An integrative classification of physical activity and sedentary behavior and their relationship with cardiometabolic risk in European adolescents: the HELENA study

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Abstract

Introduction

Evidence suggests that moderate-vigorous physical activity (MVPA) and sedentary behavior (SB) independently affect various health parameters. However, children are commonly classified as physically active or inactive without considering time spent in SB. The aim of this study was to determine the association between an integrative classification of physical activity including both MVPA and SB with a clustered cardiometabolic risk score in European adolescents. **Methods** A cross-sectional study was conducted in adolescents (n= 548; boys 47.3%; 14.7 ± 1.2y) from 10 European cities. MVPA and SB were 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 (high and low) ("High-SB & Inactive", "Low-SB & Inactive", High-SB & Active", and "Low-SB & Active"). A clustered cardiometabolic risk score was computed using the HOMA index, systolic blood pressure, triglycerides, total cholesterol/HDL-c, sum 4 skinfolds, and cardiorespiratory fitness (CRF). Univariate general linear models were performed to assess the effects of each category and cardiometabolic risk score.

Results

The cardiometabolic risk score was lower in adolescents meeting the MVPA recommendation,

and it decreased with lower sedentary time. Intermediate categories (“Low-SB & Inactive” and

"High-SB & Active") did not show significant association in comparison with the higher or lower categories. 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" to "active", but not from "high to low-SB".

Conclusion

Being physically active has shown to be the most significant and protective outcome in adolescents in order to reduce cardiometabolic risk. Reducing SB does not exhibit a large effect. Thus, future physical activity guidelines for children should focus mainly on increasing the MVPA recommendations.

Keywords: Sedentary behavior, physical activity, exercise, cardiometabolic health, children, accelerometry.

Introduction

Evidence indicates that regular physical activity is associated with numerous health benefits in adolescents such as body composition (Moliner-Urdiales et al., 2009; Jiménez-Pavón et al., 2013a), cardiorespiratory fitness (Ruiz et al., 2015; Santos et al., 2014,), markers of insulin resistance (Jiménez-Pavón et al., 2013b), and cardiovascular disease risk factors (Ruiz et al., 2009; Rendo-Urteaga et al., 2015; Marques et al., 2015; Herman et al., 2015). Despite these benefits, a large percentage of adolescents (43.2% boys and 72.5% girls) do not currently meet the established recommendation of at least 60 minutes of moderate-vigorous physical activity (MVPA) every day (Ruiz et al., 2011). Further, they spend much of their time (around 71%) in sedentary behaviors (SB) (Ruiz et al., 2011).

Total daily physical activity is composed of a broad spectrum of movement behaviors in a 24-hour period: i) SB, ii) light-intensity physical activity (LIPA), and iii) MVPA. While both LIPA and MVPA promote a healthy profile (Pedersen & Saltin, 2015; Tremblay et al., 2016), spending large amounts of time in sedentary activities (<1.5 metabolic equivalents: METs, e.g., sitting or reclining posture) and being physically inactive (i.e., not achieving the established recommendations for physical activity) have shown a strong association with morbidity and mortality (Koster et al., 2012; Booth et al., 2012).

The independent associations of total daily physical activity, MVPA, LIPA, and SB time have been exhibited for several health markers (Bakrania et al., 2016; Tremblay et al., 2016). Therefore, reallocating all movement behaviors during a day appears to be a new approach for studies have begun to explore different combinations of patterns among SB, LIPA/SB ratio, and MVPA in order to categorize children and adolescents in a more integrative way (Spittaels et al., 2012; Santos et al., 2014; Marques et al., 2015; Herman et al., 2015; Loprinzi et al., 2015; Rendo-Urteaga et al., 2015).

Studies investigating the associations between clustered cardiometabolic risk score and the combined effect of physical activity and SB using an objective method are lacking. Indeed, few studies have used this methodology, and they have mainly focused on fitness and adiposity in children and adolescents (Santos et al., 2014; Marques et al., 2015; Martinez-Gomez et al., 2011; Hernan et al., 2015; Loprinzi et al., 2015). This information could be essential to establish future public health strategies, thus improving trends in childhood physical activity so as to reduce the prevalence of coronary and metabolic diseases in adulthood (Tremblay et al., 2016; Lätt et al., 2015; Azevedo et al., 2016; WHO, 2010).

The aim of this study was to determine the association between a clustered cardiometabolic risk score and an integrative classification of physical activity, which involves the combination of: i) high vs. low-SB time and ii) physically inactive vs. active, both objectively measured using accelerometry.

Method

improving global health status (Tremblay et al., 2016; Loprinzi et al., 2015). In this regard, some The Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study (HELENA-CSS) is a multicenter study performed in 10 European cities belonging to nine 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 yr. Data collection took place between 2006 and 2008. A sample of 3,528 adolescents met the HELENA general inclusion criteria. However, only 1089 of these were randomly selected in each city for blood collection. 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 (TC/HDL), Sum 4 skinfolds and cardiorespiratory fitness (CRF)] and accelerometry were included in the analysis. The study was performed following the ethical guidelines of the 1964 Declaration of Helsinki (revision of Edinburgh 2000), the Good Clinical Practice, and the legislation about 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 (Moreno et al., 2008).

