



**HAL**  
open science

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

Carlos Cristi-Montero, Palma Chillon, Idoia Labayen, José A. Casajus, Marcela Gonzalez-Gross, Jeremy Vanhelst, Xyannis Manios, Luis Moreno, Francisco B Ortega, Jonatan R Ruiz

### ► To cite this version:

Carlos Cristi-Montero, Palma Chillon, Idoia Labayen, José A. Casajus, Marcela Gonzalez-Gross, et al.. Cardiometabolic risk through an integrative classification combining physical activity and sedentary behavior in European adolescents: HELENA study. *Journal of Sport and Health Science*, 2019, 8, pp.55-62. 10.1016/j.jshs.2018.03.004 . hal-02358854

**HAL Id: hal-02358854**

**<https://hal.univ-lille.fr/hal-02358854>**

Submitted on 25 Aug 2020

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0 International License

Original article

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

Carlos Cristi-Montero<sup>a,\*</sup>, Palma Chillón<sup>b</sup>, Idoia Labayen<sup>c</sup>, José A. Casajus<sup>d</sup>,  
Marcela Gonzalez-Gross<sup>e</sup>, Jérémy Vanhelst<sup>f</sup>, Yannis Manios<sup>g</sup>, Luis A. Moreno<sup>d</sup>,  
Francisco B. Ortega<sup>b</sup>, Jonatan R. Ruiz<sup>b</sup>, on behalf of the HELENA study group

<sup>a</sup> IRyS Group, Physical Education School, Pontificia Universidad Católica de Valparaíso, Valparaíso 2340000, Chile

<sup>b</sup> PROMoting FITness and Health through physical activity research group (PROFITH), Department of Physical Education and Sports, Faculty of Sport Sciences, University of Granada, Granada 18001, Spain

<sup>c</sup> Department of Nutrition and Food Science, University of the Basque Country, UPV/EHU, Vitoria 01001, Spain

<sup>d</sup> Department of Health and Human Performance, School of Health Sciences, University of Zaragoza, Zaragoza 50001, Spain

<sup>e</sup> ImFINE Research Group, Facultad de Ciencias de la Actividad Física y del Deporte-INEF, Universidad Politécnica de Madrid, Madrid 28001, Spain

<sup>f</sup> Lille Inflammation Research International Center, University of Lille, Lille 59000, France

<sup>g</sup> Department of Nutrition and Dietetics, Harokopio University, Athens 10431, Greece

Received 9 September 2017; received 10 November 2017; accepted 8 December 2017

Available online 27 March 2018

## 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%;  $14.7 \pm 1.2$  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.

© 2019 Published by Elsevier B.V. on behalf of Shanghai University of Sport. This is an open access article under the CC BY-NC-ND license.

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**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,<sup>1,2</sup> higher cardiorespiratory fitness (CRF),<sup>3–5</sup> lower levels of insulin resistance markers,<sup>6</sup> and lower cardiovascular disease risk factors.<sup>7–10</sup> 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.<sup>11</sup> Furthermore, they engage in an

Peer review under responsibility of Shanghai University of Sport.

\* Corresponding author.

E-mail address: [carlos.cristi.montero@gmail.com](mailto:carlos.cristi.montero@gmail.com) (C. Cristi-Montero).

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

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),<sup>14,15</sup> spending large amounts of time in sedentary activities and being physically inactive (i.e., not achieving the established recommendations for PA)<sup>12</sup> have shown a strong association with morbidity and mortality.<sup>16,17</sup> 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);<sup>15,18</sup> 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.<sup>4,7–9,19–21</sup> For example, Roman-Viñas et al.<sup>22</sup> 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 ( $\geq 60$  min/day for MVPA), and (c) SB ( $\leq 2$  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.<sup>22</sup> 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)<sup>21</sup> have mainly focused on the association between single health markers, such as fitness and adiposity in children and adolescents.<sup>4,7,8,19,23</sup> 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.<sup>24</sup> 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.<sup>15,25–27</sup> 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)<sup>1,6,9,11</sup> is a multi-center 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.<sup>28</sup> 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.<sup>29</sup>

