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TREINAMENTO INTERVALADO DE ALTA INTENSIDADE VERSUS TREINAMENTO CONTÍNUO EM PRÉ-DIABETES E DIABETES TIPO 2: REVISÃO SISTEMÁTICA E META-ANÁLISE

Santa Maria, RS
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Dissertação apresentada ao Programa de Pós-Graduação em Reabilitação Funcional, da Universidade Federal de Santa Maria (UFSM, RS), como requisito parcial para obtenção do título de **Mestre em Reabilitação Funcional.**

Orientador: Prof. Dr. Antônio Marcos Vargas da Silva

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2017

RESUMO

TREINAMENTO INTERVALADO DE ALTA INTENSIDADE VERSUS TREINAMENTO CONTÍNUO EM PRÉ-DIABETES E DIABETES TIPO 2: REVISÃO SISTEMÁTICA E META-ANÁLISE

AUTORA: Angélica Trevisan De Nardi
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No início do século XXI, 5,2% de todos os óbitos no mundo foram atribuídos ao diabetes mellitus (DM), apresentando-se como a quinta principal causa de morte. A prevalência de diabetes também tem aumentando no Brasil, sendo o país com o quarto maior número de indivíduos acometidos por essa doença. O exercício físico, reconhecido como importante ferramenta de prevenção, controle e tratamento de DM e suas complicações, está associado com um menor risco de morbidade e mortalidade nesses indivíduos. Recentemente, o treinamento intervalado de alta intensidade (HIIT) tem sido uma alternativa ao treinamento contínuo de moderada intensidade (MICT) em diferentes populações, com adaptações fisiológicas similares ou superiores, mostrando-se uma estratégia tempo-eficiente, segura e com boa aceitação. Apesar dos estudos individuais apontarem maiores benefícios com a intervenção HIIT sobre alguns desfechos metabólicos e fisiológicos, meta-análises concluíram que HIIT versus MICT não apresentou diferença na resistência a insulina e glicose de jejum em indivíduos com diabetes mellitus tipo 2 (DM2). Desta forma, os efeitos superiores do HIIT ainda são controversos e inconclusivos sobre desfechos fisiológicos e metabólicos em indivíduos pré-diabéticos ou com DM2. Com o propósito de resumir e sintetizar evidências sobre a eficácia e os efeitos do HIIT versus MICT na capacidade funcional, variáveis fisiológicas, controle glicêmico, perfil lipídico e composição corporal em indivíduos pré-diabéticos e com DM2, o nosso estudo caracterizou-se como uma revisão sistemática e meta-análise conduzida conforme o PRISMA. A estratégia de busca foi realizada nas bases de dados PubMed (MEDLINE), EMBASE, PEDro, CENTRAL, Scopus, LILACS e Clinical Trials identificadas na literatura desde o início até julho de 2017. Dois revisores de forma independente selecionaram os estudos, extraíram os dados, avaliaram o risco de viés pela ferramenta da Cochrane e a evidência dos desfechos pela classificação de recomendação, desenvolvimento e avaliação (GRADE). Dos 818 artigos potencialmente relevantes, 7 estudos foram incluídos na revisão sistemática e 5 na meta-análise. Esta revisão incluiu 64 pacientes com pré-diabetes e 120 com DM2. A meta-análise evidenciou que o HIIT promoveu aumento significativo de 3,02 mL/kg/min do VO_2máx (95% IC 1,42 a 4,61) comparado ao MICT em DM2. Nos demais desfechos avaliados, as duas modalidades de exercício induziram a efeitos semelhantes em pré-diabéticos e diabéticos. A maioria dos estudos apresentou incerto risco de viés, além de baixa e muito baixa qualidade de evidência para os desfechos pela GRADE. A partir dessa revisão, conclui-se que o HIIT tem potencial para ser utilizado como modalidade de treinamento em indivíduos pré-diabetes e com DM2, com efeitos similares ao MICT em desfechos cardiometabólicos e superiores sobre a capacidade funcional. PROSPERO CRD42016047151

Palavras-chaves: treinamento intervalado de alta intensidade, pré-diabetes, diabetes mellitus tipo 2, revisão sistemática.

ABSTRACT

HIGH-INTENSITY INTERVAL TRAINING VERSUS CONTINUOUS TRAINING IN PREDIABETES AND TYPE 2 DIABETES: SYSTEMATIC REVIEW AND META-ANALYSIS

AUTHOR: Angélica Trevisan De Nardi
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At the beginning of the 21st century, it was estimated that 5.2% of all deaths in the world to diabetes mellitus (DM), which makes this disease the fifth leading cause of death. The prevalence of diabetes has also increased in Brazil, being the country with the fourth largest number of individuals affected by this disease. Physical exercise, recognized as an important tool for the prevention, control and treatment of DM and its complications, is associated with a lower risk of mortality in these individuals. Recently, high-intensity interval training (HIIT) has been an alternative to continuous moderate intensity training (MICT) in different populations, with similar or higher physiological adaptations, showing a time-efficient, safe and well accepted strategy. Although individual studies show greater benefits with HIIT intervention on some metabolic and physiological outcomes, meta-analyzes have concluded that HIIT versus MICT showed no difference in insulin resistance and fasting glucose in subjects with type 2 diabetes (T2D). Thus, the superior effects of HIIT are still controversial and inconclusive on physiological and metabolic outcomes in prediabetes or T2D subjects. In order to summarize and synthesize evidence on the efficacy and effects of HIIT versus MICT on functional capacity, physiological variables, glycemic control, lipid profile and body composition in prediabetes subjects and T2D, our study was characterized as a systematic review and meta-analysis conducted according to the PRISMA. The search strategy was performed in the PubMed (MEDLINE), EMBASE, PEDro, CENTRAL, Scopus, LILACS and Clinical Trials databases to identify literature from inception to July 2017. Two reviewers independently selected studies, extracted data, assessed risk of bias by the Cochrane tool, and evidence of outcomes by classification of recommendation, evaluation, development, and evaluation (GRADE). From 818 potentially relevant records, 7 studies were included in systematic review and 5 in meta-analysis. This review included 64 patients with prediabetes and 120 with T2D. The meta-analysis evidenced that HIIT promoted a significant increase of 3.02 mL/kg/min of VO_2max (95% CI 1.42 to 4.61) compared to MICT in T2D. In the other outcomes evaluated, the two modalities of exercise induced similar effects in prediabetes and diabetics. Most of the studies present an uncertain risk of bias, low and very low quality of evidence for the outcomes assessed by GRADE. From this review, it is concluded that HIIT has the potential to be used as a training modality in prediabetes and T2D individuals, with similar effects to MICT in cardiometabolic outcomes and superior on functional capacity. PROSPERO CRD42016047151.

Keywords: high-intensity interval training, prediabetes, type 2 diabetes mellitus, systematic review.

SUMÁRIO

1. INTRODUÇÃO

A prevalência de diabetes mellitus (DM) tem aumentado nas últimas três décadas e está crescendo mais rapidamente em países de baixa e média renda (WORLD HEALTH ORGANIZATION, 2016). O Brasil é considerado o país com o quarto maior número de indivíduos acometidos por essa patologia (ALMEIDA-PITITTO et al., 2015). No início do século XXI, 5,2% de todos os óbitos no mundo foram atribuídos a essa doença, apresentando-se como a quinta principal causa de morte (MILECH et al., 2016). Estima-se que em 2030 haverá 400 milhões de pessoas com DM em todo o mundo (WILD et al., 2004; WORLD HEALTH ORGANIZATION, 2016).

A diabetes é uma doença metabólica caracterizada por hiperglicemia resultante de defeitos da secreção de insulina, da ação da insulina, ou ambos (AMERICAN DIABETES ASSOCIATION, 2017). A maioria dos casos de diabetes se enquadra em duas categorias: diabetes tipo 1 ou tipo 2. Na diabetes de tipo 1, responsável por 5-10% dos casos, a causa é uma deficiência absoluta da secreção de insulina resultante da destruição autoimune das células β, produtoras de insulina no pâncreas. A diabetes mellitus de tipo 2 (DM2), que acomete entre 90-95% dos casos, resulta de um defeito progressivo da secreção de insulina e resistência à insulina (HOMA) (AMERICAN DIABETES ASSOCIATION, 2017).

A hiperglicemia crônica da diabetes está associada a danos em longo prazo que induzem a múltiplas disfunções e falência orgânicas, especialmente em olhos, rins, nervos, coração e vasos sanguíneos (AMERICAN DIABETES ASSOCIATION, 2017), aumentando a taxa de morbidade e mortalidade (HAMADA; GULLIFORD, 2016; ROGLIC; UNWIN, 2010).

De acordo com a Organização Mundial de Saúde (WORLD HEALTH ORGANIZATION, 2006), o alto risco de desenvolver diabetes relaciona-se com parâmetros glicêmicos acima do normal, como observado em indivíduos pré-diabéticos, dos quais cerca de 70% desenvolverá a diabetes (AMERICAN DIABETES ASSOCIATION, 2017). Os critérios de diagnóstico para pré-diabetes se baseiam em glicose de jejum alterada, com valores de 100–125mg/dL (5,6–6,9mmol/L), tolerância à glicose diminuída de 140-199mg/dL (7,8-11,0mmol/L) e níveis de hemoglobina glicada (HbA1c) entre 5,7-6,4% (AMERICAN DIABETES ASSOCIATION, 2017; WORLD HEALTH ORGANIZATION, 2006). Além disso, o risco para o desenvolvimento da diabetes aumenta com a idade, obesidade, falta de atividade física e ocorrem com maior frequência em pessoas hipertensas ou com dislipidemia

(ASSOCIATION AMERICAN DIABETES, 2017; WORLD HEALTH ORGANIZATION, 2006).

Considerando a alta prevalência de DM2 e seu impacto relevante sobre a saúde da população, é necessário rastreamento e diagnóstico precoce, com o intuito de reduzir as taxas de morbidade e mortalidade. Os critérios para diagnóstico incluem valor de glicose de jejum ≥126 mg/dL (7,0 mmol/L), resposta ao teste oral de tolerância à glicose ≥200 mg/dL (11,1 mmol/L), HbA1c de 6,5% ou superior ou em pacientes com sintomas clássicos de hiperglicemia ou crise hiperglicêmica (AMERICAN DIABETES ASSOCIATION, 2017).

Dentre as formas de prevenção e tratamento, o exercício físico está associado com um menor risco de morbidade (COLBERG et al., 2010; THOMAS; ELLIOTT; NAUGHTON, 2006) e mortalidade nesses indivíduos (SLUIK et al., 2012; WEN et al., 2011). Os efeitos benéficos do exercício no controle glicêmico em pré-diabéticos ou com DM2 têm sido demonstrados em vários estudos (BOULE et al., 2008; EARNEST, 2008; SCHWINGSHACKL et al., 2014; THOMAS; ELLIOTT; NAUGHTON, 2006; UMPIERRE et al., 2011), utilizando diferentes modalidades de treinamento.

Meta-análise mostrou que o exercício aeróbico, o exercício de resistência e a combinação de ambos foram associados a declínios nos níveis de HbA1c em comparação com os participantes do grupo controle, especialmente se realizado por um tempo superior a 150 minutos por semana (UMPIERRE et al., 2011). Também foi observado que o aconselhamento do exercício físico combinado com apoio dietético está associado com níveis menores de HbA1c (UMPIERRE et al., 2011). A combinação de várias intervenções que incluem dieta, treinamento físico aeróbico e de resistência são eficazes em reduzir a perda de peso, melhorar a glicemia de jejum alterada e a tolerância à glicose em populações adultas pré-diabéticas (AGUIAR et al., 2014), além de proporcionar custo-efetividade para prevenir a DM2 entre indivíduos com maior risco (TOSCANO et al., 2015).

O exercício também é associado à melhora da aptidão física, dos fatores de risco cardiovasculares modificáveis, escore de risco de 10 anos para doença arterial coronariana (BALDUCCI et al., 2010), qualidade de vida (MYERS et al., 2013; NICOLUCCI et al., 2012) e ao menor risco de mortalidade em indivíduos diabéticos (SLUIK et al., 2012).

Conforme a American Diabetes Association e o American College of Sports Medicine, recomenda-se um mínimo de 150 minutos/semana de exercício aeróbico moderado, em associação com 2-3 sessões por semana de treinamento de resistência (AMERICAN DIABETES ASSOCIATION, 2017; COLBERG et al., 2016), equivalentes a 75

minutos/semana de atividade vigorosa (AMERICAN DIABETES ASSOCIATION, 2017; GARBER, C. E. et al., 2011).

Embora ambas as modalidades de exercício sejam apropriadas para a maioria dos indivíduos com diabetes (COLBERG et al., 2016), a alta intensidade parece ser superior ao exercício contínuo na melhora de desfechos metabólicos (GARBER, C. E. et al., 2011; JANSSEN; ROSS, 2012; MITRANUN et al., 2014), capacidade funcional, redução de fatores de risco cardiovasculares (HOLLEKIM-STRAND et al., 2014; MITRANUN et al., 2014) e redução da mortalidade (WEN et al., 2011).

Neste contexto, vem se destacando os protocolos de treinamento intervalado de alta intensidade (HIIT), como uma alternativa ao treinamento moderado contínuo (MICT) em diferentes populações (BABRAJ et al., 2009; GIBALA et al., 2006; GIBALA et al., 2012; GRACE et al., 2017; HWANG; WU; CHOU, 2011; XIE et al., 2017) com adaptações fisiológicas similares ou superiores, mostrando-se uma estratégia tempo-eficiente (GIBALA et al., 2012; GIBALA; MCGEE, 2008; WEN et al., 2011), segura e com boa aceitação (BARTLETT et al., 2011; JUNG et al., 2015; JUNG; BOURNE; LITTLE, 2014; THUM et al., 2017). O HIIT é caracterizado por breves explosões repetidas de exercícios intensos, intercalados com períodos de descanso ou de exercício de baixa intensidade (GIBALA et al., 2012; GIBALA; MCGEE, 2008). A escolha do protocolo HIIT com respeito à intensidade do exercício, duração do intervalo e recuperação ativa ou passiva tem uma profunda e variável influência sobre as respostas fisiológicas (FRANCOIS; LITTLE, 2015).

As possíveis modalidades de exercícios usados para o HIIT incluem caminhadas, ciclismo, natação, esportes em equipe, treinamentos em circuito e exercícios de resistência (FRANCOIS; LITTLE, 2015). A intensidade do exercício pode ser determinada utilizando o consumo máximo de oxigênio (VO_2máx), percentual de VO_2máx, frequência cardíaca máxima (FCmáx), percentual da FCmáx, FC de reserva ou percepção subjetiva de esforço (escala de Borg) (GARBER et al., 2011; JUNEAU et al., 2014; MANN; LAMBERTS; LAMBERT, 2013).

