HUMAN MOVEMENT (ISSN 1899-1955)
2023; 24(1): 32–45

Effect of chronic High Intensity Interval Training on glycosylated haemoglobin in people with type 2 diabetes: a meta-analysis

© Wroclaw University of Health and Sport Sciences

review paper
DOI: https://doi.org/10.5114/hm.2023.107247

MARÍA CRISTINA ARRIETA-LEANDRO, JESSENIA HERNÁNDEZ-ELIZONDO, JUDITH JIMÉNEZ-DÍAZ
University of Costa Rica, San Pedro Montes de Oca, Costa Rica

ABSTRACT
Type 2 diabetes is a chronic disease with an increasing prevalence all over the world. The treatment includes an integral intervention with medical treatment, healthy diet, and regular exercise. High Intensity Interval Training has been recently proposed as part of this treatment to improve glycaemic control. The aim of this meta-analysis is to determine the effect of High Intensity Interval Training on glycosylated haemoglobin in people with type 2 diabetes during at least 12 weeks of intervention. The search was performed in EBSCOHost, Web of Science, Scopus, PubMed, and EMBASE. A total of 250 records were obtained and 22 studies met the inclusion criteria to be meta-analysed. The results showed that High Intensity Interval Training could significantly lower glycosylated haemoglobin; in the sedentary control group, glycosylated haemoglobin significantly increased, making glycaemic control worse. The improvement of glycosylated haemoglobin with High Intensity Interval Training can be influenced by diet, intensity of the intervals, and age. There were some limitations because of lack of control group and appropriate information in some studies. An adequate prescription program should be developed by a qualified professional to ensure best results.
Key words: High Intensity Interval Training, type 2 diabetes, glycaemic control, HbA1c

Introduction

Type 2 diabetes (T2D) is a chronic disease whose prevalence has been increasing in the world population during the last years. For example, only in the United States, there are 29.1 million people diagnosed with T2D (9.3% of the US population) [1]. In Poland, 8% of the population suffers from diabetes and it is estimated that 25–30% of adults with diabetes are unaware of their health condition. The prediction shows that diabetes prevalence in Poland will be 11% by 2040 [2]. In the Costa Rican population, the same trend is observed. Among people aged above 20 years, T2D prevalence equals around 10.5% [3]. Moreover, according to the Costa Rican Social Security Fund (CCSS, Caja Costarricense de Seguro Social), Costa Rican people lose an average of 13.2 years of their lives because of diabetes [3].

To take care of T2D, a multidisciplinary treatment is necessary, including drugs, healthy diet and lifestyle, and a proper exercise plan [1]. Much research has been performed with reference to this last point, with the main goal of finding the best option of exercising to ensure good glycaemic control [4].

Moreover, glycosylated haemoglobin (HbA1c) is a biochemical measure used for diabetes monitoring. It was recommended for the first time by the World Health Organization in 2006 and it presents a good overview of the glycaemic behaviour of a person during the previous 8–12 weeks [5, 6]. Although the World Health Organization guidelines indicate that HbA1c can be assessed every 8–12 weeks, recent studies recommend an optimal period of 12 weeks [7] because of the red blood cells replacement time [8].

HbA1c is widely used today in the clinical practice; it has also been proposed as a diagnostic criterion in

Correspondence address: María Cristina Arrieta-Leandro, Universidad de Costa Rica, San José, Montes de Oca, Sabanilla, Instalaciones Deportivas de la Universidad de Costa Rica, post code: 11502, Costa Rica, e-mail: mariacris0409@hotmail.com

Received: February 26, 2021
Accepted for publication: June 8, 2021

Citation: Arrieta-Leandro MC, Hernández-Elizondo J, Jiménez-Díaz J. Effect of chronic High Intensity Interval Training on glycosylated haemoglobin in people with type 2 diabetes: a meta-analysis. Hum Mov. 2023;24(1):32–45; doi: https://doi.org/10.5114/hm.2023.107247.

addition to control and monitoring. It is relatively easy to assess because it does not require any special physiological condition to be tested (e.g. minimum fasting hours). In people diagnosed with diabetes, a level of HbA1c below 6.5% is recommended for optimal glycaemic control [5, 6].

According to the American Diabetes Association and the American College of Sports Medicine (ACSM), individuals diagnosed with diabetes should practise moderate to intense aerobic exercise for 150 minutes/week, complementary with 2–3 sessions of resistance training weekly [9]. Recently, however, an alternative has been proposed, namely High Intensity Interval Training (HIIT). Some studies have compared the effect of aerobic training, resistance training, and HIIT on T2D, and the outcomes bring about different conclusions [10, 11]. Moreover, other studies tested other alternatives like structured walking, finding them potentially beneficial for glycaemic control [12, 13].

Today, there are no guidelines or protocols to follow when prescribing HIIT [10, 11]. Some authors suggest a general schedule with big intervals up to 3 minutes of high intensity (beyond 85% of maximal capacity) with rest periods between 10 seconds and 4 minutes [9]. Another important fact is that there is no standardized physiological parameter to define the maximal capacity or to establish the rest periods between intervals. Because of all this, the recent studies have applied different methodologies and, as a consequence, revealed different outcomes [9–11].

A recently published meta-analysis compared the effect of exercise vs. non-exercise on HbA1c in people with T2D and found beneficial effects of resistance training with an effect size (*ES*) of –0.15 (–0.31, 0.01), concurrent training with *ES* of –0.67 (–1.04, –0.3), and aerobic exercise with *ES* of –0.77 (–1.07, –0.46) [14]. Another recent meta-analysis presented a pre-test vs. post-test comparison and noted positive effects of HIIT on HbA1c with *ES* of –0.29 (–0.55, –0.04) when HIIT was compared with a control group with *ES* of –0.39 (–0.81, 0.02) in favour of HIIT; in a comparison with moderate intensity continuous training, *ES* was –0.37 (–0.55, –0.19) favouring HIIT. Nevertheless, the study included trials lasting 4 weeks and more [15], so it could have had accuracy problems in HbA1c measurement [7]; also, it did not provide moderator variable analysis [15].

Therefore, the aim of this meta-analysis was to determine the effect of chronic HIIT on HbA1c in people aged above 18 years with T2D after at least 12 weeks of experimental and quasi-experimental intervention. The second goal was to analyse the potential factors that could directly influence this effect.

Material and methods

Data sources and searches

This meta-analysis was performed in accordance with the PRISMA statement [16]. In October 2019, the following databases were searched: EBSCOHost (Academic Search Complete, Fuente Académica Premier, MEDLINE, and SportDiscus), Web of Science, Scopus, PubMed, and EMBASE. The Boolean phrase was "(glycated hemoglobin or glycosilated hemoglobin or hemoglobin a1c HbA1c) AND (type 2 diabetes or type 2 diabetes mellitus or t2dm) AND (hit or hiit or high intensity interval training or high intensity training or aerobic interval training or high intensity intermittent training)". The last search update was made in January 2021.

Inclusion criteria

In accordance with the PICOS criteria, the meta-analysed studies met the following inclusion criteria: the selected participants were subjects aged 18 years or above with a diagnosis of T2D and available to do exercise, pregnant women were excluded (P); the intervention involved the implementation of a HIIT protocol for at least 12 weeks (I); the comparison was between the status before and after intervention (i.e. pre-test vs. post-test) (C); the outcomes were pre-test and post-test HbA1c measures (O); and the selected studies had an experimental or quasi-experimental design (S).

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

Study selection

Data selection and codification was performed by one of the authors and then the information was checked by the other 2 authors. All the information was extracted and processed in Microsoft Office Excel®. The data involved authors, year of publication, country; information on the participants: age, sex, type of medication, physical activity level, diet; information on the methodology: training method, intervention duration, exercise frequency, duration, and intensity; information about dependent variables to calculate *ES*: pre-test and post-test HbA1c, standard deviations, and sample size. *ES* was based on the change between pre-test and post-test outcomes and calculated with the OpenMEE software [17] and the continuous random effects model [18]. Four studies did not report data necessary for meta-analysis and the authors were successfully contacted via e-mail to retrieve the information. Also, 4 articles reported HbA1c in mmol/l; to calculate *ES*, these values were converted to % with a German DiaSys Diagnostic Systems GmbH converter [19].