### 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.<sup>30</sup> Adolescents were barefoot and in light clothing during anthropometric measurements. BMI was calculated as body weight divided by the square of height ( $\text{kg}/\text{m}^2$ ). 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  $4^\circ\text{C}$ – $7^\circ\text{C}$  (for a maximum of 14 h) to the central laboratory in Bonn

(Germany) and stored there at  $-80^{\circ}\text{C}$  until assayed. TG, TC, and HDL were measured using enzymatic methods (Dade Behring, Schwalbach, Germany).<sup>31</sup> Serum concentrations of glucose and insulin were measured after an overnight fast. HOMA index calculation was used as a measure of insulin resistance.<sup>32</sup>

### 2.2.3. CRF

CRF was measured by the progressive 20-m shuttle run test. The test is valid and reliable in adolescents.<sup>33</sup> 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.<sup>34</sup>

### 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.<sup>24</sup> More recently, Andersen et al.<sup>35</sup> 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:  $(\text{value} - \text{mean})/\text{standard deviation (SD)}$ , separately for boys and girls, and for each 1-year age group. Lower values are indicative of a better profile.<sup>24</sup> 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.<sup>36</sup> 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.<sup>1,11</sup> Each epoch (time sampling interval) was set at 15 s in accordance with consensus recommendations for children and adolescents,<sup>37</sup> 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.<sup>11</sup> 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.<sup>4,8</sup> Furthermore, adolescents were dichotomized into those who met (active:  $\geq 60$  min/day in MVPA) or did not meet (inactive:  $<60$  min/day in MVPA) the current PA recommendations for youth.<sup>26</sup> 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  $\pm$  SD, and categorical variables are summarized using frequency (%). Student *t*, the Mann-Whitney *U*, and the  $\chi^2$  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 ( $\geq 60$  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  $\pm$  SD).<sup>a</sup>

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

<sup>a</sup> Student *t*, Mann-Whitney *U*, or  $\chi^2$  tests.<sup>b</sup> Sum 4 skinfolds: biceps, triceps, subscapular, and suprailliac.

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  $\pm$  SD).

