, Cherney DZ, Pyle L, et al. Renal function is associated with peak exercise capacity in adolescents with type 1 diabetes. Diabetes Care 2015;38:126–31. https://doi.org/10.2337/dc14-1742.

[49] Van Ryckeghem L, Franssen WMA, Verbaanderd E, Indesteege J, De Vriendt F, Verwerft J, et al. Cardiac function is preserved in adolescents with well-controlled type 1 diabetes and a normal physical fitness: a cross-sectional STUDY. Can J Diabetes 2021;45:718–724.e1. https://doi.org/10.1016/j.jcjd.2021.01.010.

[50] Kaya Mutlu E, Mutlu C, Taşkıran HG, Özgen İT. Relationship between physical activity level and depression, anxiety, quality of life, self-esteem, and Hba1C in adolescents with type 1 diabetes mellitus. Turkish J Physiother Rehabil Rehabil 2017;28:38–46.

[51] Williams BK, Guelfi KJ, Jones TW, Davis EA. Lower cardiorespiratory fitness in children with Type 1 diabetes. Diabet Med 2011;28:1005–7. https://doi.org/10.1111/j.1464-5491.2011.03271.x.

[52] Nadeau KJ, Regensteiner JG, Bauer TA, Brown MS, Dorosz JL, Hull A, et al. Insulin resistance in adolescents with type 1 diabetes and its relationship to cardiovascular function. J Clin Endocrinol Metab 2010;95:513–21. https://doi.org/10.1210/jc.2009-1756.

[53] Gusso S, Hofman P, Lalande S, Cutfield W, Robinson E, Baldi JC. Impaired stroke volume and aerobic capacity in female adolescents with type 1 and type 2 diabetes mellitus. Diabetologia 2008;51:1317–20. https://doi.org/10.1007/s00125-008-1012-1.

[54] Baraldi E, Monciotti C, Filippone M, Santuz P, Magagnin G, Zanconato S, et al. Gas exchange during exercise in diabetic children. Pediatr Pulmonol 1992;13:155–60. https://doi.org/10.1002/ppul.1950130306.

[55] Austin A, Warty V, Janosky J, Arslanian S. The relationship of physical fitness to lipid and lipoprotein(a) levels in Adolescents with IDDM. Diabetes Care 1993;16:421–5. https://doi.org/10.2337/diacare.16.2.421.

[56] Arslanian S, Nixon PA, Becker D, Drash AL. Impact of physical fitness and glycemic control on in vivo insulin action in adolescents with IDDM. Diabetes Care 1990;13:9–15. https://doi.org/10.2337/diacare.13.1.9.

[57] Absil H, Baudet L, Robert A, Lysy PA. Benefits of physical activity in children and adolescents with type 1 diabetes: a systematic review. Diabetes Res Clin Pract 2019;156:107810. https://doi.org/10.1016/j.diabres.2019.107810.

[58] Farooq MA, Parkinson KN, Adamson AJ, Pearce MS, Reilly JK, Hughes AR, et al. Timing of the decline in physical activity in childhood and adolescence: gateshead millennium cohort study. Br J Sports Med 2018;52:1002–6. https://doi.org/10.1136/bjsports-2016-096933.

[59] Nader, Philip R; Bradly, Robert H; Houts, Renate M; McRitchie, Susan L; ÓBrien M. Moderate-to-Vigorous Physical Activity From Ages 9 to 15 Years. JAMA 2008;300:295–305. https://doi.org/10.1001/jama.300.3.295.

[60] Brazeau AS, Rabasa-Lhoret R, Strychar I, Mircescu H. Barriers to physical activity among patients with type 1 diabetes. Diabetes Care 2008;31:2108–9. https://doi.org/10.2337/dc08-0720.

[61] Jabbour G, Henderson M, Mathieu ME. Barriers to active lifestyles in children with type 1 diabetes. Can J Diabetes 2016;40:170–2. https://doi.org/10.1016/j.jcjd.2015.12.001.

[62] Roberts AJ, Taplin CE, Isom S, Divers J, Saydah S, Jensen ET, et al. Association between fear of hypoglycemia and physical activity in youth with type 1 diabetes: The SEARCH for diabetes in youth study. Pediatr Diabetes 2020;21:1277–84. https://doi.org/10.1111/pedi.13092.

[63] Michaliszyn SF, Faulkner MS. Physical activity and sedentary behavior in adolescents with type 1 diabetes. Res Nurs Health 2010;33:441–9. https://doi.org/10.1002/nur.20393.

[64] Zaharieva DP, Addala A, Mph DO. Current and novel strategies to reduce fear of hypoglycemia as a barrier to physical activity in adults and youth with type 1 diabetes. Can J Diabetes 2022;46:1–2. https://doi.org/10.1016/j.jcjd.2021.12.004.