Quality assessment and risk of bias

Quality was assessed with the PEDro scale [20]. The results were exposed to description purposes and evaluated as a moderator variable to look for possible trends depending on quality results. Heterogeneity analysis was performed with I^2 in the OpenMEE software, subjective risk of bias was assessed with a funnel plot analysis in OpenMEE [17], and an objective analysis was conducted with Egger regression by using RStudio [21].

Sensitivity analysis

One study seemed to alter data heterogeneity, so analysis was performed with and without this trial to show the reader its impact on the results (see Figure 2b, c).

Moderator variable analysis

Moderator variables were assessed to find any possible factor affecting directly the HbA1c behaviour in the studies analysed. The categorical variables were meta-analysed with subgroup analysis and continuous variables were analysed with meta-regression, both in the OpenMEE software [17].

Ethical approval

The conducted research is not related to either human or animal use.

Results

A total of 233 studies were obtained from the different databases; 17 were added from other sources like reviews and research application updates. Among these 250 studies, 89 were duplicated records so a total of 161 articles were screened and compared with the inclusion criteria. After all the assessment, 22 studies were selected for meta-analysis (Figure 1).

A total of 564 participants were included in the analysis; among them, 361 performed the HIIT protocol. Gender analysis was not possible because most of the studies did not report the results distributed by gender. The main information about the included pa-

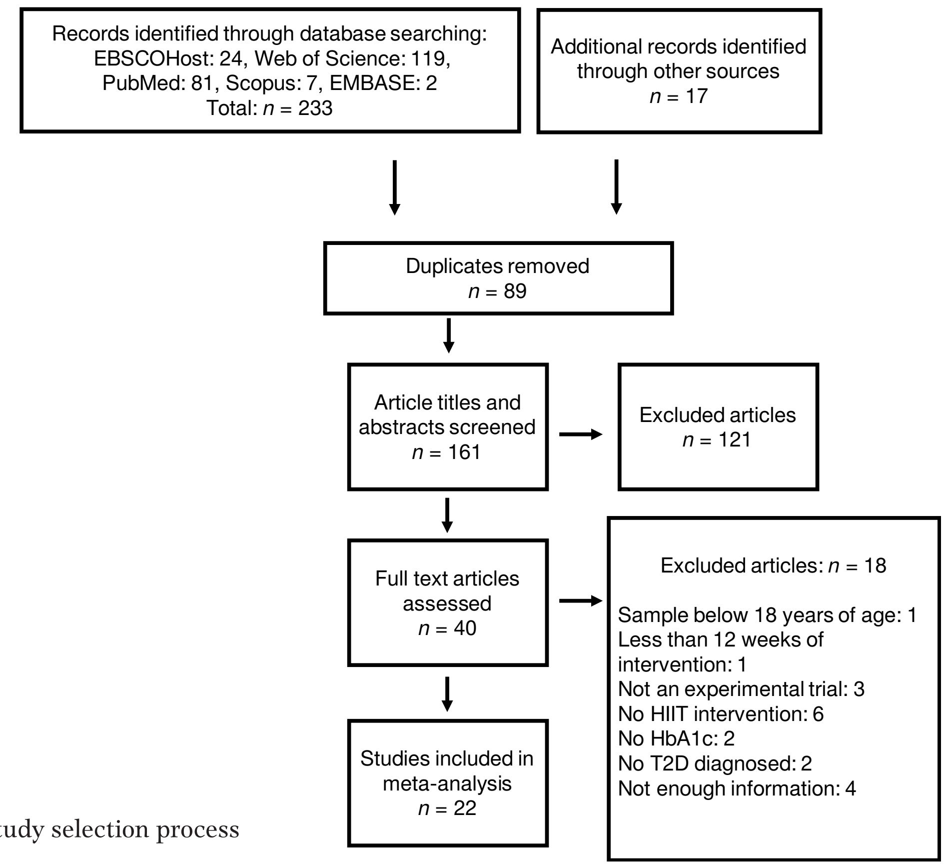
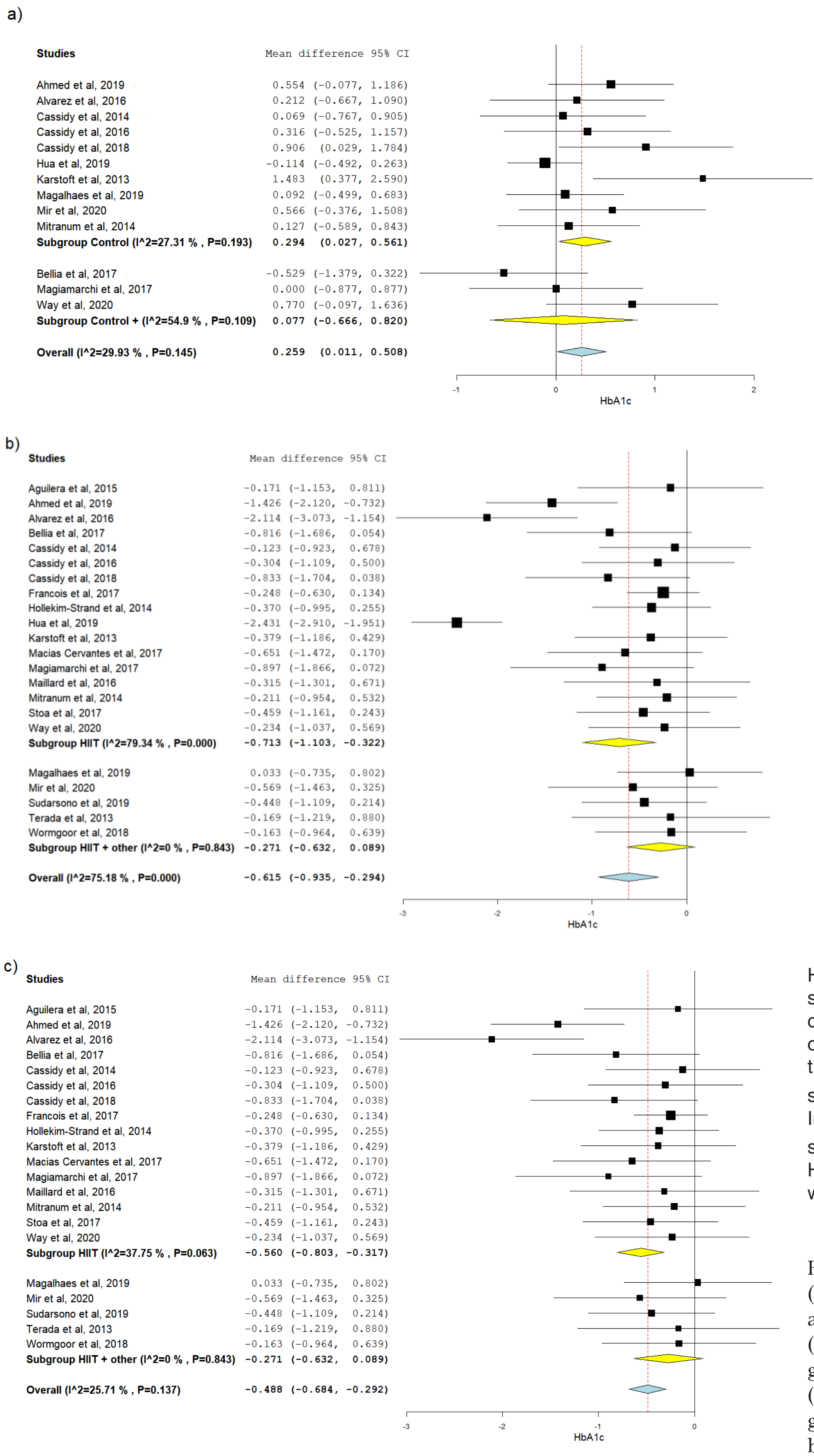