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

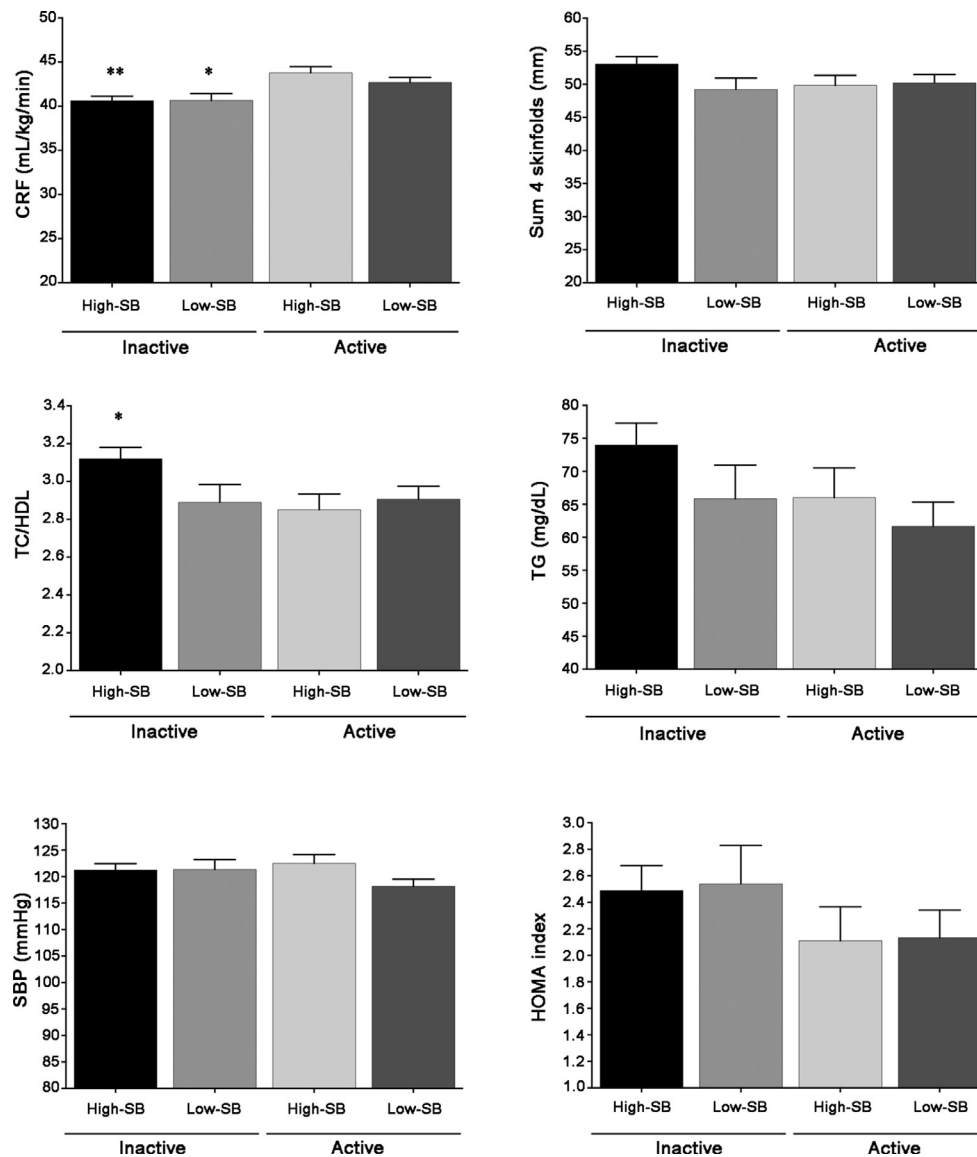


Fig. 1. Comparison across 4 categories (High-SB & Inactive ( $n = 177$ ), Low-SB & Inactive ( $n = 135$ ), High-SB & Active ( $n = 95$ ), and Low-SB & Active ( $n = 141$ )) for the 6 health parameters composing the cardiometabolic risk score. All values are mean  $\pm$  SD. Nontransformed data are presented, 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.<sup>11,26,27</sup> At the same time, emerging evidence indicates the deleterious effects of prolonged sitting on health indicators in school-aged children.<sup>38</sup> 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,<sup>10,39,40</sup> 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.<sup>2,3,6,8,11,26,38,41</sup> This finding concurs with a recently published meta-analysis,<sup>42</sup> concluding that the current evidence about objectively measured total sedentary time associated with CRF in children and

