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Association of moderate to vigorous physical activity and sedentary time
with cardiometabolic risk factors in children and adolescents

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ABSTRACT

CONTEXT: Data on the combined associations between physical activity and sedentary time with cardio-metabolic risk factors in healthy children is sparse.

OBJECTIVE: To examine the independent and combined associations between objectively measured time in moderate and vigorous intensity physical activity and sedentary time with cardio-metabolic risk factors.

DESIGN, SETTING AND PARTICIPANTS: Pooled data from 14 studies collected between 1998 and 2009 comprising 20,871 children (4-18 years) from the International Children's Accelerometry Database was used. Time spent in moderate and vigorous physical activity and sedentary time was measured using accelerometry after reanalysing raw data files. The independent associations between time in moderate and vigorous physical activity and sedentary time with outcomes were examined using meta-analysis. In combined analyses, participants were stratified by tertiles of time spent in moderate and vigorous physical activity and tertiles of sedentary time.

MAIN OUTCOME MEASURES: Waist circumference, systolic blood pressure, fasting triglycerides, HDL-Cholesterol and insulin.

RESULTS: Children accumulated 354 ± 96 min/d and 30 ± 21 min/d sedentary and in MVPA, respectively. Time in moderate and vigorous physical activity was significantly associated with all cardio-metabolic outcomes independent of sex, age, monitor wear time, time spent sedentary and waist circumference (when waist circumference was not the outcome). Sedentary time was not associated with any outcome independent of time in moderate and vigorous physical activity. In the combined analyses, higher levels of moderate and vigorous physical activity were associated with better cardiometabolic risk factors across tertiles of sedentary time. The differences in outcomes between higher and lower moderate and vigorous physical activity were greater the lower the sedentary time. The mean differences in waist circumference between the bottom and top tertiles of moderate and vigorous physical activity varied between 3.6 cm (95% CI, 2.8-4.3)

for high sedentary time to 5.6 (95% CI, 4.8-6.4) for low sedentary time. For systolic blood pressure, the mean differences were 0.7 mm Hg (95% CI, -0.07-1.6) for high sedentary time and 2.5 mm Hg (95% CI, 1.7-3.3) for low sedentary time, and for HDL-cholesterol, -2.6 mg/dL (95% CI, -1.4- -3.9) for high sedentary time and -4.5 mg/dL (95% CI, -3.3- -5.6) for low. Geometric mean differences for insulin and triglycerides showed similar variation. Children in the top tertile of MVPA accumulated >35 minutes/day in this intensity level compared with <18 minutes/day for those in the bottom tertile. In prospective analyses (N=6413, 2.1 yrs follow-up time), neither MVPA nor SED were associated with WC at follow-up, whereas a higher WC at baseline was associated with higher amounts of SED at follow-up.

CONCLUSION: Higher levels of time spent in MVPA by children and adolescents were associated with better cardio-metabolic risk factors regardless of the amount of time spent sedentary.

Introduction

National and international public health authorities agree that children and adolescents should accumulate at least 60 minutes of moderate to vigorous intensity physical activity (MVPA) daily.¹⁻⁶ Although the exact amount of physical activity needed for optimal health is unknown, recent research has established inverse cross-sectional associations between objectively measured physical activity (PA) with adiposity and cardio-metabolic risk factors in youth.⁷⁻¹⁰

Many health authorities and organisations have also recognised the potentially detrimental effects of prolonged time spent sedentary and consequently compiled guidelines for reducing the amount of sedentary time, especially TV viewing.^{3-6, 11}

Some recent reports appear to confirm the importance of reducing sedentary time in youth as they suggest that higher levels of objectively measured time spent sedentary is associated with adiposity⁸ and an adverse cardio-metabolic risk profile.¹²

Time spent in MVPA is weakly to moderately associated with time spent sedentary in youth,^{8,13} suggesting both variables may be independently associated with cardio-metabolic risk factors. However, the independent and combined associations between objectively measured time spent in MVPA and time spent sedentary in relation to cardio-metabolic risk factors in youth remain unclear.

A better understanding of the relations between physical activity and sedentary time in relation to cardio-metabolic risk factors will aid the development of physical activity interventions, counselling and public health policy.

Therefore, we examined the cross-sectional and prospective associations between MVPA and time spent sedentary with established cardio-metabolic risk factors in up to 20,871 children and adolescents (4-18 years) using a meta-analytical approach combining data from multiple cohorts in which physical activity and sedentary time have been measured objectively by accelerometry.

