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EFEITOS DO EXERCÍCIO FÍSICO SUPERVISIONADO E ESTRUTURADO NA SAÚDE CARDIOMETABÓLICA DE CRIANÇAS E ADOLESCENTES: UMA REVISÃO SISTEMÁTICA E METANÁLISE

Porto Alegre, março de 2023

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Tese apresentada como requisito parcial para obtenção do título de Doutor no Programa de Pós-Graduação em Ciências do Movimento Humano da Universidade Federal do Rio Grande do Sul.

Orientador: Dr. Giovani dos Santos Cunha

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RESUMO

Introdução: Os efeitos do exercício físico sobre a saúde cardiometabólica de crianças e adolescentes têm sido investigados a fim de identificar e melhorar parâmetros de saúde que estão relacionados a diversos fatores de risco. O objetivo do estudo foi realizar uma revisão sistemática com metanálise no intuito de avaliar os efeitos do exercício físico supervisionado e estruturado sobre saúde cardiometabólica de crianças e adolescentes. **Materiais e métodos:** A revisão foi conduzida de acordo com as recomendações Cochrane e registrada na plataforma PROSPERO. Para a seleção dos artigos foram utilizadas as plataformas de busca Embase, Cochrane, Pubmed e Scopus, em junho de 2022. Três pesquisadores independentes selecionaram os artigos que comparassem uma intervenção de exercício físico supervisionado e estruturado com um grupo controle de crianças e adolescentes de 6 a 17 anos, e que avaliassem as seguintes variáveis: dilação mediada por fluxo (FMD), velocidade de onda de pulso tornozelo-braquial (baPWV), pressão arterial sistólica e diastólica (SBP e DBP), colesterol total (TC), lipoproteínas de alta- e baixa-densidade (HDL e LDL) e a razão cintura-estatura (WtHR). A métrica escolhida para apresentação dos resultados foi a diferença média padronizada (*Standardized Mean Difference - SMD*) e os cálculos foram realizados utilizando efeitos randômicos. *Forest plots* foram gerados para apresentar os efeitos agrupados das intervenções (SMD) para cada variável, bem como os limites inferiores e superiores do intervalo de confiança 95% (IC 95%). A heterogeneidade estatística dos efeitos das intervenções entre os estudos foi avaliada usando os testes Q de Cochran e I^2 para inconsistências, sendo considerados valores elevados de heterogeneidade quando $I^2 > 50\%$. Adicionalmente, análises de sensibilidade para verificar a influência do sexo (análise incluindo ambos os sexos, meninas e meninos) e Tipo de exercício (Aeróbico, HIIT [Treinamento Intervalado de Alta-Intensidade], Combinado, Força e Esporte). Também foram conduzidas metarregressões para avaliar possíveis moderadores dos efeitos do exercício físico sobre a saúde cardiometabólica incluindo as variáveis Índice de massa corporal (IMC), Idade cronológica, frequência semanal de treinamento, duração da sessão e duração da intervenção. Valores de $P<0.05$ foram considerados significativos. **Resultados:** As intervenções de exercício físico supervisionado e estruturado melhoram significativamente a baPWV, SBP, HDL, LDL e WtHR. Na análise geral, não foram encontradas melhoras significativas no TC e DBP. Quando analisamos os sexos de forma isolada, a SBP apresentou redução significativa somente nos subgrupos ambos os sexos e meninas. Em contrapartida, para o HDL foram encontrados aumentos significativos quando foram analisados os subgrupos ambos os sexos e meninos, e para as concentrações de LDL foi encontrada uma redução significativa no subgrupo meninos. Quando os tipos de exercício foram analisados separadamente, reduções significativas foram estabelecidas para o subgrupo Aeróbico na SBP e subgrupos Aeróbico e HIIT para LDL. Idade cronológica e IMC foram consideradas variáveis moderadoras do efeito do exercício sobre a SBP, enquanto o IMC moderou os efeitos sobre HDL. Além disso, IMC e duração da intervenção moderaram os efeitos do exercício sobre WthR. **Conclusão.** Intervenções de exercício físico supervisionado e estruturado apresentaram efeitos positivos sobre indicadores de saúde cardiometabólica de crianças e adolescentes, especialmente os tipos de exercício aeróbico e HIIT, e IMC, idade cronológica e a duração da intervenção são variáveis moderadoras do efeito positivo do exercício.

Palavras-chave: Saúde cardiometabólica; rigidez arterial; função endotelial; crianças.

ABSTRACT

Introduction: The effects of physical exercise on the cardiometabolic health of children and adolescents have been investigated to identify and improve health parameters that are related to several risk factors. This systematic review and meta-analysis aimed to analyze the effects of supervised and structured physical exercise on the cardiometabolic health of children and adolescents. **Methods:** The review was conducted in accordance with Cochrane recommendations and recorded on the PROSPERO platform. For the selection of articles, the search platforms Embase, Cochrane, Pubmed and Scopus were used in June 2022. Three independent researchers selected articles that compared a supervised and structured physical exercise intervention with a control group of children and adolescents aged 6 to 17 years, and that evaluated the following variables: flow-mediated dilation (FMD), Brachial-ankle pulse wave velocity (baPWV), systolic and diastolic blood pressure (SBP and DBP), total cholesterol (TC), high- and low-density lipoproteins (HDL and LDL) and the waist-to-height ratio (WtHR). The results are presented as standardized mean differences and calculations were performed using random effects models. Statistical heterogeneity of treatment effects among studies was evaluated by Cochran Q test and the I^2 inconsistency test; it was considered that values >50% indicated high heterogeneity. In addition, sensitivity analyses were conducted to investigate the possible influence of randomization process in the included studies, the progression in training variables. In addition, sensitivity analyses were conducted to investigate the possible effect of sex (only boys, only girls or both sexes) and types of the exercise intervention (aerobic, combined, high-intensity interval training [HIIT], sport and strength) in the observed adaptations. Also, meta-regressions were performed to investigate possible moderators of the training effect on the target outcomes: chronological age, BMI, weekly training frequency, follow-up duration and session duration. Values of $P < .05$ were considered statistically significant. **Results:** Supervised and structured physical exercise interventions significantly improve baPWV, SBP, HDL, LDL and WtHR. In the general analysis, no significant improvements were found for TC and DBP. When we analyzed the sexes separately, the SBP showed a significant reduction only in both sexes and only girls' categories. In contrast, for HDL, significant increases were found when both sexes and only boys' categories were analyzed, and for LDL concentrations, a significant reduction was found in the for only boys.

When the types of exercises were analyzed separately, significant reductions were found for the aerobic category on SBP and aerobic and HIIT categories for LDL. Chronological age and BMI were considered moderating variables of the effect of exercise on SBP, while BMI moderated the effects on HDL. Furthermore, BMI and follow-up duration moderated the effects of exercise on WthR. **Conclusion:** Supervised and structured physical exercise interventions promoted improvements on the cardiometabolic health of children and adolescents, especially the aerobic and HIIT types of exercise. BMI, chronological age and duration of intervention are variables that moderate the positive effect of exercise.

Keywords: Cardiometabolic health; arterial stiffness; endothelial function; children.

Sumário

Lista de abreviaturas

AS	*Arterial stiffness* – Rigidez arterial
baPWV	*Brachial-ankle pulse wave velocity* – Velocidade de onda de pulso tornozelo braquial
CMRF	*Cardiometabolic risk factors* – Fatores de risco cardiometabólicos
DBP	*Diastolic blood pressure* – Pressão arterial diastólica
EF	*Endothelial function* - Função endotelial
FMD	*Flow-mediated dilation* – Dilatação mediada por fluxo
HDL	*High density lipoprotein* – Lipoproteína de alta densidade
HIIT	*High intensity interval training* – Treinamento intervalado de alta intensidade
IC	Intervalo de confiança
IMC	Índice de massa corporal
LDL	*Low density lipoprotein* – Lipoproteína de baixa densidade
mmHg	Miligramas de mercúrio
PWV	*Pulse wave velocity* – Velocidade de onda de pulso
SBP	*Systolic blood pressure* – Pressão arterial sistólica
SCM	Saúde cardiometabólica
TC	*Total cholesterol* – Colesterol total
TCIM	Treinamento contínuo em intensidade moderada
WtHR	*Wais-to-height ratio* – Razão cintura-estatura

1. APRESENTAÇÃO DA TESE

1.1. INTRODUÇÃO

A saúde cardiometabólica refere-se à saúde cardiovascular (coração e vasos sanguíneos) e saúde metabólica (ausência de resistência à insulina, dislipidemia e pressão arterial alta)(STEFAN; SCHICK; HARING, 2017), e o seu estudo na população pediátrica vem recebendo atenção devido às alterações em fatores de risco cardiometabólicos (CMRF) que geralmente deveriam ocorrer na idade adulta, mas atualmente tem ocorrido precocemente na infância e adolescência (CANAS; SWEETEN; BALAGOPAL, 2013; JUONALA; VIIKARI; RAITAKARI, 2013). Esta população está sendo acometida por CMRF cada vez mais cedo, e isto deve-se a fatores ambientais, genéticos e comportamentais, que consequentemente podem desencadear aumentos nos níveis de sobrepeso e obesidade, aumento do sedentarismo, desencadear hábitos alimentares inapropriados e o desenvolvimento de doenças crônicas (JI; NING; DUAN; KAPRIO *et al.*, 2014). Segundo a Organização Mundial de Saúde, estimou que em 2016, mais de 340 milhões de crianças e adolescentes com idades entre 5 e 19 anos apresentavam sobrepeso ou obesidade (BULL; AL-ANSARI; BIDDLE; BORODULIN *et al.*, 2020) e tendência de diminuição da aptidão cardiorrespiratória (TOMKINSON; LANG; TREMBLAY, 2019).

Entre os parâmetros mais utilizados para a identificação de riscos à saúde cardiometabólica e que sistematicamente vem apresentado valores anormais na população pediátrica, podemos citar a pressão arterial sistólica (SBP) e diastólica DBP), colesterol total (TC) e lipoproteínas de alta e baixa-densidade (LDL), glicemia, aptidão cardiorrespiratória, índice de massa corporal (IMC), bem como a razão cintura-estatura (WtHR) (CANAS; SWEETEN; BALAGOPAL, 2013; CANDELINO; TAGI; CHIARELLI, 2022; DE FERRANTI; STEINBERGER; AMEDURI; BAKER *et al.*, 2019; RODGERS; JONES; BOLLEDDU; VANTHENAPALLI *et al.*, 2019; TRAN; URBINA, 2020). Adicionalmente, preditores de eventos cardiovasculares como a função endotelial e rigidez arterial, que podem ser avaliados através da dilatação mediada por fluxo (FMD) e a velocidade de onda de pulso (PWV) têm sido considerados importantes indicadores da função vascular (BONETTI; LERMAN; LERMAN, 2003; CELERMAJER, 1992; CORREIA; HAYNES, 2007; HANSSEN, 2022) e consequentemente preditores de saúde cardiometabólica (DA SILVA; DA SILVA; WACLAWOVSKY; SCHAUN, 2022; TOMIYAMA; YAMASHINA, 2018). Estes indicadores são essenciais para a detecção de disfunção endotelial, que além de estar relacionada ao início do aparecimento de doenças cardiovasculares é considerado o primeiro passo para o desenvolvimento de aterosclerose, que pode ser definida como um processo inflamatório crônico e degenerativo que acomete os vasos (acúmulo de lipídios, célular inflamatórias e elementos fibrosos) e pode ter seu início durante a infância e adolescência (STRONG; MCGILL, 1969). Ou seja, tendo em vista que as alterações nos indicadores de saúde têm se manifestado precocemente, torna-se necessário identificar se crianças e adolescentes já estão expostos a esses CMRF e promover estratégias para melhorar a saúde desta população, a fim de prevenir o desenvolvimento de doenças crônicas e eventos cardiovasculares futuramente (LITWIN, 2018).

O exercício físico é uma estratégia não-farmacológica para melhorar os CMRF, pois além de ser essencial para um crescimento e desenvolvimento saudável de crianças e adolescentes, melhora os níveis de aptidão e atividade física, bem como a saúde cardiometabólica. Entretanto, os efeitos do exercício físico sobre a função endotelial e rigidez arterial ainda são pouco explorados, principalmente na população pediátrica (CHENG; SUN; YA; ZHOU *et al.*, 2022; DIAS; GREEN; INGUL; PAVEY *et al.*, 2015). A recomendação de atividade física mais recente, publicado pela Organização Mundial da Saúde, recomenda que crianças/adolescentes de 6 a 17 anos realizem uma média de 60 minutos diários de atividade física moderada à vigorosa para manter ou melhorar a saúde cardiometabólica, incluindo exercícios aeróbicos, de força muscular e exercícios de impacto (BULL; AL-ANSARI; BIDDLE; BORODULIN *et al.*, 2020). Além disso, é recomendado que o exercício físico prescrito para crianças e adolescentes seja estruturado e supervisionado, principalmente quando for realizado treinamento de força (DIAS; GREEN; INGUL; PAVEY *et al.*, 2015). Intervenções de exercício físico com abordagens multidisciplinares, ou seja, incluindo intervenções nutricionais e de mudanças de estilo de vida são consideradas eficazes na redução dos CMRF (GRACE; BIGGS; NAICKER; MOSS, 2021; HO; GARNETT; BAUR; BURROWS *et al.*, 2012; POZUELO-CARRASCOSA; CAVERO-REDONDO; HERRÁIZ-ADILLO; DÍEZ-FERNÁNDEZ *et al.*, 2018). Entretanto, é importante compreender o papel do exercício físico isoladamente, pois nesses estudos multidisciplinares, a dieta e as mudanças no estilo de vida podem ser fatores de confusão na interpretação os resultados.

Diversos efeitos positivos do exercício físico sobre os parâmetros de saúde têm sido reportados, mas ainda não está claro quais os tipos de exercício são mais efetivos para melhorar a saúde cardiometabólica de crianças e adolescentes. Além disso, faltam informações sobre os fatores moderadores dos efeitos do exercício (sexo, idade cronológica, índice de massa corporal e dos princípios fundamentais do treinamento como a frequência semanal, duração da sessão e duração da intervenção) sobre a saúde cardiometabólica. Adicionalmente, torna-se importante investigar os efeitos do exercício físico sobre os parâmetros de saúde cardiovascular (função endotelial e rigidez arterial) devido a escassez de estudos que tenham analisado esses indicadores de saúde cardiovascular nesta população.

Sendo assim, a presente revisão sistemática e metanálise tem como objetivo analisar os efeitos do exercício físico estruturado e supervisionado na saúde cardiometabólica de crianças e adolescentes. Adicionalmente, investigar o papel moderador dos diferentes tipos de exercício, sexo, IMC, idade cronológica, frequência semanal, duração das sessões e duração da intervenção na saúde cardiometabólica desta população.

1.2. OBJETIVOS

Objetivo geral

- Verificar os efeitos do exercício físico supervisionado e estruturado na saúde cardiometabólica de crianças e adolescentes.

Objetivos específicos

- Verificar os efeitos do exercício físico supervisionado e estruturado na Dilatação Mediada por Fluxo e Velocidade de onda de Pulso de crianças e adolescentes;
- Verificar os efeitos do exercício físico supervisionado e estruturado na Pressão Arterial Sistólica e Diastólica de crianças e adolescentes;
- Verificar os efeitos do exercício físico supervisionado e estruturado no TC, LDL e HDL de crianças e adolescentes;
- Verificar os efeitos do exercício físico supervisionado e estruturado na Razão Cintura-Estatura de crianças e adolescentes.

- Verificar o efeito de variáveis potencialmente moderadoras (diferentes tipos de exercício, sexo, IMC, idade cronológica, frequência semanal, duração das sessões e duração da intervenção) dos efeitos do exercício físico sobre a saúde cardiometabólica.

1.3. REVISÃO DE LITERATURA

1.3.1. Saúde cardiometabólica de crianças e adolescentes

A saúde cardiometabólica de crianças e adolescentes pode ser afetada por diversos CMRF, que estão relacionados ao desenvolvimento de doenças cardiometabólicas na vida adulta. Nesta revisão de literatura, iremos abordar alguns dos principais componentes da saúde cardiometabólica e suas alterações, bem como os efeitos do exercício físico sobre a saúde cardiometabólica na população pediátrica. Salienta-se que neste estudo os termos exercício físico supervisionado e estruturado, treinamento físico, treinamento físico-esportivo serão considerados intercambiáveis.

1.3.2. Função endotelial

O endotélio é um epitélio de camada única que reveste o interior dos vasos sanguíneos e as cavidades do coração, essencial para a manutenção da homeostase do corpo. Este tecido, além de servir como uma barreira entre o sangue e o tecido sólido, é considerado um dos órgãos endrócrinos e metabólicos mais importantes do corpo humano (GODO; SHIMOKAWA, 2017; MICHIELS, 2003). Sendo ativo e dinâmico, o endotélio tem ações importantes como a manutenção da circulação sanguínea, regulação do tônus vascular, permeabilidade microvascular, sinalização e angiogênese vascular e resposta inflamatória (KISELEVA; GLASSMAN; GREINEDER; HOOD *et al.*, 2018; PAGAN; GOMES; OKOSHI, 2018; STANEK; FAZELI; BARTUS; SUTKOWSKA, 2018). Este tecido, como regulador do tônus vascular, produz e libera mediadores da contração/relaxamento dos casos, e o principal deles é o óxido nítrico (do inglês: *Nitric Oxide*, ON) (PAGAN; GOMES; OKOSHI, 2018; SOUZA JUNIOR; ASANO; PRESTES; SALES *et al.*, 2012). Sendo assim, o funcionamento normal e saudável do endotélio é um pré-requisito fundamental para o funcionamento do sistema cardiovascular, e a perda da sua integridade (disfunção endotelial) está relacionada à diversas alterações vasculares que resultarão em doença cardiovascular. A causa da lesão do endotélio pode ser uma consequência hemodinâmica, como por exemplo o estresse de cisalhamento na parede do vaso (*sheer stress*), química, como alterações no LDL ou glicose, ou por fatores biológicos, como alterações imunes (STANEK; FAZELI; BARTUS; SUTKOWSKA, 2018).

Uma das formas mais comuns e não-invasiva de avaliar a função endotelial é através de um método denominado Dilatação Mediada por Fluxo (FMD) da artéria braquial, usualmente realizada por ultrasonografia, mensura a dilatação arterial durante a hiperemia reativa pós-oclusiva. Esta isquemia transitória provocada através de um manguito de pressão no braço provoca a liberação de óxido nítrico pelo endotélio, causando vasodilatação compensatória (CHIA; TEO; YEO, 2020; MUCKA; MIODONSKA; JAKUBIAK; STARZAK *et al.*, 2022). Quando há disfunção endotelial, a quantidade de óxido nítrico liberada não é capaz de gerar a vasodilatação esperada (CHIA; TEO; YEO, 2020). A biodisponibilidade deste potente dilatador pode ser afetada pelo exercício físico, que é uma importante estratégia não-farmacológica para melhorar a função endotelial. O exercício físico aumenta o estresse de cisalhamento na parede dos vasos de forma aguda devido ao aumento do fluxo sanguíneo, aumentando a produção de óxido nítrico de forma aguda e crônica. Visto que é relatado na literatura que uma redução de 1% na FMD aumenta o risco de doença cardiovascular no futuro em 13% (INABA; CHEN; BERGMANN, 2010), o exercício físico pode ser considerado uma importante ferramenta para preservar as funções do endotélio e prevenir doenças cardiovasculares, visto que ele pode aumentar e melhorar a dilatação vascular (GREEN; MAIORANA; O'DRISCOLL; TAYLOR, 2004; SOUZA JUNIOR; ASANO; PRESTES; SALES *et al.*, 2012).

1.3.2.1. Efeitos de intervenções de exercício físico na FMD

O estudo de Da Silva *et al.* (2020), analisou os efeitos de uma intervenção de 12 semanas de HIIT (corrida), realizado três vezes na semana na FMD de adolescentes obesas ou com peso normal e encontrou melhoras significativas após a intervenção comparadas ao grupo controle. Apesar do grupo obesas ter iniciado o treinamento com uma função endotelial reduzida (menor FMD), ambos os grupos melhoraram em torno de 4% (DA SILVA; WACLAWOVSKY; PERIN; CAMBOIM *et al.*, 2020). Resultados semelhantes foram encontrados no estudo de Chuensiri *et al.* (2018), que também encontrou melhoras significativas na FMD após intervenções de 12 semanas de HIIT e Supra-HIIT, realizado três vezes por semana em cicloergômetro com meninos obesos. Os aumentos foram de aproximadamente 2,2% para os grupos HIIT, que realizava 8 séries de 2 minutos à 90% da potência máxima e Supra-Hiit, que realizava 8 séries de 20 segundos à 170% da potência máxima (CHUENSIRI; SUKSOM; TANAKA, 2018).

O estudo de Kelly *et al.* (2004) avaliou a FMD de crianças e adolescentes com sobrepeso que realizaram uma intervenção de exercício aeróbio em cicloergômetro, quatro vezes na semana. Apesar de ter sido uma intervenção com menor duração (8 semanas), foram encontrados aumentos significativos de 1.1% na FMD do grupo exercício (KELLY; WETZSTEON; KAISER; STEINBERGER *et al.*, 2004). Em uma intervenção com treinamento de força, realizado duas vezes na semana, Yu *et al.* (2016) encontraram melhoras significativas, com aumento de 1,3% na média da FMD após 10 semanas. É interessante ressaltar que neste estudo, as crianças tinham peso normal, demonstrando que o exercício físico pode ser uma ferramenta para melhorar a função endotelial não somente de crianças e adolescentes com sobrepeso ou obesidade (YU; MCMANUS; SO; CHOOK *et al.*, 2016). Em contrapartida, em um estudo que analisou os efeitos de uma intervenção com atividades esportivas e de força realizadas três vezes na semana (jogos com bola, natação, corrida ou caminhada rápida e exercícios de força que atualizava o peso do corpo ou elásticos), Farpour-Lambert *et al.* (2009) não encontraram melhoras significativas na FMD de crianças após três meses. Uma possível explicação para a ausência de melhoras na FMD pode estar relacionada com a intensidade moderada do treinamento, que foi monitorada e realizada em 55-65% da frequência cardíaca máxima, possivelmente não sendo capaz de gerar adaptações positivas na função endotelial (FARPOUR-LAMBERT; AGGOUN; MARCHAND; MARTIN *et al.*, 2009). Visto que há poucos estudos que analisaram a FMD na população pediátrica, mais estudos são necessários para a testagem de diferentes intervenções, para compreender quais variáveis de treinamento exercem um maior efeito nesta variável.

Quando analisadas diferentes intervenções conjuntamente, a metanálise de Cheng *et al.* (2022) encontrou melhoras significativas na FMD de crianças e adolescentes com sobrepeso e obesidade. Estas melhoras ocorreram independentemente do IMC dos sujeitos (acima ou abaixo de 30 kg/m^2) ou da idade (acima ou abaixo de 14 anos) (CHENG; SUN; YA; ZHOU *et al.*, 2022).

