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Longitudinal associations between device-measured physical activity and cardiometabolic health in the transition to early adulthood

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ABSTRACT

Purposes: The aims of this study were to investigate the cross-sectional and prospective associations between accelerometer-measured physical activity and cardiometabolic health in the transition to adulthood.

Methods: Data from the 1993 Pelotas (Brazil) Birth Cohort were analysed (N=2,280). Moderate-to-vigorous intensity physical activity (MVPA, measured using a triaxial accelerometer) and cardiometabolic health (total fat mass, blood glucose, non-HDL cholesterol, triglycerides and mean resting blood pressure) were examined at age 18 and 22 years.

Results: Overall, inverse dose-response associations between MVPA and cardiometabolic health at age 18 and 22y were observed in cross-sectional analyses of data from males and females. Prospective analyses showed that, in general, MVPA declined, and cardiometabolic health worsened in this 4-year period in both males and females. Cardiometabolic health at age 22 reflected both MVPA at age 18y [β: -0.007 (95% CI: -0.014; 0.000)] and changes in MVPA from 18 to 22y [β: -0.030 (95% CI: -0.043; -0.016)] in males, but only changes in MVPA in females [β: -0.035 (95% CI: -0.058; -0.011)]. In analyses of change over time, males who improved MVPA by 20-30 minutes per day showed significant improvements in cardiometabolic health over 4 years. The magnitude of association was slightly stronger for MVPA in 10-minutes bouts than for MVPA accumulated in bouts of 1-minute, especially in females.

Conclusion: MVPA is an important predictor of cardiometabolic health in early adulthood. Strategies to prevent declines in MVPA at this life stage are required to prevent deteriorating cardiometabolic health profiles.

Keywords: physical activity; cohorts; adulthood; metabolic profile

INTRODUCTION

Non-communicable chronic diseases (NCDs) are major global health concerns. Although most NCDs usually emerge during mid-late adulthood, their risk factors tend to cluster during adolescence (1) and track into adulthood (2), leading to the development of morbidities, which in turn increases the risk of early mortality (3-5). Identification of sensitive periods for changes in behavioural and cardiometabolic risk factors is essential for preventing or delaying the occurrence of NCDs in later life.

Physical activity is critical for prevention of major NCDs (6). Recent studies show that higher levels of physical activity during adolescence are associated with improved cardiometabolic health during this life stage (7-9). Pooled analysis of data from cross-sectional studies in *The International Children's Accelerometry Database* shows that time in moderate-to-vigorous intensity physical activity (MVPA) is associated with better metabolic health in children and adolescents (7). There is also evidence to suggest that accumulation of any MVPA, regardless of the bout duration (short or long) could provide health benefits (9).

The transition to adulthood is accompanied by major life changes, which impact a range of health-related behaviours, including physical activity. A meta-analysis of prospective studies has shown that physical activity declines between adolescence and adulthood (10). However, of the 49 studies included in this meta-analysis, only three studies were conducted in low-middle income countries, and only nine studies measured changes in physical activity from adolescence to adulthood using accelerometers (none of these in low-middle income countries) (10).

Studies with accelerometer-measured physical activity are important, because self-report assessment of physical activity is prone to misclassification bias, and has limited capacity for estimating time in physical activity accumulated in bouts of short duration (11). Moreover, the relationships between physical activity and health outcomes observed in observational studies might also be susceptible to bias, due to residual or unmeasured contextual confounding factors (12).

Relationships between accelerometer-measured MVPA and cardiometabolic health during the transition from adolescence to adulthood are still poorly understood, as most evidence is from cross-sectional studies, which limit our understanding of potential causal links (12). Moreover, most studies have focused on adolescents in high-income countries (7). To date, no studies have investigated the associations between accelerometer-measured MVPA and indicators of cardiometabolic health during the transition from adolescence to early adulthood (age 20-29y) in a low-middle income country. This lack of evidence from low-income countries, where nearly 85% of the world's population resides (13), might limit our understanding of the causal links between MVPA and cardiometabolic health.

The overall aims of this study were to investigate the associations between accelerometer-measured MVPA and cardiometabolic health during the transition from adolescence to early adulthood. The specific aims were to examine: (i) cross-sectional associations between MVPA and cardiometabolic health at ages 18 and 22y; and (ii) prospective associations between MVPA at age 18 and 4-year changes in MVPA from 18 to 22y, with cardiometabolic health at age 22y. We also compared the magnitude of the associations when MVPA was defined by different bout durations (1- and 10-minutes). Given the well-known sex-differences in physical activity (14), we reported associations separately for males and females.

METHODS

This study used data from the 1993 Pelotas (Brazil) Birth Cohort. This birth cohort study includes 5,249 individuals who were born in 1993 in the city of Pelotas, Brazil, (99.7% of all births in the city). At age 18 and 22 years, all participants were invited to visit a clinic for a series of clinical measures. Written informed consent was obtained for participation in all phases of the study, including from parents or guardians when the participants were younger than 18 years. All study protocols were approved by the Ethics Committee of the Federal University of Pelotas Medical School (register number 05/2011 &

1.250.366). Additional details about the study design and protocols have been published previously (15-18).

Of the 5,249 participants enrolled in the original cohort, 4,106 and 3,810 were interviewed during the follow-up visits at ages 18 and 22y, respectively. Of the 4,106 participants who attended the 18-year clinic visit, 3,706 provided complete data on cardiometabolic health and 3,591 had valid information on MVPA; 3,161 participants had information on cardiometabolic health and 2,986 data MVPA data at age 22y. The analytical sample included 2,280 participants (43% of the original cohort) with both cardiometabolic and MVPA data at ages 18 and 22y (Supplementary Figure 1). Overall, sociodemographic characteristics of the participants whose data were included in the analyses were similar to those in the original cohort (Supplementary Table 1).

Cardiometabolic health

Total fat mass was measured following standard protocols at 18 and 22 years using Dual-energy X-ray absorptiometry (DXA; model Lunar Prodigy, GE Healthcare, USA). Pregnant women at age 18y (n=60) and 22y (n=57) were not assessed with DXA. Total fat mass (%) was estimated using Encore software (GE Lunar iDXA, GE Healthcare, USA) (16, 17). Non-fasting venous samples were collected at 18 and 22 years for measurement of glucose, high-density (HDL-C) and total cholesterol, and triglycerides using an automated enzymatic colourimetric analyzer (BS-380, Mindray,Shenzhen Mindray Bio-Medical Electronics Co., Ltd, China). Given the challenge in collecting blood samples in large population-based studies, collection of fasting blood samples was not feasible and this was therefore not an exclusion criterion. Fasting time was calculated using self-reported time of the last meal and was considered in the analyses. Results were unchanged in sensitivity analyses of data from a small number of participants who fasted for >8 hours (n = 492 and 439 at 18 and 22y, respectively). Non-HDL cholesterol was calculated as the difference between total and HDL cholesterol. Blood pressure was measured using a digital monitor (Omron brand, model 711-AC; Beijing, China) with the participant in a sitting position after resting for 10 minutes. Blood pressure was measured once at the beginning and again at the end of the assessment session. The average of two readings was used to estimate the mean resting blood pressure, calculated as 1/3 × systolic blood pressure + 2/3 x diastolic blood pressure.

At 18 and 22 years, standardized values (z-scores based on data distribution) for total fat mass, blood glucose, non-HDL cholesterol, triglycerides, and mean resting blood pressure were calculated for males and females. A composite cardiometabolic health score at each age was created as the mean of the five standardized scores. Standardized change values from age 18 to 22y were also calculated. For this, the absolute change (score at age 22y minus score at age 18y) in each variable from 18 to 22y was divided by its standard deviation at age 18y. Standard deviation at age 18y was used to ensure that within-individual changes in the metabolic profile would not be influenced by changes in the distribution at the population level, rather than changes within individuals. Outlier data (z-scores higher than 3 or lower than -3) were excluded from the analyses (n=14). Thus, a z-score of 1.0 indicates a score of 1 standard deviation above the mean of the cohort sample and lower overall scores represent improved cardiometabolic health. The use of a summary variable for cardiometabolic score based on standardized scores has been widely used in previous studies (19-23). As this score was derived from this data set, it is appropriate for investigating associations and aetiology within the cohort (24).

Accelerometer-measured physical activity

At ages 18 and 22y, participants who participated in the clinical assessment were invited to wear an accelerometer on their non-dominant wrist, 24 hours a day. The non-dominant wrist was selected because previous evidence has shown higher wear compliance than for waist-worn accelerometry, and because this offered the possibility to measure duration and quality of sleep (25, 26). At the 18y follow-up, limited availability of devices resulted in a measurement protocol designed to include 4 to 7 consecutive days of measurement, including at least one weekend day. Participants who visited the clinic on Mondays, Tuesdays or Wednesdays were monitored until the following Monday (five to seven days of measurement), whereas those who visited the clinic on Thursdays, Fridays, or Saturdays, were monitored until the following Wednesday (four to six days of measurement) (27-29). At the 22y follow-up, all participants wore the accelerometer for seven consecutive days. Accelerometer data were not

collected from participants who were not living in Pelotas at the time of data collection (due to logistic limitations accelerometers were collected by the research team at the participant's household or work), or from those with disabilities, or who were unable to wear the accelerometers due to work-restrictions. Because of device availability, different accelerometers were used at the 18y follow-up (GENEActiv; ActivInsights, Kimbolton, UK) and the 22y follow-up (ActiGraph wGT3X-BT; Pensacola, Florida, United States). Both devices provided raw acceleration data expressed in milli-*g* units. Comparability of raw acceleration data from these two devices has been demonstrated in previous studies (30-32), with high agreement between GENEActiv and ActiGraph GT3X+ data on outcomes such as wear time, moderate-to-vigorous physical activity and sleep parameters (intraclass correlation coefficients > 0.96) (32).