Physical examination

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 (Nagy et al., 2008). Adolescents were barefoot and in light clothing during anthropometric measurements. Body mass index (BMI) was calculated as body weight (biceps, triceps, subscapular, and suprailiac) on the left side of the body were measured three consecutive times with a non-elastic tape (SECA 200) to the nearest 0.1 cm and with a Holtain caliper, to the nearest 0.2 mm, respectively. Pubertal stage was assessed by a physician according to Tanner and Whitehouse (Tanner et al., 1976). SBP was measured twice by OMRON®M6 (HEM 70001). Participants were seated in a separate quiet room for 10 min with their backs supported and feet on the ground. Two SPB readings were taken at 10 min intervals, and the lowest measure was used.

Blood samples

Blood samples were collected by venipuncture at school between 8:00 am and 10:00 am 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 r.p.m. for 15 min) to avoid hemolysis. Immediately after centrifugation, the samples were stored and transported at 4–7 °C (for a maximum of 14 h) to the central laboratory in Bonn (Germany) and stored there at −80 °C until assayed [29]. TG, TC, and HDL were measured using enzymatic methods (Dade Behring, Schwalbach, Germany). HOMA index calculation was used as a measure of insulin resistance (Matthews et al., 1985).

Cardiorespiratory fitness

CRF was measured by the progressive 20-m shuttle run test. Adolescents were required to run between two lines that were located 20 m apart, while keeping the pace with audio signals divided by the square of height (kg/m^2). Waist circumference and a set of skinfold thicknesses emitted from a pre-recorded 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 two consecutive occasions or when he or she stopped due to fatigue. The last stage completed (precision of 0.5 stages) was used to calculate the VO2max from the equation developed by Leger et al. (Léger et al., 1988).

Cardiometabolic Risk Score

A clustered cardiometabolic risk score was created from the sum of SBP, TG, TC/HDL ratio, HOMA index, sum of four skinfolds, and CRF. Previously, these 6 health parameters were positively skewed and were transformed (natural log). The standardized value (Z-scores) of each variable was calculated as follows: (value - mean)/SD, separately for boys and girls, and for each 1-yr age group. Lower values are indicative of a better profile (Andersen et al., 2006). The CRF Z-score was multiplied by -1 (cardiometabolic beneficial effect).

Physical activity levels

Levels of PA and sedentary time were measured with the GT1M ActiGraph accelerometer (Actigraph MTI, model GT1M, Manufacturing, Pensacola, FL, USA). The ActiGraph has been widely validated in youth (Freedson et al., 2005). 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 criterion for

Urdiales et al., 2009). Each epoch (time sampling interval) was set at 15 s in accordance with consensus recommendations for children and adolescents (Wards et al., 2005), and bouts of 20 continuous minutes of zero counts were considered as non-wearing time periods and were removed from the analysis. At least 3 days of recording with a minimum of 480-min wear time was required for inclusion of a day in analysis. Moreover, recordings of more than 20,000 counts/minute were considered potential malfunctions of the accelerometer, and these values were excluded from the analyses.

Sedentary time, moderate and vigorous PA was defined as <100, 2000–3999 and ≥4000 counts/minute, respectively (Ruiz et al., 2011). A measure of average volume of physical activity was expressed as the sum of recorded counts divided by total daily registered time expressed in minutes (counts/min). Adolescents were classified as low or high sedentary according to the median value by age and sex, as has previously been done in the literature (Santos et al., 2013; Marques et al., 2015). 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 physical activity recommendations for youth (WHO, 2010). This allowed us to create four categories according to high vs. low-SB time and physically inactive vs. active as a proposal of an integrative classification of physical activity (i.e., “High-SB & Inactive”, “Low-SB & Inactive”, High-SB & Active” and “Low-SB & Active”).

Statistical analysis

inclusion was to record at least 8 h/day for a minimum of 3 days (Ruiz et al., 2011, Moliner-
Descriptive statistics are presented as percentages or means and standard deviation (SD). T-student, U Mann–Whitney, or Pearson chi-square tests were performed to assess differences by sex for adolescent characteristics (age, height, weight, BMI, tanner stage), physical activity 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) (table 1).

Two univariate general linear analyses (univariate GLM) were performed to assess: i) comparisons between physically inactive vs. active and low vs. high-SB groups separately with the health parameters and cardiometabolic risk score and ii) comparison between the four categories of integrative classification of physical activity ("High-SB & Inactive", "Low-SB & Inactive", High-SB & Active" and "Low-SB & Active") with the health parameters and cardiometabolic risk score.

Three different models were performed that 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 moderate-vigorous physical activity) and finally Model 3 (Model 1 + sedentary time). A Bonferroni post-hoc test comparison between groups was used in the second GLM analysis. The main analyses were performed with boys and girls combined due to the fact that 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 the IBM SPSS Statistics V.21 (SPSS, Inc. IBM, New York, USA).

