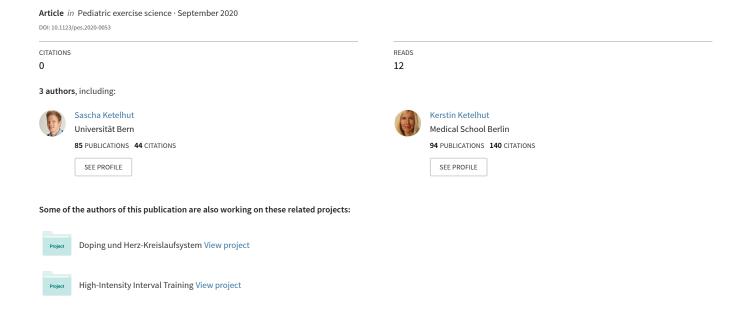
# School-Based Exercise Intervention Improves Blood Pressure and Parameters of Arterial Stiffness in Children: A Randomized Controlled Trial





# School-Based Exercise Intervention Improves Blood Pressure and Parameters of Arterial Stiffness in Children: A Randomized Controlled Trial

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**Purpose:** To evaluate the effectiveness of a school-based exercise intervention on endurance performance (EP), blood pressure (BP), and arterial stiffness in children. **Methods:** A total of 105 students (mean age = 8.2 [0.6] y; 51% girls; body mass index = 17.8 [3.0] kg/m<sup>2</sup>) were randomized to the intervention group (IG, n = 51) and control group (CG, n = 54). During a 37-week experimental period, the IG received an exercise intervention (2×45 min/wk) in addition to their regular school physical education class (3×45 min/wk). EP, peripheral and central BP, pulse pressure, augmentation pressure, augmentation index, and aortic pulse wave velocity were assessed. **Results:** Following the intervention, significant changes (P < .05) in EP, peripheral and central systolic BP, pulse pressure, augmentation index, and aortic pulse wave velocity were found in the IG. Children in the CG displayed significant changes in peripheral and central diastolic BP. An analysis of the baseline-to-post changes revealed significant between-group differences in EP (P < .001), pulse pressure (P = .028), augmentation pressure (P = .007), and aortic pulse wave velocity (P = .037) that favored the IG and in peripheral and central diastolic BP that favored the CG. **Conclusion:** The school-based exercise intervention had beneficial effects not only on EP but also on different hemodynamic parameters.

Keywords: physical activity intervention, hemodynamic measures, aerobic fitness

A growing body of literature confirms that cardiovascular diseases (CVDs) may originate in the first decade of life (46) and that relevant risk factors are already evident at a young age (13). As CVD prevention is known to be more effective than cure (34), and because the risk profile in children predicts cardiovascular morbidity and mortality decades later (15), early diagnosis, treatment, and prevention is of major importance.

Increasing physical activity levels and decreasing sedentary lifestyles are often promoted as essential components of a healthy lifestyle in children. Several systematic reviews have been published highlighting the fundamental health benefits of physical activity in this age group (14,20,41). Substantial evidence further supports the positive effects of physical activity in treating and preventing CVD (41,46).

Activity guidelines recommend that children aged 5–17 years should spend at least 60 minutes a day in moderate to vigorous intensity physical activity to improve their cardiorespiratory fitness, muscular strength, bone health, and biomarkers of cardiovascular and metabolic health. It is further known that greater amounts of physical activity (>60 min) provide additional health benefits (20). Despite the well-established positive effects of regular physical

activity on health and well-being, the current activity levels in children and youths are widely regarded as insufficient to meet recommendations (21). According to the most recent international Health Behavior in School-aged Children survey, only 13.9% of children and adolescents meet the current activity guidelines (21).

To counteract this problem, the school setting may offer an ideal environment to reach a large group of children irrespective of social-economic factors. Different research groups have shown that school-based physical activity interventions are not only effective in increasing physical activity rates in children (10) but also in improving body composition, cardiorespiratory fitness, and peripheral blood pressure (10).

Evidence suggests that, apart from pressure measured in the brachial artery, other hemodynamic parameters—such as the central pressure, the aortic pulse wave velocity (aPWV), the pulse pressure (PP), the augmentation pressure (AP), and the augmentation index (AIx)—are better related to future cardiovascular events (28,30). Data from prospective studies indicate that aPWV, a measure of arterial stiffness, is associated with a decline in endothelial function and is a precursor for future cardiovascular risk even after accounting for other established risk factors (2). Increased arterial stiffness is observed in young, healthy subjects before any increase in peripheral BP (27). Furthermore, there is evidence that poor cardiorespiratory fitness and low levels of physical activity are associated with increased arterial stiffness and endothelial dysfunction in children (43,46). Thus, aPWV has been widely recognized as a sensitive and early marker of cardiovascular outcome (26,41).