Methods

Study Design

The International Children's Accelerometry Database (ICAD, <http://www.mrc-epid.cam.ac.uk/Research/Studies/>) was established to pool data on objectively measured physical activity from studies in youth world wide. The aims, design, study selection, inclusion criteria, and methods of the ICAD project have been described in detail previously.¹⁴ Briefly, in 2008 a PubMed search for potential contributors was undertaken. From this search 19 studies using the same type of accelerometer (Actigraph), including >400 participants aged between 3 and 18 years were identified. Additional studies were identified by personal communication. In total, 25 studies were identified and approached of which 21 studies agreed to contribute data to the ICAD.¹⁴

Formal data sharing agreements were established and all partners consulted with their individual research board to confirm sufficient ethical approval had been attained for contributing data.

Participants

For the present analyses we used data on children and adolescents (4-18 years) from 14 studies from Australia, Brazil, Europe, and the US¹⁵⁻²⁴ in which data on objectively measured physical activity and at least one of the cardio-metabolic outcomes were available at one time point (N=20,871). These studies were performed between 1998 and 2009. Information on cardio-metabolic outcomes was not available from 7 studies and individuals from these studies were therefore excluded from the present analyses. Baseline and follow-up data for at least one of the outcome variables in combination with baseline physical activity data was available in 6,413 participants.

Measurements

Assessment of physical activity and sedentary time

A detailed description of the assessment of physical activity is available elsewhere.¹⁴ Briefly, all available accelerometer data from the ICAD project were

re-analysed, to provide physical activity outcome variables across studies that could be directly compared, using specifically developed and commercially available software (KineSoft, ver 3.3.20, Saskatchewan, Canada; <http://www.kinesoft.org>), Data files were reintegrated to a 60 sec epoch and non wear time was defined as 60 minutes of consecutive zeros allowing for 2 minutes of non-zeros interruptions.²⁵ All children with at least one day with at least 500 minutes of measured wear time between 7 am and midnight were included. Total physical activity was expressed as total counts, including sedentary minutes, divided by measured time per day (counts per minute, CPM). Time spent sedentary was defined as all minutes <100 counts/minute (cpm)²⁶ and MVPA time as minutes >3000 cpm,²⁶⁻²⁸ which corresponds to about 4.6 METs.²⁶

Assessment of main outcomes

Outcome variables were five established cardio-metabolic outcomes reflecting abdominal adiposity (i.e. waist circumference), glucose metabolism (i.e. fasting insulin), lipid metabolism (i.e. fasting triglycerides and HDL-cholesterol) and resting systolic blood pressure. Skewed variables (fasting insulin and triglycerides) were log transformed before analyses.

Anthropometry

Height and weight was measured using standardised clinical procedures across studies. BMI was calculated as weight (kg)/height (m)² and participants were categorised into normal-weight, overweight and obese groups according to age and sex-specific cut points.²⁹

In all studies except for the NHANES, waist circumference was measured with a metal anthropometric tape midway between the lower rib margin and the iliac crest, at the end of gentle expiration.¹⁵⁻²² In NHANES waist circumference was measured with a metal tape just above the iliac crest at the midaxillary line.³⁰

Systolic blood pressure

Systolic blood pressure (SBP) was measured in 10 of the 14 studies. Details of the measurements have been reported previously.^{17, 18, 31, 32} In the Avon Longitudinal Study of Parents and Children (ALSPAC) blood pressure was measured with a Dinamap 9301 Vital Signs Monitor (Morton Medical, London, UK). In Copenhagen School Child Intervention Study (CoSCIS) and EYHS (Denmark, Estonia, Norway and Portugal) blood pressure was measured using a Dinamap XL vital signs BP monitor (Critikron, Tampa, FL) every second minute during a 10 minute period, following a 10 minutes rest in the seated position and the average of the last three readings was used. In MAGIC and the Pelotas study blood pressure was measured twice after 5-10 minutes of seated rest using a digital Omron sphygmomanometer.

Fasting insulin, triglycerides and HDL-cholesterol

Fasting insulin was measured in seven, and fasting triglycerides and HDL-cholesterol in eight of the 14 studies at baseline according to standard clinical procedures as previously described.^{10, 16, 18, 23, 24}

Statistics

Descriptive results are expressed as mean and standard deviation (SD) for continuous variables and percentages for categorical variables. Differences between sexes were tested by ANOVA. Associations between total physical activity (CPM), MVPA and sedentary time were analysed by Pearson correlation coefficients.

Linear regression models were run separately for each study to estimate the cross-sectional associations between total physical activity (CPM), MVPA (min/d) and sedentary time (min/d) with each of the outcome variables. We thereafter mutually adjusted exposures (MVPA and sedentary time) for each other (i.e. when MVPA was modelled as the main exposure the analysis was adjusted for sedentary time and vice versa) and examined the independent associations between MVPA and sedentary time with each of the outcomes. Results were

expressed as regression coefficients representing the change in the outcome per 100 change in CPM, 10 minute change in MVPA and 60 minute change in sedentary time. Regression coefficients were thereafter combined across studies using random effects meta-analysis adjusted for sex, age, wear time and waist circumference (when WC was not modelled as the outcome).

