

Systematic Review **Acute Effects of High-Intensity Interval Training on Diabetes Mellitus: A Systematic Review**

Gabriela de Oliveira Teles 1,* [,](https://orcid.org/0000-0003-2718-1705) Carini Silva da Silva ¹ , Vinicius Ramos Rezende [2](https://orcid.org/0000-0002-3770-9289) and Ana Cristina Silva Rebelo ³

- ¹ Faculty of Physical Education and Dance, Federal University of Goiás, Goiânia 74001-970, Brazil; carinisilva@discente.ufg.br
- ² Faculty of Medicine, Federal University of Goiás, Goiânia 74001-970, Brazil; viniciusrezendeef@gmail.com
³ Department of Merphology Institute of Biological Sciences, Eederal University of Coiás Department of Morphology, Institute of Biological Sciences, Federal University of Goiás,
	- Goiânia 74001-970, Brazil; ana_rebelo@ufg.br
- ***** Correspondence: telesgabriela@discente.ufg.br; Tel.: +55-5-(62)-984382469

Abstract: This study evaluated the scientific evidence on the acute effects of high-intensity interval training (HIIT) on biochemical, cardiovascular, and metabolic parameters in patients with diabetes mellitus. The research took place using two databases (PubMed and Google Scholar) with eligible studies conducted between 2010 and 2020, using the following keywords: (1) high-intensity training/exercise; (2) interval training/exercise; (3) HIIT/exercise; AND "diabetes". Data extraction was then performed on the eligible studies through content analysis using the categories: author and year of publication; sample characteristics; methods and data collected; intervention protocol; and results found. Methodological quality was assessed using the PEDro scale. Fourteen studies were included, evaluating 168 people with diabetes (122/46 type 2/1) and 42 normoglycemic individuals, which evaluated markers such as capillary and fasting blood glucose, 24-h blood glucose profile, postprandial blood glucose, incidence, and prevalence of hyperglycemia, vascular function and pressure response and control of inflammatory markers. Physical exercise was found to have several acute beneficial effects on the health of the diabetic population, such as reduced capillary and postprandial blood glucose, blood glucose profile, and blood pressure. Moreover, HIIT seems to be a safe and effective alternative in glycemic control and associated factors, superior to continuous moderate-intensity training.

Keywords: high-intensity interval training (HIIT); physical exercise; health; hyperglycemia

1. Introduction

Currently, 463 million people aged between 29 and 70 years live with diabetes, representing 9.3% of the population, and about half of them do not know they have the disease [\[1\]](#page-12-0). In many cases, symptoms take a long time to manifest or be noticed by patients, making diabetes mellitus (DM) the silent disease of the 21st century. Brazil has the fifth highest prevalence of the disease, with close to 16.8 million cases. It is among the ten countries with the highest expenditure on health-related costs attributed to diabetes, and the cost to public health increases according to the duration of the disease and the presence of microvascular and macrovascular complications [\[2\]](#page-12-1).

Chronic microvascular and macrovascular complications related to persistent hyperglycemia are associated with increased morbidity, reduced quality of life, and increased mortality rate. Diabetes treatment is based on pharmacotherapy, adequate nutrition, and physical exercise [\[3](#page-12-2)[,4\]](#page-12-3). An intervention with physical training can promote cardiorespiratory and metabolic adjustments and adaptations that can delay the progression of diabetes and improve its prognosis [\[5](#page-12-4)[,6\]](#page-12-5).

Lack of time is one of the most common barriers to regular physical exercise by people with diabetes [\[7\]](#page-12-6). Given the low adherence and concerns about safe and effective training,

Citation: de Oliveira Teles, G.; da Silva, C.S.; Rezende, V.R.; Rebelo, A.C.S. Acute Effects of High-Intensity Interval Training on Diabetes Mellitus: A Systematic Review. *Int. J. Environ. Res. Public Health* **2022**, *19*, 7049. [https://doi.org/10.3390/](https://doi.org/10.3390/ijerph19127049) [ijerph19127049](https://doi.org/10.3390/ijerph19127049)

Academic Editor: Olivier Dupuy

Received: 14 February 2022 Accepted: 25 March 2022 Published: 9 June 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license [\(https://](https://creativecommons.org/licenses/by/4.0/) [creativecommons.org/licenses/by/](https://creativecommons.org/licenses/by/4.0/) $4.0/$).

several types of exercises have been proposed for this population. In recent decades, high-intensity interval training (HIIT) has gained prominence for requiring less time and presenting better responses in endothelial function [\[8\]](#page-12-7), increasing functional capacity [\[9\]](#page-12-8), body composition [\[10\]](#page-12-9), and in improving quality of life [\[11\]](#page-12-10) than traditional training, such as using continuous moderate intensity. HIIT is a training protocol that alternates short periods of intense exercise ($>85\%$ of the VO₂ max. or maximal heart rate) with short periods of passive or active resting [\[4\]](#page-12-3). In people with type 2 diabetes (DM2), publications show that HIIT effectively improves glycemic control, glycated hemoglobin, and cardiorespiratory fitness [\[12](#page-12-11)[,13\]](#page-12-12).