Figure 1. Flow diagram of the study selection process



HbA1c – glycosylated haemoglobin, subgroup control – pure sedentary control group, subgroup control + – control group with nutritional education or with low-level activity

subgroup HIIT – group with High Intensity Interval Training

subgroup HIIT + other – group with High Intensity Interval Training mixed with other type of training

Figure 2
(a) Forest plot for control groups and the effect on HbA1c.
(b) Forest plot for experimental groups effect on HbA1c.
(c) Forest plot for experimental groups without the study by Hua et al. [31]

Table 1. Main characteristics of the included papers

Article, year	Country	Main characteristics of the subjects					Intervention			
		n	Sex	Mean age (years)	Medication	Activity level	Duration of intervention	Frequency of exercise	Method	Diet
Aguilera Eguía et al., 2015 [22]	Chile	8	Mixed	62	NR	NR	12 weeks	5 times/ week	Treadmill and cycle ergometry	Not controlled
Ahmed et al., 2019 [23]	Egypt	20* / 20	Male	51.8* / 52.4	Pill	Sedentary	12 weeks	3 times/ week	Treadmill	Not controlled
Alvarez et al., 2016 [24]	Brazil	10* / 13	Mixed	43.1* / 45.6	Pill	Sedentary	16 weeks	3 times/ week	Walking/jogging/ running	Standardized or controlled
Bellia et al., 2017 [25]	Italy	11^{+} / 11	Mixed	56.3^{+} / 58.8	Pill	Sedentary	12 weeks	2.75 times/ week	Treadmill	Standardized or controlled
Cassidy et al., 2014 [26]	United Kingdom	11* / 12	Mixed	60* / 60	NR	NR	12 weeks	3 times/ week	Cycle ergometry	NR
Cassidy et al., 2016 [27]	United Kingdom	14* / 14	Mixed	59* / 61	Pill	Sedentary	12 weeks	3 times/ week	Cycle ergometry	Standardized or controlled
Cassidy et al., 2019 [28]	United Kingdom	11* / 11	Mixed	59* / 60	Medicine + lifestyle	NR / NR	12 weeks	3 times/ week	Cycle ergometry	Standardized or controlled
Francois et al., 2017 [29]	Canada	53	Mixed	57.7	NR	NR	12 weeks	3 times/ week	Treadmill or cycle ergometry or elliptical and elastic bands	Experimental condition
Hollekim-Strand et al., 2014 [30]	Norway	20	Mixed	58.6	NR	NR	12 weeks	3 times/ week	NR	NR
Hua et al., 2020 [31]	China	54* / 58	Mixed	43.7* / 44.3	Medicine + lifestyle	NR	12 weeks	3 times/ week	Cycle ergometry	Experimental condition
Karstoft et al., 2013 [13]	Denmark	8* / 12	Mixed	57.1* / 57.5	Medicine + lifestyle	Sedentary	16 weeks	5 times/ week	Walking/jogging/ running	Standardized or controlled
Macías-Cervantes et al., 2017 [32]	Mexico	12	NR	45.8	NR	Sedentary	16 weeks	3 times/ week	Cycle ergometry	NR
Magalhães et al., 2019 [33]	Portugal	22* / 13	Mixed	59* / 56.7	NR	NR	52 weeks	3 times/ week	Cycle ergometry	NR
Maillard et al., 2016 [35]	France	8	Female	68.2	Pill and injectable	Low	16 weeks	2 times/ week	Cycle ergometry	Standardized or controlled
Mangiamarchi et al., 2017 [34]	Chile	10^{-} / 9	Female	54.1^{-} / 57.6	Pill and injectable	Sedentary	12 weeks	3 times/ week	Cycle ergometry	Experimental condition
Mir et al., 2020 [36]	Iran	9* / 10	Male	57.7* / 58.9	Pill	Sedentary	12 weeks	3 times/ week	Treadmill	Not controlled

Mitranum et al., 2014 [37]	Thailand	15* / 14	Mixed	60.9* / 61.2	Pill	Sedentary	12 weeks	3 times/ week	Treadmill	Standardized or controlled
Støa et al., 2017 [38]	Norway	16	NR	59	Pill and injectable	Sedentary	12 weeks	3 times/ week	Walking/jogging/ running	Standardized or controlled
Sudarsono et al., 2019 [39]	Indonesia	18	Mixed	51.69	Pill	NR	12 weeks	3 times/ week	Treadmill and cycle ergometry	Standardized or controlled
Terada et al., 2013 [40]	Canada	8	Mixed	62	Medicine + lifestyle	Sedentary	12 weeks	4 times/ week	Treadmill and cycle ergometry	Standardized or controlled
Way et al., 2020 [41]	Australia	11+ / 12	Mixed	51.9+ / 56.9	Pill	Sedentary	12 weeks	3 times/ week	Cycle ergometry	Not controlled
Wormgoor et al., 2018 [42]	New Zealand	12	Male	52.2	Pill and injectable	NR	12 weeks	3 times/ week	Cycle ergometry	Standardized or controlled

NR – not reported
* control group, + control + low activity level groups, – control + nutritional advice groups

pers can be found in Table 1. Figure 2 shows the subgroup analysis corresponding to control and experimental groups.

A total of 10 studies involved pure control sedentary groups, 3 trials had a control group mixed with another kind of treatment. For example, one of them included at least 10,000 steps/day or 70,000 steps/week and another received nutritional education; because of this variety of the control groups, they were analysed in another subgroup. The results showed that being sedentary did not improve glycaemic control; on the contrary, HbA1c significantly increased in these cases, making glycaemic control worse. In the control + subgroup, glycaemic control did not present any changes (Figure 2a).

In the experimental group, *ES* was significantly lower. There were trials that involved only HIIT treatments and in 5 studies HIIT was mixed with another exercise protocol (e.g. combined with resistance training); these were analysed separately. The subgroup of HIIT revealed a significantly lower *ES* and the subgroup of HIIT + another intervention obtained lower *ES* but the difference was not significant (Figure 2b). The 5 trials of HIIT + another category were not included in the moderator variable analysis.

The heterogeneity of the results was significantly high; a sensitivity analysis was performed and it showed that the study by Hua et al. [31] brought about important heterogeneity changes. When the forest plot was obtained without this study, I^2 turned out non-significant (Figure 2c). Despite this, the results maintained significantly lower HbA1c when HIIT was performed.

The funnel plot subjective analysis shows that there is symmetry in data and the Egger regression test confirmed this in an objective way (t = –0.634, p = 0.535, slope: 0.179). This result indicates a low risk of bias in the studies included in the meta-analysis (Figure 3).

