Int J Cardiovasc Sci. 2022; 35(3), 304-315

ORIGINAL ARTICLE

Physical Activity and Cardiovascular Risk Factors in Children: A Meta-Analysis Update

Claudia Ciceri Cesa,[1] Gabriela Oliveira Gonçalves Molino,[2] Júlia Lima,[2] Raquel Barbiero Pereira,[4] Bruna Eibel,[3] Sandra Mari Barbiero,[3] Beatriz D. Schaan,[4,5] Lucia Campos Pellanda[2,3]

Instituto Federal Sul-rio-grandense – DEPEP,[1] Sapucaia do Sul, RS –Brazil
Universidade Federal de Ciências da Saúde de Porto Alegre,[2] Porto Alegre, RS – Brazil
Instituto de Cardiologia - Fundação Universitária de Cardiologia,[3] Porto Alegre, RS – Brazil
Universidade Federal do Rio Grande do Sul,[4] Porto Alegre, RS – Brazil
Hospital de Clínicas de Porto Alegre,[5] Porto Alegre, RS – Brazil

Abstract

Background: Obesity and overweight in childhood can increase the risk of developing cardiovascular disease throughout live.

Objectives: This study provides an update of a meta-analysis of randomized clinical trials (RCT) published in 2014, to assess the effects of physical activity interventions on preventing cardiovascular risk factors in childhood.

Methods: This update combines data from the previous search with new data obtained from June 2013 to June 2020. Searches were performed on PubMed, EMBASE and Cochrane CENTRAL. The RCTs enrolled used interventions with physical activity longer than six months in school children aged 6-12 years, and evaluated body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), triglyceride (TG), and low-density lipoprotein (LDL) and high-density lipoprotein (HDL) levels. Data analysis was performed using a random-effects model and a P value <0.05 was considered statistically significant.

Results: A total of 28,603 articles were retrieved, and 17 RCTs (11,952 subjects) were included. Physical activity interventions were associated with reduction in SBP [−2.11mmHg (95%CI −3.67, −0.54), $I^2$43%], DBP [−2.08mmHg (95%CI −3.68, −0,49), $I^2$65%] and TG [-0.08mmol/L (95% CI -0.13, -0.03), $I^2$0%], and increase in TC [0.17mmol/L (95%CI 0.04, 0.30), $I^2$0%]. However, the interventions were not associated with reductions in BMI [−0.03 kg/m^2 (95%CI −0.17, 0.10), $I^2$0%].

Conclusion: This update confirms and reinforces the beneficial effects of physical activity intervention in reducing systolic and diastolic blood pressure and TG levels.

Keywords: Children; Cardiovascular Diseases; Risk Factors; Physical, Activity Exercise, Public Health, Stress Test, Sports.

Introduction

The prevalence of overweight and obesity in childhood has increased in the last decade, being characterized as an alarming problem in developed and developing countries.[1,2] Obesity is an important public health challenge, and its long-term consequences are well established.[3] Overweight and obese children are likely to become obese adults. Also, they are at higher risk for developing chronic diseases such as high blood pressure, type 2 diabetes, cardiovascular disease, obstructive sleep apnea, breathing disorders, osteoarthritis and cancer.[4,5]

Thus, interventions during childhood might be beneficial to prevent these risks. The regular practice of physical activity in the long term is associated with improvement in body composition, with reduction of total and central adiposity, which contributes to a better blood pressure control, improvement of lipid and cardiorespiratory profiles,[6,7] and prevention of several chronic diseases.[8] Additionally, there is a

Mailing Address: Claudia Ciceri Cesa
Instituto Federal de Educação, Ciência e Tecnologia Sul-Rio-Grandense - IFSul Campus Sapucaia do Sul
Avenida Copacabana, 100. Postal Code: 93216-120, Sapucaia do Sul, RS - Brazil.
Email: claudia.c.cesa@gmail.com

DOI: https://doi.org/10.36660/ijcs.20210137

Manuscript received April 28, 2021; revised manuscript July 14, 2021; accepted August 13, 2021.

growing body of scientific evidence that recommends the practice of physical activity and points out the risks of sedentary behaviors.[9]

In a previous meta-analysis published in 2014,[10] our group demonstrated that physical activity was associated with a reduction in triglycerides and blood pressure levels in school children and suggested that physical activity programs aiming at cardiovascular prevention should be stimulated in this population. Since the publication of this review, other clinical trials have been published. Therefore, this update aims to discuss recent evidence of mid-term effects of physical activity.

