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Review

Exercise, health outcomes, and pædiatric obesity: A systematic review of meta-analyses

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ABSTRACT

Objectives: This study is a systematic review of meta-analyses that have addressed the effects of exercise-based interventions alone and the health outcomes (anthropometric, body composition, cardiometabolic, hepatic, vascular, and cardiorespiratory fitness parameters) in overweight and obese children and adolescents.
Design: Systematic review of meta-analysis.
Methods: Six electronic sources were searched. The inclusion criteria were: children and/or adolescents classified as overweight or obese, and previous systematic reviews and meta-analyses that included exercise interventions compared to a control group. Standardized mean differences, risk of bias, heterogeneity, and small-study effects were calculated. Subgroup analyses (intervention characteristics) were done.
Results: Eighteen meta-analyses met the inclusion criteria. The results showed improvements in some anthropometric and body composition (body mass, BMI, BMI z-score, central obesity, fat mass) and cardiometabolic (TG, fasting glucose, fasting insulin) parameters, and in cardiorespiratory fitness. For the cardiometabolic and vascular parameters, aerobic programs and interventions showed themselves to be effective if they were of four to 12 weeks, or involved a total exercise time of at least 1500 min, or involved sessions of at least 60 min.
Conclusions: The study provides indications of the appropriate dose of exercise with which to reduce health problems in the obese young population.

1. Introduction

The alarming worldwide growth of the conditions of overweight and obesity has become a major public health concern negatively affecting national health systems,[1] not only in adults,[2] but also in children and adolescents.[3] Pædiatric obesity is often carried over into adulthood[4] and is associated with adverse outcomes which include metabolic, cardiovascular, musculoskeletal, neurological, gastrointestinal, respiratory, and psychosocial disturbances,[5,6] and premature all-cause mortality.[7] The childhood obesity epidemic has been associated with obesogenic factors such as an intake of energy-dense diets, and a sedentary lifestyle with low levels of physical activity.[8] It has been suggested that exercise may play a pivotal role in treating overweight and obese children and adolescents.[9] Despite the massive amount of information regarding its benefits, generalizable conclusions that can be drawn from studies of the impact of exercise on obesity remain elusive. Sometimes, the different meta-analyses report disparate results or they only analyse a particular parameter without presenting an overview of the effects of the intervention. Very often too, they provide no specific dose-response guidelines (i.e., duration, time and number of sessions, etc.) that might be used in future interventions.

Abbreviations: PRISMA, Primary Reporting Items for Systematic Reviews and Meta-analyses; SMD, standardized mean differences; AMSTAR, Assessment of Multiple Systematic Reviews; RCTs, randomized clinical trials; BMI, body mass index; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment insulin resistance; HDL-C, high-density lipoprotein cholesterol; FMD, flow-mediated dilation; NADPH, nicotinamide adenine dinucleotide phosphate; ATP, adenosine triphosphate; cGMP, cyclic guanosine monophosphate; eNOS, endothelial nitric oxide synthase; PPAR, peroxisome proliferator-activated receptor; VLDL, very-low-density lipoprotein.

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The treatment of childhood and adolescent obesity is an active area of research.[10] Given this proliferation of systematic reviews and meta-analyses on the same topic, systematic reviews of meta-analyses could be considered to be a good alternative for determining the efficacy and effectiveness of various treatments on selected outcomes.[11] As far as we know, there has only been one systematic review of meta-analyses about exercise and childhood obesity, reporting that exercise is effective in reducing body fat percentage in overweight and obese children and adolescents, but that there is insufficient evidence that exercise reduces other measures of adiposity.[10] However, this study only analysed body composition outcomes, and did not take into account other important health parameters. On the other hand, there have been several meta-analyses that have studied the effects of exercise-based interventions on health parameters, but there has been no work attempting to provide a synthesis of this evidence.[10,12] A systematic review of meta-analyses involving different health-related parameters should help clarify both what have been the patterns of physical exercise interventions and what effects those interventions have had. In this way, specific recommendations could be made that are based on a synthesis of the scientific evidence. Therefore, the aim of the current study was to conduct a systematic review of previous meta-analyses that had addressed the effects of exercise-based interventions alone (without hypocaloric diet intervention) and the health outcomes (anthropometry, body composition, and cardiometabolic, hepatic, vascular, and cardiorespiratory fitness parameters) in overweight and obese children and adolescents.

2. Methods

This study was conducted and reported according to the general guidelines recommended by the Primary Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Statement (Supplementary file 1). The review was registered with PROSPERO CRD42017062400 at the University of York, United Kingdom.

Two researchers independently of each other (AG-H and RR-V) selected the studies. Discrepancies about study conditions were resolved through discussion. The inclusion criteria followed the PICO framework in which the PICO acronym stands for: P — patient, problem, or population; I — intervention; C — comparison, control, or comparator; O — outcome. In particular, the inclusion criteria were: children and/or adolescents classified as overweight or obese (P, population), and previous systematic reviews with meta-analyses that included structured exercise interventions (without hypocaloric diet intervention) (I, intervention) compared to a control group (non-intervention, attention control, usual care, or placebo) (C, comparison) and that analysed some health outcome (O, outcome). Meta-analyses were accepted which used studies that might combine programs of physical exercise with nutritional recommendations. Any meta-analyses that did not meet all of the above criteria were excluded from our review.

The searches covered documents in English published until 30th April 2017. Only articles in journals were accepted. The following electronic sources were searched: CINAHL, EMBASE, ERIC, MEDLINE (PubMed and OvidSP), PsycINFO, and Science Citation Index. The key terms used were: ["*Obesity*" OR "*Overweight*"] AND ["*Exercise*" OR "*Physical activity*" OR "*Intervention*"]. Also, the following limiters were used: age (children and adolescents of 6–18 years in age) and publication type (systematic review and meta-analysis).

We used a data-abstraction form to gather information about published meta-analyses and to examine their quality. Two researchers (AG-H and RR-V) coded all the studies independently of each other in a spreadsheet. We established a priori the information of interest to collect from each meta-analysis — authors and year, objective of the study, number and characteristics of the participants (age, overweight and obesity classification, ethnicity), number of individual studies, characteristics of the exercise, inclusion of studies with behavioural-nutritional programs as well as scheduled physical exercise, and the main outcome.

