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The effect of chronic high-intensity interval training programs on glycaemic control, aerobic resistance, and body composition in type 2 diabetic patients: a meta-analysis

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Abstract

Background Type 2 diabetes is an increasing health problem worldwide. HIIT has been proposed as an exercise alternative to be part of integral type 2 diabetes treatment.

Objective The aim of this meta-analysis was to determine the effect of different types of chronic HIIT on glycaemic control, aerobic resistance, and body composition in individuals above 18 years with T2D.

Design This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement and was registered with PROSPERO on November 21st, 2021.

Data sources A systematic literature search of the following databases: EbscoHost (Academic Search Ultimate, Fuente Académica Plus, MEDline and SportDiscus), Web of Science, PubMed, and EMBASE between April of 2021 and April of 2023 was conducted.

Eligibility criteria for selecting studies Eligibility criteria included (1) participants aged ≥ 18 years with a diagnosis of type 2 diabetes, (2) an HIIT protocol with detailed description, (3) control group and/or continuous aerobic training comparison group, (4) report of pre-test and post-test values for at least one of the studied variables (from glycaemic control, aerobic resistance, and/or body composition), and (5) experimental or quasi-experimental intervention design.

Analyses Meta-analysis was made by a pre–post-test between-group analysis following the inverse variance heterogeneity model for each variable, and then, a subgroup analysis by type of HIIT was conducted.

Results Of the 2817 records obtained, 180 records were included for meta-analysis. Significant improvements were found in the most part of the variables when HIIT was compared to control group, while fat-free mass kept without changes. HIIT vs. continuous aerobic training results showed an advantage in favor of HIIT for fasting blood glycemia. Subgroup analysis refers a possible advantage of SI-HIIT and SIT-HIIT in the improvement of fasting glycemia and SIT-HIIT advantage in HOMA 1-IR decrease.

Conclusions HIIT improves glycaemic control, aerobic resistance, and % fat and waist circumference, and kept fat-free mass unchanged in individuals with T2D. SI-HIIT and SIT-HIIT could be better than the other types of HIIT. HIIT benefit is similar to continuous aerobic training except for fasting blood glycemia.

Keywords HIIT · Type 2 diabetes · Glycaemic control · Aerobic resistance · Body composition

Introduction

Diabetes is a chronic and multifactorial disease whose prevalence has increased recently. According to International Diabetes Federation (IDF), there are 537 million people with diabetes in the world [1] and approximately 90% of them have type 2 diabetes (T2D) [2, 3]. In Costa Rica, diabetes

prevalence is 14.8% among people above 20 years old [4]. It is estimated that in 2045, there will be 783 million people living with diabetes worldwide [1].

The causes for the development of T2D are diverse. They are related to genetic background, high body fat mass, sedentary behavior, and other determinants, such as age, ethnicity, gestational diabetes history, and gut microbiota disorders [3, 5–8]. Because of these risk factors, the individual will develop insulin resistance, a process where insulin signal transduction is impaired, and GLUT-4 transporter

Extended author information available on the last page of the article

translocation is reduced, especially in skeletal muscle tissue. In addition, β -pancreatic damage could decrease insulin secretion. Altogether, these processes lead to a chronic high levels of fasting blood glycemia (FBG), fasting blood insulinemia (FBI) which is followed by hypoinsulinemia, and hyperglucagonemia with all comorbidity risks associated [3, 9–12].

Treatment must be multidisciplinary, where the main goal is to maintain glycaemic control through a personalized and balanced diet, an adequate exercise program, and pharmacologic therapy [13]. In addition, according to the American Diabetes Association (ADA) and the American College of Sports Medicine (ACSM), diabetic patients should engage in an aerobic exercise program for at least 150 min/week with moderate to high intensity and add 2 or 3 weekly resistance training sessions [14, 15].

One of the aerobic exercise modalities currently suggested is high-intensity interval training (HIIT), where high or maximal exercise intensity periods are combined with passive resting periods and seems an efficient and relatively simple exercise option, especially with time management [16, 17]. However, a disadvantage of HIIT is that currently, there is no standardized protocol, and the diversity of protocols implemented during the trials has given different outcomes [16–18].

A systematic review found that HIIT improves glycaemic control in one single session [19], and the main goal of this meta-analysis is to evaluate if this trend remains when HIIT is performed in a chronic mode. Recent meta-analyses had shown improvements in glycosylated hemoglobin (HbA1c), maximal oxygen consumption (VO_{2max}), peak oxygen consumption (VO_{2peak}), and fat mass when HIIT was compared with control groups [20–23]. Compared to continuous aerobic training (CONT), HbA1c, VO_{2max} , and VO_{2peak} showed HIIT advantage [20–23] and the within-group analyses reported HbA1c, FBI, VO_{2peak} , and fat mass improvement [23, 24]. However, no changes were shown in the FBG, HOMA index (HOMA 1-IR), and waist circumference (WC) [16, 23]. To our knowledge, muscular or fat-free mass were not analyzed in people with T2D following a HIIT protocol.

In this context, the aim of the present meta-analysis was to determine the effect of different types of chronic HIIT on glycaemic control, aerobic resistance, and body composition in individuals above 18 years with T2D.

Methods

Protocol registration

The current meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement [25]. The protocol was

registered in PROSPERO under the code CRD42021282723. The review protocol can be accessed through https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=282723.

Search strategy

We conducted a systematic literature search in the electronic databases: EbscoHost (Academic Search Ultimate, Fuente Académica Plus, Medline, and Sport Discus), Web of Science, PubMed, and EMBASE. Each variable was treated individually with the following combination of variations of keywords: (“HbA1c” or “glycosylated hemoglobin” or “glycated hemoglobin” or “hemoglobin A1c”) AND (“hiit” or “hit” or “high-intensity interval training” or “high-intensity training” or “sit” or “sprint interval training”) AND (“type 2 diabetes” or “type 2 diabetes mellitus” or “t2dm” or “t2d”) AND adult* NOT (“rat” or “rats” or “mouse” or “rodent” or “mice”). The search strategy and Boolean phrases can be found in the appendix 1 of the electronic supplementary material.

The first preliminary search was done between April 2021 and August 2021. Then, a formal search and screening of results against eligibility criteria were conducted between September 2021 and December 2021. Finally, the last search update was made on April, 2023. The systematic search for articles, the removal of duplicates, and article selection was performed by one author under the supervision of the other authors.

Inclusion/exclusion criteria

Studies meta-analyzed met the following *PICOS* (Population, Intervention, Comparison, Outcomes and Study) criteria. For *P*, the selected participants were individuals aged ≥ 18 year, with a diagnosis of T2D and available to exercise. Participant groups mixed with prediabetes, any other type of diabetes, or pregnant individuals were excluded. For *I*, the intervention involved the implementation of a chronic HIIT protocol with a clear description of the process. In the case of HbA1c, the protocol must have been done for at least 12 weeks. In addition, HIIT combined with other training or nutritional intervention were excluded.

For *C*, the comparison groups were a sedentary control group or a CONT group. Analysis was made between groups. Control groups performing stretching protocols, those that interrupted the current lifestyle, and those comprised of healthy subjects were not included. For *O*, the outcomes were pre-test and post-test measures of HbA1c, FBG, FBI, HOMA 1 IR, VO_{2max} , VO_{2peak} , body fat percentage (% fat), fat-free mass, and WC. The studies that had at least one of these outcomes were included. Finally, the selected studies had an experimental or quasi-experimental design for *S*.