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Numerous studies have assessed the effects of different exercise interventions on markers of arterial stiffness in adults (18). In children, studies assessing the effects of exercise on arterial stiffness are sparse. However, Chuensiri et al (7) showed acute effects of supramaximal high-intensity intermittent exercise on arterial stiffness in obese children, highlighting that alterations in arterial stiffness in children are possible. To the best of our knowledge, the effects of long-term exercise interventions on these parameters have not been evaluated in school-aged children.

Thus, the purpose of this study was to examine the effects of a regular school-based exercise intervention on endurance performance (EP), and different parameters of arterial stiffness that are used as early markers of CVD.

# **Materials and Methods**

#### **Subjects and Study Design**

The present study was conducted as a parallel-arm cluster-randomized controlled trial. A cohort of 105 students (mean age = 8.2 [0.6] y; 51% girls; body mass index [BMI] = 17.8 [3.0] kg/m²) was recruited from a pool of schools participating in the health promotion project "SMS. Sei schlau. Mach mit. Sei fit." of the German Diabetes-Center Düsseldorf in support of the project "Fitness für Kids" Verein für Frühprävention e.V.

Two primary schools, from socially disadvantaged areas, were randomly selected, and the third-grade classes were randomized to either the intervention group (IG, n = 51) or control group (CG, n = 54) using a computer-generated random number table. The school principal, teachers, and parents were provided with detailed study information. Written parental/guardian consent was obtained prior to participation in the study. Only the children who returned consent forms were eligible to participate. Children with health conditions that did not allow unrestricted physical activity engagement were excluded. Parents and children were informed about the purpose of the study and the testing procedures. The study was reviewed and approved by the research ethics board of Heinrich-Heine-University Düsseldorf and was conducted in accordance with the Declaration of Helsinki.

The study design consisted of a baseline examination where the relevant parameters were assessed, an intervention period lasting 9 months and a postexamination where the baseline measurements were repeated.

#### Measurements

Specially trained study staff members under standardized conditions performed all measurements. The same investigator obtained the pretest and posttest measurements using the same devices. The times of the measurements were recorded, and remeasurements were performed at the same time of day after the observation period to avoid circadian variation in the parameters. Parents were instructed that their children should abstain from consuming caffeinated beverages and should avoid excessive physical activity for 12 hours prior to the test day. Furthermore, subjects were asked to fast for 3-hour preceding the test.

Prior to the study, the subjects were familiarized with all experimental procedures and were subsequently tested on 2 consecutive days. The first day, anthropometric measurements, including body mass, height, and waist circumference, were registered to calculate the BMI, and waist to height ratio. Waist circumference was measured midway between the hip bone and the bottom of the ribs.

In addition, EP was assessed using the 6-minute run test. This test is a reliable and valid functional test for assessing EP in children (32,47). For this test, children in groups of 6 had to run around a volleyball field ( $18 \times 9$  m) staked out by cones for as long as 6 minutes in the school's gym. Subjects were instructed to circulate a volleyball field as often as possible in 6 minutes. During the test, children were motivated by study staff members, teachers, and other students. The test result was based on the distance covered, measured in meters.

On the second day, hemodynamic parameters (peripheral and central BP, aPWV, PP, AP, and AIx) were determined noninvasively using Mobil-O-Graph® (calibration C1, 24-h PWA monitor; IEM GmbH, Stolberg, Germany), which is a clinically validated device for hemodynamic measurements (12,16,44) with a novel transfer function-like algorithm that uses brachial cuff-based waveform recordings. Subjects rested in a seated position in a climatecontrolled room (22°C [1°C]) for 10 minutes before a minimum of 2 readings were obtained from the right arm and averaged for the analysis. Custom-fit arm cuffs were used, and the arm was extended and placed on a customized arm support so that the heart and the pressure cuff were level. To ensure that the children remained quiet during the measurement procedure, a short movie sequence ("March of the Penguins," Wild Bunch & National Geographic Films) was presented. The obtained data were processed using HMS Client-Server (version 4.7; IEM GmbH, Stolberg, Germany). The same test protocol was applied for the assessments at the end of the intervention.