Data were extracted regarding the number of participants, type of exercise programs, assessments, results of primary outcome (standardized mean difference [SMD]), risk of bias, heterogeneity, small-study effects, and methodological quality. When the SMD was unavailable, it was calculated from the weighted mean difference[13–18] or we made a request to each of the corresponding authors asking for SMD data. We used the Hedges'g SMD to homogenize all the results on the same scale, and pooled the results when there were two or more studies for a parameter, using a random-effects model. Also, the authors conducted their own meta-analyses based on the available outcome results of the individual studies nested within each meta-analysis included. Care was taken to avoid duplication, i.e., results of the same study reported in two or more different meta-analyses. Only data reported in the retrieved meta-analyses was included, i.e., not that of the original studies.[19] Subgroup analyses were conducted to determine whether exercise effects differed according to duration of study (4–12 weeks or >12 weeks), frequency of exercise (≤3 times/week or >3 times/week), duration of session (<60 min or ≥60 min), total exercise time (i.e., duration of study · session frequency · duration of session) (<1500 min or ≥1500 min) and type of exercise (aerobic, resistance, or concurrent). The cut-off points referring to the duration of study, frequency of exercise, duration of session, and total exercise time were chosen for their frequent use in meta-analyses whose target populations are obese children and young people.[13,20–22] For this, the individual results of each meta-analysis were taken for each parameter of interest. They were then categorized according to their characteristics in terms of duration, frequency, and type of exercise. This subanalysis was performed by extracting the individual data from each meta-analysis. In one case, we did not receive a reply from the corresponding author,[16] so that we used the data from a previous article of the same characteristics and the same author to carry out the subgroup analyses.[18] Cohen's categories were used to evaluate the magnitude of Hedges'g (small if $0 \le |g| \le 0.5$; medium if $0.5 < |g| \le 0.8$; and large if $|g| > 0.8$).[23] Also, I^2 values of <25%, 25–50%, and >50% were considered to represent small, medium, and large amounts of heterogeneity.[24] Finally, results for small-study effects (i.e., publication bias) were calculated using the regression-intercept approach of Egger et al.[25] All analyses were carried out using the comprehensive meta-analysis computer program (2nd version, Biostat, Englewood, New Jersey, USA).

The methodological quality of the meta-analyses was assessed using the Assessment of Multiple Systematic Reviews (AMSTAR) instrument.[26] This technique sets 11 criteria as indicators of the quality of a meta-analysis according to the responses "yes", "no", "cannot answer", or "not applicable" (the response "cannot answer" is chosen when an item is relevant but not described). Two researchers independent of each other (AG-H and RR-V) assessed the methodological quality, and disagreements were resolved by consensus with the third researcher JMS.

Inter-rater reliability was analysed using the following equation for the kappa statistic: $\kappa = [\Pr(a) - \Pr(e)]/[1 - \Pr(e)]$, where Pr(a) is the relative observed agreement among raters, and Pr(e) is the hypothetical probability of chance agreement, using the observed data to calculate the probabilities of each observer randomly assigning each category.

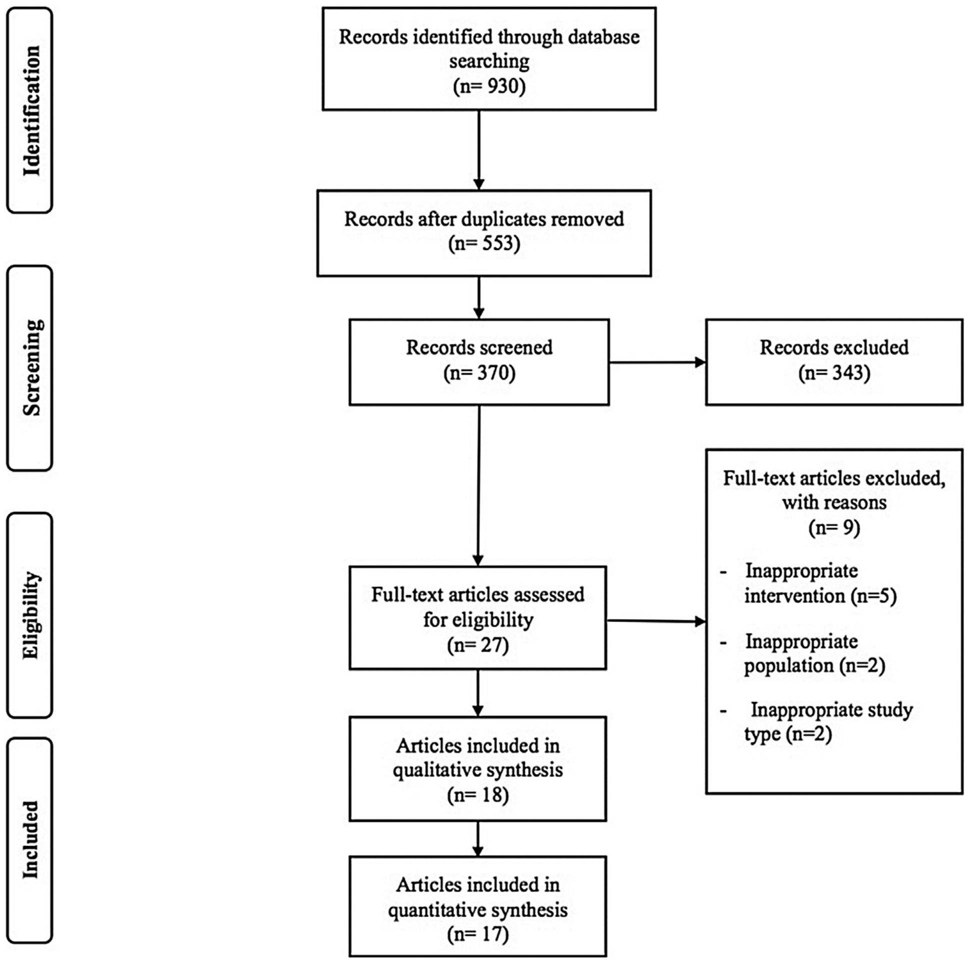

Fig. 1. Flow chart for identification of meta-analyses for inclusion in the present study.

3. Results

Of the 930 citations initially identified, 553 remained after removing duplicates. Of the 553 articles screened, the full text of 27 articles was retrieved and assessed for potential eligibility. Out of those, 9 did not fulfill the inclusion criteria: inappropriate intervention, inappropriate population, inappropriate study type, or data was duplicated in another study. The total number of papers included in the analysis was 18 (Fig. 1). The mean number of participants (children and adolescents) was 668 (standard deviation 506, maximum 2239, minimum 219). The studies were published in 16 different journals between 2006 and 2017. A list of the excluded studies accessed in full text form, including the reasons for exclusion, is given in Supplementary file 2.

