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Original article

Cardiometabolic risk through an integrative classification combining physical activity and sedentary behavior in European adolescents: HELENA study

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Abstract

Purpose: This study aims to compare adolescents' cardiometabolic risk score through an integrative classification of physical activity (PA), which involves the combination of moderate-to-vigorous physical activity (MVPA) and sedentary behavior (SB).
Methods: A cross-sectional study derived from the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study database (2006–2008) was conducted in adolescents ($n = 548$; boys, 47.3%; 14.7 ± 1.2 years) from 10 European cities. MVPA and SB were objectively measured using accelerometry. Adolescents were divided into 4 categories according to MVPA (meeting or not meeting the international recommendations) and the median of SB time (above or below sex- and age-specific median) as follows: High-SB & Inactive, Low-SB & Inactive, High-SB & Active, and Low-SB & Active. A clustered cardiometabolic risk score was computed using the homeostatic model assessment, systolic blood pressure, triglycerides, total cholesterol/high-density lipoprotein cholesterol, sum 4 skinfolds, and cardiorespiratory fitness (CRF). Analyses of covariance were performed to discern differences on cardiometabolic risk scores among PA categories and each health component.
Results: The cardiometabolic risk score was lower in adolescents meeting the MVPA recommendation and with less time spent in SB in comparison to the high-SB & Inactive group ($p < 0.05$). However, no difference in cardiometabolic risk score was established between High-SB or Low-SB groups in inactive adolescents. It is important to note that CRF was the only variable that showed a significant modification (higher) when children were compared from the category of physically inactive with "active" but not from high- to low-SB.
Conclusion: Being physically active is the most significant and protective outcome in adolescents to reduce cardiometabolic risk. Lower SB does not exhibit a significant and extra beneficial difference.

Keywords: Accelerometry; Cardiovascular disease; Exercise; Metabolic disease; Sedentary lifestyles

1. Introduction

Evidence indicates that regular physical activity (PA) is associated with numerous health benefits in adolescents, such as healthier body composition,[1,2] higher cardiorespiratory fitness (CRF),[3–5] lower levels of insulin resistance markers,[6] and lower cardiovascular disease risk factors.[7–10] Despite these benefits, a large percentage of adolescents (43.2% boys; 72.5% girls) do not meet the established recommendation of at least 60 min of moderate-to-vigorous physical activity (MVPA) every day.[11] Furthermore, they engage in an

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excessive amount of sedentary behaviors (SBs)—activities characterized by an energy expenditure ≤1.5 metabolic equivalents (METs), such as television viewing, seated video game playing, and prolonged sitting in school[12] —which have been found to have deleterious associations with risk of cardiometabolic disease regardless of PA level.[13] However, adolescents spend much of their time (around 71%) in SB.[11]

Total daily spectrum of movement behaviors is composed by: (a) SB, (b) light-intensity PA (LPA), (c) moderate-intensity PA, and (d) vigorous-intensity PA. Although both LPA and MVPA promote a healthy profile (lower cardiometabolic risk),[14,15] spending large amounts of time in sedentary activities and being physically inactive (i.e., not achieving the established recommendations for PA)[12] have shown a strong association with morbidity and mortality.[16,17] In this sense, the independent associations of total daily PA, MVPA, LPA, and SB time have been observed for several health markers (e.g., waist circumference, body mass index (BMI), glycated hemoglobin);[15,18] hence, some studies have begun to explore combinations of patterns across SB, LPA/SB ratio, and MVPA to categorize children and adolescents' PA patterns in a more integrative way.[4,7–9,19–21] For example, Roman-Viñas et al.[22] used an interesting combination of 3 recommendations for 24-h movement guidelines in children: (a) sleep duration (9–11 h/night for sleep duration), (b) PA (≥60 min/day for MVPA), and (c) SB (≤2 h/day screen time). On the one hand, this study found that only a small percentage of children from 12 countries met all of these recommendations (7%); on the other hand, it was shown that those who met more than 1 recommendation had a lower association with adiposity.[22] This kind of approach reinforces the importance of using a more integrative way to classify PA to customize intervention programs to improve overall health of the population.