O HIIT traz uma série de benefícios em desfechos clínicos e respostas glicêmicas em indivíduos saudáveis (BATACAN et al., 2017), obesos (FISHER et al., 2015), com DM2 (GRACE et al., 2017) e desordens cardiometabólicas (HWANG; WU; CHOU, 2011). Foram observadas melhoras em HbA1c, HOMA, glicose e insulina de jejum, índice de massa corporal (GRACE et al., 2017), lipídeos sanguíneos, diminuição da gordura corporal (BATACAN et al., 2017; FISHER et al., 2015), melhora da circunferência da cintura, frequência cardíaca em repouso e pressão arterial (BATACAN et al., 2017). O maior impacto

sobre VO_2máx também foi favorável ao HIIT quando comparado ao exercício contínuo de moderada intensidade em sujeitos saudáveis (BACON et al., 2013; MILANOVIC; SPORIS; WESTON, 2015), com DM2 (GRACE et al., 2017; JELLEYMAN et al., 2015), doença cardiovascular (HWANG; WU; CHOU, 2011; WESTON et al., 2014; XIE et al., 2017) síndrome metabólica e obesidade (HWANG; WU; CHOU, 2011; WESTON et al., 2014).

Além disso, o caráter tempo-eficiente do HIIT melhora rapidamente o controle glicêmico em indivíduos pré-diabéticos (FRANCOIS et al., 2014; LITTLE et al., 2014), além de reduzir HOMA, glicose de jejum, HbA1c em indivíduos com DM2 quando comparado ao grupo sem exercício (ALVAREZ et al., 2016; CASSIDY et al., 2016; JELLEYMAN et al., 2015). Entretanto, quando comparado o HIIT ao MICT, meta-análises não demonstraram diferença na resistência a insulina e glicose de jejum em indivíduos DM2 (JELLEYMAN et al., 2015; LIUBAOERJIJIN et al., 2016).

De acordo com o estudo de Jelleyman et al. (2015), o HIIT comparado ao MICT nas variáveis de HOMA, glicose de jejum e HbA1c não apresentou diferença significativa quando considerado o subgrupo DM2 e síndrome metabólica. Ao contrário desses resultados, recente meta-análise evidenciou melhores efeitos do HIIT na redução da HbA1c em indivíduos com DM2 (LIUBAOERJIJIN et al., 2016). Portanto, esses achados apontam para controvérsias quanto aos efeitos metabólicos destas duas modalidades de exercício em sujeitos com DM2 (JELLEYMAN et al., 2015; LIUBAOERJIJIN et al., 2016).

É importante destacar que ambas as revisões apresentam limitações. Jelleyman et al., 2015, considerou na mesma análise de subgrupo os indivíduos com DM2 e síndrome metabólica. Porém, a síndrome metabólica é definida por um conjunto de fatores de risco como adiposidade abdominal, dislipidemia, hipertensão arterial sistêmica e resistência à insulina que aumentam as chances de desenvolver DM2 (GRUNDY et al., 2004; WILSON et al., 2005). Sendo assim, os resultados encontrados podem apresentar viés por considerar no mesmo subgrupo indivíduos com respostas metabólicas distintas. Já a revisão sistemática realizada por Liubaoerjijin et al., 2016, utilizou abordagens distintas para o exercício de alta intensidade, como treinamento intervalado e treinamento contínuo. Na meta-análise geral, os autores combinaram diferentes intervenções (HIIT versus MICT e treinamento contínuo de baixa intensidade, e MICT versus treinamento contínuo de alta e baixa intensidade). Ambas meta-análises não reportaram variáveis fisiológicas.

Ensaios clínicos randomizados mostram controvérsias dos efeitos similares e superiores do HIIT ao MICT na pressão arterial sistólica e diastólica (HOLLEKIM-STRAND et al., 2014; KARSOFT et al., 2013; MITRANUN et al., 2014), no perfil lipídico e na

composição corporal de indivíduos com DM2 (KARSOFT et al., 2013; TERADA et al., 2013; MITRANUN et al., 2014; MAILLARD et al., 2016) e pré-diabéticos (JUNG et al., 2015; ROBINSON et al., 2015). Embora o HIIT tenha maior influência no aumento do VO_2máx do que o MICT em pacientes com desordens cardiometabólicas (HWANG; WU; CHOU, 2011; JELLEYMAN et al., 2015; WESTON; WISLØFF; COOMBES, 2014; XIE et al., 2017), indivíduos pré-diabéticos (JUNG et al., 2015; ROBINSON et al., 2015) e com DM2 (KARSOFT et al., 2013; HOLLEKIM-STRAND et al., 2014; MITRANUN et al., 2014), ainda há incertezas sobre a intensidade de exercício mais eficaz na busca do melhor controle cardiometabólico.

Dessa forma, revisões sistemáticas comparando o HIIT ao MICT podem fornecer uma perspectiva mais precisa sobre a evidência atual dos efeitos de diferentes intensidades nas variáveis fisiológicas e metabólicas de indivíduos pré-diabéticos e com DM2. Assim, o objetivo do presente estudo foi comparar os efeitos do treinamento intervalado de alta intensidade versus treinamento contínuo de moderada intensidade sobre marcadores de saúde cardiometabólicos em indivíduos pré-diabéticos e com DM2.

A questão de pesquisa consiste: O HIIT apresenta efeitos superiores ao MICT na melhora da capacidade funcional (estimada pela medida do VO_2máx), de marcadores fisiológicos e metabólicos em pré-diabetes e DM2?

O artigo é apresentado nas páginas seguintes e padronizado conforme as normas da revista ***Archives of Physical Medicine and Rehabilitation,*** fator de impacto 3,289, Qualis A1 (Educação Física).

2. ARTIGO

HIGH-INTENSITY INTERVAL TRAINING VERSUS CONTINUOUS TRAINING IN PREDIABETES AND TYPE 2 DIABETES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Abstract

Objective: To compare the effect of high-intensity interval training (HIIT) versus moderate-intensity continuous training (MICT) on functional capacity and cardiometabolic health markers of individuals with prediabetes and type 2 diabetes (T2D).

Data sources: Literature searching was carried out until July 2017 in PubMed (MEDLINE), EMBASE, PEDro, CENTRAL, Scopus and LILACS databases selecting papers related to topic research and unpublished documents were pursued through Clinical Trials (website).

Study selection: Randomized clinical trials that compared the HIIT and MICT in prediabetes and T2D adults (18 years or over) with or without cardiovascular risk factors.

Data extraction: Two reviewers independently selected the studies, extracted the data, and assessed the risk of bias according to Cochrane Handbook. Quality of evidence for each outcome effect estimate was graded according to the GRADE working group of evidence.

Data synthesis: From 818 potentially relevant records, 7 studies were included in systematic review and 5 in meta-analysis. This review included 64 patients (83% females) with prediabetes and 120 with T2D (57% females). HIIT promoted significantly increased of 3.02mL/kg/min of VO_2max (95% IC 1.42 to 4.61) compared to MICT. No differences were found between two modalities of exercises considering the outcomes HbA1c, systolic and diastolic blood pressure, total cholesterol, HDL and LDL cholesterol, triglycerides, BMI and waist-to-hip. Most of the studies presented unclear risk of bias, and low and very low quality of evidence evaluated by GRADE.

Conclusion: HIIT has potential to be used as a treatment modality for prediabetes and T2D individuals, proposed as a time-efficient intervention that induces cardiometabolic adaptations similar to MICT and provides greater benefits in terms of VO_2max improvement in T2D. However, it is suggested more studies with greater methodological rigor and with a larger sample size for strengthening the quality of current evidence. PROSPERO: CRD42016047151.

Keywords: high-intensity interval training, prediabetes, type 2 diabetes mellitus, systematic review

Abbreviations:

T2D: Type 2 diabetes

HIIT: High-intensity training interval

MICT: Moderate intensity training continuous

VO_2max: Maximum oxygen consumption

HbA1c: Glycated hemoglobin

HOMA: Insulin resistance

BMI: Body mass index

HDL: High-density lipoprotein

LDL: Low-density lipoprotein

Introduction

Type 2 diabetes (T2D) has increased in the last decades, accounts for 90–95% of all cases of diabetes, defined as "noninsulin-dependent diabetes" with progressive loss of insulin secretion and peripheral insulin resistance[1]. A high-risk for diabetes development, besides the increase in age, obesity, and lack of physical activity, are individuals with prediabetes, which present blood glucose concentrations higher than normal, but not high enough to be classified as diabetes[1,2].

The lifestyle change with adoption and maintenance of physical activity is one of the cornerstones to prevent and delay the prediabetes and T2D incidence. Aerobic exercise training is associated with beneficial effects on clinical outcomes and glycemic profile in T2D[3], with decrease in glycated hemoglobin (HbA1c)[3,4], increase maximum oxygen consumption (VO_2max)[3–5] and benefit on insulin sensitivity[6]. Moreover, it has been established in literature that regular physical activity can reduce the risk of T2D in people with impaired glucose tolerance[7,8].

American Diabetes Association recommends at least 150min/week of moderate to vigorous intensity physical activity or shorter durations (minimum 75min/week) of vigorous intensity or interval training and dietary changes to prevent or delay the onset of T2D in populations at high risk and with prediabetes[9]. However, while diabetic patients seem to comply well with dietetic and pharmacologic interventions, their exercise levels remain low[1,10]. Time lack has been appointed how the main barrier to non adherence to physical activity[11,12]. In this sense, high-intensity interval training (HIIT) is an option in order to encourage physical activity participation and reduce the risk of chronic diseases[13]. This exercise modality implies in a training programmed by brief intermittent bursts of intense exercise, interspersed with periods of rest or low-intensity exercise[10,14].

It is suggested that more vigorous physical activity may provide similar or greater benefits than moderate intensity exercise for metabolic health[15–17], cardiovascular disease risk factors[15,18]; as well as in all-cause mortality reduction[19]. Previous reviews have shown inconsistent results when assessing the effects of moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT) on metabolic profile of individuals with T2D[16,17]. Important limitations were observed in these reviews, such as considering in the same analysis, individuals with metabolic syndrome and T2D[17], and different approaches with interval and continuous training to high-intensity exercise[16]. Furthermore, the effects of different exercise intensities on physiological variables in individuals with prediabetes and T2D are still uncertain and were not reported in both reviews.

Therefore, this systematic review and meta-analysis aimed to evaluate randomized clinical trials that compared the effect of HIIT versus MICT on physiological and metabolic variables of individuals with prediabetes and T2D. The research question was as follows: Is HIIT more effective than MICT in the improving of functional capacity and cardiometabolic health markers in individuals with prediabetes and T2D?

Methods

This systematic review and meta-analysis was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement[20] and recorded in International Prospective Register of Systematic Review (PROSPERO) – CRD42016047151.

Search strategy and study selection

A comprehensive literature search was conducted through the PubMed (MEDLINE), EMBASE, Physiotherapy Evidence Database (PEDro), Cochrane Central Register of

Controlled Trials (CENTRAL), Scopus and LILACS databases to identify literature from inception to July 2017 related to research question. The search was conducted with no publication year or language limits.

The search terms used included *type 2 diabetes mellitus, prediabetes, high-intensity interval training, moderate intensity continuous training*, and terms associated with a high-sensitivity strategy for the search of randomized clinical trials[21]. The complete search strategy used on PubMed (MEDLINE) database can be assessed online in the systematic review protocol https://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016047151. The search strategy was adapted for the other databases and the results of searches also were cross-checked to locate and eliminate duplicates. Reference lists of the included papers and of reviews were also screened. To reduce publication bias, unpublished documents were pursued through Clinical Trials (website).

Eligibility criteria

Two reviewers (ATD and TT) independently assessed the identified publications and selected them by title and abstract based on the following inclusion criteria: clinical trials that compared the use of HIIT and MICT in prediabetes and T2D adults (18 years or over) with or without cardiovascular risk factors. When only a relevant title without a listed abstract was available, a full copy of the article was assessed for evaluation. The reviewers were previously trained and calibrated for papers selection (Kappa= 0.90). Any discrepancies were solved through discussion and consensus of a third reviewer (AMVS). For the purpose of this review, we considered the modalities of high-intensity interval training and moderate intensity continuous training as reported in the primary studies.

A final decision about inclusion was made based on the full-text paper of the potentially relevant studies in accordance with the following exclusion criteria: (1) non-

random allocation of subjects or no 2 or more-arm longitudinal clinical trial; (2) to include patients with metabolic syndrome, gestational diabetes and diabetic neuropathy; (3) to evaluate HIIT or MICT associated with another intervention, e.g. diet restriction, resistance training; (4) to compare the effect of different intensities of exercise on fasting; (5) to report short intervention time (<2 weeks); (6) absence of similar follow-up for subjects of both groups evaluated in the same way; and (7) did not assessed at least one of the following outcome: VO_2max (measured for functional capacity), HbA1c, fasting glucose, fasting insulin, insulin resistance, systolic and diastolic blood pressure, total cholesterol, high density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, triglycerides, body mass index (BMI), waist circumference, waist-to-hip ratio assessed pre and post intervention. In case of studies reporting the same sample, we included those that contemplated more outcomes.

Data extraction

Two reviewers (ATD and TT) independently collected the following data from eligible studies: author and publication year; individual participants' demographic characteristics (age, sex); number of individuals per group (intervention and control); exercise type and intensity; duration and frequency of training; dropout and adherence. When papers provided insufficient data for inclusion in the analysis, the correspondent author were contacted to determine whether additional data could be provided.

Assessment of risk of bias and quality of evidence

Both reviewers (ATD and TT) independently assessed (Kappa=0.90) the risk of bias based on the published specific study design-related risk bias assessed forms (*Cochrane*

Handbook for Systematic Reviews of Interventions 5.0.1)[22]. The criteria assessment included random sequence generation and allocation concealment, blinding of subjects and examiners, blinding of outcome assessors, description of losses and exclusions and selective reporting. The evaluation of the studies was performed by rating each of the study criteria as low, high or unclear risk of bias (no information or uncertainty over the potential for bias). For the final classification of risk of bias, disagreements between the reviewers were solved by consensus. Authors were contacted via e-mail (at least twice) for missing or unclear information.

Quality of evidence for each outcome effect estimate was classified according to the grading of recommendation, assessment, development and evaluation (GRADE)[23].

Statistical analysis

Data analyses were performed according to the Cochrane statistical guidelines[22] using Review Manager software (RevMan version 5.3; Cochrane Collaboration, Copenhagen, Denmark, 2014). Only the data from studies with T2D individuals were meta-analyzed. In the study conducted by Mitranun et al.[24], we performed the imputation of standard deviation for fasting glucose, HbA1c, total cholesterol, LDL, HDL, triglycerides by the central tendency value based on the studies included in this review.

In each study, weighted mean differences (WMDs) between the HIIT and MICT at baseline and end-of-trial were calculated using a random effect model for outcomes fasting glucose, HbA1c, VO_2max, systolic and diastolic blood pressure, total cholesterol, HDL and LDL cholesterol, triglycerides, BMI and waist-to-hip. Statistical significance was defined as $p \leq 0.05$.