[65] Ortega FB, Ruiz JR, Castillo MJ, Sjöström M. Physical fitness in childhood and adolescence: a powerful marker of health. Int J Obes 2008;32:1–11. https://doi.org/10.1038/sj.ijo.0803774.

[66] Brown FM, Bruemmer D, Collins BS, Hilliard ME, Isaacs D, Johnson EL, et al. Facilitating positive health behaviors and well-being to improve health outcomes. Standards of Care in Diabetes — 2023;2023(46):68–96.

[67] Cardinali P, Rapetti E, Migliorini L. Fear of hypoglycemia in Italian mothers of children with type 1 diabetes: the mediating role of resilience. Heal Psychol Res 2021;9:18–20. https://doi.org/10.52965/001c.27439.

[68] Han M, Qie R, Shi X, Yang Y, Lu J, Hu F, et al. Cardiorespiratory fitness and mortality from all causes, cardiovascular disease and cancer: dose-response meta-analysis of cohort studies. Br J Sports Med 2022;56:733–9. https://doi.org/10.1136/bjsports-2021-104876.

[69] Ruiz JR, Ortega FB, Rizzo NS, Villa I, Hurtig-Wennlöf A, Oja L, et al. High cardiovascular fitness is associated with low metabolic risk score in children: The European Youth Heart Study. Pediatr Res 2007;61:350–5. https://doi.org/10.1203/pdr.0b013e318030d1bd.

[70] Santos R, Mota J, Okely AD, Pratt M, Moreira C, Coelho-e-Silva MJ, et al. The independent associations of sedentary behaviour and physical activity on cardiorespiratory fitness. Br J Sports Med 2014;48:1508–12. https://doi.org/10.1136/bjsports-2012-091610.

[71] Leiva AM, Martínez MA, Cristi-Montero C, Salas C, Ramírez-Campillo R, Díaz Martínez X, et al. El sedentarismo se asocia a un incremento de factores de riesgo cardiovascular y metabólicos independiente de los niveles de actividad física. Rev Med Chile 2014;145:458–67.

[72] Narici M, De VG, Franchi M, Paoli A, Moro T, Marcolin G, et al. Impact of sedentarism due to the COVID-19 home confinement on neuromuscular, cardiovascular and metabolic health: Physiological and pathophysiological implications and recommendations for physical and nutritional countermeasures. Eur J Sport Sci 2021;21:614–35. https://doi.org/10.1080/17461391.2020.1761076.

[73] Chang X, Wang Z, Guo H, Xu Y, Ogihara A. Effect of physical activity/exercise on cardiorespiratory fitness in children and adolescents with type 1 diabetes: a scoping review. Int J Environ Res Public Health 2023;20:1–10. https://doi.org/10.3390/ijerph20021407.

[74] Eckstein ML, Aberer F, Dobler FJR, Aziz F, Heise T, Sourij H, et al. Association of HbA1c with VO2max in Individuals with type 1 diabetes: a systematic review and meta-analysis. Metabolites 2022;12:1017. https://doi.org/10.3390/metabo12111017.

[75] Karakelides H, Asmann YW, Bigelow ML, Short KR, Dhatariya K, Coenen-Schimke J, et al. Effect of insulin deprivation on muscle mitochondrial ATP production and gene transcript levels in type 1 diabetic subjects. Diabetes 2007;56:2683–9. https://doi.org/10.2337/db07-0378.

[76] Monaco CMF, Hughes MC, Ramos SV, Varah NE, Lamberz C, Rahman FA, et al. Altered mitochondrial bioenergetics and ultrastructure in the skeletal muscle of young adults with type 1 diabetes. Diabetologia 2018;61:1411–23. https://doi.org/10.1007/s00125-018-4602-6.

[77] Krause MP, Riddell MC, Hawke TJ. Effects of type 1 diabetes mellitus on skeletal muscle: Clinical observations and physiological mechanisms. Pediatr Diabetes 2011;12:345–64. https://doi.org/10.1111/j.1399-5448.2010.00699.x.

[78] American Diabetes Association. 5. Facilitating Behavior Change and Well-being to Improve Health Outcomes: Standards of Medical Care in Diabetes—2022. Diabetes Care 2022;45:S60–82. https://doi.org/10.2337/dc22-S005.

[79] O'Connell SM, Cooper MN, Bulsara MK, Davis EA, Jones TW. Reducing rates of severe hypoglycemia in a population-based cohort of children and adolescents with type 1 diabetes over the decade 2000–2009. Diabetes Care 2011;34:2379–80. https://doi.org/10.2337/dc11-0748.