The majority of studies published to date using an integrative methodology to classify PA combining SB and MVPA (high/low SB and meeting/not meeting PA recommendations)[21] have mainly focused on the association between single health markers, such as fitness and adiposity in children and adolescents.[4,7,8,19,23] Computing a more comprehensive indicator such as a clustering of cardiometabolic risk factors has proven to be a better marker of cardiovascular health in children than single risk factors likely from day-to-day fluctuations in both risk factors and PA.[24] Therefore, there is a need to study the effect of this kind of integrative PA methodology on the cluster of cardiometabolic health.

Having an integrative PA classification would be essential to establish future public health strategies, thus improving trends in childhood PA so as to reduce the prevalence of coronary and metabolic diseases in adulthood.[15,25–27] Consequently, the aim of this study was to compare adolescents' cardiometabolic risk score and each of its components through an integrative classification of PA, which involves the following 4 categories: (a) high *vs.* low SB time and (b) physically inactive *vs.* active—both measured using accelerometry.

2. Materials and methods

2.1. Study design

The Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study (HELENA-CSS)[1,6,9,11] is a multicenter study performed in 10 European cities in 9 countries. The HELENA-CSS was designed to obtain reliable and comparable data on nutrition and health-related parameters from a sample of European adolescents aged 12.5–17.5 years. Data collection took place between 2006 and 2008. A sample of 3528 adolescents met the HELENA general inclusion criteria, which can be found elsewhere.[28] In the present study, 548 adolescents with valid data on cardiometabolic risk factors (homeostasis model assessment (HOMA) index, systolic blood pressure (SBP), triglycerides (TG), total cholesterol by high-density lipoprotein cholesterol ratio (TC/HDL), sum of 4 skinfolds, and CRF), and accelerometry data were included in the analyses. The study was performed following the ethical guidelines of the 1964 Declaration of Helsinki (revision of Edinburgh 2000), the Good Clinical Practice, and legislation regarding clinical research in humans in each of the participating countries. The protocol was approved by the Human Research Review Committees of the involved centers. Furthermore, all parents/guardians signed an informed consent form, and the adolescents agreed to participate in the study.[29]

2.2. Physical examination

2.2.1. Measurements

Body weight was measured to the nearest 0.1 kg with an electronic scale (SECA 861; SECA, Hamburg, Germany). Body height was measured barefoot with a telescopic stadiometer (SECA 225) to the nearest 0.1 cm.[30] Adolescents were barefoot and in light clothing during anthropometric measurements. BMI was calculated as body weight divided by the square of height (kg/m^2). Waist circumference was measured with a nonelastic tape (SECA 200) to the nearest 0.1 cm and bicipital, tricipital, subscapular, and suprailiac skinfold thicknesses on the left side of the body with a caliper to the nearest 0.2 mm (Holtain Ltd., Dyfed, UK). All anthropometric measurements were taken 3 times and the mean was recorded. The sum of 4 skinfolds was used instead of BMI because CRF is included in our outcome variable and was expressed relative to body weight. SBP was measured (OMRON M6, HEM 70001; Omron, Kyoto, Japan) with participants seated in a separate quiet room for 10 min with their backs supported and feet on the ground. Two SBP readings were taken at 10-min intervals, and the lowest measure was recorded.

2.2.2. Blood samples

Blood samples were collected by venipuncture at school between 8:00 a.m. and 10:00 a.m. after a 10-h overnight fast. Blood was collected in heparinized tubes and then immediately placed on dry ice and centrifuged within 30 min (3500 rpm for 15 min) to avoid hemolysis. Immediately after centrifugation, the samples were stored and transported at 4˚C–7˚C (for a maximum of 14 h) to the central laboratory in Bonn

(Germany) and stored there at −80°C until assayed. TG, TC, and HDL were measured using enzymatic methods (Dade Behring, Schwalbach, Germany).[31] Serum concentrations of glucose and insulin were measured after an overnight fast. HOMA index calculation was used as a measure of insulin resistance.[32]

2.2.3. CRF

CRF was measured by the progressive 20-m shuttle run test. The test is valid and reliable in adolescents.[33] Adolescents were required to run between 2 lines that were located 20 m apart while keeping pace with audio signals emitted from a prerecorded CD with an initial speed of 8.5 km/h that increased by 0.5 km/h every minute (1 min equals 1 stage). The test ended either when the adolescent failed to reach the end line concurrent with the audio signals on 2 consecutive occasions or when he or she stopped because of fatigue. The last stage completed (precision of 0.5 stage) was used to estimate CRF from the equation developed by Léger et al.[34]