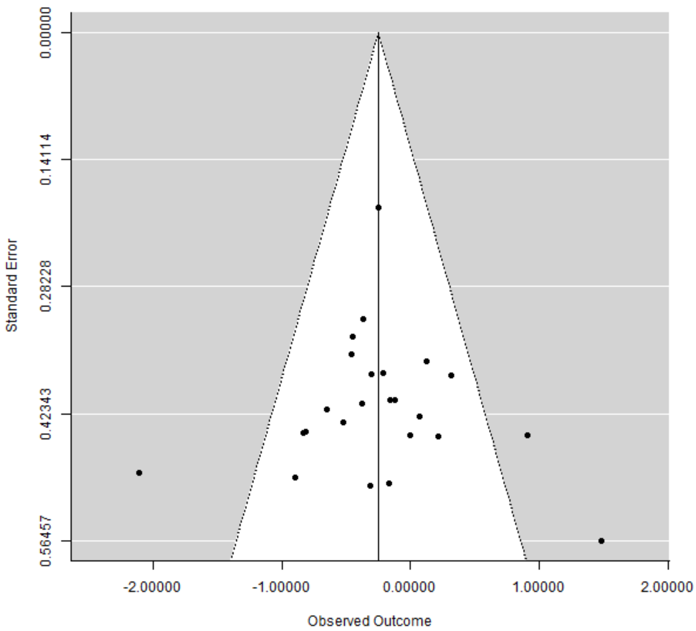


Figure 3. Funnel plot analysis of bias

Quality assessment of the meta-analysed studies was performed with the PEDro scale [20] and is displayed in Table 2. There is an important detail about this evaluation. Because of the trials design, it was not possible to blind the subjects and therapists; for that reason, all the studies were assigned 0 in these items. This, however, does not necessarily mean that the risk of bias was increased. The meta-regression analysis revealed no significant trend in *ES* depending on the quality score (Table 3); all 22 studies meta-analysed were included in this meta-regression.

Table 2. Included trials quality assessment performed with PEDro scale

Study	Eligibility criteria specified	Randomization of groups	Allocation concealed	Similar group at baseline	Blinding of subjects	Blinding of therapists	Blinding of assessors	Outcomes over 85% of initial participants	All the subjects received treatment or control condition	Results between groups reported	Point measures and variability measures reported	Total
Aguilera Eguía et al., 2015 [22]	1	1	0	?	0	0	1	1	0	1	1	6
Ahmed et al., 2019 [23]	1	1	1	?	0	0	0	0	1	1	1	6
Alvarez et al., 2016 [24]	1	1	0	1	0	0	1	1	1	1	0	7
Bellia et al., 2017 [25]	1	1	0	1	0	0	0	0	1	1	0	5
Cassidy et al., 2014 [26]	1	1	0	?	0	0	?	?	1	1	1	5
Cassidy et al., 2016 [27]	1	1	1	1	0	0	0	0	1	1	1	7
Cassidy et al., 2019 [28]	1	1	1	1	0	0	0	0	1	1	1	7
Francois et al., 2017 [29]	1	1	0	?	0	0	0	1	1	1	1	6
Hollekim-Strand et al., 2014 [30]	1	1	0	1	0	0	0	0	1	1	1	6
Hua et al., 2020 [31]	1	1	0	1	0	0	0	1	1	1	1	7
Karstoft et al., 2013 [13]	1	1	0	1	0	0	1	1	1	1	1	8
Macías-Cervantes et al., 2017 [32]	1	1	0	1	0	0	0	?	1	1	1	6
Magalhães et al., 2019 [33]	1	1	1	1	0	0	0	0	1	1	1	7
Maillard et al., 2016 [35]	1	1	0	1	0	0	0	1	1	1	1	7
Mangiamarchi et al., 2017 [34]	1	0	0	1	0	0	0	1	1	1	0	5
Mir et al., 2020 [36]	1	1	0	?	0	0	0	1	1	1	1	6
Mitranum et al., 2014 [37]	1	1	0	1	0	0	0	1	1	1	1	7
Støa et al., 2017 [38]	1	0	0	1	0	0	0	1	1	1	1	6
Sudarsono et al., 2019 [39]	1	1	0	1	0	0	1	0	1	0	1	6
Terada et al., 2013 [40]	1	1	1	1	0	0	0	1	1	1	1	8
Way et al., 2020 [41]	1	1	1	1	0	0	0	1	1	1	1	8
Wormgoor et al., 2018 [42]	1	1	1	1	0	0	?	1	1	1	0	7

0 – no, 1 – yes, ? – no clear information in the study

Table 3. Meta-regression results for continuous moderator variables

Factor	β	Data range	*p*
Age (years)	0.096	44.3–68.2	< 0.01*
Frequency of exercise (times/week)	0.162	2.75–5	0.541
Number of intervals	0.002	2.75–60	0.912
High interval duration (s)	0.001	8–240	0.528
Low interval duration (s)	0.004	12–240	0.222
Quality of studies (PEDro scale)	–0.048	5–8	0.780

* $p < 0.05$

Type of diet

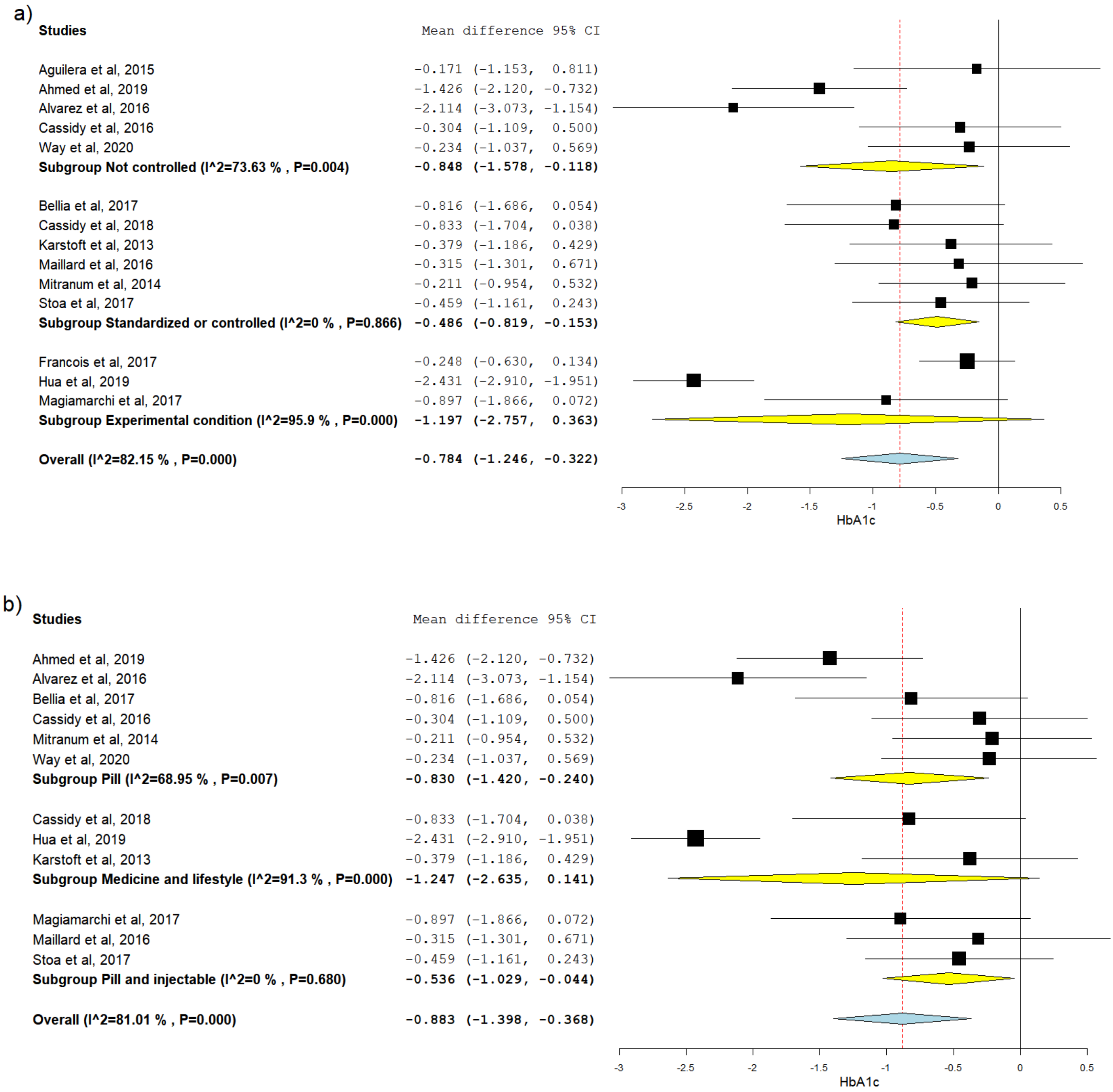
As for the diet intervention (Figure 4a), the studies with a standardized or controlled diet and those that did not control the diet presented significantly lower *ES* than the studies that made diet part of the experimental condition. It is important to highlight that there are few studies in the experimental condition category and this *ES* could not be accurate.

