UNIVERSIDADE ESTADUAL PAULISTA
"JÚLIO DE MESQUITA FILHO"
Campus de Presidente Prudente

ÍTALO RIBEIRO LEMES

EFEITOS DO TREINAMENTO RESISTIDO NA SÍNDROME METABÓLICA

Uma revisão sistemática e meta-análise

Um ensaio clínico randomizado

Presidente Prudente

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Dissertação apresentada à Faculdade de Ciências e Tecnologia – FCT/UNESP – Campus de Presidente Prudente, para obtenção do título de Mestre no Programa de Pós-Graduação *Stricto Sensu* em Fisioterapia.

Orientador: Prof. Dr. Jayme Netto Júnior

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Dedicatória

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“O sucesso nasce do querer, da determinação e persistência em se chegar a um objetivo. Mesmo não atingindo o alvo, quem busca e vence obstáculos, no mínimo fará coisas admiráveis.”

José de Alencar

“A tarefa não é tanto ver aquilo que ninguém viu, mas pensar o que ninguém ainda pensou sobre aquilo que todo mundo vê.”

Arthur Schopenhauer

SUMÁRIO

Esta dissertação está apresentada em consonância com as normas do modelo alternativo de dissertação do Programa de Pós-Graduação *Stricto Sensu* em Fisioterapia da Faculdade de Ciências e Tecnologia – FCT/UNESP – Campus de Presidente Prudente. O conteúdo desse trabalho contempla o material originado a partir da pesquisa intitulada "Efeitos do treinamento resistido na síndrome metabólica" que foi realizada em duas etapas:

1 – Desenvolvimento de revisão sistemática e meta-análise, realizado durante estágio de pesquisa na *The University of Sydney*, *Faculty of Health Sciences*, *Sydney – Austrália*, financiado pela Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) na modalidade BEPE (Bolsa de Estágio de Pesquisa no Exterior) – Processo 2014/05419-2;

2 – Ensaio clínico randomizado, realizado na Universidade Estadual Paulista, no Laboratório de Fisioterapia Desportiva (LAFIDE) da Faculdade de Ciências e Tecnologia – FCT/UNESP, campus de Presidente Prudente, também financiado pela Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) na modalidade Bolsa de Mestrado no País – Processo 2013/10857-6.

Sendo assim, o presente material está dividido nas seguintes sessões:

- **Introdução:** para contextualização do tema pesquisado;
- **Artigo 1:** Lemes IR, Ferreira PH, Linares SN, Machado AF, Pastre CM, Netto Junior J. *Effects of resistance training on metabolic syndrome: a systematic review and meta-analysis of randomized controlled trials*.

Em revisão pelo periódico ***British Journal of Sports Medicine***.

- **<u>Artigo 2</u>:** Lemes IR, Linares SN, Alves T, Figueiredo MPF, Pastre CM, Netto Junior J. F*unctional training on metabolic syndrome, muscular strength and quality of life: a randomized controlled trial*.

Em revisão pelo periódico ***Diabetology & Metabolic Syndrome***.

- **<u>Conclusões</u>:** a partir de ambas as pesquisas realizadas.
- **<u>Referências</u>:** utilizadas no texto de introdução.
- **<u>Anexos</u>:** normas dos periódicos.

Ressalta-se que cada artigo está apresentado de acordo com as normas dos seus respectivos periódicos, exceto as figuras, que foram inseridas no corpo do texto. As normas de cada periódico encontram-se em anexo ao final do texto.

A Síndrome Metabólica (SM) é definida pelo *National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III)*[1] e aceita pela I Diretriz Brasileira de Diagnóstico e Tratamento da Síndrome Metabólica (I-DBSM)[2] como a presença de três ou mais dos seguintes aspectos: obesidade ou circunferência abdominal (>102cm p/ homens e >88cm para mulheres), triglicérides (≥150mg/dL ou ≥1,69mmol/L), HDL-colesterol (<40mg/dL ou <1,03mmol/L p/ homens e <50mg/dL ou <1,29mmol/L p/ mulheres), pressão arterial (sistólica ≥130mmHg ou diastólica ≥85mmHg) e glicemia de jejum (≥110mg/dL ou ≥6,11mmol/L).

Estudos apontam que aproximadamente 25% da população ocidental possui SM[3] e, em escala mundial, esse valor pode chegar a 28,5% em homens e 40,5% em mulheres[4,5]. No Brasil, em recente revisão sistemática[6], encontrou-se média de prevalência geral de 29,6%.

A presença dos fatores de risco ligados a SM aumenta as chances de desenvolvimento de doenças cardiovasculares e diabetes mellitus tipo 2, e está ainda intimamente ligada ao estilo de vida adotado. Sabe-se que o hábito sedentário e a má alimentação têm impacto direto nos fatores de risco da SM e, portanto, podem estar indiretamente relacionados ao desenvolvimento dessa síndrome. Neste cenário, evidências[7] apontam que funções reduzidas de desempenho físico e cardiorrespiratório, causados pelo hábito sedentário em jovens adultos, podem ser importantes indicativos de risco do desenvolvimento da SM.

Apesar do hábito sedentário não compor os critérios de diagnóstico da SM, parece um importante aspecto relacionado ao desenvolvimento da doença. Pesquisas

relacionadas ao treinamento físico, de resistência[8-11] e de força[8-10,12], têm sido realizadas para esclarecer os efeitos dessa prática nas relações entre saúde e doença, dentre as quais se encontra a SM.

Jurca *et al.*[13] realizaram estudo associando força muscular e incidência da SM, e encontraram dados indicando que homens praticantes de treinamento de força têm uma taxa de risco 34% menor de desenvolver SM quando comparado àqueles que não praticam nenhum tipo de atividade física. Sendo assim, os autores descrevem a força muscular como inversamente associada à incidência dessa síndrome. Também acreditam que variações no tratamento e prevenção podem ocorrer por meio do treinamento.

A modalidade mais utilizada para o ganho de força muscular é o treinamento resistido (TR), utilizado em academias de musculação, onde os exercícios praticados visam o movimento específico, trabalhando grupos musculares isolados e proporcionando, assim, o ganho de força do segmento trabalhado. Esta modalidade específica de treinamento físico tem apresentado, em estudos recentes, resultados controversos em relação aos fatores de risco da SM. Algumas pesquisas demonstram efeitos positivos para glicemia em jejum e triglicérides[14], circunferência abdominal[8,9,12] e pressão arterial[9]. Entretanto, em pesquisas de mesma natureza, nenhum efeito foi observado para quaisquer dos cinco fatores que compõem a SM[10,15,16].

Por outro lado, diferentes métodos de treinamento resistido têm surgido nos últimos anos, destacando-se o treinamento resistido funcional (TRF), que utiliza exercícios adaptados com o intuito de melhor atender as populações que não têm a mesma qualidade e vigor físico de pessoas integralmente saudáveis[17].

A metodologia por trás do TRF passa por princípios de biomecânica e bases neurológicas atuantes no controle corporal, e baseia-se em uma prescrição coerente e segura de exercícios que permitem que o corpo humano seja estimulado de forma que diversos sistemas sejam beneficiados[17,18], respeitando sempre os princípios da individualidade biológica e especificidade. Para tanto, o TRF proporciona trabalhos múltiplos, recrutando diferentes grupos musculares tanto na execução do movimento como na estabilização corporal, utilizando pranchas inclinadas e superfícies instáveis[19], exigindo, além das contrações necessárias para execução do movimento, equilíbrio e contrações musculares isométricas constantes.

Considerando esta variação do treinamento resistido, não foi encontrado na literatura científica nenhum estudo que tenha verificado os efeitos do treinamento funcional em pessoas com SM, o que expõe uma importante lacuna a ser estudada. Ainda, acredita-se que o amplo recrutamento muscular proporcionado pelo TRF seja capaz de promover alterações significantes nos fatores de risco da SM. Torna-se, portanto, de suma importância a realização de ensaio clínico abordando o treinamento funcional como intervenção, bem como a realização de revisão sistemática e meta-análise para elucidar os efeitos do treinamento resistido de forma geral.

Nesse sentido, os objetivos da presente pesquisa foram determinar, por meio de revisão sistemática e meta-análise, os efeitos do treinamento resistido sobre cada um dos fatores de risco da SM e, por meio de ensaio clínico, verificar os efeitos do treinamento funcional sobre esses fatores de risco, força muscular e qualidade de vida de pessoas com SM.

EFFECTS OF RESISTANCE TRAINING ON METABOLIC SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Keywords: metabolic syndrome x; resistance training; cardiovascular diseases; diabetes mellitus, type 2.

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ABSTRACT

Background: Metabolic syndrome (MS) is the clustering of risk factors for cardiovascular diseases, such as hyperglycemia, dyslipidemia, increased waist circumference and hypertension. Regular physical activity is an important strategy for the treatment and prevention of metabolic and clinical changes to metabolic syndrome (MS). Resistance training (RT) is a low-cost method that can be used in the treatment and prevention of cardiovascular events. However this method has produced controversial results in relation to the risk factors of MS. **Aim:** To summarize the effects of resistance training on MS risk factors. **Methods:** The Medline, PEDro, EMBASE, SPORTDiscus and The Cochrane Library databases were searched from their earliest records to 10 January 2015. Only randomized controlled trials that compared resistance training with a control group were included in this review. The quality and data of the included studies were assessed by two independent reviewers. The pooled mean differences between RT and control group were calculated using a fixed-effect model. **Results:** The pooled effect showed a reduction of 0.04 mmol/L (95% CI -0.12, 0.21; $p>0.05$) for fasting plasma glucose, 0.00 (95% CI -0.05, 0.04; $p>0.05$) for HDL-cholesterol, 0.03 (95% CI -0.14, 0.20; $p>0.05$) for triglycerides, 1.39 mmHg (95% CI -0.19, 2.98; $p=0.08$) for diastolic blood pressure and 1.09 cm (95% CI -0.12, 2.30; $p=0.08$) for waist circumference. Only systolic blood pressure presented a significant reduction, of 4.08 mmHg (95% CI 1.33, 6.82; $p<0.01$) following RT. Inconsistency (I^2) for all meta-analysis was 0%. **Conclusion:** Resistance training can be an effective treatment for the reduction of systolic blood pressure levels, and to ameliorate clinical parameters in individuals with metabolic syndrome.

INTRODUCTION

Metabolic syndrome (MS) is a clustering of clinical and biochemical disorders related to abdominal fat, elevated levels of fasting glucose and triglycerides, low levels of HDL-cholesterol and elevated blood pressure [1 2]. Individuals with MS have a greater risk of developing cardiovascular diseases and type 2 diabetes mellitus, and consequently have an increased risk of premature death[3]. Therefore, treatment and prevention of changes in these risk factors are of substantial importance.

Regular physical activity is an important strategy in the treatment and prevention of metabolic and clinical changes and is therefore an essential part of any health and rehabilitation program[1 2]. Among the most practiced exercise modalities are aerobic training and resistance training, both of which have been studied in different situations[4-8]. Resistance training (RT) is an effective and low-cost method for the treatment and prevention of cardiovascular events, and has been recommended by respected organizations[9]. RT is widely accepted as a successful method of increasing muscle strength[10], lean mass[11] and perception of physical capacity[12]. Moreover, authors found inverse associations between muscular fitness[13] and strength, and the incidence of MS, showing that people practicing resistance training have a 34% lower chance of developing this syndrome[14].

However, this method has produced different results in relation to the clustering of alterations to MS. Some authors have found positive results in reducing fasting plasma glucose and triglycerides [15], waist circumference [16-18] and blood pressure[18]. In contrast to these favorable effects, other trials have shown no effect

on MS risk [11 19 20]. Such a discrepancy in scientific literature represents a serious confounding factor for clinical practitioners regarding the effectiveness of this method.

Variance between methods of resistance training application, in terms of intensity, volume, and time of intervention may be the cause of such conflicting results in literature. Meta-analysis, in this case, allows the results of independent studies to be grouped, allowing readers to form a better understanding.

To the best of the authors' knowledge, there is only one previous meta-analysis[21] that has examined the effects of RT on metabolic syndrome. The authors included studies in the English language published up to 2007, with the primary outcome glycemic control measured in HbA1c and fat mass percentage. Also, the authors did not evaluate the methodological quality of the included studies. The present study, meanwhile, searched trials published in any language up to 10 January 2015. In addition, the methodological quality of the included studies was assessed and the overall quality of the evidence, and the strength of the recommendation, was evaluated. Thus, the purpose of this systematic review and meta-analysis was to summarize the effects of resistance training on MS risk factors, in comparison with a control group.

MATERIALS AND METHODS

Literature search

The Medline, PEDro, EMBASE, SPORTDiscus and The Cochrane Library databases were searched from their earliest records to 10 January 2015, in order to identify randomized controlled trials that use resistance training as an exercise treatment for metabolic syndrome. The search strategy used a combination of terms

to identify randomized controlled trials, metabolic syndrome and resistance training (Appendix Table 1). The reference list of the included studies was checked to find potential studies that could be used in this review. There were no language or period of publication restrictions.

Study Selection

Only randomized controlled trials that compared resistance training with a control group (no intervention) were included in this review. Studies that used diet intervention were included if this intervention was equal for all the groups in the study. Trials were eligible if they included participants with metabolic syndrome and assessed the components of this syndrome: elevated fasting plasma glucose, triglycerides, HDL-cholesterol, blood pressure and waist circumference. As the aim of the study was to summarize the effect on all MS risk factors, studies that did not evaluate at least four of these outcomes were excluded. All types of resistance training, irrespective of intensity, frequency or duration, were eligible for inclusion.

Data Extraction and Quality Assessment

Two reviewers (IRL and SNL) independently assessed risk of bias of the trials using the PEDro scale[22 23]. If trials were already listed on the PEDro database (http://www.pedro.org.au/), these scores were adopted. A PEDro score of 7 or greater was considered “high quality”, those with a score of 5 or 6 were considered “moderate quality” and those with a score of 4 or less “poor quality”. Any disagreements in the scoring of trials were resolved consensually. Methodological quality was not an

inclusion criterion. Two reviewers (IRL and SNL) also independently extracted outcome data using a standardized data extraction form.

The GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach was used by two independent reviewers (IRL and SNL) to evaluate the overall quality of evidence and the strength of the recommendation[24 25], as advocated by the Cochrane Back Review Group[26]. The overall quality of evidence was initially regarded as "High" but downgraded by one level for each of three factors encountered: design limitations (>25% of participants from studies with low quality methods - PEDro score <7 points); inconsistency of results (substantial I^2 square statistic); imprecision (<400 participants in total for each outcome). Publication bias assessment with a funnel plot was not performed and indirectness was not considered for this review due to the presence of a specific population, relevant outcome measures and direct comparisons.

The following factors were used to define the quality of evidence: high quality - further research is unlikely to change our confidence in the estimate of effect; moderate quality - further research is likely to have an important impact on our confidence in the estimate of effect and might change the estimate; low quality - further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality - we are uncertain about the estimate.

Outcome data included final mean, SD and sample size values. When final values were not available change scores were used. When there was insufficient information, the authors were contacted. If necessary, data was imputed or calculated using methods recommended in the Cochrane Handbook for Systematic Reviews of

Interventions. Blood pressure values were expressed in mmHg, waist circumference in centimeters, glucose, triglycerides and HDL-cholesterol in mmol/l. Where appropriate, data was converted to these units of measurement.

This systematic review was registered in an international database of systematic reviews in health and social care. (Available: registration number CRD42015016538; http://www.crd.york.ac.uk/PROSPERO/).

Statistical Analysis

Pooling was carried out using Comprehensive Meta-Analysis software, version 2.2.064 (Biostat, Englewood, NJ). When trials were sufficiently homogeneous (i.e., an I^2 value less than 50%), pooled effects were calculated using fixed-effect models, whereas random effects were used to estimate the pooled effects of heterogeneous trials (i.e., an I^2 of 50% or more). Mean difference (MD) with 95% confidence intervals was calculated.

RESULTS

Description of included studies.

After the removal of duplicates, the search strategy identified 333 titles. Screening of titles and abstracts identified 19 potentially eligible articles and 7 original trials were included[15-17 19 27-29]. One further study[30] was included after checking the reference list of included trials. The reasons for excluding articles were: intervention not appropriate (n=6), e.g. resistance plus aerobic training, data not appropriate (n=3), population not appropriate (n=2) (Figure 1; Appendix Table 2).

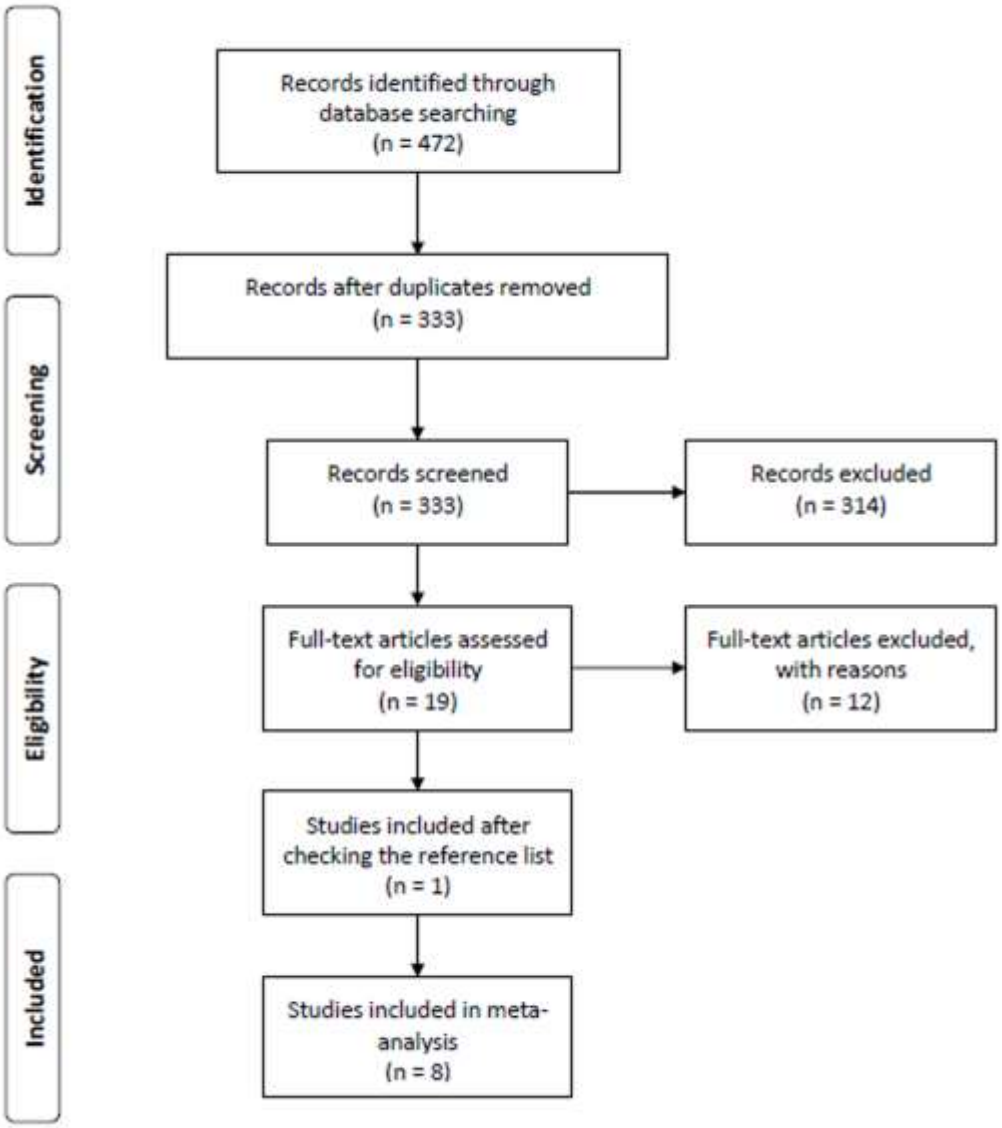

Figure 1. Flow chart of studies included.

Three studies included only men[15 19 28], and five included a mixed sample of men and women, with 65%[29], 44.8%[27], 36%[30], 39.5%[17] and 63%[16] of women, respectively. The training period ranged from 12 weeks to 9 months and all studies had an incremental workload, in intensity or volume. Table 1 shows the characteristics of the included trials.