Raw acceleration was processed and MVPA was calculated with R-package GGIR (33). The GGIR is open-source software which can process raw accelerometer data from different device brands. This included a post-calibration process using local gravity (34), non-wear detection (35), and calculation of the vector magnitude of activity-related acceleration using the Euclidian Norm minus 1 *g* (ENMO= $\sqrt{x^2 + y^2 + z^2 - 1}$) (33) Records with post-calibration error <0.2, with at least one complete 24-h cycle, with data collected every 15-min on at least two days were included in the analyses. Moderate-to-vigorous physical activity was estimated in 5-sec epochs as time spent with acceleration higher than 100m*g*. This threshold was chosen because previous studies have demonstrated that 100 m*g* approximates the range of acceleration values corresponding to walking and close to the estimate for 3 metabolic equivalents of task (MET) for adults (36). Minutes of MVPA accumulated in bouts of 1 and 10 minutes were calculated. Bouts of MVPA were identified as time windows with activities that started with 5-s epoch value equal to or higher than 100 m*g* and for which 80% (48 seconds for bouts of 1 minute; 8 minutes for bouts of 10 minutes) of subsequent 5-s epoch values were equal to or higher than the 100 m*g* threshold. This approach has been widely used in previous studies with raw accelerometry data (28, 29, 33, 36-38). In the present study, we focused mainly on MVPA with bouts lasting at least one minute (to minimize signals related to random wrist movement) and bouts lasting at least 10 minutes, as recommended in previous physical activity guidelines (39).

Covariates

The following confounding variables were assessed with standard questionnaires used across the Pelotas Birth Cohort Studies (15-18). The variables assessed at birth and included in these analyses were: birth weight (grams), maternal pre-gestational BMI ($kg/m^{2,}$), maternal education (years of schooling at time of the birth), family income (measured as multiples of minimum monthly income at time of birth). The following confounder variables were assessed at age 18: participant education (years of schooling at age 18y), smoking status at age 18y (never; former; occasional; regular), alcohol consumption in the past month at age 18y (none; less than once per month, 2-4 times per month; more than once a week), and total daily energy intake at 18 years (kcals/day). Participants completed a food frequency questionnaire at age 18 years with a recall period of one year; responses to 88 items were used to calculate energy intake (40). This questionnaire provides reasonable energy intake assessment for habitual food consumption and was based on Dietary Guidelines for the Brazilian Population (41). These variables were selected because bivariate analyses indicated they were associated with both the exposure and outcome variables ($p < 0.20$) and are not mediators in the causal pathway between MVPA and cardiometabolic health.

Statistical analyses

Participants' characteristics were described using means, standard deviations and proportions. Crude and adjusted linear regression analyses were used to examine the associations between MVPA and cardiometabolic health in three steps. All analyses were performed separately for males and females due to gender differences in both physical activity levels and changes in both physical activity and metabolic profiles. First, cross-sectional analyses between MVPA and metabolic health at ages 18 and 22 were conducted. Second, we investigated the longitudinal associations between MVPA at age 18y, and changes in MVPA from age 18 to 22y, with cardiometabolic health at age 22y. Third, to add robustness to our analyses, we examined longitudinal associations between MVPA at age 18y, and changes in MVPA from age 18 to 22y, with changes in cardiometabolic heath from age 18 to 22y

(presented as supplementary material). To account for the potential non-linearity of the associations between MVPA and cardiometabolic health, the regression models included quadratic-terms for MVPA. In the prospective analyses, interaction terms between MVPA at age 18 and changes in MVPA were included in the models to account for different associations between changes in MVPA according to baseline levels of MVPA. Adjusted models included low birth weight, maternal BMI, family income, maternal education, participant education, smoking, alcohol consumption and total energy consumption at age 18, which were assessed at birth or age 18 as previously described. In all analyses MVPA in bouts of 1 and 10 minutes were used in separated models as the exposure variable. To aid interpretation of the analyses, results are expressed as predictive margins for metabolic profile for each 10 minutes in MVPA and in change in MVPA. Predictive margins were estimated with the adjusting covariates set according to the categories presented in Table 1. To limit estimates to realistic values of MVPA, predictive margins estimates were restricted to MVPA levels between the 5th and 95th percentiles of the MVPA distribution. Assumptions for regression analyses were checked using residual and leverage-versus-residual-squared plots. Given the number of comparisons and the potential for type 1 error, interpretation of findings was based on the size of differences and overlap of confidence intervals. All analyses were performed using Stata 16.1.

RESULTS

Descriptive characteristics and physical activity variables of the analytical sample are presented in Table 1 for males and females. Males spent more time in MVPA than females regardless of bout criteria. At age 18, males spent on average 125 (SD: 72; 5th centile: 34 minutes; 95th centile: 256 minutes) minutes per day in MVPA (1-minute bout), whereas females spent on average 84 (SD: 46; 5th centile: 27 minutes; 95th centile: 172 minutes) minutes/day in MVPA. In males, total time in MVPA with 1-minute bout duration was around twice as high as time in 10-min bouts. Among females, time spent in bouts lasting 1 minute was nearly 3 times higher than in bouts lasting at least 10 minutes. On average, total minutes in MVPA decreased from 18 to 22y in males and females, and the decline was greater in males than females regardless of bout duration. About one in five participants (22% of males and 20% of females) increased their total minutes of MVPA in 1 minute bouts from age 18y to 22y; 23% of males and 27% of females increased their MVPA in bouts lasting at least 10 minutes.

Descriptions of the individual cardiometabolic markers at each age and changes in males and females from age 18 to 22y are shown in Table 2. Except for glucose values, all markers increased (worsened) over 4 years. The highest increase was observed for triglyceride levels in males [z-score: 0.54 (SD: 1.43)] and females [z-score: 0.46 (SD: 1.28)]. The average increase in the composite metabolic score profile was 0.29 (SD: 0.65) z-scores in males and 0.25 (SD: 0.60) in females.

Cross-sectional associations between MVPA in bouts lasting 1 and 10 minutes and the cardiometabolic health at age 18 and 22y are presented for males in Figure 1 and Supplementary Table 2. Inverse dose response associations between MVPA and cardiometabolic health were observed regardless of bout criteria and age. At age 18y, predictive estimates indicated that more than 100 minutes of MVPA in 1 min bouts or more than 50 minutes of MVPA in 10 min bouts tended to be associated with composite metabolic scores lower than the sample average. The corresponding thresholds at age 22y were >75 minutes (1 minute-bouts) and >25 minutes in 10 minutes-bouts. (Figure 1).

Inverse cross-sectional associations between MVPA and cardiometabolic health were also observed among females (Figure 2 and Supplementary Table 3). At age 18, >80 minutes of MVPA in 1 minute-bouts, and >30 minutes of MVPA in 10-minute bouts were associated with a cardiometabolic health score lower than the sample average score. The corresponding values for age 22y were >50 minutes (1 minute-bouts) and 15 minutes (10 minute-bouts).

Prospective associations between MVPA at age 18 and changes in MVPA over 4 years with metabolic profile at 22y are presented for males in Figure 3 and Supplementary Table 4. Among males, changes in MVPA were inversely associated with cardiometabolic health at 22y, across all deciles of MVPA at age 18y, regardless of bout criteria. As shown by the beta coefficients in Supplementary Table 4, associations between changes in MVPA from age 18 to 22y and cardiometabolic health at age 22y,

were stronger than associations between MVPA at 18y and cardiometabolic health at age 22y. Interactions between MVPA at 18y and changes in MVPA were observed ($p < 0.1$), suggesting that the associations between changes in MVPA with metabolic profile at 22y vary by MVPA level at age 18, with more marked associations in the lowest quartile of MVPA. Overall, for any given change in MVPA from age 18 to 22y, cardiometabolic health at age 22y was better in those with higher MVPA at age 18y.

Among females, although there were visual indications of differences in cardiometabolic health according to MVPA at age 18y, the 95% confidence intervals of the predicted values substantially overlapped for all levels of change in MVPA (Figure 4 and Supplementary Table 4). However, changes in MVPA in 1- and 10-minutes bout from 18y to 22y were inversely associated with the cardiometabolic health at age 22y, especially among those in the lower centiles of the MVPA distribution at age 18y. There was a strong interaction between MVPA in 10-minute bouts at age 18y and changes in MVPA with metabolic profile at age 22y ($p=0.003$). Among those in the highest MVPA centiles at age 18y, the cardiometabolic health profile did not vary greatly with changes in MVPA, whereas decreases in MVPA from 18 to 22y were strongly associated with worse cardiometabolic metabolic profiles at age 22y among those in the lowest centiles of MVPA at age 18y.

Associations between MVPA at age 18 and changes in MVPA over 4 years with changes in cardiometabolic health are presented in Supplementary Figure 2 and Supplementary Table 5 for males and females. There were inverse dose-response relationships, which were similar for 1 min and 10 min bouted MVPA. Changes in MVPA were more strongly associated than MVPA at age 18, with changes in cardiometabolic health, with some interactions ($p<0.1$), as shown in Supplementary Table 5. Overall, declines in MVPA were strongly associated with declines in cardiometabolic health among those in the lowest centiles of MVPA at age 18y. Among females, those in the top quartile of MVPA at age 18 did not show changes in cardiometabolic health with changing MVPA. Those with the lowest levels of MVPA at age 18 had large changes in the cardiometabolic health score with changing MVPA.

DISCUSSION

The aims of this study were to investigate the cross-sectional and prospective associations between accelerometer-measured physical activity and cardiometabolic health during the transition from adolescence to adulthood. In this unique large population based Brazilian cohort, we found that levels of MVPA at age 18 are important, but that declines and improvements in MVPA over 4-years are associated with declines and improvements in cardiometabolic health respectively, especially among those least active at age 18. Our observations reinforce the findings of studies with mid-age adults which suggest that there are health gains from becoming more active, irrespective of past activity levels (42, 43).

The transition from adolescence to adulthood is accompanied by many changes in physiological, behavioural and health outcomes (44). In our study, over a 4-year period, there were significant changes in total MVPA; using 1 minute-bout data, in most participants there was a decline (up to 120 min/day in males and up to 80 min/day in females), but about one in five participants increased their MVPA. Over the same period, there were small declines or improvements in cardiometabolic health, which largely mirrored the declines or improvements in MVPA. Although changes in cardiometabolic health markers were small, and perhaps not clinically important at the individual level at the age of 22y, if these changes persist and accumulate over several years, they might trigger the development of major non-communicable chronic diseases during adulthood (44, 45).