1.3.3. Rigidez arterial

Com o envelhecimento, é natural que haja um enrijecimento da vasculatura e este aumento da rigidez arterial tem sido associado ao aumento de risco cardiovascular, e também considerado um preditor independente de infarto (SHIRWANY; ZOU, 2010; YIMING; ZHOU; LV; PENG *et al.*, 2017). Além disso, o aumento da rigidez das artérias centrais tem efeitos deletérios que afetam doenças como aterosclerose, diabetes e doença renal (ZIEMAN; MELENOVSKY; KASS, 2005). Atualmente, estudos mostraram que, ao invés de haver só uma relação de causa/efeito entre a disfunção endotelial e a rigidez arterial, a relação oposta também pode ser verdadeira: a rigidez arterial contribuindo para a disfunção endotelial. Em relação a isso, pode haver um ciclo vicioso onde o enrijecimento das artérias leva às alterações no endotélio que, consequentemente, pioram o enrijecimento (SHIRWANY; ZOU, 2010).

A rigidez arterial é medida diretamente através da Velocidade de Onda de Pulso (PWV), a qual reflete a elasticidade arterial e tem sido considerada um preditor de eventos cardiovasculares e de mortalidade (YIMING; ZHOU; LV; PENG *et al.*, 2017). A contração do ventrículo esquerdo durante a sístole gera uma onda de pulso que é propagada pela árvore arterial e a PWV é calculada como a distância percorrida pela onda dividida pelo tempo (TOMIYAMA; YAMASHINA, 2018; VLACHOPOULOS; AZNAOURIDIS; STEFANADIS, 2010). Convencionalmente, PWV é medida na carótida-femoral para acessar a rigidez arterial central, mas também pode ser mensurada a PWV tornozelo-braquial (baPWV). A PWV carótida-femoral é medida através de tonometria, Doppler ou oscilometria, enquanto a baPWV é mensurada através de oscilometria (TOWNSEND; WILKINSON; SCHIFFRIN; AVOLIO *et al.*, 2015), após serem presos manguitos de pressão nas 4 extremidades (braços e pernas), e a distância é calculada pela altura, ou seja, a PWV é apresentada em distância/tempo (m/s ou cm/s). Ambas as metodologias têm correlação com o método invasivo padrão-ouro (TOMIYAMA; YAMASHINA, 2018). Estudos recentes mostram que a PWV obtida de forma não-invasiva um marcador de danos vasculares é também um preditor independente de mortalidade geral e de mortalidade por doença cardiovascular em pacientes com hipertensão (LAURENT; COCKCROFT; VAN BORTEL; BOUTOUYRIE *et al.*, 2006). Além disso, um aumento da PWV está associado ao aumento da pressão arterial sistólica e diastólica (ELKA, 2018).

De acordo com a literatura, o aumento da espessura do vaso ou a diminuição do seu diâmetro, decorrente do acúmulo de placas, o que pode resultar em um aumento da PWV, sendo esta resposta influenciada por idade e pressão arterial. Sendo assim, o aumento da rigidez arterial leva à um aumento da PWV, o que tem sido relacionado ao início do processo aterosclerótico (KIM; KIM, 2019; WEBER; AMMER; RAMMER;

ADJI *et al.*, 2009). É reportado na literatura que crianças e adolescentes, principalmente quando acometidos por hipertensão ou obesidade, já apresentam alterações significativas na PWV (KULSUM-MECCI; GOSS; KOZEL; GARBUTT *et al.*, 2017). O exercício físico, assim como exerce efeito sobre a FMD, também exerce efeito sobre a rigidez arterial. Os mecanismos fisiológicos que explicam a possível redução da PWV induzida por exercício, incluem o relaxamento das células musculares lisas através do aumento do estresse de cisalhamento e atividade do ON, redução do estresse oxidativo, inflamação e de CMRF, como por exemplo a pressão arterial (KIM; KIM, 2019). Este efeito do exercício físico é importante, visto que tem sido reportado na literatura que um aumento de 1 m/s na PWV está associado ao aumento de 12% no risco de eventos cardiovasculares, especialmente em indivíduos que já apresentam risco para o desenvolvimento de doenças cardiovasculares (VLACHOPOULOS; AZNAOURIDIS; STEFANADIS, 2010). Obviamente, uma redução na PWV pode reduzir o risco cardiovascular.

1.3.3.1. Efeitos de intervenções de exercício físico na PWV

Os efeitos do exercício físico na PWV ainda não são conclusivos, visto que na literatura são encontrados diferentes resultados após as intervenções. O estudo de Chuensiri *et al.* (2018), já citado anteriormente, encontrou reduções significativas na baPWV após intervenções de HIIT e Supra-HIIT em cicloergômetro. As crianças que participaram dos grupos de exercício, reduziram em média 0,67 m/s (HIIT) e 0,20 (Supra-HIIT) após as 12 semanas de intervenção. Ou seja, quando o exercício é prescrito em alta intensidade, pode ocorrer a melhora da PWV desta população (CHUENSIRI; SUKSOM; TANAKA, 2018).

Quando analisado o exercício de pular corda, Sung *et al.* (2018) realizaram uma intervenção de 12 semanas com frequência de cinco vezes por semana, com meninas adolescentes com pré-hipertensão. Após este período, foram encontradas melhoras na PWV, com reduções de 0,8 m/s (SUNG; PEKAS; SCOTT; SON *et al.*, 2019). Esta melhora também foi encontrada em dois estudos que analisaram os efeitos de uma intervenção de exercício combinado (aeróbico + força) de 12 semanas, realizada três vezes na semana, com adolescentes obesas, Wong *et al.* (2018) e Son *et al.* (2017), encontraram reduções significativas de PWV de 1 e 1,23 m/s, respectivamente (SON; KIM; JEON; KANG *et al.*, 2017; WONG; SANCHEZ-GONZALEZ; SON; KWAK *et al.*, 2018).

Em contrapartida, utilizando uma prescrição diferente de exercício físico, o estudo de Lee *et al.* (2010), realizou uma intervenção com atividades esportivas (futebol, basquete e corda) com ou sem treinamento de força em circuito, três vezes na semana. Após 10 semanas de treinamento, os adolescentes obesos que participaram dos grupos de exercício não melhoraram a PWV (LEE; SONG; KIM; LEE *et al.*, 2010). O mesmo ocorreu no estudo de Bharath *et al.* (2018), que não encontraram resultados positivos na baPWV de meninas adolescentes obesas após 12 semanas de treinamento combinado, realizado cinco vezes na semana (BHARATH; CHOI; CHO; SKOBODZINSKI *et al.*, 2018). Esta ausência de melhoras também foi encontrada no estudo de Horner *et al.* (2015), que analisaram os efeitos de intervenções com o exercício de força e aeróbico de forma isolada, realizado três vezes por semana. Após três meses, os adolescentes obesos que participaram dos grupos exercício não apresentaram reduções significativas na PWV de forma significativa (HORNER; KUK; BARINAS-MITCHELL; DRANT *et al.*, 2015).

Na metanálise de Cheng *et al.* (2022) que analisou os efeitos de diferentes tipos de exercício sobre a PWV, encontrou reduções significativas após as intervenções. A partir de subanálises, verificou-se que a PWV diminuiu significativamente somente em crianças até 14 anos e com IMC abaixo de 30 kg/m^2. Adicionalmente, somente as intervenções com exercício aeróbico e de HIIT induziram reduções significativas na PWV em comparação ao exercício de força e combinado. A partir destes resultados, que evidenciam melhoras na PWV em indivíduos menores de 14 anos, hipotetiza-se existir um limiar de idade relacionado aos efeitos positivos induzidos por exercício físico sobre a plasticidade de remodelação vascular (CHENG; SUN; YA; ZHOU *et al.*, 2022). Os efeitos do exercício sobre a PWV são influenciados pela idade cronológica, lembrando que a idade isolada já é um fator de induz aumento da rigidez arterial (COCKCROFT; WILKINSON; WEBB, 1997; WALLACE, 2012). Além disso, a redução da PWV somente em crianças com IMC até 30 kg/m^2 pode ter ocorrido devido às características da remodelação da estrutura vascular, que pode ser responsável pelos efeitos em longo-prazo decorrentes da obesidade, onde intervenções de exercício físico curtas não são efetivas para reverter estas alterações. Na comparação entre os diferentes tipos de exercício, o exercício de força quando analisado isoladamente ou conjuntamente com o exercício aeróbico (combinado), não foi efetivo para promover melhoras na PWV, resultado semelhante ao encontrado por estudos com indivíduos adultos (CECILIATO; COSTA; AZEVEDO; SOUSA *et al.*, 2020; ZHANG; QI; XU; SUN *et al.*, 2018).

1.3.4. Pressão arterial

A pressão arterial é a pressão, medida em milímetros de mercúrio (mmHg) dentro do sistema arterial e é convencionalmente separada em pressão arterial sistólica e diastólica. A SBP é a pressão sanguínea máxima durante a contração dos ventrículos, que estão repletos de sangue, enquanto a DBP é a pressão mínima imediatamente antes da próxima contração, quando há um relaxamento do coração. Uma pressão arterial ideal é aquela que perfunde adequadamente todos os sistemas do corpo sem causar danos. Qualquer órgão não adequadamente perfundido poderá sofrer dano isquêmico ou será incapaz de realizar a sua função de forma adequada. A principal alteração da pressão arterial é a hipertensão, podendo causar danos aos órgãos, que poderão desencadear eventos cardiovasculares como infarto e acidente vascular cerebral (WA., 1990). A pressão arterial é a principal determinante da rigidez arterial, ou seja, alterações na pressão arterial levarão à alterações na rigidez arterial (ELKA, 2018; PAINI; BOUTOUYRIE; CALVET; TROPEANO *et al.*, 2006).

As consequências da hipertensão e as estratégias (farmacológicas ou não-farmacológicas) para a redução da pressão arterial são amplamente estudadas na literatura, tanto na população adulta e idosa quanto na população pediátrica. Isto porque há associação da pressão arterial com os eventos cardiovasculares, demonstrando ser um fator de risco para o desenvolvimento de doenças e eventos cardiovasculares (ELKA, 2018).

Nos Estados Unidos, um estudo do *Centers for Disease Control and Prevention* mostrou que 1 a cada 25 jovens de 1 a 19 anos tem hipertensão, sendo que 1 a cada 10 tem pressão arterial elevada (em torno de 800.000), anteriormente chamado de pré-hipertensão, esta condição é mais comum em jovens obesos (FLYNN; KAELBER; BAKER-SMITH; BLOWEY *et al.*, 2017). É importante ressaltar que uma pressão arterial elevada na infância correlaciona-se com uma pressão ainda mais elevada na vida adulta e com o desenvolvimento da hipertensão arterial no início da vida adulta (CHEN; WANG, 2008). Ou seja, a investigação das alterações na pressão arterial, assim como pesquisas sobre intervenções que exerçam efeito sobre esta variável na população pediátrica são necessárias, pois prevenir a hipertensão arterial na infância pode reduzir os fatores de risco cardiometabólicos na vida adulta (CHEN; WANG, 2008).

O exercício físico é uma importante ferramenta não farmacológica para reduzir a pressão arterial, tanto sistólica como diastólica, e isto ocorre porque a prática regular de exercício potencializa a contração muscular cardíaca, ejetando sangue de forma mais eficiente, reduzindo a pressão arterial em longo-prazo. Algumas das adaptações fisiológicas que ocorrem em decorrência do exercício físico estão relacionadas ao aumento no débito cardíaco, redistribuição do fluxo sanguíneo e elevação da perfusão circulatória para os músculos que estão em atividade (ARAÚJO, 2001). Os efeitos do exercício físico podem variar dependendo do tipo de exercício e dos componentes do treinamento físico (duração da sessão, frequência semanal, etc.). Atualmente, há recomendações que o exercício seja realizado em intensidade moderada por 30 minutos cinco vezes na semana (ou 150 minutos semanais), ou 75 minutos semanais em intensidade vigorosa, para prevenir ou tratar a hipertensão. Além disso, é desejável que também seja incluído o exercício de força, duas a quatro vezes por semana (KHAN; HEMMELGARN; HERMAN; BELL *et al.*, 2009; PESCATELLO; FRANKLIN; FAGARD; FARQUHAR *et al.*, 2004). Apesar de já haver um consenso de que o exercício físico pode reduzir a pressão arterial, principalmente o aeróbico, ainda não está claro qual é a prescrição de treinamento ótima, principalmente na população pediátrica (CORNELISSEN; SMART, 2013; HANSSEN; BOARDMAN; DEISEROTH; MOHOLDT *et al.*, 2022).

1.3.4.1. Efeitos de intervenções de exercício físico na Pressão Arterial

A pressão arterial sistólica e diastólica de meninos com sobrepeso ou obesos foi avaliada no estudo de Cvetkovic *et al.* (2018). Nesta pesquisa, foi realizada uma intervenção de 12 semanas de futebol ou HIIT, realizados três vezes por semana. Apesar dos resultados de SBP e DBP terem mostrado uma tendência de redução, não foram encontradas diferenças significativas após o treinamento (CVETKOVIC; STOJANOVIC; STOJILJKOVIC; NIKOLIC *et al.*, 2018). Buchan *et al.* (2013) analisaram os efeitos do HIIT sobre a pressão arterial de adolescentes saudáveis e também não encontraram reduções significativas na DBP, em contrapartida, foram encontradas reduções significativas de 5 mmHg na SBP após sete semanas de intervenção, com o exercício sendo realizado três vezes por semana (BUCHAN; OLLIS; YOUNG; COOPER *et al.*, 2013).

Uma estratégia interessante para realizar intervenções de exercício físico em crianças e adolescentes é aplicá-las nas escolas, aumentando assim a aderência a intervenção. Neste contexto, um estudo de Delgado-floody *et al.* (2018) mesmo com um longo período de intervenção, não encontraram reduções significativas na SBP e DBP de crianças após 28 semanas de sessões de HIIT inserido duas vezes por semana na educação física escolar (DELGADO-FLOODY; ESPINOZA-SILVA; GARCIA-PINILLOS; LATORRE-ROMAN, 2018). No entanto, o recente estudo de Meng *et al.* (2022) encontrou reduções significativas de 5 mmHg na SBP de adolescentes obesos, com intervenções de HIIT e treinamento contínuo com intensidade moderada realizados três vezes por semana durante 12 semanas. Semelhante ao estudo supracitado, não foram encontradas reduções significativas para DBP (MENG; YUCHENG; SHU; YU, 2022).

Quando analisamos intervenções com o exercício de pular corda realizado 5 vezes por semana, Kim *et al.* (2007) não estabeleceram reduções significativas na SBP e DBP em adolescentes obesos (KIM; IM; KIM; PARK *et al.*, 2007). Em um estudo semelhante, Sung et al. (2018) encontraram reduções significativas de 6 mmHg na SBP de meninas adolescentes com pré-hipertensão. O mesmo ocorreu no estudo de Kim *et al.* (2019) que encontraram reduções significativas de 6,7 mmHg somente para a SBP de adolescentes obesas. Nestas duas intervenções, a DBP não foi alterada após as 12 semanas (KIM; SON; HEADID III; PEKAS *et al.*, 2020).

Lembrando que o exercício aeróbico é o mais indicado para a população hipertensa e diversas intervenções foram realizadas com este tipo de exercício, sendo algumas realizadas com crianças e adolescentes. Em 1998, no estudo de Ewart *et al.*, foi realizada uma intervenção com exercício aeróbico e, após 18 semanas, as meninas adolescentes que participaram do grupo exercício reduziram significativamente a SBP em 6 mmHg, enquanto a DBP não foi alterada (EWART; YOUNG; HAGBERG, 1998). Em outra intervenção de 18 semanas, Knox *et al.* (2012), prescrevendo exercício aeróbico de caminhada realizado 2 vezes por semana, não encontraram reduções significativas tanto na DBP quanto na SBP (KNOX; BAKER; DAVIES; REES *et al.*, 2012). Em uma curta intervenção com crianças e adolescentes com sobrepeso que realizaram exercício aeróbico, Kelly *et al.* (2004) também não encontraram reduções significativas para estas variáveis após uma intervenção de 8 semanas, com o exercício em cicloergômetro sendo realizado quatro vezes por semana (KELLY; WETZSTEON; KAISER; STEINBERGER *et al.*, 2004).

1.3.5. Colesterol

O Colesterol, do ponto de vista fisiológico e clínico, é um dos lípides mais importantes, pois é precursor de hormônios esteroides, dos ácidos biliares e da vitamina D, constitui membranas celulares e atua na ativação de enzimas. As lipoproteínas são responsáveis pelo transporte dos lípides (geralmente hidrofóbicos), pois permitem a sua solubilização, no meio aquoso. Duas lipoproteínas ricas em colesterol, que são classificadas de acordo com as suas densidades, são as lipoproteínas de baixa densidade (LDL) e de alta densidade (HDL) (FALUDI AA, 2017).

O início do processo aterosclerótico tem relação com a deposição de LDL na parede arterial, ou seja, uma alteração indesejada de níveis de LDL está relacionada à disfunção endotelial, assim como a rigidez arterial. Em contrapartida, o HDL é capaz de remover o colesterol das artérias e levá-lo para o fígado, pois esta lipoproteína realiza este transporte reverso e tem atividade anti-inflamatória, antiagregante, vaso-relaxante e antioxidantes que previnem o acúmulo de colesterol na parede arterial (IBORRA; RIBEIRO; NEVES; CHARF *et al*., 2008). Sendo assim, o HDL é fortemente e inversamente associado à eventos cardiovasculares enquanto o LDL e o Colesterol total são diretamente associados (EMERGING RISK FACTORS; DI ANGELANTONIO; SARWAR; PERRY *et al*.; MORTENSEN; NORDESTGAARD, 2020). Há evidências de que os altos níveis de colesterol na infância e adolescência permanecem em níveis elevados na vida adulta. Atualmente, nos Estados Unidos, cerca de 7% das crianças e adolescentes de 6 a 19 anos apresentam elevados níveis de Colesterol Total (TSAO; ADAY; ALMARZOOQ; ALONSO *et al*., 2022). Ou seja, o manejo dos lípides na população pediátrica é fundamental para prevenir futuras doenças cardiovasculares na vida adulta (DOBASHI, 2022).

O exercício físico é uma importante estratégia não farmacológica e de baixo custo financeiro para melhorar os níveis de colesterol no sangue, aumentando os níveis de HDL ou reduzindo os níveis de LDL e Colesterol total. Apesar dos efeitos do exercício físico no HDL não estarem claros, em princípio eles estão relacionados à capacidade antioxidante e anti-inflamatória desta lipoproteína, ocorrendo principalmente com o exercício aeróbico (RUIZ-RAMIE; BARBER; SARZYNSKI, 2019). Enquanto isso, o exercício físico pode não afetar substancialmente o LDL (IBORRA; RIBEIRO; NEVES; CHARF *et al*., 2008). Segundo evidências da literatura, é importante ressaltar que os efeitos do exercício físico sobre o colesterol são dependentes da intensidade e duração das sessões de treinamento (COOK; KAVEY, 2011).

1.3.5.1. Efeitos de intervenções de exercício físico nas concentrações de Colesterol

Buchan *et al*. (2013) investigaram os efeitos do HIIT sobre a lipemia de adolescentes saudáveis durante sete semanas de intervenção (3 vezes por semana) e identificaram reduções significativas no LDL. Enquanto isso, não foram encontradas diferenças significativas para o HDL (BUCHAN; OLLIS; YOUNG; COOPER *et al.*, 2013). O mesmo resultado foi encontrado no estudo de Chuensiri *et al.* (2017), que analisou os efeitos do HIIT e Supra-HIIT em cicloergômetro em meninos obesos e estabeleceu reduções significativas de 24 mg.dL^{-1} no LDL. Também não foram encontradas diferenças significativas para o HDL. Quando analisado o exercício de pular corda, Kim *et al.* (2007) não encontraram difereças significativas para CT, HDL e LDL após seis semanas de intervenção realizado cinco vezes por semana.

O tipo de exercício mais recomendado para tratar alterações no CT é o aeróbico, sendo assim, no estudo de Kelly *et al.* (2004) foram avaliados crianças e adolescentes com sobrepeso que foram expostos a uma intervenção de exercício aeróbio em cicloergômetro, realizado quatro vezes na semana, durante oito semanas. Foi encontrado um aumento significativo de aproximadamente 4 mg.dL^{-1} somente para o HDL, enquanto LDL e CT não foram alterados (REILLY; JACKSON; MONTGOMERY; KELLY *et al.*, 2004). Karacabey (2009) analisou o efeito do exercício aeróbico sobre a lipemia, mas com a caminhada/corrida leve, em meninos obesos, três vezes na semana, durante 12 semanas, encontrando reduções significativas de 20,3 mg.dL^{-1} no LDL e aumentos significativos de 7,1 mg.dL^{-1} no HDL (KARACABEY, 2009).

Quando avaliamos os efeitos do treinamento de força, Yu *et al.* (2016) realizaram uma intervenção de 10 semanas, com o exercício sendo realizado duas vezes por semana, com adolescentes não-obesos. Foram encontradas reduções significativas de aproximadamente 7 mg.dL^{-1} no LDL, enquanto não foram encontradas diferenças significativas para o HDL e CT (YU; MCMANUS; SO; CHOOK *et al.*, 2016). Quando os efeitos do treinamento combinado (força + aeróbio e força + HIIT) sobre a lipemia foram analisados, Faria *et al.* (2020) não estabeleceram diferenças significativas no HDL, LDL e CT após 12 semanas de treinamento, realizado duas vezes por semana (FARIA; MENDONCA; SANTOS; KENNEDY *et al.*, 2020). Em contrapartida, Zehsaz *et al.* (2016) encontraram melhoras significativas no CT, HL e LDL de crianças após uma intervenção de treinamento combinado realizado durante 16 semanas (ZEHSAZ; FARHANGI; GHAHRAMANI, 2017).

Em recente metanálise, Chen *et al.* (2021) analisaram os efeitos de intervenções de exercício físico aeróbico e de força sobre LDL, HDL e CT de crianças com sobrepeso ou obesas. Foram encontradas reduções significativas somente para LDL e CT para ambos os tipos de exercício comparados aos grupos controle. Ou seja, o exercício físico aeróbico e de força não foram significativamente associados a melhoras no HDL de crianças. Os autores especulam que as intervenções não atingiram o limiar de intensidade e de duração da sessão necessários para alterar o HDL (CHEN; LIN; LIN; XU *et al*., 2021). O mesmo ocorreu no estudo de Busnatu *et al*. (2022), que avaliou diferentes intervenções e seus efeitos sobre o HDL e LDL de crianças com sobrepeso, não encontrando diferenças significativas para o HDL, enquanto foram encontradas reduções significativas para o LDL (BUSNATU; SERBANOIU; LACRARU; ANDREI *et al*., 2022). Em contrapartida, recente metanálise de Kelley *et al*. (2022) com crianças e adolescentes obesos, encontrou um aumento signiicativo de 12,2% no HDL e LDL, contudo, somente em resposta ao exercício aeróbico (KELLEY; KELLEY; PATE, 2022).

1.3.6. Razão cintura-estatura

A razão cintura-estatura (WtHR) é uma forma simples, rápida e de baixo custo financeiro para realizar a triagem de diferentes populações. O cálculo utiliza a circunferência da cintura como uma medida da adiposidade abdominal e ajusta para o tamanho do indivíduo dividindo pela sua estatura. Ou seja, quanto maior for este índice, maiores são os riscos à saúde cardiometabólica (MADRUGA; MORAES SILVA; SCHERER ADAMI, 2016).