Statistical heterogeneity of the treatment effect among studies was assessed using Cochran's Q-Test and the inconsistency I^2 test, in which values above 30% and 50% were considered indicative of moderate and high heterogeneity[22].

Results

Study selection

The search strategy identified 818 potentially relevant records. After exclusion duplicates and screening titles and abstracts, we retrieved 27 full-text papers for more detailed information. A total of 7 clinical trials were included for the qualitative synthesis and 5 for the quantitative analyses. The process of study selection and the reasons for exclusions are summarized in Fig. 1.

Study characteristics

The main characteristics of the included studies are presented in Table 1. The studies were published between 2013 and 2016 and had a total of 64 patients with prediabetes (83% females), average age of 51.5±10 years, and 120 patients with T2D (57% females), average age of 61.7±6 years.

The duration of studies ranged from 12 to 16 weeks for T2D groups and 2 to 4 weeks for prediabetes groups. Different protocols of HIIT and MICT were used in the included studies. The exercise type, length session and intensity varied widely between studies. All the exercises were performed post meal and monitored by direct supervision or objective measures such as heart rate monitors or accelerometers. Moreover, subjects were instructed to not alter their dietary intake habit and medication throughout the study period.

Three studies with T2D[24–26], reported data on adherence, being of 91% and 96% for HIIT and MICT, respectively. Only one study with prediabetes[27] reported adherence to the intervention, occurring in 89% in the HIIT group and in 71% in the MICT group.

In the study of Terada et al., one participant was excluded from fasting glucose and HbA1c analyses due to discontinuation of medication[25].

Effects of interventions

VO_2max

Maximal O_2 consumption was reported by three studies in 89 participants with T2D[24,26,28] (Fig 2A). The mean difference in the VO_2max from was 3.02 mL/kg/min (95%CI 1.42 to 4.61, I^2=0%), significantly favoring HIIT (p<0.001).

Two studies with 64 prediabetes individuals reported that HIIT and MICT improved VO_2max after intervention, however without difference between the two exercise conditions[27,29].

Fasting glucose

Baseline and post-intervention fasting glucose was reported by four studies[24–26,30] that including a total of 82 participants with T2D (Fig 2B). There was no change in fasting glucose when comparing HIIT with MICT [WMD=0.11 (95%CI:-0.45, 0.67, I^2=0%, p=0.70)].

In prediabetes individuals, only one study reported this outcome, with a total of 38 participants. MICT showed a greater reduction in fasting glucose (5.9±1.0 vs 5.6±1.0), which was not seen after HIIT (5.6±1.2 vs 5.7±1.1)[29].

HbA1c

All the studies with T2D evaluated HbA1c, with a total of 119 participants[24–26,28,30]. There was a trend of improvement in HbA1c with HIIT, but the difference between interventions was not statistically significant [WMD=-0.17 (95%CI: -0.36 to 0.02, I^2= 0%, p=0.07)] (Fig 2C).

The studies with prediabetes did not evaluate this outcome.

HOMA

Two studies with T2D reported the insulin resistance outcome[24,28] with a total of 65 participants. In both studies, HOMA decreased after the MICT session (2.8±1.3 vs 2.3±1.5)[24], (2.6±1 vs 2.5±0.9)[28]. However, a decreased HOMA value following HIIT was observed only in one study (3.1±1.4 vs 2.5±1.1)[24]. Significant differences were not found between groups.

One study with prediabetes, with a total of 38 participants, demonstrated neither that HIIT nor MICT impacted in the HOMA concentrations[29].

Fasting insulin

Of all clinical trials included in this study, only one with prediabetes, with a total of 38 participants, demonstrated that neither HIIT nor MICT impacted in the fasting insulin concentrations[29].

Blood pressure

Three studies with T2D, with a total of 89 participants, demonstrated that there was no change in systolic [WMD=-2.92 (95%CI -7.62 to 1.78, I^2=0%, p=0.22)] and diastolic blood pressure [WMD=-2.14 (95%CI -4.37 to 0.09, I^2=0%, p=0.06)] between HIIT and MICT[24,26,28].

One study with prediabetes, with a total of 26 participants, demonstrated that systolic and diastolic blood pressure decreased at one-month follow-up for both conditions[27]; however, only systolic blood pressure reported significant difference (132±14 vs 124±10; p<0.001).

Total cholesterol

Four studies with T2D, with a total of 83 participants[24–26,30], demonstrated that there was no change in total cholesterol between HIIT and MICT groups [WMD=-0.16 (95%CI -0.68 to 0.35, I^2= 40%, p=0.50)].

The studies with prediabetes did not evaluate this outcome.

HDL and LDL cholesterol

Four studies with T2D, with a total of 83 participants[24–26,30], found no difference between the interventions in the HDL [WMD=0.07 (95% CI -0.06 to 0.19, I^2= 47%, p=0.29)] and LDL cholesterol [WMD=-0.06 (95%CI -0.41 to 0.28, I^2=67%, p=0.71)].

The studies with prediabetes did not evaluate this outcome.

Triglycerides

Four studies with T2D, with a total of 83 participants[24–26,30], demonstrated that there was no change in triglycerides between HIIT and MICT groups [WMD=0.14 (95%CI -0.27 to 0.55, I^2= 27%,p=0.49)].

The studies with prediabetes did not evaluate this outcome.

BMI

All the studies with T2D evaluated BMI, with a total of 120 participants[24–26,28,30]. There was no difference in BMI [WMD=-0.62 (95%CI -1.32 to 0.08, I^2=0%, p=0.08)] comparing HIIT and MICT.

The studies with prediabetes demonstrated that BMI decreased after the two exercise conditions[27,29]; however, without significance difference between the groups.

Waist-to-hip ratio

Four studies with T2D, with a total of 83 participants[24–26,30] demonstrated that there was no change in waist-to-hip ratio between HIIT and MICT groups [WMD=0.02 (95%CI -0.02 to 0.05, I^2=69%, p=0.33)].

The studies with prediabetes did not evaluate this outcome.

Waist circumference

Two studies with T2D[25,30], with a total of 31 participants demonstrated that waist circumference decreased after both intervention, but no significant difference between groups.

One study with prediabetes, with a total of 26 participants, demonstrated that waist circumference did not change significantly from baseline to one-month follow up in either HIIT or MICT ($p > 0.05$)[27].

Risk of bias

The risk of bias final assessment of the included studies is displayed in Table 2. Statement of the randomization method was observed in all evaluated papers; however, the method adequate used to generate the random sequence was reported only in one study[25]. Most studies were scored as low risk of bias for "incomplete outcome data". In the other domains predominated the risk of bias unclear. Low-quality evidence was judged according to the GRADE for HbA1c and VO_2max outcomes and very low quality for fasting glucose outcome (Table 3).

Discussion

This is the first systematic review that compared the effect of the HIIT versus MICT on functional capacity and physiological markers in prediabetes and T2D adults. The main finding of this meta-analysis was that the VO_2max values were significantly increased in individuals with T2D submitted to the HIIT [WMD=3.02 (95%IC 1.42 to 4.61), I^2=0%, p=0.0002]. Although the reduction on HbA1c, diastolic blood pressure and BMI were not significant, there was a trend of greater effects by HIIT. The results revealed that the two modalities of exercise induced similar effects on variables fasting glucose, systolic blood pressure, total cholesterol, HDL, LDL, triglycerides and waist to hip-ratio.

Previous meta-analyses showed that HIIT and MICT are effective for improvements functional capacity, evidenced by increased VO_2max in different populations[15,17,31–34]. However, HIIT is likely to elicit greater increases VO_2max that MICT in patients with cardiometabolic disorder[15,17,32,34] and in healthy individuals[31,33]. The superiority of HIIT for aerobic fitness has important clinical implications given that VO_2max is a stronger predictor of cardiovascular risk[35] and it improvement is associated with reduction of morbidity and mortality for cardiovascular diseases as well as diabetes prevalence[15,36,37]. The mechanisms involved in the superiority of HIIT can be justified by changes in stroke volume of the heart induced by increased cardiac contractility[38,39], increased skeletal muscle oxidative capacity and changes in glucose transport[39–42], which improves mitochondrial function generating more ATP[43,44], thus increasing aerobic capacity.

Both modalities of exercise did not significantly affect fasting glucose [WMD=0.11 (95%IC -0.45 to 0.67), I^2=0%, p= 0.68] and HbA1c values [WMD=-0.17 (95%IC -0.36 to 0.02), I^2= 0%, p=0.07]; however, the HIIT had a greater tendency to improve glycated

hemoglobin in T2D. Any reduction in HbA1c is likely to reduce the risk of macrovascular and microvascular complications in T2D[45].

In prediabetes, only one study reported the fasting glucose outcome, which showed significant reduction to MICT[29]. Recent meta-analyses also have shown no difference between HIIT and MICT on fasting glucose in a group of patients that included T2D[16,17]. On the other hand, the analysis by Liubaoerjijin et al.[16] observed greater improvement in HbA1c with HIIT [WMD=-0.23 (95%IC -0.43 to -0.02), I^2=0%, p=0.03][16]. We could not confirm these findings because the systematic review by Jelleyman et al.[17] presented a broad inclusion criterion and the authors considered for same subgroup analysis individuals with metabolic syndrome and T2D, which demonstrate different metabolic responses. Moreover, the review by Liubaoerjijin et al.[16] considered different approaches for high-intensity exercise, such as interval and continuous training and did not include the study by Hollekim-Strand et al.[28], which was included in our review together with study from Maillard et al.[30].

A possible explanation for absence of difference on metabolic outcomes would be the free living dietary intake between the participants of studies and the time between the last exercise session and the measurement of the blood parameters that varied between the studies. In the study by Karsoft et al.[26], the measurement was performed at least 48 hours after and up to 8 days after the last exercise session; Mitranun et al.[24] measured 48-72 hours after the last exercise session, and the study by Terada et al.[25] and Maillard et al.[30] did not reported this data. The long interval after the intervention of exercise may cause detraining effects in individuals, which results in similar benefits between groups[26].Thus, the feasibility and efficacy for glucose regulation comparing the two modalities of exercise need further investigation.

The insulin resistance was evaluated in two studies with T2D[24,28] and one in prediabetes individuals[29]; the fasting insulin was verified only in one of the studies with

prediabetes[29], and thus, the data could not be meta-analyzed. We emphasize the importance to evaluate these outcomes in prediabetes and T2D due the molecular defect in the insulin action to be associated with increased risk for cardiovascular disease[46,47].

HIIT showed no superior effect on systolic and diastolic blood pressure in prediabetes and T2D individuals, though there was a trend of greater decrease in the diastolic blood pressure in T2D [MD=-2.14 (95%IC -4.37 to -0.09), p=0.06, I^2=0%]. The mechanisms involved in the blood pressure decline mediated by exercise training can be to improvements in peripheral vascular structure and function, with an increase in popliteal artery distensibility[42] and endothelial function[48]. The lack of significant difference observed in blood pressure comparing HIIT versus MICT is possible due to few clinical trials reporting this variable.

In relation the lipid profile of individuals with T2D, the results of this meta-analysis suggest that there is no significant difference from one intervention to another. This can be justified because were individuals within the normal range of total cholesterol, HDL and LDL, which did not caused great changes after exercise. Moreover, the fact there was no modification and control of diet may attenuate the beneficial effects of exercise on lipid profile. However, is important to point out that comparing the total cholesterol, HDL, LDL and triglycerides between HIIT and MICT groups showed heterogeneity of 40%, 47%, 67% and 27% in the I^2 test, respectively. This can be justified by methodological differences between studies as such as duration, frequency and intensity of exercises. Studies in prediabetes individuals did not evaluate these outcomes.

This review also found that HIIT decreased BMI more than MICT in both populations, however without statistical significant effect in prediabetes[27,29] and T2D individuals [WMD=-0.62 (95% IC -1.32 to 0.08), I^2=0%, p=0.08]. Most individuals with prediabetes and T2D included in the studies were considered overweight (≥25–29.99 kg/m^2) and obese (≥30

kg/m^2)[49]. It is important to point out that high BMI is associated with higher risk for developing T2D[50,51] and complications cardiovascular[51,52]. Moreover, there is relationship between BMI at the time of a diabetes diagnosis and the risk of death[1,53,54]. Thus, the tendency of HIIT to reduce BMI is vitally important to public health and needs further investigation.

The waist circumference and waist-to-hip ratio are indicators to central obesity and also have been associated with T2D risk[50,55]. Our meta-analysis showed similar effect with the HIIT and MICT for the waist-to-hip ratio, however significant heterogeneity was also observed (I^2=69%), which may be partly justified by lower methodological quality of included studies. While the waist circumference was reported in few studies[25,27,30] and did not demonstrate superiority of some type of exercise. Further studies need to explore the relationship between central adiposity, diabetes, cardiovascular disease and greater long-term cardiometabolic risk.

In this systematic review, quality of studies was assessed using Cochrane risk of bias tool[22] and most items (77.8%) were classified as showing a unclear risk of bias due to insufficient information or uncertainty about the potential for bias. This finding demonstrated that well-designed future studies should be conducted. According to the GRADE, the risk of bias for outcomes VO_2max, fasting glucose and HbA1c were considered serious because in most of the studies, blinding and randomization were not properly performed. Furthermore, few studies were included and with small sample size.

Limitations

Our meta-analyses consists some limitations. First, only five studies with T2D and two with prediabetes individuals were included, with small sample size in each group (≤20) and mostly with methodological limitations. The studies used different HIIT protocols with variety of exercise modalities, intervals, intensities, volumes, duration and different ways of determining the intensities of HIIT or MICT. Another challenge was the lack of clear

information on some data. We are grateful to the authors who provided these data[25,26,28,30], but in other cases we had to estimate standard deviation values from other similar trials in the review[24]. Based on these aspects, there is a need more research with greater methodological rigor and with larger sample size for strengthening the quality of current evidence and determine which modality of exercise would be better on cardiometabolic markers in prediabetes and T2D individuals.

Conclusion

The results of our meta-analysis demonstrate that HIIT has potential to be used as a treatment modality for prediabetes and individuals with T2D, proposed as a time-efficient intervention that induces cardiometabolic adaptations similar to MICT. In addition, HIIT may provide greater benefits on functional capacity in patients with T2D. Such improvements may reflect important implications for the health, well-being, quality of life, and morbidity of individuals with T2D.

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References

1. American Diabetes Association. Standards of medical care in diabetes - 2017. *Diabetes Care* 2017;40(Suppl 1):S1-S135.

2. Tabák, A. G., Herder, C., Rathmann, W., Brunner, E. J. & Kivimäki, M. Prediabetes: a high-risk state for diabetes development. *Lancet* 2012;379(9833):2279-2290. doi:10.1016/S0140-6736(12)60283-9.

3. Grace, A., Chan, E., Giallauria, F., Graham, P. L. & Smart, N. A. Clinical outcomes and glycaemic responses to different aerobic exercise training intensities in type II diabetes: a systematic review and meta - analysis. *Cardiovasc. Diabetol.* 2017;16(1):37. doi:10.1186/s12933-017-0518-6.