#### Intervention

Throughout the 9-month intervention period, both the IG and CG participated in their regular physical education classes 3×45 minutes a week following the normal curriculum of the Hessian Ministry of Culture. The IG received an additional exercise intervention of 2×45 minutes per week consisting of a supervised structured physical activity. The program was obligatory and was part of the school timetable. The program was conducted by qualified physical education teachers who were specially trained in workshops. The content of the intervention was based on the movement concept of the exercise program "Fitness für Kids," which is characterized by an intensive interval regimen. The changes between short bouts of exercise interspersed with rest periods allow for a relatively high-intensity workload. Furthermore, the program guarantees a high degree of active movement. Each session commenced with a 5- to 10-minute warm-up and ended with a 5-minute cool-down. Following the warm-up, participants performed a variety of movement tasks and various running, ball game, relay, and coordination tasks aimed at enhancing basic motor skills. All contents were appropriate for children and could easily be performed in the school's gym without special equipment. During the movement tasks, children were verbally motivated to exert a high degree of effort corresponding to a value of 15 to 18 on the Borg ratings of perceived exertion scale, with which the children were familiarized in advance (4).

#### **Statistical Analyses**

All statistical analyses were performed using IBM SPSS Statistics (version 22.0; SPSS, Chicago, IL). The results are reported as means (SDs) and 95% confidence intervals (CIs) unless stated otherwise. Multilevel linear models with random effects for schools and classes were used to analyze the effectiveness of the exercise intervention. Differences in changes (follow-up-baseline) were used

as the effect estimates, and they are reported as the mean change with 95% CI adjusted for confounders (age, sex, BMI, and the variables at baseline). Differences in baseline values between the IG and CG were investigated using independent samples *t* test. A *P* value < .05 was considered to indicate statistical significance.

#### Results

Table 1 contains the baseline characteristics for all participants. According to the age- and sex-specific percentiles, 21.0% (IG 24%; CG 19%) of the children were overweight or obese (29).

With respect to German age-, height-, and sex-specific percentiles for peripheral systolic BP, 49.52% of the children were defined as hypertensive (39). In the IG, 55.5% of the boys and

45.4% of the girls were hypertensives by means of peripheral BP. In the CG, 48.27% of the boys and 52% of the girls were measured as hypertensive.

The IG and the CG displayed significant differences with respect to height, weight, and BMI. The groups did not differ at baseline concerning waist to height ratio, peripheral BP (SBP or DBP), or central BP (systolic or diastolic). The same was true for PP, AP, AIx, and aPWV.

Records of the exercise lessons indicated that an average of 96.3% of the scheduled exercise sessions was completed. The session attendance rates were 91% for the IG and 93% for the CG.

The changes in baseline and follow-up values are presented in Tables 2 and 3. Significant differences in the mean changes were detected for EP (Table 1), PP, AP, and aPWV (Table 2) favoring

Table 1 Subjects' Characteristics at Baseline

Items	Total (N = 105)	IG (n = 51)	CG (n = 54)	P value for difference
Boys/girls, n	47/58	18/33	29/25	
Age, y	8.2 (0.6)	8.1 (0.6)	8.3 (0.6)	.258
Height, cm	135.2 (6.1)	135.8 (5.7)	134.6 (6.3)	.002
Weight, kg	32.8 (7.2)	35.5 (8.1)	30.2 (5.0)	.002
BMI, kg/m <sup>2</sup>	17.8 (3.0)	19.1 (3.3)	16.6 (2.2)	.026
WHtR	0.47 (0.05)	0.49 (0.06)	0.45 (0.03)	.453
Hypertensive <sup>a</sup>	52	25	27	

Abbreviations: BMI, body mass index; CG, control group; IG, intervention group; WhtR, waist to height ratio. Note: Values are presented as mean (SD), unless stated otherwise.