Diversos autores consideram a WtHR uma forma mais de sensível para avaliar os indivíduos do que o IMC, além de ser mais prático de avaliar, permite que os mesmos valores limites sejam utilizados tanto para crianças quanto para adolescentes e adultos (ASHWELL; GUNN; GIBSON, 2012). Além disso, a WtHR pode ser considerada uma preditora de CMRF e consequentemente de doença cardiovascular. A identificação de alterações nesses valores está relacionada à saúde cardiometabólica (HARA; SAITOU; IWATA; OKADA *et al*., 2002; KAHN; IMPERATORE; CHENG, 2005; SAVVA; TORNARITIS; SAVVA; KOURIDES *et al*., 2000). O exercício físico pode afetar os valores de WtHR, mesmo quando as intervenções nutricionais não são realizadas, o que possivelmente afetaria mais ainda esses valores. Se houver uma intervenção nutricional combinada ao exercício, existe uma probabilidade maior de maximizar os resultados de emagrecimento com reduções significativas da circunferência da cintura. Sendo assim, torna-se interessante avaliar intervenções somente com exercício físico, que não incentivaram ou realizaram modificações nos hábitos alimentares para identificar o efeito do exercício de forma isolada na WtHR.

1.3.6.1. Efeitos de intervenções de exercício físico na Razão Cintura-estatura

Wong *et al*. (2018) analisaram os efeitos do exercício físico combinado realizado três vezes por semana durante 12 semanas sobre a WtHR de adolescentes obesas. Neste estudo, foram encontradas reduções significativas de 0,03 na WtHR concomitantemente com reduções na circunferência da cintura, da massa corporal e do percentual de gordura. O programa de exercício demonstrou ser eficaz para melhorar significativamente as variáveis supracitadas, melhorando a saúde cardiometabólica das adolesentes (WONG; SANCHEZ-GONZALEZ; SON; KWAK *et al*., 2018).

Delgado-Floody *et al*. (2018) realizaram uma intervenção de HIIT por 28 semanas, realizada duas vezes por semana em meninas e meninos com sobrepeso e obesidade. Após este o período de intervenção, foram encontradas reduções de 0,02 na WtHR somente no grupo intervenção de meninas obesas, apesar do percentual de gordura ter tido reduções significativas em todos os quatro grupos de intervenção (meninos com sobrepeso, meninos com obesidade, meninas com sobrepeso e meninas com obesidade). Este resultado demonstra que a intervenção com HIIT foi mais efetiva para meninas com obesas (DELGADO-FLOODY; ESPINOZA-SILVA; GARCIA-PINILLOS; LATORRE-ROMAN, 2018). Uma redução significativa semelhante ocorreu no estudo de Baghersalimi *et al*. (2019) que realizou uma intervenção de HIIT realizado três vezes por semana durante oito semanas com meninas obesas. No grupo que realizou exercício físico, foi encontrada uma redução significativa de 0,03 na WtHR (BAGHERSALIMI; FATHI; KAZEMI, 2019). Em contrapartida, Martinez-Vizcaíno *et al*. (2022) realizou uma intervenção de 8 meses, com jogos tradicionais realizados em alta intensidade em meninos e meninas. Após o período de intervenção, não foram encontradas diferenças significativas na WtHR (MARTINEZ-VIZCAINO; SORIANO-CANO; GARRIDO-MIGUEL; CAVERO-REDONDO *et al*., 2022). Comparando o efeito do exercício aeróbico e HIIT, Buchan *et al*. (2011) realizaram uma intervenção de oito semanas, realizado três vezes por semana em adolescentes de ambos os sexos e não encontraram diferenças significativas na WtHR após as intervenções (BUCHAN; OLLIS; THOMAS; BUCHANAN *et al*., 2011).

2. ARTIGO

SYSTEMATIC REVIEW AND META-ANALYSIS ARTICLE

Supervised and structured physical exercise effects on cardiometabolic health of children and adolescents: A systematic review and meta-analysis

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Declarations

Conflicts of Interest: All authors declare no potential conflict of interest related to this article.

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Authors' contributions: NCB and GSC conceived the idea and design of the article. CDFP, JBM, NCB and SVM performed the literature search, data acquisition, analysis and/or interpretation. CDFP, GSC, JBM, NCB and SVM drafted and/or critically reviewed the work. All authors read and approved the final version.

ABSTRACT

Background and objective: This systematic review and meta-analysis aimed to analyze the effects of supervised and structured physical exercise on the cardiometabolic risk factors (CMRF) of children and adolescents. **Methods:** PubMed, Cochrane Library, Embase and Scopus platforms databases were searched in June of 2022. Three independent investigators selected articles that compared a supervised and structured physical exercise intervention with a control group of children and adolescents aged 6-17 years, and that evaluated the following variables: flow-mediated dilation (FMD), brachial-ankle pulse wave velocity (baPWV), systolic and diastolic blood pressure (SBP and DBP), total cholesterol (TC), high- and low-density lipoproteins (HDL and LDL) and the waist-to-height ratio (WtHR). Random effect was used, and the effect size (ES) was calculated by using the standardized mean difference with a 95% confidence interval. **Results:** 51 studies were included, with a total of 6190 participants. Supervised and structured physical exercise interventions significantly reduced baPWV (0.72 m/s), SBP (2.08 mmHg), LDL (8.17 mg.dL^{-1}) and WtHR (0.01), and increased HDL (2.61 mg.dL^{-1}). In the general analysis, no significant improvements were found for TC and DBP. When analyzing the sexes separately, SBP showed a significant reduction in the categories of both sexes and only girls (3.12 and 2.17 mmHg, respectively). In contrast, for HDL, significant increases were found when the categories of both sexes and only boys were analyzed (2.01 and 5 mg.dL^{-1}, respectively), and for LDL concentrations, a significant reduction was found in the for only boys (15.10 mg.dL^{-1}). When the types of exercise were analyzed separately, significant reductions were found for the aerobic exercise on SBP (3.11 mmHg), and aerobic and HIIT for LDL (21.33 and 15.24 mg.dL^{-1}). Chronological age and BMI showed moderated effects on SBP, while BMI showed moderated effects on HDL. Furthermore, BMI and intervention duration showed moderate effects on WthR. **Conclusion:** Supervised and structured physical exercise interventions showed positive effects on CMRF of children and adolescents, especially the aerobic and HIIT exercises. In addition, BMI, chronological age, and the duration of the intervention are variables that presented moderating positive effects on CMRF. PROSPERO register number: CRD42022344094.

Keywords: Cardiometabolic health; arterial stiffness; endothelial function; children.

Key Points

- The cardiometabolic health of children and adolescents can be improved through physical exercise interventions;
- Aerobic and HIIT exercises have more beneficial results compared to other types of exercise;
- The greater the chronological age and BMI, the greater the effect of physical exercise in reducing SBP and the greater the BMI or the shorter the duration, the greater the effect of physical exercise in reducing WtHR.

INTRODUCTION

The cardiometabolic health of children and adolescents is receiving increasing attention due to alterations in cardiometabolic risk factors (CMRF) that usually occur in adulthood but are currently occurring earlier in childhood and adolescence [1-5]. Therefore, it is necessary to identify whether children and adolescents are already being exposed to CMRF and promote strategies to improve this population's health indicators to prevent the development of chronic diseases and cardiovascular events in the future [4]. This population is being affected by these risk factors at an earlier age, and this is due to environmental, genetic, and behavioral factors, which will result in increased levels of overweight and obesity status, an increased sedentary lifestyle, and poor eating habits [6]. According to the World Health Organization, it was estimated that in 2016, more than 340 millions of children and adolescents aged 5–19 years were overweight or obese [7], and with decreasing trends in cardiorespiratory fitness, which is related to a sedentary lifestyle, the health of this population and these numbers tend to worsen [8].

Among the most commonly used health parameters to identify cardiometabolic risks, which have shown abnormal values in the pediatric population, we can mention systolic and diastolic blood pressure (SBP and DBP, respectively), concentrations of total cholesterol (TC), and high- and low-density lipoproteins (HDL and LDL, respectively), fasting blood glucose, cardiorespiratory fitness, body mass index (BMI), and waist-to-height ratio (WtHR)[3, 9, 10]. Additionally, predictors of cardiovascular events, such as endothelial function and arterial stiffness, which can be assessed through flow-mediated dilation (FMD) and pulse wave velocity (PWV), have been considered important markers of vascular function [11-14] and consequently, predictors of cardiometabolic health [13,14]. It has been reported that for every 1% reduction in FMD or 1 m/s increase in PWV, the risk of future cardiovascular disease (CVD) or mortality increased by 13% and 15%, respectively [15, 16].

These health markers are essential for detecting endothelial dysfunction, which, in addition to being related to the onset of CVD, are considered the first step towards atherosclerosis, which can be defined as a chronic inflammatory and degenerative process that affects the vessels (lipids, inflammatory cells, and fibrous element accumulation) and begins in childhood and adolescence [17, 18]. That is, since these changes already appear at this early stage of life, in addition to changes in the more traditional health parameters, it becomes necessary to identify whether children and adolescents are already exposed to these risks and promote strategies to improve the health parameters of this population to prevent the development of chronic diseases and cardiovascular events in the future [4].

One of the available strategies to improve the CMRF is physical exercise, which, in addition to being essential for the healthy growth and development of children and adolescents, improves cardiometabolic health levels. However, the effects of physical exercise on endothelial function and arterial stiffness are still less explored, especially in the pediatric population [19, 20]. The most recent physical activity guide, published by the World Health Organization, recommends that children/adolescents aged 6–17 years should engage in an average of 60 min of moderate-to-vigorous physical activity daily to maintain or improve cardiometabolic health, including aerobic, muscle, and bone strengthening exercises [21]. Physical exercise interventions with multidisciplinary approaches, including nutritional interventions and lifestyle changes are considered effective in improving health and CMRF [22-24]. However, it is important to understand the role of physical exercise alone, as in these multidisciplinary studies, diet and lifestyle changes can be confounding factors in interpreting of the results.

Several beneficial effects of physical exercise on traditional CMRF have been reported; however, it is still unclear which types of exercise are most effective in improving cardiometabolic health. In addition, there is a lack of information on the moderating factors of the exercise effects, such as sex, chronological age, BMI, and training principles (weekly frequency, session duration, and follow-up duration of the interventions). It is also important to investigate the effects of physical exercise on cardiovascular health, such as endothelial function and arterial stiffness, as there are few studies that have analyzed these variables in pediatric population.

Therefore, this systematic review and meta-analysis aimed to analyze the effects of supervised and structured physical exercise on the cardiometabolic health of children and adolescents. Furthermore, this study aimed to investigate the effects of different types of exercise, sex, BMI, weekly frequency, duration of sessions, and follow-up duration of the interventions on cardiometabolic health.

MATERIALS AND METHODS

This systematic review was conducted using a predetermined protocol established according to the recommendations of the Cochrane Handbook [25] and the protocol was registered at the international prospective register of systematic reviews (PROSPERO number registration: CRD42022344094, available in https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022344094). The results are reported in accordance with the preferred reporting items for systematic reviews and meta-analyses statement (Supplementary Material 1, available online) [26].

Search strategy

The retrieval date of the electronic databases was searched until June 2022, with no restriction on the year of publication, and the following electronic databases were acessed: MEDLINE (accessed by PubMed), Cochrane Library, Embase, and Scopus. The search terms included "children", "adolescent", "exercise", "cholesterol", "HDL", "LDL", "systolic blood pressure", "diastolic blood pressure", "waist-to-height ratio", "flow-mediated dilation", "arterial stiffness" and related entry terms. The search included no time or language restrictions and only eligible full texts in English, Portuguese or Spanish were considered for this review.

Study Eligibility

The included studies were those that met the following eligibility criteria: Clinical trials (randomized or not) of supervised and structured exercise; with a control group, that didn't go through any physical exercise intervention; participants aged between 6 to 17 years old with no reported illness such as diabetes, cardiovascular, mental or orthopedic disease, or any other that restricted them from physical exercise; studies that evaluated FMD, baPWV, SBP, DBP, TC, HDL, LDL and WtHR and reported means and respective dispersion values of these outcomes at baseline and after the proposed intervention. All types of supervised and structured exercise, irrespective of intensity, frequency, or session duration were considered eligible.

The exclusion criteria were as follows: (1) studies that did not provide information regarding associations between the intervention and chosen outcomes, (2) control group performed an intervention, [27] studies that did not present the structure of the exercise intervention, (4) duplicate publications, and (5) editorials, animal studies, observational studies, review articles, case reports, and case series.

Study selection and Data Extraction

The retrieved studies were exported to EndNote^{TM} 20 to screen for duplicates. Three investigators simultaneously and independently performed the study selection and data extraction (C.P., J.M. and N.B.). Of these researchers, two extracted half of the data (C.P. and J.M.), and one extracted all of the data (N.B.) for checking purposes. The reviewers were not blinded to the authors, institutions, or manuscript journals. Abstracts that did not provide sufficient information regarding the inclusion and exclusion criteria were retrieved for the full-text evaluation. If needed, the corresponding author of the article was contacted to obtain data that were not available in the article. All disagreements were resolved through consensus. A standardized document was used for data extraction using spreadsheet editor Excel version 16.54 (Microsoft, Washington, DC, USA). The outcomes of interest extracted were FMD (%), baPWV (m/s), SBP and DBP (mmHg), TC, HDL, and LDL (mg.dL^{-1}), and WtHR. If the measurement unit used was another, such as mmol/L or cm/s, unit conversion was performed.

Quality assessment of the studies

Two independent reviewers (N.B and S.) independently assessed the methodological quality of the included studies. For this purpose, the tool for the assessment of study quality and reporting in exercise training studies, proposed by Smart et al. (2015). The TESTEX scale uses 12 criteria with some criteria having more than one possible point, for a maximum score of 15 points (5 points for study quality and 10 points for reporting). As such, the assessment included the following items for study quality: (1) specified eligibility criteria; (2) specified randomization; (3) allocation concealment, that is, patients are unaware of which group they would be allocated; (4) similar groups at baseline, with no significant difference after randomization; (5) blinding of assessor; and the following items for study reporting; (6) outcome measures evaluated in at least 85% of patients; (7) intention-to-treat analysis; (8) reporting of statistical comparison between groups; (9) point measures and measures of variability for all reported outcomes; (10) monitoring of activities in the control group; (11) whether relative exercise intensity remained constant; (l2) relative volume and energy expenditure of the exercise. The quality score of the papers were based on terciles, where 0 to 5 points were considered low quality, 6 to 10 points were considered medium quality, and 11 to 15 points were considered high quality [28].

Data analysis

The pooled effect estimates were computed from the change scores between the baseline and the end of intervention, their SDs, and the number of participants. Data from intention-to-treat analyses were entered whenever available in the included studies. The authors were contacted through e-mails for unreported data, and if no answer returned or if the data requested were not available, the studies were excluded.

The results are presented as standardized mean differences (a measure of effect, recommended to be used when the study report efficacy of an intervention on continuous measurements, especially in cases of different measurement methods) and calculations were performed using random effects models. Statistical heterogeneity of treatment effects among studies was evaluated by Cochran Q test and the I^2 inconsistency test; it was considered that values >50% indicated high heterogeneity [25]. In addition, sensitivity analyses were conducted to investigate the possible influence of randomization process in the included studies, the progression in training variables. In addition, sensitivity analyses were conducted to investigate the possible effect of sex (boys, girls or both sexes) and types of the exercise intervention (aerobic, combined, high-intensity interval training [HIIT], sport and strength) in the observed adaptations. Also, meta-regressions were performed to investigate possible moderators of the training effect on the target outcomes: chronological age (years), BMI (kg/m^2), weekly training frequency (number of sessions per week), follow-up duration (weeks), and session duration (minutes).

Forest plots were generated to present the pooled effects and standardized mean differences with 95% confidence intervals (CIs). Values of $P < .05$ were considered statistically significant. All analyses were performed using Software OpenMeta Analyst, version 10.10 [29].

RESULTS

Studies Selection

The database search yielded a total of 11,198 citations. After adjusting for duplicates, 9,973 studies remained in total. Of these, 9,787 were discarded after reviewing the titles and abstracts because they did not meet the eligibility criteria. After full-text reading of the remaining 186 articles, 136 were deleted. After finalizing the selection of studies, 51 articles were included in the analyses (Figure 1). Of these, three trials were included twice because they met the eligibility criteria for two comparison [30-32] and one trial was included four times because it met the eligibility criteria for four comparison groups [33]. No additional studies were identified after checking the references of the included papers. No relevant unpublished studies were included in the study.

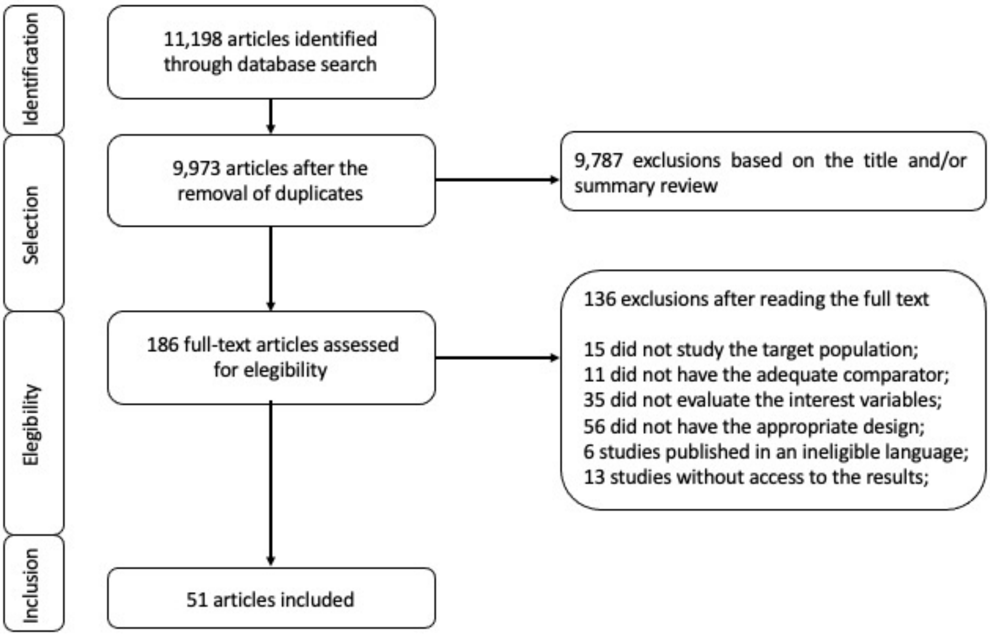


Figure 1 - Flowchart of the study design

Studies Characteristics

In total, 6,190 participants were included in the meta-analysis. Among these, 31% of the studies analyzed only boys, 27% analyzed only girls and 49% analyzed both sexes. Three studies analyzed only girls and only boys [31-34]. The characteristics of the 69 included studies are available in Supplementary Material 2 (available online).

Methodological Quality of the Included Trials

The study quality of the 51 included studies, obtained through the TEXTEX scale, is shown on Table 1.

Table 1 - Study quality

	Study quality					Study reporting							
Studies	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**TESTEX score**
Baghersalimi et al. 2019	1	1	0	1	0	1	0	2	1	0	1	1	9
Bharath et al. 2018	1	1	0	1	0	1	0	2	0	0	1	1	8
Benson et al. 2008	1	1	0	1	1	3	1	2	1	1	1	1	14
Brinco et al. 2021	1	0	0	1	0	1	0	2	1	1	1	1	9
Buchan et al. 2011	0	0	0	1	0	1	0	2	0	0	1	1	6
Buchan et al. 2013	0	0	0	1	0	2	0	2	1	0	1	1	8
Chuensiri et al. 2017	1	1	0	1	0	0	0	2	1	1	0	1	8

Continued…	Study quality					Study reporting							
Studies	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**TESTEX score**
Cvetkovic et al. 2018	1	0	0	1	1	2	0	2	1	0	0	1	9
Davis et al. 2019	1	1	1	1	0	2	1	2	1	1	0	1	12
Delgado-Floody et al. 2018	1	0	0	1	0	1	0	2	0	0	0	1	6
Eliakim et al. 2000	0	0	0	1	1	1	0	2	0	0	0	1	6
Ewart et al. 1998	1	0	0	0	1	1	0	2	1	0	0	0	6
Faria et al. 2020	1	1	0	1	1	2	1	2	1	0	1	1	12
Farpour-Lambert et al. 2009	1	1	1	1	1	2	1	2	1	1	0	1	13
Fripp & Hodgson 1987	0	0	0	1	0	1	0	2	0	0	1	1	6
García-Hermoso et al. 2020	1	1	0	1	1	2	1	2	1	0	0	0	10
Giannaki et al. 2016	0	1	0	1	0	3	0	2	0	0	1	1	9
Jeon et al. 2013	1	0	0	1	0	1	0	2	0	0	1	1	7
Karacabay 2009	1	0	0	1	0	1	0	2	0	0	0	1	6
Kelly et al. 2004	0	0	1	1	0	1	0	2	0	0	1	1	7
Kim et al. 2007	0	0	1	1	0	1	0	2	0	0	1	1	7
Kim et al. 2020	1	0	0	1	0	1	0	2	0	1	1	1	8
Knox et al. 2012	0	0	0	1	0	1	0	2	1	1	0	0	6
Larsen et al. 2018	0	1	0	0	0	1	0	2	0	0	0	1	5
Lee et al. 2010	0	0	0	1	0	1	0	2	0	0	0	1	5
Martínez-Vizcaíno et al. 2008	1	1	0	1	0	2	1	1	1	0	0	1	9
Martínez-Vizcaíno et al. 2014	1	1	1	1	0	1	1	1	1	1	0	1	10
Martínez-Vizcaíno et al. 2022	0	0	1	1	0	3	1	1	1	1	1	1	11
McMurray et al. 2002	1	0	0	0	0	1	0	1	0	0	0	1	4
Meng et al. 2022	1	1	1	1	0	2	0	1	0	0	1	1	9
Norris et al. 1992	0	0	0	1	0	1	0	1	0	0	0	0	3
Oliveira et al. 2021	0	1	1	1	0	3	0	1	0	0	1	1	9
Pahoo et al. 2020	0	0	0	1	0	2	0	1	0	0	1	1	6
Patsopoulou et al. 2017	0	0	1	1	0	1	1	1	1	0	0	0	6
Racil et al. 2013	0	0	0	1	0	1	0	1	0	0	1	1	5
Resaland et al. 2011	0	0	0	1	0	2	0	1	1	0	0	0	5
Resaland et al. 2017	0	0	0	0	0	1	0	1	1	0	0	0	3
Rosenkraz et al. 2012	0	1	0	1	0	1	0	1	1	0	1	1	7
Salcedo Aguilar et al. 2010	0	0	1	1	0	2	1	1	1	0	1	1	9
Seo et al. 2012	1	0	0	1	0	1	0	1	0	0	1	1	6
Son et al. 2017	1	0	1	1	0	1	0	1	0	1	1	1	8
Stoedefalke et al. 2000	0	0	0	1	0	1	0	1	0	0	0	1	4
Sung et al. 2018	1	0	1	1	0	1	1	1	0	1	1	1	9

Continued…	Study quality					Study reporting							
Studies	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**TESTEX score**
Tsang et al. 2009	1	1	0	1	1	3	0	1	1	1	0	0	10
van Biljon et al. 2018	0	0	0	1	0	1	0	1	0	0	0	1	4
Vasconcellos et al. 2015	1	1	1	1	1	1	0	1	1	0	1	1	10
Wong et al. 2008	1	0	0	1	0	2	0	1	0	0	1	1	7
Wong et al. 2018	1	0	1	1	0	1	0	1	0	1	1	1	8
Yu et al. 2016	0	1	1	1	1	2	0	1	0	0	1	1	9
Zehsaz et al. 2016	1	0	0	1	0	1	0	1	0	1	1	1	7
Zorba et al. 2011	0	0	0	1	0	1	0	1	0	0	0	1	4
						Median TESTEX score=							7.52

TESTEX scale items: 1 – Eligibility criteria specified (1 point); 2 – Randomization specified (1 point); 3 – Allocation concealment (1 point); 4 - Groups similar at baseline (1 point); 5 - Blinding of assessor (for at least one key outcome – 1 point); 6 - Outcome measures assessed in 85% of patients (3 points); 7 - Intention-to-treat analysis (1 point); 8 - Between-group statistical comparisons reported (2 points); 9 - Point measures and measures of variability for all reported outcome measures (1 point); 10 - Activity monitoring in control groups (1 point); 11 - Relative exercise intensity remained constant (1 point); 12 - Exercise volume and energy expenditure. Total out of a possible: 15 points.