The comparability of our findings with previous studies is limited by the scarcity of studies with device-measures of physical activity during this life stage. In children and adolescents aged 6–18 years, a recent systematic review and meta-analyses of longitudinal, observational prospective cohort, randomized controlled trials and intervention studies found a small but significant association between MVPA at baseline and clustered cardiometabolic risk at follow-up (46). In a previous study of the 1993 Pelotas Birth Cohort, our group has reported cross-sectional associations between combinations of self-reported sedentary time and physical activity and cardio-metabolic health at ages 11, 15 and 18, but did not find

prospective associations between self-reported sedentary time and physical activity at 11 and 15 with cardio-metabolic risk factors at age 18y (8). Another study in this cohort also found that accelerometer measured physical activity at age 18y was negatively associated with HbA1c at age 18y in boys only, but no prospective associations were observed (47). A Danish study with self-reported physical activity data also found no prospective associations between physical activity at baseline and metabolic profile (48). Differences between our current findings and those from previous studies might be explained by the fact that MVPA may change markedly in intervals between surveys and these changes were not taken into account in previous studies (8, 47). Moreover, different measures of physical activity (self-reported or accelerometer) might explain the difference in findings (23, 48).

Our study provides important insights into accelerometer measured physical activity. The cross-sectional data indicate that the 'thresholds' of MVPA associated with better cardiometabolic health than the average for the sample were around 50 and 30 minutes/day when MVPA was assessed in 10-min bouts in males at age 18 and 22y respectively. Current guidelines based on self-reported PA suggest 60 minutes/day for adolescents and 150-300 minutes of MVPA per week (average of 30 minutes/day for adults) (6). These thresholds were higher when MVPA was assessed in 1-min bouts, indicating that more time in 'sporadic' activity may be required for the same metabolic benefit, compared with MVPA in 10 min bouts, as has been demonstrated in previous studies (7, 49).

These thresholds were also lower for females than males, and there were sex differences in levels of MVPA at 18y and in 4-year changes in MVPA (both lower in females). The magnitude of most of the associations between these levels and changes in MVPA with cardiometabolic health at age 22y was also less marked in females. This might be explained by the smaller range of 4-year change in MVPA in the females, and lower levels of MVPA in young women. Our findings confirm the well-known sex differences in levels of physical activity (14), and improves understanding of sex differences in the association between physical activity and cardiometabolic health during early adulthood (48). Further investigations of these sex differences is warranted.

Our study has several strengths. MVPA was measured using accelerometry at two time points in a large sample of Brazilian adolescents. Device-measured MVPA is less susceptible to biases that are intrinsic to self-reported measures of physical activity (11). Moreover, the use of device-measured MVPA accumulated in different bout lengths provided the opportunity to explore how less structured activities (i.e. activities that were not sustained for at least 10 minutes) are associated with cardiometabolic health. Furthermore, the prospective design and our analytical approach accounted for the interactions between baseline level of MVPA and changes in MVPA, and how these influence cardiometabolic health during this important transition period. Finally, to date, this is the first study to investigate the associations between MVPA and metabolic profile in the transition from adolescence to adulthood, and the only one from a large middle-income country. Previous studies were conducted with adolescents in the US and Western Europe, hence limiting our understanding of these relationships in countries that may have different patterns of physical activity (2, 7).

Limitations of our study should also be considered. Our analyses included only 43% of the original cohort, which may have introduced bias in our findings, yet the analytical sample was similar to the original cohort in terms of sociodemographic and behavioural characteristics. Although the analyses included a range of confounding variables, residual confounding due to unmeasured variables cannot be ruled out. However, results from the final models, which included adjustment for a range of confounding variables, were similar to the results of the crude models. Although our analytical approach minimises reverse causation, the associations between changes in MVPA and changes in metabolic profile could, to some extent, be influenced by reverse causation. It was not feasible to assess blood samples in a fasted condition. However, the results were unchanged in sensitivity analyses that included only participants who fasted for at least eight hours. This has also been demonstrated in previous analyses of data from the same cohort (50). Finally, there are inherent limitations in the management of accelerometer data, for example in relation to decisions about what constitutes moderate intensity physical activity (e.g. raw acceleration of 100mg in 5-second epochs in a 24h period).

In conclusion, we found that MVPA and changes in MVPA during the transition from adolescence to adulthood are major determinants of metabolic health at age 22y. Declining levels of MVPA between 18 and 22y in both males and females were associated with declines in metabolic profile, and improvements in MVPA, seen in about one quarter of participants, were associated with improvements in metabolic profile, especially among young men. Strategies to improve levels of MVPA in young women, and prevent declines, particularly among young men, could improve metabolic profiles at this life-stage.

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Conflict of interest
All authors declare no conflicts of interest and that the results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of the present study do not constitute endorsement by ACSM.

Availability of data and materials
This study was conducted using data from the 1993 Pelotas (Brazil) Cohort Study. There are no linked research data sets for this submission. The data used are confidential and the datasets used in this analysis are available from the corresponding author on reasonable request.

Ethical Approval
The 1993 Pelotas (Brazil) Birth Cohort Study was approved by the Medical School Ethics Committee from the Federal University of Pelotas.

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Contributors
GM conceived and designed the study, conducted the analyses, contributed to data interpretation and wrote the first draft of the manuscript. AM, HG and FCW are Pelotas Birth Cohort CIs who contributed to survey design and data collection. They contributed to data interpretation, reviewing and editing. BS, IS, UE and WB contributed to data interpretation, and reviewed and edited several drafts. All authors approved the final manuscript.

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Table 1: Sociodemographic characteristics of analytical sample. 1993 Pelotas (Brazil) Birth Cohort Study (n=2,280)

	Male (n=1,088)	Female (n=1,192)
Birth weight (grams), mean (SD)	3240 (528)	3111 (517)
Family income at time of birth, mean (SD)[a]	4.3 (6.0)	4.3 (5.4)
Maternal pre-gestational BMI (Kg/m^2), n (%)		
< 20.0	260 (24.6)	253 (21.7)
20.0 – 24.9	573 (54.1)	648 (55.5)
25.0 – 29.9	176 (16.6)	216 (18.5)
30.0 +	50 (4.7)	51 (4.4)
Maternal education at time of birth, n (%)		
0-4	278 (25.6)	319 (26.8)
5-8	531 (48.9)	555 (46.7)
9-11	188 (17.3)	223 (18.8)
12+	89 (8.2)	92 (7.7)
Participant education at age 18y, n (%)		
0-8	564 (51.9)	404 (33.9)
9+	522 (48.7)	788 (66.1)
Smoking status at age 18y, n (%)		
Never	866 (79.6)	969 (81.3)
Former	69 (6.3)	86 (7.2)
Occasional	34 (3.1)	41 (3.4)
Regular	119 (10.9)	96 (8.1)
Alcohol consumption in the past month at age 18y, n (%)		
None	270 (24.8)	360 (30.2)
Less than once per month	233 (21.4)	490 (27.4)
2-4 times per month	150 (13.8)	180 (15.1)
More than once a week	435 (40.0)	325 (27.3)

Energy intake at age 18y in Kcal, mean (SD)	3334 (2030)	2849 (1952)
MVPA (minutes/day) at age 18y, mean (SD)		
1-minute bout	125 (72)	84 (46)
10-minute bout	58 (49)	29 (27)
MVPA (minutes/day) at age 22y, mean (SD)		
1-minute bout	81 (56)	53 (32)
10-minute bout	27 (34)	14 (16)
Changes in MVPA from 18 to 22y, mean (SD)		
1-minute bout	-44 (67)	-31 (41)
10-minute bout	-30 (48)	-14 (27)

[a] multiples of minimum monthly income. Minimum monthly income was approximately US$ 31.00 in 1993 (year of birth for this cohort) (18).

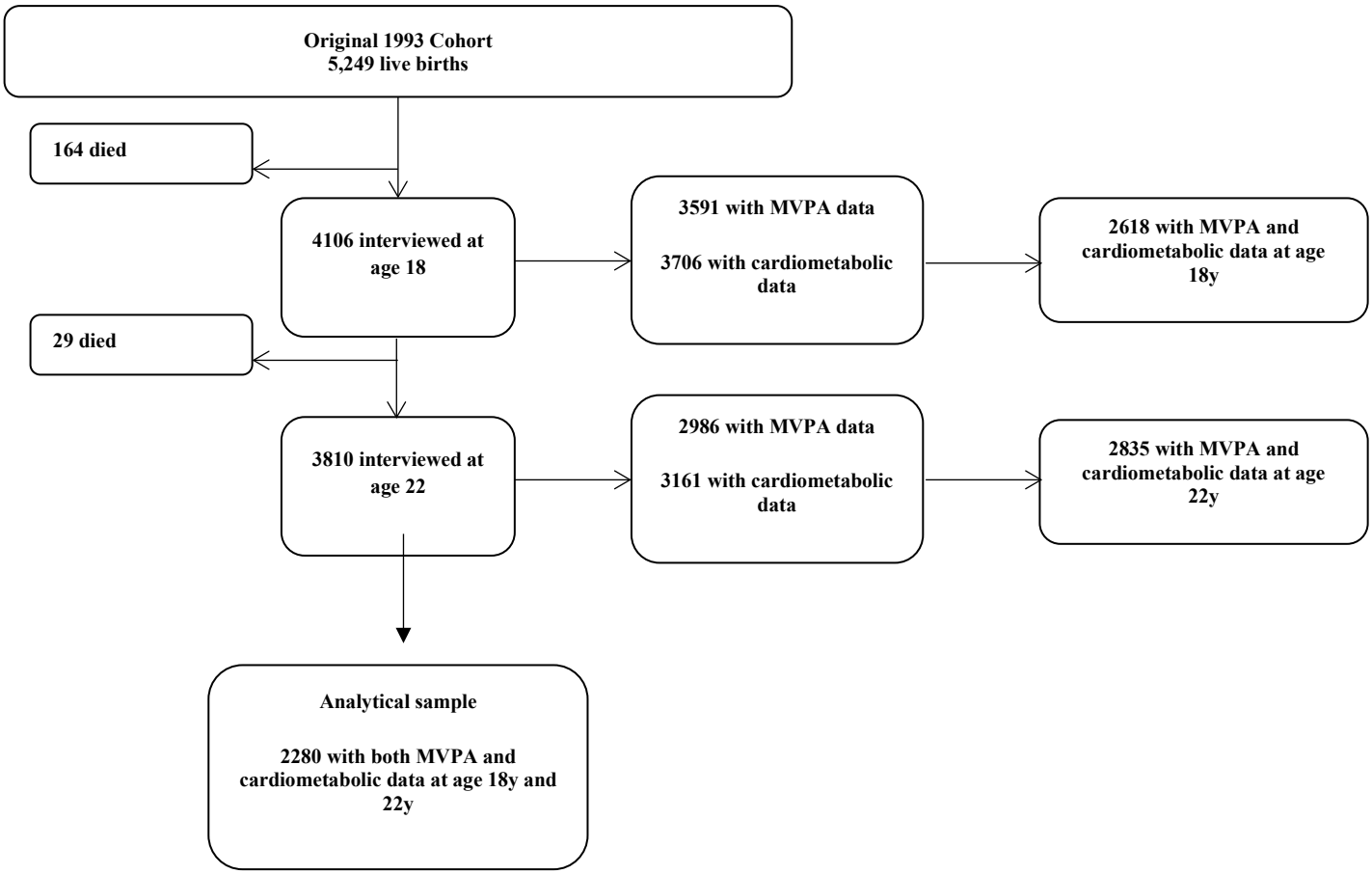
Supplemental Digital Content: Mielke et al_supplementary.docx