Results

Adolescent characteristics are shown in Table 1. On average, adolescents spent 542.8 min/day^{-1} (69.7%) in SB and 60.2 min/day^{-1} in MVPA (7.7%). Boys were significantly more active (~20 MVPA min/day^{-1}) than girls. 43.0% of the study adolescents achieved the recommended levels of PA (>60 min/day^{-1} of MVPA), and there was a large and significant difference between boys and girls, 61.7% vs. 26.2% respectively ($p<0.001$). Girls had higher levels of Sum 4 skinfolds (40%) and TG (20.7%) than boys, but they exhibited lower levels of SBP (7.5%) and CRF (25.1%) (all $p<0.005$).

Table 2 shows the comparison between high vs. low-SB time and physically inactive vs. active adolescents for various health parameters and cardiometabolic risk score. On the one hand, when active and inactive groups are compared, only two parameters (CRF and cardiometabolic risk score) exhibited significant differences ($p<0.05$) with both models 1 and 3 (model 3: adjusted for age, sex, BMI, accelerometer wear time, and additionally by sedentary time). The remaining health parameters are equal for all models. On the other hand, when comparing low and high-SB groups, TC/HDL, TG, and cardiometabolic risk score showed significant differences with model 1 ($p<0.05$). Nonetheless, when the analysis was adjusted for age, sex, BMI, accelerometers wear time, and additionally by MVPA time (model 2), this statistical difference disappears except for the cardiometabolic risk score. Overall, being physically active exhibited high cardiometabolic protection independent of sedentary level.

Figure 1 depicts multiple comparisons across the four categories of the six health parameters composing the cardiometabolic risk score. CRF ($F=6.46$; $p<0.0001$) and TC/HDL ($F=3.69$; $p<0.01$) present a significant overall effect among groups. Both “High-SB & Inactive” and “Low-SB & Inactive” groups showed significant differences in comparison with the “High-SB & Active” group in CRF ($p<0.001$ and $p<0.049$, respectively). In addition, significant differences are observed between “High-SB & Inactive” and “High-SB & Active” in TC/HDL ($p<0.030$). There were no significant differences for the remaining 4 health parameters: TG ($F=2.14$; $p=0.094$), Sum 4 skinfolds ($F=1.99$; $p=0.114$), HOMA ($F=1.02$; $p=0.380$), and SBP ($F=1.64$; $p=0.177$).

Figure 2 shows the comparisons across the four categories of the integrative classification of physical activity on cardiometabolic risk. A significant reduction in cardiometabolic risk score is observed when adolescents meet the physical activity recommendation and at the same time reduce sedentary time (overall effect $F=6.55$; $p<0.0001$). 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 ($p<0.010$ and $p<0.001$, respectively).

Discussion

The main findings of our study exhibit a significant lower cardiometabolic risk score when European adolescents meet the MVPA recommendation and a non-significant difference when sedentary time is reduced. These results suggest prioritizing attention to meeting the MVPA recommendations in early ages in order to reduce cardiometabolic risk.

Currently, there is widespread consensus on the fact that meeting the guideline level of MVPA protects against chronic diseases in children and adolescents (Ruiz et al., 2009; WHO, 2010). At the same time, emerging evidence indicates the deleterious effects of prolonged sitting on health indicators in school-aged children (Carson et al., 2016). Therefore, there is a real need to change physical activity behaviors at an early age.

Our results show that adolescents who are physically active have higher levels of CRF and a healthier cardiometabolic risk score, even when adjusting the data by sedentary time. Previous evidence confirms these results (Carson et al., 2016; Ruiz et al., 2009; WHO, 2010; Ruiz et al., 2015; Jiménez-Pavón et al., 2013a; Jiménez-Pavón et al., 2013b; Peterson et al., 2014; Marques et al., 2015). This outcome was corroborated in a recently published meta-analysis, concluding that evidence about objectively measured total sedentary time adjusted for MVPA associated with CRF in children and adolescents is limited (Cliff et al., 2016).

Regarding the proposal of the integrative classification of physical activity, recent and diverse studies have used a combination between MVPA and the time spent in SB in children and adolescents. The main variables that have been analyzed are CRF (Santos et al., 2014; Marques et al., 2015; Martinez-Gomez et al., 2011) and indices of adiposity (Hernan et al., 2015; Loprinzi et al., 2015). Nonetheless, to the best of our knowledge, only one study has previously analyzed a clustered cardiometabolic risk score in adolescents (Rendo-Urteaga et al., 2015). This study used assessed using a questionnaire. Thus, children were divided into 2 groups based on the total time spent on SB per day (<2h or >2h) according to the American Academy of Pediatrics guidelines, limiting a more holistic approach on total daily physical activity (Tremblay et al., 2016). The results of the abovementioned study were less statistically significant on each variable (HOMA, TC/HDL, SBP, TG, Sum 4 skinfolds and CRF) than ours.