Table 2 Intervention Effects for Outcomes

	IG		CG			
Outcome	Baseline	Follow-up	Baseline	Follow-up	Difference in mean change (95% CI) <sup>a</sup>	P value
EP, m	772.5 (122.6)	802.9 (136.5)*	918.3 (124.7)	876.8 (124.8)	62.0 (28.6 to 95.4)	<.001
BMI, kg/m <sup>2</sup>	19.1 (3.3)	19.42 (3.6)	16.6 (2.2)	16.68 (1.9)	0.27 (-0.11 to 0.66)	.164
WHtR	0.49 (0.06)	0.49 (0.05)	0.45 (0.03)	0.44 (0.03)	0.012 (-0.006 to 0.03)	.189

Abbreviations: BMI, body mass index; CI, confidence interval; CG, control group; EP, endurance performance; IG, intervention group; WHtR, waist to height ratio. Note: Values are presented as mean (SD). Baseline and follow-up data are unadjusted values while between-group comparisons are adjusted.

Table 3 Intervention Effects for Hemodynamic Outcomes

Outcome	IG		CG			
	Baseline	Follow-up	Baseline	Follow-up	Difference in mean change (95% CI) <sup>a</sup>	P value
pSBP, mm Hg	120.2 (8.3)	111.7 (7.7)*	112.8 (7.9)	114.8 (8.9)	-2.5 (-7.5 to 2.5)	.315
pDBP, mm Hg	70.3 (8.9)	70.1 (7.2)	70.0 (6.2)	66.8 (6.5)*	3.7 (1.1 to 6.4)	.006
cSBP, mm Hg	104.5 (8.4)	98.1 (7.4)*	99.4 (7.8)	99.8 (9.2)	-1.9 (-6.4 to 2.5)	.350
cDBP, mm Hg	72.8 (8.8)	72.3 (7.0)	72.0 (6.2)	68.8 (6.5)*	3.8 (1.2 to 6.4)	.005
PP, mm Hg	49.9 (9.2)	41.6 (8.5)*	42.8 (7.5)	47.9 (10.5)	-3.45 (-6.5 to -0.4)	.028
AP, mm Hg	8.3 (5.8)	5.8 (3.3)*	7.3 (3.6)	8.1 (4.9)	-2.3 (-4.0 to -0.6)	.007
AIx, %	31.0 (10.9)	26.6 (8.6)*	31.0 (8.7)	29.4 (11.2)	-3.2 (-6.9 to 0.5)	.088
aPWV, m/s	4.8 (0.3)	4.5 (0.3)*	4.6 (0.3)	4.6 (0.4)	-0.2 (-0.4 to -0.01)	.037

Abbreviations: AIx, augmentation index; AP, augmentation pressure; aPWV, aortic pulse wave velocity; BMI, body mass index; cDBP, central diastolic blood pressure; CI, confidence interval; CG, control group; cSBP, central systolic blood pressure; IG, intervention group; pDBP, peripheral diastolic blood pressure; PP, pulse pressure; pSBP, peripheral systolic blood pressure. Values are presented as mean (SD). Baseline and follow-up data are unadjusted values while between-group comparisons are adjusted. 
aEffect estimates are mean changes from linear mixed models with the change in outcome adjusted for age, BMI, sex, and baseline values of outcome.

\*P < .05 different from baseline.

<sup>&</sup>lt;sup>a</sup>German age-, sex-, height-specific reference values (39).

<sup>&</sup>lt;sup>a</sup>Effect estimates are mean changes from linear mixed models with the change in outcome adjusted for age, BMI, sex, and baseline values of outcome.

<sup>\*</sup>P < .05 different from baseline.

the IG. Although AIx was lower in the IG compared with the CG, the between-group differences slightly failed to reach statistical significance.

Concerning the peripheral and central diastolic BP, significant differences in the mean change were detected, favoring the CG.

Furthermore, the IG showed a significant decrease in peripheral (-4.34 mm Hg; 95% CI, -8.5 to -0.2) and central (-3.93 mm Hg; 95% CI, -7.5 to -0.3) systolic BP, PP (-2.82 mm Hg; 95% CI, -4.8 to -0.8), AP (-1.67 mm Hg; 95% CI, -2.9 to -0.5), AIx (-4.23%; 95% CI -6.8 to -1.6), and aPWV (-0.18 [0.35] m/s; 95% CI, -0.3 to 0.0) after the intervention period. The CG exhibited no significant changes in the respective parameters throughout the intervention period. Peripheral diastolic BP was significantly decreased in the CG throughout the intervention period (-4.17 mm Hg; 95% CI, -7.7 to -0.7). The same was true for central diastolic BP (-4.29 mm Hg; 95% CI, -6.0 to -0.6). No significant changes in the same parameters were evident in the IG.