4. Umpierre, D., Ribeiro, P. A., Kramer, C. K. *et al.* Physical activity advice only or structured with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. *JAMA* 2017;305(17):1970-1979. doi: 10.1001/jama.2011.576.

5. Boule, N. G., Haddad, E., Kenny, G. P., Wells, G. A. & Sigal, R. J. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. *JAMA* 2000;286(10):1218-1227. doi:10.1001/jama.286.10.1218.

6. Way, K. L., Hackett, D. A., Baker, M. K. & Johnson, N. A. The effect of regular exercise on insulin sensitivity in type 2 diabetes mellitus: a systematic review and meta-anlysis. *Diabetes Metab J* 2016;40(4):253-271. doi: 10.4093/dmj.2016.40.4.253

7. Aune, D., Norat, T., Leitzmann, M., Tonstad, S. & Vatten, L. J. Physical activity and the risk of type 2 diabetes: a systematic review and dose – response meta-analysis. *Eur. J. Epidemiol.* 2015;30(7):529-542. doi:10.1007/s10654-015-0056-z.

8. Jeon, C., Lokken, R., Hu, F. & van Dam, R. Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review. *Diabetes Care* 2007;30(3):744-752. doi:10.2337/dc06-1842.

9. Colberg, S. R., Sigal R. J., Fernhall, B. *et al.* Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. *Diabetes* 2016;39(11):2065-2079. doi:10.2337/dc16-1728.

10. Gibala, M. J., Little, J. P., Macdonald, M. J. & Hawley, J. A. Physiological adaptations to low-volume, high-intensity interval training in health and disease. *J Physiol.* 2012;590(5):1077-1084. doi:10.1113/jphysiol.2011.224725.

11. Kimm, S. Y., Glynn, N. W., McMahon, R. P., Voorhees, C. C., Striegel-Moore, R. H., Daniels, S. R. *et al.* Self-perceived barriers to activity participation among sedentary adolescent girls. *Med Sci Sport. Exerc.* 2006;38(3):534-540. doi:10.1249/01.mss.0000189316.71784.dc.

12. Trost, S. G., Owen, N., Bauman, A. E., Sallis, J. F. & Brown, W. Correlates of adults' participation in physical activity: review and update. *Med Sci Sport. Exerc* 2002;34(12):1996-2001. doi:10.1249/01.MSS.0000038974.76900.92.

13. Gibala, M. J. & Little, J. P. Just HIT it! A time-efficient exercise strategy to improve muscle insulin sensitivity. *J Physiol.* 2010;588(Pt 18):3341-3342. doi:10.1113/jphysiol.2010.196303.

14. Gibala, M. J. & Mcgee, S. L. Metabolic adaptations to short-term high-intensity interval training: a little pain for a lot of gain? *Exerc Sport Sci Rev.* 2008;36(2):58-63. doi: 10.1097/JES.0b013e318168ec1f.

15. Hwang, C.-L., Wu, Y.-T. & Chou, C.-H. Effect of aerobic interval training on exercise capacity and metabolic risk factors in people with cardiometabolic disorders. *J. Cardiopulm. Rehabil. Prev.* 2011;31(6):378-385. doi:10.1097/HCR.0b013e31822f16cb.

16. Liubaoerjijin, Y., Terada, T., Fletcher, K. & Boule, N. G. Effect of aerobic exercise intensity on glycemic control in type 2 diabetes: a meta-analysis of head-to-head randomized trials. *Acta Diabetol* 2016;53(5):769-781. doi:10.1007/s00592-016-0870-0.

17. Jelleyman, C., Yates, T., O'Donovan, G. *et al.* The effects of high-intensity interval training on glucose regulation and insulin resistance: a meta-analysis. *Obes Rev* 2015;16(11):942-961. doi:10.1111/obr.12317.

18. Balducci, S., Zanuso, S., Cardelli, P. *et al.* Effect of high- versus low-intensity supervised aerobic and resistance training on modifiable cardiovascular risk factors in type 2 diabetes; The Italian Diabetes and Exercise Study (IDES). *PLoS One* 2012;7(11):e49297. doi:10.1371/journal.pone.0049297.

19. Wen, C. P., Wai, J. P., Tsai, M. K. *et al.* Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *Lancet* 2011;378(9798):1244-1253. doi:10.1016/S0140-6736(11)60749-6.

20. Moher, D., Liberati, A., Tetzlaff, J. & Altman, D. G. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statment. *Ann. Inter Med* 2009;151(4):264-269. doi: 10.1371/journal.pmed.1000097

21. Robinson, K. A. & Dickersin, K. Development of a highly sensitive search strategy for the retrieval of reports of controlled trials using PubMed. *Int J Epidemiol.* 2002;31(1):150-153.

22. Higgins, J. P. T. & Green, S. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0*. *The Cochrane Collaboration*. 2011.

23. Balshem, H., Helfand, M., Schünemann, H. J. *et al.* GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol.* 2011;64(4):401-406. doi:10.1016/j.jclinepi.2010.07.015.

24. 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 Sport.* 2014;24(2):e69-76. doi:10.1111/sms.12112.

25. Terada, T., Friesen, A., Chahal, B. S., Bell, G. J., McCargar, L. J., Boulé, N. G. 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.

26. Karsoft, K., Winding, K., Knudsen, S. H. *et al.* The effects of free-living interval-walking training on glycemic control, body composition, and physical fitness in type 2 diabetic patients. *Diabetes Care* 2013;36(2):228-236. doi:10.2337/dc12-0658.

27. Jung, M. E., Bourne, J. E., Beauchamp, M. R., Robinson, E. & Little, J. P. High-intensity interval training as an efficacious alternative to moderate-intensity continuous training for adults with prediabetes. *J Diabetes Res.* 2015;2015. doi:10.1155/2015/191595.

28. Hollekim-Strand, S. M., Bjørgaas, M. R., Albrektsen, G., Tjønna, A. E., Wisløff, U., Ingul, C. B. 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.2014.07.971.

29. Robinson, E., Durrer, C., Simtchouk, S. *et al.* 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(5):508-516. doi:10.1152/japplphysiol.00334.2015.

30. Maillard, F., Rousset, S., Pereira, B. *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.

31. Bacon, A. P., Carter, R. E., Ogle, E. A. & Joyner, M. J. VO_2 max Trainability and High Intensity Interval Training in Humans: A Meta-Analysis. *PLoS One* 2013;8(9):e73182. doi:10.1371/journal.pone.0073182.

32. Weston, M., Taylor, K. L., Batterham, A. M. & Hopkins, W. G. Effects of low-volume high-intensity interval training (HIT) on fitness in adults: a meta-analysis of controlled and non-controlled trials. *Sport. Med* 2014;44(7):1005-1017. doi:10.1007/s40279-014-0180-z.

33. Milanović, Z., Sporiš, G. & Weston, M. Effectiveness of high-intensity interval training (HIT) and continuous endurance training for VO_2max improvements: a systematic review and meta-analysis of controlled trials. *Sport. Med* 2015;45(10):1469-1481. doi:10.1007/s40279-015-0365-0.

34. Xie, B., Yan, X., Cai, X. & Li, J. Effects of high-intensity interval training on aerobic capacity in cardiac patients: a systematic review with meta-analysis. *Biomed Res Int* 2017;2017(5420840). doi: 10.1155/2017/5420840.

35. Myers, J., McAuley, P., Lavie, C. J., Despres, J. P., Arena, R., Kokkinos, P. Physical activity and cardiorespiratory fitness as major markers of cardiovascular risk: their independent and interwoven importance to health status. *Prog. Cardiovasc. Dis.* 2015;57(4):306-314. doi:10.1016/j.pcad.2014.09.011.

36. 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 Sport. Med* 2013;48(16):1227-1234. doi:10.1136/bjsports-2013-092576.

37. Batacan, R. J., Duncan, M., Dalbo, V., Tucker, P. & Fenning, A. Effects of high-

intensity interval training on cardiometabolic health: a systematic review and meta-analysis of intervention studies. *Br J Sport. Med* 2017;51(6):494-503. doi:10.1136/bjsports-2015- 095841.

38. Helgerud, J., Høydal, K., Wang, E. *et al.* Aerobic high-intensity intervals improve VO_2max more than moderate training. *Med Sci Sport. Exerc.* 2007;39(4):665-671. doi:10.1249/mss.0b013e3180304570.

39. Cassidy, S., Thoma, C., Hallsworth, K. *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.

40. Burgomaster, K. A., Heigenhauser, G. J. F., Gibala, M. J., Kirsten, A. & Heigenhauser, G. J. F. Effect of short-term sprint interval training on human skeletal muscle carbohydrate metabolism during exercise and time-trial performance. *J Appl Physiol* 2006;100(6):2041-2047. doi:10.1152/japplphysiol.01220.2005.

41. Burgomaster, K. A., Cermak, N. M., Phillips, S. M, Benton, C. R, Bonen, A., Gibala, M. J. Divergent response of metabolite transport proteins in human skeletal muscle after sprint interval training and detraining. *Am J Physiol Regul Integr Comp Physiol* 2007;292(5):1970-1976. doi:10.1152/ajpregu.00503.2006.

42. Rakobowchuk, M., Tanguay, S., Burgomaster, K. A., Howarth, K. R., Gibala, M. J., MacDonald, M. J. Sprint interval and traditional endurance training induce similar improvements in peripheral arterial stiffness and flow-mediated dilation in healthy humans. *Am J Physiol Regul Integr Comp Physiol* 2008;295(1):R236-R243. doi:10.1152/ajpregu.00069.2008.

43. Wisløff, U., Støylen, A. , Loennechen, J. P. *et al.* Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. *Circulation* 2007;115(24):3086-3095. doi:10.1161/CIRCULATIONAHA.106.675041.

44. Little, J. P., Gillen, J. B., Percival, M. E. *et al.* Low-volume high-intensity interval training reduces hyperglycemia and increases muscle mitochondrial capacity in patients with type 2 diabetes. *J Appl Physiol* 2011;111(6):1554-1560. doi:10.1152/japplphysiol.00921.2011.

45. Stratton, I. M., Adler, A. I., Neil, H. A. *et al.* Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes: prospective observational study. *BMJ*. 2000;321(7258):405–412.doi: 10.1136/bmj.321.7258.405

46. Defronzo, R. A. & Abdul-ghani, M. Assessment and treatment of cardiovascular risk in prediabetes : impaired glucose tolerance and impaired fasting glucose. *AJC* 2011;108(3):3B-24B. doi:10.1016/j.amjcard.2011.03.013.

47. Kim, J., Chae, Y. K. & Chernoff, A. The risk for coronary heart disease according to insulin resistance with and without type 2 diabetes. *Endocr Res.* 2013;38(4):195-205. doi:10.3109/07435800.2013.766800.

48. Tjønna, A. E., Lee, S. J., Rognmo, Ø. *et al.* Aerobic interval training versus continuous moderate exercise as a treatment for the metabolic syndrome: a pilot study. *Circulation* 2008;118(4):346-355. doi:10.1161/CIRCULATIONAHA.108.772822.

49. WHO Consultation. Obesity: preventing and managing the global epidemic. *World Heal Organ Tech Rep Ser*. 2000;894.

50. Vazquez, G., Duval, S., Jacobs, D. R. & Silventoinen, K. Comparison of body mass

index, waist circumference, and waist/hip ratio in predicting incident diabetes: a meta-analysis. *Epidemiol Rev* 2007;29:115-128. doi:10.1093/epirev/mxm008.

51. Gray, N., Picone, G., Sloan, F. & Yashkin, A. The relationship between BMI and onset of diabetes mellitus and its complications. *South Med.* 2015;108(1):29-36. doi:10.14423/SMJ.0000000000000214.

52. Li, W., Katzmarzyk, P. T., Horswell, R. *et al.* Body mass index and heart failure among patients with type 2 diabetes mellitus. *Circ Hear. Fail* 2015;8(3):455-463. doi:10.1161/CIRCHEARTFAILURE.114.001837.

53. Katzmarzyk, P. T., Hu, G., Cefalu, W. T., Mire, E. & Bouchard, C. The importance of waist circumference and BMI for mortality risk. *Diabetes Care* 2013;36(10):3128-3130. doi:10.2337/dc13-0219.

54. Tobias, D., Pan, A., Jackson, C. L. *et al.* Body-mass index and mortality among adults with incident type 2 diabetes. *N Engl J Med* 2014;370(3):233-244. doi:10.1056/NEJMoa1304501.

55. Jafari-koshki, T., Mansourian, M., Mohsen, S. & Amini, M. Association of waist and hip circumference and waist-hip ratio with type 2 diabetes risk in first-degree relatives. *J. Diabetes Complications* 2016;30(6):1050-1055. doi:10.1016/j.jdiacomp.2016.05.003.

Figure legends

Figure 1. Flow Diagram

Figure 2. Effect of high-intensity training versus moderate intensity continuous training on maximum oxygen consumption (VO_2max) (A), fasting glucose (B), glycated hemoglobin (HbA1c) (C).