Methods

This systematic review is an update of the review published in 2014. All included studies in the 2014 review were considered in this update, in addition to studies published between 01 June 2013 and 15 June 2020. Details of our previous systematic review can be found in Cesa et al.,[10] all steps were performed according to the Cochrane Collaboration[11] and the Preferred Reporting Items for Systematic Review and Meta-analyses: the PRISMA Statement.[12]

Eligibility criteria

Eligible studies were randomized clinical trials (RCTs) with students aged from 6 to 12 years old, submitted to a single or main intervention of supervised physical activity. Population criteria were school children irrespective of body weight (normal-weight, overweight and obese). Interventions were exercises with a minimum of 150 minutes per week for at least 6 months. A control group with no intervention or undergoing lower-intensity exercise (e.g., ordinary physical education classes with a duration of less than 150 minutes per week) should be included. A minimum target of 150 minutes per week was chosen as it is the amount of physical activity a person should engage in to be considered physically active.[13,14] The variables included in the protocol were risk factors for the development of cardiovascular disease: systolic and diastolic blood pressure (SBP and DBP, respectively), body mass index (BMI), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), fasting glucose and C-reactive protein (CRP).

To be included in the protocol, the RCT should meet the inclusion criteria and have at least one of the primary or secondary outcomes. The authors whose articles did not present the size of the intervention effect in the experimental and control group were contacted by e-mail in the attempt of obtaining missing information. In case of unsuccess, the studies were excluded. Studies with nutritional intervention were included only if the physical activity was the main intervention. For articles from multiple publications, the most recent publication was included, the previous ones were used for complementary information.

Information sources

The online databases searched were MEDLINE (accessed by PubMed), EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL). The following terms were used: “obesity”, “overweight”, “child nutrition disorders", "child", "school", "student", "exercise", "exercise therapy", "exercise movement techniques", "motor activity", "sports", "physical education and training", in addition to a highly sensitive strategy for the search for randomized clinical trials.[15] The search strategy for PUBMED is shown in Appendix I. The authors searched and verified reference lists of systematic reviews and previously published meta-analysis to identify primary studies. This review had no language restrictions.

Study selection and data extraction

For this update, titles and abstracts of all articles identified by the search strategy were evaluated by three independent researchers in duplicate (B.E, C.C.C. and S.M.B). Those abstracts that did not provide enough information about inclusion and exclusion criteria were selected for a full-text evaluation. Disagreements between reviewers were evaluated by a third reviewer and solved by consensus (L.C.P). The outcomes extracted were: BMI (Kg/m^2– weight in kilograms divided by the square of the height in meters), SBP and DBP (mmHg), TC and triglycerides (TG) (mmol/L), HDL-c and LDL-c (mmol/L).

Assessment of risk of bias

To assess the internal quality of the studies, we evaluated each RCT according to the Cochrane Collaboration’s tool for assessing risk of bias.[16] To be considered of good quality, the studies needed to present

a clear description of the generation of suitable sequences, including description of the allocation concealment, blinding of the researcher, participants, assessors and evaluators of results, analysis of intention-to-treat and description of losses and exclusions. Concealed allocation was considered if the terms were described as "central", "web-based" or "telephone randomization", or full explanation. For the intention-to-treat analysis, the number of randomized participants and the number of patients analyzed should be the same; exceptions were patients who were lost to follow-up or asked to leave the study (they withdrew their consent). Three reviewers independently performed a quality assessment and, for each criterion, the studies were classified as adequate, not adequate or unclear/unreported.

Data analysis

All analyses were conducted using Review Manager version 5.3 (Cochrane Collaboration). For continuous outcomes, if the unit of measurement was consistent across trials, results were presented as weighted mean difference, with 95% confidence intervals (CIs). Pooled-effect estimates were obtained using the final values.[17] Calculations were performed using a random-effect model and the statistical method used was inverse variance. Statistical heterogeneity of the treatment effects among studies was assessed using the Cochran's Q test and the inconsistency I^2 test, and values above 25% and 50% were considered indicative of moderate and high heterogeneity, respectively.[18]

Sensitivity analysis was performed to evaluate differences in the intervention approach (intervention group: physical education classes + physical exercise program; control group: physical education classes or other types of intervention approaches). Heterogeneity between studies was also evaluated in terms of intensity and duration of the intervention and follow-up. A p-value < 0.05 was considered statistically significant. Funnel plots were constructed to assess the risk of publication bias (Appendix II).