There was no gender or date of publication limit, and all the records published in Spanish, English, and Portuguese were reviewed. In addition, conference abstracts that met the criteria and showed all the necessary data to meta-analyze were included.

Quality and risk-of-bias assessment

Study quality was assessed with the TESTEX scale [26] (Table 5). Heterogeneity was studied with I^2 and Cochran's Q tests, and the risk of bias was assessed with the Doi Plot and the LFK index. These last indicators assess asymmetry through the results and are recommended for $n = 20$ or less meta-analysis because of its greater sensitivity. LFK index between ± 1 shows low or no asymmetry, whereas a greater index suggests asymmetry. Doi Plot displays the density distribution of the observed effect sizes against the standard error of each study included in the meta-analysis [27], an example can be found in Fig. 1, and all the plots assessed during this study can be found in the appendix 7 of the electronic supplementary material. Meta-analyses were done using the MetaXL software [28, 29]. Sensitivity analysis identified outliers [29]; the results without outliers that changed the risk of bias or effect sizes (ES) can

be found in the results section (Tables 2 and 3). Finally, evidence support was assessed with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) scale for meta-analysis [30]. GRADE criteria conducted can be found in the appendix 2 of the electronic supplementary material.

Data extraction

One author extracted the data from the selected papers under the supervision of the other authors. The extracted data included authors, publication year, the country where the study was conducted, sample size, age, type of medication, and whether the diet was controlled. In addition, exercise protocol information was extracted: movement pattern, intervention length, weekly frequency, interval intensity, interval duration, resting periods for HIIT, and movement pattern, intensity, and session duration for continuous aerobic training. Finally, necessary numerical data for meta-analysis were recorded: pre-test mean and standard deviation, post-test mean and standard deviation, and sample size for each group.

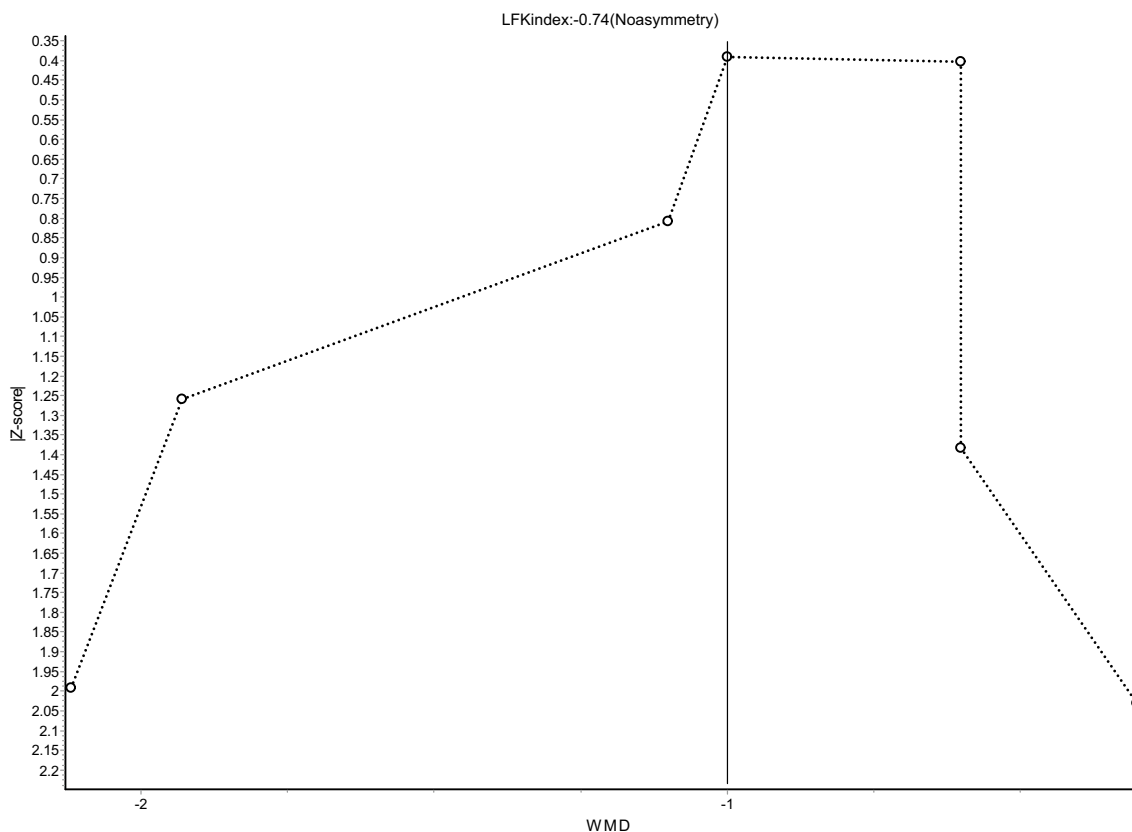


Fig. 1 Doi Plot example with LFK index

Meta-analyses

One author conducted the meta-analyses under the supervision of the other authors. Before the meta-analysis, the change score between pre-test and post-test was calculated. Mean change was obtained by subtracting pre-test from post-test. After getting the change score, a between-groups analysis was conducted, and individual and global effect sizes (ES) were calculated with Meta XL software [29], following the inverse variance heterogeneity model (IVhet) [31]. Comparison between global ES was made with the intervention group (HIIT) vs. control group and HIIT vs. CONT. Depending on literature availability, the variables that showed up on 15 or more selected articles were classified and meta-analyzed by type of HIIT, according to the classification proposed by Wen et al. [32]. Following HIIT type analysis, subgroup analysis was performed with the Review Manager Software® [33]. Variables appearing in less than 15 studies were processed as a unique HIIT type to estimate the global ES and comparisons with the control group and CONT.

Results

A systematic search was done individually for each variable (Fig. 2). An article could have been chosen or excluded more than once depending on how many variables it assessed. The detailed search results can be found in the appendix 3 of the electronic supplementary material. A total of 2699 studies were obtained from the different databases, and 118 were added from other sources (e.g., reviews and search updates). From these 2817 studies, 805 were duplicated records; thus, 2012 articles were screened by title and abstract and compared with the inclusion criteria. Then, 444 records were selected for full-text assessment, and 264 were excluded for different reasons (Fig. 2). Finally, a total of 180 records were included for meta-analysis, and these records were distributed through 41 individual articles.