Heterogeneity across studies was examined by the I^2 statistics. To explore possible reasons for heterogeneity between studies in the exposure effects, the following study-level covariates were included in meta-regression models;³³ mean age, median wear time, proportion of girls, and proportion of normal-weight, overweight and obese individuals.

Due to sex and age differences in MVPA and sedentary time, in combined associations analyses we first stratified each outcome by sex and age-group (≤ 7 years; 7 to 10 years; 10 to 13 years and ≥ 13 years) for MVPA and sedentary time. These groups were then recombined into nine new tertile groups with a similar mean age (ranging from 11.2 to 11.4 years). Sex and age adjusted means and 95% CI for each outcome and tertile group were calculated and a linear trend in the outcome across levels of MVPA within tertiles of sedentary time was tested by ANOVA. Mean difference and its 95% CI between the bottom and top tertiles of MVPA across sedentary categories were calculated for WC, SBP and HDL. Geometric Ratio and its 95% CI from bottom to top tertiles of MVPA across sedentary categories were calculated for fasting insulin and triglycerides because they are lognormal distributed.

Baseline and follow-up data on waist circumference were available in a sub-sample of 6413 participants. To estimate the prospective association between baseline MVPA and sedentary time with follow-up measures of waist circumference, a similar approach to that described above was used, with additional adjustment in the models for follow-up time and the baseline value of the outcome variable.

There were no significant MVPA by sedentary time interactions for any of the analyses.

Since the analysis was an exploratory analysis of observational data rather than a confirmatory analysis of a clinical trial, formal correction for multiple testing was not done. All the analyses were conducted using Stata/SE 11.2 (StataCorp LP, College Station, TX, USA). All significance testing were 2-sided and a P level <0.05 denotes statistical significance.

Results

The baseline characteristics of the studies and sample are summarised in **Table 1** and **Table 2**. Overall, 74.9% of children were categorised as normal weight, 17.7% as overweight and 7.4% as obese. Children's physical activity was monitored for an average of 5.2 days (median 835 min/d; 25th and 75th percentiles; 777 and 924 min/d) and 92.3% of children provided three or more days of valid recordings (>500 min/d).

Boys were significantly more active than girls and spent about 55% more of average daytime in MVPA. Conversely, girls spent on average approximately 5% more of the daytime sedentary. Time spent sedentary was moderately inversely correlated with time spent in MVPA ($r=-0.34$, $P<0.0001$) and strongly inversely correlated with total physical activity (CPM; $r=-0.70$, $P<0.0001$). MVPA was strongly correlated with overall physical activity ($r=0.83$, $P<0.0001$), explaining 68.9% of the variance in total physical activity.

Total physical activity (CPM) was significantly and inversely associated with waist circumference, fasting insulin and triglycerides after adjustment for sex, age, and waist circumference when fasting insulin and triglycerides were the outcomes. MVPA was significantly and inversely associated with all cardio-metabolic outcomes after adjustment for the same confounding variables as above. Time spent sedentary was significantly and positively associated with fasting insulin

after adjustment for confounders, but not with any of the other cardio-metabolic outcomes (**Table 3**).

We thereafter modelled the associations between MVPA with the cardio-metabolic outcomes after additional adjustment for time sedentary and the covariates mentioned above (**Table 3 and eFigure 1a-e**). The associations between MVPA and all cardio-metabolic outcomes remained statistically significant independent of time spent sedentary. In opposite, time spent sedentary was not associated with any of the outcomes after additional adjustment for MVPA (**Table 3 and eFigure 2a-e**).

Meta-regression analysis was used to examine the sources of heterogeneity when modelling the association between time in MVPA and outcome variables (eFigure 1a-e). When modelling associations between MVPA and waist circumference, heterogeneity ($I^2 = 93\%$) was partly explained by different associations between MVPA and WC across BMI groups (P for interaction=0.00004).