Table 1. Characteristics of included studies.

Study name	Patient characteristics and sample size	Participants (inclusion/exclusion criteria)	Study length	Interventions	Metabolic syndrome risk factors assessed and time points
Castaneda 2002[29]	n = 62 RT group = 29 Control group = 31 % Female = 65% RT group = 68% Control group = 61% Age (Mean ± SD) RT group = 66 ± 2 Control group = 66 ± 1	Inclusion: Confirmation of diabetes diagnosis by fasting plasma glucose ≥ 7.0 mmol/l or use of diabetic medications. Exclusion: myocardial infarction (within past 6 months) and any unstable chronic condition, including dementia, alcoholism, dialysis, retinal hemorrhage or detachment, or current participation in resistance training.	3 days p/ week for 16 wks.	RT: 5 exercises; intensity: 60-80% 1RM; dose: 9 S/MG/W; Training sessions: Supervised. Control group: continued usual medical care, received Spanish translated diabetes recommendations for self-management, and were not given dietary counseling.	Triglycerides HDL-C Fasting plasma glucose SBP DBP WC Baseline 16 wks
Dunstan 2002[27]	n = 29 RT group = 16 Control group = 13 %Female = 44.8% RT group = 37,5% Control group = 53,8% Age (Mean ± SD) RT group = 67.6 ± 5.2 Control group = 66.9 ± 5.3	Inclusion: Overweight and sedentary; had established but not optimally controlled type 2 diabetes, were not taking insulin and were nonsmokers. Exclusion: history or physical findings suggestive of ischemic heart disease, systemic diseases, uncontrolled hypertension and advanced diabetic neuropathy or retinopathy.	3 days p/ week for 6 months.	RT: 9 exercises; intensity: 50-85% 1RM; dose: 9 S/MG/W; Training sessions: Supervised. Control group: offered static stretching exercises.	Triglycerides HDL-C Fasting Plasma Glucose SBP DBP WC Baseline 3 months 6 months
Kukkonen-Harjula 2005[28]	N = 68 RT group = 26 Aerobic group = 20	Inclusion: Age 35-50 years, BMI range of 30-40 kg/m^2 and waist circumference over 100 cm.	3 days p/ week for 6 months.	All groups performed a 2-month very-low-energy diet before training programs.	Triglycerides HDL-C Fasting Plasma Glucose

	Control group = 22 All males Age (Mean ± SD) All participants = 42.6 ± 4.6	Exclusion: Regular medication; plenty of physical activity; smokers; resting blood pressure > 160/105 mmHg; fasting serum cholesterol >8 mmol L^1; triglycerides >4 mmol L^1; blood glucose >6.7 mmol L^1.		RT: 6 exercises; intensity: 60-80% 1RM; dose: 9 S/MG/W. AT: 60-70% VO_2 max; dose: 135 min/week. Training sessions: 1 weekly training session was supervised. Control group: advised not to increase physical activity.	SBP DBP WC Baseline 2 months 8 months 31 months
Sigal 2007[30]	n = 251 RT group = 64 Aerobic group = 60 Combined group = 64 Control group = 63 % Female = 36% RT group = 37% Aerobic group = 35% Combined group = 37% Control group = 35% Age (Mean ± SD) RT group = 54.7 ± 7.5 Aerobic group = 53.9 ± 6.6	Inclusion: type 2 diabetes for more than 6 months and a baseline hemoglobin A1c value of 6.6% to 9.9%. Exclusion: current insulin therapy; participation in exercise 2 or more times weekly or in any resistance training during the previous 6 months; changes during the previous 2 months in oral hypoglycemic, antihypertensive, or lipid- lowering agents or body weight; serum creatinine level of 200 mmol/L or greater; proteinuria greater than 1 g/d; blood pressure greater than	3 days p/ week for 6 months.	Before randomization, all participants entered a 4-week run-in phase to assess adherence. RT: 7 exercises; intensity: 7-9 RM; dose: 6-9 S/MG/W. AT: 60-75% VO_2 max; dose: 45-135 min/week. Combined group: RT + AT. Training sessions: Individual exercise supervision was	Triglycerides HDL-C SBP DBP WC Baseline 3 months 6 months

	Combined group = 53.5 ± 7.3 Control group = 54.8 ± 7.2	160/95 mmHg; restrictions in physical activity because of disease; presence of other medical conditions that made participation inadvisable.		provided weekly for the first 4 weeks after randomization and biweekly thereafter. Control group: asked to revert to pre-study activity levels.	
Stensvold 2010[17]	n = 43 RT group = 11 Aerobic group = 11 Combined group = 10 Control group = 11 % Female = 39,5% Age (Mean ± SD) RT group = 50.9 ± 7.6 Aerobic group = 49.9 ±10.1 Combined group = 52.9 ± 10.4 Control group = 47.3 ± 10.2	Inclusion: Patients with metabolic syndrome according to International Diabetes Federation. Exclusion: unstable angina pectoris, uncompensated heart failure, myocardial infarction during the past 4 wk, complex ventricular arrhythmias, and kidney failure.	Sessions 3 days p/ week for 12 weeks.	RT: 7 exercises; intensity: 60-80% 1RM; dose: 9 S/MG/W. AT: 70-95% HR_{peak}; dose: 129 min/week. Combined group: RT (1x p/wk) + AT (2x p/wk). Training sessions: Supervised. Control group: was instructed not to change their dietary patterns or physical activity levels during the study period.	Triglycerides HDL-C Fasting Plasma Glucose SBP DBP WC Baseline 12 wks
Saremi 2011[15]	n= 21 RT group = 11 Control group = 10 All male Age (Mean ± SD) All participants = 45,25 ±	Inclusion: Males with the metabolic syndrome (based International Diabetes Federation); Low physical activity level (less than 30 minutes of physical activity per day); Aged between 20-60.	Sessions 3 days p/ week for 12 weeks.	RT: intensity: 30-85% 1RM; dose: 6-9 SMG/W. Training sessions: Supervised. Control group: not participate in any regular exercise**.**	Triglycerides HDL-C Fasting Plasma Glucose WC Baseline 12 wks

	4,3	Exclusion: Cardiovascular disease; Musculoskeletal problems; Receiving any other treatments.			
Venojarvi 2013[19]	n = 144 RT group = 49 Aerobic group = 48 Control group = 47 All males Age (Mean ± SD) RT group = 54 ± 6.1 Aerobic group = 55 ± 6.2 Control group = 54 ± 7.2	Inclusion: age 40-65 years; BMI between 25.1 and 34.9 kg/m^2; and fasting plasma glucose between 5.6 and 6.9 mmol/L. Exclusion: earlier detection of IGT and engagement in prescribed diet or exercise programs, engagements in regular and physically very rigorous activities and usage of medication affecting glucose balance.	Sessions 3x p/ week for 12 weeks.	RT: 50-85% 5RM; dose: 125 min/wk. AT: 55-75% of Heart Rate reserve; dose: 103 min/wk. Training sessions: Supervised. Control group: not participate in any regular exercise**.**	Triglycerides HDL-C Fasting Plasma Glucose SBP DBP WC Baseline 12 wks
Earnest 2014[16]	n = 262 RT group = 73 Aerobic group = 72 Combined group = 76 Control group = 41 %Female = 63% RT group = 59% Aerobic group = 62% Combined group = 64% Control group = 68% Age (Mean ± SD) RT group = 57 ± 9 Aerobic group = 54 ± 9 Combined group = 55 ± 8 Control group = 59 ±8	Inclusion: type 2 diabetes; sedentary (not participating in RT and Aerobic exercise. Exclusion: history of stroke, advanced neuropathy or retinopathy, or other serious medical condition contraindicated for exercise or that may prevent adherence to the study protocol.	Sessions 3 days p/ week for 9 months.	RT: 7 exercises; intensity: 10-12 RM; dose: 6-9 S/MG/W. AT: 65% VO_{2peak}; dose: 150 min/wk. Combined group: 2x p/wk of RT and 3-5x p/wk of aerobic training. Training sessions: Supervised. Control group: Offered weekly stretching and relaxation classes.	Triglycerides HDL-C Fasting Plasma Glucose SBP DBP WC Baseline 9 months

RT: Resistance Training; **AT:** Aerobic Training; **RM:** Repetition Maximum; **CHD:** Coronary Heart Disease; **BMI:** Body Mass Index; **HDL-C:** High Density Lipoprotein Cholesterol; **SBP:** Systolic Blood Pressure; **DBP:** Diastolic Blood Pressure; **WC:** Waist Circumference; **IGT:** Impaired Glucose Tolerance; **S/MG/W:** Sets for each muscle group per week; **HR:** Heart rate.

Methodological quality

One study[30] was considered "high quality", three studies[17 28 29] were considered "moderate quality", and four studies[15 16 19 27] were considered "poor quality". All included trials had random allocation, between group comparisons and provided points and estimates of variability. Concealed allocation was performed in two studies[17 30]. Because of the nature of the interventions, blinding of participants and therapists was not possible. Assessor blinding was implemented in 12.5% of included studies[29]. In addition, 50% of studies had adequate follow-up[17 28-30], and 25% included an intention-to-treat analysis[29 30]. Complete details are reported in Appendix Table 3.

Resistance training as an exercise treatment of metabolic syndrome

The results for the meta-analysis comparing the effects of resistance training with a control group show that resistance training is not superior to control intervention (no intervention) in improving fasting plasma glucose (seven studies, I^2=0%, MD 0.04 [95%CI, -0.12, 0.21]), HDL-cholesterol (eight studies, I^2=0%, MD 0.00 [95%CI, -0.05, 0.04]), triglycerides (eight studies, I^2=0%, MD 0.03 [95%CI, -0.14, 0.20]), diastolic blood pressure (seven studies, I^2=0%, MD 1.39 [95%CI, -0.19, 2.98]) and waist circumference (eight studies, I^2=0%, MD 1.09 [95%CI, -0.12, 2.30]). However, the results of pooling data show that resistance training is significantly superior to control groups in reducing systolic blood pressure (seven studies, I^2=0%, MD 4.08 [95%CI, 1.33, 6.82]) (**Figure 2 and 3**).

<<Insert Figure 2 and 3>>

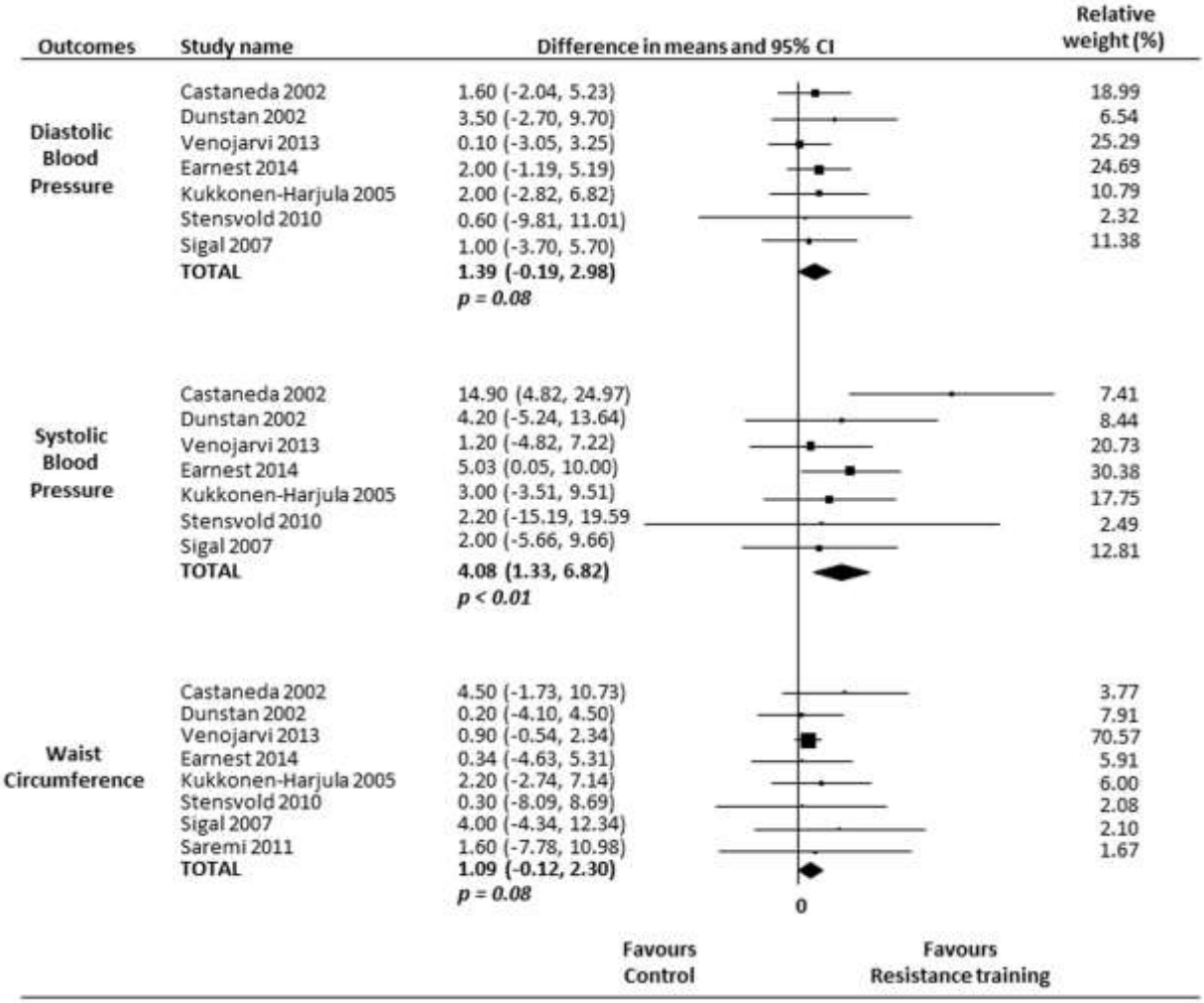

Figure 2. Effects of resistance training on clinical parameters of metabolic syndrome.

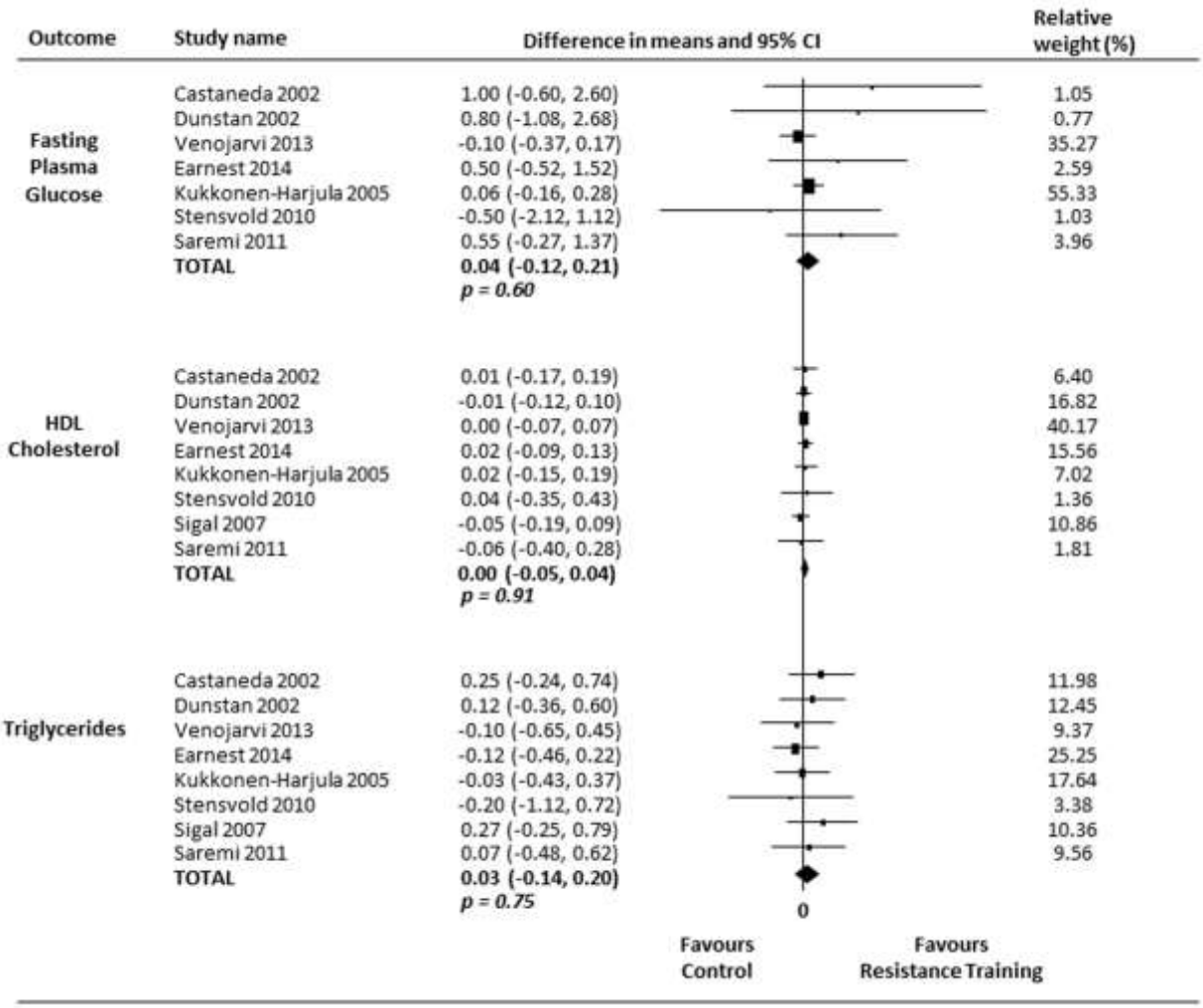

Figure 3. Effects of resistance training on metabolic parameters of metabolic syndrome.

Secondary exploratory analysis

Exploratory analysis was performed comparing low methodological quality (PEDro ≤ 4) vs moderate/high methodological quality (PEDro ≥ 5) studies (Appendix Figure 10-15), and short-term (< 6 months) vs long-term (≥ 6 months) studies (Appendix Figure 4-9). Potential influences of these aspects were not detected because comparisons of subgroups revealed no differences in pooled estimates with overlapping confidence intervals**.** However, long-term trials seem to be more effective than short-term in reducing blood pressure. A slight positive effect on systolic

blood pressure and waist circumference was also observed in moderate/high quality studies when compared with low quality ones.

Based on the GRADE system (Appendix Table 4), pooled data of HDL-Cholesterol, triglycerides, systolic blood pressure, diastolic blood pressure and waist circumference were classified as moderate-quality evidence. The evidence for fasting plasma glucose was classified as low-quality. Quality of evidence was downgraded one level because of the risk of bias, and one level because of imprecision of findings.

DISCUSSION

This systematic review and meta-analysis demonstrated that RT is associated with a reduction in systolic blood pressure. Moreover, there seems to be a trend that resistance training slightly improves diastolic blood pressure and waist circumference. RT had no effect on metabolic parameters, i.e. fasting glucose, HDL-cholesterol and triglycerides.

The results of this study are in agreement with previous meta-analyses. Authors have found reduced blood pressure, especially systolic, after resistance training[4 21 31]. The reduction found was statistically significant (4.1 mmHg), but the clinical relevance of this reduction is perhaps more important. In a major prospective study, the authors found evidence to suggest that a reduction of 3 mmHg in blood pressure can improve the risk of cardiovascular disease by up to 5%[32].

Although the differences in the reduction of diastolic blood pressure and waist circumference observed were not statistically significant, they play an important role when considering clustering of the risk factors, especially in adults over 50 years[9 21]. Any reduction of the risk factor values, no matter how small, means patients would no longer be classified as having

metabolic syndrome[33 34]. Thus, the present study reinforces the importance of physical training as an important strategy in the treatment and prevention of this syndrome.

Regarding metabolic outcomes, the results corroborate those of Cornelissen et al.[31]. The authors did not find any significant changes in fasting glucose, HDL-cholesterol and triglyceride values. When the studies were considered individually, only one found significant positive changes in HDL-C[28] and one showed improvement in triglyceride and fasting plasma glucose values[15]. Both studies used only male subjects, however, little information is available in literature to show that this fact has been instrumental in divergent findings with other clinical trials. Whereas 62.5% of the studies included in this review comprised volunteers of both sexes, and metabolic changes caused by menopause may influence the behavior of these risk factors[35], further research is needed with specific populations to better understand these effects.