Results

Description of studies

In our previous systematic review,[10] 23,091 potentially relevant citations were retrieved and from June 2014 to June 2020 another 5,512 articles were identified (total 28,603). Six studies met the inclusion criteria, which were added to the previous 11 selected,[10] resulting in 17 studies included in this paper. Figure 1 shows the diagram flow of the studies in this review. Table 1 summarizes the characteristics of all studies (Appendix III).

Risk of bias

Of the six included studies, 47% had adequate sequence generation, 35% reported adequate allocation concealment, 29% reported adequate blinding of clinical assessors, 71% performed intention-to-treat analyses and 94% described losses to follow-up exclusions. Table 2 describes the risk of bias of the studies (Appendix IV).

Effects of the interventions

Body mass index

Of 17 studies, 13 [Vandongen et al.,[19] Barbeau et al.,[20] Donnelly et al.,[21] Kriemler et al.,[22] Li et al.,[23] Faude et al.,[24] Jansen et al., Thivel et al.,[26] Weintraub et al.,[27] Martínez-Vizcaíno et al.,[28] Naiman et al.,[29] Jones et al.,[30] Sacchetti et al.,[31] n = 11,952, evaluated BMI. Physical activity interventions were not associated with changes in BMI when compared to less intensive physical activity interventions or no intervention (Figure 2), similarly to what was observed previously.[10]

Lipid profile

Total cholesterol, cholesterol fractions and triglycerides

Three studies [Vandongen et al.,[19] Walther et al.,[32] Jones et al.,[30], n = 499, evaluated TC. Physical activity interventions were associated with TC increase when compared to less intensive or no intervention (Figure 3), which is not different from previous findings.[10] Two studies , Jones et al.,[30] Muller et al.,[33] evaluated LDL-c (n = 287) and HDL-c (n = 328). Physical activity interventions were not associated with changes in LDL-c or in HDL-c when compared to less intensive or no intervention (Figure 3). Triglycerides were evaluated in four [Kriemler et al.,[22] Walther et al., [32] Jones et al., 2015; [30] Muller et al.,[33] studies (n = 981). Physical activity interventions were associated with reductions in TG when compared to less intensive physical activity interventions or no intervention, similarly to what was previously shown.[10] (Figure 3)