The combined association analyses between time spent in MVPA and sedentary time with the cardio-metabolic outcomes are shown in **Figure 1 a-e**. Higher levels of MVPA were associated with significantly lower values of waist circumference, systolic blood pressure, fasting insulin and fasting triglycerides and higher values of HDL-Cholesterol across tertiles for sedentary time. The differences in outcomes between higher and lower MVPA were greater the lower the sedentary time. The mean differences (95% CI) between the bottom and top tertiles of MVPA across sedentary categories varied between 3.6 (95% CI; 2.8–4.3) and 5.6 (95% CI; 4.8–6.4) for WC (cm); 0.7 (95% CI; -0.07–1.6) and 2.5 (95% CI; 1.7–3.3) for SBP (mmHg); -2.6 (95% CI; -1.4--3.9) and -4.5 (95% CI; -3.3--5.6) for HDL-Cholesterol (mg/dL); The ratio between bottom and top tertiles of MVPA across sedentary categories varied between 1.39 (1.27–1.53) and 1.71 (1.53–1.91) for insulin, and 1.15 (1.09–1.21) and 1.27 (1.20–1.35) for triglycerides, suggesting a 71% and 27% difference between extreme MVPA groups for fasting insulin and triglycerides, respectively.

Youth in the top tertile of MVPA accumulated >35 minutes per day in this intensity level compared with <18 minutes per day for those in the low tertile. Data on waist circumference were available from 7 studies (N=6413) at two different time points with a median follow up time of 2.1 years (range 0.3 to 8.0 yrs). Neither time in MVPA ($\beta=0.00024$; 95% CI, -0.0057–0.0062) nor sedentary time ($\beta=-0.0024$; 95% CI, -0.0057–0.0010) was associated with waist circumference at follow up after adjustment for sex, age, wear time (min/d), follow-up time and baseline waist circumference.

We then examined whether baseline waist circumference was associated with time spent in MVPA and sedentary time at follow up. Baseline waist circumference was not associated with time in MVPA at follow up ($\beta=-0.0037$; 95% CI, -0.60–0.052).

In contrast, a higher baseline waist circumference was associated with increased time spent sedentary ($\beta=0.40$; 95% CI, 0.19–0.61) adjusted for sex, baseline age, baseline sedentary time, wear time, and follow up time (**Figure 2**).

Discussion

Time spent in MVPA is associated with multiple cardio-metabolic risk factors independent of time spent sedentary and other confounding factors. Belonging to the top tertile for MVPA is associated with favourable metabolic health regardless of the amount of time spent sedentary. In contrast, time spent sedentary is unrelated to these risk factors after adjusting for time spent in MVPA. Neither time spent in MVPA nor time spent sedentary predicted a higher waist circumference in prospective analyses. However, baseline waist circumference predicted increased time spent sedentary at follow up.

Strengths of our study include the large sample size, which allowed us to stratify our sample into nine different groups with reasonably large samples in each stratum when examining the combined associations between time in MVPA, sedentary time and cardio-metabolic outcomes. Another strength includes the

meta-analyses of 14 individual studies providing more robust estimates of the observed associations. Time in MVPA and sedentary time were measured objectively reducing the possibility of misclassification and raw individual data files were cleaned, processed and reanalysed in a standardized manner in all children.¹⁴

The observational study design limits inferences of causality. However, the cross-sectional associations between time in MVPA and the cardio-metabolic risk factors independent of sedentary time were consistent in our meta-analyses and in the combined association analyses. It is unlikely that the metabolic risk factors per se lead to lower levels of physical activity whereas it is biologically plausible that physical activity affects multiple cardio-metabolic outcomes, possibly with the exception of adiposity. Indeed, results from exercise interventions suggest that both moderate and vigorous intensity exercise reduce the postprandial triacylglycerol concentrations in normal-weight³⁴ and overweight children³⁵, improves insulin sensitivity in overweight children^{36, 37} and improves systolic blood pressure in normotensive adolescents.³⁸

Although we controlled for confounding factors, we cannot exclude the possibility that unmeasured (e.g. genotype and dietary intake) or poorly measured confounders explain our observations. Our intensity threshold for MVPA (3000 cpm) was higher compared with some other previous studies in children.¹⁰ However, when reanalysing our data using a lower intensity threshold of 2000 cpm, the observations were materially unchanged (data not shown).

Previous observations suggest that overall physical activity and time spent in MVPA is associated with a more healthy cardio-metabolic profile in young people.^{9, 10, 39, 40} It has also been suggested that objectively measured time spent sedentary is associated with adiposity⁸ and insulin resistance¹² in children.

Further, overall physical activity measured by accelerometry appears associated with a favourable cardio-metabolic profile independent of self-reported time spent viewing TV.⁴¹ The present results extend previous observations by meta-analysing

data from up to 14 different studies and by mutually adjusting time in MVPA and sedentary time for each other. Further, the combined associations analyses consistently confirmed that time in MVPA appears more important than time spent sedentary in relation to cardio-metabolic outcomes in children.