Authors from the studies that did not show enough numerical information for meta-analysis were contacted via e-mail, and only one of them answered. The total sample was 1374 participants diagnosed with T2D distributed through

Fig. 2 Flow diagram of the study selection process

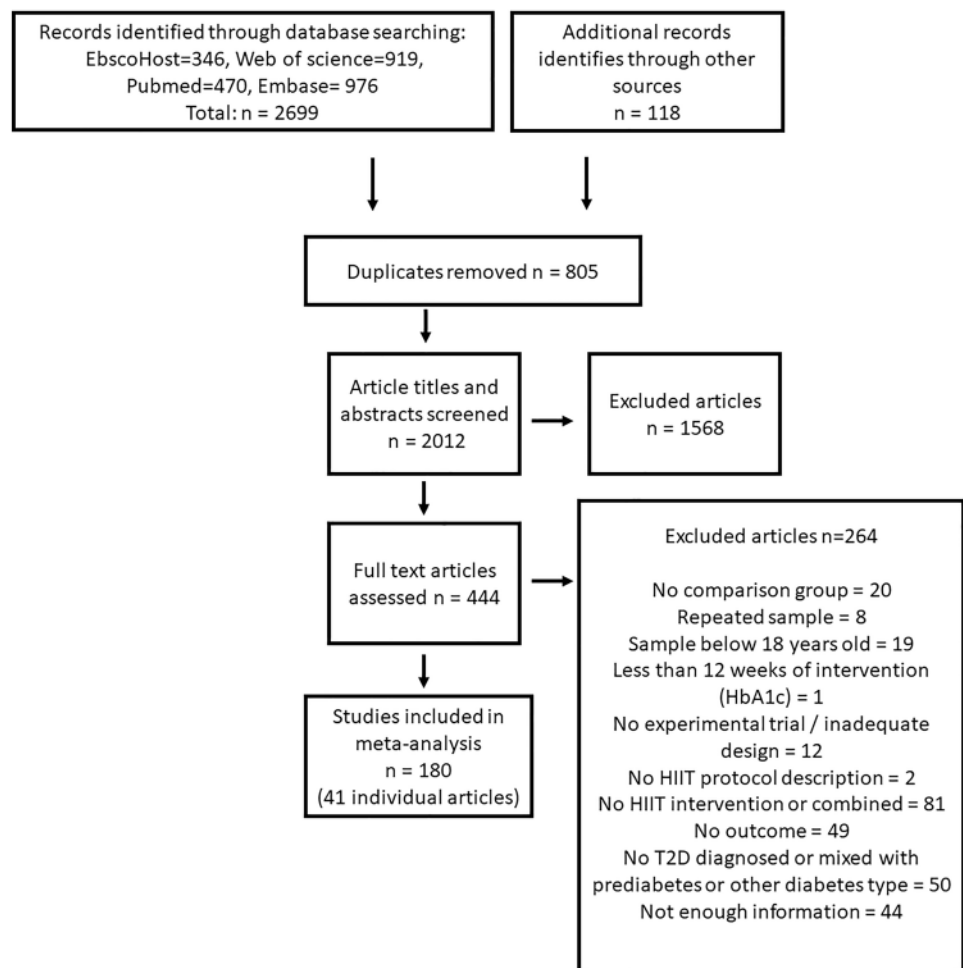


Table 1 Main characteristics of the included studies

Article	Year	Country	Average age	n	Medication	Diet	HIIT intervention		CONT intervention	
							HIIT type	Intervention	Method	Intervention
Abdelbasset et al. [34]	2019	Saudi Arabia	54.80	32	Oral medicine	Not controlled	LI-HIIT	8 weeks, 3 times/week, intervals 240 s vigorous intensity, rest 120 s	Cycle ergometry	
Abdi et al. [35]	2021	Iran	20–44	30	Oral medicine	Not controlled	LI-HIIT	12 weeks, 3 times/week, intervals 240 s vigorous intensity, rest 180 s	Treadmill	
Ahmed et al. [36]	2019	Egypt/Saudi Arabia	52.10	40	Oral medicine	Not controlled	LI-HIIT	12 weeks, 3 times/week, intervals 240 s vigorous intensity, rest 120 s	Treadmill	
Cassidy et al. [37]	2016	United Kingdom	60.00	23	Oral medicine	Standardized or controlled	LI-HIIT	12 weeks, 3 times/week, intervals 290 s vigorous intensity, rest 180 s	Cycle ergometry	
Cassidy et al. [38]	2018	United Kingdom	59.50	22	Oral medicine	Not controlled	LI-HIIT	12 weeks, 3 times/week, intervals 290 s vigorous intensity, rest 180 s	Cycle ergometry	
Dunwald et al. [39]	2019	Austria	59.05	14	Oral medicine	Not controlled	LI-HIIT	4 weeks, 3 times/week, intervals 240 s vigorous intensity, rest 180 s	Cycle ergometry	50 min, moderate intensity
Elsisi et al. [40]	2015	Egypt	57.70	40	NR	Not controlled	LI-HIIT	12 weeks, 3 times/week, intervals 240 s vigorous intensity, rest 180 s	Cycle ergometry	25 min, moderate intensity
Gentil et al. [41]	2023	Brazil	55.95	52	Oral and injectable	Not controlled	LI-HIIT	8 weeks, 2 times/week, intervals 120 s vigorous intensity, rest 120 s	Treadmill	18 min, vigorous intensity

Table 1 (continued)

Article	Year	Country	Average age	n	Medication	Diet	HIIT intervention		CONT intervention	
							HIIT type	Intervention	Method	Intervention
Ghardashi-Afousi et al. [42]	2019	Iran	54.50	59	Oral medicine	Standardized or controlled	LI-HIIT	12 weeks, 3 times/week, intervals 240 s vigorous intensity, rest 180 s	Cycle ergometry	
Hollekim-Strand et al. [43]		Norway	55.90	37		NR	LI-HIIT	12 weeks, 3 times/week, intervals 240 s vigorous intensity, rest 180 s		
Hwang et al. [44]	2019	Korea/USA	62.67	50	Oral and injectable	Standardized or controlled	LI-HIIT	8 weeks, 4 times/week, intervals 240 s vigorous intensity, rest 180 s	Cycle ergometry	32 min, moderate intensity
Karstoft et al. [45]	2013	Denmark	58.47	32	Medicine and lifestyle	Standardized or controlled	LI-HIIT	16 weeks, 5 times/week, intervals 180 s, 70% of peak calorie expenditure intensity, rest 180 s	Walking	55% of peak calorie expenditure intensity
Rasmussen-Faria et al. [46]	2021	Brazil	52.10	15	Oral medicine	Not controlled	LI-HIIT	12 weeks, 2 times/week, intervals 120 s vigorous intensity, rest 120 s	Treadmill	
Sabag et al. [47]	2020	Australia	55.85	22	NR	Not controlled	LI-HIIT	12 weeks, 3 times/week, intervals 240 s vigorous intensity, rest 240 s	Cycle ergometry	48 min, moderate intensity
Sokolovska et al. [48]	2020	Latvia	60.80	56	Oral medicine	Not controlled	LI-HIIT	16 weeks, 3 times/week, intervals 180 s vigorous intensity, rest 180 s	Walking	

Table 1 (continued)