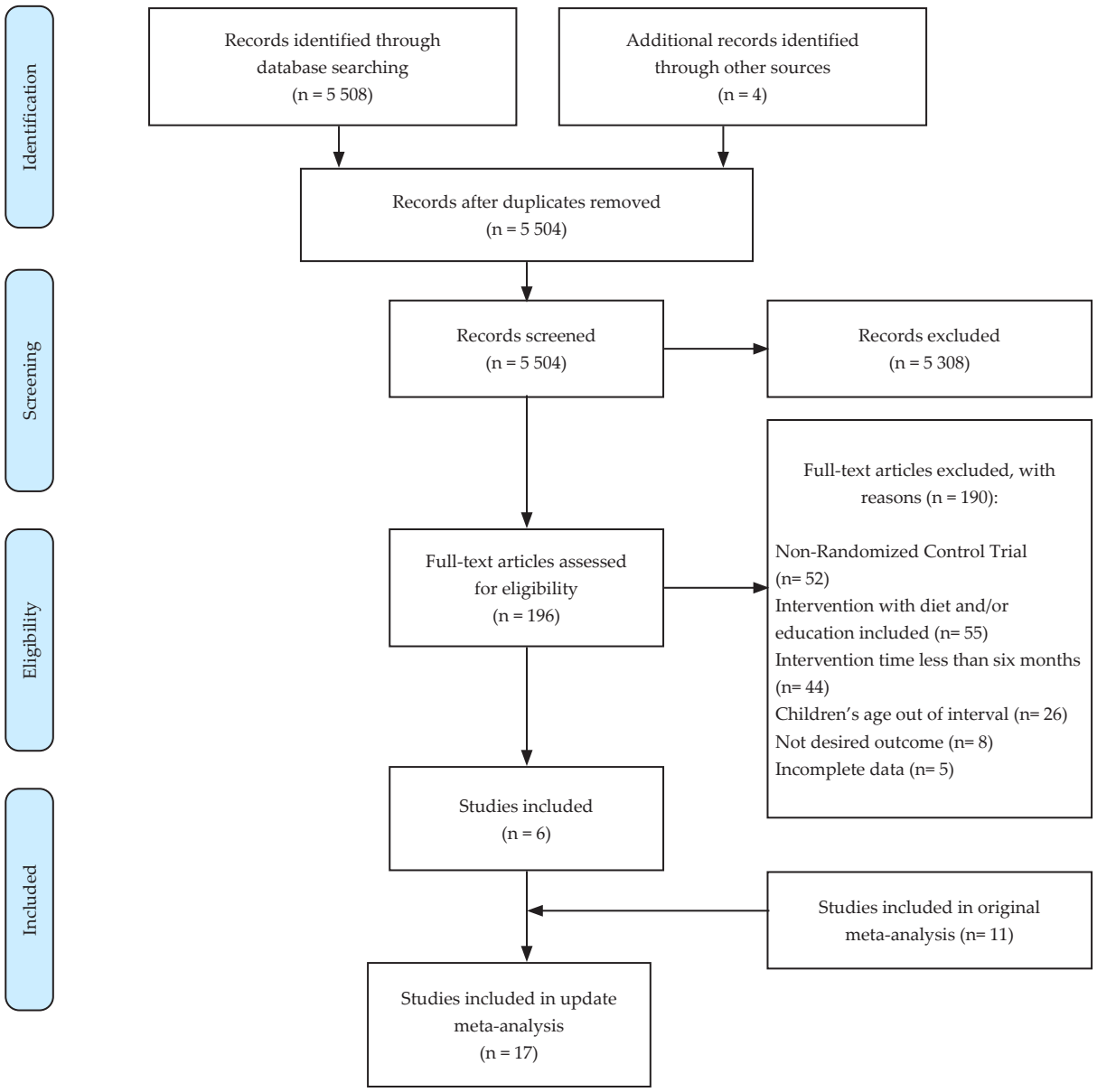

Figure 1 – Flow diagram of included studies

Blood pressure

Systolic and diastolic blood pressure

Six studies [Vandongen et al.,[19] Kriemler et al.,[22] Walther et al.,[34] Jones et al., [20] Muller et al.,[33] Aguilar-Cordero et al.,[35] n = 1,489, evaluated SBP and five studies [Vandongen et al.,[19] Kriemler et al.,[22] Walther et al.,[34] Jones et al.,[30] and Aguilar-Cordero et al.,[36] n = 1,170, evaluated DBP. Physical activity interventions were associated with reductions in SBP and DBP when compared to less intensive physical activity interventions or no intervention (Figure 4). These results are not different from the previous data.[10]

Discussion

The present study is the first update, since 2014, of the systematic review with meta-analysis including RCTs in children submitted to interventions involving physical exercises of at least six months' duration, differing from other systematic reviews[36,37] published

Appendix III – Table 1 – Characteristics of included studies[1]

Study, year	Randomized patients (n) intervention/ control	Participants	Intervention group	Control group	Intervention duration	Outcome measures
Vandongen et al., 1995	158/145	School children	Six times per week (30 minutes each) classroom sessions replacing the usual curriculum	Regular curriculum	9 months	Body mass index, systolic blood pressure, diastolic blood pressure, total cholesterol, triglycerides
Barbeau et al., 2007;	118/83	School children (black girls)	Physical education classes plus 110 minutes of out-of-school physical activity	Regular physical education classes	1 school year	Body mass index
Weintraub et al., 2008	09/12	School children	Out-of-school sports program	Traditional health education	6 months	Body mass index
Donnelly et al., 2009	814/713	School children and parents	Physical education classes (60 minutes per week) plus 90 minutes per week of moderate to vigorous physically active academic lessons (3.0–6.0 metabolic equivalents of task (MET), 10 min each) delivered intermittently throughout the school day	Regular physical education classes	3 years	Body mass index
Walther et al., 2009	105/56	School children and parents	45 minutes of physical education classes per school day	Two physical education classes per week (45 minutes each)	1 school year	Total cholesterol, triglycerides
Faude et al., 2010	11/11	Overweight children	One hour football training 3 times per week (1 hour each)	Standard sports program	6 months	Body mass index
Kriemler et al., 2010	297/205	School children	Five physical education lessons per week	Three physical education lessons per week	12 months	Body mass index, systolic blood pressure, diastolic blood pressure, total cholesterol, triglycerides
Li et al., 2010	2329/2371	School children	Two daily 10-min physical activity sessions conducted in the break between classes	No intervention. (Regular physical education classes and after-school activities)	1 school year	Body mass index