The magnitude of associations between time in MVPA and the cardio-metabolic outcomes were small and could be considered by some as not clinically meaningful. A 10 minute difference in MVPA was associated with approximately 0.5 cm difference in waist circumference and approximately a 1pmol/L difference in fasting insulin. However, the magnitude of associations may be underestimated. This is because physical activity is highly variable in children and our measure of physical activity comprising of five days on average, may not fully reflect the true activity levels of the participants. The intraclass correlation coefficient (ICC) for within individual differences in accelerometer measured physical activity is about 0.5.²⁷ Assuming all measurement error stems from within individual variability, the ICC can be used for measurement error correction by dividing the regression coefficients by the ICC.⁴² This then suggests that the true magnitudes of the associations may be at least twice as strong as those observed.

Results from the combined analyses were more substantial. Waist circumference differed by up to 5.6 cm (95% CI; 4.8–6.4) between those in the top tertiles for MVPA compared with those in the bottom tertiles. If this difference in waist circumference persists into adulthood it may confer considerable health risks as waist circumference is linearly associated with all-cause mortality.^{43, 44} For example, every 5 cm increase in waist circumference is associated with an increased relative risk of 17% and 13% for all-cause mortality in men and women, respectively.⁴³

Further, the differences in cardio-metabolic risk factors between the top and bottom tertile of MVPA were remarkable similar to the effects observed from a 12 month high intensive exercise intervention in sedentary individuals with type 2

diabetes.⁴⁵ Taken together, this suggests that the magnitude of differences in cardio-metabolic risk factors observed between high and low active healthy youth is clinically significant irrespective of the amount of time spent sedentary.

Moving from the bottom to the top tertile for MVPA requires an increase in MVPA of at least 20 minutes per day. Increasing daily activity at this intensity level can be achieved by participating in activities such as brisk walking, jogging, cycling, playing soccer, and other team sports.

Our results contradict some previous observations in adults suggesting that objectively measured sedentary time is associated with metabolic outcomes independent of time in MVPA.⁴⁶ When interpreting the differences in results between studies in children and adults the following should be considered; First, total physical activity (CPM) is significantly higher in children compared with adults. Second, differences in the definition of MVPA and differences in the relative amount of time spent sedentary between studies may also contribute to the conflicting results. Finally, the between individual variability in time in MVPA and time spent sedentary may vary between children and adults.

In contrast to studies in adults⁴⁷⁻⁴⁹ we were not able to confirm that baseline time in MVPA or sedentary time predicted any of the cardio-metabolic outcomes at follow up. This may be explained by the generally more healthy metabolic risk profile in our children compared with middle-aged adults. Other differences include higher overall levels of activity, more time accumulated in MVPA and less time spent sedentary in children compared with adults.²⁵

The observation that baseline waist circumference predicted time spent sedentary at follow up corroborates studies in children and adults^{50, 51}, supporting the hypothesis that the association between physical activity, sedentary time and weight gain may be bi-directional.

Our results have implications for public health policy and physical activity counselling. Children should be encouraged to increase their participation in physical activity of at least moderate intensity rather than reducing their overall

sedentary time as this appears more important in relation to cardio-metabolic health. However, our measure of sedentary time takes into account the accumulated time spent sedentary rather than a specific behaviour (e.g. TV viewing). Therefore, decreasing TV time in youth may still be an important public health goal as TV viewing may be associated with other unhealthy behaviours such as snacking and soft drink consumption.^{52, 53} Further TV viewing is also associated with exposure to 'adverts' that often promote unhealthy dietary habits.⁵⁴

In conclusion, higher levels of time in MVPA appear to be associated with better cardio-metabolic risk factors regardless of the amount of time spent sedentary in youth.

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Author contribution: UE and AC conceived the study; UE drafted all versions of the manuscript, interpreted the data and act as the guarantor; JAL performed the statistical analyses and contributed to data interpretation; LS cleaned and reduced the raw accelerometer data to the outcome variables and contributed to interpretation of the data; DS developed the programme for accelerometer data reduction and analyses, assisted with data cleaning and reduction and contributed to interpretation of the data; PG organised the phenotypic information and contributed to interpretation of the data; AC contributed to writing and data interpretation. All authors approved the final version of the manuscript.