Article	Year	Country	Average age	n	Medication	Diet	HIIT intervention		CONT intervention		
							HIIT type	Intervention	Method	Intervention	Method
Stoa et al. [49]	2017	Norway	59.00	38	Oral and injectable	Standardized or controlled	LJ-HIIT	12 weeks, 3 times/week, intervals 240 s vigorous intensity, rest 180 s	Walking/running	Moderate intensity	Walking/running
Way et al. [50]	2020	Australia	55.85	24	Oral medicine	Standardized or controlled	LJ-HIIT	12 weeks, 3 times/week, intervals 240 s vigorous intensity	Cycle ergometry	45 min, moderate intensity	Cycle ergometry
Aguilera-Eguía et al. [51]	2015	Chile	62.50	15	Oral and injectable	Not controlled	MI-HIIT	12 weeks, 5 times/week, intervals 60 s maximal intensity, rest 180 s	Treadmill and Cycle ergometry	45 min, moderate intensity	Treadmill and Cycle ergometry
Álvarez et al. [52]	2016	Chile	44.35	28	Oral medicine	Not controlled	MI-HIIT	16 weeks, 3 times/week, intervals 44 s maximal intensity, rest 12 s	Running		
Arefirard et al. [53]	2020	Iran	45.47	30	Oral medicine	Not controlled	MI-HIIT	6 weeks, 3 times/week, intervals 60 s maximal intensity, rest 60 s	Cycle ergometry		
Cassidy et al. [54]	2014	United Kingdom	60.00	23	NR	NR	MI-HIIT	12 weeks, 3 times/week, intervals 120 s vigorous intensity	Cycle ergometry		
Elsisi et al. [55]	2016	Egypt	45.70	60	NR	Not controlled	MI-HIIT	8 weeks, 3 times/week, intervals 60 s, maximal intensity, rest 60 s	Cycle ergometry	25 min, moderate intensity	Cycle ergometry
Findikoglu et al. [56]	2023	Turkey	56.20	63	Oral medicine	Standardized or controlled	MI-HIIT	12 weeks, 3 times/week, intervals 60 s, vigorous intensity, rest 120 s	Cycle ergometry	36 min, moderate intensity	Cycle ergometry

Table 1 (continued)

Article	Year	Country	Average age	n	Medication	Diet	HIIT intervention		CONT intervention		
							HIIT type	Intervention	Method	Intervention	Method
Ghardashi-Afousi et al. [57]	2018	Iran	54.05	52	Oral medicine	Not controlled	MI-HIIT	12 weeks, 3 times/week, intervals 90 s vigorous intensity, rest 120 s	Cycle ergometry	42 min, moderate intensity	Cycle ergometry
Golshan et al. [58]	2019	Iran	37.65	20	Oral medicine	Not controlled	MI-HIIT	8 weeks, 3 times/week, intervals 60 s vigorous intensity	Cycle ergometry		
Kazemi et al. [59]	2022	Iran	57.80	33	Oral medicine	Not controlled	MI-HIIT	12 weeks, 3 times/week, intervals 60 s vigorous intensity, rest 60 s	Cycle ergometry		
Li et al. [60]	2022	China	39.00	37	Medicine and lifestyle	Not controlled	MI-HIIT	12 weeks, 5 times/week, intervals 60 s, vigorous intensity, rest 60 s	Cycle ergometry	30 min, moderate intensity	Cycle ergometry
Macías-Cervantes et al. [61]	2017	Mexico	46.00	24	NR	NR	MI-HIIT	16 weeks, 3 times/week, intervals 60 s vigorous intensity, rest 60 s	Cycle ergometry	60 min, moderate intensity	Cycle ergometry
Mitranum et al. [62]	2014	Thailand	61.27	43	Oral medicine	Not controlled	MI-HIIT	12 weeks, 3 times/week, intervals 60 s vigorous intensity, rest 240 s	Treadmill	30 min, moderate intensity	Treadmill
Mortensen et al. [63]	2019	Denmark	55.00	21	Medicine and lifestyle	Not controlled	MI-HIIT	11 weeks, 3 times/week, intervals 60 s vigorous intensity, rest 60 s	Cycle ergometry	40 min	Cycle ergometry
Sabouri et al. [64]	2021	Iran	52.15	29	Oral medicine	Not controlled	MI-HIIT	12 weeks, 3 times/week, intervals 60 s vigorous intensity, rest 60 s	Cycle ergometry		

Table 1 (continued)

Article	Year	Country	Average age	n	Medication	Diet	HIIT intervention		CONT intervention		
							HIIT type	Intervention	Method	Intervention	Method
Saghand et al. [65]	2020	Iran	54.26	57	Oral medicine	Not controlled	MI-HIIT	8 weeks, intervals 90 s, vigorous intensity, rest 150 s	NR	40 min, moderate intensity	NR
Van Ryeckeghem et al. [66]	2022	Belgium	63.50	19	Medicine and lifestyle	Not controlled	MI-HIIT	24 weeks, 3 times/week, intervals 60 s, vigorous intensity, rest 240 s	Cycle ergometry	35 min, moderate intensity	Cycle ergometry
Wilson et al. [67]	2019	New Zealand	51.50	16	Oral and injectable	Not controlled	MI-HIIT	12 weeks, 3 times/week, intervals 120 s vigorous intensity, rest 100 s			
Winding et al. [68]	2017	Denmark	56.33	32	Medicine and lifestyle	Standardized or controlled	MI-HIIT	11 weeks, 3 times/week, intervals 60 s vigorous intensity, rest 60 s	Cycle ergometry	40 min	Cycle ergometry
Ghaedi et al. [69]	2020	Iran	55.53	28	Oral and injectable	Not controlled	SI-HIIT	10 weeks, 3 times/week, intervals 30 s vigorous intensity, rest 120 s	Cycle ergometry		
Rasmussen-Faria et al. [46]	2021	Brazil	52.10	15	Oral medicine	Not controlled	SI-HIIT	12 weeks, 2 times/week, intervals 30 s vigorous intensity, rest 30 s	Treadmill		
Asrami et al. [70]	2019	Iran	NR	35	Oral and injectable	Not controlled	SIT	8 weeks, 3 times/week, intervals 30 s maximal intensity, rest 240 s	Cycle ergometry		
Baasch-Skytte et al. [71]	2019	Denmark	61.10	44	Oral and injectable	Not controlled	SIT	10 weeks, 3 times/week, intervals 10 s maximal intensity, rest 120 s	Cycle ergometry	50 min, vigorous intensity	Cycle ergometry

Table 1 (continued)

Article	Year	Country	Average age	n	Medication	Diet	HIIT intervention		CONT intervention		
							HIIT type	Intervention	Method	Intervention	Method
Banitalebi et al. [72]	2019	Iran	55.54	28	NR	Not controlled	SIT	10 weeks, 3 times/week, intervals 30 s, maximal intensity, rest 120 s	Cycle ergometry	27 min, moderate intensity	Cycle ergometry
Gentil et al. [41]	2023	Brazil	55.95	52	Oral and injectable	Not controlled	SIT	8 weeks, 2 times/week, intervals 30 s maximal intensity, rest 30 s	Treadmill	18 min, vigorous intensity	Treadmill
Golshan et al. [58]	2019	Iran	38.40	20	Oral medicine	Not controlled	SIT	8 weeks, 3 times/week, intervals 1.5 s maximal intensity	Cycle ergometry		
Kaviani et al. [73]	2017	Canada/Iran	NR	35	NR	NR	SIT	12 weeks, 3 times/week, intervals 30 s	Cycle ergometry		
Maillard et al. [74]	2016	France	69.10	16	NR	Standardized or controlled	RST	16 weeks, 2 times/week, intervals 8 s vigorous intensity, rest 12 s	Cycle ergometry	40 min, moderate intensity	Cycle ergometry

HIIT high-intensity interval training, CONT continuous aerobic training, NR not reported, SIT sprint interval training, LI-HIIT long-interval HIIT, MI-HIIT moderate-interval HIIT, SI-HIIT short-interval HIIT

the experimental and control groups. The main information about the included papers can be found in Table 1.