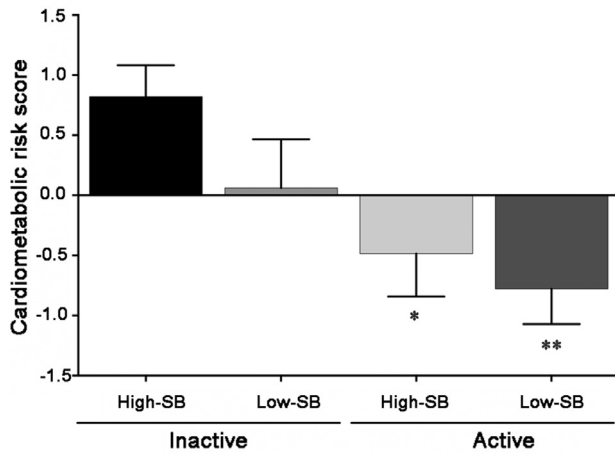


Fig. 2. Differences in cardiometabolic risk score across 4 categories (High-SB & Inactive ( $n=177$ ), Low-SB & Inactive ( $n=135$ ), High-SB & Active ( $n=95$ ), and Low-SB & Active ( $n=141$ )). All values are mean  $\pm$  SD. Non-transformed data are presented, but statistical analyses were performed 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.<sup>21</sup> The main variables analyzed are CRF<sup>4,8,23</sup> and indices of adiposity.<sup>7,19</sup> Nonetheless, to the best of our knowledge, only 1 study has previously analyzed a clustered cardiometabolic risk score in adolescents.<sup>9</sup> 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  $\geq 2$  h/day) according to the American Academy of Pediatrics guidelines, limiting a more holistic approach on total daily PA.<sup>15</sup> 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,<sup>41</sup> children, and adolescents.<sup>7,9</sup> In agreement with our findings, Boddy et al.<sup>43</sup> 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.<sup>3–5</sup> Exercise has been positively associated with increased CRF,<sup>4,5,44</sup> whereas excessive sedentary time has been related to low CRF in adolescents.<sup>4,23,45</sup> 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.<sup>46</sup> Meanwhile, in youth, time in MVPA has been associated with better CRF regardless of sedentary time.<sup>4,8</sup> 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.<sup>25</sup> Furthermore, when SB data are statistically adjusted by MVPA, the level of association appears to decrease in adiposity, cardiometabolic risk, or CRF.<sup>42</sup> 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,<sup>44</sup> 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.<sup>47</sup>

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,<sup>48</sup> which may attenuate, or even eliminate, the detrimental association of sitting time with mortality.<sup>49</sup> 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).<sup>50</sup>

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.<sup>49</sup> 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,<sup>7,38</sup> quartiles,<sup>18</sup> and median<sup>4,8</sup> cutoffs obtained in the receiver operating characteristic curve<sup>23</sup>  $<2$  h or  $\geq 2$  h,<sup>9</sup> and LPA/SB ratio,<sup>19</sup> 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.<sup>51</sup> 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.

## Acknowledgment

We thank the adolescents who participated in the study and their parents and teachers for their collaboration. The HELENA project was supported by the European Community Sixth RTD Framework Programme (contract FOOD-CT-2005-007034). The data for this study were gathered under the auspices of the HELENA project, and further analysis was additionally supported by the Spanish Ministry of Economy and Competitiveness (Grants RYC-2010-05957 and RYC-2011-09011), the Spanish Ministry of Health: Maternal, Child Health and Development Network (Grants RD08/0072 and RD16/0022), the Fondo Europeo de Desarrollo Regional (MICINN-FEDER), and the University of Granada, Plan Propio de Investigación 2016, Excellence actions: Units of Excellence; Unit of Excellence on Exercise and Health (UCEES). The content of this article reflects the authors' views alone, and the European Community is not liable for any use that may be made of the information contained herein.