In our study, regarding each individual metabolic risk factor, the only metabolic risk factor that was significantly associated with physical activity levels (using the 4 categories) was the CRF. A significant association was not found among the 4 categories and TG, TC/HDL, HOMA, Sum of 4 skinfolds, and SBP. Our results are consistent with other studies using a similar approach to physical activity classification in both adults (Peterson et al., 2014), children and adolescents (Rendo-Urteaga et al., 2015; Marques et al., 2015; Herman et al., 2015). In line with what we previously mentioned, CRF showed a significant improvement when adolescents pass from the most inactive and sedentary category to another more active category, indicating its relevance once again as part of cardiometabolic health (Boddy et al., 2014). CRF is considered a useful diagnostic and prognostic health indicator in children and adolescents (Ruiz et al., 2015; Santos et al., 2014). Exercise has been positively associated with an increased CRF (Santos et al., 2014, García-Hermoso et al., 2016), but excessive sedentary time has been related with low CRF in adolescents (Santos et al., 2014, Martinez-Gomez et al., 2011; Rey-López, 2013). In adults, an additional hour of sedentary time was associated with a -0.12 and a -0.24 MET (metabolic equivalent) difference in CRF for men and women, respectively (Kulinski et al, 2014), while in youth, time in MVPA has been associated with better CRF independent of sedentary time a mixed methodology where MVPA was assessed using an accelerometer; however, SB was (Marques et al., 2015; Santos et al., 2014). This evidence may indicate the importance of increasing total daily physical activity level either through increasing the LIPA/SB ratio or by increasing MVPA, because CRF seems to be more sensitive than the other health parameters in detecting any beneficial physiological changes.

We found that cardiometabolic risk score was notably lower when physical activity 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. This result is consistent the study by Rendo-Urteaga et al., 2015 in adolescents. They employed an integrative classification of physical activity using an accelerometer to assess MVPA as well as a questionnaire to determine SB (Rendo-Urteaga et al., 2015). It was concluded that the cardiometabolic risk score was lower in the most physically active adolescents. However, there were no statistically significant differences observed between the groups.

Intervention studies on SB have shown a significant, although very small, effectiveness on reducing BMI in children and adolescents (Azevedo et al., 2016). Statistically, when SB data are adjusted by MVPA the level of association appears to decrease on adiposity, cardiometabolic, or CRF (Cliff et al., 2016). Thus, this may explain not having found a significant association in both intermediate categories ("Low-SB & Inactive" and "High-SB & Active") in comparison with the higher or lower categories. As a result, it could be suggested that intensity plays an important role in achieving the health benefits of exercise in youth (García-Hermoso et al., 2016), but a minimal intensity is required. Physical activity exceeding 2 METs has been associated with lower

LIPA/SB ratio (Loprinzi et al., 2015; Spittaels et al., 2012), making inter-studies comparisons 2016).

In this regard, reallocating or substituting sedentary time with LIPA is maybe not the best solution for this population as opposed to the case of adults who are much more sedentary (Tremblay et al., 2016; Loprinzi et al., 2015). In this sense, an interesting study (2-year follow-up study) found that vigorous physical activity rather than SB was a better predictor of overweight and obesity in pubertal boys (Lätt et al., 2015). Furthermore, this may explain why CRF is so relevant in reducing cardiometabolic risk score (García-Hermoso et al., 2016).

It may be of interest to carry out longitudinal studies in order to understand how childhood influences adolescence and adulthood with regards to changes in physical activity and SB and their effect on cardiometabolic health. Moreover, an objective measurement to evaluate a continuum of physical activity (sedentary to vigorous physical activity intensity) is a highly recommended methodology as well as a parallel qualitative analysis describing how time is spent in children and adolescents. Finally, future physical activity guidelines for children should mainly prioritize meeting the MVPA recommendations, and in second place reducing SB.

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 (Herman et al., 2015; Peterson et al., 2014), quartile (Bakrania et al., 2016), median (Santos et al., 2014; Marques et al., 2015), cut-offs obtained in the ROC curve (Martinez-Gomez et al., 2011), <2h or >2h (Rendo-Urteaga et al., 2015), and adiposity in mid-childhood, whereas exceeding 3 METs in needed to benefit CRF (Collings et al., difficult. Furthermore, it is important to bear in mind that a cross-sectional study does not allow the analysis of causal relationships. Besides these limitations, our study presents some strength such as the diverse geographic origin of the samples and its standardized methodology to assess PA and SB using an accelerometer. Additionally, to the best of our knowledge, this is the first study to use objective measurement and integrative classification of physical activity to evaluate the association between MVPA and SB with cardiometabolic risk in a large sample of European adolescents.

Conclusion

Our study suggests that increasing MVPA and reducing sedentary level is associated with a better cardiometabolic risk score in an integrative physical activity classification. However, the most significant and protective outcome in adolescents in order to reduce cardiometabolic risk is meet MVPA recommendation.

References

1. Ruiz JR, Huybrechts I, Cuenca-García M, Artero EG, Labayen I, Meirhaeghe A, Vicente-Rodriguez G, Polito A, Manios Y, González-Gross M, Marcos A, Widhalm K, Molnar D, Kafatos A, Sjöström M, Moreno LA, Castillo MJ, Ortega FB; HELENA study group. Cardiorespiratory fitness and ideal cardiovascular health in European adolescents. Heart. 2015 May 15;101(10):766-73.