Meta-Analysis of FMD

Data concerning FMD were available from four studies that compared physical exercise intervention groups with control groups, with a total of 124 participants (Figure 2). No significant differences were found for FMD (ES: 0.384; 95% CI, –0.132 to 0.900; P= 0.145; I2: 49%, Table 2).

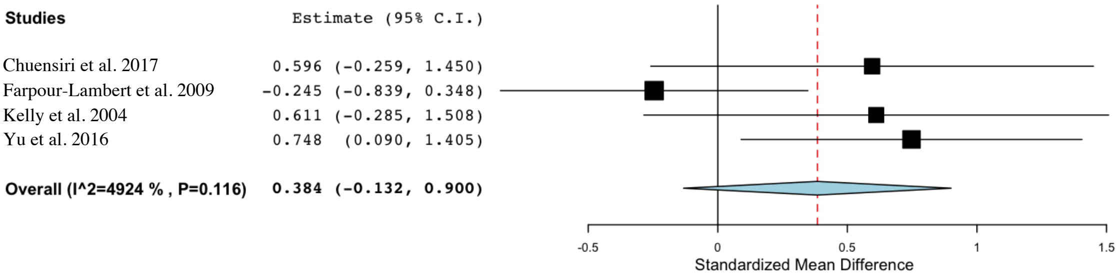


Figure 2 - Standardized mean differences in total flow dilation mediated (%) promoted by exercise and control (no intervention). CI indicates confidence interval; Std diff, standardized difference.

Furthermore, subgroup analysis suggested that in studies that analyzed both sexes (three studies), FMD was not changed after physical exercise interventions (ES: 0.338; 95% CI, –0.336 to 1.011; P= 0.326; I^2: 63%, Table 2). Only boy's category did not have enough studies to be analyzed separately and there was no study for the only girl's category, therefore, there was no subgroup analysis for these categories. When we analyzed the type of exercise, HIIT, aerobic, combined, and strength did not have enough studies to be analyzed separately and there was no study for the combined category, therefore, there was no subgroup analysis for these categories.

Table 2. Summary of the results of meta-analyses and sensitivity analyses.

		Meta-analysis			**Heterogeneity**
Analyses	**Number of comparisons**	**Effect size**	**95% IC**	**p value**	**I^2**
FMD					
General analyses	4	0.384	-0.132 to 0.900	.145	49.243
Both sexes	3	0.338	-0.336 to 1.011	.326	63.494
Only boys	-	-	-	-	-
Only girls	-	-	-	-	-
baPWV					
General analyses	6	-0.487	-0.780 to -0.193	.001*	0
Both sexes	-	-	-	-	-
Only boys	-	-	-	-	-
Only girls	4	-0.544	-0.909 to -0.180	.003*	6.085
Aerobic	-	-	-	-	-
Combined	3	-0.422	-0.850 to 0.006	.054	3.402
HIIT	-	-	-	-	-
Sports	2	-0.531	-1.154 to 0.093	.095	43.874
Strength	-	-	-	-	-
SBP					
General analyses	44	-0.200	-0.330 to -0.069	.003*	76.483
Both sexes	21	-0.277	-0.368 to -0.185	<.001*	
Only boys	13	-0.025	-0.236 to 0.186	.818	58.498
Only girls	10	-0.373	-0.732 to -0.015	.041*	88.693
Aerobic	3	-0.284	-0.533 to -0.036	.025*	0
Combined	5	-0.970	-2.186 to 0.246	.118	90.595

Continued…		**Meta-analysis**			**Heterogeneity**
Analyses	**Number of comparisons**	**Effect size**	**95% IC**	**p value**	**I^2**
HIIT	11	-0.077	-0.276 to 0.121	.446	0
Sports	22	-0.143	-0.301 to 0.015	.076	81.713
Strength	3	-0.219	-0.652 to 0.215	.323	20.345
DBP					
General analyses	42	-0.092	-0.210 to 0.027	.129	68.727
Both sexes	19	-0.242	-0.409 to -0.075	.004*	62.605
Only boys	13	0.131	-0.007 to 0.270	.063	17.041
Only girls	10	0.054	-0.112 to 0.220	.526	45.189
Aerobic	3	-0.158	-0.665 to 0.349	.541	68.119
Combined	5	-0.181	-0.791 to 0.429	.561	68.923
HIIT	11	0.060	-0.139 to 0.259	.554	0
Sports	19	-0.154	-0.327 to 0.020	.083	81.506
Strength	3	-0.062	-0.446 to 0.322	.752	0
TC					
General analyses	31	-0.146	-0.301 to 0.009	.064	74.175
Both sexes	15	-0.206	-0.607 to 0.195	.314	85.733
Only boys	10	-0.028	-0.134 to 0.078	.607	0
Only girls	5	-0.070	-0.204 to 0.064	.304	19.388
Aerobic	5	-0.463	-1.450 to 0.523	.357	92.349
Combined	3	0.058	-0.320 to 0.436	.763	0
HIIT	5	-0.274	-0.595 to 0.048	.095	0
Sports	13	-0.017	-0.092 to 0.058	.655	0
Strength	3	0.001	-0.340 to 0.342	.996	0
HDL					
General analyses	29	0.217	0.051 to 0.383	.010*	54.151
Both sexes	15	0.204	0.053 to 0.356	.008*	7.383
Only boys	9	0.383	0.013 to 0.756	.042*	64.861
Only girls	3	-0.401	-1.259 to 0.457	.360	85.56
Aerobic	6	0.467	-0.033 to 0.968	.067	75.197
Combined	4	0.213	-0.142 to 0.568	.240	0
HIIT	6	0.055	-0.607 to 0.717	.871	76.913
Sports	9	0.180	-0.011 to 0.371	.064	29.564
Strength	3	0.370	-0.219 to 0.960	.218	61.936
LDL					
General analyses	29	-0.338	-0.550 to -0.125	.002*	80.893
Both sexes	15	-0.211	-0.596 to 0.174	.282	84.075
Only boys	10	-0.599	-1.011 to -0.187	.004*	82.976

Continued…		Meta-analysis			Heterogeneity
Analyses	**Number of comparisons**	**Effect size**	**95% IC**	**p value**	**I²**
Only girls	4	-0.092	-0.237 to 0.052	.211	0
Aerobic	6	-1.056	-1.870 to -0.242	.011*	89.342
Combined	3	-0.027	-0.405 to 0.350	.887	0
HIIT	5	-0.490	-0.908 to -0.072	.022*	29.933
Sports	11	-0.045	-0.141 to 0.052	.365	0
Strength	3	-0.234	-0.838 to 0.371	.449	64.433
WtHR					
General analyses	10	-0.277	-0.552 to -0.002	.048*	57.108
Both sexes	2	-0.165	-0.673 to 0.343	.524	0
Only boys	3	-0.056	-0.306 to 0.194	.659	0
Only girls	5	-0.513	-1.087 to 0.061	.080	78.239
Aerobic	-	-	-	-	-
Combined	-	-	-	-	-
HIIT	6	-0.252	-0.531 to 0.027	.077	0
Sports	3	-0.003	-0.195 to 0.190	.977	0
Strength	-	-	-	-	-

Abbreviations: FMD: Flow-mediated dilation; baPWV: Brachial-ankle pulse wave velocity; HIIT: High-intensity interval training; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TC: Total cholesterol; HDL: High density lipoproteins; LDL: Low density lipoprotein; WtHR: Waist-to-height ratio. * Indicates significative difference in comparison to control group ($p<0.05$).

Meta-Analysis of baPWV

Data concerning baPWV were available from six studies that compared physical exercise intervention groups with control groups, with a total of 186 participants (Figure 3). Exercise was associated with a reduction in baPWV compared with no intervention (ES: -0.487; 95% CI, –0.780 to -0.193; P= 0.001; I2: 0%, Table 2). Exercise led to a reduction in baPWV levels of approximately 0.72 m/s in the intervention groups compared to the control group, who did not exercise or undergo any intervention.

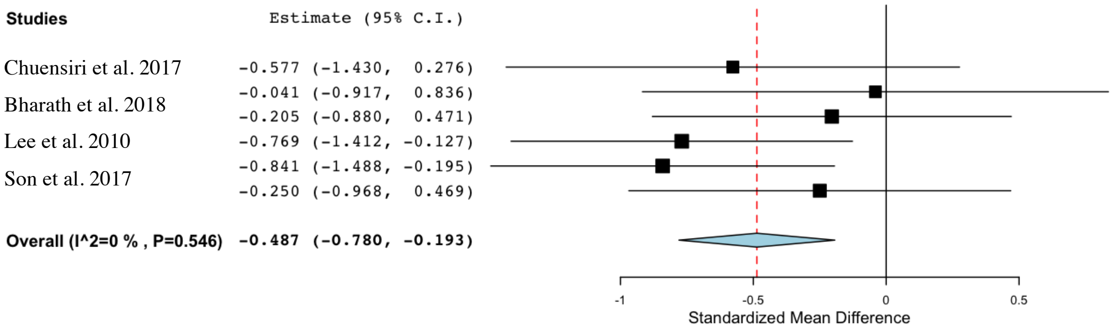


Figure 3 - Standardized mean differences in total brachial-ankle pulse wave velocity (m/s) promoted by exercise and control (no intervention). CI indicates confidence interval; Std diff, standardized difference.

Furthermore, subgroup analysis suggested that in studies that analyzed only girls (four studies), baPWV was significantly reduced (0.82 m/s) after the interventions (ES: -0.544; 95% CI, –0.909 to -0.180; P= 0.003; I^2: 6%, Table 2). Only boy's and both sexes categories did not have enough studies to be analyzed separately, therefore, there was no subgroup analysis for these categories. When we analyzed the type of exercise, sport and combined categories did not show significant results (ES: -0.531; 95% CI, –1.154 to 0.093; P = 0.095; I^2: 43% and ES: -0.422; 95% CI, –0.850 to 0.006; P = 0.054; I^2: 3%, respectively, Table 2). HIIT category did not have enough studies to be analyzed separately, and there was no study for the strength and aerobic categories, therefore, there was no subgroup analysis for these categories.

The results of the meta-regression analysis showed that mean chronological age, BMI, Weekly training frequency, Follow-up duration, and Session duration were not associated with improvements in baPWV after physical exercise interventions (Table 3)

Table 3: Meta-regression of Moderators of the cardiometabolic health

Outcome/moderator	Number of study estimates	β	95% IC	p value
baPWV	6			
Age	5	-0.001	-0.231 to 0.229	.996
BMI	6	0.026	-0.100 to 0.153	.683
Follow-up duration	6	-0.174	-0.549 to 0.201	.363
Session duration	5	0.048	-0.026 to 1.222	.204
Weekly frequency	6	-0.053	-0.368 to 0.262	.741
SBP	38			
Age	34	-0.067	-0.106 to -0.028	<.001*
BMI	36	-0.051	-0.076 to -0.026	<.001*

Outcome/moderator	Number of study estimates	β	95% IC	p value
Follow-up duration	38	0.004	-0.001 to 0.010	.091
Session duration	37	0.002	-0.001 to 0.006	.229
Weekly frequency	36	-0.028	-0.156 to 0.099	.664
HDL	29			
Age	24	-0.052	-0.131 to 0.027	.194
BMI	25	0.036	0.012 to 0.061	.004*
Follow-up duration	29	0.003	-0.016 to 0.023	.728
Session duration	26	0.007	-0.003 to 0.018	.186
Weekly frequency	29	0.023	-0.151 to 0.196	.797
LDL	27			
Age	24	-0.015	-0.122 to 0.092	.783
BMI	24	-0.036	-0.085 to 0.013	.151
Follow-up duration	27	0.008	-0.016 to 0.032	.509
Session duration	25	0.002	-0.006 to 0.009	.648
Weekly frequency	27	0.171	-0.084 to 0.427	.189
WtHR	6			
Age	6	-0.062	-0.144 to 0.020	.137
BMI	6	-0.073	-0.119 to -0.028	.001*
Follow-up duration	6	0.029	0.009 to 0.048	.004*
Session duration	6	0.002	-0.016 to 0.020	.828
Weekly frequency	6	0.134	-0.055 to 0.323	.164

Abbreviations: β: Coefficients; baPWV: Brachial-ankle pulse wave velocity; BMI: body mass index; SBP: Systolic blood pressure; HDL: High density lipoproteins; LDL: Low density lipoprotein; WtHR: Waist-to-height ratio. * Indicates significant moderating effect ($p<0.05$).

Meta-Analysis of SBP

Data concerning SBP were available from 38 studies that compared physical exercise intervention groups with control groups, with a total of 5335 participants (Figure 4). Exercise was associated with a reduction in SBP compared with no intervention (ES: -0.200; 95% CI, –0.330 to -0.069; P= 0.003; I^2: 76%, Table 2). Exercise led to a reduction in SBP levels of approximately 2.08 mmHg in the intervention groups compared to the control group, who did not exercise or undergo any intervention.

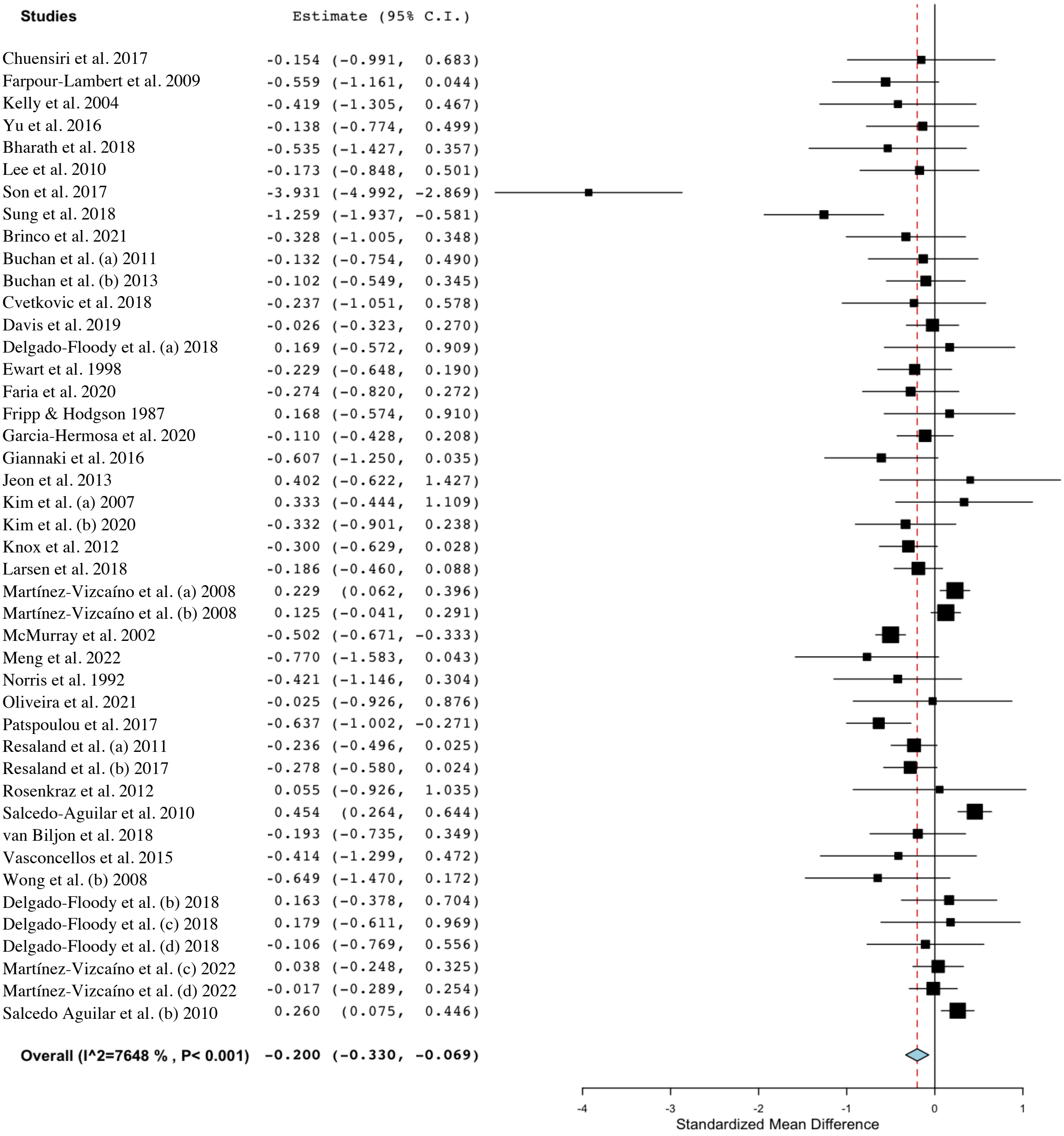


Figure 4 - Standardized mean differences in systolic blood pressure (mmHg) promoted by exercise and control (no intervention). CI indicates confidence interval; Std diff, standardized difference.

Furthermore, subgroup analysis suggested that in studies that analyzed only girls (10 studies) and both sexes (21 studies), SBP was significantly reduced after interventions (2.17 mmHg in only girls, ES: -0.373; 95% CI, –0.732 to -0.015; P = 0.041; I^2: 88%, Table 2 and 3.12 mmHg in both sexes, ES: -0.277; 95% CI, –0.368 to -0.185; P<0.001; I^2: 7%, Table 2). Only boy's category (13 studies) did not obtain a significant result (ES: -0.025; 95% CI, –0.236 to 0.186; P= 0.818; I^2: 58%, Table 2). When we analyzed the type of exercise, the aerobic (three studies) showed a significant reduction in SBP (3.11 mmHg) after the interventions (ES: -0.284; 95% CI, –0.533 to -0.036; P= 0.025; I^2: 0%, Table 2). However, the other categories did not show significant results (HIIT [seven studies {ES: -0.077; 95% CI, –0.276 to 0.121; P= 0.446; I^2: 0%}], Sport [19 studies {ES: -0.143; 95% CI, –0.301 to 0.015; P= 0.076; I^2: 81%}], Strength [three studies {ES: -0.219; 95% CI, –0.652 to 0.215; P= 0.323; I^2: 20%}] and Combined [five studies {ES: -0.970; 95% CI, –2.186 to 0.246; P= 0.118; I^2: 90%}], Table 2).

The results of the meta-regression analysis showed that mean age and BMI were inversely associated with SBP changes (β: –0.067; 95% CI, –0.106 to –0.028; P<0.001 e β: –0.051; 95% CI, –0.076 to –0.026; P<0.001, respectively, Table 3). In contrast, weekly training frequency, follow-up duration, and session duration were not associated with improvements in SBP after physical exercise interventions. That is, the greater the chronological age and BMI, the greater the effect of physical exercise in reducing SBP.

Meta-Analysis of DBP

Data concerning DBP were available from 36 studies that compared physical exercise intervention groups with control groups, with a total of 5,170 participants (Figure 5). No significant differences were found for DBP (ES: –0.092; 95% CI, –0.210 to 0.027; P= 0.129; I^2: 68%, Table 2).

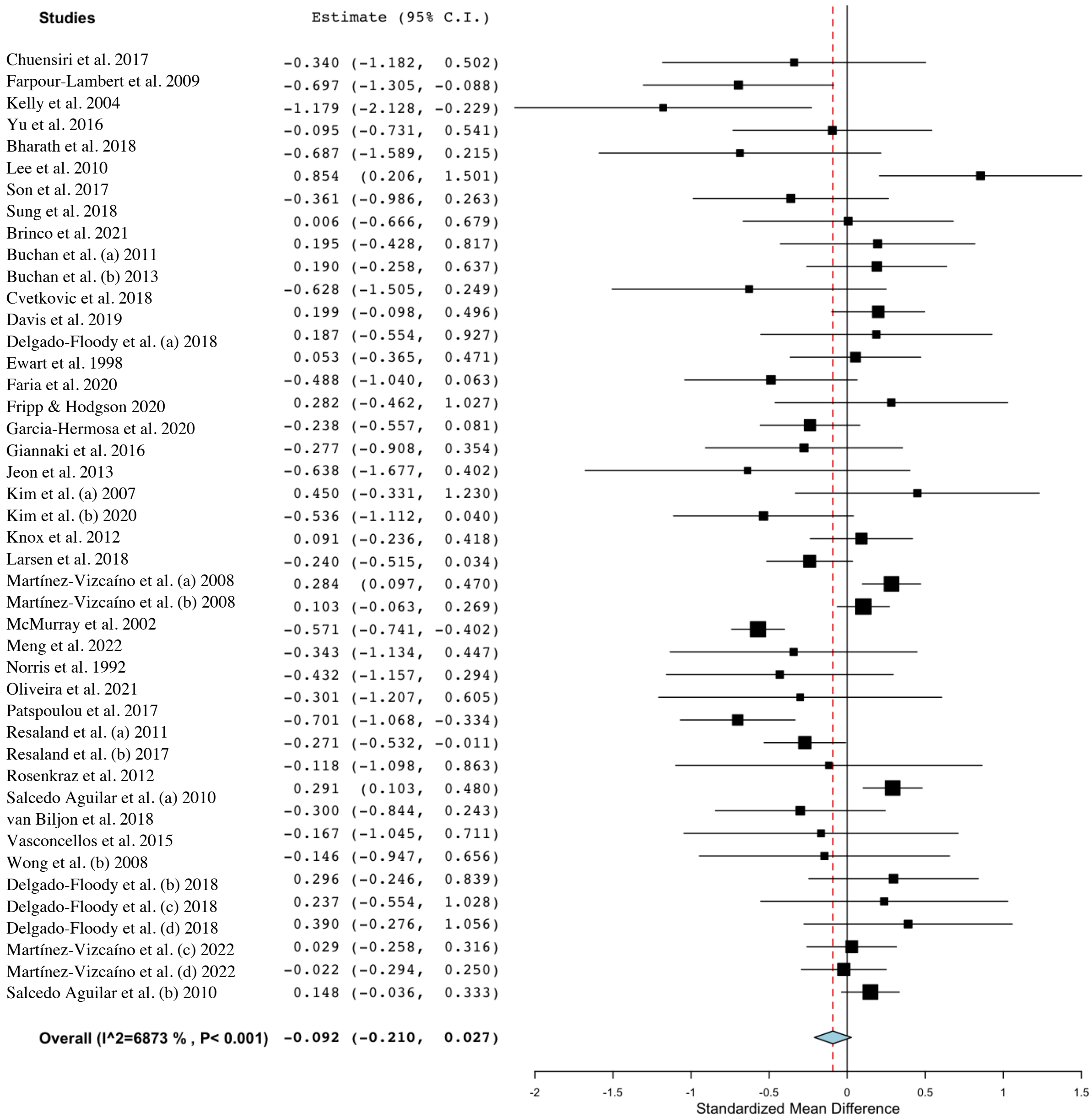


Figure 5 - Standardized mean differences in diastolic blood pressure (mmHg) promoted by exercise and control (no intervention). CI indicates confidence interval; Std diff, standardized difference.