Some studies have compared the effects of HIIT with continuous moderate-intensity training (CMIT) on indicators of cardiovascular risk in people with diabetes. De Nardi et al. (2018) compared the effects of HIIT with CMIT on functional capacity and cardiometabolic markers in people with DM2 (maximum oxygen volume; glycated hemoglobin; blood pressure; lipid profile; body mass index; and waist-to-hip ratio). Through a systematic review and meta-analysis, the authors concluded that HIIT promotes more significant benefits to functional capacity as evidenced by the 3.02 mL/Kg/min increase (confidence interval $1.42-4.61$) in VO₂ max. in this population. The study did not find differences between the modalities for the glycemia and blood pressure variables or in the other cardiometabolic markers [\[4\]](#page-12-3).

Considering the growing range of studies on HIIT and the concern over the efficacy and safety of protocols, understanding the effects on the physiological markers of health in this population is necessary. Therefore, the present study analyzed literature concerning the acute effects of HIIT on biochemical, cardiovascular, and metabolic parameters in patients with diabetes.

2. Materials and Methods

This systematic literature review study was performed according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) [\[14\]](#page-12-13). The search was performed in two databases (PubMed and Google Scholar) with eligible studies conducted between 2010 and 2020, written in Portuguese or English. The following keywords were used in the surveys: (1) high-intensity training/exercise; (2) interval training/exercise; (3) HIIT/exercise; AND "diabetes". The protocol for this study was registered in the PROSPERO Systematic Review Protocols Registry under ID: CRD42021250255.

The title and abstract of the articles found were read to verify the presence of keywords. Then, the articles that met the eligibility criteria were separated for a full reading. After selecting the eligible studies, data were extracted in a standardized way, and a database was created in the Excel 2016 (Microsoft, Redmond, WA, USA) platform containing the information from each study. This process was carried out by two researchers independently. Any disagreements were resolved by consensus or by the participation of a third researcher.

2.1. Eligibility Criteria

The criteria were established according to the PICOS approach (Population, Intervention, Comparator, Outcomes, and Study Design). In addition, a minimum score of 6 in the assessment of methodological quality using the PEDro scale was accepted as a criterion.

2.1.1. Population

The present review included studies involving adults diagnosed with type 1 or 2 diabetes, aged over 18 years, of both sexes, who were not included in any regular exercise program.

2.1.2. Intervention

Studies reporting the acute effect of HIIT, comparing or not with CMIT on biochemical, cardiovascular, and metabolic parameters in patients with diabetes, were included. Studies had to assess the acute (one session) effect and present the results to be included.

CMIT was considered a comparator of the HIIT. The included studies could therefore have a control group or a group that performed CMIT.

2.1.4. Outcomes

The primary outcome of this review is glycemic control, given the importance of this marker for the health of patients with diabetes. Other outcomes were expected, including cardiovascular and metabolic markers such as blood pressure, lipid profile, inflammatory indicators, and C-reactive protein.

2.2. Study Design

Randomized clinical trials and case studies were considered, involving a HIIT session.

2.3. Data Extraction

The extracted data were entered into an Excel spreadsheet (2016) (Microsoft, Redmond, WA, USA) according to the eligibility criteria using pre-established categories, such as author and year of publication; sample characteristics; methods and data collected; intervention protocol; and results found.

2.4. Evaluation of Methodological Quality

The methodological quality of the included studies was assessed using the PEDro scale translated into Portuguese, and the minimum score used was 6 [\[15\]](#page-12-14).

3. Results

The flowchart describing the search and selection of studies is shown in Figure [1.](#page-2-0) After reading the articles in full, 14 were included in the total that met all the criteria.

Figure 1. PRISMA flowchart for the search and selection of studies.