The results of this study should be viewed with caution, as most of the studies included have low methodological quality, which can cause interpretation bias of positive results. Researches with better methodological quality are required in order to elucidate the effects of RT training on clinical and metabolic risk factors of MS.

Our secondary exploratory analysis also did not reveal any potential influence of subgroups of intervention time and methodological quality. But the number of studies in the subgroup analyses prevent any definitive conclusion about the influence of these factors.

Strengths and limitations

The strengths of this systematic review are its search protocol and the inclusion of studies in any language. The PEDro scale was used rather than the Cochrane Risk of Bias tool to assess risk of bias as the PEDro scale has been shown to have acceptable reliability[23] and validity[22 36], whereas two studies have reported reliability limitations with the Cochrane tool[37 38]. Another

strength of this review is that the training effect was explored through quantitatively pooled trials. In addition, the inconsistency (I^2) of the meta-analysis was 0% for all risk factors, and the overall quality of the evidence was assessed with the GRADE approach.

A limitation of this review is that publication bias was not assessed with a funnel plot, as tests for funnel plot asymmetry should be used only when there are at least 10 studies included in the meta-analysis[26]. In addition, no attempt was made to find unpublished trials in clinical registries and conferences, which could also be considered a limitation, along with the small number of studies included. With a larger number of trials, the evidence quality would be more reliable.

CONCLUSION

In summary, resistance training can be used as an effective treatment to reduce systolic blood pressure levels and to ameliorate clinical parameters in people with metabolic syndrome. These changes may improve the diagnostic status of patients with metabolic syndrome.

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Competing interests: None.

What are the contributions of this review?

- This meta-analysis shows that RT promotes a reduction of approximately 4.1 mmHg in systolic blood pressure.
- There was no statistical difference between RT and control in reducing diastolic blood pressure and waist circumference, but the observed effects may be clinically relevant.
- RT can be considered to improve the clinical parameters of metabolic syndrome.

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Appendix Table 1. Search strategy (up to January 10th 2015).

MEDLINE

1. 'clinical trial' OR 'controlled trial' OR 'randomized controlled trial' OR 'randomised controlled trial' OR 'randomized' OR 'randomised' OR 'trial' OR 'controlled clinical trial'
2. 'metabolic syndrome' OR 'metabolic syndrome x'
3. 1 and 2
4. 'resisted training' OR 'resistance training' OR 'resisted exercise' OR 'resistance exercise' OR 'strength training' OR 'strength exercise'
5. 3 and 4
6. Animal
7. 5 not 6

EMBASE

1. 'clinical trial' OR 'controlled trial' OR 'randomized controlled trial' OR 'randomised controlled trial' OR 'randomized' OR 'randomised' OR 'trial' OR 'controlled clinical trial'
2. 'metabolic syndrome' OR 'metabolic syndrome x'
3. 1 and 2
4. 'resisted training' OR 'resistance training' OR 'resisted exercise' OR 'resistance exercise' OR 'strength training' OR 'strength exercise'
5. 3 and 4
6. Animal
7. 5 not 6

THE COCHRANE LIBRARY

1. 'clinical trial' OR 'controlled trial' OR 'randomized controlled trial' OR 'randomised controlled trial' OR 'randomized' OR 'randomised' OR 'trial' OR 'controlled clinical trial'
1. 'metabolic syndrome' OR 'metabolic syndrome x'
2. 1 and 2
3. 'resisted training' OR 'resistance training' OR 'resisted exercise' OR 'resistance exercise' OR 'strength training' OR 'strength exercise'
4. 3 and 4
5. Animal
6. 5 not 6

Filter: "trials".

SPORTDiscus

1. 'clinical trial' OR 'controlled trial' OR 'randomized controlled trial' OR 'randomised controlled trial' OR 'randomized' OR 'randomised' OR 'trial' OR 'controlled clinical trial'
2. 'metabolic syndrome' OR 'metabolic syndrome x'

3. 1 and 2
4. ‘resisted training’ OR ‘resistance training’ OR ‘resisted exercise’ OR ‘resistance exercise’ OR ‘strength training’ OR ‘strength exercise’
5. 3 and 4
6. Animal
7. 5 not 6

PEDro

Abstract & Title: metabolic syndrome
Therapy: strength training
Method: clinical trial

Appendix Table 2. Potentially eligible articles excluded after full text evaluation.

Author, year	Title	Reason for exclusion
Tsuzuku 2007	Favorable effects of non-instrumental resistance training on fat distribution and metabolic profiles in healthy elderly people.	Healthy subjects.
Kemmler 2009	Exercise decreases the risk of metabolic syndrome in elderly females.	Mixed training – Aerobic plus resistance.
Levinger 2009	Inflammation, hepatic enzymes and resistance training in individuals with metabolic risk factors.	No evaluation of metabolic syndrome risk factors.
Balducci 2010	Effect of an intensive exercise intervention strategy on modifiable cardiovascular risk factors in subjects with type 2 diabetes mellitus: A randomized controlled trial: The Italian Diabetes and Exercise Study (IDES).	Mixed training – Aerobic plus resistance.
Ho 2010	Twelve weeks of moderate aerobic, resistance and combination exercise training improves chronic disease risk factors in overweight and obese subjects.	Conference abstract.
Bateman 2011	Comparison of aerobic versus resistance exercise training effects on metabolic syndrome (from the Studies of a Targeted Risk Reduction Intervention Through Defined Exercise -- TRRIDE-AT/RT).	No control group.
Stensvold 2012	Effect of exercise training on inflammation status among people with metabolic syndrome.	No evaluation of metabolic syndrome risk factors.
Conceição 2013	Sixteen weeks of resistance training can decrease the risk of metabolic syndrome in healthy postmenopausal women.	Healthy subjects.
Kemmler 2013	Long-term exercise and risk of metabolic and cardiac diseases: The erlangen fitness and prevention study.	Mixed training – Aerobic plus resistance.
Rodriguez-Escudero 2013	Effect of a lifestyle therapy program using cardiac rehabilitation resources on metabolic syndrome componentes.	Mixed training – Aerobic plus resistance.
Venojarvi 2013	12 Weeks' aerobic and resistance training without dietary intervention did not influence oxidative stress but aerobic training decreased atherogenic index in middle-aged men with impaired glucose regulation.	No evaluation of metabolic syndrome risk factors.
Bouchonville 2014	Weight loss, exercise or both and cardiometabolic risk factors in obese older adults: Results of a randomized controlled trial.	Mixed training – Aerobic plus resistance.

Appendix table 3. Risk of bias of included studies (PEDro).

Study	Eligibility criteria specified	Random allocation	Concealed allocation	Groups similar at baseline	Participant blinding	Therapist blinding	Assessor blinding	Adequate follow-up	Intention to treat analysis	Between group comparisons	Point estimates and variability	Total (0-10)
Castaneda 2002	No	Yes	No	No	No	No	Yes	Yes	Yes	Yes	Yes	6
Dunstan 2002	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4
Kukkonen-Harjula 2005	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5
Sigal 2007	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Stensvold 2010	Yes	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	6
Saremi 2011	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4
Venojarvi 2013	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4
Earnest 2014	No	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4

Appendix table 4. Quality summary of outcome assessment (GRADE).

Outcomes	Quality Assessment			Patient, n		Effect	Quality
	Risk of Bias ‡	Inconsistency §	Imprecision ¶	RT Group	Control Group	MD† (95% CI)	
Fasting Plasma Glucose Seven studies	Serious limitation (-1)	No serious inconsistency	Serious imprecision (-1)	202	168	0.04 (-0.12, 0.20)	Low
HDL-Cholesterol Eight studies	Serious limitation (-1)	No serious inconsistency	Serious imprecision	266	231	-0.00 (-0.05, 0.04)	Moderate
Triglycerides Eight studies	Serious limitation (-1)	No serious inconsistency	Serious imprecision	266	231	0.03 (-0.14, 0.20)	Moderate
Diastolic Blood Pressure Seven studies	Serious limitation (-1)	No serious inconsistency	Serious imprecision	255	221	1.39 (-0.19, 2.98)	Moderate
Systolic Blood Pressure Seven studies	Serious limitation (-1)	No serious inconsistency	Serious imprecision	255	221	4.08 (1.33, 6.82)	Moderate
Waist Circumference Eight studies	Serious limitation (-1)	No serious inconsistency	Serious imprecision	266	231	1.09 (-0.12, 2.30)	Moderate

† Mean Difference (MD) of the resistance training group compared with the control group.

‡ More than 25% of participants from studies with low methodological quality (Physiotherapy Evidence Database (PEDro) score <7 points).

§ Substantial I^2 (>75%).

¶Fewer than 400 participants for each outcome.

Appendix figure

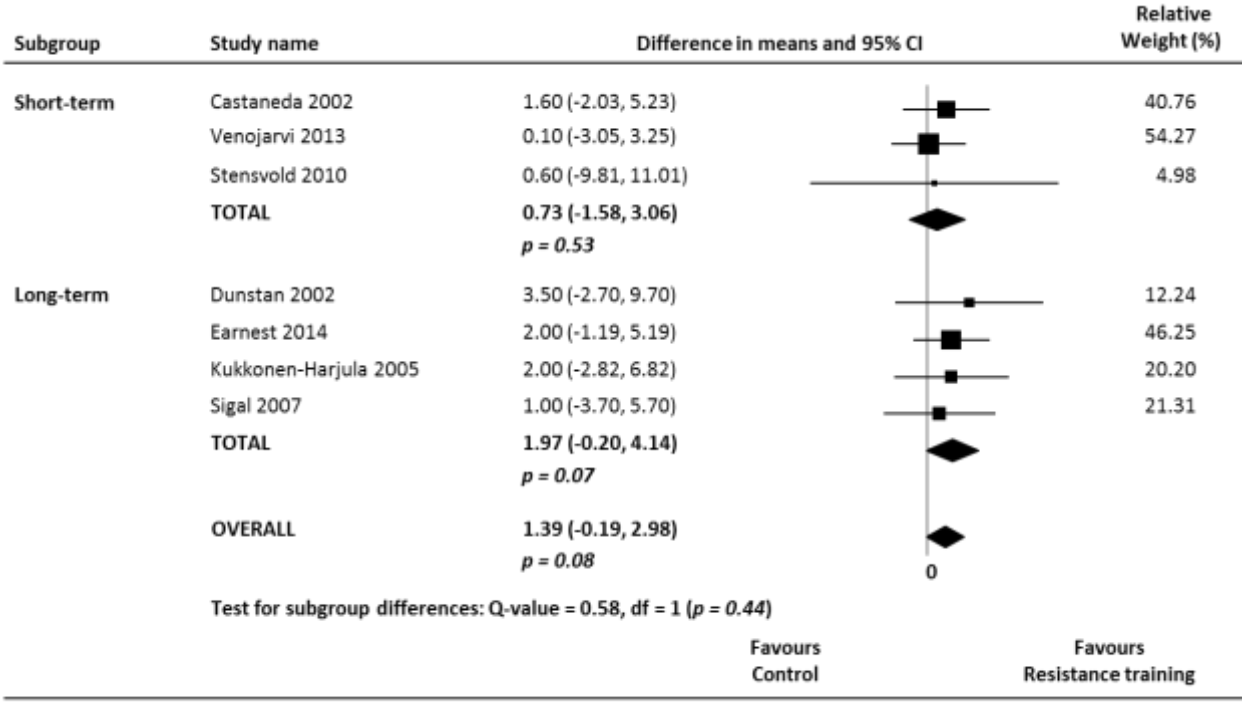

Figure 4. Forest plot (short vs. long-term) showing pooled MD with 95% CI for diastolic blood pressure.

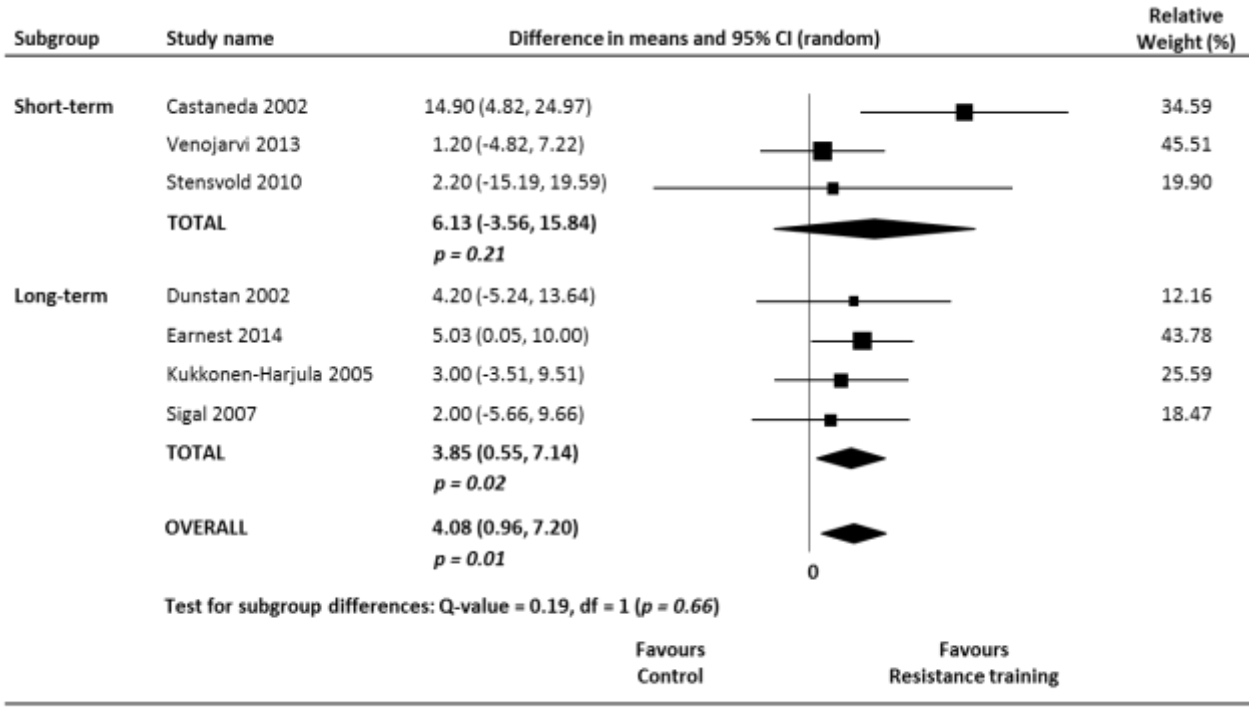

Figure 5. Forest plot (short vs. long-term) showing pooled MD with 95% CI for systolic blood pressure.

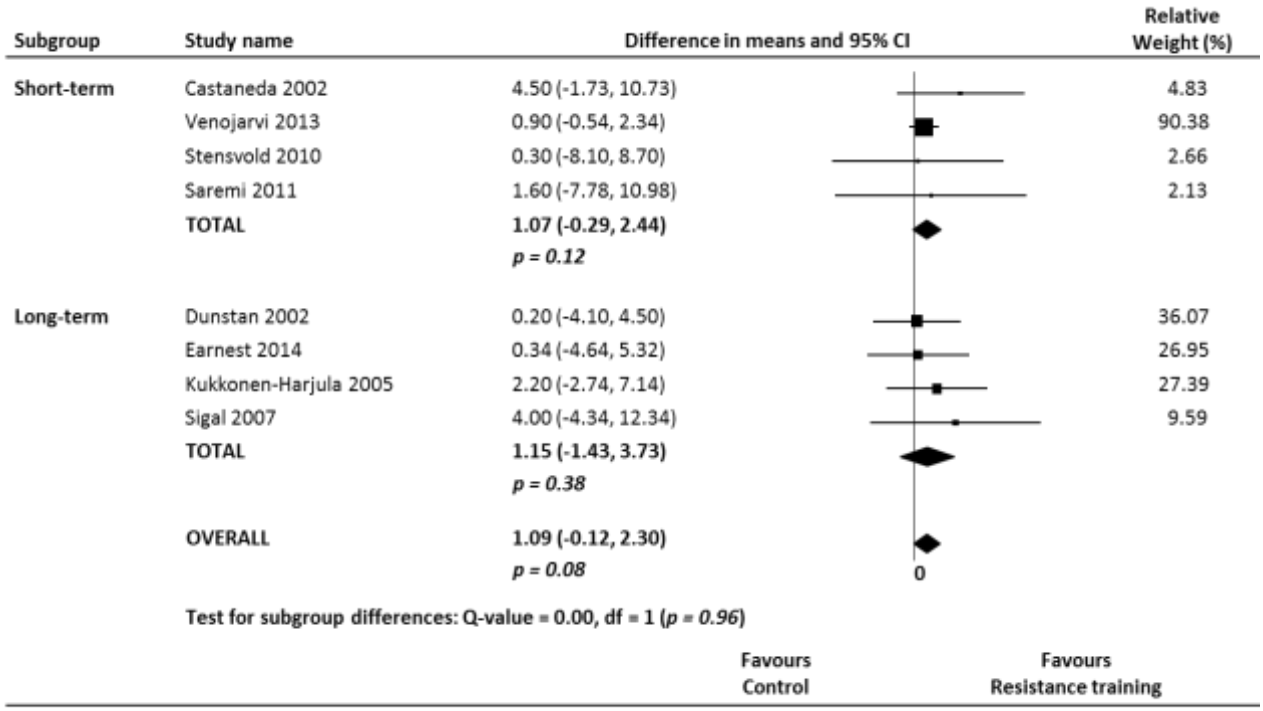

Figure 6. Forest plot (short vs. long-term) showing pooled MD with 95% CI for waist circumference.

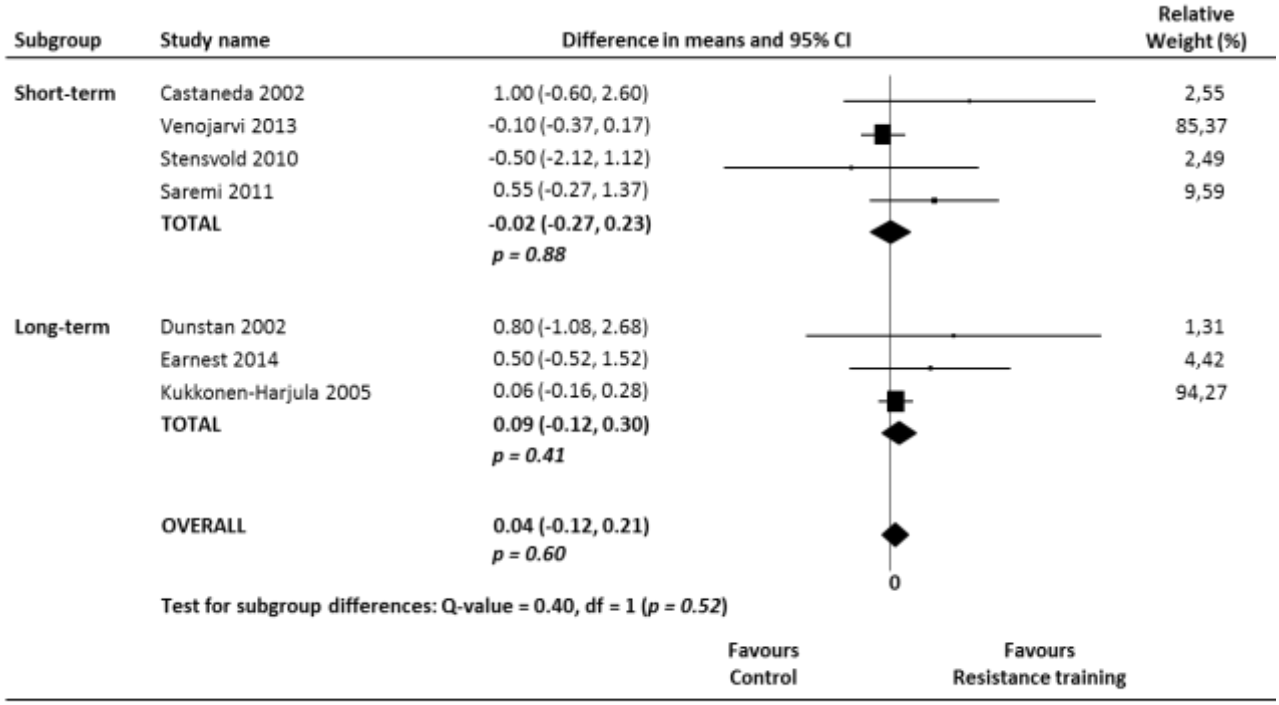

Figure 7. Forest plot (short vs. long-term) showing pooled MD with 95% CI for fasting glucose.