Furthermore, subgroup analysis suggested that in studies that analyzed both sexes (19 studies), DBP was significantly reduced after the interventions (2.28 mmHg, ES: -0.242; 95% CI, –0.409 to -0.075; P= 0.004; I^2: 62%, Table 2). However, only girls (9 studies) and only boys (12 studies) categories did not obtain a significant result (ES: 0.054; 95% CI, –0.112 to 0.220; P= 0.526; I^2: 45% e ES: 0.131; 95% CI, –0.007 to 0.270; P= 0.063; I^2: 17%, respectively, Table 2). When we analyzed the type of exercise, no category showed significant results (HIIT [eight studies {ES: 0.060; 95% CI, –0.139 to 0.259; P= 0.554; I^2: 0%}], Sport [17 studies {ES: -0.154; 95% CI, –0.327 to 0.020; P= 0.083; I^2: 81%}], Aerobic [three studies {ES: -0.158; 95% CI, –0.665 to 0.349; P= 0.541; I^2: 68%}], Strength [three studies {ES: -0.062; 95% CI, –0.446 to 0.322; P= 0.752; I^2: 0%}] and Combined [five studies ES: -0.181; 95% CI, –0.791 to 0.429; P= 0.561; I^2: 68%}], Table 2).

Meta-Analysis of TC

Data concerning TC were available from 31 studies that compared physical exercise intervention groups with control groups, with a total of 3,480 participants (Figure 6). No significant differences were found for TC (ES: –0.146; 95% CI, –0.301 to 0.009; P= 0.064; I^2: 74%, Table 2).

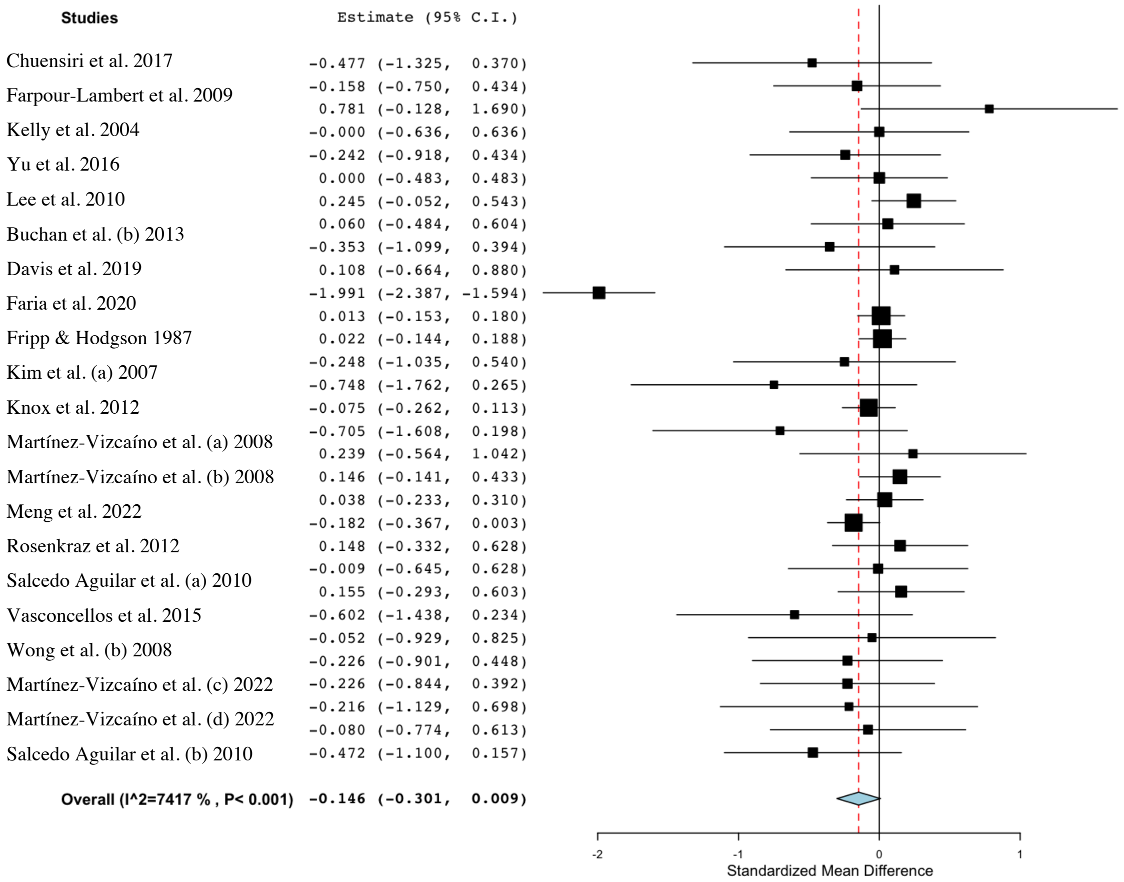


Figure 6 - Standardized mean differences in total cholesterol (mg.dL^{-1}) promoted by exercise and control (no intervention). CI indicates confidence interval; Std diff, standardized difference.

Furthermore, subgroup analysis suggested that in studies that analyzed both sexes (15 studies [ES: -0.206; 95% CI, –0.607 to 0.195; P= 0.314; I^2: 85%], Table 2), only girls (four studies [ES: -0.070; 95% CI, –0.204 to 0.064; P= 0.304; I^2: 19%], Table 2) e only boys (nine studies [ES: -0.028; 95% CI, –0.134 to 0.078; P= 0.607; I^2: 0%], Table 2) no significant differences were found. When we analyzed the type of exercise, no category showed significant results (HIIT [five studies {ES: -0.274; 95% CI, –0.595 to 0.048; P= 0.095; I^2: 0%}], Sport [10 studies {ES: -0.017; 95% CI, –0.092 to 0.058; P= 0.655; I^2: 0%}], Aerobic [five studies {ES: -0.463; 95% CI, –1.450 to 0.523; P= 0.357; I^2: 92%}], Strength [three studies {ES: 0.001; 95% CI, –0.340 to 0.342; P= 0.996; I^2: 0%}] and Combined [three studies ES: 0.058; 95% CI, –0.320 to 0.436; P= 0.763; I^2: 0%}], Table 2).

Meta-Analysis of HDL

Data concerning HDL were available from 29 studies that compared physical exercise intervention groups with control groups, with a total of 1,516 participants (Figure 7). Exercise was associated with an increase in HDL compared with no intervention (ES: 0.217; 95% CI, 0.051 to 0.383; P= 0.010; I^2: 54%, Table 2). Exercise led to an increase in HDL levels of approximately 2.61 mg·dL^{-1} in the intervention groups compared to the control group, who did not exercise or undergo any intervention.

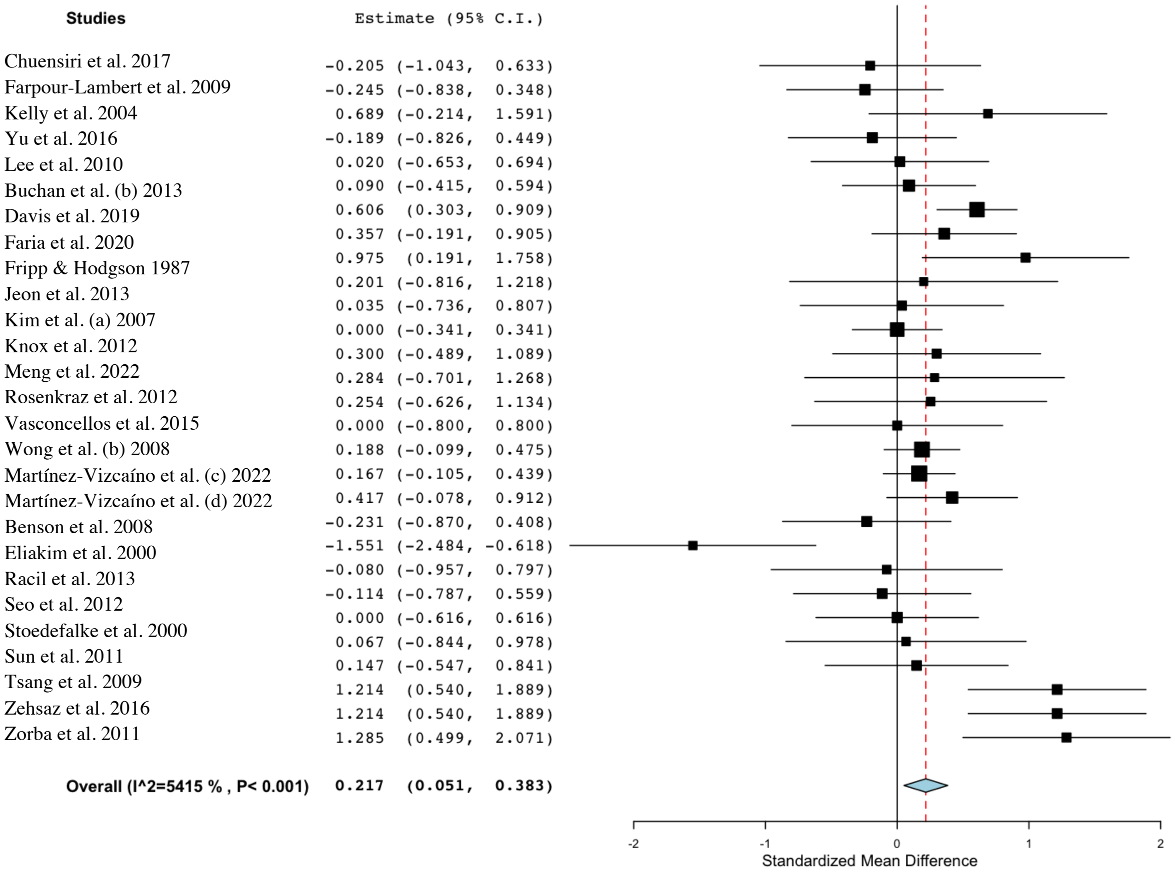


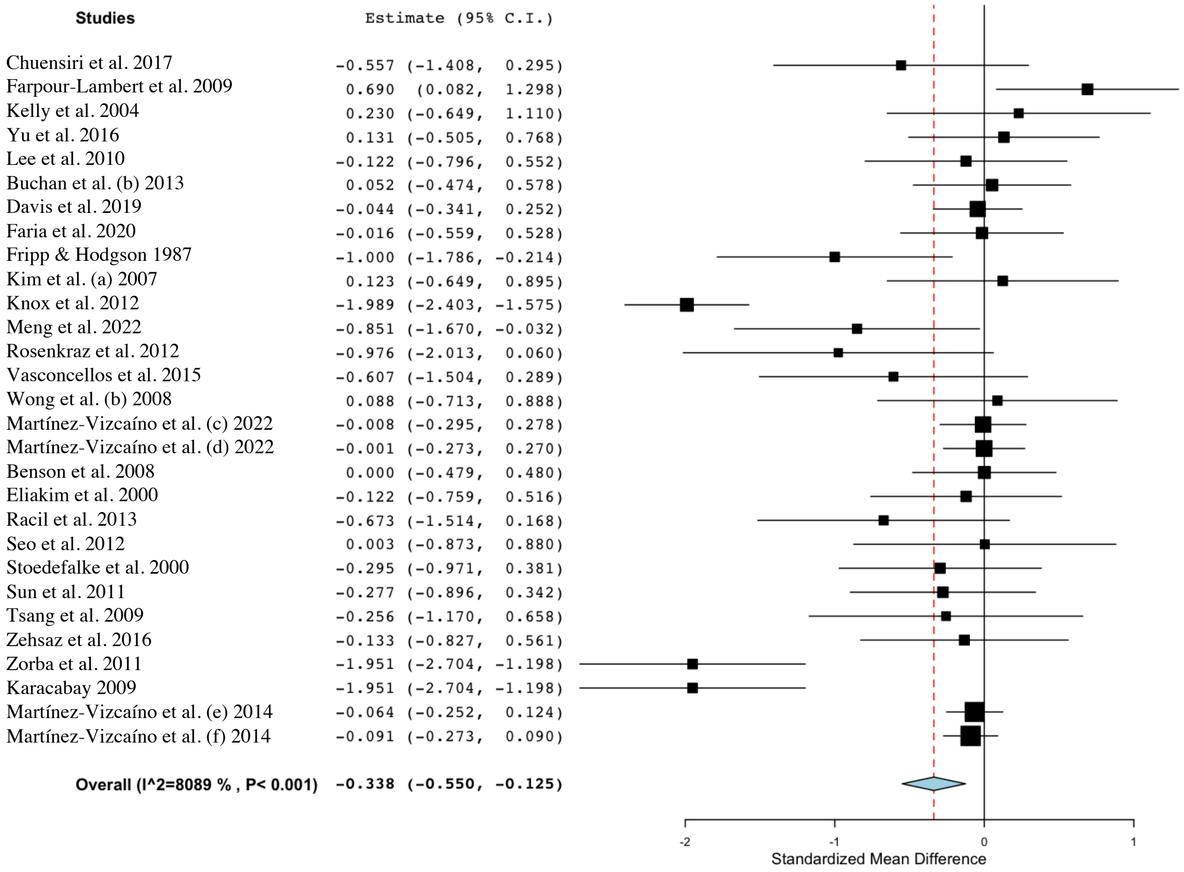
Figure 7 - Standardized mean differences in total HDL (mg.dL^{-1}) promoted by exercise and control (no intervention). CI indicates confidence interval; Std diff, standardized difference.

Furthermore, subgroup analysis suggested that in studies that analyzed only boys (nine studies) and both sexes (15 studies), HDL was significantly increased after the interventions (5 mg·dL^{-1} in only boys, ES: 0.383; 95% CI, 0.013 to 0.753; P = 0.042; I^2: 64%, Table 2 and 2.01 mg·dL^{-1} in both sexes, ES: 0.204; 95% CI, 0.053 to 0.356; 0.008; I^2: 7%, Table 2). Only girl's category (three studies) did not obtain a significant result (ES: -0.401; 95% CI, –1.259 to 0.457; P= 0.360; I^2: 83%, Table 2). When we analyzed the type of exercise, no category showed significant results (HIIT [six studies {ES: 0.055; 95% CI, –0.607 to 0.717; P= 0.871; I^2: 76%}], Sport [eight studies {ES: 0.180; 95% CI, –0.011 to 0.371; P= 0.064; I^2: 29%}], Aerobic [six studies {ES: 0.467; 95% CI, –0.033 to 0.968; P= 0.067; I^2: 75%}], Strength [three studies {ES: 0.370; 95% CI, –0.219 to 0.960; P= 0.218; I^2: 61%}] and Combined [four studies{ES: 0.213; 95% CI, –0.142 to 0.568; P= 0.240; I^2: 0%}], Table 2).

Results of the meta-regression analysis showed that BMI was directly associated with HDL changes (β: 0.036; 95% CI, 0.012 to 0.061; P= 0.004, Table 3). In contrast, mean age, weekly training frequency, follow-up duration, and session duration were not associated with improvements in HDL after physical exercise interventions. That is, the greater the BMI, the greater the effect of physical exercise in increasing HDL.

Meta-Analysis of LDL

Data concerning LDL were available from 29 studies that compared physical exercise intervention groups with control groups, with a total of 2,382 participants (Figure 8). Exercise was associated with a reduction in LDL compared with no intervention (ES: –0.338; 95% CI, –0.550 to –0.125; P= 0.002; I^2: 80%, Table 2). Exercise led to a reduction in LDL levels of approximately 8.17 $mg{\cdot}dL^{-1}$ in the intervention groups compared to the control group, who did not exercise or undergo any intervention.



Studies	Estimate (95% C.I.)
Chuensiri et al. 2017	-0.557 (-1.408, 0.295)
Farpour-Lambert et al. 2009	0.690 (0.082, 1.298)
Kelly et al. 2004	0.230 (-0.649, 1.110)
Yu et al. 2016	0.131 (-0.505, 0.768)
Lee et al. 2010	-0.122 (-0.796, 0.552)
Buchan et al. (b) 2013	0.052 (-0.474, 0.578)
Davis et al. 2019	-0.044 (-0.341, 0.252)
Faria et al. 2020	-0.016 (-0.559, 0.528)
Fripp & Hodgson 1987	-1.000 (-1.786, -0.214)
Kim et al. (a) 2007	0.123 (-0.649, 0.895)
Knox et al. 2012	-1.989 (-2.403, -1.575)
Meng et al. 2022	-0.851 (-1.670, -0.032)
Rosenkraz et al. 2012	-0.976 (-2.013, 0.060)
Vasconcellos et al. 2015	-0.607 (-1.504, 0.289)
Wong et al. (b) 2008	0.088 (-0.713, 0.888)
Martínez-Vizcaíno et al. (c) 2022	-0.008 (-0.295, 0.278)
Martínez-Vizcaíno et al. (d) 2022	-0.001 (-0.273, 0.270)
Benson et al. 2008	0.000 (-0.479, 0.480)
Eliakim et al. 2000	-0.122 (-0.759, 0.516)
Racil et al. 2013	-0.673 (-1.514, 0.168)
Seo et al. 2012	0.003 (-0.873, 0.880)
Stoedefalke et al. 2000	-0.295 (-0.971, 0.381)
Sun et al. 2011	-0.277 (-0.896, 0.342)
Tsang et al. 2009	-0.256 (-1.170, 0.658)
Zehsaz et al. 2016	-0.133 (-0.827, 0.561)
Zorba et al. 2011	-1.951 (-2.704, -1.198)
Karacabay 2009	-1.951 (-2.704, -1.198)
Martínez-Vizcaíno et al. (e) 2014	-0.064 (-0.252, 0.124)
Martínez-Vizcaíno et al. (f) 2014	-0.091 (-0.273, 0.090)
Overall (I^2=8089 % , P< 0.001)	**-0.338 (-0.550, -0.125)**

Figure 8 - Standardized mean differences in total LDL (mg.dL^{-1}) promoted by exercise and control (no intervention). CI indicates confidence interval; Std diff, standardized difference.

Furthermore, subgroup analysis suggested that in studies that analyzed only boys (10 studies), LDL was significantly reduced after interventions (15.10 mg.dL^{-1}, ES: -0.599; 95% CI, -1.011 to -0.187; P= 0.004; I^2: 82%, Table 2). Only girls (four studies) and both sexes (15 studies) categories did not obtain a significant result (ES: -0.092; 95% CI, –0.237 to 0.052; P= 0.211; I^2: 0% and ES: -0.211; 95% CI, –0.596 to 0.174; P= 0.282; I^2: 84%, respectively, Table 2). When we analyzed the type of exercise, the HIIT (five studies) and aerobic category (six studies) showed a significant reduction in LDL after the interventions (15.24 mg.dL^{-1} in HIIT, ES: -0.490; 95% CI, –0.908 to -0.072; P= 0.022; I^2: 29% and 21.33 mg.dL^{-1} in aerobic, ES: -1.056; 95% CI, –1.870 to -0.242; P= 0.011; I^2: 89%, respectively, Table 2). However, the other categories did not show significant results (Sport [nine studies {ES: -0.045; 95% CI, –0.141 to 0.052; P= 0.365; I^2: 0%}], Strength [three studies {ES: -0.234; 95% CI, –0.838 to 0.371; P= 0.449; I^2: 64%}] and Combined [three studies {ES: -0.027; 95% CI, –0.405 to 0.350; P= 0.887; I^2: 0%}], Table 2).

Results of meta-regression analysis showed that mean age, BMI, weekly training frequency, follow-up duration, and session duration were not associated with improvements in LDL after the physical exercise interventions.

Meta-Analysis of Waist-to-Height Ratio

Data concerning WtHR were available from six studies that compared physical exercise intervention groups with control groups, with a total of 705 participants (Figure 9). Exercise was associated with a reduction in WtHR compared with no intervention (ES: –0.277; 95% CI, –0.552 to –0.002; P= 0.048; I^2: 57%, Table 2). Exercise led to a reduction in WtHR of approximately 0.01 in the intervention groups compared to the control group, who did not exercise or undergo any intervention.

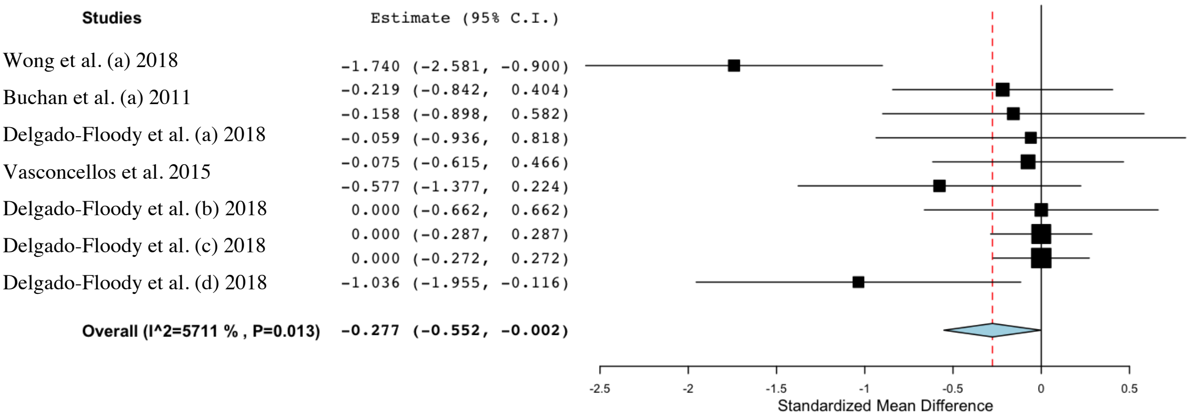


Figure 9 - Standardized mean differences in Waist-to-Height Ratio promoted by exercise and control (no intervention). CI indicates confidence interval; Std diff, standardized difference.

Furthermore, subgroup analysis suggested that in studies that analyzed both sexes (two studies, ES: -0.165; 95% CI, –0.673 to 0.343; P= 0.524; I^2: 0%, Table 2), only girls (four studies, ES: -0.513; 95% CI, –1.087 to 0.061; P= 0.080; I^2: 78%, Table 2) and only boys (two studies, ES: -0.056; 95% CI, –0.306 to 0.194; P= 0.659; I^2: 0%, Table 2) no significant differences were found. When we analyzed the type of exercise, the HIIT (three studies) and sport category (two studies) did not obtain a significant result (ES: -0.252; 95% CI, –0.531 to 0.027; P= 0.077; I^2: 0% and ES: -0.003; 95% CI, –0.195 to 0.190; P= 0.977; I^2: 0%, respectively, Table 2). Combined category did not have enough studies to be analyzed separately, and there was no study for the strength and aerobic categories, therefore, there was no subgroup analysis for these categories.

Results of meta-regression analysis showed that BMI was inversely associated (β: - 0.073; 95% CI, -0.119 to -0.028; P= 0.001, Table 3) and follow-up duration was directly associated (β: 0.029; 95% CI, 0.009 to 0.048; P= 0.004, Table 3) with WtHR changes. In contrast, mean age, weekly training frequency e session duration were not associated with improvements in WtHR after the physical exercise interventions. That is, the greater the BMI or the shorter the duration, the greater the effect of physical exercise in reducing WtHR.