Type of medication

In the type of medication analysis (Figure 4b), all groups significantly improved HbA1c, regardless of the type of pharmacological treatment received by the participants. In the category where the studies included participants without pharmacological treatment, treated with lifestyle changes, no significant improvement was observed.

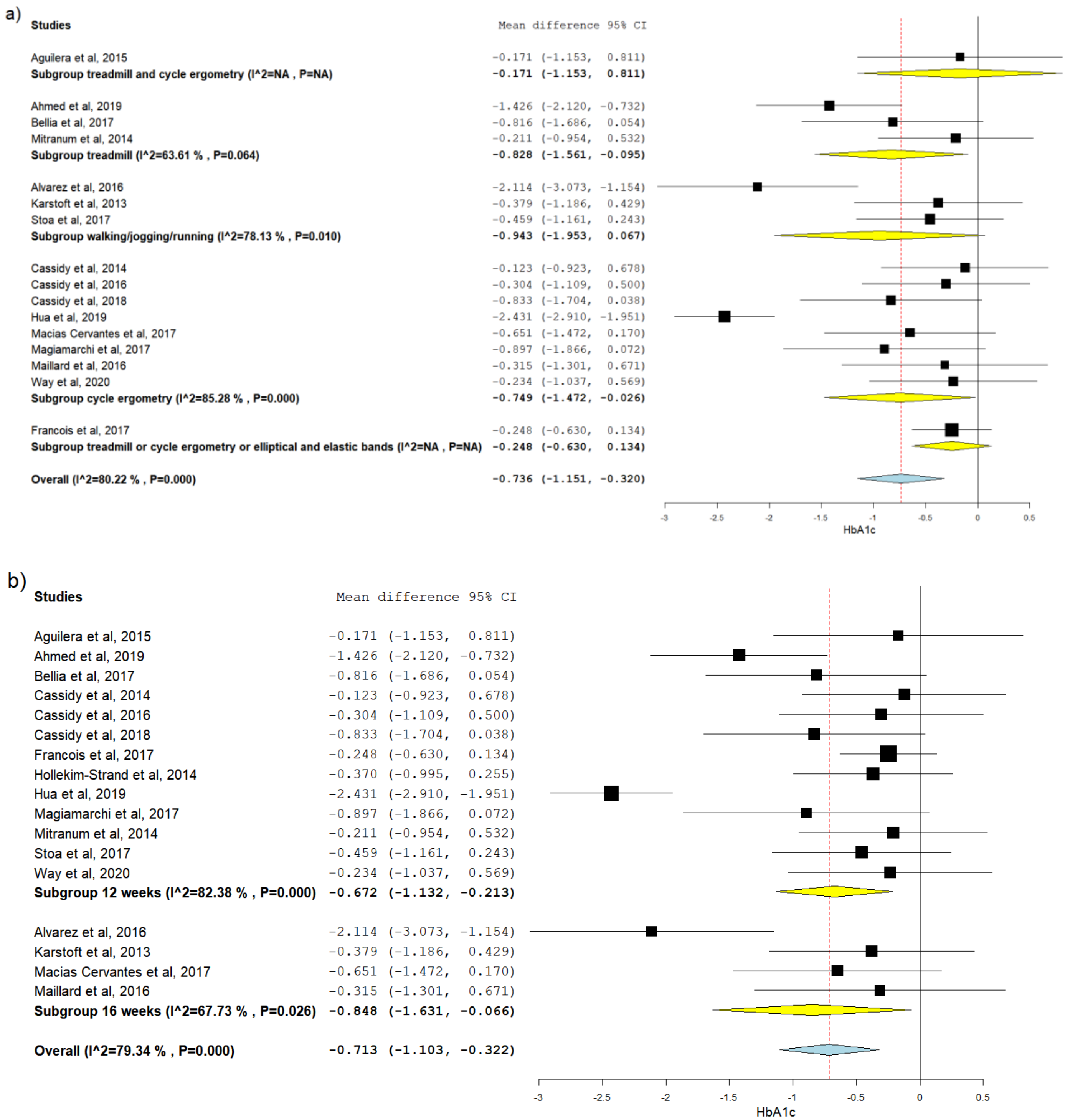
Method of exercise

In the subgroup analysis of exercise method, the cycle ergometer and the treadmill presented significantly lower *ES* (Figure 5a).



HbA1c – glycosylated haemoglobin

Figure 4. (a) Effect of High Intensity Interval Training on HbA1c depending on diet intervention.
(b) Effect of High Intensity Interval Training on HbA1c depending on received medication



HbA1c – glycosylated haemoglobin

Figure 5. (a) Effect of High Intensity Interval Training on HbA1c depending on the type of exercise performed. (b) Effect of High Intensity Interval Training on HbA1c depending on the number of intervention weeks

Intervention duration

In the studies included, the interventions lasted 12 or 16 weeks; their duration was analysed as a categorical variable (Figure 5b). Trials that endured 16 weeks revealed a better improvement in *ES* but both categories, as well as the overall group, presented significantly lower outcomes.

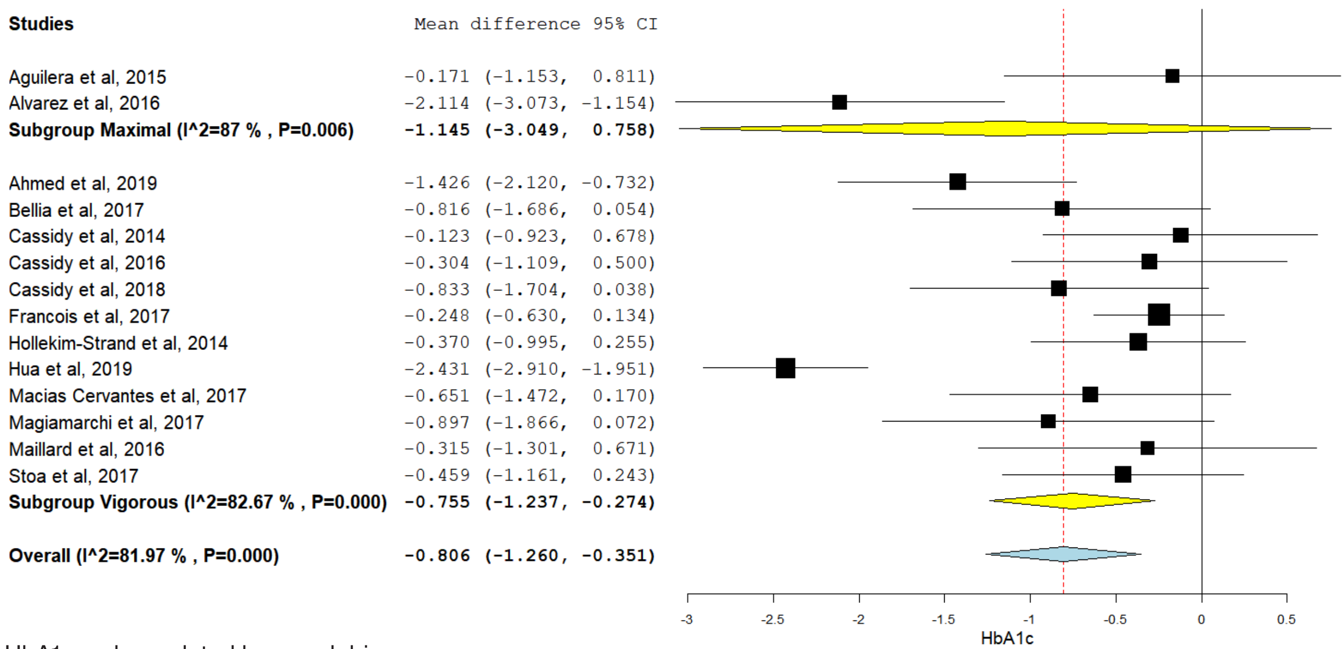
High interval intensity

The intensity of the high interval was measured with different physiological parameters in the analysed trials. For that reason, all the information concerning this topic was classified in accordance with the ACSM guidelines [43] as very light, light, moderate, vigorous, or maximal. Those studies that involved an intensity progress during the trial, the different intensities were averaged for analysis purposes. All the high intervals in the trials presented vigorous or maximal intensity (Figure 6), and *ES* was significantly lower in the overall analysis. In the subgroup analysis, the vigorous intensity kept significantly lower but the maximal subgroup was not significantly different.