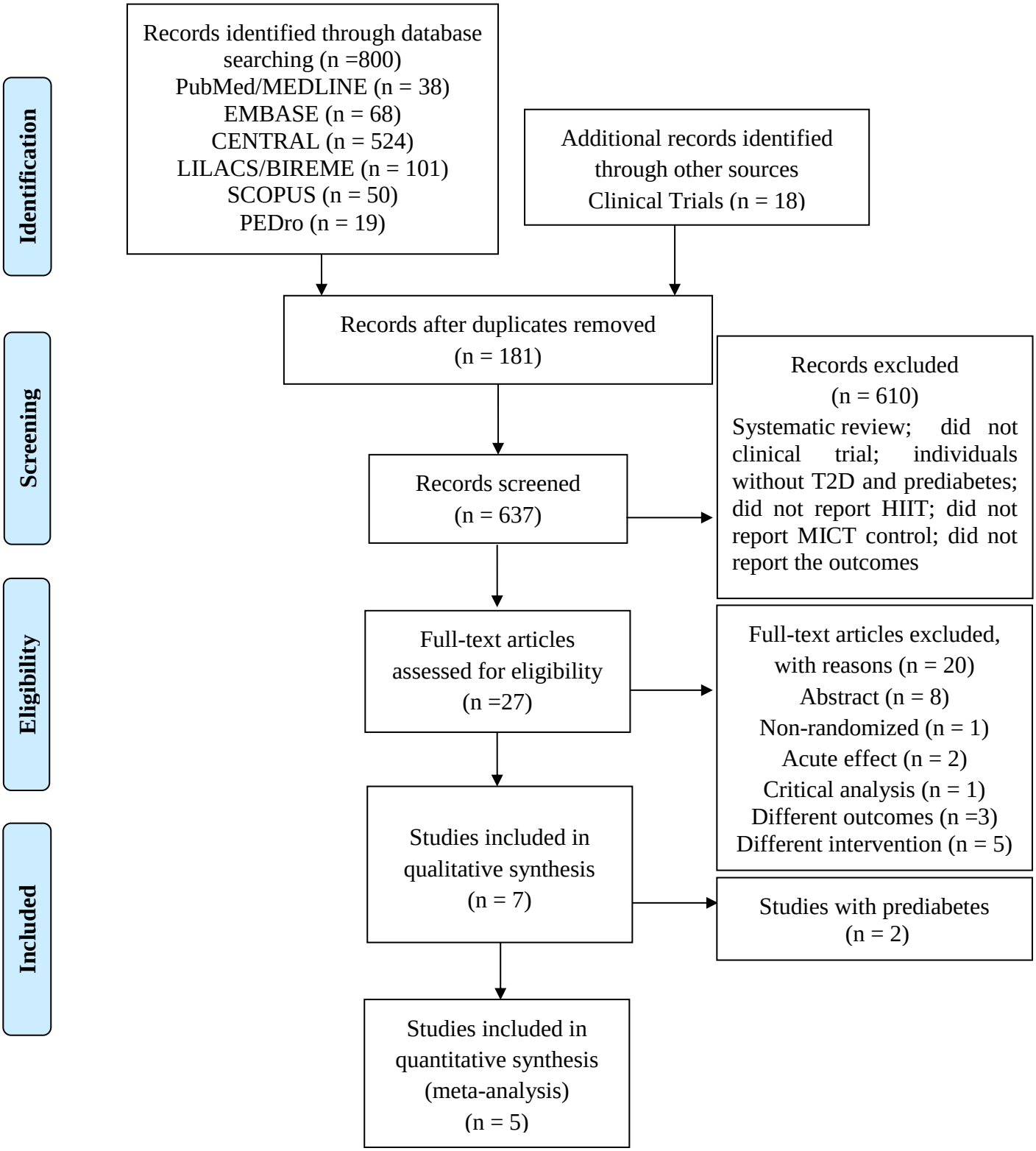
Identification
Screening
Eligibility
Included
Records identified through database searching (n =800)
PubMed/MEDLINE (n = 38)
EMBASE (n = 68)
CENTRAL (n = 524)
LILACS/BIREME (n = 101)
SCOPUS (n = 50)
PEDro (n = 19)
Additional records identified through other sources
Clinical Trials (n = 18)
Records after duplicates removed (n = 181)
Records screened (n = 637)
Records excluded (n = 610)
Systematic review; did not clinical trial; individuals without T2D and prediabetes; did not report HIIT; did not report MICT control; did not report the outcomes
Full-text articles assessed for eligibility (n =27)
Full-text articles excluded, with reasons (n = 20)
Abstract (n = 8)
Non-randomized (n = 1)
Acute effect (n = 2)
Critical analysis (n = 1)
Different outcomes (n =3)
Different intervention (n = 5)
Studies included in qualitative synthesis (n = 7)
Studies with prediabetes (n = 2)
Studies included in quantitative synthesis (meta-analysis) (n = 5)

Figure 1

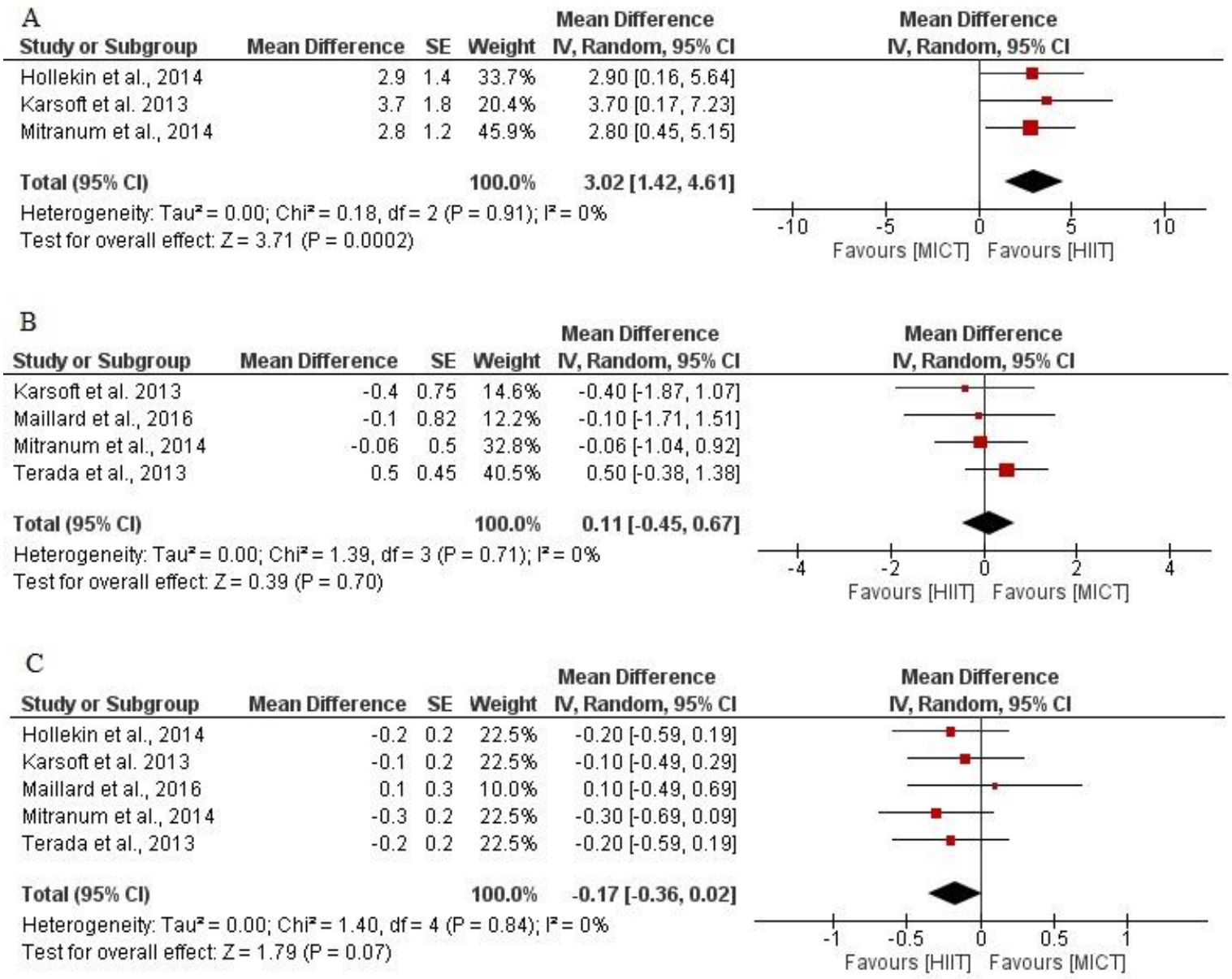
A
Study or Subgroup | Mean Difference | SE | Weight | Mean Difference IV, Random, 95% CI
Hollekin et al., 2014 2.9 1.4 33.7% 2.90 [0.16, 5.64]
Karsoft et al. 2013 3.7 1.8 20.4% 3.70 [0.17, 7.23]
Mitranum et al., 2014 2.8 1.2 45.9% 2.80 [0.45, 5.15]
Total (95% CI) 100.0% 3.02 [1.42, 4.61]
Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 2 (P = 0.91); I² = 0%
Test for overall effect: Z = 3.71 (P = 0.0002)
Mean Difference IV, Random, 95% CI
-10 -5 0 5 10
Favours [MICT] Favours [HIIT]
B
Study or Subgroup | Mean Difference | SE | Weight | Mean Difference IV, Random, 95% CI
Karsoft et al. 2013 -0.4 0.75 14.6% -0.40 [-1.87, 1.07]
Maillard et al., 2016 -0.1 0.82 12.2% -0.10 [-1.71, 1.51]
Mitranum et al., 2014 -0.06 0.5 32.8% -0.06 [-1.04, 0.92]
Terada et al., 2013 0.5 0.45 40.5% 0.50 [-0.38, 1.38]
Total (95% CI) 100.0% 0.11 [-0.45, 0.67]
Heterogeneity: Tau² = 0.00; Chi² = 1.39, df = 3 (P = 0.71); I² = 0%
Test for overall effect: Z = 0.39 (P = 0.70)
Mean Difference IV, Random, 95% CI
-4 -2 0 2 4
Favours [HIIT] Favours [MICT]
C
Study or Subgroup | Mean Difference | SE | Weight | Mean Difference IV, Random, 95% CI
Hollekin et al., 2014 -0.2 0.2 22.5% -0.20 [-0.59, 0.19]
Karsoft et al. 2013 -0.1 0.2 22.5% -0.10 [-0.49, 0.29]
Maillard et al., 2016 0.1 0.3 10.0% 0.10 [-0.49, 0.69]
Mitranum et al., 2014 -0.3 0.2 22.5% -0.30 [-0.69, 0.09]
Terada et al., 2013 -0.2 0.2 22.5% -0.20 [-0.59, 0.19]
Total (95% CI) 100.0% -0.17 [-0.36, 0.02]
Heterogeneity: Tau² = 0.00; Chi² = 1.40, df = 4 (P = 0.84); I² = 0%
Test for overall effect: Z = 1.79 (P = 0.07)
Mean Difference IV, Random, 95% CI
-1 -0.5 0 0.5 1
Favours [HIIT] Favours [MICT]

Figure 2

Table 1. Characteristics of included studies

Author and year	Participants	Groups	Sample size (%female)	Age, y (SD)	Duration (frequency)	Exercise type	Length/ session (min)	Intensity (%VO_2peak)*	Dropout (%)	Adherence (%)
HOLLEKIN et al. 2014	T2D	HIIT	20(40%)	58.6(5)	12 weeks 3 days/week	Walking uphill on a treadmill.	40	4 x 4min 90-95% HRmax	17%	NR
		MICT	17(35%)	54.7(5.3)		Walking/ cycling	≥10min - 210min/week	~70% HRmax	26%	NR
KARSTOFT et al. 2013	T2D	HIIT	12(42%)	57.5(8.3)	16 weeks 5 days/week	Free-living Walking	60	3min >70% 3min < 70%	8%	85%
		MICT	12(33%)	60.8(7.6)		Free-living Walking	60	> 55%	8%	94%
MAILLARD et al. 2016	T2D	HIIT	8(100%)	68.2(5.4)	16 weeks 2 days/week	Cycling program	20	60 cycles x (8s 77-85% HRmax, 12s active recovery)	0%	NR
		MICT	8(100%)	70.1(6.8)		Cycling program	40	55 - 60% HRR	11%	NR
MITRANUN et al. 2014	T2D	HIIT	14(64%)	61.2(10.5)	12 weeks 3 days/week	Walking on treadmill	Wk_{1-2} = 30 Wk_{3-6} = 30 Wk_{7-12} =40	50% 4x1min 80% - 4min 50% 6x1min 85% - 4min 60%	7%	≥80%
		MICT	14(64%)	61.7(10.1)		Walking on treadmill	Wk_{1-2} = 30 Wk_{3-6} = 30 Wk_{7-12} =40	50% 60% 65%	7%	≥80%
TERADA et al. 2013	T2D	HIIT	7(43%)	62(3)	12 weeks 5days/week	Walking on treadmill / cycling	Wk_{1-4} = 30 Wk_{5-8} = 45 Wk_{9-12} =60	1min 100% VO_2reserve 3min 20% VO_2reserve	0%	97%
		MICT	8(50%)	63(5)		Walking on treadmill / cycling	Wk_{1-4} = 30 Wk_{5-8} = 45 Wk_{9-12}=60	40% VO_2reserve	0%	97%

Table 1 (Continued)

Author and year	Participants	Groups	Sample size (%female)	Age, y (SD)	Duration (frequency)	Exercise type	Length/ session (min)	Intensity (%VO_2 peak)*	Dropout (%)	Adherence (%)
JUNG et al. 2015	Prediabetes	HIIT	10 (80%)	51(10)	4 weeks 3days/week	Walking	25	4-10 x1 min ~90% HRpeak/ 1min of low intensity	33%	89%
		MICT	16 (88%)	51(10)		Walking	20-50	~65% HRpeak	6%	71%
ROBINSON et al. 2015	Prediabetes	HIIT	20 (85%)	52(10)	2 weeks 5days/week	Walking	4-10	4-10 x 1min ~85-90% HRpeak/ 1min rest period	0%	NR
		MICT	18 (79%)	52(10)		Walking	20-50	~60-65% HRpeak	5%	NR

HIIT High-intensity interval training; MICT Moderate-intensity continuous training; y year; HRmax heart rate maximum; HRR heart rate reserve; * Unless stated otherwise; NR not reported

Table 2. Risk of bias

Author and year	Bias domains					
	Randomization	Allocation concealment	Blinding (participants and personnel)	Blinding (outcome assessment)	Incomplete outcome data	Selective reporting
Hollekin-Strand et al. 2014	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Karstoft et al. 2013	Unclear	Unclear	Unclear	Low	Low	Low
Maillard et al. 2016	Unclear	Unclear	Unclear	Unclear	Low	Low
Mitranum et al. 2014	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Terada et al. 2013	Low	Unclear	High	Unclear	Low	Low
Jung et al. 2015	High	Unclear	Unclear	Unclear	Low	Unclear
Robinson et al. 2015	Unclear	Unclear	Unclear	Unclear	Low	Unclear

"Low" (low risk of bias), "High" (high risk of bias) or "Unclear" (no information or uncertainty over the potential for bias).

Table 3. Quality of evidence

Quality assessment						№ of patients		Effect	Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**HIIT**	**MICT**	**Absolute (95% CI)**		
VO_2max										
3	randomized trials	serious [a]	not serious	not serious	serious [b]	46	43	MD 3.02 ml/kg/min higher (1.42 lower to 4.61 higher)	⊕⊕◯◯ LOW	IMPORTANTE
Fasting glucose										
4	randomized trials	serious [a]	not serious	not serious	serious [b]	41	41	MD 0.11 mmol/L higher (0.45 lower to 0.67 higher)	⊕◯◯◯ VERY LOW	CRÍTICO
HbA1c										
5	randomized trials	serious [a]	not serious	not serious	serious [b]	61	58	MD 0.17 % lower (0.36 lower to 0.02 higher)	⊕⊕◯◯ LOW	CRÍTICO

CI: Confidence interval; **MD:** Mean difference

a. Most of the studies were not blinded and problems with the form of randomization were detected. b. Few studies and few patients assessed.

3. CONCLUSÃO

A partir da realização dessa revisão sistemática e meta-análise, é possível afirmar que o treinamento intervalado de alta intensidade tem potencial para ser usado como uma modalidade de prevenção e tratamento em indivíduos pré-diabetes e diabetes tipo 2.

O HIIT comparado ao treinamento contínuo de moderada intensidade proporcionou similares adaptações cardiometabólicas em indivíduos pré-diabéticos e com diabetes tipo 2; com benefícios superiores sobre o consumo máximo de oxigênio em diabéticos, o que representa importantes implicações clínicas, pois reflete na melhora da capacidade funcional e contribui na redução dos fatores de risco cardiovasculares.