2.2.4. Cardiometabolic risk score

A clustered cardiometabolic risk score was created from the sum of SBP, TG, TC/HDL ratio, HOMA index, sum of 4 skinfolds, and CRF Z-score. This risk profile was previously used in a cross-sectional study of 1732 randomly selected 9- and 15-year-old school children from 3 European countries.[24] More recently, Andersen et al.[35] confirmed in a sample of 15,794 youths aged 6−18 years, which included the HOMA index rather than fasting glucose, the sum of 4 skinfolds instead of BMI or waist circumference, and CRF, that the composite risk score improved substantially.

These 6 health parameters were positively skewed and were transformed (natural log). The standardized value (Z-score) of each variable was calculated as follows: (value − mean)/standard deviation (SD), separately for boys and girls, and for each 1-year age group. Lower values are indicative of a better profile.[24] The CRF Z-score was multiplied by −1 (cardiometabolic beneficial effect).

2.2.5. PA levels

Levels of PA and sedentary time were measured with the GT1M ActiGraph accelerometer (Actigraph Corp., Pensacola, FL, USA). The ActiGraph has been widely validated in youth.[36] Adolescents were asked to wear the accelerometer during the daytime for 7 consecutive days and were also instructed to wear the accelerometer attached tightly on the hip by an elastic belt on the right side. They were only permitted to remove it when bathing or doing other water-based activities. The inclusion criterion was to record at least 8 h/day for a minimum of 3 days.[1,11] Each epoch (time sampling interval) was set at 15 s in accordance with consensus recommendations for children and adolescents,[37] and bouts of 20 continuous min of 0 count were considered as nonwearing periods and were removed from the analyses. Moreover, recordings of more than 20,000 counts/min (cpm) were considered potential malfunctions of the accelerometer, and these values were excluded from the analyses.

Sedentary time and MVPA were defined as <100 cpm and >2000 cpm, respectively.[11] PA average was expressed as the sum of recorded counts divided by total daily registered time expressed in minutes (cpm). Adolescents were classified as low or highly sedentary using the median split method by age and sex, as used previously in the literature.[4,8] Furthermore, adolescents were dichotomized into those who met (active: ≥ 60 min/day in MVPA) or did not meet (inactive: <60 min/day in MVPA) the current PA recommendations for youth.[26] This allowed us to create 4 categories according to high *vs.* low SB time and physically inactive *vs.* active as a proposal of an integrative classification of PA (i.e., High-SB & Inactive, Low-SB & Inactive, High-SB & Active, and Low-SB & Active).

2.3. Statistical analysis

Continuous variables are summarized using mean ± SD, and categorical variables are summarized using frequency (%). Student *t*, the Mann-Whitney *U*, and the χ^2 tests were used to assess differences between sex and adolescent characteristics (age, height, weight, and BMI), PA level (sedentary time, MVPA, accelerometer wearing time, % meeting PA guidelines, and % high sedentary time), and health parameters (CRF, sum 4 skinfolds, TC/HDL ratio, TG, SBP, and HOMA index; Table 1). Analysis of covariance (ANCOVA) was performed to assess (a) comparisons between physically inactive *vs.* active and low *vs.* high SB groups separately with the health parameters and cardiometabolic risk score and (b) comparisons between the 4 categories of integrative classification of PA (High-SB & Inactive, Low-SB & Inactive, High-SB & Active, and Low-SB & Active) with the health parameters and cardiometabolic risk score. Cardiometabolic risk factor clustering and each health parameter were the primary and secondary outcomes in this study, respectively.

Three different models were performed and were adjusted to several covariates in the following manner: Model 1 (adjusted for age, sex, BMI, accelerometer wear time, and study center as a random factor), Model 2 (Model 1 + time spent at MVPA), and Model 3 (Model 1 + sedentary time). A Bonferroni *post hoc* test comparison between groups was used in the second ANCOVA analysis. The main analyses were performed with boys and girls combined because no significant interaction was found between sex and PA/sedentary time groups. The level of significance was set at $p < 0.05$. Data were analyzed using IBM SPSS Statistics (Version 21.0; IBM Corp., Armonk, NY, USA).