When HIIT was compared with a control group, the between-group meta-analysis showed significant improvements in glycaemic control variables (HbA1c, FBG, FBI, and HOMA 1-IR). Furthermore, almost all types of HIIT protocols mimic this trend. HIIT also improved VO_{2peak} , VO_{2max} , % fat, and waist circumference. However, the fat-free mass did not show significant changes. Inconsistency among data was low to moderate, and it was lower in the cases of sensitivity analysis (outliers can be found in the appendix 4 of the electronic supplementary material). LFK index showed asymmetry between data, which suggests a high risk of publication bias (Table 2).

Subgroup analysis showed an advantage of short-interval HIIT (SI-HIIT), and sprint interval training (SIT-HIIT) over other types of HIIT for FBG, and SIT-HIIT was better in the improvement of HOMA 1-IR (Table 2). When comparing HIIT to CONT, the benefit of both training modalities was similar in all variables, except for FBG which had a significant advantage for HIIT. Almost all types of HIIT showed no differences. Inconsistency fluctuated from very low to low, and a few exceptions improved with sensitivity analysis (outliers can be found in the appendix 4 of the electronic supplementary material). Asymmetry and a high risk of publication bias were prevalent in all variables except for the FBI. There were no differences between types of HIIT in the subgroup analysis (Table 3).

The GRADE scale assessed evidence support. The results showed a very low-to-low certainty for HIIT vs. control group and low-to-moderate certainty for HIIT vs. CONT, allowing for future changes in the current results when more evidence becomes available (Table 4).

The TESTEX scale assessed quality; the scores are between 7 and 12 points out of 15 points, which is the total possible score (Table 5). A detailed description of the quality assessment can be found in the appendix 5 of the electronic supplementary material.

Discussion

Main findings

Glycaemic control variables improved with HIIT compared to controls, and ES were similar between HIIT and CONT. In the case of HbA1c, the current results are similar to Lora-Pozo et al. [20], Brondani-de Mello et al. [22], and Qiu et al. [21]. In contrast, Liu et al. [23] reported a non-significant ES for this variable. In the HIIT vs. CONT comparison, HbA1c ES result is similar as De Nardi et al. [16] and Lora-Pozo et al. [20] findings; however, Liu et al. [23] and Qiu et al. [21] found significant differences in favor of HIIT.

To the best of our knowledge, the only meta-analysis that assessed FBG was the study of Liu et al. [23] in the HIIT vs. control group, and there was no difference between groups, which is contrary to what we found. HIIT vs. CONT for FBG was evaluated by De Nardi et al. [16] and Liu et al. [22], and their outcomes are different to ours. In the case of FBI and HOMA 1-IR, the only meta-analysis we found was Liu et al. [23]; they did not find significant results in the HIIT vs. control group, which is different from the present results.

The HIIT mode analysis showed improvements in almost all types of HIIT in the HIIT vs. the control group variables. HbA1c, LI-HIIT, and MI-HIIT results are similar to Brondani-de Mello et al. [22], but SI-HIIT outcomes were different. The subgroup analysis showed significant differences only when HIIT was compared to a control group. SI-HIIT and SIT-HIIT had a significantly higher benefit over the other types of HIIT at reducing FBG, and SIT-HIIT was better than the others at decreasing HOMA 1-IR (Fig. 3). It is essential to highlight that these significant types of HIIT have a smaller sample size and higher inconsistency (i.e., HOMA 1-IR). In some cases, the LFK index assessment was impossible because of the sample size (e.g., $n=2$). When possible, the LFK index was >2 ; therefore, there was an increased risk of publication bias.

Secondary outcomes

Compared to the control group, aerobic resistance, fat mass, and waist circumference improved with HIIT; the fat-free mass remained unchanged. The HIIT vs. CONT analysis remained unchanged except for VO_{2max} . The only VO_{2peak} analysis was made by Liu et al. [23], and their results are similar to ours in the HIIT vs. control group. Still, in the HIIT vs. CONT, in contrast to our outcomes, they reported significant differences in favor of HIIT. After the sensitivity analysis, our ES also favored HIIT significantly (Table 3).

The present VO_{2max} results are similar to those by Lora-Pozo et al. [20], Qiu et al. [21], and Brondani-de Mello et al. [22] for HIIT vs. control group. On the contrary, for the HIIT vs. CONT comparison, De Nardi et al. [16], Lora-Pozo et al. [20], and Qiu et al. [21] found that the HIIT benefit is higher than CONT, while we did not find significant changes.

Qiu et al. [21] reported a significant reduction in % fat with a small ES. In the present study, the estimated ES was high based on the meta-analysis of a larger sample. The current HIIT vs. CONT outcomes were similar to Liu et al. [23] and Qiu et al. [21]. The present meta-analysis is the first to assess fat-free mass for HIIT in T2D individuals. The ES was not significant in any of the comparisons; therefore, HIIT reduced % fat without affecting fat-free mass. Although, until we searched, no waist circumference analysis was found for HIIT vs. the control group, our results showed a significant reduction with HIIT. Liu et al. [23]

Table 2 HIIT vs. control group effect meta-analysis results on the analyzed variables

Variable	Comparison	Between-group analysis (IVhet model)					Subgroup differences (IVhet model)			
		Number of articles	n	I^2 (%)	p (Cochran's Q)	LFK index	Global effect size	95% CI	χ^2	$p =$ (Between groups)
HbA1c	HIIT vs. CG	16	444	66	0.00	-3.18	-0.62	-0.87, -0.37		
	LJ-HIIT vs. CG	8	244	77	0.00	-4.65	-0.67	-1.01, -0.34	1.10	0.58
	MI-HIIT vs. CG	7	202	54	0.04	-1.49	-0.54	-0.89, -0.20		
	SI-HIIT vs. CG	1	10	0	N/A	N/A	-0.91	-2.64, 0.82		
	#HIIT vs. CG	15	385	34	0.10	-2.98	-0.56	-0.73, -0.40		
	#LJ-HIIT vs. CG	7	185	36	0.15	-3.98	-0.60	-0.78, -0.41		
	#MI-HIIT vs. CG	6	179	0	0.47	-2.55	-0.37	-0.59, -0.15		
	HIIT vs. CG	22	637	67	0.00	-3.33	-1.04	-1.71, -0.38	19.72	0.0002
	LJ-HIIT vs. CG	8	248	60	0.01	-3.55	-0.98	-1.69, -0.28		
	MI-HIIT vs. CG	9	261	12	0.34	-0.44	-0.81	-1.22, -0.40		
Fasting blood FBG	SI-HIIT vs. CG	2	38	0	0.35	N/A	-3.87*	-5.48, -2.25		
	SIT-HIIT vs. CG	3	90	51	0.13	2.12	-3.18*	-4.71, -1.65		
	#LJ-HIIT vs. CG	7	238	33	0.17	-0.74	-0.93	-1.4, -0.46		
	HIIT vs. CG	16	488	76	0.00	-0.14	-2.07	-3.14, -1.00		
	LJ-HIIT vs. CG	4	136	92	0.00	-0.54	-3.10	-6.29, 0.1	7.45	0.06
	MI-HIIT vs. CG	7	159	9	0.36	-2.02	-1.03	-1.77, -0.29		
	SI-HIIT vs. CG	1	28	0	N/A	N/A	-1.51	-5.08, 2.06		
	SIT-HIIT vs. CG	4	125	0	1.00	-2.79	-2.40	-3.16, -1.65		
	#HIIT vs. CG	15	468	5	0.39	0.76	-1.71	-2.15, -1.27		
	#LJ-HIIT vs. CG	3	116	0	0.90	4.25	-1.99	-2.80, -1.18		
HOMA 1-IR	HIIT vs. CG	17	535	89	0.00	5.04	-1.60	-2.42, -0.77		
	LJ-HIIT vs. CG	6	218	60	0.03	1.38	-1.06	-1.62, -0.50	8.36	0.04
	MI-HIIT vs. CG	8	233	65	0.01	-0.43	-0.92	-1.45, -0.38		
	SI-HIIT vs. CG	1	28	0	N/A	N/A	-0.51	-1.05, 0.03		
	SIT-HIIT vs. CG	2	55	91	0.00	N/A	-2.02**	-2.84, -1.2		
	#LJ-HIIT vs. CG	5	195	0	0.76	1.47	-1.30	-1.62, -0.98		
	#MI-HIIT vs. CG	7	213	42	0.11	-0.63	-0.69	-1.15, -0.23		
	HIIT vs. CG	11	325	77	0.00	3.59	4.03	2.21, 5.86	0.92	0.63
	LJ-HIIT vs. CG	5	175	88	0.00	4.92	4.09	1.12, 7.07		
	MI-HIIT vs. CG	5	140	62	0.03	1.44	3.86	1.99, 5.73		
VO _{2peak}	SI-HIIT vs. CG	1	10	0	N/A	N/A	4.28	-1.58, 10.14		
	#LJ-HIIT vs. CG	4	141	61	0.05	1.99	6.12	4.27, 7.97		
	#MI-HIIT vs. CG	4	111	27	0.25	3.36	4.63	3.13, 6.13		