## 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.

## References

- Moliner-Urdiales D, Ruiz JR, Ortega FB, Rey-Lopez JP, Vicente-Rodriguez G, España-Romero V, et al. Association of objectively assessed physical activity with total and central body fat in Spanish adolescents; the HELENA Study. *Int J Obes (Lond)* 2009;**33**:1126–35.
- Jiménez-Pavón D, Fernández-Vázquez A, Alexy U, Pedrero R, Cuenca-García M, Polito A, et al. Association of objectively measured physical activity with body components in European adolescents. *BMC Public Health* 2013;**13**:667. doi:10.1186/1471-2458-13-667.
- Ruiz JR, Huybrechts I, Cuenca-García M, Artero EG, Labayen I, Meirhaeghe A, et al. Cardiorespiratory fitness and ideal cardiovascular health in European adolescents. *Heart* 2015;**101**:766–73.
- Santos R, Mota J, Okely AD, Pratt M, Moreira C, Coelho-E-Silva MJ, et al. The independent associations of sedentary behaviour and physical activity on cardiorespiratory fitness. *Br J Sports Med* 2014;**48**:1508–12.
- Armstrong N. Young people are fit and active—fact or fiction? *J Sport Heal Sci* 2012;**1**:131–40.
- Jimenez-Pavon D, Ruiz JR, Ortega FB, Martinez-Gomez D, Moreno S, Urzauqui A, et al. Physical activity and markers of insulin resistance in adolescents: role of cardiorespiratory fitness levels—the HELENA study. *Pediatr Diabetes* 2013;**14**:249–58.
- Herman KM, Chaput JP, Sabiston CM, Mathieu ME, Tremblay A, Paradis G. Combined physical activity/sedentary behavior associations with indices of adiposity in 8- to 10-year-old children. *J Phys Act Heal* 2015;**12**:20–9.
- Marques A, Santos R, Ekelund U, Sardinha LB. Association between physical activity, sedentary time, and healthy fitness in youth. *Med Sci Sports Exerc* 2015;**47**:575–80.
- Rendo-Urteaga T, de Moraes ACF, Collese TS, Manios Y, Hagströmer M, Sjöström M, et al. The combined effect of physical activity and sedentary behaviors on a clustered cardio-metabolic risk score: the Helena study. *Int J Cardiol* 2015;**186**:186–95.
- Tarp J, Brond JC, Andersen LB, Moller NC, Froberg K, Grontved A. Physical activity, sedentary behavior, and long-term cardiovascular risk in young people: a review and discussion of methodology in prospective studies. *J Sport Health Sci* 2016;**5**:145–50.
- Ruiz JR, Ortega FB, Martínez-Gómez D, Labayen I, Moreno LA, De Bourdeaudhuij I, et al. Objectively measured physical activity and sedentary time in European adolescents: the HELENA study. *Am J Epidemiol* 2011;**174**:173–84.
- Tremblay MS, Aubert S, Barnes JD, Saunders TJ, Carson V, Latimer-Cheung AE, et al. Sedentary Behavior Research Network (SBRN)—Terminology Consensus Project process and outcome. *Int J Behav Nutr Phys Act* 2017;**14**:75. doi:10.1186/s12966-017-0525-8.
- Saunders TJ, Chaput JP, Tremblay MS. Sedentary behaviour as an emerging risk factor for cardiometabolic diseases in children and youth. *Can J Diabetes* 2014;**38**:53–61.
- Pedersen BK, Saltin B. Exercise as medicine—evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scand J Med Sci Sport* 2015;**25**:1–72.
- Tremblay MS, Carson V, Chaput JP, Connor Gorber S, Dinh T, Duggan M, et al. Canadian 24-hour movement guidelines for children and youth: an integration of physical activity, sedentary behaviour, and sleep. *Appl Physiol Nutr Metab* 2016;**41**(Suppl. 3):S311–27.
- Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. *Compr Physiol* 2012;**2**:1143–211.
- Koster A, Caserotti P, Patel KV, Matthews CE, Berrigan D, van Domelen DR, et al. Association of sedentary time with mortality independent of moderate to vigorous physical activity. *PLoS One* 2012;**7**:e37696. doi:10.1371/journal.pone.0037696.
- Bakrania K, Edwardson CL, Bodicoat DH, Esliger DW, Gill JMR, Kazi A, et al. Associations of mutually exclusive categories of physical activity