Jansen et al., 2011	1240/1382	School children	Three physical education classes per week plus additional sports and play activities outside school hours (voluntary)	Two physical education classes	8 months	Body mass index
Thivel et al., 2011	229/228	Lean and obese school children	Two physical education classes per week plus 2 times additional exercise classes (2 times, 60 minutes each = 120 minutes per week)	Two physical education classes per week	6 months	Body mass index
Walther et al., 2011	141/91	School children	One hour of regulated sports activities, including 15 minutes of endurance training five times a week	One hour of current sports activity two times a week	2 school years	Systolic blood pressure, diastolic blood pressure
Martínez-Vizcaíno et al., 2014	420/492	School children	Two 90-minute physical activity sessions during the weekdays in the evening from 4 to 5.30 pm and one 150-minute session on Saturday morning each week	Conventional physical education curriculum	9 months	Body mass index
Sacchetti et al., 2014	212/216	School children	30-minute physical exercise daily	Regular physical education classes	2 years	Body mass index
Naiman et al., 2014	110/110	School children	Two hours of out-of-school physical activities five times per week	Regular after school routine	9 months	Body mass index
Muller et al., 2015	202/164	School children	60 minutes of physical exercise at school daily (5 hours per week)	Two physical education classes (45 minutes each) weekly	4 years	Systolic blood pressure, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides
Jones et al, 2015	19/18	School children	90 minutes of physical exercise twice a week	45 min week	7 months	Body mass index, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol
Aguilar-Cordero et al., 2019	49/49	Overweight and obese children	A program of games based on physical activity, with four 90-minute sessions per week during the nine months of the school year, plus theoretical-practical sessions on nutrition	Only received theoretical-practical sessions on nutrition	9 months	Systolic blood pressure, diastolic blood pressure

Note: A p<0.05 was considered statistically significant in all included studies

Table 2 – Risk of bias of included studies

Study, year	Adequate sequence generation	Allocation concealment	Blinding of investigator	Blinding of participant	Blinding of assessors	Blinding of outcome assessors	Intention-to-treat analysis	Description of losses and exclusions
Vandongen et al., 1995	Not reported	Not reported	Not reported	Not reported	Yes	Unclear	No	Yes
Barbeau et al., 2007	Not reported	Unclear	Not reported	Not reported	Not reported	Not reported	Yes	Yes
Weintraub et al., 2008	Yes	Unclear	No	No	No	Not reported	Yes	Yes
Donnelly et al., 2009	Not reported	Unclear	No	No	Yes	Not reported	Not reported	Yes
Walther et al., 2009	Not reported	Unclear	No	No	Yes	Not reported	Yes	Yes
Faude et al., 2010	Yes	Not reported	Not reported	Not reported	Not reported	Not reported	No	Yes
Kriemler et al., 2010	Yes	Adequate	No	No	Yes	Not reported	Yes	Yes
Li et al., 2010	Yes	Not reported	Not reported	Not reported	Not reported	Not reported	No	Yes
Jansen et al., 2011	Yes	Not reported	No	No	No	No	Yes	No
Thivel et al., 2011	Not reported	Not reported	Not reported	Yes	Not reported	Not reported	Yes	Yes
Walther et al., 2011	Not reported	Adequate	No	No	No	Not reported	No	Yes
Martínez-Vizcaíno et al., 2014	Yes	Adequate	No	Not reported	No	Not reported	Yes	Yes
Sacchetti et al., 2014	Not reported	Not reported	No	Not reported	Not reported	Not reported	Yes	Yes
Naiman et al., 2014	Not reported	Adequate	No	No	No	No	Yes	Yes
Muller et al., 2015	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Yes	Yes
Jones et al, 2015	Yes	Adequate	No	Not reported	Yes	Not reported	Yes	Yes
Aguilar-Cordero et al., 2019	Yes	Adequate	No	No	Not reported	Not reported	Yes	Yes

after the original meta-analysis.[10] As in the original publication, we found that the interventions proposed in the RCTs included in this update were not associated with any change in the BMI. Data were extracted from four of the five new articles involving BMI measures included in the update. Muller et al.,[33] used BMI in percentile and not in kg/m², so their study was not included.