A total of 234 studies were included in these 18 meta-analyses[13–18,20–22,27–35]; the numbers of studies that overlapped among the meta-analyses are given in Supplementary file 3.

The characteristics (interventions and outcomes) of the meta-analyses included are summarized in Supplementary file 4. There were three meta-analyses[16,18,30] that had as an inclusion criterion an age of 2–18 years, although the actual age range of the subjects of these studies was from 7.9 to 17.4 years old.

Most meta-analyses analysed included randomized clinical trials (RCTs) except for three[20–22] which included non-RCT but controlled trials. These meta-analyses had non-RCT studies with two[20,34] or more groups.[22] Regardless of the type of study (RCT, or RCT plus non-RCT), the meta-analyses were analysed conjointly.

The studies included overweight/obese,[13–18,27,30–35] only obese,[20,27,29] or only overweight[21,28] children and adolescents. The participants were children,[20,21,28] adolescents,[31,32] or both.[13–18,22,27,29–31,33–35]

The meta-analyses satisfied at least 7 AMSTAR criteria[20,21,31] and five satisfied all the criteria[15,16,18,34,35] (Supplementary file 5). Similarly, the questions with most negative responses (10 responses) were: “Was an a priori design provided?” and “Was a list of studies (both included and excluded) provided?”.

A description of the overall findings of each meta-analysis is given in Table 1. Forest plots are shown in Supplementary file 6. Effects of exercise (subanalysis) according to duration of study, session frequency, duration of session, and total exercise time are given in Table 2 and type of exercise is given in Supplementary file 7.

Table 1 presents a summary of the results. Pooling these body weight results, we found a small overall effect size ($g = -0.23$; 95% CI, −0.41 to −0.05; $p = 0.013$; $I^2 = 35.8\%$), with no small-study bias (Egger regression intercept = −1.92, 95% CI −3.19 to 0.12, $p = 0.052$). A reduction in BMI was observed in three meta-analyses,[15,31,32] with effect sizes from small ($g = -0.36$) to medium ($g = -0.78$) and heterogeneity from low ($I^2 = 0\%$) to high ($I^2 = 84.7\%$).[15] Pooling these BMI results, we found a medium overall effect size ($g = -0.50$; 95% CI, −0.70 to −0.30; $p = 0.006$; $I^2 = 77.5\%$) and no indication of small-study bias (Egger regression intercept = 2.16, 95% CI −3.89 to 0.43, $p = 0.158$). The pooled effect size of fat mass percentage was small ($g = -0.38$; 95% CI, −0.55 to −0.21; $p < 0.001$; $I^2 = 45.2\%$). There was no indication of small-study bias (Egger regression inter-

Table 1
Effects of exercise on anthropometric, body composition, cardiometabolic health, and physical fitness parameters.

Parameter	Type of exercise	Study (n)	Subjects (n)	Hedge's *g* (95% CI) [I^2 (%)]	Pooled[a]
Anthropometric and body composition parameters					
Body mass					
Atlantis et al.[27]	Without specification[b]	11	365	−0.21 (−0.49 to 0.07) [42.7%]	**−0.23 (−0.41 to −0.05) [35.8%]**
García-Hermoso et al.[14]	Combined	9	365	−0.31 (−0.66 to 0.04) [54.5%]	
Stoner et al.[32]	Without specification[b]	14	487	−0.21 (−0.14 to 0.56) [0%]	
Body mass index					
García-Hermoso et al.[14]	Combined	9	365	−0.28 (−0.61 to 0.04) [47.0%]	**−0.50 (−0.70 to −0.30) [77.5%]**
Kelley et al.[15]	Without specification[b]	20	971	**−0.78 (−1.13 to −0.43) [84.7%]**	
McGovern et al.[30]	Without specification[b]	11	433	−0.02 (−0.21 to 0.18) [0%]	
Ruotsalainen et al.[31]	Without specification[b]	7	217	**−0.36 (−0.64 to −0.08) [0%]**	
Stoner et al.[32]	Without specification[b]	22	554	**−0.36 (−0.08 to −0.65) [0%]**	
Body mass index z-score					
Kelley et al.[18]	Without specification[b]	10	835	**−0.51 (−0.68 to −0.34)** [25.9%]	
Kelley et al.[16]	Aerobic	20	1451	**−0.21 (−0.31 to −0.10)** [NR]	
Kelley et al.[16]	Strength	5	250	**−0.27 (−0.47 to −0.07)** [NR]	
Kelley et al.[16]	Combined	9	395	0.09 (−0.16 to 0.34) [NR]	
Central obesity					
Atlantis et al.[27]	Without specification[b]	5	156	−0.20 (−0.60 to 0.10) [0%]	**−0.20 (−0.41 to −0.01) [0%]**
García-Hermoso et al.[14]	Combined	3	195	−0.17 (−0.45 to 0.11) [0%]	
Fat mass (%)					
Atlantis et al.[27]	Without specification[b]	5	369	**−0.40 (−0.70 to −0.10) [48.4%]**	**−0.38 (−0.55 to −0.21) [45.2%]**
García-Hermoso et al.[14]	Combined	5	272	−0.48 (−1.01 to 0.04) [70.0%]	
McGovern et al.[30]	Without specification[b]	6	358	**−0.52 (−0.73 to −0.30) [0%]**	
Stoner et al.[32]	Without specification[b]	13	391	−0.16 (−0.13 to 0.44) [0%]	
Fat mass (kg)					
García-Hermoso et al.[14]	Combined	7	66	−0.47 (−1.51 to 0.57) [58.0%]	
Fat-free mass (kg)					
García-Hermoso et al.[14]	Combined	7	312	0.05 (−0.11 to 0.22) [28.0%]	0.005 (−0.18 to 0.19) [0%]
Stoner et al.[32]	Without specification[b]	12	324	0.03 (−0.14 to 0.45) [56.0%]	
Visceral fat					
González-Ruiz et al.[22]	Without specification[b]	15	1107	−0.66 (−0.97 to −0.35) [33.6%]	
Subcutaneous fat					
González-Ruiz et al.[22]	Without specification[b]	14	1072	−0.35 (−0.52 to −0.19) [36.8%]	
Cardiometabolic parameters					
High-density lipoprotein					
Escalante et al.[21]	Aerobic	5	260	0.12 (−0.37 to 0.13) [83.0%]	0.33 (−0.09 to 0.75) [74.9%]
Escalante et al.[21]	Combined	3	106	**0.50 (0.88–0.11) [0%]**	
Low-density lipoprotein					
Escalante et al.[21]	Aerobic	4	232	**−0.49 (−0.76 to −0.21) [87.0%]**	−0.43 (−1.01 to 0.15) [82.5%]
Escalante et al.[21]	Combined	2	62	0.08 (−0.42 to 0.58) [0%]	
Triglycerides					
Escalante et al.[21]	Aerobic	4	210	**−0.55 (−0.83 to −0.27) [76.0%]**	**−0.45 (−0.80 to −0.09) [59.3%]**
Escalante et al.[21]	Combined	3	106	−0.34 (−0.73 to 0.04) [0%]	
Total cholesterol					
Escalante et al.[21]	Aerobic	2	115	−0.15 (−0.52 to 0.22) [0%]	−0.56 (−1.12 to 0.01) [69.2%]
Escalante et al.[21]	Combined	2	62	0.17 (−0.33 to 0.67) [0%]	
Fasting glucose					
García-Hermoso et al.[28]	Aerobic	7	260	**−0.39 (−0.68 to −0.14) [19.0%]**	**−0.57 (−0.77 to −0.37) [32.9%]**
Marson et al.[33]	Aerobic	8	296	−0.35 (−0.90 to 0.19) [78.3%]	
Marson et al.[33]	Strength	4	96	−0.36 (−0.73 to 0.11) [64.5%]	
Marson et al.[33]	Combined	3	116	−0.36 (−1.62 to 0.90) [90.4%]	
Fasting insulin					
García-Hermoso et al.[28]	Aerobic	7	307	**−0.40 (−0.63 to −0.17) [0%]**	**−0.42 (−0.60 to −0.24) [28.0%]**
Marson et al.[33]	Aerobic	10	391	**−0.56 (−0.90 to −0.21) [60.2%]**	
Marson et al.[33]	Strength	4	96	−0.34 (−0.81 to 0.12) [17.4%]	
Marson et al.[33]	Combined	4	139	−0.41 (−0.89 to 0.07) [48.9%]	
HOMA-IR					
Marson et al.[33]	Aerobic	5	211	**−0.56 (−1.01 to −0.11) [55.2%]**	
C-reactive protein					
García-Hermoso et al.[13]	Without specification[b]	9	427	−0.33 (−0.72 to 0.06) [71.1%]	
Adiponectin					
García-Hermoso et al.[35]	Without specification[b]	10	246	**0.32 (0.02–0.63) [36.5%]**	
Leptin					
García-Hermoso et al.[35]	Without specification[b]	5	94	−0.43 (−0.91 to 0.05) [49.1%]	
Resistin					
García-Hermoso et al.[35]	Without specification[b]	2	39	−0.14 (−0.77 to 0.48) [0%]	
Hepatic parameters					
Aspartate aminotransferase					
González-Ruiz et al.[22]	Without specification[b]	4	254	−0.18 (−0.46 to 0.08) [5.2%]	
Alanine aminotransferase					
González-Ruiz et al.[22]	Without specification[b]	6	370	−0.15 (−0.40 to 0.11) [27.4%]	