A falta de tempo é um dos principais motivos a não adesão e à prática de atividade física regular; o que dificulta a realização de 150 minutos de exercício por semana, conforme recomendado para este perfil de população. Sendo assim, ofertar programas de treinamento de alta intensidade supervisionados é uma estratégia interessante e adequada para a promoção da saúde, prevenção e tratamento de indivíduos pré-diabéticos e diabetes tipo 2. Além da eficiência temporal, o HIIT é considerado uma estratégia segura, com boa aceitação, com resultados cardiometabólicos similares ao exercício contínuo e superiores sobre a capacidade funcional.

Entretanto, devido algumas limitações encontradas nos estudos primários como pequeno tamanho amostral, randomização não adequada e falta de clareza nas informações de aspectos metodológicos, destaca-se a importância de conduzir pesquisas bem delineadas para fortalecer a qualidade das evidências atuais.

Dessa forma, acredito ter encerrado esta etapa na minha vida acadêmica com substancial contribuição para o meio científico no que tange o uso do treinamento intervalado de alta intensidade em pré-diabetes e diabetes tipo 2. Saliento a imensa satisfação com a realização e o resultado deste trabalho, o qual me proporcionou desafios e grande aprendizado. Acredito que deparar-se com novas informações e conteúdos é sempre uma estratégia para o crescimento pessoal e profissional. Além disso, a interação com pesquisadores, pós-graduandos e acadêmicos, contribuiu de maneira inigualável para a produção do conhecimento e desenvolvimento da ciência.

REFERÊNCIAS BIBLIOGRÁFICAS

AGUIAR, E. J. et al. Efficacy of interventions that include diet, aerobic and resistance training components for type 2 diabetes prevention: a systematic review with meta-analysis. **Int J Behav Nutr and Phys Act**., v. 11, n. 2, p. 1–10, 2014.

ALMEIDA-PITITTO, B. et al. Type 2 diabetes in Brazil: epidemiology and management. **Diabetes, Metab Syndr Obes**., v. 8, p. 17–28, 2015.

ALVAREZ, C. et al. Low-volume high-intensity interval training as a therapy for type 2 diabetes. **Int J Sports Med**., v.37, n.9, p. 723-729, 2016.

AMERICAN DIABETES ASSOCIATION. Standards of medical care in diabetes — 2017. **J Diabetes Care**, v. 40, n. Suppl 1, p. S1-S135, 2017.

BABRAJ, J. A. et al. Extremely short duration high intensity interval training substantially improves insulin action in young healthy males. **BMC Endocr Disord**., v. 9, n. 3, p. 1–8, 2009.

BACON, A. P. et al. VO_2max trainability and high intensity interval training in humans: a meta-analysis. **PLoS One**, v. 8, n. 9, p. e73182, 2013.

BALDUCCI, S. et al. Effect of an intensive exercise intervention strategy on modifiable cardiovascular risk factors in subjects with type 2 diabetes mellitus. **Arch Intern Med**., v. 170, n. 20, p. 1794–1803, 2010.

BARTLETT, J. D. et al. High-intensity interval running is perceived to be more enjoyable than moderate-intensity continuous exercise: Implications for exercise adherence. J Sports Sci, v. 29, n.6, p. 547-553, 2011.

BATACAN, R. B. J. et al. Effects of high-intensity interval training on cardiometabolic health: a systematic review and meta-analysis of intervention studies. **Br J Sports Med**., v. 51, n. 6, p. 494–503, 2017.

BOULE, N. G. et al. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus a meta-analysis of controlled clinical trials. **JAMA**, v. 286, n. 10, p. 11–15, 2001.

CASSIDY, S. 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**, v. 59, n. 1, p. 56–66, 2016.

COLBERG, S. R. et al. Exercise and type 2 diabetes: The American College of Sports Medicine and the American Diabetes Association: Joint position statement. **Diabetes Care**, v. 33, n. 12, e147-67, 2010.

COLBERG, S. R. et al. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. **Diabetes Care**, v. 39, n. 11, p. 2065–2079, 2016.

EARNEST, C. P. Exercise interval training: An improved stimulus for improving the physiology of pre-diabetes. **Med Hypotheses**, v. 71, n. 5, p. 752–761, 2008.

FISHER, G. et al. High intensity interval- vs moderate intensity- training for improving cardiometabolic health in overweight or obese males: a randomized controlled trial. **PLoS**

One, v. 10, n. 10, p. e0138853, 2015.

FRANCOIS, M. E. et al. “Exercise snacks” before meals: a novel strategy to improve glycaemic control in individuals with insulin resistance. **Diabetologia**, v.57, n.7, p. 1437–1445, 2014.

FRANCOIS, M. E.; LITTLE, J. P. Effectiveness and safety of high-intensity interval training in patients with type 2 diabetes. **Diabetes Spectr**., v. 28, n. 1, p. 39–44, 2015.

GIBALA, M. et al. Physiological adaptations to low-volume, high-intensity interval training in health and disease. **J Physiol**., v. 590, n. Pt 5, p. 1077–1084, 2012.

GIBALA, M. J. et al. Short-term sprint interval versus traditional endurance training: similar initial adaptations in human skeletal muscle and exercise performance. **J Physiol**., v. 575, n. Pt 3, p. 901–911, 2006.

GIBALA, M. J.; MCGEE, S. L. Metabolic adaptations to short-term high-intensity interval training: a little pain for a lot of gain? **Exerc Sport Sci Rev**., v. 36, n. 2, p. 58–63, 2008.

GRACE, A. et al. Clinical outcomes and glycaemic responses to different aerobic exercise training intensities in type II diabetes: a systematic review and meta - analysis. **Cardiovas Diabetol**., v. 16, n. 1, p. 37, 2017.

GRUNDY, S. M. et al. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. **Circulation**, v. 109, n. 3, p. 433–438, 2004.

HAMADA, S.; GULLIFORD, M. C. Mortality in individuals aged 80 and older with type 2 diabetes mellitus in relation to glycosylated hemoglobin, blood pressure, and total cholesterol. **J Am Geriatr Soc**., v. 64, n.7, p. 1425–1431, 2016.

HOLLEKIM-STRAND, S. M. et al. High-intensity interval exercise effectively improves cardiac function in patients with type 2 diabeles mellitus and diastolic dysfunction. **J Am Coll Cardiol**., v. 64, n. 16, p. 1758–1760, 2014.

HWANG, C.L.; WU, Y.T.; CHOU, C.H. Effect of aerobic interval training on exercise capacity and metabolic risk factors in people with cardiometabolic disorders. **J Cardiopulm Rehabil Prev**, v. 31, n. 6, p. 378–385, 2011.

JANSSEN, I.; ROSS, R. Vigorous intensity physical activity is related to the metabolic syndrome independent of the physical activity dose. **Int J Epidemiol**., v. 41, n. 4, p. 1132–1140, 2012.

JELLEYMAN, C. et al. The effects of high-intensity interval training on glucose regulation and insulin resistance: a meta-analysis. **Obes Rev**., v. 16, n. 11, p. 942-961, 2015.

JUNEAU, M. et al. Provocative issues in heart disease prevention. **Can J Cardiol**., v. 30, n. 12 Suppl, p. S401–S409, 2014.

JUNG, M. E. et al. High-intensity interval training as an efficacious alternative to moderate-intensity continuous training for adults with prediabetes. **J Diabetes Res.**, v. 2015, n. 191595, p. 1-9, 2015.

JUNG, M. E.; BOURNE, J. E.; LITTLE, J. P. Where does hit fit ? an examination of the

affective response to high-intensity intervals in comparison to continuous moderate- and continuous vigorous- intensity exercise in the exercise intensity-affect continuum. **PLoS One**, v. 9, n. 12, p. e114541, 2014.

KARSOFT, K. et al. The effects of free-living interval- walking training on glycemic control, body composition, and physical fitness in type 2 diabetic patients. **Diabetes Care**, v. 36, n. 2, p. 228–236, 2013.

LITTLE, J. P. et al. Effects of high-intensity interval exercise versus continuous moderate-intensity exercise on postprandial glycemic control assessed by continuous glucose monitoring in obese adults. **App Physiol Nutr Metab**., v. 39, n.7, p. 835-841, 2014.

LIUBAOERJIJIN, Y. et al. Effect of aerobic exercise intensity on glycemic control in type 2 diabetes: a meta-analysis of head-to-head randomized trials. **Acta Diabetol**, v. 53, n. 5, p. 769–781, 2016.

MAILLARD, F. et al. High-intensity interval training reduces abdominal fat mass in postmenopausal women with type 2 diabetes. **Diabetes Metab**, v. 42, n. 6, p. 433–441, 2016.

MANN, T.; LAMBERTS, R. P.; LAMBERT, M. I. Methods of prescribing relative exercise intensity: Physiological and practical considerations. **Sports Med**., v. 43, n. 7, p. 613–625, 2013.

GARBER, C. E. et al. Quantity and quality of exercise for developing and maintaining neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. **Med Sci Sports Exerc**., v.43, n.7, p. 1334–59, 2011.

MILANOVIC, Z.; SPORIS, G.; WESTON, M. Effectiveness of high-intensity interval training (hit) and continuous endurance training for VO_2max improvements: a systematic review and meta-analysis of controlled trials. **Sports Med**., v. 45, n. 10, p. 1469–1481, 2015.

MILECH, A. et al. **Diretrizes da Sociedade Brasileira de Diabetes (2015-2016).** São Paulo:A.C.Farmacêutica, 2016.

MITRANUN, W. et al. Continuous vs interval training on glycemic control and macro- and microvascular reactivity in type 2 diabetic patients. **Scand J Med Sci Sports.**, v. 24, n. 2, p. e69-76, 2014.

MYERS, V. H. et al. Exercise training and quality of life in individuals with type 2 diabetes. **Diabetes Care**, v. 36, p. 1884–1890, 2013.

NICOLUCCI, A. et al. Relationship of exercise volume to improvements of quality of life with supervised exercise training in patients with type 2 diabetes in a randomised controlled trial: The Italian Diabetes and Exercise Study (IDES). **Diabetologia**, v. 55, n. 3, p. 579–588, 2012.

ROBINSON, E. et al. 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**, v. 119, n. 5, p. 508–516, 2015.

ROGLIC, G.; UNWIN, N. Mortality attributable to diabetes: Estimates for the year 2010. **Diabetes Res Clin Pract**., v. 87, n. 1, p. 15–19, 2010.

SCHWINGSHACKL, L. et al. Impact of different training modalities on glycaemic control

and blood lipids in patients with type 2 diabetes: a systematic review and network meta-analysis. **Diabetologia**, v. 57, n.9, p. 1789–1797, 2014.

SLUIK, D. et al. physical activity and mortality in individuals with diabetes mellitus: a prospective study and meta-analysis. **Arch Intern Med**., v. 172, n. 17, p. 1285–1295, 2012.

TERADA, T. et al. Feasibility and preliminary efficacy of high intensity interval training in type 2 diabetes. **Diabetes Res Clin Pract**., v. 99, n. 2, p. 120–129, 2013.

THOMAS, D.; ELLIOTT, E. J.; NAUGHTON, G. A. Exercise for type 2 diabetes mellitus (review). **Cochrane Database Syst Rev**., n. 3, p. CD002968, 2006.

THUM, J. S. et al. High-intensity interval training elicits higher enjoyment than moderate intensity continuous exercise. **PLoS One**, v. 12, n.1, p. e0166299, 2017.

TOSCANO, C. M. et al. Cost - effectiveness of a national population - based screening program for type 2 diabetes: the Brazil experience. **Diabetol Metab Syndr**., v. 7, p. 95, 2015.

UMPIERRE, D. et al. Physical activity advice only or structured exercise training and association with hba1c levels in type 2 diabetes. **JAMA**, v. 305, n. 17, p. 1790–1799, 2011.

WEN, C. P. et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. **Lancet**, v. 378, n. 9798, p. 1244–1253, 2011.

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**., v. 48, n. 16, p. 1227–1234, 2014.

WESTON, M. et al. Effects of low-volume high-intensity interval training (HIT) on fitness in adults: a meta-analysis of controlled and non-controlled trials. **Sports Med**, v. 44, n. 7, p. 1005–1017, 2014.

WILD, S. et al. Global prevalence of diabetes: estimates for the year 2000 and projection for 2030. **Diabetes Care**, v. 27, n. 5, p. 1047–1053, 2004.

WILSON, P. W. F. et al. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. **Circulation**, v. 112, n. 20, p. 3066–3072, 2005.

WORLD HEALTH ORGANIZATION. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia. Ed. WHO/IDF consultation. p. 1-50, 2006.

WORLD HEALTH ORGANIZATION. Global Report on Diabetes. p. 1–88, 2016.

XIE, B. et al. Effects of high-intensity interval training on aerobic capacity in cardiac patients: a systematic review with meta-analysis. **BioMed Res Int**., v. 2017, p. 5420840, 2017.

Universidade Federal de Santa Maria - UFSM

Projeto na Íntegra

Data/Hora: 15/05/2017 22:47
Autenticação:
2A75.3625.02AF.614D.E308.4704.67D0.384A
Consulte em http://www.ufsm.br/autenticacao

Título: TREINAMENTO INTERMITENTE DE ALTA INTENSIDADE VERSUS TREINAMENTO CONTÍNUO EM PRÉ-DIABETES E DIABETES TIPO 2: REVISÃO SISTEMÁTICA DE ENSAIOS CLÍNICOS

Número: 044857 **Classificação:** Pesquisa **Registrado em:** 07/11/2016

Situação: Em andamento **Início:** 01/07/2016 **Término:** 31/03/2018

Avaliação: Avaliado **Última avaliação:** 02/03/2017

Fundação: Não necessita contratar fundação **Número na fundação:** *Não se aplica*

Supervisor financeiro: *Não se aplica*

Proteção do conhecimento: Projeto não gera conhecimento passível de proteção

Público alvo: **Público envolvido:** **Tipo de público:** Geral

Tipo de evento: Não se aplica **Carga Horária:** *Não se aplica* **Alunos matriculados:** *Não se aplica*
Alunos concluintes: *Não se aplica*

Palavras-chave: diabetes tipo 2, pré-diabéticos, treinamento intermitente, treinamento contínuo

Resumo: A prevalência de diabetes tem aumentado nas últimas três décadas e está crescendo mais rapidamente em países de baixa e média renda. No início do século 21, a diabetes tornou-se a quinta principal causa de morte no mundo. Dentre as formas de prevenção e tratamento, a atividade física está associada com um menor risco de morbidade e mortalidade nesses indivíduos. Recentemente, o treinamento intermitente de alta intensidade (HIIT) tem se tornado uma alternativa para o exercício moderado contínuo em diversas populações, sendo sugerido como uma atividade física que pode conferir maiores benefícios para a saúde metabólica. Entretanto, ainda não está claro na literatura os efeitos superiores do HIIT quando comparado ao treinamento contínuo de moderada intensidade. A partir disso, através da realização de uma revisão sistemática, discutiremos evidências recentes para esclarecer se o HIIT é uma alternativa de exercício tempo-eficiente a ser implementado com efeitos superiores ao MICT em indivíduos pré-diabéticos e com DM2. O objetivo desta revisão sistemática será comparar os efeitos do treinamento intermitente de alta intensidade com o treinamento contínuo de moderada intensidade sobre variáveis metabólicas, fisiológicas e funcionais em pacientes pré-diabéticos e/ou com diabetes tipo 2. A revisão sistemática será conduzida conforme a recomendação do PRISMA e registrada no PROSPERO.