3. Results

Adolescent characteristics are shown in Table 1. In synthesis, adolescents spent 69.7% of the day in SB and 7.7% in MVPA. Boys were significantly more active than girls (MVPA), and the recommended level of PA (≥ 60 min/day of MVPA) was achieved by the 43.1% of adolescents. Girls had higher levels of sum 4 skinfolds and lower levels of SBP and CRF than boys.

Table 2 shows the comparisons between high *vs.* low SB time and physically inactive *vs.* active adolescents for various

Table 1
Comparison of demographic and cardiometabolic characteristics between adolescent boys and adolescent girls (mean ± SD).[a]

	All ($n = 548$)	Boy ($n = 259$)	Girl ($n = 289$)	p
Age (year)	14.7 ± 1.2	14.8 ± 1.2	14.7 ± 1.1	0.296
Height (cm)	165.1 ± 9.8	169.5 ± 10.2	161.2 ± 7.5	**<0.001**
Weight (kg)	57.3 ± 12.4	59.6 ± 13.2	55.3 ± 11.2	**<0.001**
BMI (kg/m^2)	20.9 ± 3.4	20.6 ± 3.3	21.2 ± 3.5	**0.041**
Sedentary time (min/day)	542.8 ± 86.8	535.8 ± 92.7	549.0 ± 80.8	0.077
MVPA (min/day)	60.2 ± 24.9	70.5 ± 26.5	51.1 ± 19.2	**<0.001**
Accelerometer wearing time (min/day)	777.9 ± 98.3	784.4 ± 103.0	772.0 ± 93.6	0.092
Meeting PA guidelines *n* (%)	236 (43.1)	160 (61.8)	76 (26.3)	**<0.001**
High sedentary *n* (%)	272 (49.6)	134 (51.7)	138 (47.8)	0.392
CRF (mL/kg/min)	41.4 ± 7.9	46.3 ± 7.2	37.0 ± 5.7	**0.002**
Sum 4 skinfolds (mm)[b]	50.8 ± 25.2	41.9 ± 23.7	58.7 ± 23.9	**<0.001**
TC/HDL	3.0 ± 0.6	2.9 ± 0.6	3.0 ± 0.7	0.121
TG (mg/dL)	68.9 ± 35.4	62.1 ± 29.5	75.0 ± 39.0	**<0.001**
SBP (mmHg)	120.7 ± 14.7	125.3 ± 15.2	116.5 ± 13.0	**0.001**
HOMA index	2.4 ± 2.0	2.4 ± 2.4	2.5 ± 1.6	0.543
Cardiometabolic risk score	0.12 ± 3.66	−0.12 ± 3.59	0.34 ± 3.70	0.138

[a] Student *t*, Mann-Whitney *U*, or χ^2 tests.
[b] Sum 4 skinfolds: biceps, triceps, subscapular, and suprailiac.
Abbreviations: BMI = body mass index; CRF = cardiorespiratory fitness; HOMA = homeostasis model assessment; MVPA = moderate-to-vigorous physical activity; PA = physical activity; SBP = systolic blood pressure; TC/HDL = ratio between total cholesterol and high-density lipoprotein; TG = triglycerides.

health parameters and cardiometabolic risk score. When active and inactive groups were compared, only 2 parameters (CRF and cardiometabolic risk score) exhibited significant differences ($p < 0.05$) with both Models 1 and 3. There were no significant differences in the remaining health parameters. In addition, when comparing low- and high-SB groups, TC/HDL, TG, and cardiometabolic risk score showed significant differences in Model 1 ($p < 0.05$). Nonetheless, when the analyses were additionally adjusted for MVPA time, these differences became nonsignificant, except for the cardiometabolic risk score (Model 2).

Fig. 1 depicts multiple comparisons of the 6 health parameters composing the cardiometabolic risk score across the 4 categories. CRF ($p < 0.001$) and TC/HDL ($p < 0.01$) presented a significant overall effect across groups. Both High-SB & Inactive and Low-SB & Inactive groups showed lower significant differences in comparison with the High-SB & Active group in CRF ($p < 0.001$ and $p < 0.05$, respectively). In addition, a significant difference was observed between High-SB & Inactive and High-SB & Active in TC/HDL ($p < 0.05$), in favor of the latter. There were no significant differences for the remaining 4 health parameters: TG ($p = 0.09$), sum 4 skinfolds ($p = 0.11$), HOMA index ($p = 0.38$), and SBP ($p = 0.17$).