Table 1 (*Continued*)

Parameter	Type of exercise	Study (n)	Subjects (n)	Hedge's *g* (95% CI) [I^2 (%)]	Pooled[a]
Gamma-glutamyl transferase					
González-Ruiz et al.[22]	Without specification[b]	2	78	**−0.73 (−1.20 to −0.25) [0%]**	
Intrahepatic fat					
González-Ruiz et al.[22]	Without specification[b]	5	155	**−0.80 (−1.12 to −0.48) [0%]**	
Vascular parameters					
Systolic blood pressure					
García-Hermoso et al.[29]	Without specification[b]	9	410	**−0.46 (−0.66 to −0.24) [27.0%]**	
Diastolic blood pressure					
García-Hermoso et al.[29]	Without specification[b]	7	254	**−0.28 (−0.55 to 0.00) [78.0%]**	
Flow-mediated dilation					
Dias et al.[17]	Without specification[b]	6	219	**0.55 (0.17–0.93) [51.0%]**	
Carotid intima-media thickness					
García-Hermoso et al.[34]	Without specification[b]	6	303	**−0.31 (−0.54 to −0.07) [47.3%]**	
Cardiorespiratory fitness					
Saavedra et al.[20]	Aerobic	6	203	**0.46 (0.12–0.79) [35.2%]**	**0.33 (0.09–0.57) [28.9%]**
Saavedra et al.[20]	Combined	4	146	0.15 (−0.17 to 0.48) [0%]	

Bold face text indicates $p < 0.05$.

[a] Pooled refers to totals avoiding double counting by excluding duplicated articles in each of the corresponding meta-analyses (see Supplementary file 6).

[b] These works do not specify the type of exercise included, but instead speak of exercise in general without making any distinction in terms of content.

cept = 1.42, 95% CI −3.24 to 0.39, p = 0.118). For central obesity (waist circumference and/or waist-to-hip ratio), there were two meta-analyses[27,28] giving a pooled small effect size (g = −0.20; 95% CI, −0.41 to −0.01; p = 0.047; I^2 = 0%) with no small-study bias (Egger regression intercept = 0.65, 95% CI −2.40 to 1.10, p = 0.385).

With respect to the subgroup analysis, aerobic programs achieved small improvements in all parameters (medium improvements in BMI, g = −0.64, and visceral fat, g = −0.80) except for central obesity and fat-free mass, while resistance or concurrent programs achieved improvements only in BMI (g = −0.31 and −0.40, respectively) and BMI z-score (only concurrent programs, g = −0.97) (Table 1). The duration of the session and the weekly frequency did not seem to influence the parameters studied since, except for body mass and fat-free mass, the improvements were independent of these characteristics of the program. For the duration of the session in particular, there were improvements in BMI, BMI z-score, fat mass (%), visceral fat, and subcutaneous fat independently of whether the sessions lasted less than or more than 60 min. Programs of four to 12 weeks were only effective in improving BMI, BMI z-score, and visceral and subcutaneous fat, with more than 12 weeks of intervention being required to achieve improvements in the rest of the parameters. Programs of 1500 min or more were effective in improving BMI, BMI z-score, fat mass (%), visceral fat, and subcutaneous fat.