Table 2 (continued)

Variable	Comparison	Between-group analysis (IVhet model)							Subgroup differences (IVhet model)	
		Number of articles	n	I^2 (%)	p (Cochran's Q)	LFK index	Global effect size	95% CI	χ^2	p =(Between groups)
VO_{2max}	HIIT vs. CG	3	79	92	0.00	-4.86	5.63	0.73, 10.53	N/A	N/A
% Fat	HIIT vs. CG	15	377	69	0.00	1.46	-2.67	-4.40, -0.94		
	LJ-HIIT vs. CG	5	175	2	0.39	0.2	-1.91	-3.08, -0.75	4.05	0.26
	MI-HIIT vs. CG	5	132	0	0.62	2.23	-2.79	-3.86, -1.72		
	SI-HIIT vs. CG	2	38	0	0.98	N/A	-0.21	-2.89, 2.46		
	SJT-HIIT vs. CG	3	90	93	0.00	-0.14	-4.75	-11.14, 1.63		
	#HIIT vs. CG	14	342	5	0.39	2.54	-2.10	-2.86, -1.35		
	#SIT-HIIT vs. CG	2	55	65	0.09	N/A	-1.33	-5.36, 2.73		
Fat-free mass	HIIT vs. CG	5	137	0	0.95	-2.47	0.19	-1.20, 1.59	N/A	N/A
Waist circumference	HIIT vs. CG	5	165	62	0.03	-1.68	-2.90	-4.82, -0.98	N/A	N/A
	#HIIT vs. CG	4	142	0	0.51	-0.81	-1.88	-3.04, -0.72		

Significant effect size written with bold font HIIT vs. CG

HIIT high-intensity interval training, CG control group, LJ-HIIT long-interval HIIT, MI-HIIT moderate-interval HIIT, SI-HIIT short-interval HIIT, SJT-HIIT sprint interval training, N/A not applicable

#Post-sensitivity analysis results

*Statistically different from LJ-HIIT and MI-HIIT

***Statistically different from SI-HIIT and MI-HIIT

Table 3 HIIT vs. continuous aerobic training effect meta-analysis results on the analyzed variables

Variable	Comparison	Between-group analysis (IVhet model)					Subgroup differences (IVhet model)			
		Number of articles	<i>n</i>	<i>I</i> ² (%)	<i>p</i> (Cochran's <i>Q</i>)	LFK index	Global effect size	95% CI	χ^2	<i>p</i> = (Between groups)
HbA1c	HIIT vs. CONT	13	347	10	0.34	-1.61	-0.12	-0.24, 0.01		
	LJ-HIIT vs. CONT	7	210	0	0.46	-2.54	-0.16	-0.29, -0.02	2.79	0.42
Fasting blood FBG	MI-HIIT vs. CONT	6	151	5	0.38	-0.58	-0.15	-0.39, 0.09		
	RST vs. CONT	1	16	0	N/A	N/A	0.1	-0.19, 0.39		
	HIIT vs. CONT	16	379	0	0.49	1.60	-0.21	-0.40, -0.02		
	LJ-HIIT vs. CONT	6	149	0	0.80	4.56	-0.26	-0.51, -0.01	0.15	0.98
	MI-HIIT vs. CONT	8	211	37	0.14	-1.72	-0.17	-0.80, 0.47		
Fasting blood FBI	SIT vs. CONT	1	29	0	N/A	N/A	-0.15	-2.50, 2.20		
	RST vs. CONT	1	16	0	N/A	N/A	-0.1	-0.92, 0.72		
	#MI-HIIT vs. CONT	7	187	0	0.62	-0.35	-0.11	-0.39, 0.17		
	HIIT vs. CONT	9	250	41	0.1	-0.72	-0.43	-1.57, 0.71		
	LJ-HIIT vs. CONT	4	106	73	0.01	4.49	-0.3	-3.37, 2.76	0.03	0.87
	MI-HIIT vs. CONT	5	144	0	0.71	-5.99	-0.55	-1.53, 0.44		
	#HIIT vs. CONT	8	186	0	0.69	-1.14	-0.92	-1.70, -0.14		
	#LJ-HIIT vs. CONT	3	82	0	0.57	4.55	-1.56	-2.85, -0.28		
	HIIT vs. CONT	12	380	56	0.01	-5.33	0.01	-0.45, 0.46		
	LJ-HIIT vs. CONT	4	123	81	0.00	-3.24	0.13	-0.59, 0.85	1.32	0.52
VO_{2peak}	MI-HIIT vs. CONT	7	237	0	0.98	-1.59	-0.42	-0.79, -0.05		
	SIT-HIIT vs. CONT	1	20	0	N/A	N/A	-0.5	-1.64, 0.64		
	#HIIT vs. CONT	11	356	1	0.44	-0.58	-0.34	-0.59, -0.10		
	#LJ-HIIT vs. CONT	3	89	0	0.81	-4.39	0.27	0.07, 0.47		
	HIIT vs. CONT	11	287	34	0.12	4.47	0.04	-0.97, 1.06		
	LJ-HIIT vs. CONT	5	132	61	0.04	0.29	-0.09	-1.61, 1.44	0.62	0.43
	MI-HIIT vs. CONT	6	155	0	0.55	2.17	0.63	-0.64, 1.91		
	#LJ-HIIT vs. CONT	4	108	0	0.47	1.56	0.57	-0.19, 1.32		
	#MI-HIIT vs. CONT	5	115	0	0.83	-0.84	1.81	-0.12, 3.75		
	HIIT vs. CONT	8	246	27	0.21	-1.06	2.83	1.72, 3.95	N/A	N/A
% Fat	HIIT vs. CONT	13	362	0	0.96	-2.20	0.25	-0.47, 0.97	0.38	0.94
	LJ-HIIT vs. CONT	4	130	28	0.24	-3.5	0.18	-1.61, 1.98		
	MI-HIIT vs. CONT	7	172	0	1.00	-1.42	0.42	-0.83, 1.68		
	SIT-HIIT vs. CONT	1	44	0	N/A	N/A	-0.20	-3.76, 3.36		
	RST vs. CONT	1	16	0	N/A	N/A	0.20	-1.23, 1.63		