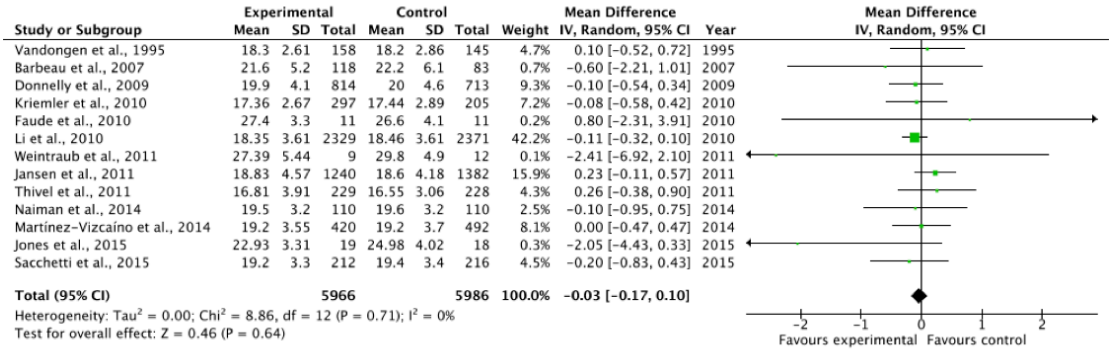

Figure 2 – Absolute changes in body mass index (BMI, kg/m²) for physical activity intervention vs. controls.
CI: confidence interval; SD: standard deviation. Weights are from random-effects analysis.

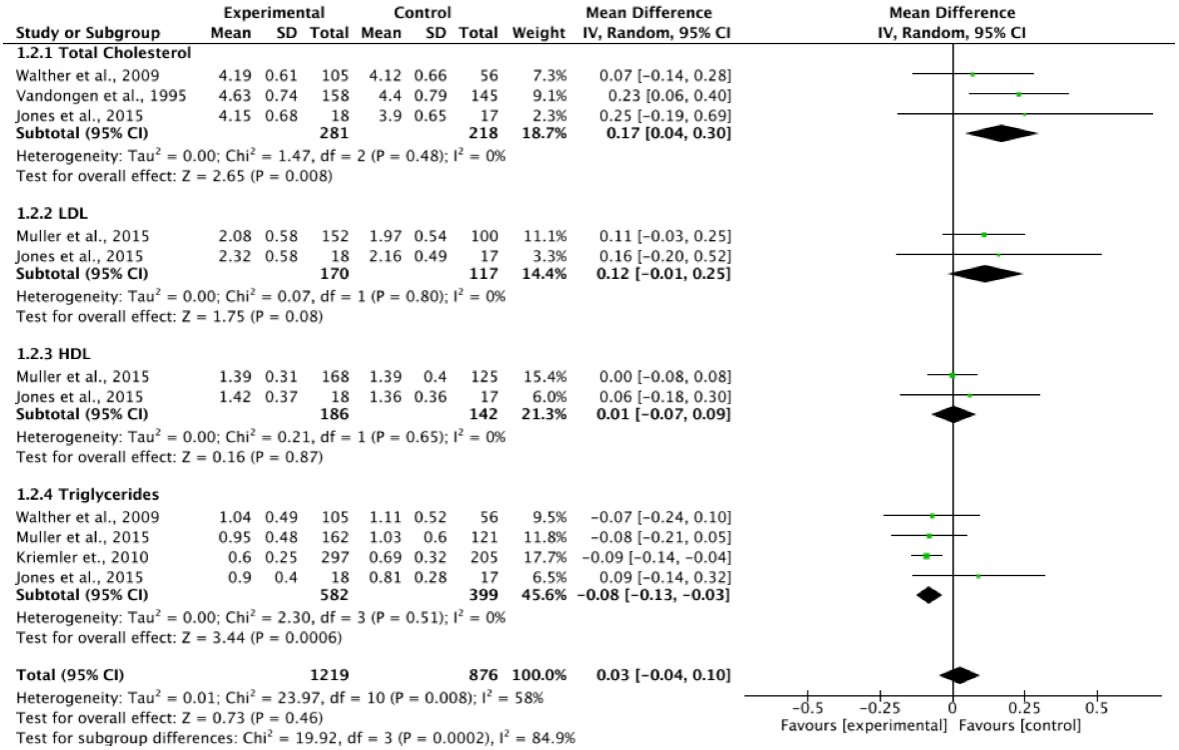

Figure 3 – Absolute changes in total cholesterol, LDL-c, HDL-c and triglycerides (mmol/L) for physical activity intervention vs. controls.
CI: confidence interval; SD: standard deviation. Weights are from random-effects analysis.