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Data access: UE and JL retain full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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FIGURE LEGENDS

Figure 1. Combined associations of time spent sedentary and in MVPA on waist circumference (**Figure 1a**), systolic blood pressure (**Figure 1b**) fasting insulin (**Figure 1c**), fasting triglycerides (**Figure 1d**), and fasting HDL-Cholesterol (**Figure 1e**) stratified by tertiles of sedentary time and time in MVPA. Mean time (min/d) spent sedentary in the low, middle and high tertile groups were 268.0 (range 28.0 to 399) min/d; 351.6 (range 203.0 to 479.8) min/d; and 433.3 (range 262.3 to 755.8) min/d, respectively. Mean time spent in MVPA was 12.0 (range 0 to 27.2) min/d; 27.0 (range 8.4 to 45.7) min/d; and 52.5 (range 20.6 to 185.0) min/d in the low, middle and high MVPA groups. The mean age ranged between 11.2 yrs and 11.4 yrs across tertile groups. Data for each group are sex and age adjusted means (geometric means for fasting insulin and triglycerides) and 95% CI (P for trend<0.0001 for all outcomes across all sedentary tertiles except for systolic blood pressure in the high sedentary group; P for trend=0.11).

Figure 2. Meta analysis of the prospective associations (β -coefficients and 95% CI) between baseline waist circumference and time spent sedentary at follow up. The β -coefficients represent the difference in time spent sedentary (min per day) for one cm difference in baseline waist circumference. The model is adjusted for sex, age, monitor wear time, baseline time spent sedentary, and follow up time.

Table 1. Cohort characteristics and measurements (data are mean and standard deviations unless otherwise stated).

Study	Country and year of measurement	N (boys/girls)		Follow-up time	Age range (years)	Height (cm)	Weight (kg)	BMI (kg/m ²)	Waist (cm)	Secondary sex					Birth weight (g)
										Stage					
ALSPAC	UK 2003/04 and 2005/06	3158	3436		10-15	151.9 (8.2)	44.7 (10.7)	19.2 (3.4)	68.6 (9.5)	1510 (22.9)	2334 (35.4)	1820 (27.6)	804 (12.2)	125 (1.9)	3409 (551)
Ballabeina	Switzerland 2008 and 2009	299	300		4-8	113.4 (6.3)	20.3 (3.4)	15.7 (1.6)	53.2 (4.4)	NA					
CSCIS	Denmark 2001/02 and 2004/05	356	311		6-11	124.5 (7.1)	25.2 (5.3)	16.1 (2.0)	56.4 (6.1)	454 (75.8)	126 (21.0)	19 (3.2)	0	0	NA
Denmark EYHS	Denmark 1997/98 and 2003/04	607	751		9-16	148.8 (15.5)	42.1 (14.5)	18.5 (3.1)	63.4 (8.3)	807 (59.4)	129 (9.5)	27 (2.0)	187 (13.8)	208 (15.3)	3396 (587)
Estonia EYHS	Estonia 1998/99	294	366		9-16	152.7 (17.5)	44.6 (15.8)	18.4 (3.1)	62.4 (8.1)	281 (42.6)	60 (9.1)	57 (8.6)	132 (20.0)	130 (19.7)	3540 (598)
KISS	Switzerland 2005 and 2006	235	260		6-14	136.6 (13.2)	33.0 (10.2)	17.3 (2.8)	58.6 (7.1)	345 (69.7)	102 (20.7)	33 (6.7)	12 (2.4)	2 (0.4)	3357 (568)
MAGIC	Scotland	205	213		4-5	102.7	17.3	16.3	51.3	NA					NA

	2002					(4.3)	(2.4)	(1.5)	(3.6)						
NHANES 03/04	US 2003/04	1193	1154		6-18	153.9 (17.7)	53.9 (22.1)	21.9 (5.9)	75.3 (15.8)	NA					NA
NHANES 05/06	US 2005/06	1225	1229		6-18	152.7 (18.0)	52.8 (22.4)	21.7 (6.0)	74.9 (16.1)	NA					NA
Norway EYHS	Norway 1999/2000	194	190		9-10	139.2 (6.4)	33.2 (5.9)	17.0 (2.2)	60.3 (5.7)	315 (82.1)	64 (16.7)	5 (1.2)	0	0	3459 (587)
PEACH	UK 2006/07 and 2008/09	605	635		10-13	145.7 (7.3)	39.8 (9.5)	18.6 (3.4)	66.9 (9.1)	NA					NA
Pelotas	Brazil 2006/07	238	217		13-14	158.0 (8.4)	51.1 (12.0)	20.3 (3.8)	68.6 (8.4)	NA					3218 (533)
Portugal EYHS	Portugal 1999/00 and 2008	610	613		9-16	141.5 (13.7)	38.8 (13.2)	18.9 (3.5)	63.3 (8.3)	422 (34.5)	471 (38.5)	29 (2.4)	75 (6.1)	226 (18.5)	3385 (526)
SPEEDY	UK 2007	878	1098		9-11	141.0 (6.6)	36.5 (8.3)	18.2 (3.2)	64.1 (8.4)	NA					3349 (582)

Table 1 cont.