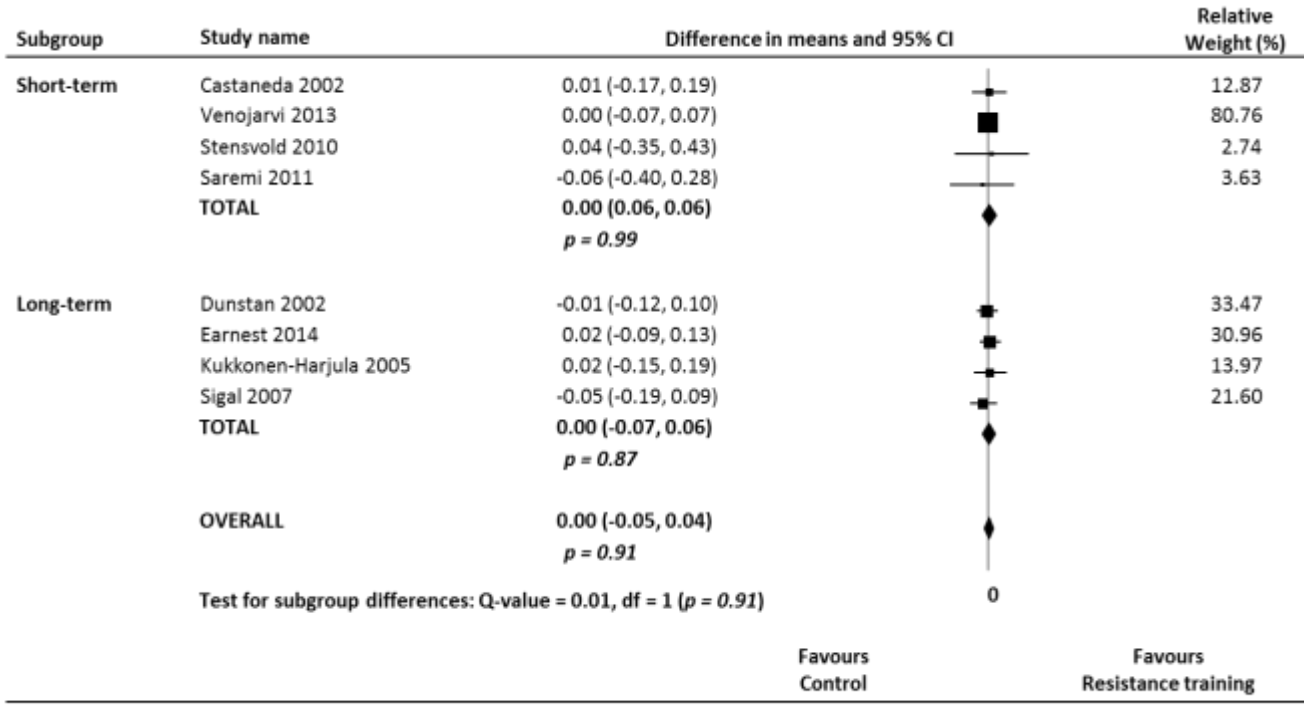

Figure 8. Forest plot (short vs. long-term) showing pooled MD with 95% CI for HDL-cholesterol.

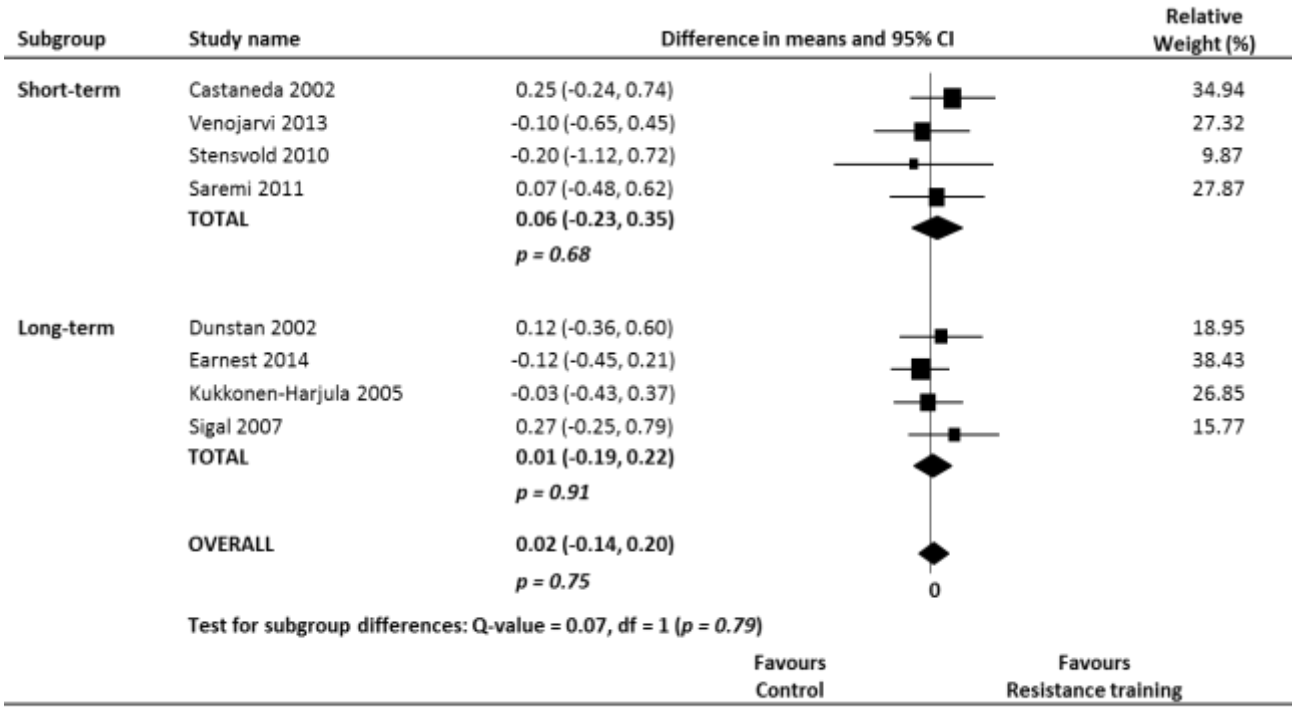

Figure 9. Forest plot (short vs. long-term) showing pooled MD with 95% CI for triglycerides.

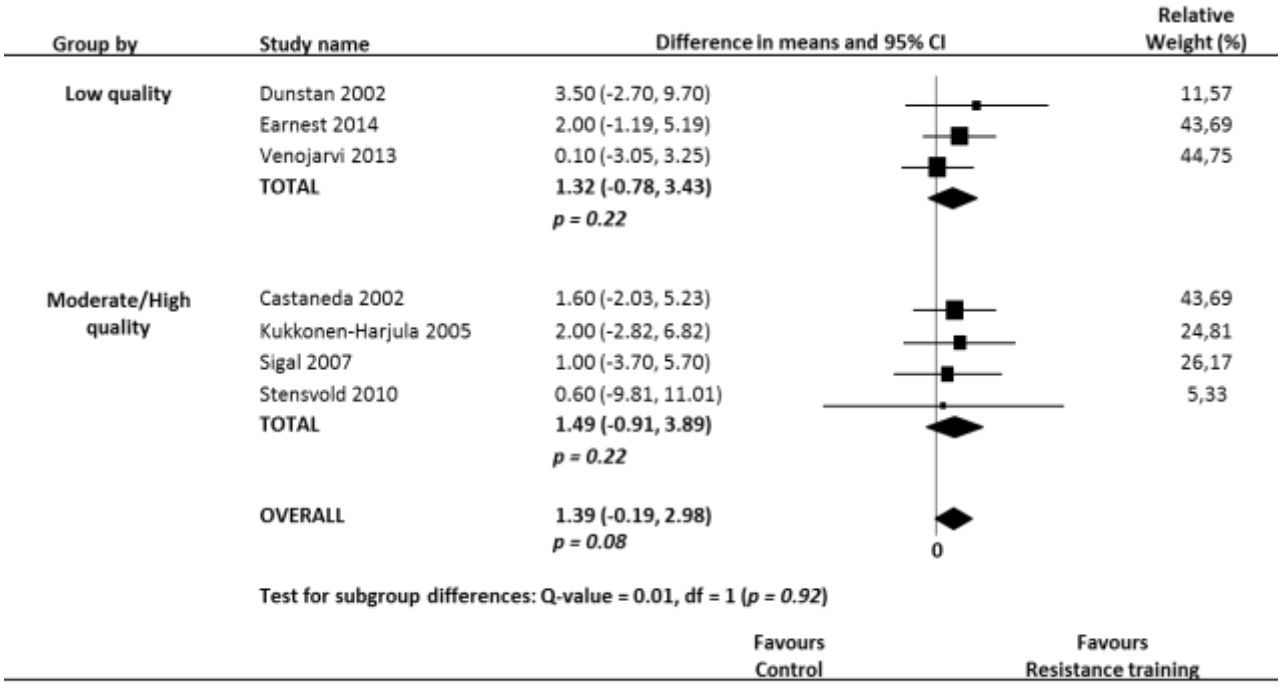

Figure 10. Forest plot (low vs moderate/high quality) showing pooled MD with 95% CI for diastolic blood pressure.

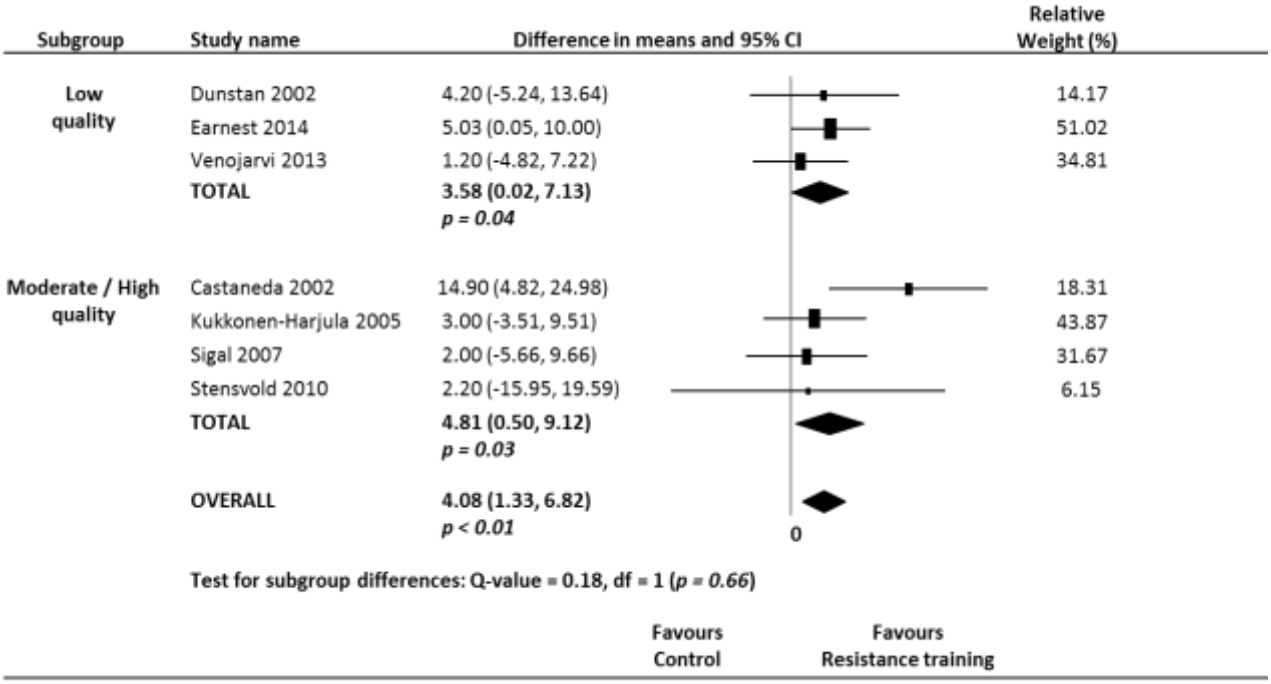

Figure 11. Forest plot (low vs moderate/high quality) showing pooled MD with 95% CI for systolic blood pressure.

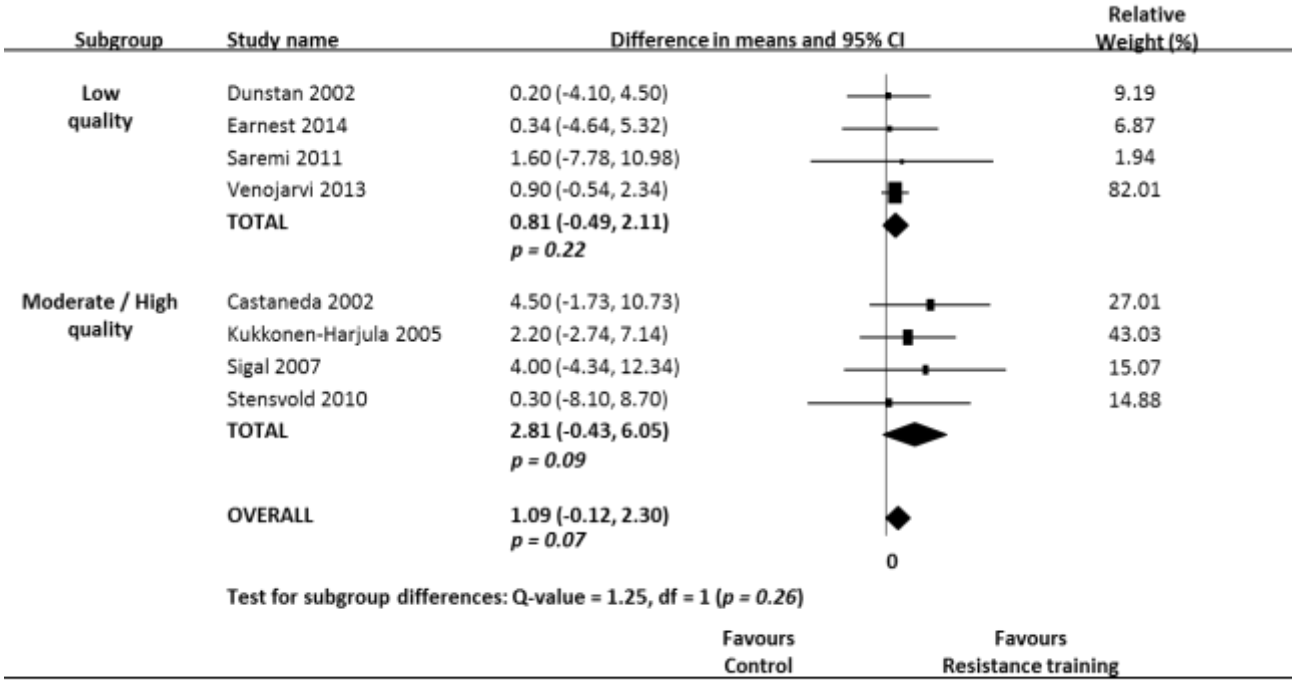

Figure 12. Forest plot (low vs moderate/high quality) showing pooled MD with 95% CI for waist circumference.

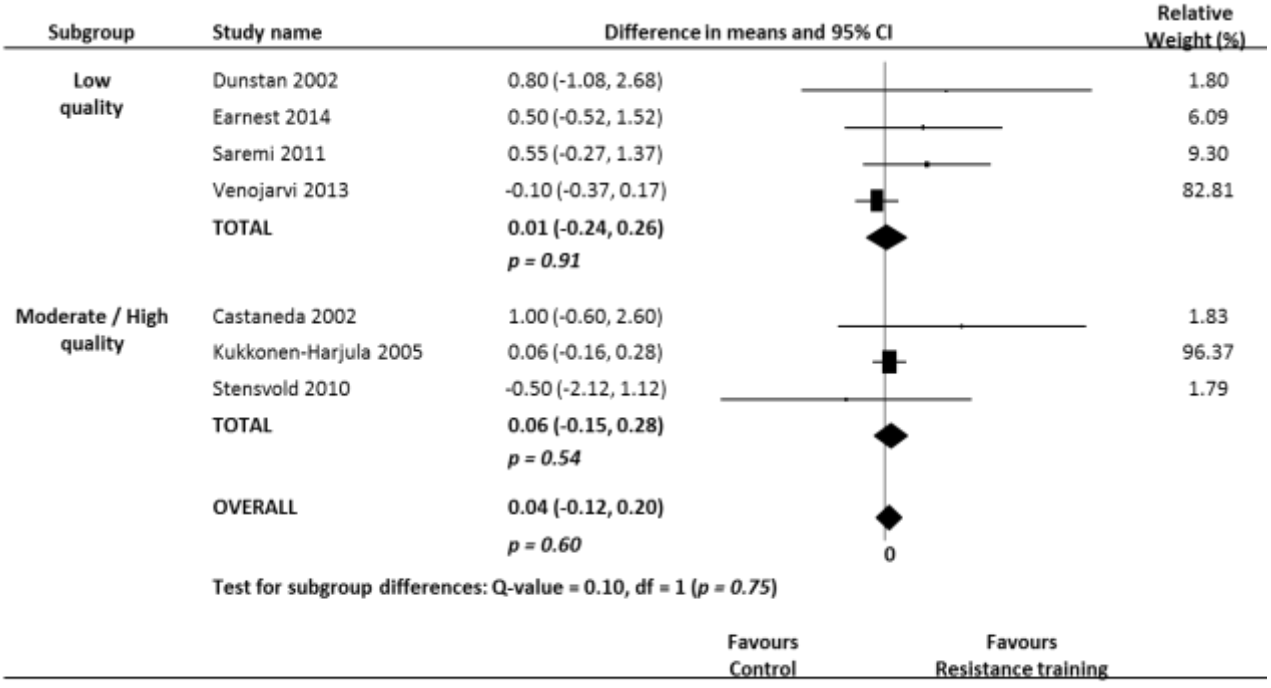

Figure 13. Forest plot (low vs moderate/high quality) showing pooled MD with 95% CI for fasting glucose.

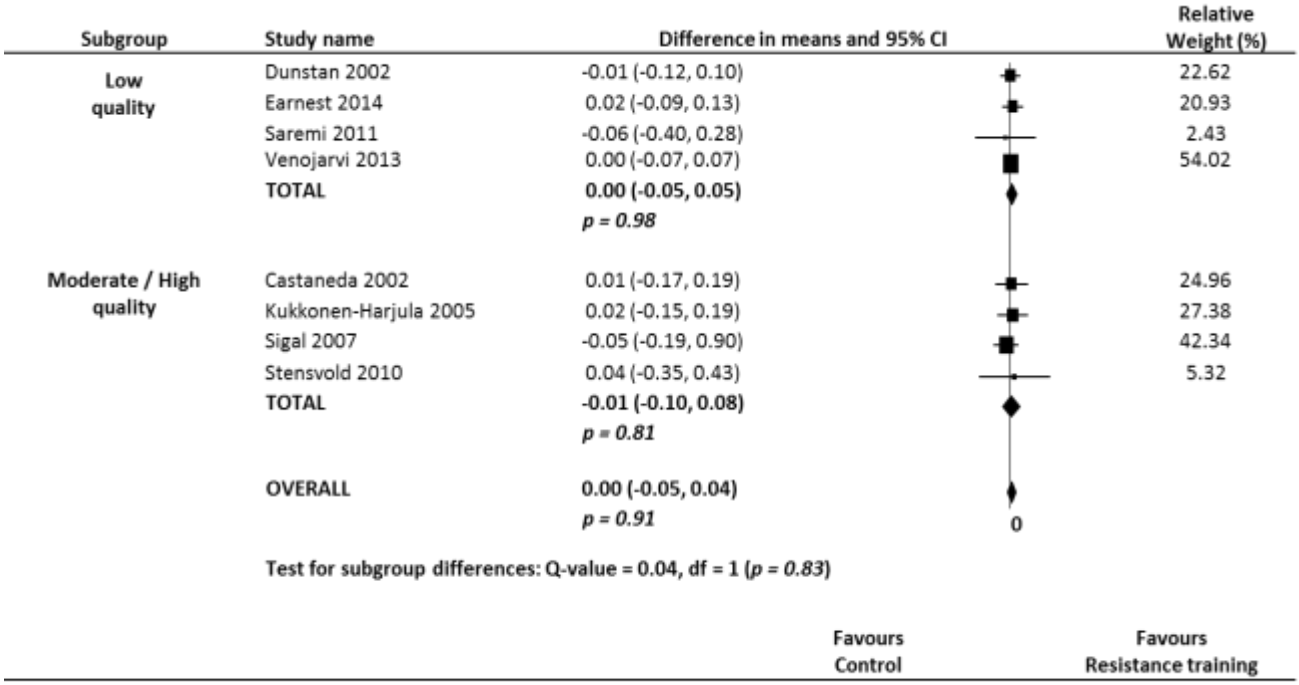

Figure 14. Forest plot (low vs moderate/high quality) showing pooled MD with 95% CI for HDL-cholesterol.