Of the 14 studies evaluated, all performed a maximal exercise test before the intervention to diagnose possible exercise-related problems or to indicate session intensity. In addition, all studies performed an aerobic training session, one of which compared aerobic training with resistance training, and 64% of the studies had a control group (no exercise) in the comparison. Eight studies (57%) evaluated the effect of exercise in the postprandial period, seven studies used a standardized diet for participants, and one used online food control. As for the methods, five studies used continuous glucose monitoring (24 h or 32 h) to verify values such as postprandial mean and peak glucose, in addition to the incidence and predominance of hyperglycemia.

The methodological quality of the studies is reported in Table [1,](#page-3-0) with a minimum score of 6. The characteristics of the study participants are shown in Table [2.](#page-4-0) Table [3](#page-5-0) contains the characteristics of the training methods and protocols of the included studies. Finally, the results are shown in Table [4.](#page-7-0)

Table 1. PEDro score for the included studies.

DM2, type 2 diabetes mellitus; DM1, type 1 diabetes mellitus; NG, normoglycemic; TN, trained; SD, sedentary; AH, arterial hypertension; NAH, normal awareness of hypoglycemia; IAH, impaired awareness of hypoglycemia; N, number of participants; BMI, body mass index; F, female; M, male.

Table 3. Study training methods and protocols.

HIIT, high-intensity interval training; CMIT, continuous moderate-intensity training; CONT, control; MIN, minute; blood pressure; HR, heart rate; HRM, heart rate maximum; HRR, heart rate reserve; SPE, subjective perception of effort; AT, anaerobic threshold; W, watts; Wmax, maximum watts; VO₂ max., maximum oxygen volume; REHIT, reduced exertion high-intensity interval training; EPOC, excess post-exercise oxygen consumption.

Table 4. *Cont*.

4. Discussion

This study reviewed in the literature the acute effects of HIIT on biochemical, cardiovascular, and metabolic parameters in patients with diabetes. It was found that that HIIT improves capillary blood glucose levels and factors associated with cardiovascular risk in people with diabetes, emphasizing the glycemic profile, blood pressure, vascular function, and inflammatory indicators when compared to CMIT or control groups.

We also want to clarify that the results obtained in studies that did not evaluate a control group should be reviewed, and we suggest further studies on the topic.

4.1. Capillary Blood Glucose Levels

There is a consensus on the beneficial effect of physical exercise on glycemic control in diabetics. Molecular, physiological and metabolic mechanisms related to glycemic control, induced by exercise, generate several adaptations, including increased concentration and translocation of GLUT-4 in the plasma membrane, improved uptake of muscle glucose, in addition to the increase in muscle fibers that are more sensitive to insulin, and the activity of glycolytic and oxidative enzymes [\[12\]](#page-12-11).

Santiago et al. (2017) found a reduction in capillary blood glucose of 27.4% after MTCT and 26.9% after HIIT [\[24\]](#page-12-23). Mendes et al. (2019) assessed blood glucose every 10 min after the exercise session and found that the hypoglycemic effect lasted for 50 min and that it was greater using HIIT [\[20\]](#page-12-19). It is important to note that the authors used a protocol of lower intensity than the others, being 70% of the HRR, while other researchers define HIIT as >85% of the HRM. Viana et al. (2019) demonstrated that HIIT, whether guided by HR or by SPE, promotes a more expressive reduction in blood glucose than CMIT [\[26\]](#page-13-1).

There is no consensus on the factors leading to a greater reduction in blood glucose by HIIT compared to continuous exercise. However, the high levels of muscle fiber recruitment, the use of muscle glycogen, and the increased insulin sensitivity previously observed during HIIT may increase exercise-induced muscle glucose uptake during and after [\[29\]](#page-13-8).

4.2. Postprandial Blood Glucose and Time/Exposure to Hyperglycemia

Gillen et al. (2012) assessed through continuous glucose monitoring that HIIT was effective in glycemic control three hours after eating, in peak glucose, in postprandial mean, and in hyperglycemia time [\[27\]](#page-13-2). Karstoft et al. (2014) compared the effects of HIIT with the CMIT and found a reduction in postprandial blood glucose, more expressive after HIIT [\[18\]](#page-12-17). The physiological mechanisms involved in reducing postprandial blood glucose after HIIT are still controversial, but it is possible to speculate that the increased insulin sensitivity in skeletal muscle, the high degree of muscle fiber recruitment, or the use of glycogen may be involved. Furthermore, insulin-independent mechanisms associated with HIIT, such as GLUT-4 translocation and increased endothelial function for up to 72 h, seem to contribute to this effect [\[27\]](#page-13-2).