Table 1 presents a summary of the results. The pooled results showed a reduction in TG (g = −0.45; 95% CI, −0.80 to −0.09; p = 0.014; I^2 = 59.3%), with no small-study bias (Egger regression intercept = −3.00, 95% CI −6.62 to 11.8, p = 0.501). The pooled effect sizes for fasting glucose and insulin were medium (g = −0.57; 95% CI, −0.77 to −0.37; p < 0.001; I^2 = 32.9%) and small (g = −0.42; 95% CI, −0.60 to −0.24; p < 0.001; I^2 = 28.0%), respectively. There was indication of small-study bias for fasting glucose (Egger regression intercept = −2.77, 95% CI −4.55 to −0.99, p = 0.004) and insulin (Egger regression intercept = −3.30, 95% CI −4.66 to −1.94, p < 0.001). Systolic and diastolic blood pressure both decreased with small effect sizes (g = −0.46 and −0.28, respectively) and medium and high heterogeneity (I^2 = 27.0% and 78.0%, respectively), but flow-mediated dilation increased with medium effect size (g = 0.55) and heterogeneity (51.0%). In the subgroup analysis, whether or not a type of program was effective depended on the parameter being considered. Thus, aerobic programs improved LDL-C, TG, fasting glucose, fasting insulin, HOMA-IR, intrahepatic fat, systolic blood pressure, and flow-mediated dilation, while resistance programs were found to do so only for fasting glucose, fasting insulin, and intrahepatic fat, and the combination of the two programs improved HDL-C, fasting glucose, and leptin (Table 1). Concerning the duration of the program, weekly frequency, and duration of the session, with the pooling of the results, it seemed in general that short duration programs (four to 12 weeks) or low frequency (≤3 sessions/week) or long session duration (≥60 min) gave improvements in seven parameters: HDL-C, fasting glucose, fasting insulin, HOMA-IR, intrahepatic fat, systolic blood pressure, and carotid intima-media thickness. Programs of 1500 min or more were effective in improving HDL-C, LDL-C, TG, TC, fasting glucose and insulin, HOMA-IR, and intrahepatic fat. In general, however, the results were heterogeneous, and differed depending on the parameter studied.

The pooled cardiorespiratory fitness results showed a small increase (g = 0.33; 95% CI, 0.08–0.57; p = 0.008; I^2 = 28.9%), with no small-study bias (Egger regression intercept = −2.41, 95% CI −3.27 to 8.11, p = 0.356). Regarding the subanalysis, the results showed that improvements in cardiorespiratory fitness require aerobic programs of three weekly sessions, or more than 60 min per session, or more than 1500 min total exercise time (Table 2).

4. Discussion

This systematic review has given a critical synthesis of the findings of several meta-analyses, all of which addressed a similar research question: are exercise-based interventions effective at improving anthropometric and body composition, cardiometabolic, hepatic, and vascular parameters, and cardiorespiratory fitness in overweight and obese children and adolescents?

Overall, exercise interventions seem to favour a reduction in body weight, BMI, central obesity, fat mass percentage, triglycerides, insulin resistance markers, and cardiorespiratory fitness, but the pooled data showed only small effects. These small effects could be due to different confounding variables in each of the individual studies. In this sense, several biologically plausible mechanisms could explain the effects of exercise in modulating the anthropometric (body mass, BMI, central obesity, fat mass) and cardiovascular (triglycerides, fasting glucose, fasting insulin) parameters. To the best of our knowledge, this review is the first study to have analysed the effectiveness of physical-exercise based interventions on a large number of parameters, as well as performing a subanalysis of the programs' characteristics.

Table 2
Effects of exercise on anthropometric and body composition parameters, cardiometabolic health, vascular parameters, and physical fitness as a function of duration of study, session frequency, duration of session, and total time of exercise. The data are Hedge's *g*.