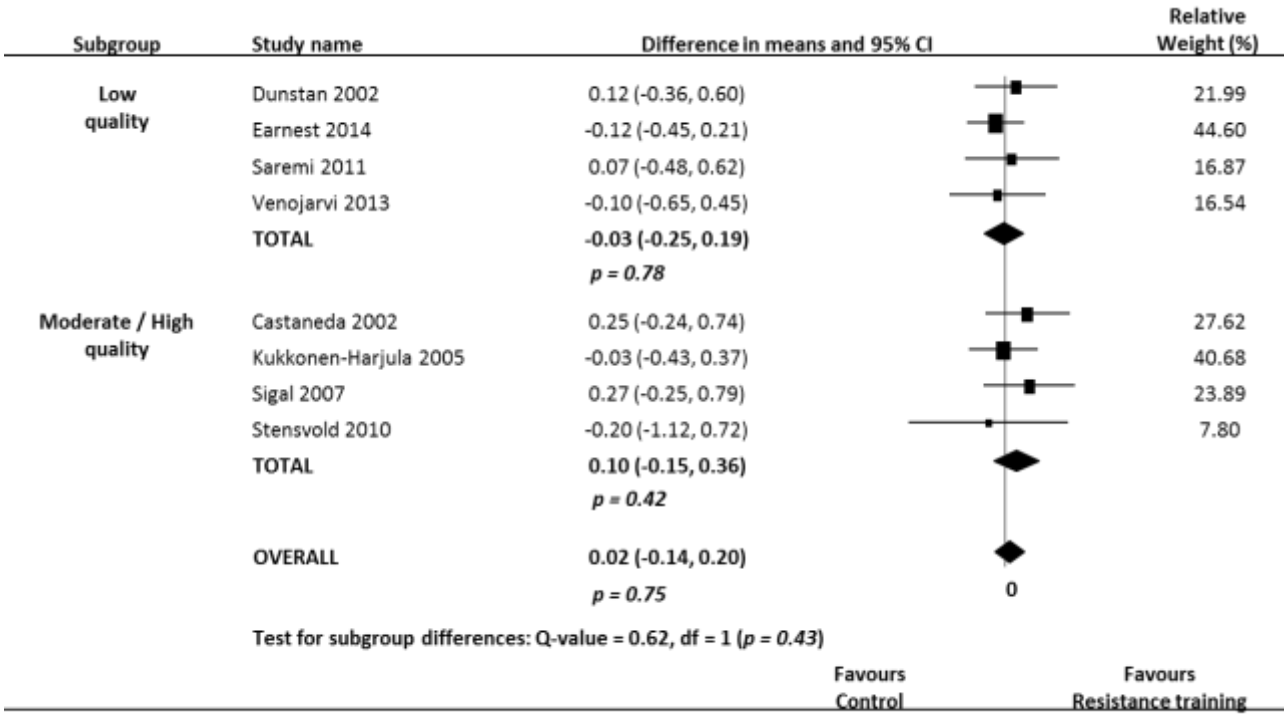

Figure 15. Forest plot (low vs moderate/high quality) showing pooled MD with 95% CI for triglycerides.

PROSPERO Registration - **Registration number CRD42015016538;**

Available: http://www.crd.york.ac.uk/PROSPERO/

UNIVERSITY of York
Centre for Reviews and Dissemination

NHS
National Institute for Health Research

PROSPERO International prospective register of systematic reviews

Effects of resistance training on metabolic syndrome: a systematic review and meta-analysis of randomized controlled trials

Italo Ribeiro Lemes, Paulo Henrique Ferreira, Aryane Flauzino Machado, Carlos Marcelo Pastre, Jayme Netto Junior

Citation
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Review question(s)
Summarize the effects of resistance training on MS risk factors compared to a control group.

Searches
Database: MEDLINE, PEDro, EMBASE, SPORTDiscus and The Cochrane Library.

There are no restrictions on language or publication period.

Types of study to be included
Only randomized controlled trials that compared resistance training versus control group (no intervention) will be included in this review. Studies that used a diet intervention were included if this intervention was equal to all groups. Trials will be eligible if they included participants with metabolic syndrome and abnormalities, and assessed the components of this syndrome: fasting plasma glucose, triglycerides, HDL-cholesterol, blood pressure and waist circumference. Studies that did not evaluate these outcomes will be excluded. All types of resistance training used in trials, irrespective of intensity, frequency or duration, will be eligible to be included.

Condition or domain being studied
Metabolic syndrome. The components are: fasting plasma glucose, HDL-cholesterol, triglycerides, blood pressure and waist circumference.

Participants/ population
Patients with metabolic syndrome (at least three of the five components).

Intervention(s), exposure(s)
Resistance training (RT) appears in the current scenario as an effective and low-cost method to be used as treatment and prevention of cardiovascular events, and has been indicated by respected organizations. RT is widely accepted as a successful method to increase muscle strength, lean mass and perception of physical capacity. Moreover, authors found inverse associations between muscular fitness, muscular strength and incidence of MS, showing that people practicing resistance training have 34% lower chances to developing this syndrome.

Comparator(s)/ control
Control groups who did not undergo any training.

Outcome(s)
Primary outcomes
Changes in fasting plasma glucose, HDL-cholesterol, triglycerides, blood pressure and waist circumference.

Blood outcomes measured after a fasting night. Blood pressure and waist circumference measured through standard recommendations.

Secondary outcomes
None

None

Risk of bias (quality) assessment
Two reviewers independently will assess trials methodological quality using the PEDro scale. If trials were already listed on the PEDro database (http://www.pedro.org.au/), we will adopt these scores. A PEDro score of 7 or greater will be considered "high quality", those with a score of 5 or 6 will be considered "moderate quality" and those with a score of 4 or less "poor quality". Any disagreements in the scoring of trials will be resolved consensually. Methodological quality will be not an inclusion criterion. Two reviewers also independently will extract outcome data using a standardized data extraction form.

The GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach will be used by two independent reviewers to evaluate the overall quality of evidence and the strength of the recommendation, as advocated by the Cochrane Back Review Group. The overall quality of evidence will be initially regarded as "High" but downgraded by 1 level for each of three factors encountered: limitations in the design (>25% of participants from studies with low quality methods - PEDro score <7 points); inconsistency of results (substantial I2 square statistic); imprecision (<400 participants in total for each outcome). Publication bias will be not assessed with a funnel plot and indirectness will be also not considered for this review due to the presence of a specific population, relevant outcome measures and direct comparisons.

Strategy for data synthesis
Baseline demographic data and characteristics of the studies will be extracted from included trials. Outcome data include mean, SDs and sample sizes. When there is insufficient information in trial reports, data will be imputed or calculated using methods recommended in the Cochrane Handbook for Systematic Reviews of Interventions. Outcome data will be extracted from final values (after training period) or from change scores. Blood pressure values will be expressed in mmHg, waist circumference in centimeters, glucose, triglycerides and HDL-cholesterol in mmol/l. Where appropriate, data will be transformed to these units of measurement.

Analysis of subgroups or subsets
None planned.

Dissemination plans
A paper will be submitted to a leading journal in this field.

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Anticipated or actual start date
01 July 2014

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Sao Paulo Research Foundation (FAPESP), grant #2014/05419-2

Conflicts of interest
None known

Language
English

Country
Australia, Brazil

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Humans; Metabolic Syndrome X; Resistance Training

Stage of review
Ongoing

Date of registration in PROSPERO
09 February 2015

Date of publication of this revision
09 February 2015

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

Functional training on metabolic syndrome, muscular strength and quality of life: a randomized controlled trial

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ABSTRACT

Background: Resistance and aerobic training have been used as treatment and prevention strategies of metabolic syndrome. However, the effects of different methods, such as functional training, applied in this population deserves to be investigated. The aim of this clinical study was to investigate the effects of 12 weeks of functional training on metabolic syndrome risk factors, muscular strength and quality of life. **Methods:** This study was carried out between January and July 2014 in Presidente Prudente, Brazil. 36 participants, both sex, between 40 and 60 years old, with metabolic syndrome, were randomized in training group and control group. Intervention group underwent a 12-week functional periodized training 3 times per week and control group were instructed to not change their habitual activities. Metabolic syndrome risk factors, muscular strength and quality of life were assessed before and after intervention. **Results:** Training group presented significantly reduction in systolic blood pressure (127.7 ± 18.48 to 119.37 ± 15.55; $p<0.05$). Also, it was observed worsening in fasting glucose (5.38 ± 1.60 to 5.57 ± 1.01; $p<0.05$), HDL-cholesterol (1.15 ± 0.25 to 1.08 ± 0.23; $p<0.05$) levels and body composition of control group, while training group remained statistically unchanged. Percentual change in muscular strength of training group was up to 44%, being statistically higher than control group ($p<0.05$). Quality of life was improved in training group in six of eight domains of the quality of life questionnaire ($p<0.05$). **Conclusions:** Functional training can improve systolic blood pressure and muscular strength. Moreover, it is able to maintain HDL-cholesterol levels and body composition values.

Clinical trial registry number: RBR-8rz4yq

Available: http://www.ensaiosclinicos.gov.br/.

Keywords: metabolic syndrome x; resistance training; muscle strength; quality of life.

BACKGROUND

Metabolic syndrome (MS) is characterized by changes in waist circumference values, blood pressure, triglycerides, HDL-cholesterol and fasting glucose. These changes increase the chances of developing cardiovascular disease (CVD) and type 2 diabetes mellitus, and even premature death[1-3]. Studies indicate a prevalence rate of 25% for western population[4], and more than 30% among middle-aged adults in Brazil [5]. Globally these values reach 28.5% in men and 40.5% in women[6-8]. Given this extremely worrying scenario, different strategies for treatment and prevention have been studied, mainly related to insertion of physical activity in daily life of this population.

Although sedentary lifestyle is not a diagnostic criteria for MS, it is an important aspect related to development of this disease since that physical inactivity has impact on primary risk factors of this syndrome, such as obesity, high blood pressure, dyslipidemia and diabetes. Therefore, intervention in routine through physical training is fundamental to improve health of this population. Several clinical trials show the effects of aerobic exercise providing metabolic and clinical benefits in patients with MS[9-11]. Although resistance training has also shown some positive effects in this population[11, 12, 5], real benefits of this method still remain uncertain, especially when it comes to periodization, individualization and implementation of training.

Thus, physical training intervention seems to be the best way to prevent and treat[13]. However, training modalities described in the literature, aerobic and resistance training, are not the only ones present in clinical field. Different types of training can be and should be explored in order to promote health. As a variation of resistance training appeared the functional training (FT), which is a method with many adherents in recent years, mainly because contain dynamic and easy application exercises providing contractions of different muscle groups

simultaneously[14, 15]. This training method is being increasingly investigated and has been proven effective in improving pain, physical function, balance and muscular strength in different populations[16-19]. Thus, it is believed that the simultaneously contraction of muscle groups could promote a better musculoskeletal adaptation and improve metabolic responses[20]. Moreover, although increasingly addressed in clinical practice, the effects of this training method on metabolic responses of specific diseases, such as MS, remain unknown.

With so many existing physical training methods, it is important to investigate the effects of different methods, especially in patient populations. Thus, the aim of this study was to investigate the effects of 12 weeks of functional training on metabolic syndrome risk factors, muscular strength and quality of life.

METHODS

Participants

Adults men and women with MS according to Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III - NCEP ATP III) criteria[6] were recruited from community using advertisements in newspaper, flyers and posters in places with high circulation of people. Then, interviews were scheduled with eligible patients to check the inclusion criteria. Calculation of sample size was made based on previous findings of muscular strength[11]. With 5% level of significance a sample size of twenty one participants per group was stipulated. MS was defined as presence of at least three of the five components: Triglycerides (> 1.69mmol/L), fasting blood glucose (> 6.11mmol/L), HDL-cholesterol (< 1.03mmol/L for men and < 1.29mmol/L for women), waist circumference (>102cm for men and > 88cm for women) and blood pressure (> 130mmHg or > 85mmHg).

Inclusion criteria were as following: aged between 40 and 60 years, be sedentary for at least previous 6 months (self-reported), do not have amenorrhea, infectious disease, musculoskeletal injuries or respiratory dysfunctions. At start of the study all subjects signed an informed consent with all information about the study, and also were asked to present a medical consent allowing the exercise practice. The study had been previously approved by the Ethics Committee in Research of the Univ. Estadual Paulista (UNESP), and is registered in a clinical trial registry database (http://www.ensaiosclinicos.gov.br/rg/RBR-8rz4yq/).

Intervention

The study was carried out at *Studio Salus,* located in Presidente Prudente, Sao Paulo, between October/2013 and June/2014. Participants were randomized using software (Microsoft Office Excel 2007) and a computer-generated random list was used for allocation. Initially, 22 volunteers were allocated to the training group and 21 in the control group. To avoid bias, randomization was stratified by age and sex. Those located in the intervention group underwent a 12-week periodized training program, 3 times per week. Training sessions were supervised by professionals and consisted of 8 exercises (5 for upper body and 3 for lower body). Upper body exercises were adapted with inclined boards and unstable surfaces, providing the participant to work different muscle groups simultaneously. Exercises that used the inclined board in the supine position, providing contraction of all anterior chain, were bench press and behind neck lat pulldown. Exercises that used the inclined board in the prone position, providing contraction of the entire posterior chain, were triceps and biceps pulley. For upright row exercise was used an unstable surface, providing contraction of the lower limbs and constant proprioception. The lower limb exercises were leg press, knee extension and leg curl.

The resistance training was periodized and week 4 and 9 were considered recuperative, where participants had no training sessions. Intensity in the first 3 weeks were between 30-40% of 1RM, and progressed from 40% to 100% between week 5 to 12. Table 1 shows the progression loads over 12 weeks. Participants from control group (CG) were instructed to keep their normal activities. All evaluations were made before and after intervention.

Table 1. Training program periodization.

Week	Sets X Repetitions	% of 1RM test
1	2 X 12	30 - 40
2	2 X 16	30 - 40
3	2 X 20	30 - 40
4	**Recuperative**	
5	1 X 16 / 12 / 9	40 / 50 / 60
6	1 X 12 / 9 / 6	50 / 60 / 70
7	1 X 10 / 8 / 6	60 / 70 / 80
8	1 X 8 / 6 / 4	70 / 80 / 90
9	**Recuperative**	
10	1 X 6 / 4 / 2 / 4 / 6	80 / 90 / 100 / 90 / 80
11	1 X 6 / 4 / 2 / 2 / 4 / 6	80 / 90 / 100 / 100 / 90 / 80
12	1 X 6 / 4 / 2 / 2 / 2 / 4 / 6	80 / 90 / 100 / 100 / 100 / 90 / 80

1RM: One-repetition maximum.

Procedures

Metabolic syndrome risk factors

Participants were instructed to remain fasted for 12 hours and then a sample of 5ml of blood were collected by a professional nurse. The samples were sent to a commercial clinical laboratory, where through standard procedures were carried out analysis of fasting glucose, HDL-cholesterol and triglycerides. Blood pressure were assessed after 15 minutes resting in sitting position, and waist circumference measured with subject in orthostatic position.

Metabolic Syndrome z score (MetSyn z score) was calculated using individual data and standard deviation of all participants at baseline[12, 5, 21].

Muscular strength

Upper and lower body muscular strength were measured by the one repetition maximum test-1RM[22]. The test began by using a weight between 30-50% of body mass for lower limbs and 10-20% for upper limbs, and increments of 20-30% for lower limbs and 5% for upper limbs were applied. Perceived strength of the individual was also considered. The test was completed when participant reached his maximum load when executing the exercise movement without mechanical failure. No more than 5 attempts to establish the maximum load were allowed. If 5 attempts were concluded before maximum load, another test were realized after a minimum of 48 hours[23]. All 1RM tests were supervisioned by a physical education professional. For upper body was used biceps curl and triceps skull crushers exercises, and for lower body was used the leg-press, knee extension and leg curl.

Body composition

Body weight and height was assessed in a standard digital scale (Tanita BC 554, Ironman/Inner Scanner, Illinois, USA) and portable stadiometer, respectively. Lean mass and percentage of body fat were measured by bioimpedance (Tanita, BC model 418, Segmental Body Composition Analyzer, Illionois, USA). All measures were assessed using the recommendations of manufacturer.

Quality of life

Quality of life was measured by The Medical Outcomes Study – Short Form 36 (SF-36), a questionnaire that is widely accepted and used in studies with MS[24, 25]. This questionnaire consists in 8 domains: physical function, physical role, bodily pain, general health, vitality, social function, emocional role and mental health. The same interviewer applied the questionnaire before and after intervention.

Statistical analysis

Data are presented as means ± standard deviation (SD), mean difference (final – baseline values) and percentual changes. Normality was assessed by Kolmogorov-Smirnov test and the Student t test was used when normal distribution was found. When found nonparametric distribution the Wilcoxon test was used to comparison between moments and Mann-Whitney test to comparison between groups. The level of significance was set at $p < 0.05$ for all tests.

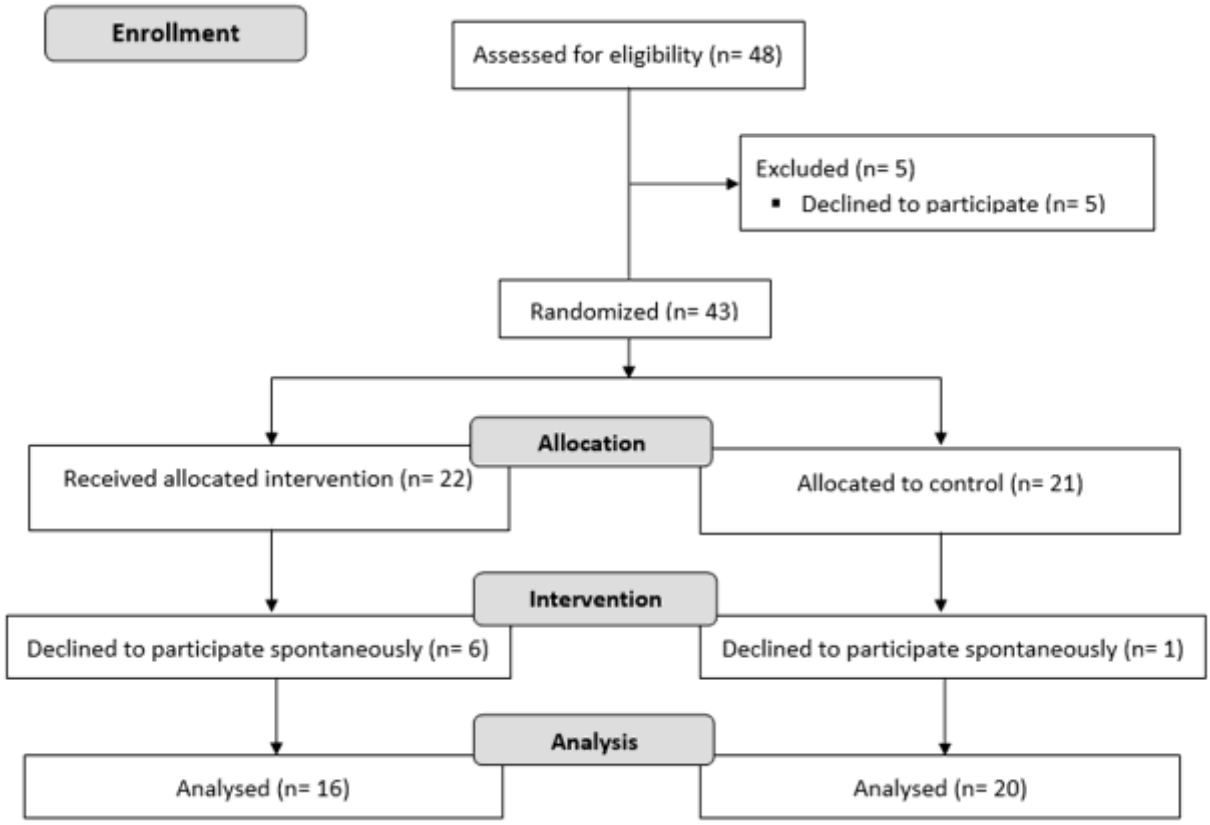

Figure 1. Flowchart of participants.