The meta-regression analysis showed a significant impact of age on the results (Table 3). Regression presented a positive correlation: the older the participant, the smaller effect HIIT had on HbA1c (*ES* = +0.096 for each subsequent year of age). The performance variables that revealed progression during the trial were averaged for analysis purposes. All other continuous variables showed no significant trends and their ranges are depicted in Table 3.

Discussion

The experimental HIIT group revealed a significant reduction in *ES* of HbA1c; in the trials that implemented only a HIIT protocol without any other training, *ES* was bigger. Among these studies, those by Ahmed et al. [23], Alvarez et al. [24], and Hua et al. [31] presented the biggest changes (*ES* = –1.426, *ES* = –2.114, *ES* = –2.431, respectively). Seven of the 17 only-HIIT studies had *ES* below the overall, but all the 17 studies indicated a negative size effect. This is consistent with the meta-analysis by Jang et al. [14], who found significant *ES* when comparing the HIIT and control groups. On the contrary, Liu et al. [15] did not observe significant differences in HbA1c in comparison with controls, but noted a difference in comparison with continuous aerobic exercise; on the other hand, De Nardi et al. [11] did not find significant differences in comparison with continuous aerobic exercise. An important detail about these previous meta-analyses is that they involved fewer studies than this meta-analysis, and De Nardi et al. [11] included participants diagnosed with prediabetes; these can be possible reasons for the differences in the results.



HbA1c – glycosylated haemoglobin

Figure 6. Effect of High Intensity Interval Training on HbA1c depending on the high interval intensity [43]

In some of the trials analysed, HIIT was complemented with another type of training and *ES* reduction was not significant, but there were only 5 studies applying this method. It is important to highlight that all of these 5 studies presented smaller *ES* than the overall and actually Magalhães et al. [33] implied positive *ES* without significant changes. It is therefore necessary to perform more research to obtain a clear picture of the effect of HIIT complemented with some other training alternatives.

A recent meta-analysis showed a comparison between HIIT, moderate intensity training, low intensity training, and control in affecting HbA1c in T2D participants [44]. A significant reduction of HbA1c was found when HIIT was performed, as in the present meta-analysis. HIIT turned out more beneficial than control and low intensity training. There was no significant difference between HIIT and moderate intensity training [44].

A possible explanation for the HbA1c reduction could be the effect of HIIT on appetite [45]; it was proved that HIIT reduced ghrelin plasma levels in obese diabetic subjects and also increased glucagon-like peptide-1 concentrations in obese and normal weight diabetics. Ghrelin plasma levels reduction helps to improve appetite control and regulate energy intake. The improvement of glucagon-like peptide-1 concentrations enhances insulin metabolism. Both factors can contribute to HbA1c reduction [46, 47].

A significant increase of *ES* was observed in the control groups, corresponding with a negative effect of sedentarism on diabetes control. The study by Karstoft et al. [13] presented the biggest *ES* (+1.483), and only Hua et al. [31] indicated negative *ES* (–0.114) between the sedentary control group studies. There were 3 trials that had control groups mixed with nutritional education or low-level activity; these did not reveal significant changes, whereas the pure sedentary control group had a significant increase in *ES*. The results show that being sedentary not only is unsuitable to improve glycaemic control, but also worsens the status of this chronic disease. This confirms the importance of an integrated treatment (diet, medication, and exercise) to obtain better glycaemic control, already reported in the literature [14].

With reference to the moderator variable analysis, there are some aspects to highlight. Concerning the diet, when it was controlled or standardized or the participants were instructed to continue their usual habits without any control, the results were better than when diet constituted part of the experimental condition. This reflects the influence of diet on T2D treatment. In the case of the type of medication, all the pharmacologic alternatives presented a significant *ES* reduction but when participants with lifestyle modification without medication were included, the results were not satisfactory. These facts again imply the importance of an integrated treatment where it is necessary to combine healthy lifestyle with exercise and pharmacologic treatment for better T2D control [48].

Sex analysis was not possible because of lack of appropriate information in the studies meta-analysed. A study published as an ACSM meeting abstract found a bigger reduction of HbA1c in males when they followed an aerobic training, resistance training, and flexibility training program [49].

The other moderator variable analysis showed that the best HIIT program involved a cycle ergometer or treadmill used for at least 12 weeks; better results were achieved with 16 weeks and with the high interval in vigorous intensity in accordance with ACSM guidelines [43]. Maximal intensity did not imply significant results; as it only appeared in 2 studies, further research is needed to draw conclusions about maximal intensity.

The meta-regression analysis showed no trend concerning exercise frequency, number of intervals, or interval duration; so, when the protocol was prescribed in the ranges displayed in Table 3, the result in HbA1c was satisfactory. The analysis revealed a significant trend with reference to age: the older the person, the smaller reduction in HbA1c the *ES* indicated. In the study by Hua et al. [31], the average age was 44.3 years, and, the lowest in this meta-analysis, its *ES* equalled –2.431. On the other hand, Maillard et al. [35] involved the oldest participants, with an average age of 68.2 years, and *ES* was –0.315. It illustrates the trend found in the meta-regression results.

A recent review indicated that HIIT could be beneficial for glycaemic control in patients of any age; however, it remains unclear if this benefit is the same for all ages, so further investigation is recommended to make a specific evaluation concerning the participants' age [50]. That prediction is consistent with this meta-regression analysis, which found significant differences in HbA1c reduction depending on age.

Among the strengths of this meta-analysis, there is the quality analysis, performed in accordance with the PEDro scale (with the assumption that it was not possible to blind the subjects and therapists because of the design of the studies). There is a low risk of bias in the trials analysed, so the results are reliable. Moreover, as revealed in the meta-regression analysis (Table 3), there is no influence of the quality score on the results. Another strength of this study is that papers published in Spanish or English were included and there was no publishing year restriction in the search.

On the other hand, this meta-analysis included T2D-diagnosed participants only; prediabetes individuals were excluded. The intervention length was filtered in accordance with the newest recommendations for HbA1c assessment (at least 12 weeks) [7, 8]. In addition, to our knowledge, this is the only meta-analysis evaluating moderator variables and proposing a HIIT protocol.

Among the limitations of this study, there are design weaknesses, lack of control groups in many trials, and lack of randomization in 2 studies. In the moderator variable analysis, it was not possible to include all the information because there was not enough information in some studies. Furthermore, some trial designs combined HIIT and other training modalities; these could not be included in the moderator variable analysis. There was another case with control groups in which nutritional education, diet, or another exercise were part of the intervention; this made them non-strict control groups.

Conclusions

HIIT has a beneficial effect on HbA1c in people diagnosed with T2D and this effect is influenced by diet, training program intensity, and age. Keeping sedentary despite medical treatment can worsen glycaemic control. It is important to take into account the frequency, intensity, and length of intervention, interval duration, and the number of intervals when making prescription; this should be done by qualified professionals.