Figure 1: Cross-sectional association between moderate-to-vigorous physical activity in bouts of 1 and 10 minutes with metabolic profile in males. 1993 Pelotas (Brazil) Birth Cohort Study. The red dashed line represents the average metabolic profile. Predictive margins for metabolic profile were calculated for each 10 minutes in MVPA. The highest values on the x axes represent the 95th percentile of the MVPA distributions. Adjusted models included low birth weight, maternal BMI, family income, maternal education, participant education, smoking, alcohol consumption and total energy consumption at age 18y.

Figure 2: Cross-sectional association between moderate-to-vigorous physical activity according to different bout criteria and metabolic profile in females. 1993 Pelotas (Brazil) Birth Cohort Study. The red dashed line represents the average metabolic profile. Predictive margins for metabolic profile were calculated for each 10 minutes in MVPA. The highest values on the x axes represent the 95th percentiles of the MVPA distributions. Adjusted models included low birth weight, maternal BMI, family income, maternal education, participant education, smoking, alcohol consumption and total energy consumption at age 18y.

Figure 3: Metabolic profile at age 22y according to changes in moderate-to-vigorous physical activity from 18 to 22y and MVPA at age 18y in males. 1993 Pelotas (Brazil) Birth Cohort Study. The red dashed line represents the average metabolic profile. Predictive margins for metabolic profile were calculated for each 10 minute change in MVPA. The x axes show the 5th to 95th percentiles of changes in the MVPA distributions. Adjusted models included low birth weight, maternal BMI, family income, maternal education, participant education, smoking, alcohol consumption, total energy consumption, and cardiometabolic health at age 18y.

Figure 4: Metabolic profile at age 22y according to changes in moderate-to-vigorous physical activity from 18 to 22y and MVPA at age 18y in females. 1993 Pelotas (Brazil) Birth Cohort Study. The red dashed line represents the average metabolic profile. Predictive margins for metabolic profile were calculated for each 10 minute change in MVPA. The x axes show the 5th to 95th percentiles of changes in the MVPA distributions. Adjusted models included low birth weight, maternal BMI, family income, maternal education, participant education, smoking, alcohol consumption, total energy consumption, and cardiometabolic health at age 18y.



Supplementary Figure 1: Flowchart of data collected on physical activity and cardiometabolic health in the 1993 Pelotas Birth Cohort Study.

Supplementary Table 1: Comparison of sociodemographic variable in the original cohort (N=5249) and the analytical sample (N=2280).

Variables	Original Cohort N (%)	Analytical sample (43.4% of the original cohort)*	p value
Gender			0.017
Male	2603 (49.6)	41.8	
Female	2645 (50.4)	45.1	
Family income (perinatal)			0.083
1st quartile	1428 (27.8)	40.9	
2nd quartile	1169 (22.8)	44.6	
3th quartile	1264 (24.6)	45.6	
4th quartile	1276 (24.8)	43.6	
Maternal education (perinatal)			0.070
0-4 years	1468 (28.0)	40.7	
5-8 years	2424 (46.2)	44.8	
9-11 years	923 (17.6)	44.5	
12+ years	427 (8.2)	42.4	
Birth weight			0.914
< 2500g	510 (9.8)	43.6	
≥ 2500g	4722 (90.2)	43.3	
Maternal pre-gestational BMI (Kg/m^2)			0.655
<20.0 kg/m^2	1147 (22.5)	44.7	
20.0-24.9 kg/m^2	2825 (55.4)	43.2	
25.0-29.9 kg/m^2	880 (17.3)	44.6	
≥ 30.0 kg/m^2	245 (4.8)	41.2	

*** Proportion of participants of the original cohort included in the analyses according to sociodemographic variables.**

Supplementary Table 2: Cross-sectional association between moderate-to-vigorous physical activity according to different bout criteria and cardiometabolic health in males. 1993 Pelotas (Brazil) Birth Cohort Study.

Bout criteria	Linear		Quadratic	
	β (95%CI)	p value	β (95%CI)	p value
18 years				
1-minute bout	-0.022 (-0.036; -0.008)	0.002	0.0004 (0.0001; 0.0008)	0.025
10-minute bout	-0.024 (-0.038; -0.009)	0.001	0.0005 (0.0000; 0.0010)	0.045
22 years				
1-minute bout	-0.028 (-0.044; -0.012)	0.001	0.0003 (-0.0002; 0.0009)	0.232
10-minute bout	-0.037 (-0.057; -0.018)	<0.001	0.0005 (-0.0002; 0.0013)	0.152

Results expressed as regression coefficients representing the change in the outcome per 10-minute difference in daily MVPA

Supplementary Table 3: Cross-sectional association between moderate-to-vigorous physical activity according to different bout criteria and cardiometabolic health in females. 1993 Pelotas (Brazil) Birth Cohort Study.

Bout criteria	Linear		Quadratic	
	β (95%CI)	p value	β (95%CI)	p value
18 years				
1-minute bout	-0.021 (-0.042; 0.001)	0.066	0.0002 (-0.0007; 0.0011)	0.657
10-minute bout	-0.024 (-0.052; 0.003)	0.086	-0.0001 (-0.0023; 0.0021)	0.907
22 years				
1-minute bout	-0.022 (-0.055; 0.011)	0.186	0.0002 (-0.0018; 0.0023)	0.817
10-minute bout	-0.052 (-0.103; -0.001)	0.044	0.0026 (-0.0047; 0.0100)	0.483

Results expressed as regression coefficients representing the change in the outcome per 10-minute difference in daily MVPA

Supplementary Table 4: Cardiometabolic health at age 22y according to changes in moderate-to-vigorous physical activity from 18 to 22y and MVPA at age 18y in males and females. 1993 Pelotas (Brazil) Birth Cohort Study.

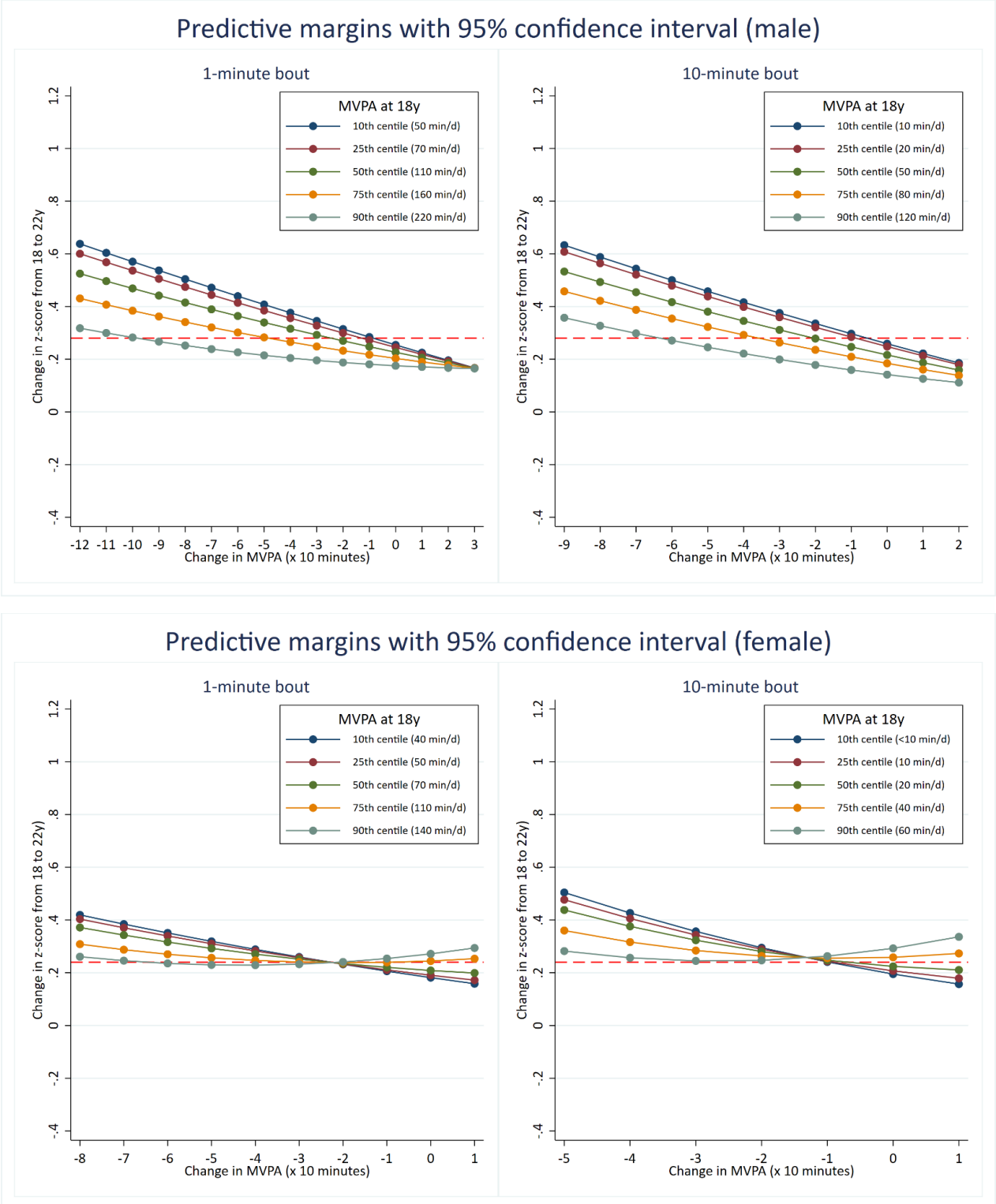
Bout criteria	MVPA at age 18y		Changes in MVPA		Interaction MVPA 18y x changes	
	β (95%CI)	p value	β (95%CI)	p value	β (95%CI)	p value
Males						
1-minute bout	-0.007 (-0.014; 0.000)	0.063	-0.030 (-0.043; -0.016)	<0.001	0.001 (0.000; 0.002)	0.046
10-minute bout	-0.013 (-0.025; -0.002)	0.026	-0.032 (-0.049; -0.015)	<0.001	0.001 (-0.001; 0.004)	0.296
Females						
1-minute bout	0.000 (-0.012; 0.012)	0.948	-0.035 (-0.058; -0.011)	0.004	0.003 (0.000; 0.006)	0.030
10-minute bout	0.000 (-0.023; 0.023)	0.994	-0.050 (-0.079; -0.020)	0.001	0.013 (0.004; 0.021)	0.003

* Quadratic terms were suppressed from the table.