RESULTS

During the training 6 volunteers from intervention group and 1 from control group dropped out spontaneously for personal reasons. Of the 36 participants who completed the study, 13 were women and 23 were men. Figure 1 shows the flow chart of participants and Table 2 shows the baseline characteristics of all subjects in both groups.

Table 2. Baseline subject characteristics (mean ± SD).

	Functional training	Control group
n	16	20
Age	51.81 ± 6.17	49.6 ± 5.87
Sex (male/female)	10/6	13/7
Height (cm)	164.43 ± 11.45	167.5 ± 9.47
Weight (kg)	85.31 ± 9.33	77.15 ± 15.49
BMI (kg/m^2)	31.72 ± 3.80*	27.32 ± 3.96
Medications in use		
Antihypertensive agentes *n (%)*		
Total#	8 (50)	6 (28,6)
Beta blocker	4 (25)	1 (4,8)
Angiotensin receptors antagonist	4 (25)	3 (14,3)
Inhibitor of angiotensin converting enzyme	0 (0)	0 (0)
Calcium channel blockers	1 (6,3)	0 (0)
Diuretics	5 (31,3)	2 (9,5)
Lipid lowering agents *n (%)*		
Total#	3 (18,8)	3 (14,3)
Statin	3 (18,8)	0 (0)
Fibrate	1 (6,3)	0 (0)
Others	0 (0)	3 (14,3)
Oral hypoglycemic agents *n (%)*		
Total#	6 (37,5)	1 (4,8)
Sulfonylureas	1 (6,3)	0 (0)
Metformin	5 (31,3)	0 (0)
Inhibitor of DPP 4	1 (6,3)	0 (0)
Others	2 (12,5)	1 (4,8)

BMI: Body Mass Index; **Cm:** Centimeters; **Kg:** Kilograms; **DPP:** Dipeptidyl peptidase 4.
*Significant difference (p<0,05) between training and control group.
#The same participant can take more than one medicine in the same category.

Metabolic syndrome risk factors and body composition

Table 3 shows baseline and final values, and the difference between moments. Regarding risk factors of metabolic syndrome, there was improvement only in systolic blood pressure (SBP) values on FT group ($p<0.05$). For fasting plasma glucose, FT presented no statistical difference, while CG presented significant increase ($p<0.05$). Regarding HDL-cholesterol levels, only CG decreased significantly ($p<0.05$). There was no statistical difference in comparison between groups for any of the risk factors of MS.

Regarding to body fat percentage and absolute values of lean body mass, training group showed no statistically significant changes between moments, while control group presented increased the fat percentage values and reduced lean mass values ($p<0.05$).

Table 3. Body composition and MS risk factors.

Outcome	Training group (n=16)	Control group (n=20)
Fasting plasma glucose (mmol/L)		
Baseline	5.16 ± 1.02	5.38 ± 1.60
Final	5.45 ± 0.67	5.57 ± 1.01▪
Δ	0.29 ± 0.66	0.19 ± 1.23
Triglycerides (mmol/L)		
Baseline	1.88 [1.07 – 7.30]	1.57 [0.74 – 4.23]
Final	1.90 [0.90 – 5.92]	1.60 [0.63 – 5.26]
Δ	-0.04 [-2.15 – 0.88]	0.00 [-1.11 – 1.68]
HDL-cholesterol (mmol/L)		
Baseline	1.00 ± 0.30	1.15 ± 0.25
Final	0.96 ± 0.24	1.08 ± 0.23▪
Δ	-0.04 ± 0.15	-0.06 ± 0.10
Non-HDL cholesterol (mmol/L)		
Baseline	138.25 ± 47.05	156 ± 38.45
Final	138.43 ± 29.78	159.6 ± 39.64
Δ	0.18 ± 38.20	3.60 ± 14.87
TOTAL-cholesterol/HDL-cholesterol (mmol/L)		
Baseline	4.76 ± 1.23	4.78 ± 1.69
Final	4.95 ± 1.23	5.02 ± 1.54▪
Δ	0.17 ± 0.94	0.24 ± 0.49
Waist circumference (cm)		
Baseline#	108.50 ± 9.37	97.70 ± 10.64
Final	108.83 ± 9.90	98.06 ± 11.04
Δ	0.33 ± 2.27	0.36 ± 1.40
Systolic blood pressure (mmHg)		
Baseline#	127.70 ± 18.48	115.25 ± 12.78
Final	119.37 ± 15.55▪	117.32 ± 18.11
Δ	-8.33 ± 13.60	2.07 ± 20.88
Diastolic blood pressure (mmHg)		
Baseline#	82.49 ± 9.54	72.99 ± 9.90
Final	79.47 ± 8.64	75.32 ± 14.44
Δ	-3.02 ± 9.96	2.32 ± 15.26
MetSyn z score		
Baseline#	1.99 ± 2.91	-1.18 ± 2.17
Final	1.84 ± 2.25	-0.64 ± 2.51
Δ	-0.14 ± 1.64	0.53 ± 1.63
Body fat (%)		
Baseline	35.02 ± 9.53	29.67 ± 5.92
Final	34.31 ± 10.01	30.84 ± 5.52▪
Δ	-0.71 ± 1.99*	1.17 ± 1.79
Lean body mass (Kg)		
Baseline	55.49 ± 10.77	54.28 ± 11.78
Final	55.96 ± 10.50	53.77 ± 11.49▪
Δ	0.47 ± 2.21*	-0.51 ± 0.95

Δ Mean difference; # Baseline difference between groups ($p<0.05$); ▪ Significant difference in relation to baseline ($p<0.05$); * Significant difference in change in relation to control group ($p<0.05$); Triglycerides expressed in median and minimum and maximum values.

Muscular strength

Baseline values of 1RM test and percentual change are shown in Table 4. When comparing percentage gain between groups, training group is significantly superior to control group ($p<0.05$) for the following exercises, biceps curl, triceps skull crushers, leg curl and leg press.

Table 4. Muscular strength values.

Exercise	Training group (n=16)	Control group (n=20)
Biceps curl		
Baseline	21.75 ± 8.38	24.94 ± 8.92
Δ%	30.45 ± 12.71*	6.55 ± 18.29
Triceps skull crushers		
Baseline	15.50 ± 6.63	15.89 ± 6.37
Δ%	44.19 ± 24.45*	6.36 ± 22.28
Leg extension		
Baseline	87.50 ± 38.60	83.21 ± 28.80
Δ%	36.85 ± 14.79	20.41 ± 30.21
Leg curl		
Baseline	51.25 ± 21.48	61.05 ± 19.19
Δ%	43.64 ± 25.68*	-0.23 ± 14.68
Leg press		
Baseline	97.18 ± 35.48	100.52 ± 31.78
Δ%	37.64 ± 17.30*	6.16 ± 17.54

Δ%: Mean percentual of change;
*Significant difference in relation to control group (p<0,001).

Quality of life

Figure 2 show baseline and final values of quality of life domains of SF-36 questionnaire. Training group presented significant improvement for physical role, bodily pain, vitality, social function, emocional role and mental health ($p<0.05$).

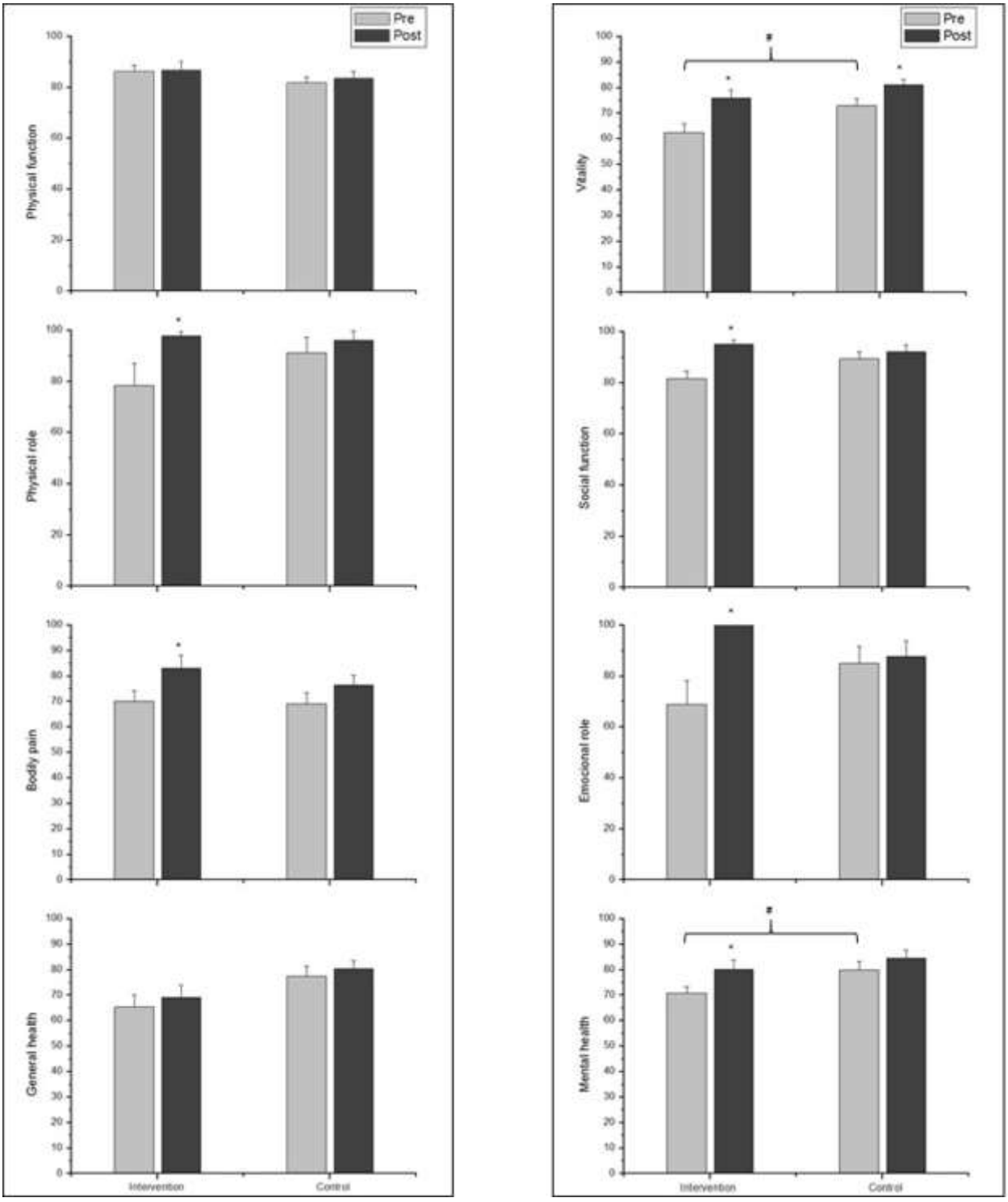

Figure 2. Pre and post values of the Medical Outcome Study Short Form-36 (SF-36). *Significant difference compared to pre value ($p<0.05$). #Significant difference between groups ($p<0.05$).

DISCUSSION

The aim of this study was to investigate the effects of 12 weeks of functional training on risk factors of metabolic syndrome, muscular strength and quality of life. Only SBP in FT had a significant reduction compared to baseline. CG presented significant increase in fasting plasma glucose, and there was no difference between moments in diastolic blood pressure (DBP), triglycerides and waist circumference for both groups. There was also a significant decline in HDL-cholesterol values for CG, while FT maintained their values statistically unchanged. For muscular strength, FT had significantly superior gains compared to control group, with increase of up to 44%.

Metabolic syndrome risk factors

It is known that resistance training decreases blood pressure about 2 or 3 mmHg[26], however, in our study this magnitude was higher (127.70 ± 18.48 to 119.37 ± 15.55). Castaneda *et al.*[27] in a clinical trial with 16 week of conventional resistance training also found significant reducing in SBP. Moreover, Dunstan and collaborators[28], also using resistance training as intervention, found a reduction in SBP and DBP after 6 months of training. In addition, a systematic review and meta-analysis[29], although with a high inconsistency (94.9%), also showed statistically significant reduction in favor of resistance training. Although some data in the literature corroborate those of the present study in relation to blood pressure, recent researches with 12 weeks[11, 30] and 9 months[31] of intervention, authors found no significant reduction in blood pressure values. Such differences in results can be explained by variations in intensity, frequency, exercises, volume and time of intervention.

Functional training did not promoted changes in HDL-cholesterol, triglycerides and waist circumference values. Previous studies suggest that resistance training has little or no effect on

improvement in triglycerides and HDL[29, 32-34] levels, and also suggest caution when recommend this training method to improve lipid profile[35]. It is believed that these variables are more susceptible to dietary changes, therefore dietary intervention combined with functional training should be investigated. However, with present results obtained from this study, it can be assumed that maintenance of these values could be positive since that control group showed a significant worsening in HDL.

Body compostition

Regarding to body composition, our study did not show significant effects on training group. However, in control group, body fat percentage values increased while lean mass decreased, both with statistical difference. There is evidence that resistance training has fundamental role in maintaining lean body mass, especially in health promotion programs[36, 22], therefore, our findings corroborate the literature[31, 37, 34, 38] that resistance training do not change, statistically, body composition values in this population. Moreover, according to literature, prevention of weight gain may be fundamental in reducing rates of obesity[32].

Muscular strength and quality of life

Muscular strength values after intervention show that functional training is as effective as conventional resistance training in promoting gains in muscular strength[37, 5, 36, 33], without necessarily changing body composition. After intervention, participants showed improvement of at least 30%, moreover, percentage gain values of trained group were higher, statistically, than control group for all muscle groups assessed, except for leg extension exercise, where there was no statistical difference. According Jurca *et al.*[39], muscular strength

is inversely associated with incidence of MS, and studies show that muscle mass and strength are important protective factors in this scenario [40].

Regarding quality of life, groups were heterogeneous at baseline in two of eight domains and although training group had significant improvement in 6 domains, no differences were found between the groups after intervention. These findings do not corroborate Tsai *et al.*[25] that worse values were found in overweigth people. On the other hand, Landaeta-Diaz *et al.*[24] indicate that exercise programs is an important strategy for promoting quality of life in adults. Regardless of domains where training has shown positive effects and differences compared to control group, it is believed that regular practice of physical training promotes physical, emotional and social benefits. Although three months of intervention was not able to improve quality of life completely, longer interventions may provide more obvious benefits.

Limitations

Although this study has been controlled, it is important to talk about some limitations. The main limitation is regarding to diet and medications in use. Since the aim of study was to analyze the isolated effect of functional training, participants were instructed to maintain their nutritional habits and not change medications in use. Thus, none follow-up survey of caloric intake or change in medications was done. This fact becomes limiting regarding to changes that could be caused by higher caloric intake, a normal situation in sedentary people who begin regular physical activity, or by changes in medications use. It is also believed that dietary interventions associated with exercise are able to cause even more significant effects in this population.

Another limitation to be considered is related to 1RM test reliability. Ritti-Dias *et al.*[41] compared 1RM tests between sedentary and active people who have already practiced

resistance training. After four tests in four different days the sedentary group showed differences up to 11% between first and last test, indicating the importance of reliabilty in these cases. Although in our study we did not carried out the reliability test, all evaluated exercises showed gains more than 11%, therefore, this limitation can be attenuated.

CONCLUSIONS

In summary, we conclude that functional training was effective in reduce systolic blood pressure and maintain HDL and body composition values in people with metabolic syndrome. However this results need caution because the data have presented baseline heterogeneity in several outcomes. In addition, functional training was effective in significantly increase muscular strength.

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COMPETING INTEREST

None.

AUTHORS' CONTRIBUTIONS

IRL, SNL, TA, MPFF and JMJ participated in the design of the study. CMP, JNJ and IRL performed the statistical analysis. IRL, SNL, MPFF and TA participated in coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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Appendix - Brazilian Clinical Trials Registry (REBEC)

12/03/2015 Registro Brasileiro de Ensaios Clínicos

USUÁRIO SENHA

PT | ES | EN

NOTÍCIAS | SOBRE | AJUDA | CONTATO

BUSCA AVANÇADA

HOME / ENSAIOS REGISTRADOS /

RBR-8rz4yq

Efeitos de dois programas de treinamento resistido periodizado nos marcadores da síndrome metabólica e na aptidão funcional

Data de registro: 6 de Jan. de 2014 às 16:26

Last Update: 23 de Fev. de 2015 às 10:38

Tipo do estudo:

Intervenções

Título científico:

PT-BR: Efeitos de dois programas de treinamento resistido periodizado nos marcadores da síndrome metabólica e na aptidão funcional

EN: Effects of two periodized resisted training programs on markers of metabolic syndrome and functional fitness

Identificação do ensaio

Número do UTN: U1111-1151-9031

Título público:

PT-BR: Efeitos de dois programas de musculação na saúde e no desempenho físico

EN: Effects of two bodybuilding programs in health and physical performance

Acrônimo científico:

Acrônimo público:

Identificadores secundários:

Número do parecer: 306.947

Órgão emissor: Comite de Ética em Pesquisa da Faculdade de Ciências e Tecnologia - Universidade Estadual Paulista "Júlio de Mesquita Filho" - Presidente Prudente

17378813.0.0000.5402 - CAAE

Órgão emissor: Plataforma Brasil

Patrocinadores

Patrocinador primário: Universidade Estadual Paulista "Júlio de Mesquita Filho"

Patrocinadores secundários:

Instituição: Departamento de Fisioterapia

Instituição: Laboratório de Fisioterapia Desportiva

Fontes de apoio financeiro ou material:

Instituição: Universidade Estadual Paulista "Júlio de Mesquita Filho"

http://www.ensaiosclinicos.gov.br/rg/RBR-8rz4yq/ 1/6

Instituição: Fundação de Amparo à Pesquisa do Estado de São Paulo

Condições de saúde

Condições de saúde ou problemas:

PT-BR: Síndrome x metabólica, estilo de vida sedentário

EN: Metabolic syndrome x, sedentary lifestyle

Descritores gerais para as condições de saúde:

PT-BR: **C18:** Doenças nutricionais e metabólicas

ES: **C18:** Enfermedades nutricionales y metabólicas

EN: **C18:** Nutritional and metabolic diseases

Descritores específicos para as condições de saúde:

PT-BR: **C18.452.394.968.500.570:** Síndrome X Metabólica

ES: **C18.452.394.968.500.570:** Síndrome X Metabólico

EN: **C18.452.394.968.500.570:** Metabolic Syndrome X

PT-BR: **F01.829.458.705:** Estilo de Vida Sedentário

ES: **F01.829.458.705:** Estilo de Vida Sedentario

EN: **F01.829.458.705:** Sedentary Lifestyle

Intervenções

Categorias das intervenções

Other

Intervenções:

PT-BR: Grupo experimental: 40 voluntários serão randomizados em 2 grupos de treinamento (20 sujeitos cada), e participarão de 30 sessões de exercícios em uma academia de musculação, 3 vezes por semana. Cada sessão terão duração de 40 a 50 minutos, consistindo de 8 exercícios (5 para membros superiores e 3 para membros inferiores).
Grupo controle: 20 sujeitos serão orientados a permanecerem sedentários, com alimentação normal, durante o mesmo período de treinamento do grupo experimental. Este grupo receberá aulas e palestras semanais a respeito de exercício físico e saúde.