Parameter	Duration of study (weeks)		Weekly session frequency (number)		Duration of session (min)		Total time of exercise[a] (min)	
	4–12	>12	≤3	>3	<60	≥60	<1500	≥1500
Anthropometry & body composition								
Body mass (kg)	−0.22 (−0.47 to 0.03)	−0.23 (−0.44 to −0.02)*	−0.25 (−0.49 to −0.01)*	−0.14 (−0.38 to 0.10)	−0.38 (−0.60 to −0.16)	0.01 (−0.27 to 0.29)	−0.33 (−0.88 to 0.21)	−0.15 (−0.32 to 0.02)
Body mass index	−0.62 (−0.93 to −0.31)#	−0.30 (−0.49 to −0.10)#	−0.57 (−0.88 to −0.26)#	−0.47 (−0.75 to −0.19)#	−0.55 (−0.83 to −0.28)#	−0.53 (−0.92 to −0.14)#	−0.27 (−0.45 to −0.09)*	−0.46 (−0.57 to −0.34)#
Body mass index z-score[b]	−0.39 (−0.59 to −0.20)#	−0.71 (−0.94 to −0.47)#	−0.73 (−1.09 to −0.36)#	−0.43 (−0.63 to −0.22)#	−0.43 (−0.66 to −0.20)#	−0.66 (−0.95 to −0.36)#	−0.34 (−0.57 to −0.10)*	−0.74 (−0.97 to −0.50)#
Central obesity	−0.22 (−0.52 to 0.07)	−0.19 (−0.47 to 0.09)	−0.18 (−0.51 to 0.15)	−0.18 (−0.45 to 0.09)	−0.25 (−0.50 to 0.01)	−0.12 (−0.47 to 0.22)	−0.25 (−0.62 to 0.11)	−0.14 (−0.39 to 0.11)
Fat mass (%)	−0.31 (−0.66 to 0.03)	−0.41 (−0.61 to −0.22)#	−0.46 (−0.72 to −0.20)#	−0.34 (−0.57 to −0.11)*	−0.43 (−0.66 to −0.20)*	−0.34 (−0.59 to −0.08)*	−0.34 (−0.75 to 0.08)	−0.42 (−0.61 to −0.24)#
Fat-free mass (kg)	0.01 (−0.19 to 0.20)	–	−0.01 (−0.21 to 0.21)	0.03 (−0.38 to 0.45)	−0.13 (−0.38 to 0.11)	0.19 (−0.09 to 0.47)	−0.18 (−0.42 to 0.06)	0.26 (−0.02 to 0.55)
Visceral fat	−0.88 (−1.33 to −0.44)#	−0.59 (−0.96 to −0.22)*	−0.46 (−0.73 to −0.19)*	−0.95 (−1.71 to −0.20)*	−0.80 (−1.39 to −0.22)*	−0.48 (−0.79 to −0.17)*	–	−0.65 (−0.97 to −0.32)#
Subcutaneous fat	−0.55 (−1.07 to −0.02)*	−0.32 (−0.48 to −0.15)*	−0.29 (−0.53 to −0.05)*	−0.49 (−0.68 to −0.30)#	−0.35 (−0.58 to −0.12)*	−0.38 (−0.62 to −0.13)*	–	−0.33 (−0.46 to −0.21)#
Cardiometabolic health								
HDL-C	0.56 (0.14–0.97)*	−0.26 (−0.60 to 0.09)	0.54 (0.11–0.97)*	−0.35 (−0.74 to 0.02)	0.32 (−0.58 to 1.22)	0.33 (0.01–0.65)*	–	0.22 (0.01–0.43)*
LDL-C	−0.38 (−0.73 to −0.03)*	−0.34 (−0.67 to −0.01)*	−0.46 (−0.74 to −0.17)*	–	−0.54 (−0.89 to −0.19)*	−0.20 (−0.53 to 0.13)	–	−0.38 (−0.64 to −0.13)*
TG	−0.35 (−0.65 to −0.06)*	−0.64 (−1.82 to 0.54)	−0.24 (−0.51 to 0.03)	−0.91 (−1.65 to −0.17)#	−0.62 (−1.38 to 0.14)	−0.27 (−0.56 to 0.01)	–	−0.52 (−0.75 to −0.28)#
TC	−0.31 (−0.70 to 0.07)	–	−0.31 (−0.70 to 0.07)	–	−0.66 (−1.87 to 0.56)	−0.42 (−0.86 to 0.03)	–	−0.79 (−1.12 to −0.47)#
Fasting glucose	−0.61 (−0.86 to −0.36)#	−0.51 (−0.84 to −0.19)#	−0.43 (−0.63 to −0.22)#	−0.81 (−1.19 to −0.42)#	−0.67 (−0.99 to −0.36)#	−0.50 (−0.76 to −0.22)#	−0.49 (−0.86 to −0.13)*	−0.63 (−0.89 to −0.34)#
Fasting insulin	−0.55 (−0.84 to −0.27)#	−0.28 (−0.49 to −0.07)*	−0.41 (−0.62 to −0.19)*	−0.48 (−0.86 to −0.10)*	−0.36 (−0.58 to −0.13)*	−0.53 (−0.81 to −0.25)#	−0.46 (−0.82 to −0.10)*	−0.47 (−0.69 to −0.24)#
HOMA-IR	−0.37 (−0.69 to −0.05)*	−0.28 (−0.57 to 0.01)	−0.28 (−0.52 to −0.04)*	−0.53 (−1.15 to −0.08)*	−0.35 (−0.67 to −0.03)*	−0.30 (−0.59 to −0.02)*	−0.21 (−0.63 to 0.21)	−0.38 (−0.63 to −0.12)*
C-reactive protein	−0.14 (−0.43 to 0.14)	−0.98 (−2.11 to 0.15)	−0.11 (−0.33 to 0.11)	−0.79 (−1.92 to 0.34)	−0.47 (−1.25 to 0.18)	−0.20 (−0.53 to 0.13)	−0.01 (−0.27 to 0.25)	−0.72 (−1.44 to 0.01)
Adiponectin	0.36 (0.06–0.65)*	–	0.19 (−0.17 to 0.56)	0.47 (0.09–0.86)	0.39 (0.08–0.71)*	0.17 (−0.32 to 0.66)	0.33 (−0.14 to 0.80)	0.41 (−0.20 to 1.01)
Leptin	−0.43 (−0.91 to 0.05)	–	−0.49 (−1.07 to 0.10)	–	−0.09 (−0.88 to 0.71)	−0.71 (−1.25 to −0.18)*	–	−0.49 (−1.07 to 0.10)
Aspartate aminotransferase	−0.07 (−0.50 to 0.36)	–	−0.12 (−0.47 to 0.23)	–	−0.32 (−0.63 to 0.00)	0.07 (0.42–0.57)	–	−0.18 (−0.46 to 0.09)
Alanine aminotransferase	−0.16 (−0.55 to 0.23)	−0.16 (−0.42 to 0.09)	−0.13 (−0.37 to 0.11)	−0.27 (−0.75 to 0.19)	−0.16 (−0.41 to 0.07)	−0.14 (−0.60 to 0.32)	–	−0.15 (−0.40 to 0.11)
Intrahepatic fat	−0.80 (−1.18 to −0.41)#	–	−0.80 (−1.18 to −0.41)#	–	–	−0.80 (−1.18 to −0.41)#	–	−0.80 (−1.12 to −0.48)#
Vascular parameters								
Systolic blood pressure	−0.61 (−0.89 to −0.34)#	−0.34 (−0.73 to 0.06)	−0.57 (−0.87 to −0.27)*	−0.48 (−0.87 to −0.09)*	−0.29 (−0.52 to −0.06)*	−0.82 (−1.23 to −0.41)#	−0.53 (−1.02 to −0.04)*	−0.46 (−0.67 to −0.25)#
Diastolic blood pressure	−0.52 (−1.18 to 0.14)	–	−0.04 (−0.79 to 0.71)	−0.74 (−1.59 to 0.10)	−0.07 (−0.39 to 0.25)	−1.47 (−3.09 to −0.05)	−0.22 (−0.76 to 0.33)	−0.54 (−0.13 to 0.22)
Flow-mediated dilation	0.55 (0.17–0.93)*	–	0.43 (−0.07 to 0.93)	1.02 (0.45–1.58)#	0.54 (−0.39 to 1.47)	0.62 (0.28– 0.95)#	0.72 (0.43–1.00)#	–
Carotid intima-media thickness	−0.73 (−1.17 to −0.28)*	−0.11 (−0.42 to 0.20)	−0.31 (−0.54 to −0.07)*	–	–	−0.31 (−0.54 to −0.07)*	–	−0.33 (−0.66 to −0.01)*
Physical fitness								
Aerobic fitness	0.19 (−0.16 to 0.55)	0.51 (0.21–0.81)	0.24 (−0.03 to 0.51)	0.59 (0.07–1.11)*	0.31 (−0.01 to 0.62)	0.37 (0.03–0.78)*	0.40 (−0.01 to 0.87)	0.31 (0.08–0.54)*

[a] Total time of exercise = duration of study·session frequency·duration of session.
[b] This subanalysis was performed with only one study (Kelley et al.[17]) since in the other study[15] it was impossible to access all the data needed to perform the calculation.
* $p < 0.05$.
\# $p < 0.001$.