Supplementary Table 5: Association between changes in moderate-to-vigorous physical activity according to different bout criteria and changes on cardiometabolic health from age 18 to 23y in males. 1993 Pelotas (Brazil) Birth Cohort Study.

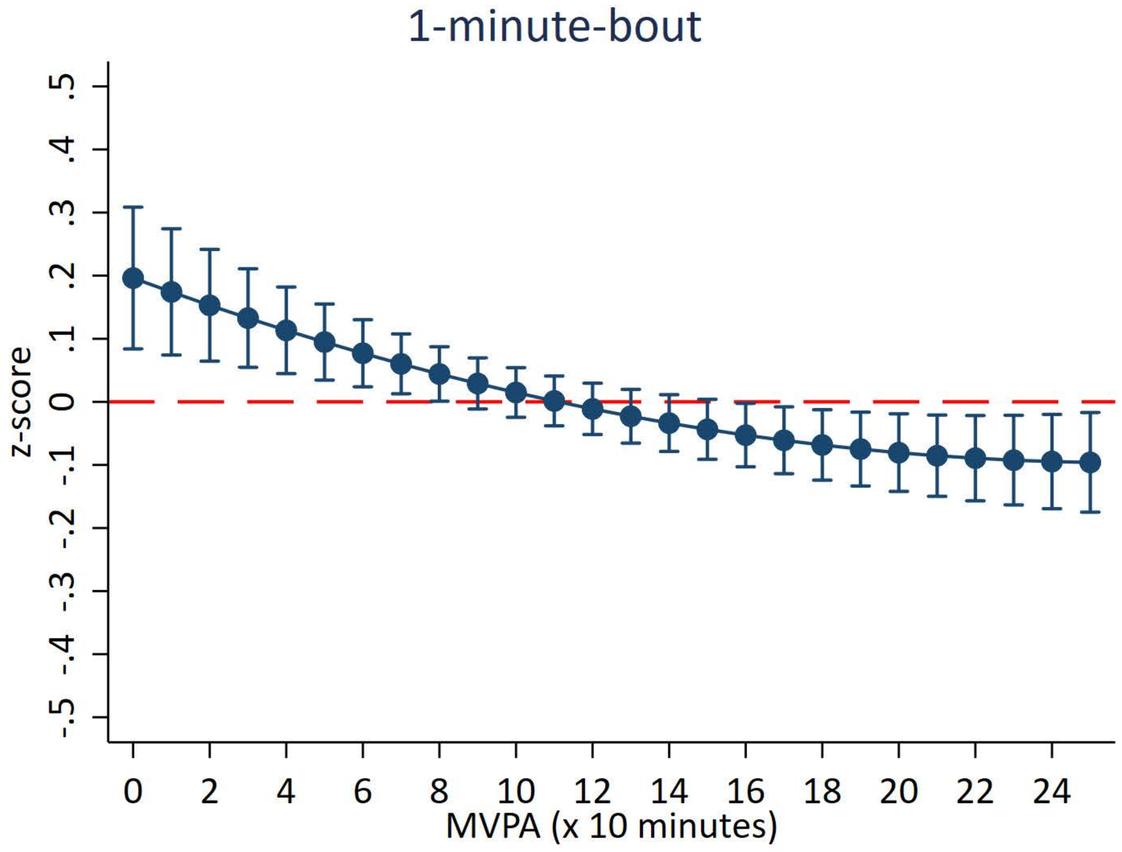
Bout criteria	MVPA age 18y		Changes in MVPA		Interaction MVPA 18y x changes	
	β (95%CI)	p value	β (95%CI)	p value	β (95%CI)	p value
Males						
1-minute bout	-0.005 (-0.014; 0.004)	0.309	-0.037 (-0.053; -0.021)	<0.001	0.001 (0.000; 0.003)	0.028
10-minute bout	-0.011 (-0.025; 0.004)	0.145	-0.039 (-0.060; -0.019)	<0.001	0.002 (-0.001; 0.005)	0.200
Females						
1-minute bout	0.009 (-0.006; 0.024)	0.235	-0.041 (-0.071; -0.012)	0.006	0.004 (0.001; 0.008)	0.018
10-minute bout	0.017 (-0.012; 0.046)	0.248	-0.046 (-0.083; -0.009)	0.015	0.014 (0.003; 0.024)	0.010

* Quadratic term were suppressed from the table.



Supplementary Figure 2: Association between changes in moderate-to-vigorous physical activity in bouts of 1 and 10 minutes and changes on cardiometabolic health from age 18 to 23y in males. 1993 Pelotas (Brazil) Birth Cohort Study. The red dashed line represents the average change in metabolic profile. Predictive margins for metabolic profile were calculated for each 10 minute change in MVPA. The x axes show the 5th to 95th percentiles of changes in the MVPA distribution.

18y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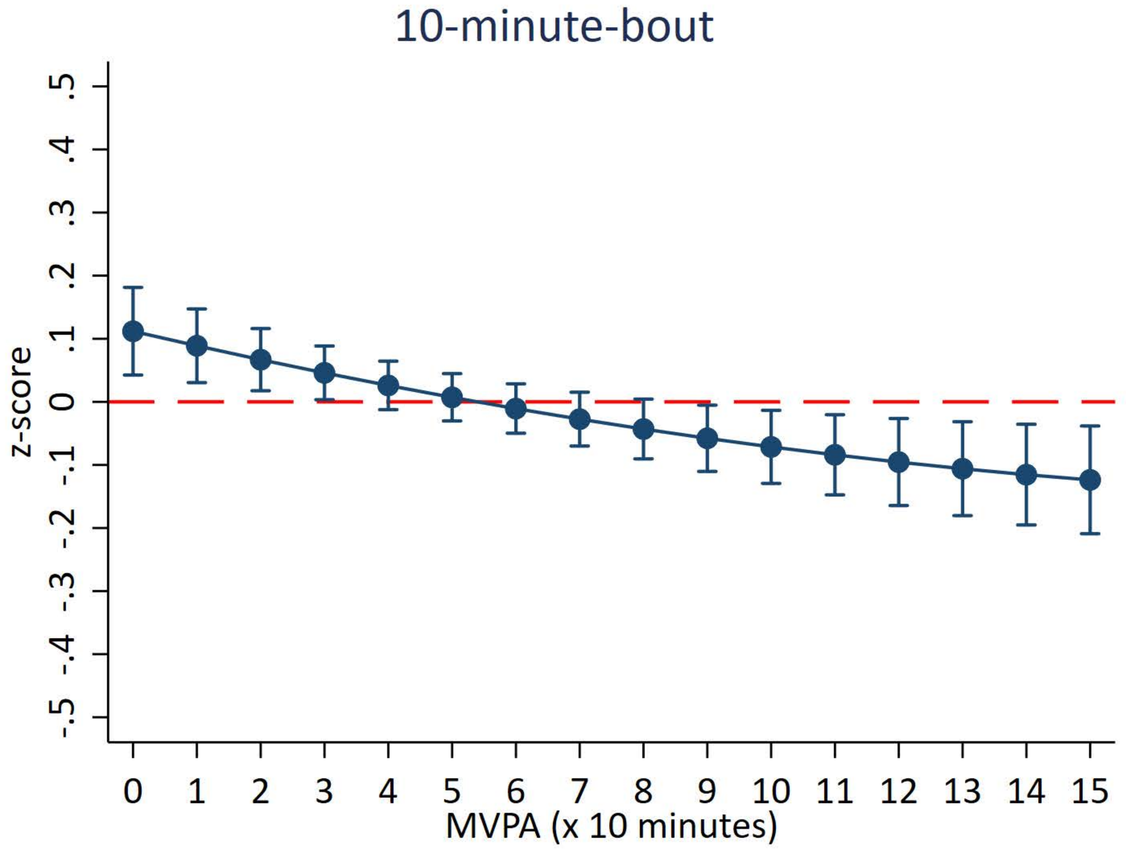
MVPA (x 10 minutes)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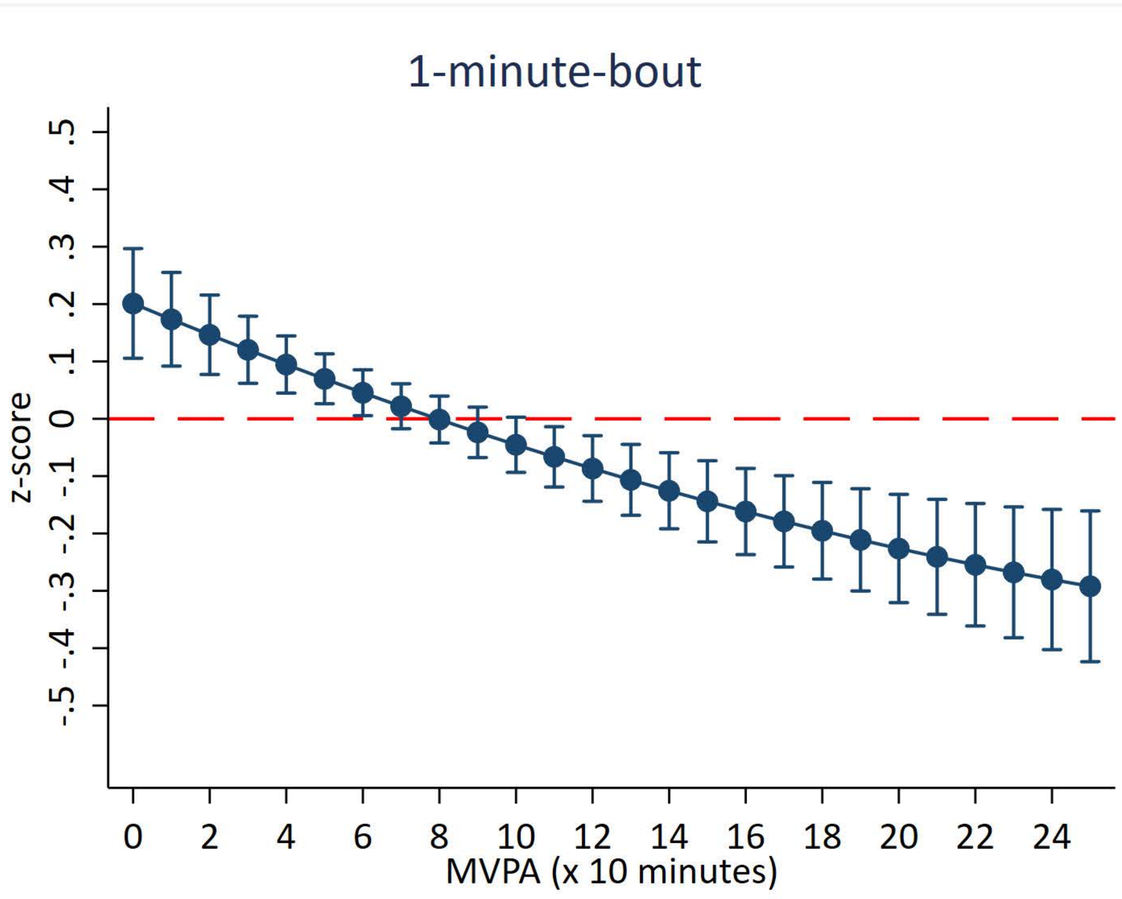
MVPA (x 10 minutes)