Terada et al. (2016) performed a HIIT and CMIT training session with people with diabetes after fasting and after breakfast and verified the glycemic behavior in the following 24 h using continuous glucose monitoring. The authors concluded that when training was performed after fasting, postprandial blood glucose values were lower than with training performed after breakfast [\[28\]](#page-13-3). Other authors who investigated the hypoglycemic effects of fasting training concluded that the practice after an overnight fast and before using fast-acting insulin helps to maintain glycemic stability, regardless of the mode or intensity of exercise. This means that the patient does not need to consume carbohydrates to avoid hypoglycemia during training [\[25\]](#page-13-0). However, the authors of this study did not evaluate long-term protocols. Further studies are needed to investigate whether regular fasting exercise improves long-term glycemic control.

Metcalf et al. (2018) found that a training session reduced time and the prevalence of hyperglycemia, being more expressive in HIIT than in CMIT [\[22\]](#page-12-21). On the other hand, Jayawardene et al. (2017) found different results when verifying that HIIT promoted higher glycemic levels and greater exposure to hyperglycemia than CMIT [\[17\]](#page-12-16), and this

may be attributed to greater cellular stress and subsequent vascular dysfunction. There is also evidence of a strong correlation between postprandial hyperglycemia and the risk of adverse cardiovascular events [\[22\]](#page-12-21). Thus, physical exercise seems to have a cardioprotective effect in the diabetic population, regardless of the protocol.

4.3. 24 h Glycemic Profile and Hypoglycemia

Using continuous glucose monitoring, Gillen et al. (2012) showed that a single HIIT session reduced mean 24 h glucose and did not increase the risk of hypoglycemia [\[27\]](#page-13-2). Metcalfe et al. (2018) compared the acute effects of HIIT and CMIT, and found that CMIT promoted a greater effect on the 24 h glycemic profile than the HIIT protocols [\[22\]](#page-12-21). Greater sensitivity to insulin throughout the body can explain this prolonged glycemic control, which is observed immediately after exercise and persists for up to 96 h [\[30\]](#page-13-9).

There is a need for discussion regarding the risk of hypoglycemia following highintensity exercise in this population. However, this risk decreases with good professional follow-up, adequate control of variables before, during, and after exercise, and a balanced diet. Scott et al. (2019) and Terada et al. (2016) found that a training session of several protocols did not increase the incidence of fasting hypoglycemia in the following 24 h or at night in diabetics [\[25](#page-13-0)[,28\]](#page-13-3). These last authors also found that HIIT promoted a greater reduction in nocturnal and fasting blood glucose than CMIT. Rooyackers et al. (2017) concluded that HIIT decreases the symptoms of hypoglycemia in normoglycemics, and attenuates the cognitive dysfunction induced by hypoglycemia in diabetics [\[23\]](#page-12-22).

HIT appears to be superior to CMIT in several biochemical aspects in patients with diabetes, but there are still controversies regarding the superiority of one protocol over the other in the 24 h glycemic profile and hypoglycemia; as a result, further studies need to be performed.

4.4. Blood Pressure and Vascular Function

In addition to improving glycemic control, reducing cardiovascular risk also has positive implications for DM2 morbidity, mortality, and health care costs. For example, a 2.1/0.9 mmHg decrease in blood pressure (BP) resulted in a 10% reduction in major cardiovascular events in DM2 [\[31\]](#page-13-10) patients.

Santiago et al. (2017) evaluated BP after one HIIT session and one CMIT session and found a blood pressure reduction using both protocols, being more expressive 30 min after training [\[24\]](#page-12-23). Viana et al. (2019) evaluated the BP for 24 h following exercise and found a reduction in this resulting from HIIT guided by the subjective perception of exertion, but not from CMIT, and in the HIIT it was suggested by the participant's heart rate [\[26\]](#page-13-1). The type of exercise also influences this BP control. Francois et al. (2015) found that HIIT cardio training (training based on stimulating the cardiovascular system to gain physical endurance) increased arterial dilation one hour after training, and that HIIT resistance training improved endothelial function in both diabetics and normoglycemics [\[13\]](#page-12-12).

The mechanisms that guide BP variation during and after exercise are related to hemodynamic, humoral, and neural factors [\[26](#page-13-1)[,32\]](#page-13-11). Increased blood flow to skeletal muscles during physical exercise increases the stress on the vascular wall, inducing a greater release of nitric oxide and, consequently, vasodilation. With this decrease in peripheral vascular resistance, there is a drop in BP [\[32\]](#page-13-11).