Fig. 2 shows the comparisons across the 4 categories of the integrative classification of PA on cardiometabolic risk (High-SB & Inactive: score = 0.822 (95% confidence interval (CI): 0.308−1.336); Low-SB & Inactive: score = 0.062 (95%CI: 0.733−0.856); High-SB & Active: score = −0.484 (95%CI: −1.187 to 0.218); and Low-SB & Active: score = −0.778 (95%CI: −1.353 to −0.203)). A significant reduction in cardiometabolic risk score is observed when adolescents meet the PA recommendation and at the same time reduce sedentary time ($p < 0.001$). In particular, the most significant differences were found between the High-SB & Inactive group and both the High-SB & Active and the Low-SB & Active groups ($p < 0.01$ and $p < 0.001$, respectively).

Table 2
Comparisons between inactive *vs.* active and low *vs.* high SB groups for single health parameters and cardiometabolic risk score (mean ± SD).

	Physical activity level				Sedentary time			
	Inactive ($n = 312$)	Active ($n = 236$)	p		Low ($n = 276$)	High ($n = 272$)	p	
			Model 1	Model 3			Model 1	Model 2
CRF (mL/kg/min)	40.6 ± 0.3	42.7 ± 0.4	**<0.001**	**0.001**	42.2 ± 0.4	41.2 ± 0.4	0.155	0.814
Sum 4 skinfolds (mm)	51.8 ± 0.8	50.9 ± 1.0	0.490	0.265	50.1 ± 0.9	52.8 ± 1.0	0.087	0.209
TC/HDL	3.0 ± 0.0	2.8 ± 0.0	0.060	0.265	2.8 ± 0.0	3.0 ± 0.0	**0.019**	0.099
TG (mg/dL)	70.4 ± 2.3	63.0 ± 2.9	0.060	0.225	62.4 ± 2.7	72.7 ± 2.9	**0.022**	0.225
SBP (mmHg)	121.2 ± 0.8	120.2 ± 1.0	0.497	0.899	119.0 ± 1.0	121.5 ± 1.0	0.128	0.261
HOMA index	2.5 ± 0.1	2.1 ± 0.1	0.094	0.105	2.1 ± 0.1	2.3 ± 0.1	0.392	0.888
Cardiometabolic risk score	0.52 ± 0.14	−0.52 ± 0.25	**0.001**	**0.020**	−0.66 ± 0.23	0.55 ± 0.27	**0.001**	**0.045**

Notes: ANCOVA models. Nontransformed data are presented, but statistical analyses were performed on log-transformed data. Boldface indicates statistical significance ($p < 0.05$). Model1: Adjusted for age, sex, body mass index, accelerometer wear time, and study center (random factor). Model 2: Model 1 + time spent at moderate-to-vigorous physical activity. Model 3: Model 1 + sedentary time.
Abbreviations: ANCOVA = analysis of covariance; CRF = cardiorespiratory fitness; HOMA = homeostasis model assessment; SBP = systolic blood pressure; TC/HDL = ratio between total cholesterol and high-density lipoprotein; TG = triglycerides.