Discussion

This systematic review and meta-analysis aimed to analyze the effects of supervised and structured physical exercise on the cardiometabolic health of children and adolescents. The main findings of this study demonstrate that: (1) physical exercise interventions are efficient in inducing positive effects on cardiometabolic health, significantly reducing bapWV, SBP, LDL, and WthR and increasing HDL; (2) some of these effects are mediated by sex and type of exercise used in the intervention; (3) when sex categories were analyzed separately, a significant SBP reduction was found in studies of both sexes and only girls, a significant increase in HDL was found in studies of both sexes and only boys, and a significant reduction in LDL was found in only boys; (4) individual analysis on the type of exercise categories revealed a significant reduction in SBP for aerobic exercise, and also in LDL for aerobic and HIIT exercises; (5) for the types of exercise, effects experienced by the aerobic exercise for the SBP and aerobic and HIIT exercises for the LDL variable were found; and (6) mean age and BMI moderating SBP results, BMI moderating HDL, and BMI and follow-up duration moderating WthR. These findings were found to be statistically significant, and we will compare them with data available in the literature.

In the present study, the endothelial function assessed through FMD did not obtain significant results after the physical exercise interventions in children and adolescents. Although few, some meta-analyses have analyzed the effects of physical exercise on the cardiovascular health of children and adolescents. Contrary to our findings, Cheng et al. (2022) observed improvements in FMD after physical exercise interventions with overweight and obese children, compared with the control group (no intervention). Subgroup analysis demonstrated that physical exercise increased FMD regardless of BMI (above or below 30 kg/m^2) and age (below or above 14 years old) [19]. Dias et al. (2015) also found favorable results in FMD of obese children after physical exercise intervention, with an increase of 1.54% being observed [20]. The main reason for improvements in FMD be expected with physical exercise is due to the increase in the bioavailability of nitric oxide that ensues. Physical exercise increases shear stress on the vessel wall acutely in response to increased blood flow, increasing acute and chronic oxide nitric production, increasing vasodilation, and consequently improving vascular function. These FMD increases are important for cardiometabolic health, because a 1% reduction in FMD is associated with a 13% increase in cardiovascular events [15].

Although substantial results have been reported by different studies that analyzed FMD, contrary to expectations, the present meta-analysis did not find a significant result. This rather contradictory result may be due to one of our four studies included in the meta-analysis. The study by Farpour-Lambert et al. (2009) [35] was the only one that did not obtain a significant increase in FMD after physical exercise intervention. This is probably due to the moderate-intensity of the physical exercise intervention, if we compare it with the intensity of the other three included studies, resulting in not being effective in improving FMD. Another possibility for explain our result is the small number of studies included, despite their low heterogeneity (49%). In addition, the eligibility criteria for this meta-analysis were strict and only included studies conducting structured and supervised exercises. Studies where in physical exercise was performed through video games or took place without professional supervision were not considered. Studies with physical exercise interventions combined with other interventions, such as nutritional guidance or changes in lifestyle habits, were also not included, as this would increase the heterogeneity of the studies, could affect the results, and be a confounding factor. Essentially, we would not be able to dissociate whether the observed effect was due to physical exercise or changes in habits that affected the results. Thus, the results of the present study show that FMD can be unaffected by physical exercise interventions in children and adolescents. Therefore, more interventions are needed to identify the best way exercise prescription to improve FMD.

As an important marker of cardiometabolic health, arterial stiffness, assessed through baPWV, significantly decreased by 0.72 m/s after the interventions. In addition, to finding beneficial results regarding FMD, the study by Cheng et al. (2022) found a reduction in PWV after physical exercise interventions. When subanalyses were performed, PWV decreased only in children up to 14 years of age, with BMI below 30 kg/m^2, and only in interventions with aerobic and HIIT. These results that show improvements only in individuals younger than 14 years suggest the effects of physical exercise on promoting vascular plasticity and structural remodeling may have a chronological age threshold. The effects of physical exercise on PWV are influenced by the subjects' age, especially since chronological age alone is already a factor that increases arterial stiffness [36]. Furthermore, the reduction in PWV only in children with BMI up to 30 kg/m^2 may have occurred due to the remodeling characteristics of the vascular structure, which may be responsible for the long-term effects resulting from obesity, where short interventions are not enough to reverse these changes [19]. Comparisons of different types of exercise showed that the strength category, when analyzed alone or together with aerobic (combined), was not effective in promoting improvements, which was expected and found in other studies [37, 38]. The present study also found significant PWV reductions after structured and supervised exercise interventions, demonstrating improvement in arterial stiffness in children and adolescents. However, no significant differences were found when the types of exercise were analyzed separately. Since only one study performed intervention with HIIT and no studies were found with aerobic and strength, performing a subanalysis with these types of exercise was impossible.

In the adult population, there are contradictory results about the effects of strength training. Some studies have found improvements in PWV with this type of exercise [39], while others have not found an effect [37, 38, 40], and unfavorable results have also been found, as in the study by Li et al. (2014), who found an increase of 3 m/s in PWV after a high-intensity strength training intervention (> 80% of 1 maximum repetition) [41] . A possible explanation for this finding is that the acute increase in blood pressure after vigorous strength training affected arterial stiffness. However, according to the authors, the interpretation of these findings is inconclusive since this meta-analysis included studies with very different intervention methodologies and several confounding factors (medication and diet). The types of exercise in the present study, sport and combined, may not have obtained a significant difference due to the strength component of the combined training (aerobic plus strength), since the aerobic exercises are more effective, according to the literature. Also, since the sport category included different sports modalities, it may be that the intensity of these modalities was not sufficiently to induce adaptative responses in comparison to aerobic interventions.

Regarding differences between sex, the present study found a greater effect size for only girls (ES: -0.544), with a reduction of 0.81 m/s, which is a greater reduction than that of all together in the general analysis. Although sub-analyses were not performed for both sexes and only boys, as each category had only one article, it was possible to verify that only girls may be more responsive to this variable when evaluated separately. Additionally, none of the potential moderators analyzed in the present study was related to changes in PWV, unlike the aforementioned study, which found greater effects when participants had BMI above 30 kg/m^2 [19]. The possible absence of moderators for the baPWV data may be because the six studies included in the analysis are methodologically similar, which results in a low heterogeneity of the results. Therefore, to deepen knowledge regarding the influence of sex, age, BMI, type of exercise, and different training variables on arterial stiffness, it is suggested that more interventions be carried out, mainly with longer follow-up (> 12 weeks), since the articles found had shorter interventions.

A 1 m/s increase in PWV has been associated with a 15% increase in the mortality risk from CVD [16]. Therefore, the results of the present meta-analysis for PWV are very significant even if the analyzed individuals do not yet have cardiovascular diseases because reducing PWV with these interventions is important in maintaining and improving cardiometabolic health. Moreover, this adds to the studies' suggestions that PWV predicts blood pressure progression and may be a valuable tool for predicting the outcome risk of hypertension in young adults [42]. Furthermore, since arterial stiffness is a common subclinical process in most cardiovascular diseases, the findings of this meta-analysis support that exercise can be included as an intervention for the management of CMRF in children and adolescents.

Regarding the blood pressure results found in the present study, with significant reductions in SBP and no differences in DBP, when we evaluate the subanalysis, we can observe that it was possibly the results of studies with girls (whether they were analyzed alone or together with boys), which made the results obtain significance in SBP. This is because only in the general analysis and in the categories only girl's and both sexes were significant reductions found. Corroborating the guidelines that reinforce the importance and indicate aerobic exercises to manage blood pressure in prehypertensive and hypertensive individuals [43], as this type of exercise is able to reduce blood pressure even in individuals with resistant hypertension [44], in this study only the aerobic exercise obtained a significant reduction in SBP (3.1 mmHg). On the one hand, studies found in the literature did not find significant differences when comparing types of exercise; regardless of the type of exercise, a reduction in blood pressure is expected, especially in SBP [45-47]. On the other hand, some studies found significant improvements only with aerobic exercise [48]. Even though studies with hypertensive children and adolescents were not included in the present meta-analysis, a significant improvement in SBP was still found for the aerobic exercise, while the other types of exercise did not reach this significance. A possible explanation for the lack of significant reductions in DBP could be due to the condition of the participants included in the studies, who were not hypertensive and physical exercise interventions tend to reduce both SBP and DBP in this population [49]. Even if no significant reduction in DBP was found, it is important to emphasize that the elevation of SBP better predicts the risk for CVD when compared to DBP [50, 51]. Furthermore, systolic arterial hypertension is more common with aging [52]. When projecting long-term improvements, a 10 mmHg reduction in SBP may be associated with a 40% reduction in the risk of death from stroke and approximately 30% less mortality risk from ischemic heart disease in middle-aged people. Even a long-term reduction of 2 mmHg can result in a 10% reduction in mortality from myocardial infarction and approximately a 7% reduction in the mortality risk from ischemic heart disease [51]. Therefore, reducing blood pressure in children and adolescents, even if only systolic, is an important result for the cardiometabolic health of individuals and may represent a reduction in the risk of death from CVD in the future.

Regarding SBP moderating factors, the higher BMI and mean age, the greater the effect size in reducing the SBP. It is reported in the literature that overweight or obese children and adolescents have higher values of SBP and DBP [53]; they are at greater risk of developing CVD. This was found in the present study, as interventions where the mean BMI of the participants was closer to 30 (overweight), the highest mean SBP values were found [35, 54-60]. The same also occurred with age, where interventions with average age of the participants was higher, SBP values were also higher [54, 56, 57, 59-62].

It is also important to investigate other CMRF equally important for cardiovascular health such as TC, HDL, and LDL concentrations. As the formation of fatty plaques in the arteries (atherosclerosis) begins in childhood/adolescence with lesions called fatty streaks, which are associated with cardiovascular health, it is important that we pay appropriate attention to these components to prevent its pathological progression [18]. Individuals with elevated TC (>200 $mg.dL^{-1}$) have approximately twice the risk of coronary artery disease compared with individuals with healthy values (<180 $mg.dL^{-1}$)[63]. Evidence shows that physical exercise interventions are able to reduce TC and LDL and increase HDL in adults, children, and adolescents [64], and together with other lifestyle interventions, it is the first line of treatment for early stage dyslipidemia. Kelley et al. (2021), who investigated the effects of physical exercise on the CMRF of children and adolescents with obesity, found significant HDL increases (5.3 $mg.dL^{-1}$) and LDL reductions (17.5 $mg.dL^{-1}$) with aerobic interventions, while no significant reductions were found in TC [64].These results are similar to the present study, where in a significant increase in HDL of approximately 2.16 $mg.dL^{-1}$ and a reduction in LDL of 8.17 $mg.dL^{-1}$ were found. Given that subjects had normal levels of LDL and HDL (no reported dyslipidemia), these results suggest that physical exercise interventions may help prevent lifelong cholesterol changes. When we take into account sex and types of exercise, a significant increase in HDL was found for the interventions that evaluated only boys and both sexes, with no differences between the types of exercise, while a significant reduction in LDL was found in only boys for aerobic and HIIT interventions. Mean age was moderating HDL results; that is, the greater the age, the greater the effect of physical exercise on HDL improvements.

Waist circumference and height comprise the WtHR and are related to cardiometabolic health and CMRF. The WtHR is a measure of central obesity and is considered the most effective anthropometric measurement possible for screening cardiometabolic diseases [9], superior to BMI and waist circumference measurements alone [65]. The present study found improvements in this variable after the physical exercise interventions; the greater BMI of the participants, the greater the effect of physical exercise on the WtHR, and the greater the follow-up duration, the smaller the effect. Maintaining physical exercise interventions, particularly in the clinical population is difficult and long interventions have lower adherence when compared to shorter interventions [66]. In this way, the results of the present study, which found smaller effect sizes on the WtHR variable during longer interventions (1 to 2 years) [32, 33]. The physical exercise effects on WtHR could potentially occur during the initial weeks of longer interventions, because when compared with shorter interventions analyzed in the present study (approximately 10 weeks), the effect size was smaller the longer the intervention lasted. BMI has been shown to be a moderator of WtHR, as well as for SBP and HDL, demonstrating that individuals with higher BMI values may be more responsive to physical exercise interventions.

Limitations and future research prospects

When conducting this systematic review with meta-analysis and meta-regression, there are some limitations that deserve attention. First, it is important to emphasize that most of the included studies have low scores in the evaluation of the quality of the studies, generating an average value of 7.52 points out of a total of 15, demonstrating a high risk of methodological bias. Many intervention studies are carried out with convenience samples; therefore, they do not present clear eligibility criteria for the inclusion of subjects. In addition, many studies did not randomize the groups or did not detail how this randomization was done. Regarding the blinding of study evaluators, almost none of the studies performed it, but it is important to emphasize that this blinding is rarely considered in physical exercise intervention studies.

In the present study, for some results obtained, high heterogeneity was found, and even performing sensitivity and moderation analyses, it was not possible to identify the cause of this result. This may have occurred due to the small number of studies included in the subanalyses of some variables. Like all reviews, meta-analyses are limited by available or obtained data. Since few studies were found for some variables (FMD, bapWV, and WtHR), it reinforces the need for further investigations on the physical exercise effects on these parameters in the pediatric population.

Conclusion

The present meta-analysis showed that supervised and structured physical exercise interventions promote reductions in baPWV, SBP, LDL, and WtHR while promoting an increase in HDL in children and adolescents. Furthermore, boys seem to be more responsive to improve HDL and LDL, while girls are more responsive to improve SBP. The aerobic exercise was more effective in promoting improvements in SBP and LDL, and HIIT exercise was more effective to improve LDL. The SBP is moderated by the participants' mean age and BMI, while the HDL depends on the BMI, and the WtHR on the BMI and Follow-up duration. Session duration and weekly training frequency did not show moderating effects on any of the analyzed variables; the frequency of physical exercise interventions or session duration did not interfere with the results. Therefore, supervised and structured physical exercise can be an interesting way to maintain or improve the cardiometabolic health of children and adolescents.

REFERENCES

1. Canas JA, Sweeten S, Balagopal PB. Biomarkers for cardiovascular risk in children. Curr Opin Cardiol. 2013 Mar;28(2):103-14.

2. Candelino M, Tagi VM, Chiarelli F. Cardiovascular risk in children: a burden for future generations. Ital J Pediatr. 2022 Apr 11;48(1):57.

3. de Ferranti SD, Steinberger J, Ameduri R, Baker A, Gooding H, Kelly AS, et al. Cardiovascular Risk Reduction in High-Risk Pediatric Patients: A Scientific Statement From the American Heart Association. Circulation. 2019 Mar 26;139(13):e603-e34.

4. Litwin M. Why should we screen for arterial hypertension in children and adolescents? Pediatr Nephrol. 2018 Jan;33(1):83-92.

5. Juonala M, Viikari JS, Raitakari OT. Main findings from the prospective Cardiovascular Risk in Young Finns Study. Curr Opin Lipidol. 2013 Feb;24(1):57-64.

6. Ji F, Ning F, Duan H, Kaprio J, Zhang D, Zhang D, et al. Genetic and environmental influences on cardiovascular disease risk factors: a study of Chinese twin children and adolescents. Twin Res Hum Genet. 2014 Apr;17(2):72-9.

7. Organization WH. Obesity and overweight. 2021 [cited; Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

8. Tomkinson GR, Lang JJ, Tremblay MS. Temporal trends in the cardiorespiratory fitness of children and adolescents representing 19 high-income and upper middle-income countries between 1981 and 2014. Br J Sports Med. 2019 Apr;53(8):478-86.

9. Guasch-Ferre M, Bullo M, Martinez-Gonzalez MA, Corella D, Estruch R, Covas MI, et al. Waist-to-height ratio and cardiovascular risk factors in elderly individuals at high cardiovascular risk. PLoS One. 2012;7(8):e43275.

10. Fontes A, de Oliveira LS, Vanderlei FM, Garner DM, Valenti VE. Waist-Stature Ratio And Its Relationship With Autonomic Recovery From Aerobic Exercise In Healthy Men. Sci Rep. 2018 Oct 31;8(1):16093.

11. Correia ML, Haynes WG. Arterial compliance and endothelial function. Curr Diab Rep. 2007 Aug;7(4):269-75.

12. Bonetti PO, Lerman LO, Lerman A. Endothelial dysfunction: a marker of atherosclerotic risk. Arterioscler Thromb Vasc Biol. 2003 Feb 1;23(2):168-75.

13. Celermajer DSS, K. E., Gooch, V. M., Spiegelhalter, D. J., Miller, O. I., Sullivan,, I. D., Lloyd, J. K. Deanfield, J. E. Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. Lancet. 1992;7(340(8828)):1111-5.

14. Hanssen H. Vascular biomarkers in the prevention of childhood cardiovascular risk: From concept to clinical implementation. Front Cardiovasc Med. 2022;9:935810.

15. Inaba Y, Chen JA, Bergmann SR. Prediction of future cardiovascular outcomes by flow-mediated vasodilatation of brachial artery: a meta-analysis. Int J Cardiovasc Imaging. 2010 Aug;26(6):631-40.

16. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol. 2010 Mar 30;55(13):1318-27.

17. McGill HC, Jr., McMahan CA, Herderick EE, Malcom GT, Tracy RE, Strong JP. Origin of atherosclerosis in childhood and adolescence. Am J Clin Nutr. 2000 Nov;72(5 Suppl):1307S-15S.

18. Strong JP, McGill HC, Jr. The pediatric aspects of atherosclerosis. J Atheroscler Res. 1969 May-Jun;9(3):251-65.

19. Cheng Y, Sun Z, Ya X, Zhou L, Wang M, Wang X, et al. Effect of exercise training on arterial stiffness in obese and overweight children: a meta-analysis. Eur J Pediatr. 2022 Jul;181(7):2633-42.

20. Dias KA, Green DJ, Ingul CB, Pavey TG, Coombes JS. Exercise and Vascular Function in Child Obesity: A Meta-Analysis. Pediatrics. 2015 Sep;136(3):e648-59.

21. Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med. 2020 Dec;54(24):1451-62.

22. Pozuelo-Carrascosa DP, Cavero-Redondo I, Herráiz-Adillo A, Díez-Fernández A, Sánchez-López M, Vicente Martínez-Vizcaíno V. School-Based Exercise Programs and Cardiometabolic Risk Factors: A Meta-analysis. Pediatrics. 2018;142 (5).

23. Grace J, Biggs C, Naicker A, Moss S. Effect of Physical Activity and Nutrition Education on Body Mass Index, Blood Pressure and Biochemical Variables in Overweight and Obese Adolescents. Ann Glob Health. 2021 Jan 25;87(1):9.

24. Ho M, Garnett SP, Baur L, Burrows T, Stewart L, Neve M, et al. Effectiveness of lifestyle interventions in child obesity: systematic review with meta-analysis. Pediatrics. 2012 Dec;130(6):e1647-71.

25. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions. In: Higgins JPT, Green S, editors.: The Cochrane Collaboration; 2011.

26. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009 Aug 18;151(4):264-9, W64.

27. Getty AK, Wisdo TR, Chavis LN, Derella CC, McLaughlin KC, Perez AN, et al. Effects of circuit exercise training on vascular health and blood pressure. Prev Med Rep. 2018 Jun;10:106-12.

28. Smart NA, Waldron M, Ismail H, Giallauria F, Vigorito C, Cornelissen V, et al. Validation of a new tool for the assessment of study quality and reporting in exercise training studies: TESTEX. Int J Evid Based Healthc. 2015 Mar;13(1):9-18.

29. Wallace BC, Dahabreh, I. J., Trikalinos, T. A., Lau, J., Trow, P., & Schmid, C. H. Closing the Gap between Methodologists and End-Users: R as a Computational Back-End. Journal of Statistical Software. 2012;49(5):1-15.

30. Salcedo Aguilar F, Martinez-Vizcaino V, Sanchez Lopez M, Solera Martinez M, Franquelo Gutierrez R, Serrano Martinez S, et al. Impact of an after-school physical activity program on obesity in children. J Pediatr. 2010 Jul;157(1):36-42 e3.

31. Martinez Vizcaino V, Salcedo Aguilar F, Franquelo Gutierrez R, Solera Martinez M, Sanchez Lopez M, Serrano Martinez S, et al. Assessment of an after-school physical activity program to prevent obesity among 9- to 10-year-old children: a cluster randomized trial. Int J Obes (Lond). 2008 Jan;32(1):12-22.

32. Martinez-Vizcaino V, Soriano-Cano A, Garrido-Miguel M, Cavero-Redondo I, Medio EP, Madrid VM, et al. The effectiveness of a high-intensity interval games intervention in schoolchildren: A cluster-randomized trial. Scand J Med Sci Sports. 2022 Apr;32(4):765-81.

33. Delgado-Floody P, Espinoza-Silva M, Garcia-Pinillos F, Latorre-Roman P. Effects of 28 weeks of high-intensity interval training during physical education classes on cardiometabolic risk factors in Chilean schoolchildren: a pilot trial. Eur J Pediatr. 2018 Jul;177(7):1019-27.

34. Martinez-Vizcaino V, Sanchez-Lopez M, Notario-Pacheco B, Salcedo-Aguilar F, Solera-Martinez M, Franquelo-Morales P, et al. Gender differences on effectiveness of a school-based physical activity intervention for reducing cardiometabolic risk: a cluster randomized trial. Int J Behav Nutr Phys Act. 2014 Dec 10;11:154.

35. Farpour-Lambert NJ, Aggoun Y, Marchand LM, Martin XE, Herrmann FR, Beghetti M. Physical activity reduces systemic blood pressure and improves early markers of atherosclerosis in pre-pubertal obese children. J Am Coll Cardiol. 2009 Dec 15;54(25):2396-406.

36. Cockcroft JR, Wilkinson IB, Webb DJ. The Trevor Howell Lecture. Age, arterial stiffness and the endothelium. Age Ageing. 1997 Dec;26 Suppl 4:53-60.

37. Ceciliato J, Costa EC, Azevedo L, Sousa JC, Fecchio RY, Brito LC. Effect of Resistance Training on Arterial Stiffness in Healthy Subjects: A Systematic Review and Meta-Analysis. Curr Hypertens Rep. 2020 Jul 15;22(8):51.

38. Zhang Y, Qi L, Xu L, Sun X, Liu W, Zhou S, et al. Effects of exercise modalities on central hemodynamics, arterial stiffness and cardiac function in cardiovascular disease: Systematic review and meta-analysis of randomized controlled trials. PLoS One. 2018;13(7):e0200829.

39. Li S, Chen W, Srinivasan SR, Berenson GS. Childhood blood pressure as a predictor of arterial stiffness in young adults: the bogalusa heart study. Hypertension. 2004 Mar;43(3):541-6.

40. Ashor AW, Lara J, Siervo M, Celis-Morales C, Oggioni C, Jakovljevic DG, et al. Exercise modalities and endothelial function: a systematic review and dose-response meta-analysis of randomized controlled trials. Sports Med. 2015 Feb;45(2):279-96.

41. Li Y, Hanssen H, Cordes M, Rossmeissl A, Endes S, Schmidt-Trucksass A. Aerobic, resistance and combined exercise training on arterial stiffness in normotensive and hypertensive adults: A review. Eur J Sport Sci. 2015;15(5):443-57.

42. Koivistoinen T, Lyytikainen LP, Aatola H, Luukkaala T, Juonala M, Viikari J, et al. Pulse Wave Velocity Predicts the Progression of Blood Pressure and Development of Hypertension in Young Adults. Hypertension. 2018 Mar;71(3):451-6.

43. Pescatello LS, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA, et al. American College of Sports Medicine position stand. Exercise and hypertension. Med Sci Sports Exerc. 2004 Mar;36(3):533-53.

44. Lopes S, Mesquita-Bastos J, Garcia C, Bertoquini S, Ribau V, Teixeira M, et al. Effect of Exercise Training on Ambulatory Blood Pressure Among Patients With Resistant Hypertension: A Randomized Clinical Trial. JAMA Cardiol. 2021 Nov 1;6(11):1317-23.

45. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc. 2013 Feb 1;2(1):e004473.

46. Costa EC, Hay JL, Kehler DS, Boreskie KF, Arora RC, Umpierre D, et al. Effects of High-Intensity Interval Training Versus Moderate-Intensity Continuous Training On Blood Pressure in Adults with Pre- to Established Hypertension: A Systematic Review and Meta-Analysis of Randomized Trials. Sports Med. 2018 Sep;48(9):2127-42.

47. Ramos JS, Dalleck LC, Tjonna AE, Beetham KS, Coombes JS. The impact of high-intensity interval training versus moderate-intensity continuous training on vascular function: a systematic review and meta-analysis. Sports Med. 2015 May;45(5):679-92.

48. Halbert JA, Silagy CA, Finucane P, Withers RT, Hamdorf PA, Andrews GR. The effectiveness of exercise training in lowering blood pressure: a meta-analysis of randomised controlled trials of 4 weeks or longer. J Hum Hypertens. 1997 Oct;11(10):641-9.

49. de Sousa EC, Abrahin O, Ferreira ALL, Rodrigues RP, Alves EAC, Vieira RP. Resistance training alone reduces systolic and diastolic blood pressure in prehypertensive and hypertensive individuals: meta-analysis. Hypertens Res. 2017 Nov;40(11):927-31.

50. Kannel WB, Schwartz MJ, McNamara PM. Blood pressure and risk of coronary heart disease: the Framingham study. Dis Chest. 1969 Jul;56(1):43-52.

51. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R, Prospective Studies C. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002 Dec 14;360(9349):1903-13.

52. Strandberg TEaP, K. What is the most important component of blood pressure? Current Opinion in Nephrology and Hypertension. 2003;12(3):293-7.

53. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012 Sep 25;345:e4759.

54. Bharath LP, Choi WW, Cho JM, Skobodzinski AA, Wong A, Sweeney TE, et al. Combined resistance and aerobic exercise training reduces insulin resistance and central adiposity in adolescent girls who are obese: randomized clinical trial. Eur J Appl Physiol. 2018 Aug;118(8):1653-60.

55. Kim ES, Im JA, Kim KC, Park JH, Suh SH, Kang ES, et al. Improved insulin sensitivity and adiponectin level after exercise training in obese Korean youth. Obesity (Silver Spring). 2007 Dec;15(12):3023-30.

56. Kim J, Son WM, Headid Iii RJ, Pekas EJ, Noble JM, Park SY. The effects of a 12-week jump rope exercise program on body composition, insulin sensitivity, and academic self-efficacy in obese adolescent girls. J Pediatr Endocrinol Metab. 2020 Jan 28;33(1):129-37.

57. Patsopoulou A, Tsimtsiou Z, Katsioulis A, Malissiova E, Rachiotis G, Hadjichristodoulou C. Evaluating the Efficacy of the Feeding Exercise Randomized Trial in Overweight and Obese Adolescents. Child Obes. 2017 Apr;13(2):128-37.

58. Chuensiri N, Suksom D, Tanaka H. Effects of High-Intensity Intermittent Training on Vascular Function in Obese Preadolescent Boys. Child Obes. 2018 Jan;14(1):41-9.

59. Vasconcellos F, Seabra A, Cunha F, Montenegro R, Penha J, Bouskela E, et al. Health markers in obese adolescents improved by a 12-week recreational soccer program: a randomised controlled trial. J Sports Sci. 2016;34(6):564-75.

60. Sung KD, Pekas EJ, Scott SD, Son WM, Park SY. The effects of a 12-week jump rope exercise program on abdominal adiposity, vasoactive substances, inflammation, and vascular function in adolescent girls with prehypertension. Eur J Appl Physiol. 2019 Feb;119(2):577-85.

61. Cvetkovic N, Stojanovic E, Stojiljkovic N, Nikolic D, Scanlan AT, Milanovic Z. Exercise training in overweight and obese children: Recreational football and high-intensity interval training provide similar benefits to physical fitness. Scand J Med Sci Sports. 2018 Aug;28 Suppl 1:18-32.

62. Giannaki CD, Aphamis G, Tsouloupas CN, Ioannou Y, Hadjicharalambous M. An eight week school-based intervention with circuit training improves physical fitness and reduces body fat in male adolescents. J Sports Med Phys Fitness. 2016 Jul-Aug;56(7-8):894-900.

63. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics--2012 update: a report from the American Heart Association. Circulation. 2012 Jan 3;125(1):e2-e220.

64. Kelley GA, Kelley KS, Pate RR. Exercise and Cardiovascular Disease Risk Factors in Children and Adolescents With Obesity: A Systematic Review With Meta-Analysis of Randomized Controlled Trials. Am J Lifestyle Med. 2022 Jul-Aug;16(4):485-510.

65. Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. Obes Rev. 2012 Mar;13(3):275-86.

66. Woodard CM, Berry MJ. Enhancing adherence to prescribed exercise: structured behavioral interventions in clinical exercise programs. J Cardiopulm Rehabil. 2001 Jul-Aug;21(4):201-9.

Supplementary Materials

Supplementary Material 1- Prisma checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	5-6
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	6
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	7
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	7
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	7
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	8-9
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	8-9
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	8
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	9
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	N/A
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	8-9

Section and Topic	Item #	Checklist item	Location where item is reported
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	9
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	8-9
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	9
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	9
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	9
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	9
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	N/A
Study characteristics	17	Cite each included study and present its characteristics.	Supplementary material
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	10-11
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	12-25
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	N/A
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	12-25
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	13-16
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	12-25
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	25
	23b	Discuss any limitations of the evidence included in the review.	30-31
	23c	Discuss any limitations of the review processes used.	30-31
	23d	Discuss implications of the results for practice, policy, and future research.	30-31
OTHER INFORMATION			

Section and Topic	**Item #**	**Checklist item**	**Location where item is reported**
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	6
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	6
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	2
Competing interests	26	Declare any competing interests of review authors.	2
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	2

Supplementary Material 2- Characteristics of the included studies

Study	Sample; Age at baseline; Sex	Outcomes	Follow-up duration	Weekly training frequency	Session duration (min)	Physical exercise	Intensity
Baghersalimi et al. (2019)	n= 32; I: 9.86, C: 9.66; obese girls	WtHR	8 weeks	3		Walking	75-85% predicted HRmax
Bharath et al. (2018)	n= 40; I: 15.6, C: 14.8; obese girls	baPWV, SBP, DBP	12 weeks	5	60	Resistance band exercises and treadmill walking	Moderate: 15-20 RM and 40-70% HRR
Benson et al. (2008)	n= 78; I: 12.3, C: 12.2; boys and girls	TC, HDL, LDL	12 weeks	2		Upper and lower body strength exercises using free weights and ankle weights	High: 15-18 RPE
Brinco et al. (2021)	n= 41; I: 7.86, C: 8.08; overweight/obese boys	SBP, DBP	12 weeks	2	20	Lower body plyometrics, plyometric speed and agility drills	
Buchan et al. (2011)	n= 47; I: 16.7, C: 16.3; boys and girls	SBP, DBP, WtHR	8 weeks	3		Running	Maximal effort
Buchan et al. (2013)	n= 89; I: 16.8, C: 16.6; boys and girls	SBP, DBP, TC, HDL, LDL	7 weeks	3	~10	Running	Maximal effort
Chuensiri et al. (2017)	n= 48; I: 11, C:10.6; obese boys	FMD, baPWV, SBP, DBP, TC, HDL, LDL	12 weeks	3		Cycle ergometer	90% peak power output
Cvetkovic et al. (2018)	n= 42; I: 12; C: 12; overweight/obese boys	SBP, DBP	12 weeks	2	60	Soccer	

Continued... **Study**	**Sample; Age at baseline; Sex**	**Outcomes**	**Follow-up duration**	**Weekly training frequency**	**Session duration (min)**	**Physical exercise**	**Intensity**
Davis et al. (2019)	n= 175; I: 9.6, C: 9.7; overweight/obese boys and girls	SBP, DBP, TC, HDL, LDL	8 months	5	40	Aerobic activities (e.g., tag, jump rope)	
Delgado-Floody et al. (2018)	n= 197; 8.39; overweight boys, overweight girls, obese boys, and obese girls	SBP, DBP, WtHR	28 weeks	2	60	Circuit (running, jumping, throwing)	80-95% predicted HRmax
Eliakim et al. (2000)	n= 38; 16; boys	TC, HDL, LDL	5 weeks	5	30	Endurance-type training (running, aerobic dance, and competitive sports) and occasional weight-lifting	
Ewart et al. (1998)	n= 99; 9; girls	SBP, DBP,	18 weeks		50	Aerobic exercises	
Faria et al. (2020)	n= 76; I: 16.1, C:16.5; boys and girls	SBP, DBP, TC, HDL, LDL	12 weeks	2		Treadmill run and strength exercises	>90% Vmax and 15-20 RM/8-10 RM (increasing workloads)
Farpour-Lambert et al. (2009)	n= 44; I: 9.1, C: 8.8; obese boys and girls	FMD, DBP, SBP, TC, HDL, LDL	3 months	3	60	Aerobic and strengthening body weight and elastic band exercises	55-65% VO2max

Continued... Study	Sample; Age at baseline; Sex	Outcomes	Follow-up duration	Weekly training frequency	Session duration (min)	Physical exercise	Intensity
Fripp & Hodgson (1987)	n= 14; I: 15.7, C: 15.9; boys	SBP, DBP, TC, HDL, LDL	9 weeks	3	60-80	Free weights and machine gym equipments	
García-Hermoso et al. (2020)	n= 170; I: 10.18, C: 10.02; boys and girls	SBP, DBP	8 weeks	5	30	Cooperative physical games and sports games	Moderate-vigorous
Giannaki et al. (2016)	n= 39; 16; boys	SBP, DBP	8 weeks	2	25	Circuit training (push ups, triceps dips, step-on-the-box, wall ball, bicep curls with elastic bands for resistance, sit-ups, standing calf raises with medicine ball, and back raises)	
Jeon et al. (2013)	n= 15; overweight/obese boys and girls	SBP, DBP, HDL, LDL	12 weeks	2	50	Walking exercises and band exercises	55-75% predicted HRmax and 70% 1RM
Karacabay (2009)	n= 40; I: 11.8, C: 11.2; obese boys	HDL, LDL	12 weeks	3	65	Walking and jogging	60-65% HHR
Kelly et al. (2004)	n= 25; 11; overweight boys and girls	FMD, SBP, DBP, TC, HDL, LDL	8 weeks	4	30-50	Stationary cycling	50-80% VO2peak
Kim et al. (2007)	n= 26; 17; obese boys	SBP, DBP, TC, HDL, LDL	6 weeks	5	40	Jump rope	
Kim et al. (2019)	n= 48; I: 15, C: 15; girls	SBP, DBP	12 weeks	5	50	Jump rope	40-70% HRR

Continued... **Study**	**Sample; Age at baseline; Sex**	**Outcomes**	**Follow-up duration**	**Weekly training frequency**	**Session duration (min)**	**Physical exercise**	**Intensity**
Knox et al. (2012)	n= 182; I: 12.4, C: 12.1; boys and girls	SBP, DBP, TC, HDL, LDL	18 weeks	2	60	Brisk walking	
Larsen et al. (2018)	n= 291; I: 9.3, C: 9.3; boys and girls	SBP, DBP	10 weeks	3	40	Small-sided ball games, mainly football	
Lee et al. (2010)	n= 54; 12-14 ; obese boys and girls	baPWV, SBP, TC, LDL	10 weeks	3	60	Soccer, basketball, football, baseball, hockey, badminton, healthrobics, rope skipping, and mountain climbing	60-80% VO2max
Martínez-Vizcaíno et al. (2008)	n= 1,044; I: 9.4/9.4, C: 9.5/9.4; boys/girls	SBP, DBP, TC	24 weeks	3	90	Sports with alternative equipment (pogo sticks, frisbees, jumping balls, parachutes, and so on), cooperative games, dance, recreational athletics, and muscular strength exercises	Moderate
Martínez-Vizcaíno et al. (2014)	n= 712; I: 9.4/9.4, C: 9.5/9.4; boys/girls	LDL	9 months	3	90 and 150 min	Basic sports games, tradicional games, and other outdoor activities such as cycling or gymkhanas	Moderate-vigorous
Martínez-Vizcaíno et al. (2022)	n= 562; I: 9.89/10.03, C: 10.12/10.04; boys/girls	SBP, DBP, TC, HDL, LDL, WtHR	8 months	4	53	Traditional games	Vigorous

Continued... **Study**	**Sample; Age at baseline; Sex**	**Outcomes**	**Follow-up duration**	**Weekly training frequency**	**Session duration (min)**	**Physical exercise**	**Intensity**
McMurray et al. (2002)	n= 1,140; I: 12.3, C: 12.1; boys and girls	SBP, DBP	8 weeks	3	30	Minisoccer, cone soccer, adapted handball, three-aside basketball, floor hockey, keep-away soccer, aerobic tag, fast pass, and partner's strength and endurance circuit, among others.	90-100% MAS, about 80-90% HRmax
Meng et al. (2022)	n= 45; I: 11.4, C:11; obese boys	SBP, DBP, TC, HDL, LDL	12 weeks	3	11	Running	
Norris et al. (1992)	n= 60; I: 16.7, C: 16.7; boys and girls	SBP, DBP	10 weeks	2	25-30	Aerobic exercise to music.	70-75% HRmax
Oliveira et al. (2021)	n= 21; I: 13.3, C: 13.2; boys	SBP, DBP	4 weeks	3	25	Running	90% MAS
Pahoo et al. (2020)	n= 45; I: 11.13, C: 11.2; overweight/obese boys and girls	HDL	12 weeks	3	45	Running	100-110% MAS
Patsopoulou et al. (2017)	n= 181; I: 14.04, C: 14.04; overweight/obese boys and girls	SBP, DBP	3 months	3	45	Team sports and running games	
Racil et al. (2013)	n= 34; I: 15.6, C: 15.9; obese girls	TC, HDL, LDL	12 weeks	3	20	Running	100-110% MAS

Continued… **Study**	**Sample; Age at baseline; Sex**	**Outcomes**	**Follow-up duration**	**Weekly training frequency**	**Session duration (min)**	**Physical exercise**	**Intensity**
Resaland et al. (2011)	n= 259; I: 9.2, C: 9.2; boys and girls	SBP, DBP	2 years	5	60	Running, relay racing, obstacle courses and various forms of active play of high-intensity nature	Moderate-vigorous
Resaland et al. (2017)	n= 259; I: 9.2, C: 9.2; boys and girls	SBP	2 years	5	~42	Ballgames, active play that included a variety of fun activities and games, gymnastics, running, relay racing, obstacle courses and jumping rope	Moderate-vigorous
Rosenkraz et al. (2012)	n= 18; I: 8.6, C: 9.6; boys and girls	SBP, DBP, TC, HDL, LDL	8 weeks	2	30	Running	100-130% MAS
Salcedo Aguilar et al. (2010)	n= 1,109; 9-11; boys/girls	SBP, DBP, TC	2 years	3	90	Sports with alternative equipment (pogo sticks, frisbees, jumping balls, small parachutes, etc)	
Seo et al. (2012)	n= 34; I: 14.7, C: 14.6; obese boys	TC, HDL, LDL	8 weeks	3	60	Yoga	40-60% HHR (heart-rate reserve)
Son et al. (2017)	n= 40; 15; obese prehypertensive girls	baPWV, SBP, DBP	12 weeks	3	60	Various exercises (strokes, jumps and jump rope) and badminton	40-70% HHR (heart-rate reserve)
Stoedefalke et al. (2000)	n= 38; 13-14; girls	TC, HDL, LDL	20 weeks	3	25	Treadmill running, cycle and rowing ergometry and stair stepping	75-85 Hrpeak
Sung et al. (2018)	n= 40; 15; obese prehypertensive girls	baPWV, SBP, DBP	12 weeks	5	50	Rope jumping	40-70% HHR (heart-rate reserve)

Continued... Study	Sample; Age at baseline; Sex	Outcomes	Follow-up duration	Weekly training frequency	Session duration (min)	Physical exercise	Intensity
Tsang et al. (2009)	n= 20; 13.1; overweight/obese boys and girls	TC, HDL, LDL, LDL	6 months	3	60	Kung fu	
van Biljon et al. (2018)	n= 109; 11.1; boys and girls	SBP, DBP,	5 weeks	3	23	Running	>80% predicted Hrmax
Vasconcellos et al. (2015)	n= 42; I: 14.1, C: 14.8; obese boys and girls	SBP, DBP, TC, HDL, LDL, WtHR	12 weeks	3	60	Soccer	
Wong et al. (2008)	n= 24; I: 13.8, C: 14.3; obese boys	SBP, DBP, TC, HDL, LDL, WtHR	12 weeks	2	45-62	Circuit based aerobic exercises, strength conditioning and/or resistance training, and game activities such as soccer, handball, stair-climbing exercises and other active recreational activities	50-85% predicted HRmax
Wong et al. (2018)	n= 30; I: 15.2, C:15.3; obese girls	baPWV	12 weeks	3	60	Various resistant band exercises (upper body: seated rows, biceps curl, shoulder flexion, elbow extension, and chest press; lower body: hip flexion, hip extension, calf raise, leg press, and squat) and treadmill walking	40-70% HHR (heart-rate reserve)

Continued... **Study**	**Sample; Age at baseline; Sex**	**Outcomes**	**Follow-up duration**	**Weekly training frequency**	**Session duration (min)**	**Physical exercise**	**Intensity**
Yu et al. (2016)	n= 38; I: 12.3, C:12.1; boys and girls	FMD, SBP, DBP, TC, HDL, LDL	10 weeks	2	55 min	Resistance training (elbow extension, elbow flexion, trunk extension, trunk flexion, shoulder press, knee extension, knee flexion, push ups, squats, incline dip, hip abduction, and hip adduction)	12 RM
Zehsaz et al. (2016)	n= 32; I: 10.8, C: 10.3; overweight/obese boys and girls	TC, HDL, LDL	16 weeks	2	60	Aerobic exercises, strength conditioning and/or resistance training, and game activities such as soccer, handball, stair-climbing exercises and other active recreational activities	50-85% predicted Hrmax
Zorba et al. (2011)	n= 40; 11; obese boys	TC, HDL, LDL	12 weeks	3	20-45	Walking and jogging	60-65% predicted HR

Abbreviations: ~: Approximately; C: Control group; DBP: Diastolic blood pressure; HDL: Low-density lipoprotein; HR_{max}: Maximum heart rate; HR_{peak}: Peak heart rate; HRR: Heart rate reserve; I: Intervention group; LDL: High-density lipoprotein; MAS: Maximal aerobic speed; N: Number of individuals; RM: Repetition maximum; SBP: Systolic blood pressure; TC: Total cholesterol; V: Velocity; VO_{2max}: Maximum oxygen consumption; WtHR: Waist-to-height ratio

3. CONSIDERAÇÕES FINAIS

O presente estudo traz algumas contribuições importantes para a literatura. Além de terem sido encontrados efeitos positivos do exercício físico supervisionado e estruturado sobre a saúde cardiometabólica de crianças e adolescentes, foi possível identificar que algumas variáveis possuem efeito moderador sobre esses resultados. Através de subanálises, fatores como sexo, idade cronológica, IMC, tipo de exercício e a duração da intervenção podem influenciar os parâmetros de saúde cardiometabólica. Em contrapartida, foi possível visualizar que alguns fatores não são moderadores dos resultados, como a duração das sessões e a frequência semanal de treinamento, ou seja, realizar o exercício físico mais ou menos vezes na semana e com duração de sessão menores ou maiores do que 60 minutos, não parece influenciar os resultados das variáveis analisadas. Um ponto forte do presente estudo foi o rigor metodológico da metanálise, que seguiu orientações de diretrizes internacionais, a fim de fortalecer os resultados encontrados. Destacamos também a importância da participação de investigadores cegados na seleção dos estudos, evitando o viés nesta seleção. Como diferencial dos estudos incluídos nesta revisão, podemos destacar o fato de que, para serem incluídos, os mesmos deveriam apresentar intervenções somente com exercício físico, não podendo incluir intervenções associadas, como orientações nutricionais ou palestras de estilo de vida saudável. Neste sentido, os efeitos positivos do exercício físico sobre os indicadores de saúde cardiometabólica identificados no presente estudo não sofreram efeito de interferência de outras intervenções. Por fim, é importante ressaltar que ainda há uma grande necessidade de serem avaliados os parâmetros de saúde de crianças e adolescentes, principalmente na função endotelial e rigidez arterial, pois há poucos estudos que abordam estas variáveis. Contudo, é importante que estas pesquisas tenham metodologias bem delineadas, principalmente quanto às descrições do treinamento/intervenção, para que os resultados dos estudos sejam mais confiáveis e possíveis de serem reproduzidos.

4. REFERÊNCIAS

ARAÚJO, C. Fisiologia do exercício físico e hipertensão arterial: uma breve introdução. **Revista Hipertensão**, 4, n. 3, p. 5, 2001.

ASHWELL, M.; GUNN, P.; GIBSON, S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. **Obes Rev**, 13, n. 3, p. 275-286, Mar 2012.

BAGHERSALIMI, M.; FATHI, R.; KAZEMI, S. The effect of eight-week walking program on plasma levels of amino acids in early/mid pubertal obese girls. **Med J Islam Repub Iran**, 33, p. 128, 2019.

BHARATH, L. P.; CHOI, W. W.; CHO, J. M.; SKOBODZINSKI, A. A. *et al*. Combined resistance and aerobic exercise training reduces insulin resistance and central adiposity in adolescent girls who are obese: randomized clinical trial. **Eur J Appl Physiol**, 118, n. 8, p. 1653-1660, Aug 2018.

BONETTI, P. O.; LERMAN, L. O.; LERMAN, A. Endothelial dysfunction: a marker of atherosclerotic risk. **Arterioscler Thromb Vasc Biol**, 23, n. 2, p. 168-175, Feb 1 2003.

BUCHAN, D. S.; OLLIS, S.; THOMAS, N. E.; BUCHANAN, N. *et al*. Physical activity interventions: effects of duration and intensity. **Scand J Med Sci Sports**, 21, n. 6, p. e341-350, Dec 2011.

BUCHAN, D. S.; OLLIS, S.; YOUNG, J. D.; COOPER, S. M. *et al*. High intensity interval running enhances measures of physical fitness but not metabolic measures of cardiovascular disease risk in healthy adolescents. **BMC Public Health**, 13, p. 498, May 24 2013.

BULL, F. C.; AL-ANSARI, S. S.; BIDDLE, S.; BORODULIN, K. *et al*. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. **Br J Sports Med**, 54, n. 24, p. 1451-1462, Dec 2020.

BUSNATU, S. S.; SERBANOIU, L. I.; LACRARU, A. E.; ANDREI, C. L. *et al*. Effects of Exercise in Improving Cardiometabolic Risk Factors in Overweight Children: A Systematic Review and Meta-Analysis. **Healthcare (Basel)**, 10, n. 1, Jan 1 2022.

CANAS, J. A.; SWEETEN, S.; BALAGOPAL, P. B. Biomarkers for cardiovascular risk in children. **Curr Opin Cardiol**, 28, n. 2, p. 103-114, Mar 2013.

CANDELINO, M.; TAGI, V. M.; CHIARELLI, F. Cardiovascular risk in children: a burden for future generations. **Ital J Pediatr**, 48, n. 1, p. 57, Apr 11 2022.