22y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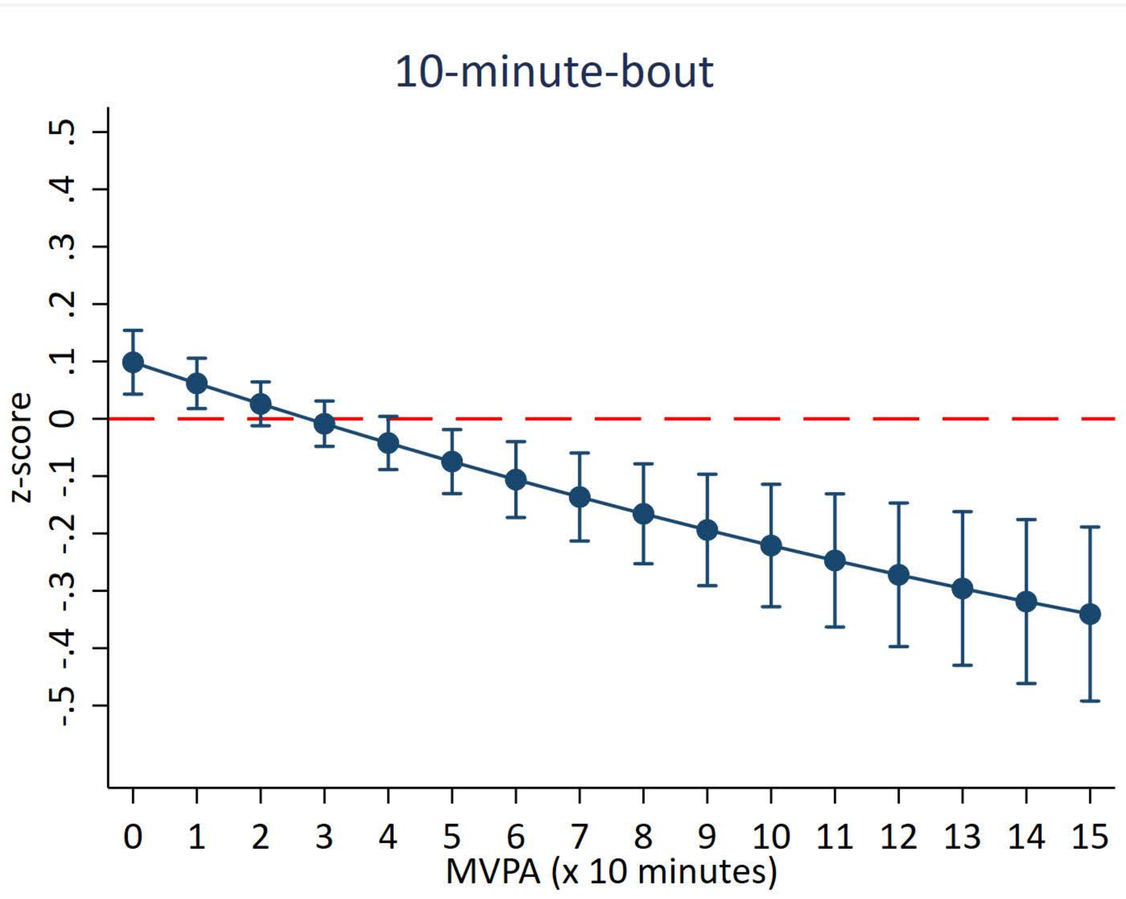
MVPA (x 10 minutes)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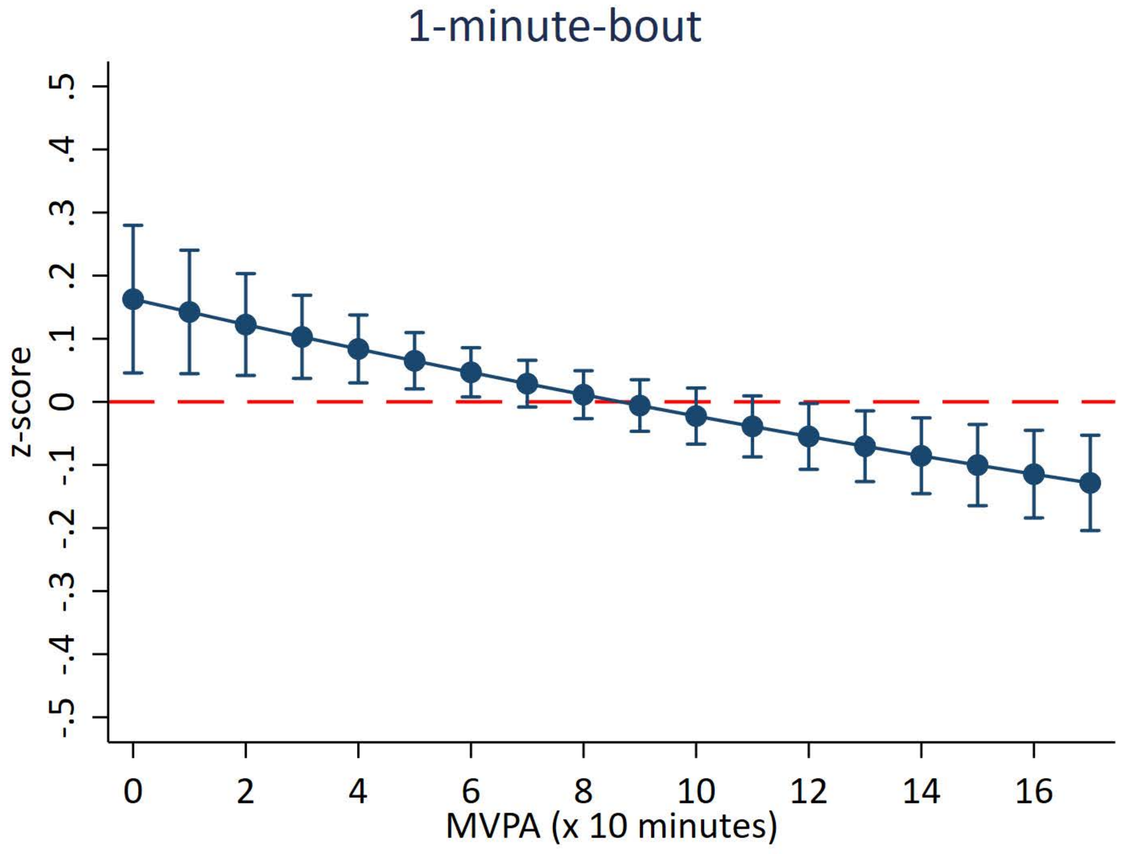
MVPA (x 10 minutes)