#### **Discussion**

The current study aimed to evaluate the effects of a school-based physical activity intervention on EP, BP, and parameters of arterial stiffness in 8-year-old children from a low social-economic background. The primary findings of this study were that a 9-month supervised exercise intervention was effective in improving EP and reducing peripheral and central systolic BP, PP, AP, AIx, and aPWV in the IG.

According to the baseline data (BMI and BP), the children of both groups displayed a high prevalence of obesity and hypertension. Thus, the sample enrolled in this study must be classified as at risk. This high prevalence might be due to the schools being located in an area of Düsseldorf with a very low social-economic status and a very high percentage of children with a migration background. It is known that low social status and migration background are associated with a higher prevalence of hypertension (19).

The positive effects of an additional exercise intervention on EP correspond to the current literature (23,31). Even though the 6-minute run is only an indirect method for accessing endurance capacity, a high correlation between the distance covered in the test and the maximal oxygen uptake has been proven (48). The fact that maximal oxygen uptake is related to cardiovascular risk factors and mortality (11,37) underscores the need for interventions to enhance cardiorespiratory fitness as early as possible.

The children in the IG showed a significant reduction in their peripheral systolic BP, whereas the children in the CG displayed a slight increase in this measurement. These results are in accordance with previous reports indicating significant effects of school-based exercise interventions on peripheral systolic BP in children (10,41). However, other studies failed to detect positive effects on BP in this young age group (5). Apart from general differences in the study designs, and sample, this discrepancy might be attributed to the higher exercise intensity in the present study. As stated before, the intervention consisted of intermittent exercise of higher intensity. The majority of observational studies have focused on continuous physical activity of moderate intensity. However, research emphasizes the importance of incorporating more activities of vigorous intensity for improving the health of children and youth (6,24). Nonetheless, we must be careful of premature assumptions because the exercise intensity was not objectively documented in the present study. These results are of interest and clinical relevance because BP levels are known to track from childhood into adulthood (3). Lowering BP levels at a young age may thus reduce the cardiovascular risk profile in later life.

After the intervention, the diastolic BP was higher in the IG when compared with that of the CG. Together with a lower systolic BP in the IG after the intervention, this resulted in a lower PP in the IG. Studies have shown that a larger PP may contribute to the development of arteriosclerosis and arterial stiffness (49). Furthermore, large PP in childhood plays an essential role in the development of subclinical vascular damage in adulthood (17).

Even though most interventional studies in children have failed to detect considerable effects on diastolic BP, one other study demonstrated a decrease in the CG (35). Based on the data obtained, it is difficult to explain this result because no significant changes in peripheral resistance were observed in any group.

Apart from peripheral BP, the oscillometric device also assesses central BP, detecting significant reductions in central systolic BP for the IG and slight increases in the CG. This finding is in line with that of Beck et al (1), who observed a significant reduction in central systolic BP after 8 weeks of resistance or endurance training in slightly older prehypertensive subjects. To the best of our knowledge, there are no data in children accessing central BP and its influence on cardiovascular outcomes. We found a significant reduction in the central diastolic BP of the CG compared with that of the IG.

Throughout the intervention, the aPWV was significantly lower in the IG compared with the CG. The aPWV is a direct measure of arterial stiffness and has been shown to be reliable and reproducible (38).

Increased central arterial stiffness is an important predictor of cardiovascular events and mortality (2). Apart from aging, poorer cardiorespiratory fitness and lower levels of physical activity have been associated with increased arterial stiffness and endothelial dysfunction among children (42). Higher levels of leisure-time physical activity are linked to decreased aortic intima-media thickness and increased maximal brachial artery flow-mediated dilatation capacity in adolescents (42). In 18- to 35-year-old participants. Beck et al (1) found a reduction in aPWV after an 8-week endurance training of 11%. Regrettably, almost no studies have assessed the effects of exercise interventions on aPWV in children. Only Meucci et al (36) investigated the effects of a shortterm 8-week game-based movement intervention in children, but they were unable to demonstrate any significant changes in aPWV. The discrepancy in the results may be attributed to a longer intervention period and possibly higher exercise intensity in the present study.

The AP and AIx are measures of pulse wave reflection which are associated with cardiovascular risk (40) and have been shown to be independent predictors of cardiovascular events and all-cause mortality (33). In the present study, AP and AIx significantly decreased in the children of the IG throughout the exercise intervention period. Furthermore, significant between-group differences that favored the IG could be detected in AIx.

The detected changes in hemodynamic parameters may be primarily attributed to shear stress-induced improvements in endothelial function and the distribution of vasoactive substances (1).