Study	DBP (mmHg)	SBP (mm Hg)	Insulin (pmol/L)*	Triglycerides (mg/dL)*	HDL-Cholesterol (mg/dL)	Total PA (cpm)	Sedentary (min/d)	MVPA (min/d)
ALSPAC	58.7 (6.5)	105.5 (9.9)	NA	NA	NA	597 (189)	356 (75)	35 (21)
Ballabeina	NA	NA	NA	NA	NA	702 (182)	236 (65)	22 (13)
CSCIS	58.1 (6.0)	98.7 (8.5)	21.1 (19.7; 22.6)	20.1 (16.6; 25.9)	57.5 (10.8)	738 (198)	268 (62)	36 (20)
Denmark EYHS	61.3 (6.2)	104.9 (10.0)	49.1 (47.6; 50.7)	29.3 (21.6; 39.4)	58.3 (13.1)	581 (248)	356 (107)	30 (23)
Estonia EYHS	61.2 (7.1)	105.9 (11.3)	47.1 (45.1; 49.3)	26.6 (21.2; 35.1)	54.4 (11.2)	625 (243)	343 (106)	38 (26)
KISS	NA	NA	50.2 (47.3; 53.1)	23.6 (16.6; 27.8)	63.3 (13.5)	647 (210)	278 (99)	44 (23)
MAGIC	60.8 (6.6)	97.0 (7.8)	NA	NA	NA	756 (187)	192 (57)	26 (16)
NHANES 03/04	57.7 (11.6)	106.8 (10.3)	58.3 (55.2; 61.5)	31.7 (23.2; 44.0)	54.4 (12.7)	541 (226)	375 (106)	27 (21)
NHANES 05/06	58.0 (10.9)	108.0 (10.6)	63.5 (60.3; 66.8)	30.9 (22.8; 41.7)	54.4 (13.1)	526 (228)	378 (105)	24 (20)

Norway EYHS	62.6 (5.8)	102.9 (7.6)	NA	30.5 (24.7; 35.9)	59.5 (12.0)	711 (293)	325 (102)	45 (27)
PEACH	NA	NA	NA	NA	NA	570 (170)	362 (72)	29 (17)
Pelotas	68.2 (11.2)	110.7 (14.1)	NA	NA	NA	388 (144)	491 (93)	20 (16)
Portugal EYHS	55.0 (6.4)	96.9 (9.8)	28.2 (27.1 (29.3))	23.6 (18.9; 33.6)	60.2 (12.7)	562 (215)	367 (94)	29(21)
SPEEDY	NA	NA	NA	NA	NA	602 (180)	352 (63)	28 (17)

BMI, body Mass Index; DBP, Diastolic Blood Pressure; SBP, Systolic Blood Pressure; PA, Physical activity; MVPA, moderate-to-vigorous physical activity; CPM, counts per minute, NA, Data Not Available

Sexual maturity according to secondary sex staging based on public hair in boys and breast development in girls, data are N and frequencies in each group from 1 to 5

*Median and inter quartilerange

To convert conventional units for triglycerides and HDL-Cholesterol to SI units multiply by 0.0259

Table 2. Baseline descriptive characteristics of participants stratified by sex (n=20,871). Data are mean and SD unless otherwise stated.

	Boys (N=10,098)	Girls (N=10,773)	P
Age (years)	11.3 (2.9)	11.3 (2.8)	0.48
Weight (kg)	43.1 (17.7)	42.7 (15.6)	0.037
Height (cm)	147.4 (17.5)	145.6 (15.1)	<0.0001
Waist (cm)	67.5 (12.4)	66.8 (12.1)	<0.0001
BMI (kg/m ²)	19.1 (4.2)	19.4 (4.5)	<0.0001
Ethnicity (% white) ^a	74.1	76.1	
Normal-weight (%)	76.2	73.7	
Overweight (%)	16.7	18.6	
Obese (%)	7.1	7.7	
<u>Sexual maturity^b</u>			
Stage 1 N (%)	1983 (48.3)	1551 (40.0)	
Stage 2 N (%)	1186 (28.9)	791 (20.4)	
Stage 3 N (%)	386 (9.4)	582 (15.0)	
Stage 4 N (%)	271 (6.6)	531 (13.7)	
Stage 5 N (%)	279 (6.8)	423 (10.9)	
Birth weight (g) ^c	3457 (588)	3342 (536)	<0.0001
Diastolic BP (mm Hg) ^d	58.5 (8.7)	59.4 (8.3)	<0.0001
Systolic BP (mm Hg)	105.5 (10.9)	104.2 (10.4)	<0.0001
Insulin (pmol/L) ^e	35.0 (33.8; 36.1)	39.3 (38.1; 40.7)	<0.0001
Triglycerides (mg/dL) ^f	27.0 (26.6; 27.4)	28.6 (28.2; 29.0)	<0.0001
HDL (mg/dL)	56.0 (13.1)	56.8 (12.7)	0.0011
<u>Physical Activity</u>			
Total activity (CPM)	642 (226)	540 (193)	<0.0001
Sedentary (min/d)	345 (96)	363 (96)	<0.0001
MVPA (min/d)	37 (23)	24 (17)	<0.0001