Observação:

Participantes

Matrícula	Nome	Vínculo	Função	Bolsa	C.H.*	Início	Término
201570095	ANGÉLICA TREVISAN DE NARDI	Aluno de Pós-graduação	Participante		20	01/07/2016	31/03/2018
1689820	ANTONIO MARCOS VARGAS DA SILVA	Docente	Coordenador		6	01/07/2016	28/03/2017
1689820	ANTONIO MARCOS VARGAS DA SILVA	Docente	Coordenador		2	29/03/2017	31/03/2018
201670114	TAINARA TOLVES	Aluno de Pós-graduação	Colaborador		10	01/07/2016	31/03/2018
2056325	TATHIANE LARISSA LENZI	Docente	Colaborador		4	01/07/2016	31/03/2018

* carga horária semanal

Unidades vinculadas

Unidade	Função	Valor	Início	Término
04.74.00.00.0.0 - CURSO-PROGRAMA PG EM REABILITAÇÃO FUNCIONAL	Responsável		01/07/2016	31/03/2018

Classificações

Tipo de classificação	Classificação
Classificação CNPq	4.08.00.00-8 - FISIOTERAPIA E TERAPIA OCUPACIONAL
Grupo do CNPq	028 - Grupo de Pesquisa em Fisiopatologia e Reabilitação Cardiorrespiratória
Linha de pesquisa	99.00.00 - LINHA DE PESQUISA INEXISTENTE
Quanto ao tipo de projeto de pesquisa	2.03 - Projeto de Dissertação

Regiões de atuação

Cidade	UF	País	Início	Término
Santa Maria	Rio Grande do Sul	Brasil	01/07/2016	31/03/2018

Atividades

Atividade	Início previsto	Início efetivo	Término previsto	Término efetivo

Anexo 2 - Protocolo PROSPERO

UNIVERSITY of York
Centre for Reviews and Dissemination

NHS
National Institute for Health Research

PROSPERO International prospective register of systematic reviews

High intensity interval training compared to moderate-intensity continuous training in prediabetes and type 2 diabetes mellitus: a protocol of a systematic review

Angélica Trevisan De Nardi, Tainara Tolves, Antônio Marcos Vargas da Silva

Citation

Angélica Trevisan De Nardi, Tainara Tolves, Antônio Marcos Vargas da Silva. High intensity interval training compared to moderate-intensity continuous training in prediabetes and type 2 diabetes mellitus: a protocol of a systematic review. PROSPERO 2016:CRD42016047151 Available from http://www.crd.york.ac.uk/PROSPERO_REBRANDING/display_record.asp?ID=CRD42016047151

Review question(s)

Does high intensity interval training (HIIT) compared to moderate-intensity continuous training (MICT) in patients prediabetes and/or type 2 diabetes improve metabolic and physiological outcomes?

Searches

A comprehensive literature search will be conducted through the PubMed (MEDLINE), Physiotherapy Evidence Database (PEDro), Cochrane Central Register of Controlled Trials (CENTRAL), Scopus and LILACS databases to identify literature that has evaluated the high intensity interval training versus moderate-intensity continuous training (MICT) in prediabetes and/or type 2 diabetes adults (> 18 years) with or without associated risk factors and/or known cardiometabolic diseases will be considered for analysis.

The search will be conducted with no publication year or language limits.

For the subject search, a combination of controlled vocabulary and text words based on the search strategy for the PubMed (MEDLINE) database will be used as follow:

(((((("Diabetes Mellitus, Type 2"[Mesh] OR "diabetes" OR "NIDDM" OR "Maturity-Onset Diabetes" OR "Diabetes Mellitus, Noninsulin-Dependent" OR "Diabetes Mellitus, Adult-Onset" OR "Adult-Onset Diabetes Mellitus" OR "Diabetes Mellitus, Adult Onset" OR "Diabetes Mellitus, Ketosis-Resistant" OR "Diabetes Mellitus, Ketosis Resistant" OR "Ketosis-Resistant Diabetes Mellitus" OR "Diabetes Mellitus, Maturity-Onset" OR "Diabetes Mellitus, Maturity Onset" OR "Diabetes Mellitus, Non Insulin Dependent" OR "Diabetes Mellitus, Non-Insulin-Dependent" OR "Non-Insulin-Dependent Diabetes Mellitus" OR "Diabetes Mellitus, Noninsulin Dependent" OR "Diabetes Mellitus, Slow-Onset" OR "Diabetes Mellitus, Slow Onset" OR "Slow-Onset Diabetes Mellitus" OR "Diabetes Mellitus, Stable" OR "Stable Diabetes Mellitus" OR "Diabetes Mellitus, Type II" OR "Maturity-Onset Diabetes Mellitus" OR "Maturity Onset Diabetes Mellitus" OR "MODY" OR "Type 2 Diabetes Mellitus" OR "Noninsulin-Dependent Diabetes Mellitus"))) OR (("Prediabetic State"[Mesh] OR "Prediabetic States" OR "State, Prediabetic" OR "States, Prediabetic" OR "Prediabetes"))) AND (("Exercise Therapy"[Mesh] OR "Therapy, Exercise" OR "Exercise Therapies" OR "Therapies, Exercise" OR "exercise rehabilitation" OR "exercise intervention" OR "interval exercise" OR "high intensity exercise" OR "high intensity interval exercise" OR "interval training" OR "interval exercise" OR "high intensity training" OR "intensity training" OR "high intensity interval training" OR "intermittent exercise" OR "vigorous intensity" OR "exercise intensity" OR "High Intensity Intermittent Exercise" OR "Intermittent Training."))) AND ((((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh] OR ("clinical trial"[tw]) OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])) OR ("latin square"[tw]) OR placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR follow-up studies[mh] OR prospective studies[mh] OR cross-over studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw]))))

A sensitive search strategy will be adapted for the PEDro, CENTRAL, Scopus and LILACS databases. To reduce publication bias, unpublished documents through the ClinicalTrials.gov database will be checked. The results of

searches of various databases also will be cross-checked to locate and eliminate duplicates.

The titles and abstracts of studies will be reviewed independently by two reviewers (A.T.N and T.T) and will be selected for further review if they meet the inclusion criteria:

(1) Clinical trials that comparing the effects of HIIT versus MICT in prediabetes and/or type 2 diabetes adults (> 18 years) with or without associated risk factors and/or known cardiometabolic diseases will be considered for analysis

Any discrepancies were resolved through discussion and consensus of a third reviewer (A.M.V.S).

The final decision about inclusion will be made on the basis of the full text paper of the potentially relevant studies in accordance with exclusion criteria:

(1) Did not present a proper control group (type 2 diabetes or prediabetes or healthy individuals submitted moderate-intensity continuous training (MICT) or no intervention

(2) Did not include prediabetes or type 2 diabetes adults;

(3) Absence of similar follow-up for subjects of both groups evaluated in the same way;

(4) Did not assess insulin resistance, fasting glucose, HbA1c, fasting insulin, VO2peak and systolic/diastolic blood pressure.

Types of study to be included
Randomized controlled trials (RCTs) or prospective trials.

Condition or domain being studied
Prediabetes or type 2 diabetes individuals have received HIIT

Participants/ population
Prediabetes or type 2 diabetes patients

Intervention(s), exposure(s)
High-intensity interval training versus moderate-intensity continuous training.

Comparator(s)/ control
Studies using HIIT compared with prediabetes or type 2 diabetes or healthy individuals submitted to moderate-intensity continuous training or a control group (without performing intervention)

Outcome(s)
Primary outcomes
Metabolic health outcome (insulin resistance, fasting glucose, HbA1c or fasting insulin)

Physiological outcomes (VO2peak, and systolic/diastolic blood pressure)

Measured at baseline and after a period of HIIT

Secondary outcomes
Functional outcome (6 minute walk test)

All measured at baseline and on completion of HIIT

Risk of bias (quality) assessment
Risk of bias will be assessed according the Cochrane Handbook for Systematic Reviews of Interventions, Version 5.0.1.

Strategy for data synthesis
A descriptive synthesis is planned.

Data analysis will be performed descriptively. If data allow, further meta-analysis will be performed.

Analysis of subgroups or subsets
None planned.

Contact details for further information
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Organisational affiliation of the review
None

Review team
Miss Angélica Trevisan De Nardi, Federal University of Santa Maria
Miss Tainara Tolves, Federal University of Santa Maria
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Anticipated or actual start date
12 September 2016

Anticipated completion date
13 February 2017

Funding sources/sponsors
none

Conflicts of interest
None known

Language
English

Country
Brazil

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Diabetes Mellitus, Type 2; Exercise; Exercise Therapy; Humans; Prediabetic State

Stage of review
Ongoing

Date of registration in PROSPERO
06 September 2016

Date of publication of this revision
06 September 2016

UNIVERSITY of York
Centre for Reviews and Dissemination

NHS
National Institute for Health Research

Stage of review at time of this submission	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

ANEXO 3 – Checklist PRISMA

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	13
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	13
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	17
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	17
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	17
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	18
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	19
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	18
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	18-19
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	19
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	19
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	19
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	20
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	20

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	19
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	21
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	21
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	25
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	21
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	22
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	25
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	26
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	29
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	30
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

ANEXO 4 – Normas da revista

Archives of
Physical Medicine and Rehabilitation

Introduction

Archives of Physical Medicine and Rehabilitation publishes original articles that report on important trends and developments in physical medicine and rehabilitation and in the wider interdisciplinary field of rehabilitation. *Archives of Physical Medicine and Rehabilitation* brings readers authoritative information on the therapeutic utilization of physical and pharmaceutical agents in providing comprehensive care for persons with disabilities and for chronically ill individuals. *Archives* began publication in 1920, publishes monthly, and is the official journal of the ACRM | American Congress of Rehabilitation Medicine. Its content is cited more often than any other rehabilitation journal. A steadily increasing rate of submissions has forced the *Archives* to adopt a policy of restricting its manuscripts to topics that proved new information that may alter clinical practice or represent influential advances in the research. *Archives* will not review studies involving animal models, healthy normal samples, or small case reports, except in unusual circumstances. We may make exceptions when the clinical implications for populations of persons with chronic illness or disability are compelling. In addition, we will not review studies that report psychometric information of well-established instruments for language-specific applications.

Types of papers

Original Research: Present new and important basic and clinical information, extend existing studies, or provide a new approach to a traditional subject. Manuscripts should be limited to 3000 words of text (Introduction through Conclusions). Figures, tables, and references should be limited to the number needed to clarify, amplify, or document the text.

Brief Reports: Provide preliminary communications of new data, research methods, new ideas, and techniques. Manuscripts should be limited to 1500 words of text (or 1200 words plus 1-2 figures or tables, Introduction through Conclusions), and no more than 10 references. Brief reports should be accompanied by the appropriate reporting guideline and checklist.

The *Archives* will **not** consider case reports or animal studies for publication. Please do not submit them.

Commentaries (by Invitation): Focus on issues in physical medicine and rehabilitation. Manuscripts should be limited to 2000 words of text (Introduction through Conclusions). The Editorial Board reserves the right to ensure that the author is qualified, through education and professional experience, to write knowledgeably and appropriately about a particular subject before accepting a Commentary for publication. The Editorial Board will choose the author(s) for Invited Commentaries and the author(s)' identity will be anonymous until publication. Authors of the subject article may submit a response for a subsequent issue.

Editorials: Editorials published in *Archives* may only be written by the elected officers of ACRM, or by members of the Editorial Board. Prior to publication, all editorials are approved by the Editorial Board's Executive Committee. Editorials do not represent the opinions or positions of ACRM or the Editorial Board. Editorials should be limited to 1000 words of text.

Information/Education: The ACRM Communications Committee has developed a new feature, Information/Education Pages, which appear in the Organization News section of *Archives*.

These fact sheets are printed as tear-out pages. They are designed to provide consumer-friendly information on topics relevant to rehabilitation medicine, including basic background or overview, similar to a Wikipedia entry, or brief how-to suggestions. They are targeted toward people with disabilities, their caregivers, or clinicians; and are designed so that a practitioner can tear out and copy, or download the pages, to make them available to patients and caregivers.

Authors are invited to submit Information/Education Page manuscripts or proposals to the *Archives*' Editorial Office (ArchivesMail@archives.acrm.org). The ACRM Communications Committee will assess subject matter, content, and target reading level then provide feedback on suitability and instructions on how to proceed directly to the author. Note that this should not be considered an official peer review of the content. For more information go to http://www.acrm.org/publications/archives-of-pm-r/information-education-pages/.

Letters to The Editor: Letters are published at the discretion of the Editorial Board and should be directly related to the published article on which it comments. Letters may not reference unpublished studies or reference "in press" studies that are not publicly available. The Editorial Board reserves the right to solicit a response from the authors of the cited article. Letters must be limited to roughly 500 words of text, 1 table, and no more than 5 references.

Measurement Tools: These instrument summaries, which appear in the Organization News section of *Archives*, are designed to facilitate the selection of outcome measures by trained

clinicians. The information contained in this summary represents a sample of the peer-reviewed research available at the time of the summary's publication. The information contained in these summaries does not constitute an endorsement of the instrument for clinical practice. The views expressed are those of the summary authors and do not represent those of authors' employers, instrument owner(s), the *Archives*, the Rehabilitation Measures Database or the United States Department of Health and Human Services. Authors are invited to submit proposals for new Measurement Tools to the *Archives'* editorial office (Archivesmail@archives.acrm.org) and the office will coordinate with the ACRM Measurement Networking Group for the Rehabilitation Measures Database to determine if the proposal is suitable for publication in the *Archives*. The Networking Group can assist authors with formatting their article to meet the Measurement Tools requirements.

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Special Communications: Provide information or an objective analysis of issues in physical medicine and rehabilitation that does not qualify as a research or clinical paper or commentary. Manuscripts are peer reviewed and should be limited to 5000 words of text, exclusive of references.

Before You Begin

Ethics in Publishing

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Authors are encouraged to provide gender-specific data, when appropriate, in describing outcomes of epidemiologic analyses or clinical trials; or specifically state that there were no gender-based differences. For more information please consult the Institute of Medicine's report on "SEX-SPECIFIC REPORTING OF SCIENTIFIC RESEARCH", which can be accessed at http://www.ncbi.nlm.nih.gov/books/NBK84192/pdf/Bookshelf_NBK84192.pdf.