18y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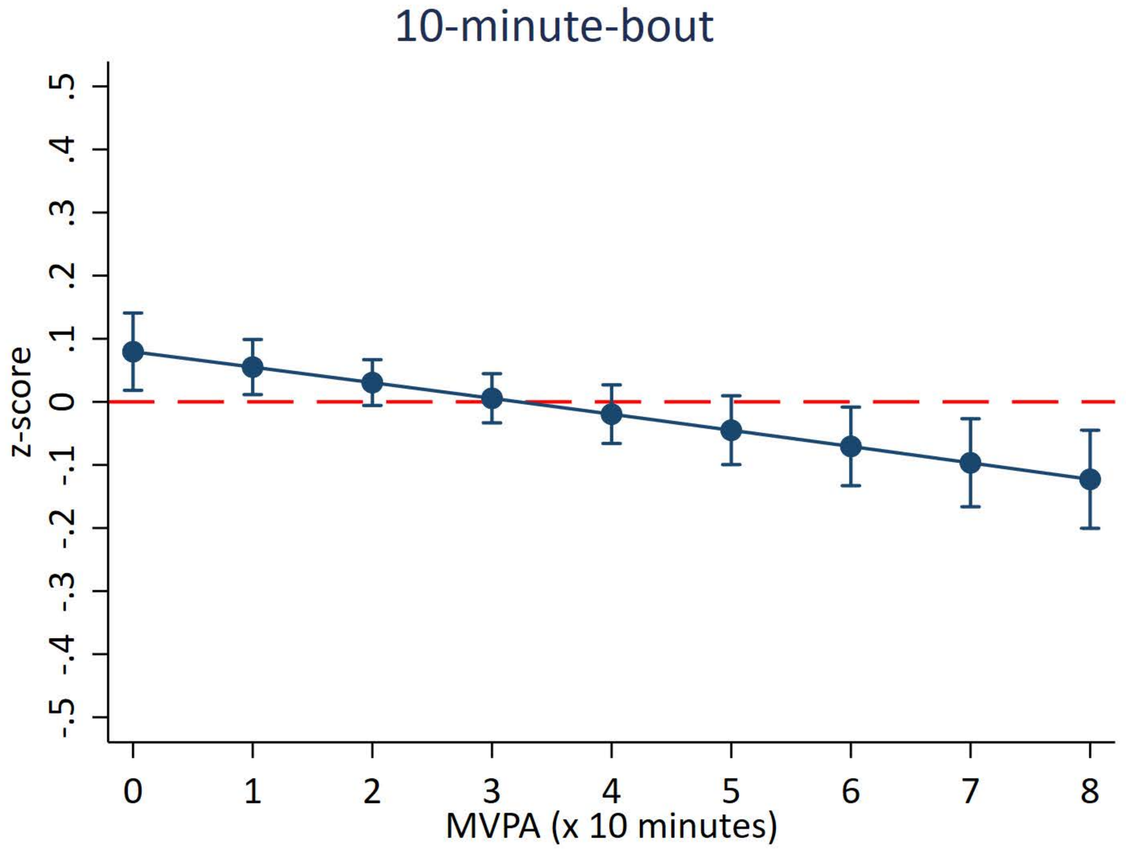
MVPA (x 10 minutes)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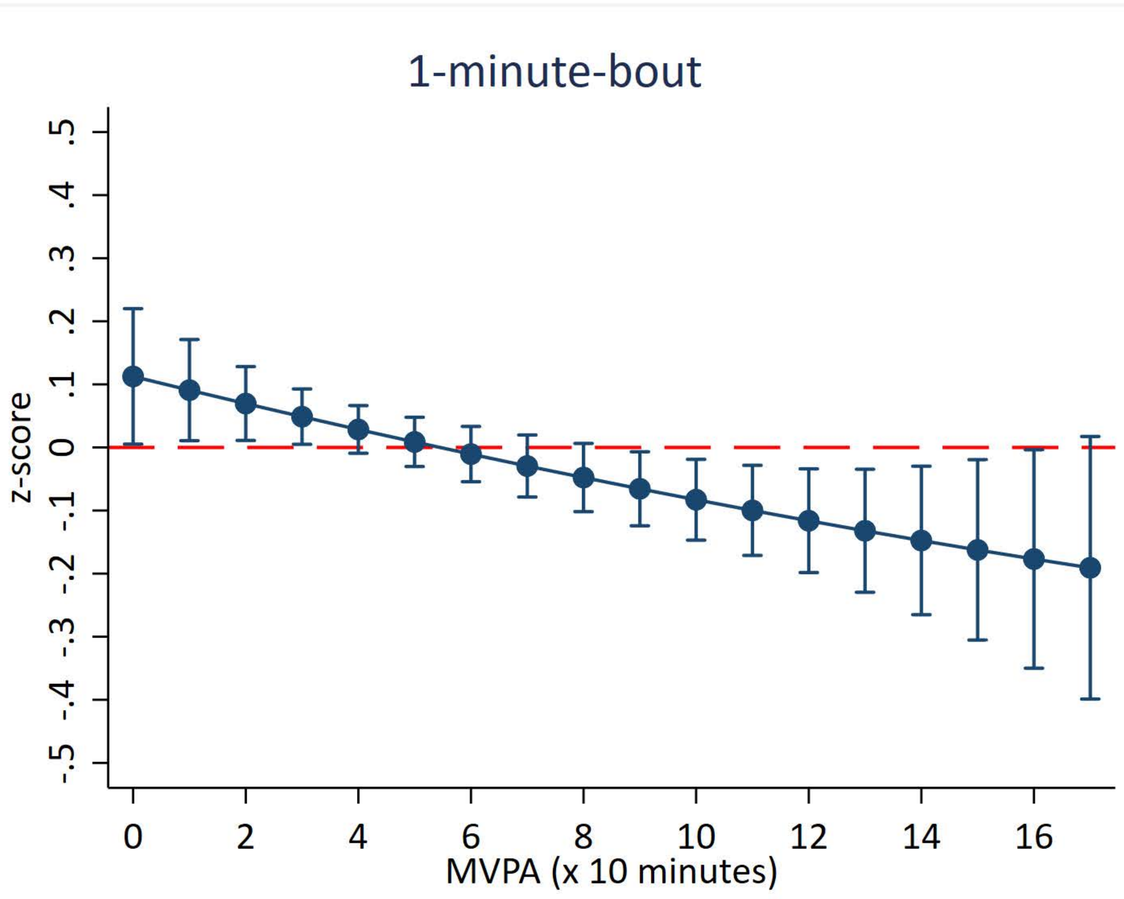
MVPA (x 10 minutes)