LIPA/SB ratio (Loprinzi et al., 2015; Spittaels et al., 2012), making inter-studies comparisons

2. Jiménez-Pavón D, Fernández-Vázquez A, Alexy U, Pedrero R, Cuenca-García M, Polito A, Vanhelst J, Manios Y, Kafatos A, Molnar D, Sjöström M, Moreno LA; HELENA Study Group. Association of objectively measured physical activity with body components in European adolescents. BMC Public Health. 2013 Jul 18;13:667. **A**

3. Jiménez-Pavón D, Ruiz JR, Ortega FB, Martínez-Gómez D, Moreno S, Urzanqui A, Gottrand F, Molnár D, Castillo MJ, Sjöström M, Moreno LA; HELENA Study group. Physical activity and markers of insulin resistance in adolescents: role of cardiorespiratory fitness levels--the HELENA study. Pediatr Diabetes. 2013 Jun;14(4):249-58. B

4. Ruiz JR, Ortega FB. Physical activity and cardiovascular disease risk factors in children and adolescents. Curr Cardiovasc Risk Rep. 2009;1(3):281–287.

5. Ruiz JR, Ortega FB, Martínez-Gómez D, Labayen I, Moreno LA, De Bourdeaudhuij I, Manios Y, Gonzalez-Gross M, Mauro B, Molnar D, Widhalm K, Marcos A, Beghin L, Castillo MJ, Sjöström M; HELENA Study Group. Objectively measured physical activity and sedentary time in European adolescents: the HELENA study. Am J Epidemiol. 2011 Jul 15;174(2):173-84.

6. Koster A, Caserotti P, Patel KV, Matthews CE, Berrigan D, Van Domelen DR, Brychta RJ, Chen KY, Harris TB. Association of sedentary time with mortality independent of moderate to vigorous physical activity. PLoS One. 2012;7(6):e37696.

7. Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. Compr Physiol. 2012,2:1143–211.

8. Bakrania K, Edwardson CL, Bodicoat DH, Esliger DW, Gill JM, Kazi A, Velayudhan L, Sinclair AJ, Sattar N, Biddle SJ, Khunti K, Davies M, Yates T. Associations of mutually exclusive categories of physical activity and sedentary time with markers of

for England. BMC Public Health. 2016 Jan 12;16(1):25.

9. Pedersen BK, Saltin B. Exercise as medicine - evidence for prescribing exercise as therapy in 26 different chronic diseases. Scand J Med Sci Sports. 2015 Dec;25 Suppl 3:1-72.

10. Marques A, Santos R, Ekelund U, Sardinha LB. Association between physical activity, sedentary time, and healthy fitness in youth. Med Sci Sports Exerc. 2015 Mar;47(3):575-80.

11. Herman KM, Chaput JP, Sabiston CM, Mathieu ME, Tremblay A, Paradis G. Combined physical activity/sedentary behaviour associations with indices of adiposity in 8- to 10-year-old children. J Phys Act Health. 2015 Jan;12(1):20-9.

12. 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 May 27;14:46.

13. Spittaels H, Van Cauwenberghe E, Verbestel V, De Meester F, Van Dyck D, Verloigne M, Haerens L, Deforche B, Cardon G, De Bourdeaudhuij I. 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 Dec 18;9:149.

14. Santos R, Mota J, Okely AD, Pratt M, Moreira C, Coelho-e-Silva MJ, Vale S, Sardinha LB. The independent associations of sedentary behaviour and physical activity on cardiorespiratory fitness. Br J Sports Med. 2014 Oct;48(20):1508-12.

15. Nagy E, Vicente-Rodriguez G, Manios Y, et al. Harmonization process and reliability assessment of anthropometric measurements in a multicenter study in adolescents. Int J

cardiometabolic health in English adults: a cross-sectional analysis of the Health Survey Obes (Lond) 2008;32(Suppl 5):S58–65.

16. 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;28:412e9.
17. Moreno LA1, De Henauw S, González-Gross M, Kersting M, Molnár D, Gottrand F, Barrios L, Sjöström M, Manios Y, Gilbert CC, Leclercq C, Widhalm K, Kafatos A, Marcos A; HELENA Study Group. Design and implementation of the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study. Int J Obes (Lond). 2008;32 Suppl 5:S4-11.
18. Andersen LB, Harro M, Sardinha LB, Froberg K, Ekelund U, Brage S, Anderssen SA. Physical activity and clustered cardiovascular risk in children: a cross-sectional study (The European Youth Heart Study). Lancet. 2006 22;368(9532):299-304.
19. Rey-López JP, Bel-Serrat S, Santaliestra-Pasías A, de Moraes AC, Vicente-Rodríguez G, Ruiz JR, Artero EG, Martínez-Gómez D, Gottrand F, De Henauw S, Huybrechts I, Polito A, Molnar D, Manios Y, Moreno LA. Sedentary behaviour and clustered metabolic risk in adolescents: the HELENA study. Nutr Metab Cardiovasc Dis. 2013 Oct;23(10):1017-24.
20. Tanner JM, Whitehouse RH. Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. Arch Dis Child 1976: 51: 170 – 179.
21. Moliner-Urdiales D, Ruiz JR, Ortega FB 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 – 1135.
22. Freedson P, Pober D, Janz KF. Calibration of accelerometer output for children. Med Sci Sports Exerc 2005;37:S523–30.

practices and research recommendations. Med Sci Sports Exerc 2005;37:S582–8.