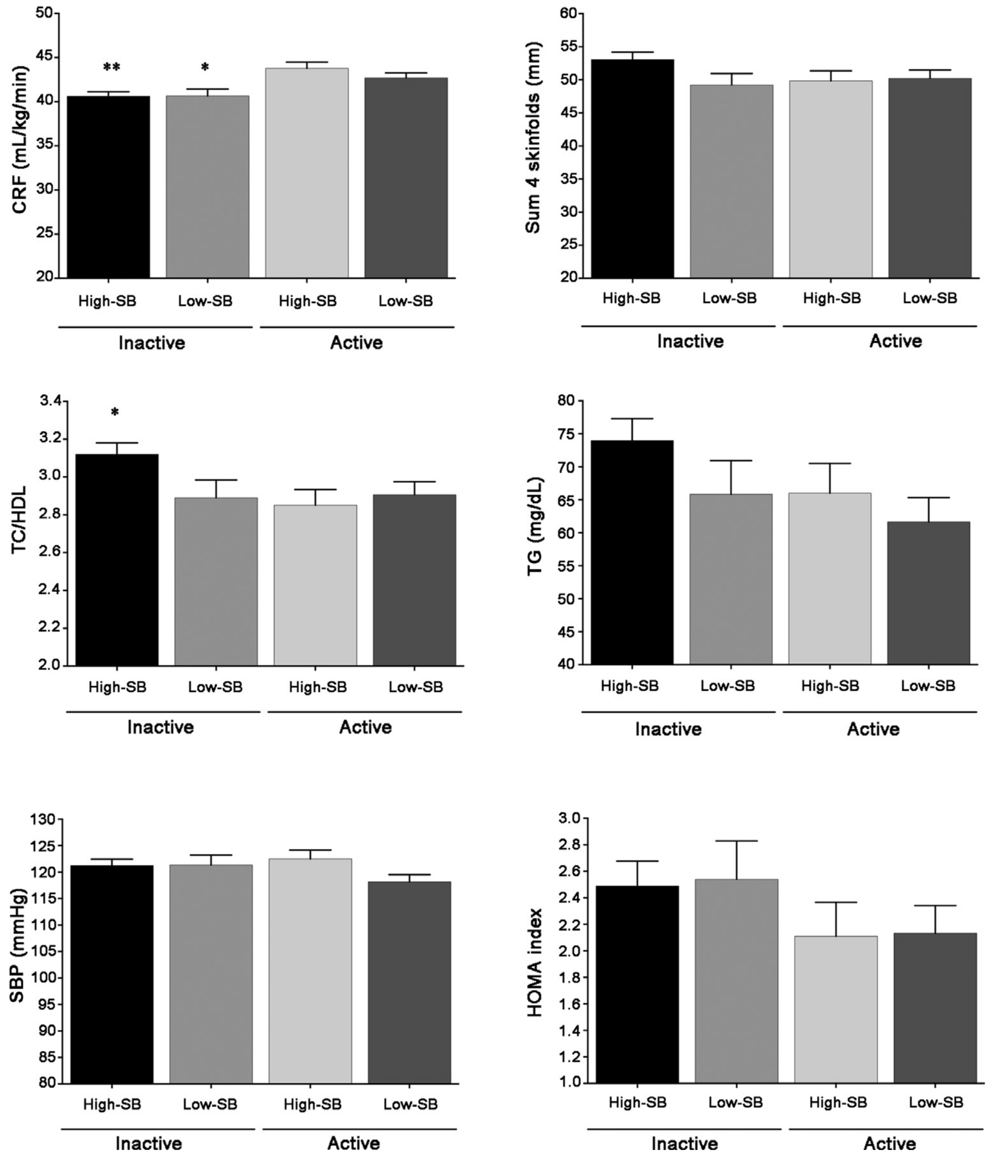

Fig. 1. Comparison across 4 categories (High-SB & Inactive ($n = 177$), Low-SB & Inactive ($n = 135$), High-SB & Active ($n = 95$), and Low-SB & Active ($n = 141$)) for the 6 health parameters composing the cardiometabolic risk score. All values are mean ± SD. Nontransformed data are presented, but statistical analyses were performed on log-transformed data. Analysis of covariance adjusted for age, sex, body mass index, accelerometer wear time, and study center (random factor). Bonferroni *post hoc* analysis was used. *$p < 0.05$, **$p < 0.001$ compared with High-SB & Active group. CRF = cardiorespiratory fitness; HOMA = homeostasis model assessment; SB = sedentary behavior; SBP = systolic blood pressure; TC/HDL = ratio between total cholesterol and high-density lipoprotein. TG = triglycerides.

4. Discussion

The present study showed that meeting the current MVPA recommendations and reducing SB time benefit cardiometabolic health in European adolescents. When using a more integrative PA classification, we found that a healthier cardiometabolic profile is present only in those who are physically active, whereas a nonsignificant difference is observed between high or low SB groups both in physically active and in inactive adolescents. These findings suggest prioritizing attention in public health to meeting the MVPA recommendations at early ages (infancy and early, middle, and late childhood) more than reducing SB time to reduce cardiometabolic risk.