Brannsether et al.,[38] evaluated differences in BMI in children aged 0-19 years for one year (The Bergen Growth Study). BMI increased slightly and with small variations during childhood, reaching the highest values at 13 years of age and decreasing in older children (the number of children aged 6-14 years was 1,167). It was pointed out that there was a higher prevalence of overweight and obesity in children aged 7-11 years and that these

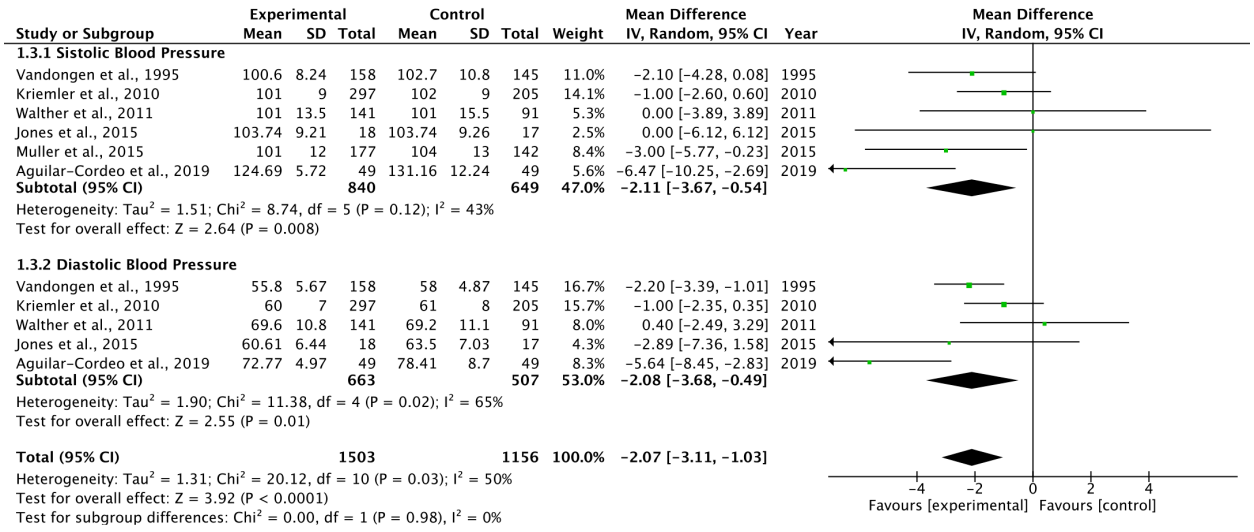

Figure 4 – Absolute changes in systolic and diastolic blood pressure (mmHg) for physical activity intervention vs. controls.
CI: confidence interval; SD: standard deviation. Weights are from random-effects analysis.

children may, for a period, be taller than those with adequate weight. Therefore, the relationship between weight and height does not change significantly until the child's growth rate decreases. In line with our original publication, it is necessary to reaffirm that BMI is not the best parameter to measure the effect of interventions performed in the clinical trials of this systematic review, precisely because an increase in the index is expected during the studied age range. In addition, only four new studies were added the original analysis of BMI, adding a total of 1,597 children to that of the original publication (n = 10,355). Thus, the observations made in the original review that there was little difference between the control and intervention groups are still valid, since all control groups received regular physical education classes whereas the intervention groups underwent additional exercise sessions. Moreover, to obtain more powerful results in reducing weight in overweight and obese children it is of utmost importance the combination of nutritional interventions (healthier eating habits and choices, lower caloric intake, etc). In this regard, Verjans-Janssen et al. conducted a systematic review of 18 studies where different approaches (physical activity, nutrition, diet, parental involvement and others) were used; 11 studies showed favorable results for BMI, six reported no change and one showed a negative outcome.[39] That review brought results of BMI's reduction, but, again, the review includes studies on combinations of multiple interventions, which differs from the current study where only studies on single physical activity interventions were included.

In addition, the present investigation corroborated the inverse relationship between blood pressure and physical activity in children and adolescents, as presented in our first review [11] and other studies.[40,41] Normal levels of blood pressure were expected as a result of improvement in cardiorespiratory fitness.[40] We may hypothesize that this positive effect may be carried into adulthood, and contribute to cardiovascular risk prevention, since we know that these risk factors (physical inactivity, increased blood pressure and excess weight) start in childhood and may persist throughout life. Furthermore, these positive findings may also indicate a protective role of these factors for hypertension in adults.[41] Liu et al.,[42] in a longitudinal cohort study with adult participants in the Bogalusa Heart Study, who had been followed since childhood, demonstrated that the increase in BMI in childhood and adulthood and its overload throughout life are significantly associated with arterial stiffness in young adults, triggered by an increasing trend of hypertension.[42]