24. World Health Organization. Global Recommendations on Physical Activity for Health. Geneva (Switzerland): World Health Organization; 2010.

25. Rendo-Urteaga T, de Moraes AC2, Collese TS, Manios Y, Hagströmer M, Sjöström M, Kafatos A, Widhalm K, Vanhelst J, Marcos A, González-Gross M, De Henauw S, Ciarapica D, Ruiz JR, España-Romero V, Molnár D, Carvalho HB, Moreno LA; HELENA Study Group. 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.

26. Carson V, Hunter S, Kuzik N, Gray CE, Poitras VJ, Chaput JP, Saunders TJ, Katzmarzyk PT4, Okely AD, Connor Gorber S, Kho ME, Sampson M, Lee H, Tremblay MS. Systematic review of sedentary behaviour and health indicators in school-aged children and youth: an update. Appl Physiol Nutr Metab. 2016 Jun;41(6 Suppl 3):S240-65.

27. Cliff DP, Hesketh KD, Vella SA, Hinkley T, Tsiros MD, Ridgers ND, Carver A, Veitch J, Parrish AM, Hardy LL, Plotnikoff RC, Okely AD, Salmon J, Lubans DR. Objectively measured sedentary behaviour and health and development in children and adolescents: systematic review and meta-analysis. Obes Rev. 2016 Apr;17(4):330-44.

28. 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 Jun;17(6):531-40.

29. Azevedo LB, Ling J, Soos I, Robalino S, Ells L. The effectiveness of sedentary behaviour

23. Ward DS, Evenson KR, Vaughn A, et al. Accelerometer use in physical activity: best interventions for reducing body mass index in children and adolescents: systematic review and meta-analysis. Obes Rev. 2016 Jul;17(7):623-35.

30. Martinez-Gomez D, Ortega FB, Ruiz JR, Vicente-Rodriguez G, Veiga OL, Widhalm K, Manios Y, Béghin L, Valtueña J, Kafatos A, Molnar D, Moreno LA, Marcos A, Castillo MJ, Sjöström M; HELENA study group. Excessive sedentary time and low cardiorespiratory fitness in European adolescents: the HELENA study. Arch Dis Child. 2011 Mar;96(3):240-6.

31. Tremblay MS, Carson V, Chaput JP, Connor Gorber S, Dinh T, Duggan M, Faulkner G, Gray CE, Gruber R, Janson K, Janssen I, Katzmarzyk PT, Kho ME, Latimer-Cheung AE, LeBlanc C, Okely AD, Olds T, Pate RR, Phillips A, Poitras VJ, Rodenburg S, Sampson M, Saunders TJ, Stone JA, Stratton G, Weiss SK, Zehr L. Canadian 24-Hour Movement Guidelines for Children and Youth: An Integration of Physical Activity, Sedentary Behaviour, and Sleep. Appl Physiol Nutr Metab. 2016 Jun;41(6 Suppl 3):S311-27.

32. Lätt E, Mäestu J, Ortega FB, Rääsk T, Jürimäe T, Jürimäe J. Vigorous physical activity rather than sedentary behaviour predicts overweight and obesity in pubertal boys: a 2-year follow-up study. Scand J Public Health. 2015 May;43(3):276-82.

33. Kulinski JP, Khera A, Ayers CR, Das SR, de Lemos JA, Blair SN, Berry JD. Association between cardiorespiratory fitness and accelerometer-derived physical activity and sedentary time in the general population. Mayo Clin Proc. 2014 Aug;89(8):1063-71.

34. Léger LA, Mercier D, Gadoury C, et al. The multistage 20 metre shuttle-run test for aerobic fitness. J Sports Sci 1988;6:93–101.

35. Boddy LM, Murphy MH, Cunningham C, Breslin G, Foweather L, Gobbi R, Graves LE, Hopkins ND, Auth MK, Stratton G. Physical activity, cardiorespiratory fitness, and

Table 1. Descriptive characteristics of adolescents.

study. Am J Hum Biol. 2014 Jul-Aug;26(4):446-51.

36. 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 Jun;46(6):1133-9.

37. Collings PJ, Westgate K, Väistö J, Wijndaele K, Atkin AJ, Haapala EA, Lintu N, Laitinen T, Ekelund U, Brage S, Lakka TA. Cross-Sectional Associations of Objectively-Measured Physical Activity and Sedentary Time with Body Composition and Cardiorespiratory Fitness in Mid-Childhood: The PANIC Study. Sports Med. 2016 Aug 24.