Furthermore, effects on the RAAS-system and the sympathovagal balance can be debated. In this respect, we have found that a similar regular exercise intervention in children showed positive effects on measures of cardiac autonomic control due to increases in cardiac vagal activity with a significant increase in highfrequency power and the root mean square of the successive

differences (RMSSD). We also found a decrease in low-frequency power and LF/HF ratio (25).

Surveys have reported that an alarming number of children do not meet the current activity recommendations (22). These data are alarming since activity patterns are known to track from childhood into adulthood (45). Furthermore, children already exhibit an increasing prevalence of CVD risk factors. This could be confirmed by the present sample, displaying a high prevalence of hypertension and obesity. However, a confirmed additional exercise intervention of only  $2 \times 45$  minutes a week was sufficient to evoke positive effects on different CVD risk factors in this young cohort.

Previous reports have concluded, in addition to the frequency and duration of physical activity, the intensity of the activity contributes to promoting the overall physical health status of an individual (6). A systematic review suggests that vigorous activities provide additional benefits beyond those of modest intensity activities (20). A recent study from Delgado-Floody et al (9) showed that a 28-week high-intensity interval training during physical education classes significantly reduced the number of hypertensive and obese children. Furthermore, short bouts of exercise—as applied in high-intensity interval training—correspond to the natural patterns of adolescents' habitual activity during school time, as a recently published study has shown (8). This may result in higher compliance.

Although exercise intensity was not objectively documented in the present study, we presume that the stronger effects observed in our study compared with those of other research groups could in part be due to the relatively high intensity of the exercise regime in our study. Higher exercise intensities may promote greater shear-stress induced nitric oxide (NO) distribution (50) and may lead to a higher reduction of sympathetic nervous activity (25).

# **Strengths and Limitations**

A strength of the present study is the fact that additional hemodynamic parameters apart from peripheral BP were assessed; these parameters have been shown to have a higher prognostic value and to be beneficial in understanding the mechanisms responsible for producing the detected effects. In addition, the duration of the exercise intervention in the present study was fairly long. This characteristic of the study may account for the stronger effects that not only allowed for functional alterations but also likely resulted in structural changes to the vascular system. Furthermore, the exercise regimen and intensity must be highlighted. The intermittent character of the exercise protocol and the intensity of the exercise bouts may be the key factors that drive the positive results. In addition, the fact that the exercise intervention was obligatory, and part of the school timetable, guaranteed a high adherence to the program.

Apart from the strengths, some weaknesses of the present study have to be discussed. First, the study sample consisted of children from a low socioeconomic background, displaying a high CVD risk profile. Thus, the results cannot be extrapolated to other populations. Another limitation of this study is that, given the extended period of the study, other confounding factors—which have not been considered—could have influenced the outcomes. In addition, the lack of knowledge about the physical activity pattern of the students outside of school throughout the treatment period represents a particular limitation. Furthermore, the heterogeneity due to the cluster randomization of the groups concerning the anthropometric data might have biased the results. However, despite significant differences in BMI and waist to height ratio, there were no significant differences in the hemodynamic

parameters at baseline. This finding may lead to the assumption that biometrical dimensions do not have a strong influence on hemodynamic parameters in these young and at-risk subjects and that group differences can be neglected. Another limitation of this study is the fact, that the maturation status of the children was not assessed. However, because it is anticipated that children (age 8.2 y) would be classified in Tanner stage I, no significant difference in maturation is expected.

Furthermore, apart from hemodynamic parameters and EP, no metabolic parameters have been assessed. Therefore, no conclusions can be drawn about whether the intervention leads to changes in metabolic risk factors. Finally, we assume that the exercise intensity in the present study may be one reason for the positive effects that we observed. Nevertheless, exercise intensity was not objectively measured but rather was assessed subjectively. However, the physical education teachers were confident that the children reached the intensity demanded.

## Conclusion

In conclusion, this study is one of the first to demonstrate that a 9-month exercise intervention not only is efficacious in improving EP and reducing peripheral BP but also can positively influence the central systolic BP, PP, AP, AIx, and aPWV in school-aged children with a high prevalence of CVD risk factors. Therefore, physical activity should be increased in this young population, especially among those at risk, to reduce the burden of future CVD. The school setting seems to be an ideal environment for creating a lifestyle pattern of regular physical activity that will carry over to adulthood.

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