HIIT can be applied in people with T2D and medical approval; the suggested regimen involves practising 2–5 times/week, with vigorous intensity intervals lasting from 8 seconds to 4 minutes, for at least 12 weeks, on a treadmill or cycle ergometer.

Acknowledgements

We would like to thank all the professors and master program participants who advised us on improving this meta-analysis.

Disclosure statement

No author has any financial interest or received any financial benefit from this research.

Conflict of interest

The authors state no conflict of interest.

References

* Studies meta-analysed

1. Franz MJ, Evert AB. Medical nutrition therapy for diabetes mellitus and hypoglycemia of nondiabetic origin. In: Mahan LK, Raymond JL (eds.), Krause's food & the nutrition care process. St. Louis: Elsevier; 2017; 586–618.
2. Zatońska K, Basiak-Rasała A, Różańska D, Karczewski M, Wołyniec M, Szuba A, et al. Changes in diabetes prevalence and corresponding risk factors – findings from 3- and 6-year follow-up of PURE Poland cohort study. BMC Public Health. 2020;20(1):843; doi: 10.1186/s12889-020-08970-5.
3. Aguilar AY. Costa Rican people lose an average of 13.2 years of life because of diabetes [in Spanish]. 2018. Available from: https://amprensa.com/2018/09/costarricenses-pierde-en-promedio-13-2-anos-de-vida-a-causa-de-la-diabetes/.
4. Buresh R, Berg K. Exercise for the management of type 2 diabetes mellitus: factors to consider with current guidelines. J Sports Med Phys Fitness. 2018;58(4):510–524; doi: 10.23736/S0022-4707.17.06969-9.
5. World Health Organization. Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus. Geneva: WHO; 2011. Available from: https://www.who.int/diabetes/publications/report-hba1c_2011.pdf.
6. Shrivastava A, Mishra P, Shrivastava N, Mishra S, Kumar V, Zaidi SNH, et al. Awareness of glycosylated haemoglobin (HbA1c) among type 2 diabetes mellitus patients in a diabetic clinic in urban Allahabad. HECS Int J Comm Health Med Res. 2018;4(2):61–64.
7. Morgen EK, Naugler C. Inappropriate repeats of six common tests in a Canadian city: a population cohort study within a laboratory informatics framework. Am J Clin Pathol. 2015;144(5):704–712; doi: 10.1309/AJCPYXDAUS2F8XJY.
8. Reynolds TM, Smellie WSA, Twomey PJ. Glycated haemoglobin (HbA1c) monitoring. BMJ. 2006;333(7568):586–588; doi: 10.1136/bmj.38947.627847.AE.
9. Da Silva DE, Grande AJ, Roever L, Tse G, Liu T, Biondi-Zoccai G, et al. High-intensity interval training in patients with type 2 diabetes mellitus: a systematic review. Curr Atheroscler Rep. 2019;21(2):8; doi: 10.1007/s11883-019-0767-9.
10. Wormgoor SG, Dalleck LC, Zinn C, Harris NK. Effects of high-intensity interval training on people living with type 2 diabetes: a narrative review. Can J Diabetes. 2017;41(5):536–547; doi: 10.1016/j.jcjd.2016.12.004.
11. De Nardi AT, Tolves T, Lenzi TL, Signori LU, da Silva AMV. High-intensity interval training versus continuous training on physiological and metabolic variables in prediabetes and type 2 diabetes: a meta-analysis. Diabetes Res Clin Pract. 2018;137:149–159; doi: 10.1016/j.diabres.2017.12.017.
12. Deguchi K, Enishi T, Sato N, Miura H, Fujinaka Y, Matsuhisa M, et al. Acute effect of fast walking on postprandial blood glucose control in type 2 diabetes.

Diabetol Int. 2016;7(2):119–123; doi: 10.1007/s13340-015-0217-z.
13. *Karstoft K, Winding K, Knudsen SH, Nielsen JS, Thomsen C, Pedersen BK, et al. The effects of free-living interval-walking training on glycemic control, body composition, and physical fitness in type 2 diabetic patients: a randomized, controlled trial. Diabetes Care. 2013;36(2):228–236; doi: 10.2337/dc12-0658.
14. Jang JE, Cho Y, Lee BW, Shin ES, Lee SH. Effectiveness of exercise intervention in reducing body weight and glycosylated hemoglobin levels in patients with type 2 diabetes mellitus in Korea: a systematic review and meta-analysis. Diabetes Metab J. 2019;43(3):302–318; doi: 10.4093/dmj.2018.0062.
15. Liu J-X, Zhu L, Li P-J, Li N, Xu Y-B. Effectiveness of high-intensity interval training on glycemic control and cardiorespiratory fitness in patients with type 2 diabetes: a systematic review and meta-analysis. Aging Clin Exp Res. 2019;31(5):575–593; doi: 10.1007/s40520-018-1012-z.
16. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009;339:b2700; doi: 10.1136/bmj.b2700.
17. Wallace BC, Lajeunesse MJ, Dietz G, Dahabreh IJ, Trikalinos TA, Schmid CH, et al. OpenMEE: intuitive, open-source software for meta-analysis in ecology and evolutionary biology. Methods Ecol Evol. 2017;8(8):941–947; doi: 10.1111/2041-210X.12708.
18. Borenstein M, Higgins JPT, Hedges LV, Rothstein HR. Basics of meta-analysis: I^2 is not an absolute measure of heterogeneity. Res Synth Methods. 2017;8(1):5–18; doi: 10.1002/jrsm.1230.
19. DiaSys Diagnostic Systems. HbA1c calculator. Available from: https://www.hba1cnet.com/hba1c-calculator/.
20. Physiotherapy Evidence Database. PEDro scale. Available from: https://www.pedro.org.au/english/downloads/pedro-scale/.
21. RStudio Team. RStudio: integrated development for R. Boston: RStudio, Inc.; 2015. Available from: http://www.rstudio.com/.
22. *Aguilera Eguía RA, Russell Guzmán JA, Soto Muñoz ME, Villegas González BE, Poblete Aro CE, Ibacache Palma A. Effect of high-intensity interval training on the reduction of glycosylated hemoglobin in type-2 diabetic adult patients [in Spanish]. Medwave. 2015;15(2):e6079; doi: 10.5867/medwave.2015.02.6079.
23. *Ahmed AS, Ahmed MS, Mahmoud WS, Abdelbasset WK, Elnaggar RK. Effect of high intensity interval training on heart rate variability and aerobic capacity in obese adults with type 2 diabetes mellitus. Biosci Res. 2019;16(3):2450–2458.
24. *Alvarez C, Ramirez-Campillo R, Martinez-Salazar C, Mancilla R, Flores-Opazo M, Cano-Montoya J, et al. Low-volume high-intensity interval training as a therapy for type 2 diabetes. Int J Sports Med. 2016;37(9):723–729; doi: 10.1055/s-0042-104935.
25. *Bellia A, Iellamo F, De Carli E, Andreadi A, Padua E, Lombardo M, et al. Exercise individualized by TRIMPi method reduces arterial stiffness in early onset type 2 diabetic patients: a randomized controlled trial with aerobic interval training. Int J Cardiol. 2017;248:314–319; doi: 10.1016/j.ijcard.2017.06.065.
26. *Cassidy SA, Thoma C, Hallsworth K, Jakovljevic DG, Parikh J, Hollingsworth KG, et al. High intensity intermittent exercise reverses abnormal cardiac function in people with type 2 diabetes: an MRI/S study. In: Boulton AJM, Del Prato S, Thorens B, Roden M, Walker M, Tack CJ, et al. (eds.), Minutes of the 49th General Assembly of the European Association for the Study of Diabetes. Diabetologia. 2014;57(Suppl. 1):1–566; S258. Available from: https://link.springer.com/content/pdf/10.1007%2Fs00125-014-3355-0.pdf.
27. *Cassidy S, Thoma C, Hallsworth K, Parikh J, Hollingsworth KG, Taylor R, et al. High intensity intermittent exercise improves cardiac structure and function and reduces liver fat in patients with type 2 diabetes: a randomised controlled trial. Diabetologia. 2016;59(1):56–66; doi: 10.1007/s00125-015-3741-2.
28. *Cassidy S, Vaidya V, Houghton D, Zalewski P, Seferovic JP, Hallsworth K, et al. Unsupervised high-intensity interval training improves glycaemic control but not cardiovascular autonomic function in type 2 diabetes patients: a randomised controlled trial. Diab Vasc Dis Res. 2019;16(1):69–76; doi: 10.1177/1479164118816223.
29. *Francois ME, Durrer C, Pistawka KJ, Halperin FA, Chang C, Little JP. Combined interval training and post-exercise nutrition in type 2 diabetes: a randomized control trial. Front Physiol. 2017;8:528; doi: 10.3389/fphys.2017.00528.
30. *Hollekim-Strand SM, Bjørgaas MR, Albrektsen G, Tjønna AE, Wisløff U, Ingul CB. High-intensity interval exercise effectively improves cardiac function in patients with type 2 diabetes mellitus and diastolic dysfunction: a randomized controlled trial. J Am Coll Cardiol. 2014;64(16):1758–1760; doi: 10.1016/j.jacc.2014.07.0971.
31. *Hua L, Lei M, Xue S, Li X, Li S, Xie Q. Effect of fish oil supplementation combined with high-intensity interval training in newly diagnosed non-obese type 2 diabetes: a randomized controlled trial. J Clin Biochem Nutr. 2020;66(2):146–151; doi: 10.3164/jcbn.19-64.
32. *Macías-Cervantes MH, Casillas LG, Sevilla MA, Figueroa A, Zarate E, Guerrero GA. Metabolic changes after two differents exercise programs in sedentary type 2 diabetic patients. Med Sci Sports Exerc. 2017;49(5S):1020; doi: 10.1249/01.mss.0000519799.35679.86.
33. *Magalhães JP, Júdice PB, Ribeiro R, Andrade R, Raposo J, Dores H, et al. Effectiveness of high-intensity interval training combined with resistance training versus continuous moderate-intensity training com-