Table 3 (continued)

Variable	Comparison	Between-group analysis (IVhet model)					Subgroup differences (IVhet model)		
		Number of articles	I^2 (%)	p (Cochran's Q)	LFK index	Global effect size	95% CI	χ^2	$p =$ (Between groups)
Fat-free mass	HIIT vs. CONT	9	41	0.10	0.36	-0.70	-2.20, 0.79	N/A	N/A
Waist circumference	HIIT vs. CONT	9	0	0.99	-0.13	-0.30	-1.69, 1.09	N/A	N/A

HIIT High-Intensity Interval Training, CONT continuous aerobic training group, LL-HIIT long-interval HIIT, MI-HIIT moderate-interval HIIT, SI-HIIT short-interval, SIT-HIIT sprint interval training, RST repeated sprint training, N/A Not applicable

Significant effect size written with bold font HIIT vs. CONT

#Post-sensitivity analysis results

Table 4 GRADE assessment results

Variable	HIIT vs. control group certainty	HIIT vs. CONT certainty
HbA1c	Low	Moderate
FBG	Low	High
FBI	Low	Low
HOMA 1-IR	Very low	Low
VO _{2peak}	Very low	Low
VO _{2max}	Very low	Low
% Fat	Moderate	Moderate
Fat-free mass	Very low	Moderate
Waist circumference	Very low	Moderate

compared HIIT vs. CONT and reported similar results to ours.

The HIIT mode analysis showed improvements in almost all types of HIIT through the variables for HIIT vs. control group, while HIIT vs. CONT remained unchanged in most cases. In addition, the subgroup analysis showed no differences between types of HIIT in any of the comparisons for aerobic resistance and %fat (Fig. 3). A more graphical chart of the obtained results can be found in the electronic supplementary material, appendix 6.

Physiological mechanisms

Recent evidence suggests that HIIT can affect different metabolic pathways. For instance, HIIT exerts an anti-inflammatory effect, especially in skeletal muscle tissue. Moreover, HIIT increases GLUT4 translocation and expression in the cellular membrane, and glucose uptake is increased. The enhanced GLUT4 activity could explain the benefits of HbA1c, FBG, FBI, and HOMA 1-IR indicators [75–78].

Another potential mechanism relates to appetite. For instance, Jiménez-Maldonado et al. [77] reported a decreased caloric intake in individuals following chronic HIIT. Indeed, HIIT can reduce ghrelin levels and increase incretin hormones, such as GLP 1 and peptide Y, which elicit a greater feeling of satiety [79]. The reduction in % fat and waist circumference might be explained by the decreased caloric output elicited by exercise and caloric intake. In addition, the improved incretin effect can increase insulin secretion and bioavailability [79, 80].

HIIT can also increase mitochondrial proteins and enhance the muscle fiber's enzymatic capacity, which will increase glucose and lipid oxidation, ATP production, energy expenditure, and cellular VO₂. These mitochondrial processes could explain insulin sensitivity, glycaemic control, energy expenditure, and, therefore, % fat and waist circumference reduction [75, 76, 81]. Consequently,

Table 5 Quality assessment scores obtained with TESTEX scale

Article, year	Score	Article, year	Score	Article, year	Score
Abdelbasset et al. [34]	10	Elsisi et al. [55]	9	Maillard et al. [74]	10
Abdi et al. [35]	8	Findikoglu et al. [56]	11	Mitranun et al. [62]	10
Aguilera-Eguía et al. [51]	7	Gentil et al. [41]	9	Mortensen et al. [63]	9
Ahmed et al. [36]	10	Ghaedi et al. [69]	8	Rasmussen-Faria et al. [46]	7
Álvarez et al. [52]	12	Ghardashi-Afousi et al. [57]	8	Sabag et al. [47]	12
Arefirard et al. [53]	9	Ghardashi-Afousi et al. [42]	11	Sabouri et al. [64]	10
Asrami et al. [70]	8	Golshan et al. [58]	8	Saghand et al. [65]	8
Baasch-Skytte et al. [71]	12	Hollekim-Strand et al. [43]	7	Sokolovska et al. [48]	10
Banitalebi et al. [72]	10	Hwang et al. [44]	11	Stoa et al. [49]	8
Cassidy et al. [54]	8	Karstoft et al. [45]	10	Van Ryckeghem et al. [66]	10
Cassidy et al. [37]	12	Kaviani et al. [39]	7	Way et al. [50]	12
Cassidy et al. [38]	10	Kazemi et al. [73]	9	Wilson et al. [67]	9
Dünnwald et al. [39]	9	Li et al. [60]	11	Winding et al. [68]	10
Elsisi et al. [40]	9	Macías-Cervantes et al. [61]	7		

the mitochondrial oxidative capacity is enhanced, which explains the increased VO_{2peak} and VO_{2max} [75, 77, 81].

At the skeletal muscle fiber level, it can be found myokine liberation. These substances have autocrine, paracrine, or endocrine effects and during exercise, the myokines released can have different effects on tissues, such as anti-inflammatory (i.e., interleukin 6 [IL-6]), lipolytic (i.e., GDF-15, irisin, and IL-6), enhanced lipid uptake (i.e., myonectin), and enhanced glucose uptake (i.e., FGF-21) [78, 82]. These effects can contribute to insulin sensitivity improvement (i.e., better glycaemic control), and reduced % fat and waist circumference.

In the fat tissue, it has been described changes in the adipokine secretion pattern. Exercise increases anti-inflammatory adipokine release and reduces pro-inflammatory adipokines. These responses can also directly affect insulin sensitivity [76].

Strengths and limitations

The present meta-analysis has strengths. First, to the best of our knowledge, this is the first multiple meta-analysis about the effect of HIIT on diverse critical variables for T2D care. In addition, this is the first analysis of fat-free mass in T2D individuals following an HIIT protocol. Indeed, the present meta-analysis considered HIIT modality for the first time, except for HbA1c and VO_{2max} [22]. These features allow for a comprehensive view of the situation and a more straightforward professional application.

Second, between the methodological strengths, this meta-analysis was conducted with only T2D participants and exclusively with HIIT protocols without mixing other exercise or nutritional intervention types. In addition, the

analysis included the IVhet model [33], which is a novel method with several advantages over the random-effects model. IVhet retains a correct coverage probability and a lower observed variance regardless of heterogeneity [31]. Moreover, IVhet model gives more weight to larger studies and less weight to smaller studies, so it is an adequate model when true effect sizes are highly heterogeneous or when there are a few large studies that dominate the meta-analysis [31]. Another important facts are sensitivity analysis, this process could identify articles that could be biasing data, and the quality assessment scale, which was specific for exercise-related interventions [26].