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		All (n=548)		Boys (n=259)		Girls (n=289)		P-value by sex
		mean	SD	mean	SD	mean	SD	
Age (years)		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
Tanner	stage I	3.5%		3.0%		3.8%		
	stage II-IV	66.2%		65.3%		67.1%		0,048
	stage V	30.3%		31.7%		29.1%		
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)		43.0 (236)		61.7 (160)		26.2 (76)		<0.001
High sedentary % (n)		49.6 (272)		51.7 (134)		47.7 (138)		0.392
CRF ($ml/kg/min-^1$)		41.4	7.9	46.3	7.2	37.0	5.7	0.002
Sum 4 skinfolds (mm)		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		2.4	2.0	2.4	2.4	2.5	1.6	0.543
Cardiometabolic risk score		0.123	3.6	-0.121	3.5	0.342	3.7	0.138

Table 1. Descriptive characteristics of adolescents.

Values are mean and SD. Bold indicates statistical significance (P-values < 0.05) using t-student, U Mann–Whitney, or Pearson chi-square tests. PA: physical activity; MVPA: moderate to vigorous physical activity; BMI: body mass index; TG: triglycerides; TC/HDL: ratio between total cholesterol and high density lipoprotein; HOMA: homeostasis model assessment; Sum 4 skinfolds: biceps, triceps, subcapsular and suprailiac; SBP: systolic blood pressure; CRF: cardiorespiratory fitness. Meeting PA guidelines %: Percentage of children meeting the physical activity recommendation. High sedentary %: Percentage of sedentary children according to the median value by age and sex.

Table 2. Comparisons between inactive vs. active and low vs. high-SB groups for various health parameters and Cardiometabolic Risk Score.

	Physical activity level						Sedentary					
	Inactive (n=312)		Active (n=236)		Model 1	Model 3	Low (n=276)		High (n=272)		Model 1	Model 2
	Mean	SEM	Mean	SEM	P-value	P-value	Mean	SEM	Mean	SEM	P-value	P-value
CRF	40.6	0.36	42.7	0.45	**<0.001**	**0.001**	42.2	0.43	41.2	0.46	0.155	0.814
Sum 4 skinfolds	51.8	0.81	50.9	1.01	0.490	0.265	50.1	0.94	52.8	1.01	0.087	0.209
TC/HDL	3.0	0.04	2.8	0.05	0.060	0.265	2.8	0.05	3.0	0.05	**0.019**	0.099
TG (mg/dL)	70.4	2.38	63.0	2.98	0.060	0.225	62.4	2.74	72.7	2.94	**0.022**	0.225
SBP (mmHG)	121.2	0.87	120.2	1.09	0.497	0.899	119.0	1.00	121.5	1.08	0.128	0.261
HOMA	2.52	0.13	2.15	0.16	0.094	0.105	2.1	0.15	2.3	0.16	0.392	0.888
Cardiometabolic risk score	0.52	0.18	-0.52	0.23	**0.001**	**0.020**	-0.66	0.22	0.55	0.23	**0.001**	**0.045**

Univariate general linear model, all values are mean and SEM. Non-transformed data are presented, but statistical analyses were performed on Log-transformed data. Bold indicates statistical significance ($p<0.05$).

Model 1. Adjusted for age, sex, body mass index, accelerometer wear time, and study center (random factor).

Model 2. Model 1 + time spent at moderate-vigorous physical activity.

Model 3. Model 1 + sedentary time.