CECILIATO, J.; COSTA, E. C.; AZEVEDO, L.; SOUSA, J. C. *et al*. Effect of Resistance Training on Arterial Stiffness in Healthy Subjects: A Systematic Review and Meta-Analysis. **Curr Hypertens Rep**, 22, n. 8, p. 51, Jul 15 2020.

CELERMAJER, D. S. S., K. E. Gooch, V. M. Spiegelhalter, D. J. Miller, O. I.

Sullivan, I. D. Lloyd, J. K. Deanfield, J. E. Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. **Lancet**, 7, n. 340(8828), p. 1111-1115, 1992.

CHEN, T.; LIN, J.; LIN, Y.; XU, L. *et al*. Effects of aerobic exercise and resistance exercise on physical indexes and cardiovascular risk factors in obese and overweight school-age children: A systematic review and meta-analysis. **PLoS One**, 16, n. 9, p. e0257150, 2021.

CHEN, X.; WANG, Y. Tracking of blood pressure from childhood to adulthood: a systematic review and meta-regression analysis. **Circulation**, 117, n. 25, p. 3171-3180, Jun 24 2008.

CHENG, Y.; SUN, Z.; YA, X.; ZHOU, L. *et al*. Effect of exercise training on arterial stiffness in obese and overweight children: a meta-analysis. **Eur J Pediatr**, 181, n. 7, p. 2633-2642, Jul 2022.

CHIA, P. Y.; TEO, A.; YEO, T. W. Overview of the Assessment of Endothelial Function in Humans. **Front Med (Lausanne)**, 7, p. 542567, 2020.

CHUENSIRI, N.; SUKSOM, D.; TANAKA, H. Effects of High-Intensity Intermittent Training on Vascular Function in Obese Preadolescent Boys. **Child Obes**, 14, n. 1, p. 41-49, Jan 2018.

COCKCROFT, J. R.; WILKINSON, I. B.; WEBB, D. J. The Trevor Howell Lecture. Age, arterial stiffness and the endothelium. **Age Ageing**, 26 Suppl 4, p. 53-60, Dec 1997.

COOK, S.; KAVEY, R. E. Dyslipidemia and pediatric obesity. **Pediatr Clin North Am**, 58, n. 6, p. 1363-1373, ix, Dec 2011.

CORNELISSEN, V. A.; SMART, N. A. Exercise training for blood pressure: a systematic review and meta-analysis. **J Am Heart Assoc**, 2, n. 1, p. e004473, Feb 1 2013.

CORREIA, M. L.; HAYNES, W. G. Arterial compliance and endothelial function. **Curr Diab Rep**, 7, n. 4, p. 269-275, Aug 2007.

CVETKOVIC, N.; STOJANOVIC, E.; STOJILJKOVIC, N.; NIKOLIC, D. *et al*. Exercise training in overweight and obese children: Recreational football and high-intensity interval training provide similar benefits to physical fitness. **Scand J Med Sci Sports**, 28 Suppl 1, p. 18-32, Aug 2018.

DA SILVA, M. R.; WACLAWOVSKY, G.; PERIN, L.; CAMBOIM, I. *et al*. Effects of high-intensity interval training on endothelial function, lipid profile, body composition and physical fitness in normal-weight and overweight-obese adolescents: A clinical trial. **Physiol Behav**, 213, p. 112728, Jan 1 2020.

DA SILVA, R. S. N.; DA SILVA, D. S.; WACLAWOVSKY, G.; SCHAUN, M. I. Effects of aerobic, resistance, and combined training on endothelial function and arterial stiffness in older adults: study protocol for a systematic review and meta-analysis. **Syst Rev**, 11, n. 1, p. 171, Aug 13 2022.

DE FERRANTI, S. D.; STEINBERGER, J.; AMEDURI, R.; BAKER, A. *et al*. Cardiovascular Risk Reduction in High-Risk Pediatric Patients: A Scientific Statement From the American Heart Association. **Circulation**, 139, n. 13, p. e603-e634, Mar 26 2019.

DELGADO-FLOODY, P.; ESPINOZA-SILVA, M.; GARCIA-PINILLOS, F.; LATORRE-ROMAN, P. Effects of 28 weeks of high-intensity interval training during physical education classes on cardiometabolic risk factors in Chilean schoolchildren: a pilot trial. **Eur J Pediatr**, 177, n. 7, p. 1019-1027, Jul 2018.

DIAS, K. A.; GREEN, D. J.; INGUL, C. B.; PAVEY, T. G. *et al*. Exercise and Vascular Function in Child Obesity: A Meta-Analysis. **Pediatrics**, 136, n. 3, p. e648-659, Sep 2015.

DOBASHI, K. Changes in Serum Cholesterol in Childhood and its Tracking to Adulthood. **J Atheroscler Thromb**, 29, n. 1, p. 5-7, Jan 1 2022.

ELKA, K. R., M.; Winata, J.; Pangemanan, J.; Panda, AL. . The Pulse Wave Velocity is Linearly Correlated with Resting Systolic and Diastolic Blood Pressure in Hypertensive Patients. **Indonesian Journal of Cardiology**, 39, p. 15-21, 2018.

EMERGING RISK FACTORS, C.; DI ANGELANTONIO, E.; SARWAR, N.; PERRY, P. *et al*. Major lipids, apolipoproteins, and risk of vascular disease. **JAMA**, 302, n. 18, p. 1993-2000, Nov 11 2009.

EWART, C. K.; YOUNG, D. R.; HAGBERG, J. M. Effects of school-based aerobic exercise on blood pressure in adolescent girls at risk for hypertension. **Am J Public Health**, 88, n. 6, p. 949-951, Jun 1998.

FALUDI AA, I. M., Saraiva JFK, Chacra APM, Bianco HT, Afiune AN, et al. . Atualização da Diretriz Brasileira de Dislipidemias e Prevenção da Aterosclerose. **Arquivos Brasileiros de Cardiologia**, 2, 109, p. 76, 2017.

FARIA, W. F.; MENDONCA, F. R.; SANTOS, G. C.; KENNEDY, S. G. *et al*. Effects of 2 Methods of Combined Training on Cardiometabolic Risk Factors in Adolescents: A Randomized Controlled Trial. **Pediatr Exerc Sci**, 32, n. 4, p. 217-226, Jul 31 2020.

FARPOUR-LAMBERT, N. J.; AGGOUN, Y.; MARCHAND, L. M.; MARTIN, X. E. *et al*. Physical activity reduces systemic blood pressure and improves early markers of atherosclerosis in pre-pubertal obese children. **J Am Coll Cardiol**, 54, n. 25, p. 2396-2406, Dec 15 2009.

FLYNN, J. T.; KAELBER, D. C.; BAKER-SMITH, C. M.; BLOWEY, D. *et al*. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. **Pediatrics**, 140, n. 3, Sep 2017.

GODO, S.; SHIMOKAWA, H. Endothelial Functions. **Arterioscler Thromb Vasc Biol**, 37, n. 9, p. e108-e114, Sep 2017.

GRACE, J.; BIGGS, C.; NAICKER, A.; MOSS, S. Effect of Physical Activity and Nutrition Education on Body Mass Index, Blood Pressure and Biochemical Variables in Overweight and Obese Adolescents. **Ann Glob Health**, 87, n. 1, p. 9, Jan 25 2021.

GREEN, D. J.; MAIORANA, A.; O'DRISCOLL, G.; TAYLOR, R. Effect of exercise training on endothelium-derived nitric oxide function in humans. **J Physiol**, 561, n. Pt 1, p. 1-25, Nov 15 2004.

HANSSEN, H. Vascular biomarkers in the prevention of childhood cardiovascular risk: From concept to clinical implementation. **Front Cardiovasc Med**, 9, p. 935810, 2022.

HANSSEN, H.; BOARDMAN, H.; DEISEROTH, A.; MOHOLDT, T. *et al*. Personalized exercise prescription in the prevention and treatment of arterial hypertension: a Consensus Document from the European Association of Preventive Cardiology (EAPC) and the ESC Council on Hypertension. **Eur J Prev Cardiol**, 29, n. 1, p. 205-215, Feb 19 2022.

HARA, M.; SAITOU, E.; IWATA, F.; OKADA, T. *et al*. Waist-to-height ratio is the best predictor of cardiovascular disease risk factors in Japanese schoolchildren. **J Atheroscler Thromb**, 9, n. 3, p. 127-132, 2002.

HO, M.; GARNETT, S. P.; BAUR, L.; BURROWS, T. *et al*. Effectiveness of lifestyle interventions in child obesity: systematic review with meta-analysis. **Pediatrics**, 130, n. 6, p. e1647-1671, Dec 2012.

HORNER, K.; KUK, J. L.; BARINAS-MITCHELL, E.; DRANT, S. *et al*. Effect of Aerobic versus Resistance Exercise on Pulse Wave Velocity, Intima Media Thickness and Left Ventricular Mass in Obese Adolescents. **Pediatr Exerc Sci**, 27, n. 4, p. 494-502, Nov 2015.

IBORRA, R. T.; RIBEIRO, I. C.; NEVES, M. Q.; CHARF, A. M. *et al*. Aerobic exercise training improves the role of high-density lipoprotein antioxidant and reduces plasma lipid peroxidation in type 2 diabetes mellitus. **Scand J Med Sci Sports**, 18, n. 6, p. 742-750, Dec 2008.

INABA, Y.; CHEN, J. A.; BERGMANN, S. R. Prediction of future cardiovascular outcomes by flow-mediated vasodilatation of brachial artery: a meta-analysis. **Int J Cardiovasc Imaging**, 26, n. 6, p. 631-640, Aug 2010.

JI, F.; NING, F.; DUAN, H.; KAPRIO, J. *et al*. Genetic and environmental influences on cardiovascular disease risk factors: a study of Chinese twin children and adolescents. **Twin Res Hum Genet**, 17, n. 2, p. 72-79, Apr 2014.

JUONALA, M.; VIIKARI, J. S.; RAITAKARI, O. T. Main findings from the prospective Cardiovascular Risk in Young Finns Study. **Curr Opin Lipidol**, 24, n. 1, p. 57-64, Feb 2013.

KAHN, H. S.; IMPERATORE, G.; CHENG, Y. J. A population-based comparison of BMI percentiles and waist-to-height ratio for identifying cardiovascular risk in youth. **J Pediatr**, 146, n. 4, p. 482-488, Apr 2005.

KARACABEY, K. The effect of exercise on leptin, insulin, cortisol and lipid profiles in obese children. **J Int Med Res**, 37, n. 5, p. 1472-1478, Sep-Oct 2009.

KELLEY, G. A.; KELLEY, K. S.; PATE, R. R. Exercise and Cardiovascular Disease Risk Factors in Children and Adolescents With Obesity: A Systematic Review With Meta-Analysis of Randomized Controlled Trials. **Am J Lifestyle Med**, 16, n. 4, p. 485-510, Jul-Aug 2022.

KELLY, A. S.; WETZSTEON, R. J.; KAISER, D. R.; STEINBERGER, J. *et al*. Inflammation, insulin, and endothelial function in overweight children and adolescents: the role of exercise. **J Pediatr**, 145, n. 6, p. 731-736, Dec 2004.

KHAN, N. A.; HEMMELGARN, B.; HERMAN, R. J.; BELL, C. M. *et al*. The 2009 Canadian Hypertension Education Program recommendations for the management of hypertension: Part 2--therapy. **Can J Cardiol**, 25, n. 5, p. 287-298, May 2009.

KIM, E. S.; IM, J. A.; KIM, K. C.; PARK, J. H. *et al*. Improved insulin sensitivity and adiponectin level after exercise training in obese Korean youth. **Obesity (Silver Spring)**, 15, n. 12, p. 3023-3030, Dec 2007.

KIM, H. L.; KIM, S. H. Pulse Wave Velocity in Atherosclerosis. **Front Cardiovasc Med**, 6, p. 41, 2019.

KIM, J.; SON, W. M.; HEADID III, R. J.; PEKAS, E. J. *et al*. The effects of a 12-week jump rope exercise program on body composition, insulin sensitivity, and academic self-efficacy in obese adolescent girls. **J Pediatr Endocrinol Metab**, 33, n. 1, p. 129-137, Jan 28 2020.

KISELEVA, R. Y.; GLASSMAN, P. M.; GREINEDER, C. F.; HOOD, E. D. *et al*. Targeting therapeutics to endothelium: are we there yet? **Drug Deliv Transl Res**, 8, n. 4, p. 883-902, Aug 2018.

KNOX, G. J.; BAKER, J. S.; DAVIES, B.; REES, A. *et al*. Effects of a novel school-based cross-curricular physical activity intervention on cardiovascular disease risk factors in 11- to 14-year-olds: the activity knowledge circuit. **Am J Health Promot**, 27, n. 2, p. 75-83, Nov-Dec 2012.

KULSUM-MECCI, N.; GOSS, C.; KOZEL, B. A.; GARBUTT, J. M. *et al*. Effects of Obesity and Hypertension on Pulse Wave Velocity in Children. **J Clin Hypertens (Greenwich)**, 19, n. 3, p. 221-226, Mar 2017.

LAURENT, S.; COCKCROFT, J.; VAN BORTEL, L.; BOUTOUYRIE, P. *et al*. Expert consensus document on arterial stiffness: methodological issues and clinical applications. **Eur Heart J**, 27, n. 21, p. 2588-2605, Nov 2006.

LEE, Y. H.; SONG, Y. W.; KIM, H. S.; LEE, S. Y. *et al*. The effects of an exercise program on anthropometric, metabolic, and cardiovascular parameters in obese children. **Korean Circ J**, 40, n. 4, p. 179-184, Apr 2010.

LITWIN, M. Why should we screen for arterial hypertension in children and adolescents? **Pediatr Nephrol**, 33, n. 1, p. 83-92, Jan 2018.

MADRUGA, J. G.; MORAES SILVA, F.; SCHERER ADAMI, F. Positive association between waist-to-height ratio and hypertension in adolescents. **Rev Port Cardiol**, 35, n. 9, p. 479-484, Sep 2016.

MARTINEZ-VIZCAINO, V.; SORIANO-CANO, A.; GARRIDO-MIGUEL, M.; CAVERO-REDONDO, I. *et al*. The effectiveness of a high-intensity interval games intervention in schoolchildren: A cluster-randomized trial. **Scand J Med Sci Sports**, 32, n. 4, p. 765-781, Apr 2022.

MENG, C.; YUCHENG, T.; SHU, L.; YU, Z. Effects of school-based high-intensity interval training on body composition, cardiorespiratory fitness and cardiometabolic markers in adolescent boys with obesity: a randomized controlled trial. **BMC Pediatr**, 22, n. 1, p. 112, Mar 1 2022.

MICHIELS, C. Endothelial cell functions. **J Cell Physiol**, 196, n. 3, p. 430-443, Sep 2003.

MORTENSEN, M. B.; NORDESTGAARD, B. G. Elevated LDL cholesterol and increased risk of myocardial infarction and atherosclerotic cardiovascular disease in individuals aged 70-100 years: a contemporary primary prevention cohort. **Lancet**, 396, n. 10263, p. 1644-1652, Nov 21 2020.

MUCKA, S.; MIODONSKA, M.; JAKUBIAK, G. K.; STARZAK, M. *et al*. Endothelial Function Assessment by Flow-Mediated Dilation Method: A Valuable Tool in the Evaluation of the Cardiovascular System. **Int J Environ Res Public Health**, 19, n. 18, Sep 7 2022.

ORGANIZATION, W. H. **Obesity and overweight**. 2021. Disponível em: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.

PAGAN, L. U.; GOMES, M. J.; OKOSHI, M. P. Endothelial Function and Physical Exercise. **Arq Bras Cardiol**, 111, n. 4, p. 540-541, Oct 2018.

PAINI, A.; BOUTOUYRIE, P.; CALVET, D.; TROPEANO, A. I. *et al*. Carotid and aortic stiffness: determinants of discrepancies. **Hypertension**, 47, n. 3, p. 371-376, Mar 2006.

PESCATELLO, L. S.; FRANKLIN, B. A.; FAGARD, R.; FARQUHAR, W. B. *et al*. American College of Sports Medicine position stand. Exercise and hypertension. **Med Sci Sports Exerc**, 36, n. 3, p. 533-553, Mar 2004.

POZUELO-CARRASCOSA, D. P.; CAVERO-REDONDO, I.; HERRÁIZ-ADILLO, A.; DÍEZ-FERNÁNDEZ, A. *et al*. School-Based Exercise Programs and Cardiometabolic Risk Factors: A Meta-analysis. **Pediatrics**, e20181033, 142 (5), 2018.

REILLY, J. J.; JACKSON, D. M.; MONTGOMERY, C.; KELLY, L. A. *et al*. Total energy expenditure and physical activity in young Scottish children: mixed longitudinal study. **Lancet**, 363, n. 9404, p. 211-212, Jan 17 2004.

RODGERS, J. L.; JONES, J.; BOLLEDDU, S. I.; VANTHENAPALLI, S. *et al*. Cardiovascular Risks Associated with Gender and Aging. **J Cardiovasc Dev Dis**, 6, n. 2, Apr 27 2019.

RUIZ-RAMIE, J. J.; BARBER, J. L.; SARZYNSKI, M. A. Effects of exercise on HDL functionality. **Curr Opin Lipidol**, 30, n. 1, p. 16-23, Feb 2019.

SAVVA, S. C.; TORNARITIS, M.; SAVVA, M. E.; KOURIDES, Y. *et al*. Waist circumference and waist-to-height ratio are better predictors of cardiovascular disease risk factors in children than body mass index. **Int J Obes Relat Metab Disord**, 24, n. 11, p. 1453-1458, Nov 2000.

SERVICES, U. S. D. o. H. a. H. Physical Activity Guidelines for Americans. SERVICES, D. o. H. a. H. Washington. 2 2018.

SHIRWANY, N. A.; ZOU, M. H. Arterial stiffness: a brief review. **Acta Pharmacol Sin**, 31, n. 10, p. 1267-1276, Oct 2010.

SON, Y.; KIM, K.; JEON, S.; KANG, M. *et al*. Effect of Exercise Intervention on Flow-Mediated Dilation in Overweight and Obese Adults: Meta-Analysis. **Int J Vasc Med**, 2017, p. 7532702, 2017.

SOUZA JUNIOR, T. P.; ASANO, R. Y.; PRESTES, J.; SALES, M. M. *et al*. Óxido nítrico e exercício: uma revisão. **Revista da Educação Física/UEM**, 23, n. 3, 2012.

STANEK, A.; FAZELI, B.; BARTUS, S.; SUTKOWSKA, E. The Role of Endothelium in Physiological and Pathological States: New Data. **Biomed Res Int**, 2018, p. 1098039, 2018.

STEFAN, N.; SCHICK, F.; HARING, H. U. Causes, Characteristics, and Consequences of Metabolically Unhealthy Normal Weight in Humans. **Cell Metab**, 26, n. 2, p. 292-300, Aug 1 2017.

STRONG, J. P.; MCGILL, H. C., Jr. The pediatric aspects of atherosclerosis. **J Atheroscler Res**, 9, n. 3, p. 251-265, May-Jun 1969.

SUNG, K. D.; PEKAS, E. J.; SCOTT, S. D.; SON, W. M. *et al*. The effects of a 12-week jump rope exercise program on abdominal adiposity, vasoactive substances, inflammation, and vascular function in adolescent girls with prehypertension. **Eur J Appl Physiol**, 119, n. 2, p. 577-585, Feb 2019.

TOMIYAMA, H.; YAMASHINA, A. Ankle-Brachial Pressure Index and Pulse Wave Velocity in Cardiovascular Risk Assessment. *In*: **Encyclopedia of Cardiovascular Research and Medicine**, 2018. p. 111-122.

TOMKINSON, G. R.; LANG, J. J.; TREMBLAY, M. S. Temporal trends in the cardiorespiratory fitness of children and adolescents representing 19 high-income and upper middle-income countries between 1981 and 2014. **Br J Sports Med**, 53, n. 8, p. 478-486, Apr 2019.

TOWNSEND, R. R.; WILKINSON, I. B.; SCHIFFRIN, E. L.; AVOLIO, A. P. *et al*. Recommendations for Improving and Standardizing Vascular Research on Arterial

Stiffness: A Scientific Statement From the American Heart Association. **Hypertension**, 66, n. 3, p. 698-722, Sep 2015.

TRAN, A. H.; URBINA, E. M. Hypertension in children. **Curr Opin Cardiol**, 35, n. 4, p. 376-380, Jul 2020.

TSAO, C. W.; ADAY, A. W.; ALMARZOOQ, Z. I.; ALONSO, A. *et al*. Heart Disease and Stroke Statistics-2022 Update: A Report From the American Heart Association. **Circulation**, 145, n. 8, p. e153-e639, Feb 22 2022.

VLACHOPOULOS, C.; AZNAOURIDIS, K.; STEFANADIS, C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. **J Am Coll Cardiol**, 55, n. 13, p. 1318-1327, Mar 30 2010.

WA., B. Chapter 16 Blood Pressure. *In*: H. KENNETH WALKER, W. D. H. a. J. W. H. (Ed.). **Clinical Methods, 3rd edition**. Boston: Butterworth Publishers, 1990.

WALLACE, B. C., Dahabreh, I. J., Trikalinos, T. A., Lau, J., Trow, P., & Schmid, C. H. Closing the Gap between Methodologists and End-Users: R as a Computational Back-End. **Journal of Statistical Software**, 49, n. 5, p. 1-15, 2012.

WEBER, T.; AMMER, M.; RAMMER, M.; ADJI, A. *et al*. Noninvasive determination of carotid-femoral pulse wave velocity depends critically on assessment of travel distance: a comparison with invasive measurement. **J Hypertens**, 27, n. 8, p. 1624-1630, Aug 2009.

WONG, A.; SANCHEZ-GONZALEZ, M. A.; SON, W. M.; KWAK, Y. S. *et al*. The Effects of a 12-Week Combined Exercise Training Program on Arterial Stiffness, Vasoactive Substances, Inflammatory Markers, Metabolic Profile, and Body Composition in Obese Adolescent Girls. **Pediatr Exerc Sci**, 30, n. 4, p. 480-486, Nov 1 2018.

YIMING, G.; ZHOU, X.; LV, W.; PENG, Y. *et al*. Reference values of brachial-ankle pulse wave velocity according to age and blood pressure in a central Asia population. **PLoS One**, 12, n. 4, p. e0171737, 2017.

YU, C. C.; MCMANUS, A. M.; SO, H. K.; CHOOK, P. *et al*. Effects of resistance training on cardiovascular health in non-obese active adolescents. **World J Clin Pediatr**, 5, n. 3, p. 293-300, Aug 8 2016.

ZEHSAZ, F.; FARHANGI, N.; GHAHRAMANI, M. Exercise training lowers serum chemerin concentration in obese children. **Science & Sports**, 32, n. 1, p. 39-45, 2017.

ZHANG, Y.; QI, L.; XU, L.; SUN, X. *et al*. Effects of exercise modalities on central hemodynamics, arterial stiffness and cardiac function in cardiovascular disease: Systematic review and meta-analysis of randomized controlled trials. **PLoS One**, 13, n. 7, p. e0200829, 2018.

ZIEMAN, S. J.; MELENOVSKY, V.; KASS, D. A. Mechanisms, pathophysiology, and therapy of arterial stiffness. **Arterioscler Thromb Vasc Biol**, 25, n. 5, p. 932-943, May 2005.