bined with resistance training in patients with type 2 diabetes: a one-year randomized controlled trial. Diabetes Obes Metab. 2019;21(3):550–559; doi: 10.1111/dom.13551.
34. *Mangiamarchi P, Caniuqueo A, Ramírez-Campillo R, Cárdenas P, Morales S, Cano-Montoya J, et al. Effects of high-intensity interval training and nutritional education in patients with type 2 diabetes [in Spanish]. Rev Med Chile. 2017;145(7):845–853; doi: 10.4067/s0034-98872017000700845.
35. *Maillard F, Rousset S, Pereira B, Traore A, de Pradel Del Amaze P, Boirie Y, et al. High-intensity interval training reduces abdominal fat mass in postmenopausal women with type 2 diabetes. Diabetes Metab. 2016; 42(6):433–441; doi: 10.1016/j.diabet.2016.07.031.
36. *Mir E, Moazzami M, Bijeh N, Hakak Dokht E, Rahimi N. Changes in SFRP5, WNT5A, HbA1c, BMI, PBF, and insulin resistance in men with type 2 diabetes after 12 weeks of combined exercise (HIIT and resistance). Int J Diabetes Dev Ctries. 2020;40(2):248–254; doi: 10.1007/s13410-019-00790-7.
37. *Mitranun W, Deerochanawong C, Tanaka H, Suksom D. Continuous vs interval training on glycemic control and macro- and microvascular reactivity in type 2 diabetic patients. Scand J Med Sci Sports. 2014; 24(2):e69–e76; doi: 10.1111/sms.12112.
38. *Støa EM, Meling S, Nyhus L-K, Strømstad G, Mangerud KM, Helgerud J, et al. High-intensity aerobic interval training improves aerobic fitness and HbA1c among persons diagnosed with type 2 diabetes. Eur J Appl Physiol. 2017;117(3):455–467; doi: 10.1007/s00421-017-3540-1.
39. *Sudarsono NC, Tulaar ABM, Jusman SWA, Soewondo P, Sudaryo MDK, Siagian M, et al. The effects of combined high-intensity interval and resistance training on glycemic control and oxidative stress in T2DM. Asian J Sports Med. 2019;10(3):e91841; doi: 10.5812/asjsm.91841.
40. *Terada T, Friesen A, Chahal BS, Bell GJ, McCargar LJ, Boulé NG. Feasibility and preliminary efficacy of high intensity interval training in type 2 diabetes. Diabetes Res Clin Pract. 2013;99(2):120–129; doi: 10.1016/j.diabres.2012.10.019.
41. *Way KL, Sabag A, Sultana RN, Baker MK, Keating SE, Lanting S, et al. The effect of low-volume high-intensity interval training on cardiovascular health outcomes in type 2 diabetes: a randomised controlled trial. Int J Cardiol. 2020;320:148–154; doi: 10.1016/j.ijcard.2020.06.019.
42. *Wormgoor SG, Dalleck LC, Zinn C, Borotkanics R, Harris NK. High-intensity interval training is equivalent to moderate-intensity continuous training for short- and medium-term outcomes of glucose control, cardiometabolic risk, and microvascular complication markers in men with type 2 diabetes. Front Endocrinol. 2018; 9:475; doi: 10.3389/fendo.2018.00475.
43. American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription, 10th ed. Philadelphia: Wolters Kluwer; 2018.
44. Lora-Pozo I, Lucena-Anton D, Salazar A, Galán-Mercant A, Moral-Munoz JA. Anthropometric, cardiopulmonary and metabolic benefits of the high-intensity interval training versus moderate, low-intensity or control for type 2 diabetes: systematic review and meta-analysis. Int J Environ Res Public Health. 2019;16(22): 4524; doi: 10.3390/ijerph16224524.
45. Afrasyabi S, Marandi SM, Kargarfard M. The effects of high intensity interval training on appetite management in individuals with type 2 diabetes: influenced by participants weight. J Diabetes Metab Disord. 2019; 18(1):107–117; doi: 10.1007/s40200-019-00396-0.
46. Mottalib A, Salsberg V, Mohd-Yusof B-N, Mohamed W, Carolan P, Pober DM, et al. Effects of nutrition therapy on HbA1c and cardiovascular disease risk factors in overweight and obese patients with type 2 diabetes. Nutr J. 2018;17(1):42; doi: 10.1186/s12937-018-0351-0.
47. Peng XV, Ayyagari R, Lubwama R, Shi L, Price-Haywood EG, Hollander P, et al. Impact of simultaneous versus sequential initiation of basal insulin and glucagon-like peptide-1 receptor agonists on HbA1c in type 2 diabetes: a retrospective observational study. Diabetes Ther. 2020;11(4):995–1005; doi: 10.1007/s13300-020-00783-4.
48. Abusaib M, Ahmed M, Nwayyir HA, Alidrisi HA, Al-Abbood M, Al-Bayati A, et al. Iraqi experts consensus on the management of type 2 diabetes/prediabetes in adults. Clin Med Insights Endocrinol Diabetes. 2020; 13:1–11; doi: 10.1177/1179551420942232.
49. Devitskaya D, Villalobos C, VanNess JM, Vosti PD, King AC, Jensen CD. Sex-specific HbA1c responses to structured exercise among patients with type 2 diabetes. Med Sci Sports Exerc. 2019;51(6S):299–300; doi: 10.1249/01.mss.0000561405.06744.80.
50. Montes de Oca García A, Gutiérrez Manzanedo J, Ponce González JG. High-intensity interval training (HIIT) as a therapeutic tool in patients with type 2 diabetes mellitus: a narrative review [in Spanish]. Retos. 2019; 36(2):633–639; doi: 10.47197/retos.v36i36.69762.