Because of the quality and risk-of-bias assessment, inconsistency and possible publication bias were detected. However, when this information was integrated into GRADE results, certainty levels ranged from moderate to very low. It is acknowledged that the current results could change with more literature availability.

Between the limitations detected, we found that information availability was insufficient; therefore, the type of HIIT analysis was impossible to perform on VO_{2max} , fat-free mass, and waist circumference. Also, there is no HIIT meta-analysis (except HbA1c and VO_{2max}); thus, the current subgroup analysis results cannot be compared to any similar study.

There were some methodological limitations. For example, the exercise protocol descriptions were heterogeneous, and it caused some difficulties in the coding process. Also, two studies did not randomize the sample, and only a few reported how they controlled possible external factors that could directly affect the results. All these factors could have contributed to increasing the inconsistency in some results.

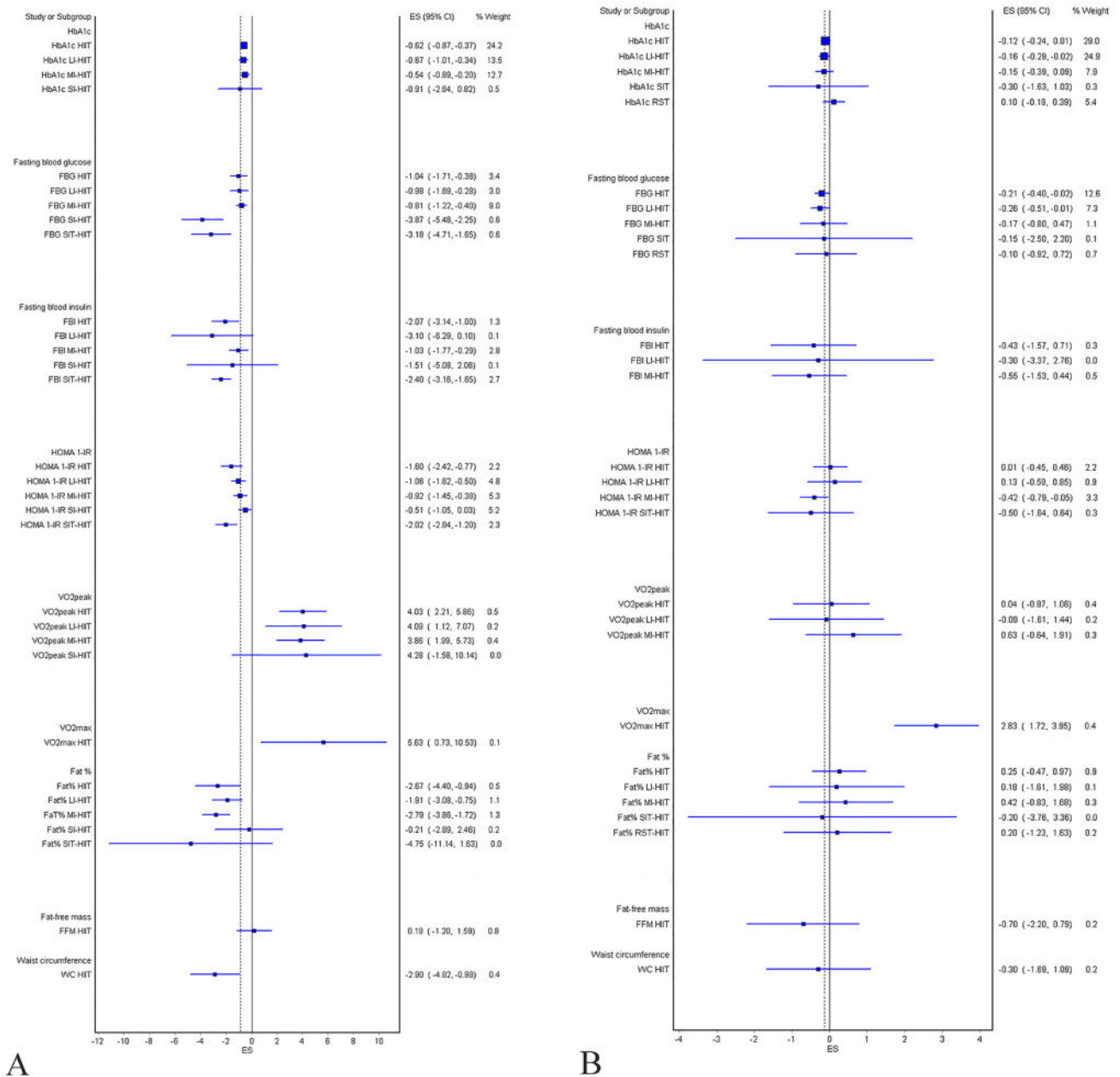


Fig. 3 Forest plot summary for the meta-analysis by type of HIIT on the different critical variables. **A** HIIT vs. control group. **B** HIIT vs. CONT

Recommendations

For future randomized and controlled trials, it is recommended to refine randomization methods adding concealment in the processes, and improve the “intention to treat” with data when possible. In addition, we recommend improving the strategies to control potential external factors affecting the results in all experimental groups and propose a standard process to describe exercise protocols.

Finally, it is also recommended to standardize methods for variable recording with the same kind of instrument and same measurement units; this will make it possible to meta-analyze all the existing data.

In professional practice, we recommend the HIIT implementation for T2D control based on a previous medical approval, with a personalized volume and progression plan, according to clinical conditions and under expert supervision.

Conclusions

The present meta-analysis showed that HIIT protocols improve HbA1c, FBG, FBI, HOMA 1-IR, VO_{2peak} , VO_{2max} , % fat, and waist circumference and keep fat-free mass unchanged in individuals with T2D. The SI-HIIT and SIT-HIIT protocols could be better than the other types of HIIT in reducing FBG, and SIT-HIIT could be better at HOMA 1-IR decrease. However, this result should be interpreted carefully, since these types of HIIT have shorter sample sizes and higher inconsistency. HIIT benefit is similar to CONT for the majority of variables, FBG showed a significant advantage in favor of HIIT. This training modality can be beneficial in professional practice, always taking into account the risk–benefit analysis, previous medical approval, and under the supervision of an expert in the field.

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Author contributions MCAL participated in the meta-analysis design, wrote and edited significant sections of the manuscript, ran the literature search, screened all identified studies based in title and abstract, made the full-text screening, and assisted in the risk of bias assessment, data extraction, and meta-analyses process. MJM contributed to statistical design and meta-analysis model, quality assessment scale, and article screening in foreign languages, and wrote significant sections of the manuscript. MGMS contributed to theoretical background of the study, meta-analysis design proposal, and interpretation of the results with physiological explanation of the outcomes obtained. JHE participated in meta-analysis design and data extraction, and also contributed to decision making when information was not clear, and she supervised the entire process. All authors reviewed and approved the final manuscript.

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Data availability All data generated or analyzed during this study are included in this article (and in the electronic supplementary material).

Declarations

Conflict of interest The authors declare that they have no conflicts of interest relevant to the content of this review.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of study formal consent is not required.

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