4.5. Hormones and Indicators of Cellular and Systemic Inflammation

Karstoft et al. (2014) found an increase in lactate and glucagon after HIIT. In 2016, the same authors found a more significant increase in lactate using HIIT over CMIT in a similar study, and that lipid oxidation increased after exercise, regardless of the protocol. Rooyackers et al. (2017) also found a significant increase in lactate and counterregulatory hormones such as adrenaline, norepinephrine, GH, and cortisol during HIIT. Jayaeardene et al. (2017) found that, during HIIT, there was an increase in blood ketone and counterregulatory hormones (epinephrine, norepinephrine, and cortisol) [\[17\]](#page-12-16).

Several inflammatory markers are associated with exercise. For example, Robinson et al. (2015) evaluated sedentary individuals at high risk of type 2 diabetes, concluding that CMIT led to a reduction in fasting glucose and in the expression of Toll-like receptor 4 (TLR4), which is an inflammatory marker associated with cardiometabolic risk factors, such as insulin resistance and atherosclerosis, while HIIT did not show such effects [\[33\]](#page-13-12). These findings provide preliminary evidence that moderate-intensity exercise may lead to greater anti-inflammatory responses in overweight or obese inactive individuals. In addition, Durrer et al. (2017) found similar effects through HIIT, by subjecting diabetic and normoglycemic patients to a HIIT session and observing a reduction in tumor necrosis factor α (TNF α), which is a group of cytokines associated with several metabolic conditions such as hypertension, dyslipidemia, obesity, and insulin resistance, and TLR2, immediately after and one hour after training [\[16\]](#page-12-15).

Therefore, it has been demonstrated that physical exercise has anti-inflammatory properties, not only in the adipose tissue, but also impacting the phenotype of immune cells and altering systemic inflammatory mediators such as cytokines and interleukins [\[34\]](#page-13-13).

5. Conclusions

Physical exercise has several acute beneficial effects on the health of the diabetic population, including improvement in capillary and fasting blood glucose, blood glucose profile, postprandial blood glucose, decreased incidence and prevalence of hyperglycemia, improved vascular function and response pressure, and control of inflammatory markers.

Thus, HIIT appears to be a safe and effective alternative for glycemic control and associated factors in diabetics. In addition, most studies comparing HIT with CMIT found better acute effects of HIIT on glycemic control and blood pressure. HIIT could have an effect on inflammatory biomarkers. There is likely to be a relationship between changes in inflammatory profile and fat loss. A controlled diet may be a good complement to reduce the inflammatory profile. Further studies are required to determine whether HIIT is a better, worse or an equivalent alternative to medium-intensity aerobic exercise to improve the inflammatory profile. Based on the results obtained in this study, we also sugest the combination of both protocols. For low physical fitness or high-risk patients, starting training programs with continuous moderate-intensity exercise with the gradual inclusion of HIIT sessions using passive recovery is advised. Larger randomized controlled trials of longer duration than those included in this meta-analysis are required to confirm these results.

Furthermore, the studies evaluated here included patients with type 1 and type 2 diabetes, so there is a limitation when analyzing the impact of HIIT on cardiometabolic parameters, regardless of the type of diabetes, given that type 1 and 2 have different genesis and mechanisms.

Author Contributions: G.d.O.T. and A.C.S.R. contributed to the conception and design of the study; G.d.O.T. and C.S.d.S. conducted the triage of the studies; G.d.O.T., C.S.d.S. and V.R.R. performed the data analysis; G.d.O.T. and C.S.d.S. wrote the first draft of the manuscript; A.C.S.R., V.R.R., C.S.d.S. and G.d.O.T. critically revised the original manuscript for important intellectual content. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable. The protocol for this study was registered in the PROSPERO Systematic Review Protocols Registry under ID: CRD42021250255.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data available on Google Drive. The data presented in this study are openly available at: [https://drive.google.com/drive/folders/1apeVEx9Wc-wnV_oxabUzcKOTyE](https://drive.google.com/drive/folders/1apeVEx9Wc-wnV_oxabUzcKOTyE-po4jY?usp=sharing)[po4jY?usp=sharing.](https://drive.google.com/drive/folders/1apeVEx9Wc-wnV_oxabUzcKOTyE-po4jY?usp=sharing) Accessed on 13 February 2022.

Conflicts of Interest: The authors declare no conflict of interest.