Currently, there is a need to change PA behaviors at an early age, and there is widespread consensus on the fact that meeting the guideline level of MVPA protects against chronic diseases in children and adolescents.[11,26,27] At the same time, emerging evidence indicates the deleterious effects of prolonged sitting on health indicators in school-aged children.[38] However, there is also evidence showing that SB has not been linked to any of the body composition variables, fasting insulin, fasting TG, HDL cholesterol, or resting SBP, once adjusted for MVPA,[10,39,40] which supports our main findings.

Our results show that physically active adolescents have higher levels of CRF and a healthier cardiometabolic risk score, even when adjusting the analyses by sedentary time. Previous evidence confirms these results.[2,3,6,8,11,26,38,41] This finding concurs with a recently published meta-analysis,[42] concluding that the current evidence about objectively measured total sedentary time associated with CRF in children and

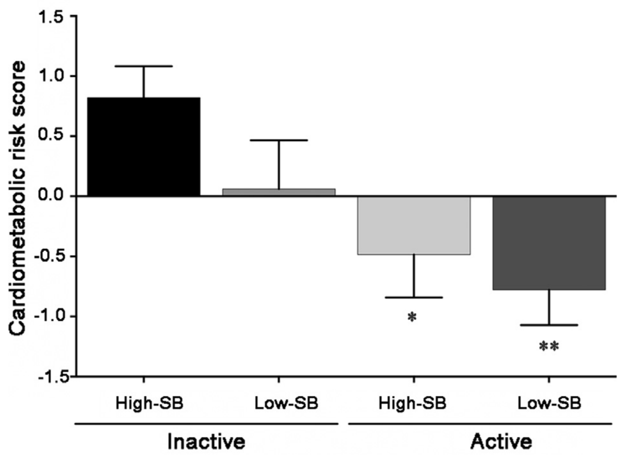

Fig. 2. Differences in cardiometabolic risk score across 4 categories (High-SB & Inactive ($n = 177$), Low-SB & Inactive ($n = 135$), High-SB & Active ($n = 95$), and Low-SB & Active ($n = 141$)). All values are mean ± SD. Non-transformed data are presented, but statistical analyses were performed on log-transformed data. Analysis of covariance adjusted for age, sex, body mass index, accelerometer wear time, and study (random factor). $*p < 0.01$, $**p < 0.001$ compared with High-SB & Inactive group. Bonferroni *post hoc* analysis was used. SB = sedentary behavior.

adolescents, but adjusted for MVPA, is limited. Thus, this type of integrative classification helps solve this type of methodological inconvenience.

Regarding the proposal of the integrative classification of PA, recent and diverse studies have used a combination of MVPA with the time spent in SB in children and adolescents.[21] The main variables analyzed are CRF[4,8,23] and indices of adiposity.[7,19] Nonetheless, to the best of our knowledge, only 1 study has previously analyzed a clustered cardiometabolic risk score in adolescents.[9] This study used a mixed methodology, where MVPA was measured using an accelerometer but SB was assessed using a questionnaire. Children were divided into 2 groups based on the total time spent on SB (<2 h/day or ≥2 h/day) according to the American Academy of Pediatrics guidelines, limiting a more holistic approach on total daily PA.[15] However, the results of this study were slightly different from ours, in which the HOMA index, TC/HDL, SBP, TG, sum of 4 skinfolds, and cardiometabolic risk score were not statistically significant in any of the 4 categories. Nonetheless, in line with our main finding, CRF was higher in the most active group.

In our study, the only individual metabolic risk factor that was significantly associated with PA levels in all categories was the CRF. There were no significant differences across the 4 categories in TG, HOMA index, sum of 4 skinfolds, or SBP, yet there was a trend showing lower (i.e., healthier) values in the active group. These results are consistent with other studies using a similar approach to PA classification in adults,[41] children, and adolescents.[7,9] In agreement with our findings, Boddy et al.[43] observed that CRF showed a significant improvement when adolescents advanced from the most inactive and sedentary category to another more active category, indicating its relevance once again as part of cardiometabolic health. For this reason, CRF is considered to be a useful diagnostic and prognostic health indicator in children and adolescents.[3−5] Exercise has been positively associated with increased CRF,[4,5,44] whereas excessive sedentary time has been related to low CRF in adolescents.[4,23,45] In adults, an additional hour of sedentary time was associated with a −0.12 metabolic equivalent (MET) and a −0.24 MET difference in CRF for men and women, respectively.[46] Meanwhile, in youth, time in MVPA has been associated with better CRF regardless of sedentary time.[4,8] This evidence may indicate the importance of increasing total daily PA level either through increasing the LPA/SB ratio or by increasing MVPA, because CRF seems to be more sensitive than the other health parameters in detecting any beneficial physiological change.