- and sedentary time with markers of cardiometabolic health in English adults: a cross-sectional analysis of the Health Survey for England. *BMC Public Health* 2016;**16**:25. doi:10.1186/s12889-016-2694-9.
19. Loprinzi PD, Cardinal BJ, Lee H, Tudor-Locke C. Markers of adiposity among children and adolescents: implications of the isotemporal substitution paradigm with sedentary behavior and physical activity patterns. *J Diabetes Metab Disord* 2015;**14**:46. doi:10.1186/s40200-015-0175-9.
  20. Spittaels H, Van Cauwenbergh E, Verbestel V, De Meester F, Van Dyck D, Verloigne M, et al. Objectively measured sedentary time and physical activity time across the lifespan: a cross-sectional study in four age groups. *Int J Behav Nutr Phys Act* 2012;**9**:149. doi:10.1186/1479-5868-9-149.
  21. Cristi-Montero C. An integrative methodology for classifying physical activity level in apparently healthy populations for use in public health. *Rev Panam Salud Publica* 2017;**41**:e161. doi:10.26633/RPSP.2017.161.
  22. Roman-Viñas B, Chaput JP, Katzmarzyk PT, Fogelholm M, Lambert EV, Maher C, et al. Proportion of children meeting recommendations for 24-hour movement guidelines and associations with adiposity in a 12-country study. *Int J Behav Nutr Phys Act* 2016;**13**:123. doi:10.1186/s12966-016-0449-8.
  23. Martínez-Gómez D, Ortega FB, Ruiz JR, Vicente-Rodríguez G, Veiga OL, Widhalm K, et al. Excessive sedentary time and low cardiorespiratory fitness in European adolescents: the HELENA study. *Arch Dis Child* 2011;**96**:240–6.
  24. Andersen LB, Harro M, Sardinha LB, Froberg K, Ekelund U, Brage S, et al. Physical activity and clustered cardiovascular risk in children: a cross-sectional study (The European Youth Heart Study). *The Lancet* 2006;**368**:299–304.
  25. Azevedo LB, Ling J, Soos I, Robalino S, Ells L. The effectiveness of sedentary behaviour interventions for reducing body mass index in children and adolescents: systematic review and meta-analysis. *Obes Rev* 2016;**17**:623–35.
  26. World Health Organization (WHO). *Global recommendations on physical activity for health*. Geneva: WHO; 2010. p. 60. doi:10.1080/11026480410034349.
  27. Riner WF, Sellhorst SH. Physical activity and exercise in children with chronic health conditions. *J Sport Health Sci* 2013;**2**:12–20.
  28. Vicente-Rodríguez G, Libersa C, Mesana MI, Béghin L, Iliescu C, Moreno Aznar LA, et al. Healthy lifestyle by nutrition in adolescence (HELENA). A new EU funded project. *Therapie* 2007;**62**:259–70.
  29. Moreno LA, De Henauf S, González-Gross M, Kersting M, Molnár D, Gottrand F, et al. Design and implementation of the healthy lifestyle in Europe by nutrition in adolescence cross-sectional study. *Int J Obes* 2008;**32**(Suppl. 5):S4–11.
  30. Nagy E, Vicente-Rodríguez G, Manios Y, Béghin L, Iliescu C, Censi L, et al. Harmonization process and reliability assessment of anthropometric measurements in a multicenter study in adolescents. *Int J Obes (Lond)* 2008;**32**(Suppl. 5):S58–65.
  31. González-Gross M, Breidenassel C, Gómez-Martínez S, Ferrari M, Béghin L, Spinneker A, et al. Sampling and processing of fresh blood samples within a European multicenter nutritional study: evaluation of biomarker stability during transport and storage. *Int J Obes (Lond)* 2008;**32**(Suppl. 5):S66–75.
  32. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985;**28**:412–9.
  33. Ortega FB, Artero EG, Ruiz JR, Vicente Rodríguez G, Bergman P, Hagströmer M, et al. Reliability of health-related physical fitness tests in European adolescents. The HELENA Study. *Int J Obes (Lond)* 2008;**32**:49–57.
  34. Léger LA, Mercier D, Gadoury C, Lambert J. The multistage 20 metre shuttle run test for aerobic fitness. *J Sports Sci* 1988;**6**:93–101.