References

- 1. International Diabetes Federation (IDF). IDF Diabetes Atlas. 2019; p. 1. Available online: <https://www.diabetesatlas.org/en/> (accessed on 26 January 2022).
- 2. American Diabetes Association. Standards of Medical Care in Diabetes-2019 Abridged for Primary Care Providers. *Clin. Diabetes* **2019**, *37*, 11–34. [\[CrossRef\]](http://doi.org/10.2337/cd18-0105) [\[PubMed\]](http://www.ncbi.nlm.nih.gov/pubmed/30705493)
- 3. World Health Organization. Global Report on Diabetes. 2016. Available online: [http://apps.who.int/iris/bitstream/handle/10](http://apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf?sequence=1&isAllowed=y) [665/204871/9789241565257_eng.pdf?sequence=1&isAllowed=y](http://apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf?sequence=1&isAllowed=y) (accessed on 26 January 2022).
- 4. De Nardi, A.T.; Tolves, T.; Lenzi, T.L.; Signori, L.U.; da Silva, A.M.V. 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. [\[CrossRef\]](http://doi.org/10.1016/j.diabres.2017.12.017) [\[PubMed\]](http://www.ncbi.nlm.nih.gov/pubmed/29329778)
- 5. Thiel, D.M.; Al Sayah, F.; Vallance, J.K.; Johnson, S.T.; Johnson, J.A. Association between Physical Activity and Health-Related Quality of Life in Adults with Type 2 Diabetes. *Can. J. Diabetes* **2017**, *41*, 58–63. [\[CrossRef\]](http://doi.org/10.1016/j.jcjd.2016.07.004) [\[PubMed\]](http://www.ncbi.nlm.nih.gov/pubmed/27692960)
- 6. Sacre, J.W.; Jellis, C.L.; Jenkins, C.; Haluska, B.A.; Baumert, M.; Coombes, J.S.; Marwick, T.H. A six-month exercise intervention in subclinical diabetic heart disease: Effects on exercise capacity, autonomic and myocardial function. *Metab. Clin. Exp.* **2014**, *63*, 1104–1114. [\[CrossRef\]](http://doi.org/10.1016/j.metabol.2014.05.007)
- 7. Egan, A.M.; Mahmood, W.A.W.; Fenton, R.; Redziniak, N.; Kyaw Tun, T.; Sreenan, S.; Mcdermott, J.H. Barriers to exercise in obese patients with type 2 diabetes. *QJM* **2013**, *106*, 635–638. [\[CrossRef\]](http://doi.org/10.1093/qjmed/hct075)
- 8. Guiraud, T.; Nigam, A.; Gremeaux, V.; Meyer, P.; Juneau, M.; Bosquet, L. High-Intensity Interval Training in Cardiac Rehabilitation. *Sport* **2012**, *42*, 587–605. [\[CrossRef\]](http://doi.org/10.2165/11631910-000000000-00000)
- 9. Weston, K.S.; Wisløff, U.; Coombes, J.S. High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: A systematic review and meta-analysis. *Br. J. Sports Med.* **2014**, *48*, 1227–1234. [\[CrossRef\]](http://doi.org/10.1136/bjsports-2013-092576)
- 10. Kelly, B.M.; Xenophontos, S.; King, J.A.; Nimmo, M.A. An evaluation of low volume high-intensity intermittent training (HIIT) for health risk reduction in overweight and obese men. *BMC Obes.* **2017**, *4*, 1–12. [\[CrossRef\]](http://doi.org/10.1186/s40608-017-0151-7)
- 11. Meyer, P.; Normandin, E.; Gayda, M.; Billon, G.; Guiraud, T.; Bosquet, L.; Nigam, A. High-intensity interval exercise in chronic heart failure: Protocol optimization. *J. Card. Fail.* **2012**, *18*, 126–133. [\[CrossRef\]](http://doi.org/10.1016/j.cardfail.2011.10.010)
- 12. Bird, S.R.; Hawley, J.A. Update on the effects of physical activity on insulin sensitivity in humans. *BMJ Open Sport Exerc. Med.* **2017**, *2*, 1–26. [\[CrossRef\]](http://doi.org/10.1136/bmjsem-2016-000143)
- 13. Francois, M.E.; Durrer, C.; Pistawka, K.J.; Halperin, F.A.; Little, J.P. Resistance-based interval exercise acutely improves endothelial function in type 2 diabetes. *Am. J. Physiol. Heart Circ. Physiol.* **2016**, *311*, H1258–H1267. [\[CrossRef\]](http://doi.org/10.1152/ajpheart.00398.2016) [\[PubMed\]](http://www.ncbi.nlm.nih.gov/pubmed/27638878)