We found that cardiometabolic risk score was notably lower when PA was higher and sedentary time lower. However, the most significant result was observed when adolescents were more active than the median of MVPA and not when they were less sedentary. These SB results could be explained in 2 ways. First, intervention studies in children and adolescents aimed at reducing time in SB have shown significant, although very low, effectiveness in lowering BMI.[25] Furthermore, when SB data are statistically adjusted by MVPA, the level of association appears to decrease in adiposity, cardiometabolic risk, or CRF.[42] This may explain not having found a significant difference in either intermediate category (Low SB & Inactive and High SB & Active) in comparison with the higher or lower categories. Second, it has been suggested that intensity plays an important role in achieving the health benefits of exercise in youth,[44] but a minimal intensity is required. PA exceeding 2 METs has been associated with lower adiposity in mid-childhood, whereas exceeding 3 METs is needed to benefit CRF.[47]

Biological rationale for the results observed in this study is that exercise (and especially the intensity) plays a key role as an epigenetic modulator both to cellular and systemic level in several tissues and organs,[48] which may attenuate, or even eliminate, the detrimental association of sitting time with mortality.[49] Indeed, a recently published meta-analysis concluded that reallocating SB to MVPA but not to LPA is effective to reduce adiposity among youths (<18 years old).[50]

It may be of interest to carry out longitudinal studies to understand how childhood influences adolescence and adulthood with regard to changes in PA and SB and their effect on cardiometabolic health. Moreover, an objective measurement to evaluate a continuum of PA (sedentary to vigorous PA intensity) is a highly recommended methodology as well as a parallel qualitative analysis describing how children and adolescents spend their time (e.g., total sedentary time *vs.* screen viewing). Finally, future PA guidelines for children should prioritize meeting the MVPA recommendations such a primary strategy on public health and reducing SB as second. This approach is supported by a currently harmonized meta-analysis of data from more than 1 million men and women, which concludes that high levels of moderate-intensity PA (i.e., 60−75 min/day) seems to eliminate the increased risk of death associated with high sitting time.[49] More studies are necessary to understand the influence of LPA on diverse health parameters in adolescents.

This study presents some limitations that are important to note. The most relevant limitation is the methodological approach used to establish the sedentary categories. Sedentary time has typically been categorized by tertiles,[7,38] quartiles,[18] and median[4,8] cutoffs obtained in the receiver operating characteristic curve[23] <2 h or ≥2 h,[9] and LPA/SB ratio,[19] thus making interstudy comparisons difficult. Furthermore, it is important to bear in mind that a cross-sectional study does not allow the analysis of causal relationships.[51] In addition to these limitations, our study presents certain strengths, such as the diverse geographic origin of the samples and its standardized methodology to assess PA and SB using accelerometry. Additionally, to the best of our knowledge, this is the first study to use objective measurement and integrative classification of PA to evaluate the association between MVPA and SB with cardiometabolic risk in a large sample of European adolescents.

5. Conclusion

Increasing MVPA and reducing sedentary time is associated with a greater cardiometabolic risk score in an integrative PA classification. However, the most significant and protective outcome in adolescents to reduce cardiometabolic risk is to meet the MVPA recommendation.

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Authors' contributions

CCM had full access to all of the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis, carried out the study concept and design, and drafted the manuscript; JRR carried out the study concept and design, drafted the manuscript, and carried out the critical revision of the manuscript for important intellectual content; PC carried out the study concept and design and carried out the critical revision of the manuscript for important intellectual content; IL, JAC, MGG, JV, YM, LAM, and FBO carried out the critical revision of the manuscript for important intellectual content. All authors have read and approved the final version of the manuscript, and agreed with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

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