Exercise helps to regulate body fat. However in the young population, it is unknown to what extent greater volumes of exercise influence body fat. Current findings showed overall a significant medium reduction in BMI (g = −0.50; 95% CI, −0.70 to −0.30; $p < 0.001$; $I^2 = 77.5\%$) and a small effect size in fat mass percentage (g = −0.38; 95% CI, −0.55 to −0.21; $p < 0.001$; $I^2 = 45.2\%$) using pooled data from five[14,15,31–32] and four meta-analyses,[14,27,30,32] respectively. Also, there was a small significant reduction in central obesity (g = −0.20; 95% CI, −0.41 to −0.01; p = 0.047; $I^2 = 0\%$). The dose-response effects of exercise on measures of adiposity remain elusive. The meta-analysis by Atlantis et al.[27] (seven out of 11 criteria in the AMSTAR assessment instrument, Supplementary file 5) that included 481 overweight boys and girls (aged ∼12 years) concluded (g = −0.21; 95% CI, −0.49 to 0.07) that 155–180 min per week of moderate to high intensity exercise was effective in reducing body fat and central obesity in overweight and obese children and adolescents. In the same line, García-Hermoso et al.[14] (nine out of 11 criteria in the AMSTAR assessment instrument, Supplementary file 5) analysed studies with overweight and obese participants, and concluded (g = −0.31; 95% CI, −0.66 to 0.04) that aerobic plus resistance exercise interventions (8–24 weeks duration) produced decreases in body weight, BMI, and fat mass, but no changes in fat-free mass and waist circumference. McGovern et al.[30] (nine out of 11 criteria in the AMSTAR assessment instrument, Supplementary file 5) found an outcome-treatment interaction between trials that measured the effect of physical activity on adiposity (moderate effect size, g = −0.52; 95% CI, −0.73 to −0.30) and trials measuring the effect on BMI (no significant effect, g = −0.02; 95% CI, −0.21 to 0.18). Stoner et al.[32] (nine out of 11 criteria in the AMSTAR assessment instrument, Supplementary file 5) found that exercise intervention reduced BMI (moderate effect, g = −0.36; 95% CI, −0.08 to −0.65), body weight, and body fat percentage (all with small effects), and noted that central obesity reduction in response to weight loss may be conditioned by obesity phenotype (BMI versus fat mass). Thus, diversity of body composition outcomes might also play a role in the heterogeneity of the meta-analyses studied. In this sense, several biologically plausible mechanisms could explain the effects of exercise in modulating adipose tissue and body composition changes. Exercise can be therapeutic in reducing body fat by increasing energy expenditure, stimulating lipid oxidation, and inhibiting lipid synthesis in the liver through the activation of the AMP-activated protein kinase pathway and free fatty acid flux to the liver.[36]

Finally, it has to be said that the present systematic review has found that exercise training indeed has an overall effect despite the great heterogeneity of the various meta-analyses that it covered. This heterogeneity might be explained by the diversity of study designs, training protocols, and characteristics of the subjects (aerobic, strength, combination, age, body composition, sex, randomization,...). In order to reduce this heterogeneity, the subanalysis was performed in terms of the characteristics of the intervention (see the Subsection "Intervention characteristics" below).

Excess adiposity and particularly abdominal obesity are linked to a raised lipid profile and a risk of developing insulin resistance and metabolic syndrome, constituting the basis for impaired vascular function.[37] A recent meta-analysis[17] (nine out of 11 criteria in the AMSTAR assessment instrument, Supplementary file 5) pooling six studies showed (g = 0.55; 95% CI, 0.17–0.93) that supervised training is a more potent stimulus than non-supervised training in enhancing (by ∼1.5%) flow-mediated dilation (FMD). The clinical relevance of this improvement in FMD had been suggested by previous prognostic studies. A meta-analysis[38] of 5547 adults associated a 1% increase in FMD with a 13% decrease in cardiometabolic events, so that the magnitude of FMD improvement found following exercise can favourably affect endothelial function in young healthy adults, indicative of another cardioprotective effect of exercise against the progression of atherosclerosis. In this context, several biologically plausible mechanisms could explain the effects of exercise in modulating endothelial function and arterial stiffness. The main physiological mechanisms involved up-regulate endothelial nitric oxide synthase activity in cell culture, animal, and human studies, with subsequent reduction in the expression of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, and stimulation of radical scavenging systems that include copper/zinc-containing superoxide dismutase, extracellular superoxide dismutase, glutathione peroxidase, and glutathione.[38] However, further research is needed to confirm these mechanisms, especially in childhood obesity during and after weight-loss exercise programs.

Another meta-analysis[21] (seven out of 11 criteria in the AMSTAR assessment instrument, Supplementary file 5) reported that aerobic exercise performed for 60 min, thrice a week, at ≤75% maximum heart rate improves LDL-c and TG concentrations in obese children, and combined exercise (≥60 min, >75% maximum heart rate) increases HDL-c concentrations. In this sense, the pooled result of the present study showing a decrease in TG (g = −0.45; 95% CI, −0.80 to −0.09; p = 0.014; $I^2 = 59.3\%$) was in accordance with the finding of the aforementioned meta-analysi[21] (g = −0.55; 95% CI, −0.83 to −0.27). Marson et al.[33] (seven out of 11 criteria in the AMSTAR assessment instrument, Supplementary file 5) demonstrated (g = −0.56; 95% CI, −1.01 to −0.11) that in overweight adolescents the improvements in the insulin sensitivity index (insulin resistance, HOMA) were similar for aerobic and for strength training, and neither were there differences in the improvements between the exercise training groups and those with combined training. Thus, the improvements in insulin sensitivity in aerobic groups found in the present study are likely explicable in part by significant increases in skeletal muscle mass with training. However, the heterogeneity in the children's and adolescents' growth, maturation, and pubertal status and the limitations of some body composition assessments (e.g., bioelectrical impedance) could well influence the final results, so that one must interpret the findings with care. The findings overall showed a significant reduction in fasting glucose (g = −0.57; 95% CI, −0.77 to −0.37; $p < 0.001$; $I^2 = 32.9\%$) and fasting insulin (g = −0.42; 95% CI, −0.60 to −0.24; $p < 0.001$; $I^2 = 28.0\%$). So the present findings have important health implications, and provide health care professionals with therapeutic strategies for the treatment of childhood obesity and the reduction of insulin resistance in the young population.