- 14. Liberati, A.; Altman, D.G.; Tetzlaff, J.; Mulrow, C.; Gøtzsche, P.C.; Ioannidis, J.P.; Moher, D. The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. *PLoS Med.* **2009**, *6*, e1000100. [\[CrossRef\]](http://doi.org/10.1371/journal.pmed.1000100) [\[PubMed\]](http://www.ncbi.nlm.nih.gov/pubmed/19621070)
- 15. Maher, C.G.; Sherrington, C.; Herbert, R.D.; Moseley, A.M.; Elkins, M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys. Ther.* **2003**, *83*, 713–721. [\[CrossRef\]](http://doi.org/10.1093/ptj/83.8.713) [\[PubMed\]](http://www.ncbi.nlm.nih.gov/pubmed/12882612)
- 16. Durrer, C.; Francois, M.; Neudorf, H.; Little, J.P. Acute high-intensity interval exercise reduces human monocyte toll-like receptor 2 expression in type 2 diabetes. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* **2017**, *312*, R529–R538. [\[CrossRef\]](http://doi.org/10.1152/ajpregu.00348.2016)
- 17. Jayawardene, D.C.; McAuley, S.A.; Horsburgh, J.C.; La Gerche, A.; Jenkins, A.J.; Ward, G.M.; O'Neal, D.N. Closed-loop insulin delivery for adults with type 1 diabetes undertaking high-intensity interval exercise versus moderate-intensity exercise: A randomized, crossover study. *Diabetes Technol. Ther.* **2017**, *19*, 340–348. [\[CrossRef\]](http://doi.org/10.1089/dia.2016.0461)
- 18. Karstoft, K.; Christensen, C.S.; Pedersen, B.K.; Solomon, T.P.J. The acute effects of interval-Vs continuous-walking exercise on glycemic control in subjects with type 2 diabetes: A crossover, controlled study. *J. Clin. Endocrinol. Metab.* **2014**, *99*, 3334–3342. [\[CrossRef\]](http://doi.org/10.1210/jc.2014-1837)
- 19. Karstoft, K.; Wallis, G.A.; Pedersen, B.K.; Solomon, T.P.J. The effects of interval vs. continuous exercise on excess post-exercise oxygen consumption and substrate oxidation rates in subjects with type 2 diabetes. *Metab. Clin. Exp.* **2016**, *65*, 1316–1325. [\[CrossRef\]](http://doi.org/10.1016/j.metabol.2016.05.017)
- 20. Mendes, R.; Sousa, N.; Themudo-Barata, J.L.; Reis, V.M. High-intensity interval training versus moderate-intensity continuous training in middle-aged and older patients with type 2 diabetes: A randomized controlled crossover trial of the acute effects of treadmill walking on glycemic control. *Int. J. Environ. Res. Public Health* **2019**, *16*, 4163. [\[CrossRef\]](http://doi.org/10.3390/ijerph16214163)
- 21. Mendes, R.; Sousa, N.; Garrido, N.; Rocha, P.; Themudo Barata José, L.; Reis Victor, M. Efficacy of Acute High-Intensity Interval Training in Lowering Glycemia in Patients With Type 2 Diabetes: Diabetes Em Movimento® Pilot Study. *Br. J. Sports Med.* **2013**, *47*, e3. [\[CrossRef\]](http://doi.org/10.1136/bjsports-2013-092558.19)
- 22. Metcalfe, R.S.; Fitzpatrick, B.; Fitzpatrick, S.; McDermott, G.; Brick, N.; McClean, C.; Davison, G.W. Extremely short duration interval exercise improves 24-h glycaemia in men with type 2 diabetes. *Eur. J. Appl. Physiol.* **2018**, *118*, 2551–2562. [\[CrossRef\]](http://doi.org/10.1007/s00421-018-3980-2)
- 23. Rooijackers, H.M.; Wiegers, E.C.; Van Der Graaf, M.; Thijssen, D.H.; Kessels, R.P.C.; Tack, C.J.; De Galan, B.E. A single bout of high-intensity interval training reduces awareness of subsequent hypoglycemia in patients with type 1 diabetes. *Diabetes* **2017**, *66*, 1990–1998. [\[CrossRef\]](http://doi.org/10.2337/db16-1535) [\[PubMed\]](http://www.ncbi.nlm.nih.gov/pubmed/28420673)