22y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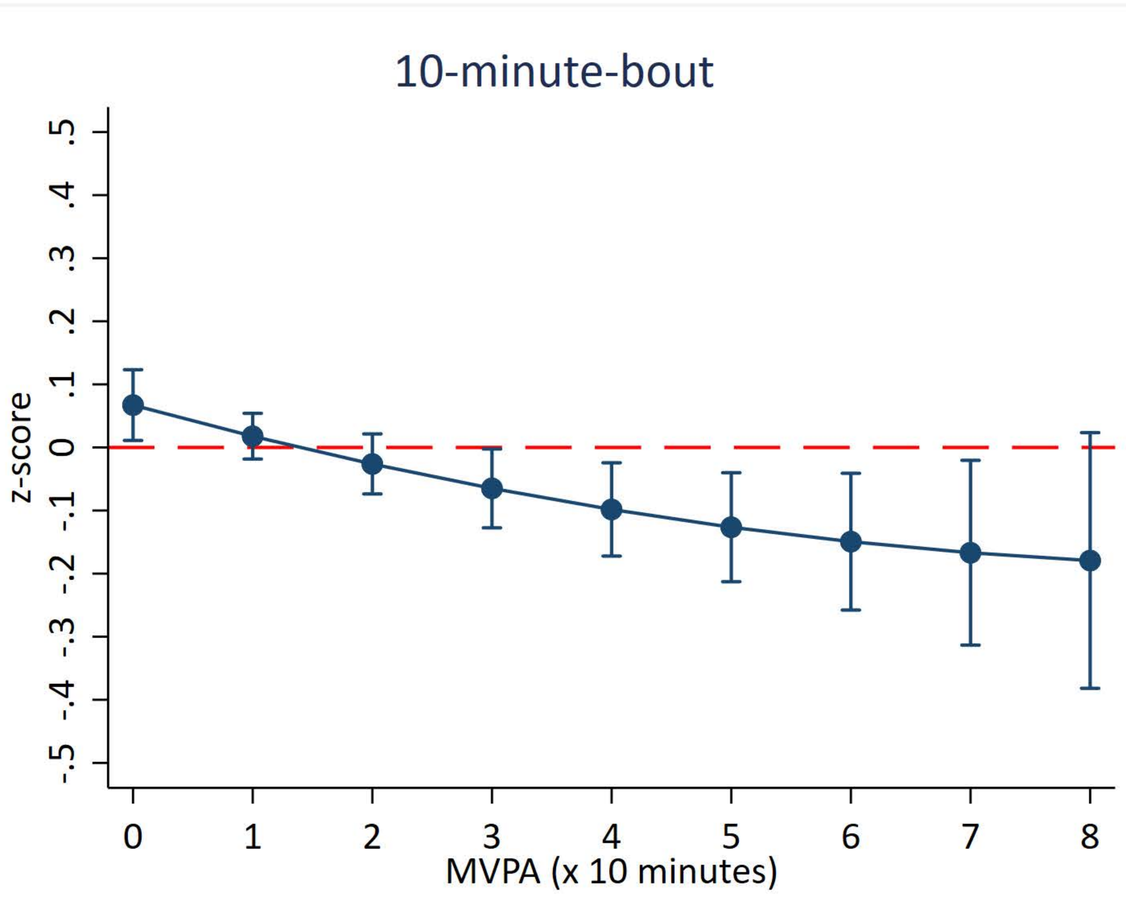
MVPA (x 10 minutes)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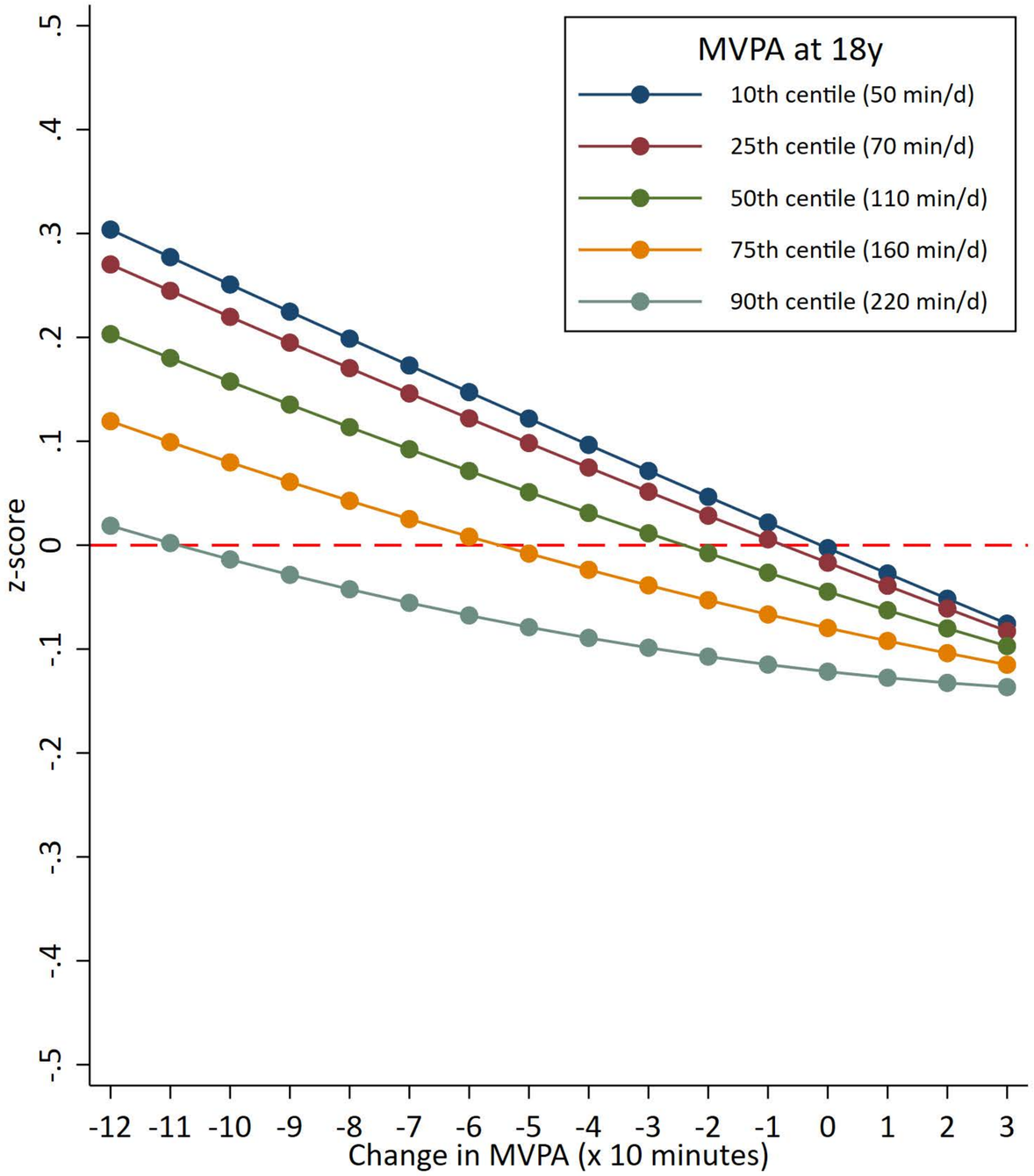
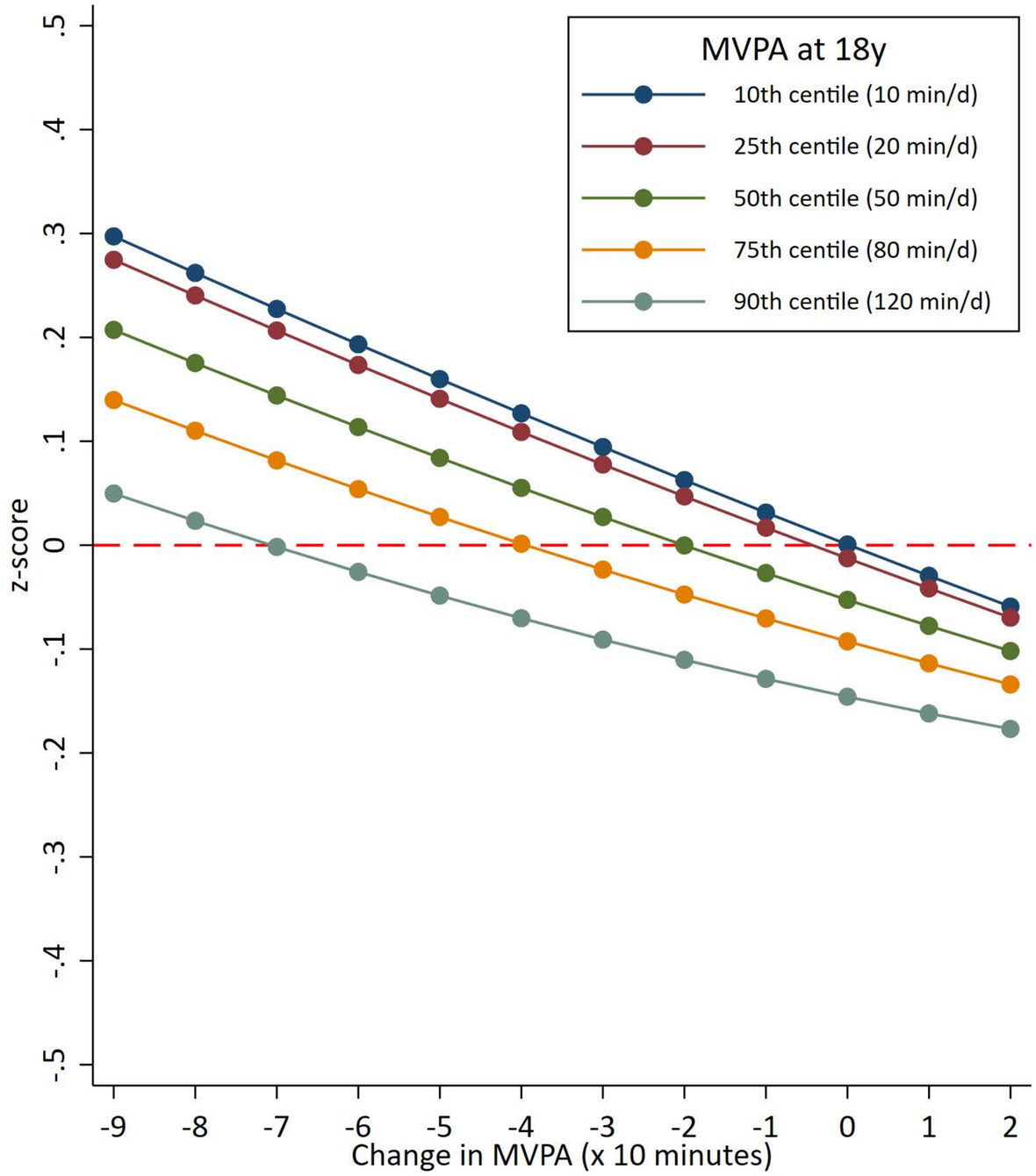
MVPA (x 10 minutes)

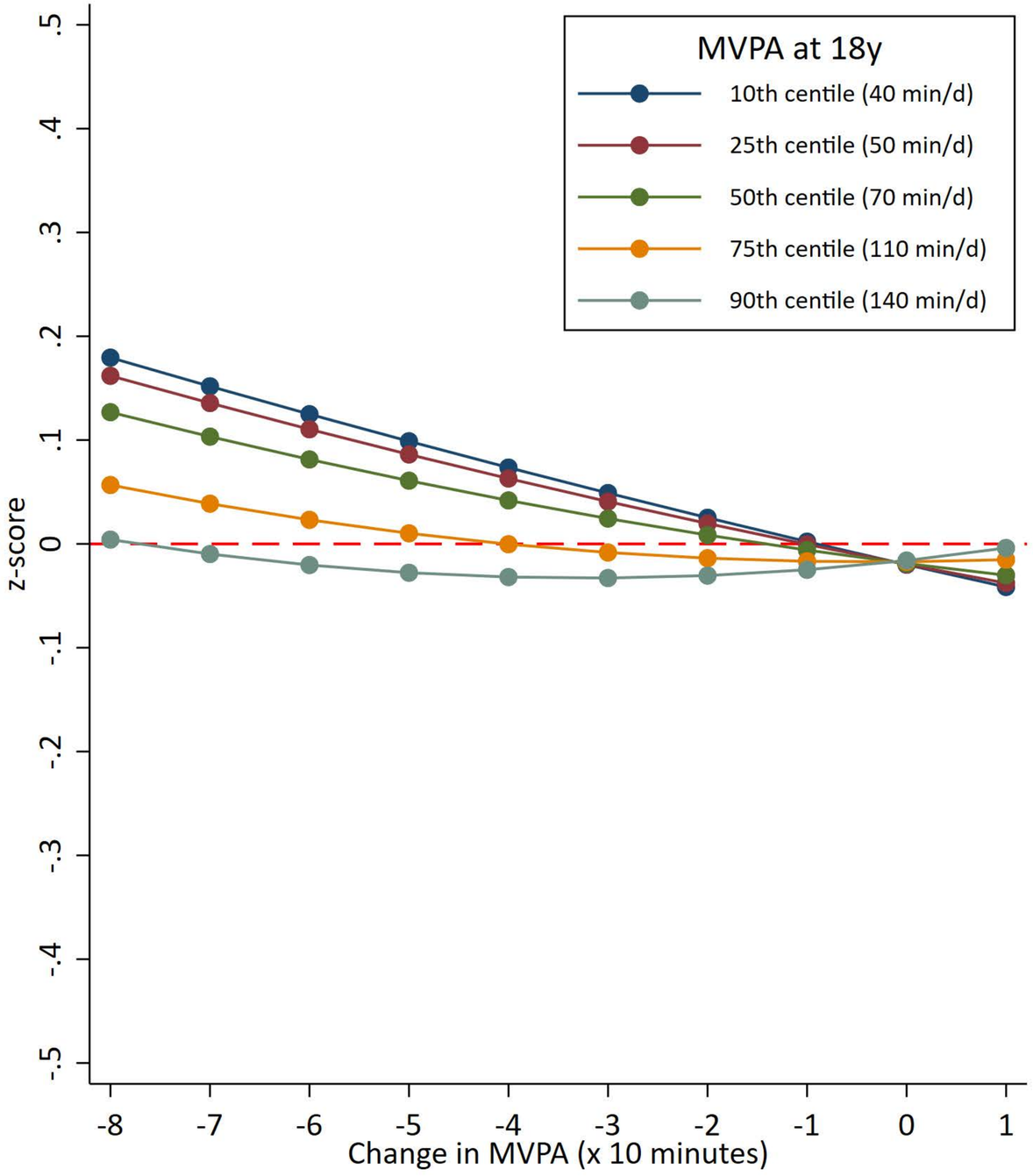
1-minute bout



10-minute bout



1-minute bout



10-minute bout