EN: Experimental group: 40 subjects will be randomized into two training groups (20 subjects each) and attend 30 sessions of exercises in a bodybuilding gym, 3 times a week. Each session will last for 40 to 50 minutes, consisting of 8 exercises (5 for upper limbs and 3 for lower limbs).
Control group: 20 subjects will be asked to remain sedentary, with normal diet, during the same period of training in the experimental group. This group will receive weekly lessons and lectures about exercise and health.

Descritores para as intervenções:

PT-BR: **G11.427.590.530.698.277:** Exercício

ES: **G11.427.590.530.698.277:** Ejercicio

PT-BR

E02.779.483.875: Treinamento de Resistência

ES

E02.779.483.875: Entrenamiento de Resistencia

Recrutamento

Situação de recrutamento: Recruitment completed

País de recrutamento

Brazil

Data prevista do primeiro recrutamento: 2013-12-01

Data prevista do último recrutamento: 2014-01-31

Tamanho da amostra alvo:	Gênero para inclusão:	Idade mínima para inclusão:	Idade máxima para inclusão:
40	-	40 Y	60 Y

Critérios de inclusão:

PT-BR

Idade entre 40 e 60 anos; possuir síndrome metabólica; não ter realizado nenhuma atividade física regular ou treinamento de musculação nos últimos 6 meses.

EN

Age between 40 and 60 years; have metabolic syndrome; no regular physical activity or strength training in the last 6 months.

Critérios de exclusão:

PT-BR

Consumo de drogas ou medicamentos que não estejam relacionados aos fatores que compõem a síndrome metabólica; apresentar amenorréia; presença de processo inflamatório ou infeccioso; episódio de lesão músculo-tendíneas ou osteoarticular nos membros superiores, inferiores ou coluna; apresentar doenças respiratórias.

EN

Use of drugs or medicines that are not related to the metabolic syndrome factors; amenorrhoea; presence of inflammation or infection; musculotendinous or osteoarticular injuries in the upper limbs, lower limbs or column; respiratory diseases.

Tipo do estudo

Desenho do estudo:

PT-BR

Ensaio clínico, terapêutico, randomizado controlado, aberto, paralelo, com 2 braços

EN

Clinical trial, therapeutic, randomized controlled, open, parallel, with 2-arm

Programa de acesso expandido	Enfoque do estudo	Desenho da intervenção	Número de braços	Tipo de mascaramento	Tipo de alocação	Fase do estudo
Nenhum	Treatment	Parallel	2	Aberto	Randomized-controlled	N/A

Desfechos

Desfechos primários:

PT-BR

Desfecho esperado: Redução da pressão arterial sistólica e diastólica, avaliada em repouso por meio de esfigmomanômetro. Considerou-se o menor valor obtido após 3 aferições. Avaliação nos momentos: basal e pós treinamento.

EN

Expected outcome: Reduction of systolic and diastolic blood pressure, measured at rest by sphygmomanometer. It was considered the lowest value obtained after 3 measurements. Assessment in moments: baseline and post training.

PT-BR

Desfecho encontrado: Redução da pressão arterial sistólica, avaliada em repouso por meio de esfigmomanômetro. Considerou-se o menor valor obtido após 3 aferições. Foi realizada análise comparativa entre os grupos e entre os momentos. Avaliação nos momentos: basal e pós treinamento.

EN

Outcome found: Reduction in systolic blood pressure, measured at rest by sphygmomanometer. It was considered the lowest value obtained after 3 measurements. Comparative analysis was performed between groups and between times. Assessment in moments: baseline and post training

Desfechos secundários:

PT-BR

Desfecho esperado (1): redução dos valores de triglicérides, avaliado por meio de exame de sangue em jejum. Avaliação nos momentos: basal e pós treinamento. Desfecho esperado (2): redução dos valores de glicemia em jejum, avaliado por meio de exame de sangue em jejum. Avaliação nos momentos: basal e pós treinamento. Desfecho esperado (3): aumento nos valores de HDL colesterol, avaliado por meio de exame de sangue em jejum. Avaliação nos momentos: basal e pós treinamento. Desfecho esperado (4): redução da medida de circunferência abdominal, avaliado por meio de fita métrica em posição ortostática. Avaliação nos momentos: basal e pós treinamento. Desfecho esperado (5): aumento da força muscular, avaliada por meio do teste de 1 repetição máxima. Avaliação nos momentos: basal e pós treinamento. Desfecho esperado (6): melhora da qualidade de vida, avaliada por meio do questionário. Avaliação nos momentos: basal e pós treinamento.

EN

Expected outcome (1): reduction of triglyceride levels, assessed by blood test fasting. Assessment in moments: baseline and post training. Expected outcome (2): reduction of blood glucose levels in fasting, assessed by blood test fasting. Assessment in moments: baseline and post training. Expected outcome (3): increase in HDL cholesterol levels, assessed by blood test fasting. Assessment in moments: baseline and post training. Expected outcome (4): reduction of abdominal circumference measurement, assessed by metric tape in the standing position. Assessment in moments: baseline and post training. Expected outcome (5): increased muscle strength assessed by 1 repetition maximum test. Assessment in moments: baseline and post training. Expected outcome (6): improved quality of life, assessed by questionnaire. Assessment in moments: baseline and post training.

PT-BR

Desfecho encontrado (1): os valores de triglicérides permaneceram estatisticamente inalterados, avaliado por meio de exame de sangue em jejum. Foi realizada análise comparativa entre os grupos e entre os momentos. Avaliação nos momentos: basal e pós treinamento. Desfecho encontrado (2):

EN

Outcome found (1): triglyceride values remained statistically unchanged, assessed by blood test fasting. Comparative analysis was performed between groups and between times. Assessment in moments: baseline and post training. Outcome found (2): the fasting blood glucose values

os valores de glicemia em jejum permaneceram estatisticamente inalterados, avaliado por meio de exame de sangue em jejum. Foi realizada análise comparativa entre os grupos e entre os momentos. Avaliação nos momentos: basal e pós treinamento. Desfecho encontrado (3): os valores de HDL colesterol permaneceram estatisticamente inalterados, avaliado por meio de exame de sangue em jejum. Foi realizada análise comparativa entre os grupos e entre os momentos. Avaliação nos momentos: basal e pós treinamento. Desfecho encontrado (4): os valores da circunferência abdominal permaneceram estatisticamente inalterados, avaliado por meio de fita métrica em posição ortostática. Foi realizada análise comparativa entre os grupos e entre os momentos. Avaliação nos momentos: basal e pós treinamento. Desfecho encontrado (5): aumento da força muscular, avaliada por meio do teste de 1 repetição máxima. Foi realizada análise comparativa entre os grupos e entre os momentos. Avaliação nos momentos: basal e pós treinamento. Desfecho encontrado (6): melhora da qualidade de vida, avaliada por meio do questionário. Foi realizada análise comparativa entre os grupos e entre os momentos. Avaliação nos momentos: basal e pós treinamento.

remained statistically unchanged, assessed by blood test fasting. Comparative analysis was performed between groups and between times. Assessment in moments: baseline and post training. Outcome found (3): HDL cholesterol values remained statistically unchanged, assessed by blood test fasting. Comparative analysis was performed between groups and between times. Assessment in moments: baseline and post training. Outcome found (4): the waist circumference values remained statistically unchanged, assessed by metric tape in the standing position. Comparative analysis was performed between groups and between times. Assessment in moments: baseline and post training. Outcome found (5): increased muscle strength assessed by 1 repetition maximum test. Comparative analysis was performed between groups and between times. Assessment in moments: baseline and post training. Outcome found (6): improved quality of life, assessed by questionnaire. Comparative analysis was performed between groups and between times. Assessment in moments: baseline and post training.

Contatos

Contatos para questões públicas

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Ethical approval – Human Research Ethics Committee

FACULDADE DE CIÊNCIAS E TECNOLOGIA - UNESP/ CAMPUS DE PRESIDENTE

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: EFEITOS DE DOIS PROGRAMAS DE TREINAMENTO RESISTIDO PERIODIZADO NOS MARCADORES DA SÍNDROME METABÓLICA E NA APTIDÃO FUNCIONAL

Pesquisador: Ítalo Ribeiro Lemes

Área Temática: Área 5. Novos procedimentos ainda não consagrados na literatura.

Versão: 1

CAAE: 17378813.0.0000.5402

Instituição Proponente: UNIVERSIDADE ESTADUAL PAULISTA JULIO DE MESQUITA FILHO

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 306.947

Data da Relatoria: 07/06/2013

Apresentação do Projeto:

O projeto trata de pesquisa experimental onde se objetiva aprofundar os conhecimentos sobre a melhor estrategia e procedimentos de um programas de atividade física destinada ao tratamento coadjuvante de portadores de síndrome metabolica em adultos de 40 a 60 anos.

Serão integrados por 60 sujeitos de ambos os sexos distribuidos em dois grupos de intervenção e um de controle constituidos por 20 sujeitos cada um. a intervenção consta de uma avaliação inicial (precedida por uma avaliação clinica realizada por medico) seguida de coleta de dados pessoais, antropometricos e clinicos e exames laboratoriais ligados ao acompanhamento dos itens marcadores de acompanhamento da síndrome metabolica. A seguir as pessoas serão submetidas a um programa de exercicios de fortalecimento muscular e atividade física progressivos de acordo com parametros iniciais individualizados. Tais periodos de intervenção serão entremeados por periodos de repouso.

Objetivo da Pesquisa:

Encontrar um de atividade física eficaz e efetivo destinado a tratamento adjuvante dos adultos portadores de síndrome metabolica que resulte em beneficio de saude e redução dos risco de complicações em partadores de síndrome metabolica em adultos.

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Avaliação dos Riscos e Benefícios:

Os riscos da atitivade fisica proposta serão minimos pois serão excluidos os pacientes portadores de uma contra indicação clinica, Por outro lado as atividades deverão ser beneficas à saude dos pacientes integrados.

Comentários e Considerações sobre a Pesquisa:

Trata-se de testar duas abordagens de programa de atividade fisica aerobica destinado a tratamento coadjuvante de portadores de sindrome metabolica, disturbio esse de alta prevalencia entre adultos e de alto risco para sobrevivencia e complicações irreversíveis.

Considerações sobre os Termos de apresentação obrigatória:

Os termos de apresentação obrigatoria foram adequadamente obedecidos.

Recomendações:

Dois pontos de natureza tecnica merecem contribuição

1- a alocação dos individuos nos grupos de comparação deveria ser aleatoria evitando-se vises de seleção.

2- Nos termo de consentimento livre e esclarecido não consta o endereço telefonico ou outro para contato dos sujeitos com os responsaveis pela pesquisa recomendando-se enfaticamente sua inclusão

O item 4 do TCLE tem redação pouco clara quanto a o que seja "COLETAS" e deveria ser substituido por "coleta de exames clinicos ou laboratoriais".

Conclusões ou Pendências e Lista de Inadequações:

Não consideramos haver pendencia a ser providenciada. Entretanto, sugerimos que seja explicitado qual será o grupo controle.

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Sim

Considerações Finais a critério do CEP:

Em reunião realizada no dia 14.06.2013, o Comitê de Ética em Pesquisa da Faculdade de Ciências e Tecnologia - Unesp - Presidente Prudente, em concordância com o parecerista, considerou o projeto APROVADO.

Obs: Lembramos que ao finalizar a pesquisa, o (a) pesquisador (a) deverá apresentar o relatório final.

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O presente projeto, seguiu nesta data para análise da CONEP e só tem o seu início autorizado após a aprovação pela mesma.

PRESIDENTE PRUDENTE, 17 de Junho de 2013

Assinador por:
Edna Maria do Carmo
(Coordenador)

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Embora diferentes metodologias tenham sido utilizadas, em relação à intensidade, volume e tempo de intervenção, o treinamento resistido, bem como o treinamento resistido funcional, pode ser utilizado como ferramenta na redução da pressão arterial sistólica. Ainda, por meio da meta-análise realizada, observou-se melhora dos parâmetros clínicos da síndrome metabólica, pressão arterial diastólica e circunferência abdominal, após intervenções com treinamento resistido.

Além disso, a partir do ensaio clínico realizado, o treinamento resistido funcional mostrou-se capaz de realizar a manutenção de algumas variáveis metabólicas, como HDL-colesterol e glicemia, e promover ganho de força muscular.

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British Journal of Sports Medicine - Instructions for Authors

For guidelines on policy and submission across our journals, please click on the links below:

Manuscript preparation

Editorial policies

Patient consent forms

Licence forms

Peer review

Submission and production processes

Twitter handles - BJSM encourages the inclusion of Twitter usernames in an author's information to encourage discussion and debate around each article.

Editorial policy

The British Journal of Sports Medicine (BJSM) aims to highlight clinically-relevant orginal research, editorials and commentary that will be of interest to the field of sport and exercise medicine. The journal is aimed at physicians, physiotherapists, exercise scientists and those involved in public policy.

Please note that references will be published online only; references should be provided as a separate data supplement.

Open Access

Authors can choose to have their article published Open Access for a fee of £1,950 (plus applicable VAT).

Colour figure charges

During submission you will be asked whether or not you agree to pay for the colour print publication of your colour images. This service is available to any author publishing within this journal for a fee of £250 per article. Authors can elect to publish online in colour

and black and white in print, in which case the appropriate selection should be made upon submission.

Article types and word counts

- Review articles
- Original reports
- Editorials
- Discussion
- Education reviews
- Mobile app Review
- Fillers
- I-test - Sports medicine radiology/imaging
- Letters to the Editor
- Supplements
- Preferred reviewers
- Plagiarism detection

The word count excludes the title page, abstract, tables, acknowledgements and contributions and the references.

Please note: Maximum word counts are strictly enforced and manuscripts that exceed these guidelines are usually rejected.

If you are not a native English speaker and would like assistance with your paper there is aprofessional editing service available.

BMJ's pre-submission checklist

Review articles

Review articles should provide concise in-depth reviews of both established and new areas in sports medicine.

Systematic reviews

Systematic reviews provide level One evidence; they form a critical part of the literature. Here we provide some ground rules for SRs of interest in this journal. These guidelines are meant to inform authors but are not absolute.

Is the review of interest to our core readership?

BJSM is a clinical journal so the topic must have relevance and some application to clinical practice. Ask the key question "will the findings change what practitioners do?"

The scope of the question and review

Very specific questions and very broad questions may both have limited appeal. Those that ask and answer 'meaty' questions that reflect clinical issues have greater interest to BJSM readers.

Is the review worth the journal space?

Succinct and focussed reviews are always of more interest. Questions that are topical, novel or controversial that will attract readers and researchers to the journal will be more likely to be accepted.

Do the authors have broad knowledge in the topic area?

We are looking for experts to synthesise the literature and to comment on the outcomes of the review in a meaningful and clinically relevant way. The conclusion that "more research is needed" does not add value for readers - it is uninformative.

So, after you consider these questions, please send in your SRs. We are open to amendments to these guidelines - contact us with your suggestions.

Please include a summary box summarising in 3-4 bullet points 'what are the new findings'.

Please provide 5 multiple choice questions (MCQs) each with 4-5 possible answers (only 1 correct answer), so the reader can test his or her understanding of the article. These MCQs will be published online only in the form of an E-learning module.

How to easily create multiple choice questions:

- Make the questions a positive single choice with only one correct answer

- Provide 4-5 answer options for each question
- The reader should be able to answer the questions need from the material provided in the article
- Problem orientated questions in form of a short case description are best
- Make sure that each question focuses only on one problem
- The answers you offer should be homogeneous: for example 5 diagnostic procedures, 5 therapeutic interventions
- Avoid options that contain vague terms such as "common," "often", "rare," "sometimes," and absolute statements such as "never" or "always"
- Avoid "all of the above" of none of the above
- Please give us an answer key for your questions! The correct answer with a short explanation for each answer
- Please check all your questions and answers carefully - do this with a colleague.

Word count: up to 4500 words (not including figure/table legends, references). Peer reviewed by 2 external reviewers.

Original reports

Papers should be a maximum of 3000 words in length (not including abstract, figure/table legends, references).

Abstracts should be a maximum of 250 words in length and structured as follows:

- Background/Aim
- Methods
- Results
- Conclusions

Please include a summary box summarising in 3-4 bullet points "what are the new findings".

Main body of the paper: We encourage short introductions when the rationale of the study is obvious, i.e. it may be as short as 3 short paragraphs if that addresses "Why we did it".

We encourage the use of subheadings in the methods, results and discussion. We find it hard to imagine a discussion that has fewer than two subheadings.

Peer reviewed by 2 external reviewers.

Discussion

This type of paper makes a comment related to a hot topic; it differs from an editorial in that it might be wider ranging and it may link (discuss) a series of papers. As with an editorial, these should be written in less than 800 words and use 8 or less references.

Editorials

BJSM welcomes editorials. The purpose of an editorial is to provide a novel perspective on a clinically-relevant issue. Please see the table of contents of BJSM for examples. We welcome suggestions for possible topics and authors.

Word count: a maximum of 800 words (not including figure/table legends, references). References: up to 8. Additional material can be posted as a supplement or on the BJSM Blog. Editorials are peer reviewed by 2 reviewers who may be external or members of the Editorial Board.

Education reviews

These are written or commissioned by the editors and should follow the proforma guidelines that will be supplied by the editorial office.

Peer reviewed by 2 external reviewers.

Mobile app Review

BJSM welcomes reviews of mobile sporting apps that have the potential for clinical use in the world of sports medicine. Such submissions should follow the format below:

- **Author** - Name, address, email and Twitter handle (if you have one)
- **Name of the mobile application** - e.g. Strava
- **Category of the mobile application** - e.g. Fitness or health
- **Platform** - e.g. iOS (iPhone 4 & above), Android (versions 2.3.3 & above), Google Glass and over 50 GPS devices (e.g. Garmin) can upload date onto the Strava website
- **Cost** - The different verions available of an app and their particular pricings
- **About the App** - Should be less than 300 words
- **Use in clinical practice** - Should be less than 150 words
- **Pros** - Up to eight bullet points, but no less than three

- **Cons** - Up to eight bullet points, but no less than three
- **References** - References are not essential and the maximum required is four
- **Screen shot** - Please provide an image of the app, such as a screen shot, for use in the article. The quality of the image must be at least 300dpi and in .tif, .jpeg, .gif or .eps format

Fillers

We try to make the best use of every page of the printed BJSM, so we use small gaps to publish fillers. Most fillers have the added advantage of entertaining readers and making them think. If the filler refers to an identifiable person we will need written consent to publication from that person or a relative. We welcome articles of up to 400 words (we also like and need much shorter ones) on topics such as:

- Any other story conveying instruction, pathos or humour.

I-test - Sports medicine radiology/imaging

I-tests aim to provide readers with a succinct imaging-based educational opportunity in a clinical context familiar to a sports medicine readership. The main thrust of the article is the diagnosis of the condition through imaging; however, the clinical presentation should be addressed as well as basic aspects of treatment (surgical or otherwise). The specific role of imaging in the diagnosis and management of the condition should be highlighted.

The "question" part of the I-test should comprise a short description of the clinical presentation (< 200 words) accompanied by up to 3 images; the "answer" should include a discussion of the clinical, imaging and management issues (< 1200 words), supplemented by up to 3 additional images and 8 references.

The "question" and "answer" parts should be submitted online as a single article following the standard formats.

Letters to the Editor

Letters to the Editor are considered for publication (subject to editing and abridgment) provided they do not contain material that has been submitted or published elsewhere.

Letters in reference to a BJSM article must not exceed 175 words (excluding references), and must be received within three weeks of publication of the article. If you are responding to an Online First article that does not have a print publication date, the article will be listed under "Online Articles."

Letters not related to a BJSM article must not exceed 400 words (excluding references).

A letter can have no more than four references and one figure or table.

A letter may not be signed by more than three authors.