- 24. Santiago, É.; Delevatti, R.S.; Bracht, C.G.; Netto, N.; Lisboa, S.C.; Vieira, A.F.; Kruel, L.F.M. Acute glycemic and pressure responses of continuous and interval aerobic exercise in patients with type 2 diabetes. *Clin. Exp. Hypertens.* **2017**, *40*, 179–185. [\[CrossRef\]](http://doi.org/10.1080/10641963.2017.1339075) [\[PubMed\]](http://www.ncbi.nlm.nih.gov/pubmed/28737464)
- 25. Scott, S.N.; Cocks, M.; Andrews, R.C.; Narendran, P.; Purewal, T.S.; Cuthbertson, D.J.; Shepherd, S.O. Fasted high-intensity interval and moderate-intensity exercise do not lead to detrimental 24-hour blood glucose profiles. *J. Clin. Endocrinol. Metab.* **2019**, *104*, 111–117. [\[CrossRef\]](http://doi.org/10.1210/jc.2018-01308)
- 26. Viana, A.A.; Fernandes, B.; Alvarez, C.; Guimarães, G.V.; Ciolac, E.G. Prescribing high-intensity interval exercise by rpe in individuals with type 2 diabetes: Metabolic and hemodynamic responses. *Appl. Physiol. Nutr. Metab.* **2019**, *44*, 348–356. [\[CrossRef\]](http://doi.org/10.1139/apnm-2018-0371) [\[PubMed\]](http://www.ncbi.nlm.nih.gov/pubmed/30230920)
- 27. Gillen, J.B.; Little, J.P.; Punthakee, Z.; Tarnopolsky, M.A.; Riddell, M.C.; Gibala, M.J. Acute high-intensity interval exercise reduces the postprandial glucose response and prevalence of hyperglycaemia in patients with type 2 diabetes. *Diabetes Obes. Metab.* **2012**, *14*, 575–577. [\[CrossRef\]](http://doi.org/10.1111/j.1463-1326.2012.01564.x)
- 28. Terada, T.; Wilson, B.J.; Myette-Cóté, E.; Kuzik, N.; Bell, G.J.; McCargar, L.J.; Boulé, N.G. Targeting specific interstitial glycemic parameters with high-intensity interval exercise and fasted-state exercise in type 2 diabetes. *Metab. Clin. Exp.* **2016**, *65*, 599–608. [\[CrossRef\]](http://doi.org/10.1016/j.metabol.2016.01.003)
- 29. Kirwan, J.P.; Sacks, J.; Nieuwoudt, S. The essential role of exercise in the management of type 2 diabetes. *Clevel. Clin. J. Med.* **2017**, *84*, S15–S21. [\[CrossRef\]](http://doi.org/10.3949/ccjm.84.s1.03)
- 30. Magkos, F.; Tsekouras, Y.; Kavouras, S.A.; Mittendorfer, B.; Sidossis, L.S. Improved insulin sensitivity after a single bout of exercise is curvilinearly related to exercise energy expenditure. *Clin. Sci.* **2008**, *114*, 59–64. [\[CrossRef\]](http://doi.org/10.1042/CS20070134)
- 31. Turnbull, F. Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus: Results of prospectively designed overviews of randomized trials. *Arch. Intern. Med.* **2005**, *165*, 1410–1419. [\[CrossRef\]](http://doi.org/10.1001/archinte.165.12.1410)
- 32. Michael, S.; Graham, K.S.; Oam, G.M.D. Cardiac autonomic responses during exercise and post-exercise recovery using heart rate variability and systolic time intervals-a review. *Front. Physiol.* **2017**, *8*, 1–19. [\[CrossRef\]](http://doi.org/10.3389/fphys.2017.00301)
- 33. Robinson, E.; Durrer, C.; Simtchouk, S.; Jung, M.E.; Bourne, J.E.; Voth, E.; Little, J.P. Short-term high-intensity interval and moderate-intensity continuous training reduce leukocyte TLR4 in inactive adults at elevated risk of type 2 diabetes. *J. Appl. Physiol.* **2015**, *119*, 508–516. [\[CrossRef\]](http://doi.org/10.1152/japplphysiol.00334.2015) [\[PubMed\]](http://www.ncbi.nlm.nih.gov/pubmed/26139217)
- 34. Gleeson, M.; Bishop, N.C.; Stensel, D.J.; Lindley, M.R.; Mastana, S.S.; Nimmo, M.A. The anti-inflammatory effects of exercise: Mechanisms and implications for the prevention and treatment of disease. *Nat. Rev. Immunol.* **2011**, *11*, 607–610. [\[CrossRef\]](http://doi.org/10.1038/nri3041) [\[PubMed\]](http://www.ncbi.nlm.nih.gov/pubmed/21818123)