  35. Andersen LB, Lauersen JB, Brønd JC, Anderssen SA, Sardinha LB, Steene-Johannessen J, et al. A new approach to define and diagnose cardiometabolic disorder in children. *J Diabetes Res* 2015;**2015**: 539835. doi:10.1155/2015/539835.
  36. Freedson P, Pober D, Janz KF. Calibration of accelerometer output for children. *Med Sci Sports Exerc* 2005;**37**(Suppl. 11):S523–30.
  37. Ward DS, Evenson KR, Vaughn A, Rodgers AB, Troiano RP. Accelerometer use in physical activity: best practices and research recommendations. *Med Sci Sport Exerc* 2005;**37**(Suppl. 11):S582–8.
  38. Carson V, Hunter S, Kuzik N, Gray CE, Poitras VJ, Chaput JP, et al. Systematic review of sedentary behaviour and health indicators in school-aged children and youth: an update. *Appl Physiol Nutr Metab* 2016;**41**(Suppl. 3):S240–65.
  39. Ekelund U, Luan J, Sherar LB, Esliger DW, Griew P, Cooper A, et al. Moderate to vigorous physical activity and sedentary time and cardiometabolic risk factors in children and adolescents. *JAMA* 2012;**307**:704–12.
  40. Ferrari GL, Oliveira LC, Araujo TL, Matsudo V, Barreira TV, Tudor-Locke C, et al. Moderate-to-vigorous physical activity and sedentary behavior: Independent associations with body composition variables in Brazilian children. *Pediatr Exerc Sci* 2015;**27**:380–9.
  41. Peterson MD, Al Snih S, Stoddard J, McClain J, Lee IM. Adiposity and insufficient MVPA predict cardiometabolic abnormalities in adults. *Med Sci Sports Exerc* 2014;**46**:1133–9.
  42. Cliff DP, Hesketh KD, Vella SA, Hinkley T, Tsiros MD, Ridgers ND, et al. Objectively measured sedentary behaviour and health and development in children and adolescents: systematic review and meta-analysis. *Obes Rev* 2016;**17**:330–44.
  43. Boddy LM, Murphy MH, Cunningham C, Breslin G, Foweather L, Gobbi R, et al. Physical activity, cardiorespiratory fitness, and clustered cardiometabolic risk in 10- to 12-year-old school children: the REACH Y6 study. *Am J Hum Biol* 2014;**26**:446–51.
  44. García-Hermoso A, Cerrillo-Urbina AJ, Herrera-Valenzuela T, Cristi-Montero C, Saavedra JM, Martínez-Vizcaíno V. Is high-intensity interval training more effective on improving cardiometabolic risk and aerobic capacity than other forms of exercise in overweight and obese youth? A meta-analysis. *Obes Rev* 2016;**17**:531–40.
  45. Rey-López JP, Bel-Serrat S, Santaliestra-Pasías A, de Moraes AC, Vicente-Rodríguez G, Ruiz JR, et al. Sedentary behaviour and clustered metabolic risk in adolescents: the HELENA study. *Nutr Metab Cardiovasc Dis* 2013;**23**:1017–24.
  46. Kulinski JP, Khera A, Ayers CR, Das SR, de Lemos JA, Blair SN, et al. Association between cardiorespiratory fitness and accelerometer-derived physical activity and sedentary time in the general population. *Mayo Clin Proc* 2014;**89**:1063–71.
  47. Collings PJ, Westgate K, Väistö J, Wijndaele K, Atkin AJ, Haapala EA, et al. Cross-sectional associations of objectively-measured physical activity and sedentary time with body composition and cardiorespiratory fitness in mid-childhood: the PANIC study. *Sport Med* 2017;**47**:769–80.
  48. Hawley JA, Hargreaves M, Joyner MJ, Zierath JR. Integrative biology of exercise. *Cell* 2014;**159**:738–49.
  49. Ekelund U, Steene-Johannessen J, Brown WJ, Fagerland MW, Owen N, Powell KE, et al. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. *The Lancet* 2016;**388**:1302–10.
  50. García-Hermoso A, Saavedra JM, Ramírez-Vélez R, Ekelund U, Del Pozo-Cruz B. Reallocating sedentary time to moderate-to-vigorous physical activity but not to light-intensity physical activity is effective to reduce adiposity among youths: a systematic review and meta-analysis. *Obes Rev* 2017;**18**:1088–95.
  51. Setia M. Methodology series module 3: cross-sectional studies. *Indian J Dermatol* 2016;**61**:261–4.