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If relevant, a statement must be included in the body of the manuscript that human experimentation was approved by the local institutional review board or conforms to the Helsinki Declaration [3], as stated in the section Manuscript Preparation, Methods. Also that

guidelines for the care/use of nonhuman animals or other species, approved by the institution, were followed as indicated in the Methods. The species must be named in the Title, Abstract, and Methods section.

Conflict of Interest

The *Archives* utilizes the ICMJE Form for Disclosure of Potential Conflicts of Interest.

During original submission, the corresponding author completes and uploads an *ICMJE* form.

If a revised paper is submitted, all authors must complete the *ICMJE* form.

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Please see the ICMJE author responsibilities regarding conflicts of interest (http://www.icmje.org/recommendations/browse/roles-and-responsibilities/author-responsibilities--conflicts-of-interest.html). It is important to note that a conflict of interest can be actual or perceived.

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Authors have read the submitted manuscript and vouch for its accuracy. All authors have participated sufficiently in the conception and design of this work and the analysis of the data (where applicable), as well as the writing of the manuscript to take public responsibility for its content. If any author (or group of authors) listed cannot verify substantial contribution, the author's name should be moved to the acknowledgment section. If requested, authors shall produce the data on which the manuscript is based for examination by *Archives* or its assignees.

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publication elsewhere and it is not presently under review by any other publisher. The manuscript will not be submitted for publication elsewhere until a decision has been made on its acceptability for publication in *Archives*. This restriction does not apply to brief abstracts or press reports published in connection with scientific meetings.

Clinical trial

While there may be occasional exceptions, the *Archives* is committed to the need for clinical trial reports to be accompanied by adequate periods of follow-up. A lack of sufficient follow-up may be detrimental to a paper's acceptance.

As of January 1, 2017 the *Archives* will ***only*** consider clinical trials that have been registered before the first patient is enrolled.

For our purposes, a clinical trial is defined as "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes" (http://www.who.int/ictrp/en). Thus, cohort and retrospective studies without an intervention do not require registration, and neither do observational studies of clinical care. However, studies of human subjects with prospective assignment of an intervention by the investigators, regardless of the size of the trial or method of assignment, must be registered.

NEW - Reporting Guidelines and Checklists

To ensure a high and consistent quality of research reporting, original research articles, including brief reports, must contain sufficient information to allow readers to understand how a study was designed and conducted. For review articles, systematic or narrative, readers should be informed of the rationale and details behind the literature search strategy.

To achieve this goal, *Archives* requires that authors upload a completed checklist for the appropriate reporting guideline during original submission. Taking the time to ensure your manuscript addresses basic reporting prerequisites will greatly improve your manuscript, and enhance the likelihood of publication. These checklists serve as a guide for the editors and reviewers as they evaluate your paper.

The EQUATOR Network (http://www.equator-network.org) is an excellent resource for key reporting guidelines, checklists, and flow diagrams. These guidelines should be especially useful for *Archives*' authors.

Click on the checklist that applies to your manuscript, download it to your computer, fill it out electronically, "save as," and upload it with your manuscript when you submit. Links to mandatory flow diagrams also are provided. Below are the most commonly used checklists

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 Randomized Controlled Trials — CONSORT — Consolidated Standards of Reporting Trials

 Observational Studies — STROBE — Strengthening the Reporting of Observational studies in Epidemiology

 Systematic Review of Controlled Trials — PRISMA — Preferred Reporting Items for Systematic Reviews and Meta-Analyses

 Study of Diagnostic accuracy/assessment scale — STARD — Standards for the Reporting of Diagnostic Accuracy Studies

 For psychometric studies the editors recommend either the COSMIN or GRRAS guideline, though the final choice is up to the author.

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Referees

All submissions will be screened by editors to determine their suitability for further review. Manuscripts that are approved for review will be evaluated by at least one recognized expert in the particular subject matter. Biostatistical review may be obtained. Peer reviewers' assessments are referred to a member of the Editorial Board, who may also critique the manuscript. The assigned Editorial Board Member will then make a final decision and communicate with the corresponding author via e-mail. Decisions are typically communicated within 60 days after the manuscript has been approved for peer review. All reviews are conducted in a double-blind fashion.

Letters to the Editors and Editorials are generally evaluated by an editorial committee, however, external reviews may also be sought.

Published annually without peer review are the ACRM | American Congress of Rehabilitation Medicine presidential address and the John Stanley Coulter Lecture. The Editorial Board does not peer review the published abstracts of posters, platform presentations of scientific papers, or audiovisual materials presented at the ACRM annual meeting. *Archives* also publishes the official documents of ACRM. These documents are not peer reviewed by *Archives* and include position papers and other materials approved by the ACRM.

Revisions

When submitting your revised manuscript, at the request of the Editorial Board, please include a document, separate from your cover letter, itemizing your response to each of the suggested revisions and any other changes you have made. Use consecutive line numbering in the text and cite line numbers for each change. In addition, highlight each change in the revised manuscript. You will upload this document in the file upload step as the "Detailed Response to Reviewers." Please note that this file should be blinded and should not include author names or institutional letterhead.

If revisions are not received within the time specified in the decision e-mail, the manuscript file will be closed. A revision received after a file has been closed will be handled as a new submission. An extension beyond the deadline may be granted at the Editorial Board's discretion, but only in extenuating circumstances, given the editors' commitment to prompt publication.

Submission of a revised manuscript includes submission of separate documents in the following order: (1) cover letter; (2) title page, including acknowledgments and explanation of any conflicts of interest; (3) main text file with highlighted changes, including an appropriate (structured or standard) abstract, keywords, list of abbreviations, body of the text, suppliers' list, references, figure legends; (4) a clean copy of the main text file with no highlighted changes, including an appropriate abstract, keywords, list of abbreviations, body of the text, suppliers' list, references, figure legends; (5) figures; (6) tables; (7) appendices; (8) supplementary files; (9) checklist; and (10) ICMJE Form for Disclosure of Potential Conflicts of Interest for each author.

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From time to time an author may receive a decision of "Reject-Resubmit" on their original submission. This is a reject but grants the author the opportunity to revise and resubmit their work under a new manuscript number at any time. The resubmission will be linked to the original submission but there will be no expectation of acceptance. The resubmission will be treated as new.

To submit a resubmission authors should note the following:

Select RESUBMISSION as the article type.

In your cover letter, please 1) reference this manuscript ID number and include an itemized list of the revisions. 2) Use line numbering in the text and reference the revisions made by page and line number in the cover letter. 3) Highlight changes made in one copy of the manuscript text. Submit another copy with all changes accepted and not highlighted. Please add "marked copy" to the file name of the highlighted version and "clean copy" to the file name of the clean version. Submit both clean and highlighted copies under the category titled Manuscript without author identifiers. Both should remain blinded for the review process.

Additional information

Unless author(s) notify the Editorial Office of alternate preferences, all accepted articles are posted online within 5 business days of release to production. Author(s) should notify the Editorial Office immediately with any requests to delay posting. This posted version will include a fully citable PDF of the author's accepted files, and will be submitted to PubMed.

Supplementary material(s), such as raw data, videos, etc., will not be included. Supplementary materials will be included when the article is typeset and published on the Articles in Press platform or in the monthly print/online issue of the journal.

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Authors should prepare manuscripts according to the "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals" [1] as developed by the International Committee of Medical Journal Editors. The Requirements are available at http://www.icmje.org.

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Manuscripts must be double-spaced throughout, including the title page, abstract, text, acknowledgments, references, individual tables, and legends. Use only standard 12-point type and spacing. Use unjustified, flush-left margins. Number the pages of the text consecutively. Put the page number in the upper or lower right-hand corner of each page. Number each line on each page of the text to facilitate peer review.

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There are no strict formatting requirements for articles at initial submission (for requirements for revised submissions, please see REVISED SUBMISSIONS section below) but all manuscripts must contain the essential elements needed to convey your manuscript, for example Abstract, Keywords, Introduction, Methods, Results, Conclusions, Artwork and Tables with Captions.

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Regardless of the file format of the original submission, at revision you must provide us with an editable file of the entire article. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the Guide to Publishing with Elsevier). See also the section on Electronic artwork.

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Original Article level 1 headings are: Methods, Results, Discussion, and Conclusions. Articles should include the level 2 subsection heading Study Limitations at the end of the Discussion section. Longer articles may need other level 2 and/or level 3 subsection headings to clarify their content, especially the Results and Discussion sections.

Other types of articles such as Commentaries and Special Communications do not require this format.

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Include these elements in the title page in the following sequence, double-spaced: (1) Running head of no more than 40 character spaces (no abbreviations); (2) Title (no abbreviations); (3) Author(s) full name(s) and highest academic degree(s); (4) The name(s) of the institution(s), section(s), division(s), and department(s) where the study was performed and the institutional affiliation(s) of the author(s) at the time of the study. An asterisk after an author's name and a footnote may indicate a change in affiliation; (5) Acknowledgment of any presentation of this material, to whom, when, and where; (6) Acknowledgment of financial support, including grant numbers and any other needed acknowledgments. Explanations of any conflicts of interest; (7) Name, address, business telephone number, and e-mail address of corresponding author; and (8) Clinical trial registration number, if applicable. Please note that clinical trial registration will now be required as of January 1, 2016. The grace period will end January 1, 2017 when registration will be mandatory.

Abstract

For articles reporting original data (Original Articles, Brief Reports) and Review Articles (including Meta-Analyses), a structured abstract is required (see the Instructions for Structured Abstracts). Authors should make sure the key elements from the Reporting Guideline (eg. CONSORT, PRISMA, etc.) they followed for their manuscript are included in the abstract as well as the body of the paper.

For other manuscripts (e.g., Commentaries, Editorials and Special Communications), include a conventional, unstructured abstract of no more than 250 words.

Keywords

All abstracts must include provide 3 to 5 Keywords identified ny the author. Keywords must be selected from the US National Library of Medicine's (NLM) *Medical Subject Headings*, which is available at http://www.nlm.nih.gov/mesh/MBrowser.html.

Abbreviations

Archives' editorial policy is to **minimize the use of abbreviations**. Fewer abbreviations make it easier for the multidisciplinary readership to follow the text. Authors should include a list of

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Main Manuscript

Introduction

State the purpose of the article. Summarize the rationale for the study or observation. Give only pertinent references, and do not review the subject extensively. Do not include data or conclusions from the work being reported. Do not include a heading for this section.

Methods

Describe the selection of the observational or experimental subjects (patients or experimental animals, including controls) clearly. Discuss eligibility of experimental subjects. Give details about randomization. Describe the methods for any blinding of observations. Identify the methods, equipment and materials, and procedures in sufficient detail to allow others to reproduce the results.

Reference established methods, including statistical methods (see below); provide very brief descriptions for methods that have been published but are not well known; describe new or substantially modified methods, give reasons for using them, and evaluate their limitations. Identify precisely all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration.

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Researchers should report and identify the specific statistical test used and the obtained statistical value. Researchers should supplement the results of any statistical value. Researchers should supplement the results of any statistical significance test with the use of effect size values or CIs. Measures of effect size or CIs should be routinely included in quantitative clinical trials reported in rehabilitation research. The statistical power values and the corresponding type II error probability should always be reported for statistically nonsignificant results.

The investigator should ensure that there is sufficient power to detect, as statistically significant, a clinically meaningful treatment effect of an *a priori* specified size [4]. References for study design and statistical methods should be to standard works (with pages stated) rather than to papers in which designs or methods were originally reported.

Specify any general use computer programs used. Avoid nontechnical uses of technical terms in statistics, such as "random" (which implies a randomizing device), "normal," "significant," "correlation," or "sample." Define statistical terms, abbreviations, and symbols.

When submitting manuscripts on randomized controlled trials (RCTs), authors must include the CONSORT (Consolidated Standards for Reporting Trials) flow diagram. See the Reporting Guidelines.

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When data are summarized in the Results section, specify the statistical methods used to analyze them. Describe the success of any blinding of observations. Report treatment complications. Give numbers of observations. Report losses to observation (ie, dropouts from a clinical trial). Present results in logical sequence in the text, tables, and illustrations. *Archives* aims to publish no more than 5 figures per manuscript so restrict tables and figures to those needed to explain arguments and to assess their support. Use graphs as an alternative to tables with many entries; do not duplicate data in graphs and tables. Do not repeat in the text all the data in the tables, illustrations, or both; emphasize or summarize only important observations.

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Discussion

Emphasize the new and important aspects of the study and the conclusions that follow from them. Do not repeat in detail data or other material given in the introduction or the Results section. Include in the Discussion section the implications of the findings and their limitations, including implications for future research. Authors should address the issue of effect magnitude, in terms of both the statistics reported and the implications of the research. Relate the observations to other relevant studies.

Study Limitations

Include the subsection (Level 2 heading), "Study Limitations" to discuss the limitations of the study.

Conclusions

Link the conclusions with the study's goals but avoid unqualified statements not supported by the data. Avoid claiming priority and alluding to work that is incomplete. State new hypotheses when warranted, but clearly label them as such. Recommendations, when appropriate, may be included.

Graphical abstract

Although a graphical abstract is optional, its use is encouraged as it draws more attention to the online article. The graphical abstract should summarize the contents of the article in a concise, pictorial form designed to capture the attention of a wide readership. Graphical abstracts should be submitted as a separate file in the online submission system. Image size: Please provide an image with a minimum of 531 × 1328 pixels (h × w) or proportionally more. The image should be readable at a size of 5 × 13 cm using a regular screen resolution of 96 dpi. Preferred file types: TIFF, EPS, PDF or MS Office files. You can view Example Graphical Abstracts on our information site.

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It is not necessary to include detailed descriptions on the program or type of grants and awards. When funding is from a block grant or other resources available to a university, college, or other research institution, submit the name of the institute or organization that provided the funding.

If no funding has been provided for the research, please include the following sentence: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Units

Metric units are required. Blood pressures in millimeters of mercury (mmHg) and all hematologic and clinical chemistry measurements using the International System of Units (SI).

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Footnotes other than for references are not allowed in the manuscript body.

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If photographs of persons are used, either the subjects must not be identifiable or the author must obtain and archive permission to publish the pictures and attest that permission has been granted in the cover letter that accompanies the manuscript submission.

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Electronic artwork

General points

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• Use a logical naming convention for your artwork files.

• Indicate per figure if it is a single, 1.5 or 2-column fitting image.

• For Word submissions only, you may still provide figures and their captions, and tables within a single file at the revision stage.

• Please note that individual figure files larger than 10 MB must be provided in separate source files.

A detailed guide on electronic artwork is available.

You are urged to visit this site; some excerpts from the detailed information are given here.

Formats

Regardless of the application used, when your electronic artwork is finalized, please 'save as' or convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):

EPS (or PDF): Vector drawings. Embed the font or save the text as 'graphics'.

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Identify statistical measures of variations such as standard deviation and standard error of the mean. Do not use internal horizontal and vertical rules. Be sure that each table is cited in the text in order. Using too many tables in relation to the length of the text may produce typesetting difficulties.

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