You will be asked to include your full address, telephone number and e-mail address. Financial associations or other possible conflicts of interest must be disclosed.

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The BMJ Publishing Group journals are willing to consider publishing supplements to regular issues. Supplement proposals may be made at the request of:

- The journal editor, an editorial board member or a learned society may wish to organise a meeting, sponsorship may be sought and the proceedings published as a supplement.
- The journal editor, editorial board member or learned society may wish to commission a supplement on a particular theme or topic. Again, sponsorship may be sought.
- The BMJPG itself may have proposals for supplements where sponsorship may be necessary.
- A sponsoring organisation, often a pharmaceutical company or a charitable foundation, that wishes to arrange a meeting, the proceedings of which will be published as a supplement.

In all cases, it is vital that the journal's integrity, independence and academic reputation is not compromised in any way.

When contacting us regarding a potential supplement, please include as much of the information below as possible.

- Journal in which you would like the supplement published
- Title of supplement and/or meeting on which it is based
- Date of meeting on which it is based

- Proposed table of contents with provisional article titles and proposed authors
- An indication of whether authors have agreed to participate
- Sponsor information including any relevant deadlines
- An indication of the expected length of each paper Guest Editor proposals if appropriate

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Video Abstracts

We welcome video abstracts to accompany accepted research articles. These allow authors to personally talk through their work beyond the restrictions of a formal article to improve the user's understanding.

Note that we will not ask you to consider submitting a video abstract until your paper has been accepted. Please do not try to upload a video abstract upon initial submission of your manuscript.

There are many tutorials online which can guide the production of a video abstract, using widely and often freely available software.Windows Movie Maker and Apple iMovie are the most common examples. Examples of video abstracts are available from *The BMJ*. Below are a few guidelines for making a video abstract. Authors may also want to ask their institution's press/media office for assistance.

- Video abstracts should not last longer than **4 minutes**.
- The content and focus of the video must relate directly to the study that has been accepted for publication, and should not stray beyond the data. We recommend that you follow the same structure as the paper itself i.e. briefly outline the background/context of the study, present your research objective, outline the methods used, present the key results and then discuss the implications of the outcomes.
- The presentation and content of the video should be in a style and in terms that will be understandable and accessible to a general medical audience. The main language should be English, but we welcome subtitles in another language. Please avoid jargon that will not be familiar to a wide medical audience, and do not use abbreviations.

- Authors usually talk directly into the camera and/or present a slideshow, but we encourage the use of other relevant visual and audio material (such as animations, video clips, still photographs, figures, infographics). If you wish to use material from previously published work or from other sources, please obtain the appropriate permissions from the relevant publisher or copyright owner.
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Please suggest up to four reviewers who the editors can approach to review if needed. First name, last name, institution and email are required. You are required to suggest at least two reviewers, and preferably, at least half of the nominated reviewers should be from a country other than your own. Reviewer nominees from the same institution as any of the authors are not permitted.

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Diabetology & Metabolic Syndrome – Guide for Authors

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General guidelines of the journal's style and language are given below.
Overview of manuscript sections for Research Articles
Manuscripts for Research Articles submitted to *Diabetology & Metabolic Syndrome* should be divided into the following sections (in this order):

- Title page
- Abstract
- Keywords
- Background
- Methods
- Results and discussion
- Conclusions
- List of abbreviations used (if any)
- Competing interests
- Authors' contributions
- Authors' information
- Acknowledgements
- Endnotes
- References
- Illustrations and figures (if any)
- Tables and captions
- Preparing additional files

The **Accession Numbers** of any nucleic acid sequences, protein sequences or atomic coordinates cited in the manuscript should be provided, in square brackets and include the corresponding database name; for example, [EMBL:AB026295, EMBL:AC137000, DDBJ:AE000812, GenBank:U49845, PDB:1BFM, Swiss-Prot:Q96KQ7, PIR:S66116].
The databases for which we can provide direct links are: EMBL Nucleotide Sequence Database (EMBL), DNA Data Bank of Japan (DDBJ), GenBank at the NCBI (GenBank), Protein Data Bank (PDB), Protein Information Resource (PIR) and the Swiss-Prot Protein Database (Swiss-Prot).
For reporting standards please see the information in the About section.

Title page

The title page should:

- provide the title of the article
- list the full names, institutional addresses and email addresses for all authors
- indicate the corresponding author

Please note:

- the title should include the study design, for example "A versus B in the treatment of C: a randomized controlled trial X is a risk factor for Y: a case control study"
- abbreviations within the title should be avoided

Abstract

The Abstract of the manuscript should not exceed 350 words and must be structured into separate sections: **Background,** the context and purpose of the study; **Methods**, how the study was performed and statistical tests used; **Results**, the main findings; **Conclusions**, brief summary and potential implications. Please minimize the use of abbreviations and do not cite references in the abstract. **Trial registration**, if your research reports the results of a controlled health care intervention, please list your trial registry, along with the unique identifying number (e.g. **Trial registration**: Current Controlled Trials ISRCTN73824458). Please note that there should be no space between the letters and numbers of your trial registration number. We recommend manuscripts that report randomized controlled trials follow the CONSORT extension for abstracts.

Keywords

Three to ten keywords representing the main content of the article.

Background

The Background section should be written in a way that is accessible to researchers without specialist knowledge in that area and must clearly state - and, if helpful, illustrate - the background to the research and its aims. Reports of clinical research should, where appropriate, include a summary of a search of the literature to indicate why this study was necessary and what it aimed to contribute to the field. The section should end with a brief statement of what is being reported in the article.

Methods

The methods section should include the design of the study, the setting, the type of participants or materials involved, a clear description of all interventions and comparisons, and the type of analysis used, including a power calculation if appropriate. Generic drug names should generally be used. When proprietary brands are used in research, include the brand names in parentheses in the Methods section.

For studies involving human participants a statement detailing ethical approval and consent should be included in the methods section. For further details of the journal's editorial policies and ethical guidelines see 'About this journal'.

For further details of the journal's data-release policy, see the policy section in 'About this journal'.

Results and discussion

The Results and discussion may be combined into a single section or presented separately. Results of statistical analysis should include, where appropriate, relative and absolute risks or risk reductions, and confidence intervals. The Results and discussion sections may also be broken into subsections with short, informative headings.

Conclusions

This should state clearly the main conclusions of the research and give a clear explanation of their importance and relevance. Summary illustrations may be included.

List of abbreviations

If abbreviations are used in the text they should be defined in the text at first use, and a list of abbreviations can be provided, which should precede the competing interests and authors' contributions.

Competing interests

A competing interest exists when your interpretation of data or presentation of information may be influenced by your personal or financial relationship with other people or organizations. Authors must disclose any financial competing interests; they should also reveal any non-financial competing interests that may cause them embarrassment were they to become public after the publication of the manuscript.

Authors are required to complete a declaration of competing interests. All competing interests that are declared will be listed at the end of published articles. Where an author gives no competing interests, the listing will read 'The author(s) declare that they have no competing interests'.

When completing your declaration, please consider the following questions:

Financial competing interests

- In the past three years have you received reimbursements, fees, funding, or salary from an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future? Is such an organization financing this manuscript (including the article-processing charge)? If so, please specify.
- Do you hold any stocks or shares in an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future? If so, please specify.
- Do you hold or are you currently applying for any patents relating to the content of the manuscript? Have you received reimbursements, fees, funding, or salary from an

organization that holds or has applied for patents relating to the content of the manuscript? If so, please specify.

- Do you have any other financial competing interests? If so, please specify.

Non-financial competing interests

Are there any non-financial competing interests (political, personal, religious, ideological, academic, intellectual, commercial or any other) to declare in relation to this manuscript? If so, please specify.

If you are unsure as to whether you, or one your co-authors, has a competing interest please discuss it with the editorial office.

Authors' contributions

In order to give appropriate credit to each author of a paper, the individual contributions of authors to the manuscript should be specified in this section.

According to ICMJE guidelines, An 'author' is generally considered to be someone who has made substantive intellectual contributions to a published study. To qualify as an author one should 1) have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) have been involved in drafting the manuscript or revising it critically for important intellectual content; 3) have given final approval of the version to be published; and 4) agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Acquisition of funding, collection of data, or general supervision of the research group, alone, does not justify authorship.

We suggest the following kind of format (please use initials to refer to each author's contribution): AB carried out the molecular genetic studies, participated in the sequence alignment and drafted the manuscript. JY carried out the immunoassays. MT participated in the sequence alignment. ES participated in the design of the study and performed the statistical analysis. FG conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

All contributors who do not meet the criteria for authorship should be listed in an acknowledgements section. Examples of those who might be acknowledged include a person who provided purely technical help, writing assistance, or a department chair who provided only general support.

Authors' information

You may choose to use this section to include any relevant information about the author(s) that may aid the reader's interpretation of the article, and understand the standpoint of the author(s). This may include details about the authors' qualifications, current positions they hold at institutions or societies, or any other relevant background information. Please refer to authors using their initials. Note this section should not be used to describe any competing interests.

Acknowledgements
Please acknowledge anyone who contributed towards the article by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data, or who was involved in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria for authorship. Please also include the source(s) of funding for each author, and for the manuscript preparation. Authors must describe the role of the funding body, if any, in design, in the collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication. Please also acknowledge anyone who contributed materials essential for the study. If a language editor has made significant revision of the manuscript, we recommend that you acknowledge the editor by name, where possible.

The role of a scientific (medical) writer must be included in the acknowledgements section, including their source(s) of funding. We suggest wording such as 'We thank Jane Doe who provided medical writing services on behalf of XYZ Pharmaceuticals Ltd.'

Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements section.

Endnotes
Endnotes should be designated within the text using a superscript lowercase letter and all notes (along with their corresponding letter) should be included in the Endnotes section. Please format this section in a paragraph rather than a list.

References
All references, including URLs, must be numbered consecutively, in square brackets, in the order in which they are cited in the text, followed by any in tables or legends. Each reference must have an individual reference number. Please avoid excessive referencing. If automatic numbering systems are used, the reference numbers must be finalized and the bibliography must be fully formatted before submission.

Only articles, clinical trial registration records and abstracts that have been published or are in press, or are available through public e-print/preprint servers, may be cited; unpublished abstracts, unpublished data and personal communications should not be included in the reference list, but may be included in the text and referred to as "unpublished observations" or "personal communications" giving the names of the involved researchers. Obtaining permission to quote personal communications and unpublished data from the cited colleagues is the responsibility of the author. Footnotes are not allowed, but endnotes are permitted. Journal abbreviations follow Index Medicus/MEDLINE. Citations in the reference list should include all named authors, up to the first six before adding 'et al.'..

Any *in press* articles cited within the references and necessary for the reviewers' assessment of the manuscript should be made available if requested by the editorial office.
An Endnote style file is available.
Examples of the *Diabetology & Metabolic Syndrome* reference style are shown below. Please ensure that the reference style is followed precisely; if the references are not in the correct style they may have to be retyped and carefully proofread.

All web links and URLs, including links to the authors' own websites, should be given a reference number and included in the reference list rather than within the text of the manuscript. They should be provided in full, including both the title of the site and the URL, as well as the date the site was accessed, in the following format: The Mouse Tumor Biology Database. http://tumor.informatics.jax.org/mtbwi/index.do. Accessed 20 May 2013. If an author or group of authors can clearly be associated with a web link, such as for weblogs, then they should be included in the reference.

Examples of the* Diabetology & Metabolic Syndrome *reference style

Article within a journal
Smith JJ. The world of science. Am J Sci. 1999;36:234-5.
Article within a journal (no page numbers)
Rohrmann S, Overvad K, Bueno-de-Mesquita HB, Jakobsen MU, Egeberg R, Tjønneland A, et al. Meat consumption and mortality - results from the European Prospective Investigation into Cancer and Nutrition. BMC Medicine. 2013;11:63.
Article within a journal by DOI
Slifka MK, Whitton JL. Clinical implications of dysregulated cytokine production. Dig J Mol Med. 2000; doi:10.1007/s801090000086.
Article within a journal supplement
Frumin AM, Nussbaum J, Esposito M. Functional asplenia: demonstration of splenic activity by bone marrow scan. Blood 1979;59 Suppl 1:26-32.
Book chapter, or an article within a book
Wyllie AH, Kerr JFR, Currie AR. Cell death: the significance of apoptosis. In: Bourne GH, Danielli JF, Jeon KW, editors. International review of cytology. London: Academic; 1980. p. 251-306.
OnlineFirst chapter in a series (without a volume designation but with a DOI)
Saito Y, Hyuga H. Rate equation approaches to amplification of enantiomeric excess and chiral symmetry breaking. Top Curr Chem. 2007. doi:10.1007/128_2006_108.
Complete book, authored
Blenkinsopp A, Paxton P. Symptoms in the pharmacy: a guide to the management of common illness. 3rd ed. Oxford: Blackwell Science; 1998.
Online document
Doe J. Title of subordinate document. In: The dictionary of substances and their effects. Royal Society of Chemistry. 1999. http://www.rsc.org/dose/title of subordinate document. Accessed 15 Jan 1999.
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Healthwise Knowledgebase. US Pharmacopeia, Rockville. 1998. http://www.healthwise.org. Accessed 21 Sept 1998.
Supplementary material/private homepage
Doe J. Title of supplementary material. 2000. http://www.privatehomepage.com. Accessed 22 Feb 2000.
University site
Doe, J: Title of preprint. http://www.uni-heidelberg.de/mydata.html (1999). Accessed 25 Dec 1999.

FTP site
Doe, J: Trivial HTTP, RFC2169. ftp://ftp.isi.edu/in-notes/rfc2169.txt (1999). Accessed 12 Nov 1999.
Organization site
ISSN International Centre: The ISSN register. http://www.issn.org (2006). Accessed 20 Feb 2007.

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Illustrations should be provided as separate files, not embedded in the text file. Each figure should include a single illustration and should fit on a single page in portrait format. If a figure consists of separate parts, it is important that a single composite illustration file be submitted which contains all parts of the figure. There is no charge for the use of color figures.

Please read our figure preparation guidelines for detailed instructions on maximising the quality of your figures.

Formats

The following file formats can be accepted:

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- DOCX/DOC (single page only)
- PPTX/PPT (single slide only)
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Figure legends

The legends should be included in the main manuscript text file at the end of the document, rather than being a part of the figure file. For each figure, the following information should be provided: Figure number (in sequence, using Arabic numerals - i.e. Figure 1, 2, 3 etc); short title of figure (maximum 15 words); detailed legend, up to 300 words.

Please note that it is the responsibility of the author(s) to obtain permission from the copyright holder to reproduce figures or tables that have previously been published elsewhere.

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Each table should be numbered and cited in sequence using Arabic numerals (i.e. Table 1, 2, 3 etc.). Tables should also have a title (above the table) that summarizes the whole table; it should be no longer than 15 words. Detailed legends may then follow, but they should be concise. Tables should always be cited in text in consecutive numerical order.

Smaller tables considered to be integral to the manuscript can be pasted into the end of the document text file, in A4 portrait or landscape format. These will be typeset and displayed in the final published form of the article. Such tables should be formatted using the 'Table object' in a word processing program to ensure that columns of data are kept aligned when the file is sent electronically for review; this will not always be the case if columns are generated by simply using tabs to separate text. Columns and rows of data should be made visibly distinct by ensuring that the borders of each cell display as black lines. Commas should not be used to indicate numerical values. Color and shading may not be used; parts of the table can be highlighted using symbols or bold text, the meaning of which should be explained in a table legend. Tables should not be embedded as figures or spreadsheet files.

Larger datasets or tables too wide for a landscape page can be uploaded separately as additional files. Additional files will not be displayed in the final, laid-out PDF of the article, but a link will be provided to the files as supplied by the author.

Tabular data provided as additional files can be uploaded as an Excel spreadsheet (.xls) or comma separated values (.csv). As with all files, please use the standard file extensions.

Preparing additional files

Although *Diabetology & Metabolic Syndrome* does not restrict the length and quantity of data included in an article, we encourage authors to provide datasets, tables, movies, or other information as additional files.
Please note: All Additional files **will be published** along with the article. Do not include files such as patient consent forms, certificates of language editing, or revised versions of the main manuscript document with tracked changes. Such files should be sent by email todmsjournal@biomedcentral.com, quoting the Manuscript ID number.
Results that would otherwise be indicated as "data not shown" can and should be included as additional files. Since many weblinks and URLs rapidly become broken, *Diabetology & Metabolic Syndrome* requires that supporting data are included as additional files, or deposited in a recognized repository. Please do not link to data on a personal/departmental website. The maximum file size for additional files is 20 MB each, and files will be virus-scanned on submission.
Additional files can be in any format, and will be downloadable from the final published article as supplied by the author. We recommend CSV rather than PDF for tabular data.

Certain supported files formats are recognized and can be displayed to the user in the browser. These include most movie formats (for users with the Quicktime plugin), mini-websites prepared according to our guidelines, chemical structure files (MOL, PDB), geographic data files (KML).

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- Title of data
- Description of data

Additional files should be named "Additional file 1" and so on and should be referenced explicitly by file name within the body of the article, e.g. 'An additional movie file shows this in more detail [see Additional file 1]'.

Additional file formats

Ideally, file formats for additional files should not be platform-specific, and should be viewable using free or widely available tools. The following are examples of suitable formats.

- Additional documentation
  - PDF (Adode Acrobat)
- Animations
  - SWF (Shockwave Flash)
- Movies
  - MP4 (MPEG 4)
  - MOV (Quicktime)
- Tabular data
  - XLS, XLSX (Excel Spreadsheet)
  - CSV (Comma separated values)

As with figure files, files should be given the standard file extensions.

Mini-websites

Small self-contained websites can be submitted as additional files, in such a way that they will be browsable from within the full text HTML version of the article. In order to do this, please follow these instructions:

1. Create a folder containing a starting file called index.html (or index.htm) in the root.
2. Put all files necessary for viewing the mini-website within the folder, or sub-folders.
3. Ensure that all links are relative (ie "images/picture.jpg" rather than "/images/picture.jpg" or "http://yourdomain.net/images/picture.jpg" or "C:\Documents and Settings\username\My Documents\mini-website\images\picture.jpg") and no link is longer than 255 characters.
4. Access the index.html file and browse around the mini-website, to ensure that the most commonly used browsers (Internet Explorer and Firefox) are able to view all parts of the mini-website without problems, it is ideal to check this on a different machine.
5. Compress the folder into a ZIP, check the file size is under 20 MB, ensure that index.html is in the root of the ZIP, and that the file has .zip extension, then submit as an additional file with your article.

Style and language

General

Currently, *Diabetology & Metabolic Syndrome* can only accept manuscripts written in English. Spelling should be US English or British English, but not a mixture.

There is no explicit limit on the length of articles submitted, but authors are encouraged to be concise.

Diabetology & Metabolic Syndrome will not edit submitted manuscripts for style or language; reviewers may advise rejection of a manuscript if it is compromised by grammatical errors. Authors are advised to write clearly and simply, and to have their article checked by colleagues before submission. In-house copyediting will be minimal. Non-native speakers of English may choose to make use of a copyediting service.

Help and advice on scientific writing

The abstract is one of the most important parts of a manuscript. For guidance, please visit our page on Writing titles and abstracts for scientific articles.

Tim Albert has produced for BioMed Central a list of tips for writing a scientific manuscript. American Scientist also provides a list of resources for science writing. For more detailed guidance on preparing a manuscript and writing in English, please visit the BioMed Central author academy.

Abbreviations

Abbreviations should be used as sparingly as possible. They should be defined when first used and a list of abbreviations can be provided following the main manuscript text.

Typography

- Please use double line spacing.
- Type the text unjustified, without hyphenating words at line breaks.
- Use hard returns only to end headings and paragraphs, not to rearrange lines.
- Capitalize only the first word, and proper nouns, in the title.
- All pages should be numbered.
- Use the *Diabetology & Metabolic Syndrome* reference format.
- Footnotes are not allowed, but endnotes are permitted.
- Please do not format the text in multiple columns.
- Greek and other special characters may be included. If you are unable to reproduce a particular special character, please type out the name of the symbol in full. **Please ensure that all special characters used are embedded in the text, otherwise they will be lost during conversion to PDF.**

Units

SI units should be used throughout (liter and molar are permitted, however).