Physical fitness is a multi-dimensional construct that includes skill- and health-related components in which cardiorespiratory fitness, musculoskeletal fitness (e.g., muscle endurance, muscle strength, muscle power), and motor fitness (e.g., balance, coordination) can be strongly influenced by lifestyle factors. Previous large cohort studies have shown the lack of cardiorespiratory fitness to be an independent risk factor for cardiovascular disease,[39] exceeding in importance even that of other classic cardiometabolic factors such as dyslipidaemia, hypertension, smoking, and obesity.[40,41]

Overall, the findings showed a significant increment in cardiorespiratory fitness (g = 0.33; 95% CI, 0.09–0.57; p = 0.008; $I^2 = 28.9\%$). Particular attention has to be paid to such changes as well as to those in the lipid and lipoprotein profiles and glucose metabolism that occur after training-type interventions in youth obesity.[42] One systematic review[20] (eight out of 11 criteria in the AMSTAR assessment instrument, Supplementary file 5) found that aerobic-exercise-based programs lasting more than 12 weeks (3000 min total exercise time) in three sessions per week (more than 60 min per session) led to better maximum oxygen uptake results. Excessive body fat is known to profoundly influence cardiorespiratory fitness, and adiposity (fat mass) depresses weight-relative maximal aerobic power.[20] Another study has demonstrated that skeletal muscle quality, such as the oxidation capacity of muscle and the muscle fibre type distribution, plays a role in the association between excess intramyocellular lipids and insulin resistance in youth obesity.[43]

The present review has shown that there is evidence that exercise improves various parameters related to health (body mass, BMI, fat mass, triglycerides, fasting glucose, fasting insulin). Surprisingly, relative to those of over 12 weeks, the 2- to 4-week programs showed greater improvements in BMI, visceral fat, and subcutaneous fat. Probably, the shorter programs do not need the strict control of the progression of exercise intensity that the longer programs do, so that their results would be more pronounced. Also, the interventions were very heterogeneous both in content – aerobic exercises,[15,16,20,21,28,29,33] strength,[15,16,33] combined (aerobic and resistance),[15,16,20,21,33] or even unspecified[17,18,22,27,30–32,34,35] and characteristics – duration of the study, session frequency, duration of the sessions, and total time and intensity. An overall consideration of the data given in Table 1 would seem to show that, in general, aerobic programs favoured changes in fifteen parameters, whereas resistance programs or the combination of the two only showed improvements in four and five parameters, respectively. These findings did not confirm those of a recent study published by García-Hermoso et al.[44] of concurrent and aerobic exercise in obese youngsters, in which combined aerobic and strength exercise led to greater benefits in most of the health parameters. With respect to the duration of the program, weekly frequency, and duration of the session, none of these seemed to be determinant in anthropometric and body composition parameters since their results are similar. However, in general and with the results pooled, for the cardiometabolic and vascular parameters it seems programs of four to 12 weeks, or of more than 60 min per session, or with a total exercise time of 1500 min or more were effective in improving HDL-C levels, fasting glucose, fasting insulin, HOMA-IR, intrahepatic fat, systolic blood pressure, and carotid intima-media thickness. This may be due to the organism's rapid adaptation to the load represented by the physical exercise program, so that an increase in the intensity may be needed in order to produce a new adaptation.

Once the scientific evidence has shown positive effects of exercise programs on the health parameters, the next step in studies on this topic might be to look at the different characteristics of the intervention programs. In particular, it appears that there still needs to be more evidence that any particular "dose" of exercise is required. It should be taken into account that, although in the field of sports the precise quantification of training programs is the norm, in the field of health, quantification of exercise programs is at best only very general in form, and sometimes almost non-existent. This is an aspect of especial interest since precise quantification is considered to be the key factor in the field of physical exercise.[45] It has also to be borne in mind that, of all the meta-analyses considered in the present study, only six[14,16,20,21,28,33] specifically reported the type of exercise taken as an inclusion criterion. This, together with the limited information on the "dose" of physical exercise, sometimes compromises the reproducibility of the studies. It therefore seems necessary to go into greater depth in this sense by proposing physical exercise programs that are developed in detail.

To the best of our knowledge, this is the first systematic review of meta-analyses that evaluates the effects of exercise-based interventions alone and the health outcomes in overweight and obese children and adolescents. However, the study has various limitations. First, the heterogeneity of the RCTs included limits the capacity to decide on an optimal exercise prescription to improve the health parameters of overweight and obese children and adolescents. Second, some of the meta-analyses considered only a small number of subjects (<219). However, the mean number of participants in the studies (668.67 participants) and the total number of studies (18 studies) could be considered good. Third, as is inherent in any meta-analysis, the current study assumed all the meta-analyses to be equal (the ecological fallacy), and it could also be the case that the pooling changed the trend of each meta-analysis analysed alone (Simpson's paradox). Fourth, overlap could have influenced the results, and an analysis was made of the potential influence of this known problem (Supplementary file 3). Fifth, some pooling was made with just a single study. However, the statistical analyses and the results are new. Sixth, we included meta-analyses with children and adolescents even though the physiological responses to exercise have been shown to be very different from 6 to 17 years in age, mainly reflecting age-dependent metabolic and musculoskeletal differences.[46] This should also be taken into consideration in doing subgroup analyses (duration of study, frequency of exercise, duration of session, and type of exercise). However, this grouping is customary when performing meta-analyses. Also, the inclusion in the subgroup analysis of both RCT and non-RCT studies for some parameters may have been a cause of bias. Seventh, six of the meta-analyses considered[20,27,30–33] included studies with both physical exercise programs and nutritional recommendations. Finally, a potential limitation of the evidence provided is that most of the meta-analyses included have a moderate risk of bias.

5. Conclusions

The results suggested that exercise-based interventions in children and adolescents improved some anthropometric (body mass, body mass index, central obesity, fat mass) and cardiovascular (TG, fasting glucose, fasting insulin) parameters and cardiorespiratory fitness. The evidence concerning other parameters, however, needs deeper study. The findings are of importance in the context of public health. But, given the difficulty in meeting international physical activity recommendations for overweight and obese children and adolescents, an individual exercise prescription that gradually progresses them up to those recommendations (i.e., 60 min daily of moderate-to-vigorous physical activity) would seem appropriate. Overall, subgroup analyses of the meta-analyses yielded pooled effects that were greater for studies with higher doses. From a general point of view, aerobic programs seem to favour healthy changes in most of the parameters evaluated (15 of 26). Regarding the duration of the program, weekly frequency, and duration of the session, although the results are heterogeneous and differ from one parameter to another, it seems that these variables are not determinant for anthropometric and body composition parameters. For cardiometabolic and vascular parameters however, programs of four to 12 weeks, or with a total exercise time of 1500 min or more, or three or even fewer weekly sessions, or sessions of 60 min each were effective in improving HDL-C, fasting glucose, fasting insulin, HOMA-IR, intrahepatic fat, systolic blood pressure, and carotid intima-media thickness. Thus these results based on scientific evidence constitute a first approximation to a specific prescription for an effective physical exercise program in the pædiatric population. The proposed dose-response relationships for the different health parameters could be applied to obtain benefits in health and to develop more effective lifestyle interventions in the obese young population.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jsams.2018.07.006.

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