In 2014, we reported that more physical activity in children was associated with a reduction in TG and an increase in TC.[11] For the new included outcomes LDL-c and HDL-c, the RCTs analyzed in this review did not

show significant results, which can be justified by the small number of individuals evaluated. The only lipid component that showed positive repercussions after intervention with physical activity was TG. These results are in line with another meta-analysis that evaluated physical activity intervention in overweight children and adolescents.[43] High levels of TG are an independent risk factor for coronary heart disease, for their potential atherogenic effects.[44] Thus, the results demonstrated in the present study corroborate the importance of the practice of physical activity as a non-pharmacological measure to control elevations in TG levels. Unlike our findings, another systematic review with meta-analysis[45] involving children and adolescents between two and 17 years of age, demonstrated that exercise is associated with LDL-c reduction. However, the authors pointed out that greater reductions in LDL-c were associated with an older age of the adolescents, which could justify the difference in relation to our study, where children between 6 and 12 years were included.

The conflicting results between physical exercise and repercussions on HDL-c levels were also highlighted in another systematic review.[46] Stoner et al.,[47] carried out a meta-analysis to assess the effects of physical exercise on cardiometabolic risk factors in adolescents with overweight or obesity and demonstrated no changes in HDL-c levels, in accordance with the present study. Longer periods of intervention with physical activity may be necessary, and aerobic exercise is more beneficial in comparison to regular strength training to improve blood lipids.[47] In disagreement with the present study, Costa et al.,[45] demonstrated in a meta-analysis that supervised physical training was associated with a reduction in TC levels compared to no intervention. However, the authors showed that the longer the duration of the follow-up, the smaller the reductions, due to the adaptation of the TC levels. This inverse association could justify the absence of changes in TC levels in the present study, considering that only interventions of at least six months' duration were included. In addition, it is well-known that the peak of TC curves in healthy children aged between 9 and 10 years is approximately 15 mg/dL higher than in younger children and adolescents.[48] Considering that in the study by Costa et al.[45] the sample had a wider age range (between 2 and 17 years), it may not have been sensitive to possible associations between age groups and borderline cholesterol values .

This systematic review has limitations due to the poor methodological quality of the included studies. The absence of blinding can be considered one of the greatest limitations among these studies, although it is usual in non-pharmacological studies. Studies that involve physical activities and no pharmacological intervention have limitations regarding learning curves, introduction and stabilization of the intervention, and combination of other interventions that do not assess physical activity. However, the interventions used in the selected papers were similar, providing strength for the analysis of several components even in a small sample. In our first[10] and in the current systematic review, several studies have been excluded due to the lack of description of the interventions, resulting in a reduced number of RCTs included and of outcomes analyzed. However, considering that these physical activity interventions are of low cost and risk, the positive findings, in favor of the interventions, should be worthy of consideration even in a small sample.

Finally, this systematic review with meta-analysis has strengths that should be mentioned. The process of article selection was conducted with strict criteria, namely RCTs, studies with an intervention period longer than six months (27 weeks), and with outcomes already mentioned in our previous systematic review additionally to HDL-c and LDL-c. In addition, children and adolescents were included regardless of baseline BMI, and the original language of the studies was not considered as an exclusion criterion.

Conclusions

This update confirms the previous findings of the beneficial effects of physical activity interventions of at least six months' duration in reducing SBP, DBP, as well as TG levels. Although no changes in other cardiovascular risk factors (BMI, TC, HDL-c and LDL-c) were detected, we believe that regular physical activity classes in schools must still be encouraged as a way of preventing diseases and promoting health for children and adolescents, primarily during pubertal development and, later, for consolidation of healthy habits throughout life.

Acknowledgements

We were thankful for general support of National Council for Scientific and Technological Development -

CNPq, Rio Grande do Sul Research Foundation (Fundação de Apoio à Pesquisa do Estado do Rio Grande do Sul – FAPERGS) and Institute of Cardiology Research Foundation (Fundo de Apoio do Instituto de Cardiologia/FUC à Ciência e Cultura – FAPICC).

Author contributions

Conception and design of the research: Cesa CC, Barbiero S, Schaan BD, Pellanda LC. Acquisition of data: Cesa CC, Molino G, Lima J, Pereira R, Eibel B, Barbiero S, Pellanda LC. Analysis and interpretation of the data: Cesa CC, Molino G, Lima J, Pereira R, Eibel B, Barbiero S, Schaan BD, Pellanda LC. Statistical analysis: Cesa CC. Writing of the manuscript: Cesa CC, Molino G, Lima J, Pereira R, Eibel B, Barbiero S, Pellanda LC. Critical revision of the manuscript for intellectual content: Cesa CC, Molino G, Lima J, Pereira R, Eibel B, Barbiero S, Schaan BD, Pellanda LC.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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