^a White/Other; 10 studies (ALSPAC, EYHS Denmark, EYHS Estonia, EYHS Norway, EYHS Portugal, NHANES 05/06, NHANES 03/04, PEACH, Pelotas, SPEEDY (Boys; N=8585; Girls; N=9248)

^b pubic hair in boys (N=3878) and breast development in girls (N=4105) from 7 studies (ALSPAC, CSCIS, EYHS Denmark, EYHS Estonia, EYHS Norway, EYHS Portugal, KISS)

^c Birth weight; 8 Studies (ALSPAC, EYHS Denmark, EYHS Estonia, EYHS Norway, EYHS Portugal, Pelotas, SPEEDY, KISS) (Boys N=5511; Girls N=6132)

^d DBP and SBP; 9 studies (ALSPAC, CSCIS, EYHS Denmark, EYHS Estonia, EYHS Norway, EYHS Portugal, MAGIC, NHANES 05/06, NHANES 03/04, Pelotas) (Boys; N=7348; Girls N=7754)

^e Fasting insulin (geometric mean and 95% CI); 7 studies (CSCIS, EYHS Denmark, EYHS Estonia, EYHS Portugal, NHANES 05/06, NHANES 03/04, KISS) (Boys N=2590; Girls N=2671)

^f Fasting triglycerides (geometric mean and 95% CI); 8 studies (CSCIS, EYHS Denmark, EYHS Estonia, EYHS Portugal, NHANES 05/06, NHANES 03/04, KISS) (Boys N=2785; Girls N=2896)

HDL, High Density Lipoprotein Cholesterol; 8 studies (CSCIS, EYHS Denmark, EYHS Estonia, EYHS Portugal, NHANES 05/06, NHANES 03/04, KISS) (Boys N=4104; Girls N=4256)

P; denote statistical differences between sex (ANOVA)

To convert conventional units for triglycerides and HDL-Cholesterol to SI units multiply by 0.0259

Table 3. Meta analysed associations between objectively measured total physical activity (CPM), time spent in MVPA (min/d) and sedentary time (min/d) with cardio-metabolic risk factors in up to 20,871 children. Data are β -coefficients (95% CI). Coefficients represent the change in the outcome for a 100 CPM change in total physical activity and a 10 minute change in time spent in MVPA and a 60 minute change in time spent sedentary. In models at the bottom of the table MVPA is additionally adjusted for sedentary time and sedentary time mutually adjusted for MVPA.

	Waist circumference (cm)	Systolic Blood Pressure (mmHg) ^a	Insulin (pmol/L) ^b	Triglycerides (mg/dl) ^b	HDL-Cholesterol (mg/dl)
Total PA (CMP)	-0.35 (-0.50;-0.16)	-0.10 (-0.26;0.05)	-0.026 (-0.033;-0.020)	-0.021 (-0.026;-0.016)	0.19 (-0.11;0.48)
MVPA (min/d)	-0.52 (-0.76;-0.28)	-0.15 (-0.30;-0.06)	-0.028 (-0.038;-0.017)	-0.017 (-0.025;-0.009)	0.25 (-0.034;0.53)
Sedentary (min/d)	0.13 (-0.094;0.358)	-0.043 (-0.21;0.20)	0.012 (0.0029;0.022)	0.014 (-0.0031;0.030)	-0.064 (-0.24;0.12)
MVPA adjusted for Sedentary (min/d)	-0.54 (-0.79;-0.30)	-0.17 (-0.30;-0.04)	-0.030 (-0.043;-0.017)	-0.014 (-0.023;-0.0046)	0.31 (0.036;0.59)
Sedentary adjusted for MVPA (min/d)	-0.12 (-0.32;0.09)	-0.10 (-0.21;0.02)	-0.009 (-0.026,0.008)	0.006 (-0.010;0.023)	0.096 (-0.098;0.29)

Data are adjusted for age, sex, wear minutes, and waist circumference (WC) (when WC is not the outcome) (WC; N=20,871; BP N=15,062; Insulin N=5261; Triglycerides N=5689; HDL N=8360)

^aSystolic Blood pressure; additionally adjusted for height

^bFasting insulin and triglycerides were log transformed

To convert conventional units for triglycerides and HDL-Cholesterol to SI units multiply by 0.0259