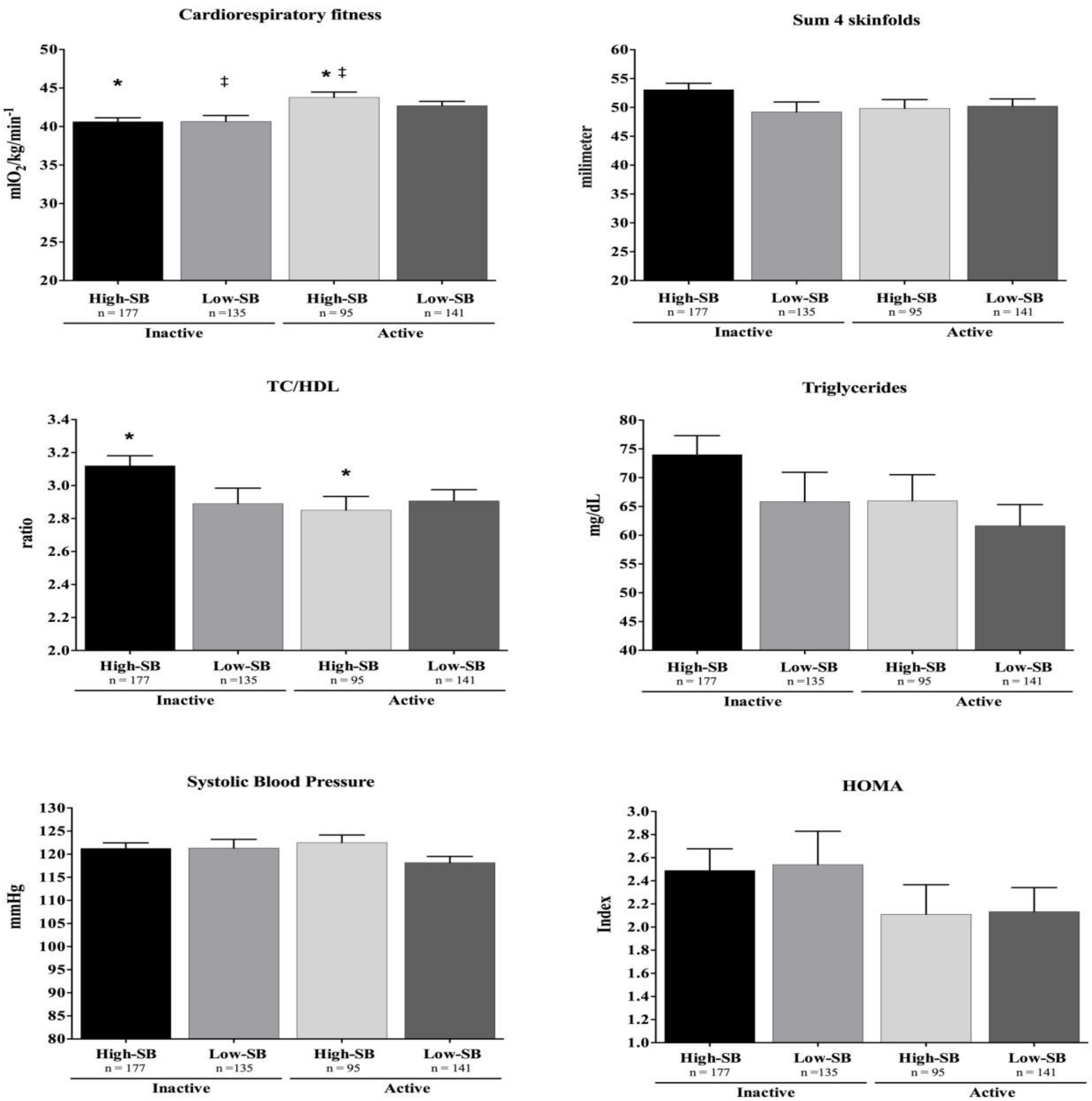

Figure 1. Comparison among four categories for the six health parameters composing cardiometabolic risk score. Univariate general linear models, all values are mean and SEM. Non-transformed data are presented, but statistical analyses were performed on Log-transformed data. Common symbols indicate statistical significance ($p<0.05$) between groups. Analysis adjusted for

Bonferroni post hoc analysis was used.

age, sex, body mass index, accelerometer wear time, and study center (random factor).

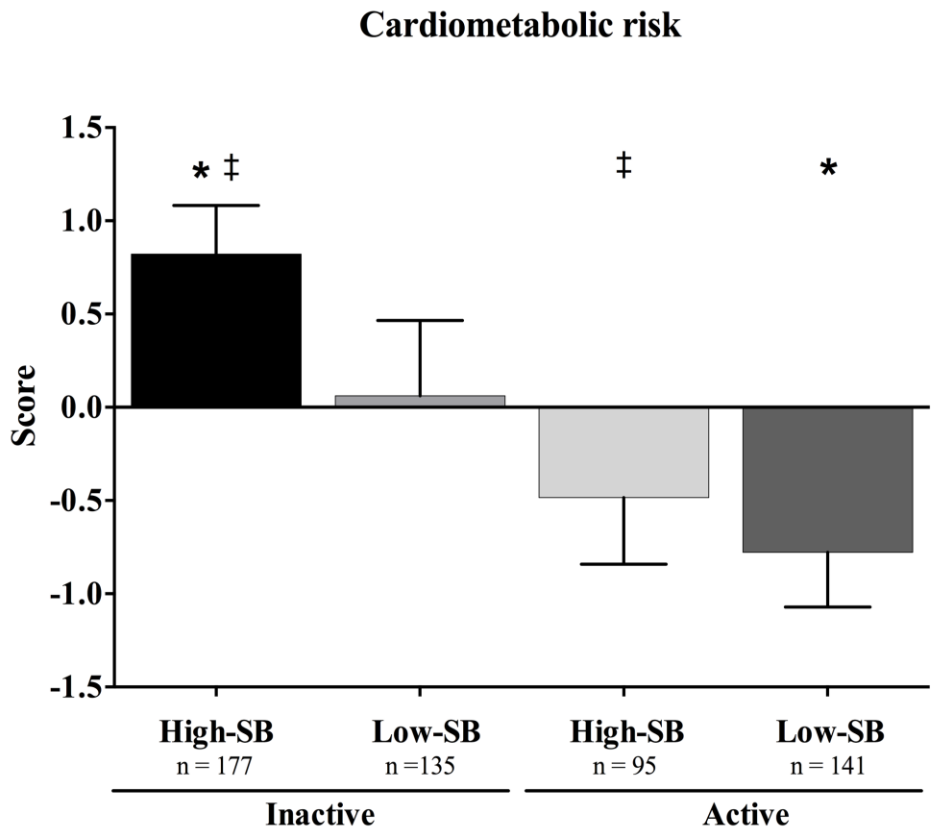

Figure 2. Differences in cardiometabolic risk score among four categories. Univariate general linear models, all values are mean and SEM. Non-transformed data are presented, but statistical analyses were performed on Log-transformed data. Analysis adjusted for age, sex, body mass index, accelerometer wear time, and study (random factor). Common symbols indicate statistical significance ($p<0.05$) between groups. Bonferroni post hoc analysis was used.