2017

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Schnurr TM

Springer Nature

info:eu-repo/semantics/article
info:eu-repo/semantics/acceptedVersion
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http://dx.doi.org/10.1038/ijo.2017.235

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Genetic predisposition to adiposity is associated with increased objectively assessed sedentary time in young children

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Abstract

Increased sedentariness has been linked to the growing prevalence of obesity in children, but some longitudinal studies suggest that sedentariness may be a consequence rather than a cause of increased adiposity. We used Mendelian randomization to examine the causal relations between body mass index (BMI) and objectively assessed sedentary time and physical activity in 3-8 year-old children from one Finnish and two Danish cohorts \( N_{\text{TOTAL}} = 679 \). A genetic risk score (GRS) comprised of 15 independent genetic variants associated with childhood BMI was used as the instrumental variable to test causal effects of BMI on sedentary time, total physical activity, and moderate-to-vigorous physical activity (MVPA). In fixed effects meta-analyses, the GRS was associated with 0.05 SD/allele increase in sedentary time \( (P=0.019) \), but there was no significant association with total physical activity \( (\text{beta}=0.011 \text{ SD/allele}, P=0.58) \) or MVPA \( (\text{beta}=0.001 \text{ SD/allele}, P=0.96) \), adjusting for age, sex, monitor wear-time and first three genome-wide principal components. In two-stage least squares regression analyses, each genetically instrumented one unit increase in BMI z-score increased sedentary time by 0.47 SD \( (P=0.072) \). Childhood BMI may have a causal influence on sedentary time but not on total physical activity or MVPA in young children. Our results provide important insights into the regulation of movement behaviour in childhood.
Introduction

Increased sedentary time and decreased physical activity have been linked to the recent increase in the prevalence of overweight and obesity among children (1, 2). However, evidence from longitudinal studies suggests that decreased physical activity and increased sedentary time may be an outcome rather than a cause of increased adiposity in children (3, 4).

Genetic variants associated with body mass index (BMI) can be utilized as instrumental variables in Mendelian randomization to test for causal relationships between adiposity and physical activity or sedentary behaviour. In 2014, Richmond et al. performed instrumental variable analyses in 4296 children 11 years of age from the UK using a genetic risk score (GRS) for obesity (5), derived from 32 gene variants identified in a published genome-wide association study (GWAS) of adult BMI (6). Genetic predisposition to higher BMI was robustly associated with longer sedentary time and lower levels of physical activity (5), suggesting causality. However, these findings remain to be replicated in younger children in whom genetic determinants of movement behaviour may be particularly discernible due to higher tendency for voluntary and spontaneous, play-oriented activity (7, 8). Further, a recent GWAS in children identified 15 loci for childhood BMI (9), making it possible to generate a more specific instrumental variable for childhood adiposity than the GRS for adult BMI used by Richmond et al. (5).

The aim of the current study was to investigate whether a GRS of 15 loci for childhood BMI is associated with objectively assessed sedentary time and physical activity in young children.

Methods

Participants

The participants of the study include 287 Danish children 3 years of age from the Småbørns Kost Og Trivsel I and II (SKOT I and II) studies (10) and 400 Finnish children from the Physical Activity and Nutrition in
Measurement of body size and composition

In the SKOT I and II studies, body weight was measured by the Tanita WB-100MA digital scale (Tanita Corporation, Tokyo, Japan) and body height by the 235 Heightronic digital stadiometer (QuickMedical, Issaquah, WA, USA). The age and gender-specific BMI z-score was calculated using the WHO Anthro software, version 3.2.2 (12). In the PANIC study, body weight was measured using the InBody® 720 bioimpedance device (Biospace, Seoul, Korea) and body height using a wall-mounted stadiometer. Age and gender-specific BMI z-score was calculated based on Finnish reference data (13).

Assessment of sedentary time, total physical activity and MVPA

In the SKOT I and II studies the ActiGraph GT3X accelerometer (ActiGraph LLC, Pensacola, FL, USA), and in the PANIC study Actiheart (Actiheart, CamNTech Ltd., Cambridge, UK) was used to assess sedentary time and physical activity. Details on the assessment of activity behaviours are provided in Supplementary Material 1.

Genotyping, SNP selection, and genetic risk score construction

Children in SKOT I and II were genotyped using the Illumina Infinium HumanCoreExome Beadchip. Children in the PANIC study were genotyped using the Illumina Custom Infinium Cardio-MetaboChip and the Illumina Infinium HumanCoreExome Beadchip (Illumina, San Diego, CA, USA) and the genotypes from the two arrays were combined (see Supplementary Material 1 for information on quality control). The SNPs included in the GRS were selected based on a previously published GWAS meta-analysis in children 2-10 years of age (9) that identified 15 independent loci associated with BMI at genome-wide significance ($p<5\times10^{-8}$). We
constructed a weighted BMI-increasing GRS by summing the number of BMI-increasing alleles weighted by the effect sizes of the variants estimated in the GWAS discovery study (Supplementary Material 1, Supplementary Table 1).

**Statistical analysis**

All association analyses were performed using R, version 3.3.1. Only children with valid physical activity and genotype data (n_{SKOT I}=208; n_{SKOT II}=71; n_{PANIC}=400) were included in the present analyses. Sedentary time, total physical activity, and moderate-to-vigorous intensity physical activity (MVPA) variables were rank inverse normally transformed to approximate normal distribution with a mean of 0 and standard deviation (SD) of 1, and the effect sizes are thus reported in SD units of the inverse normally transformed trait.

The associations of the BMI z-score as well as the BMI-increasing GRS with sedentary time, physical activity and MVPA were analysed by linear regression adjusting for age, sex, and monitor wear-time. The association of the BMI-increasing GRS with the BMI z-score was analysed by linear regression adjusting only for monitor wear-time, because the BMI z-score is age and sex-specific. The BMI-increasing GRS did not show an association with additional potential confounders in PANIC, the largest cohort included in the meta-analysis (sleep, socioeconomic status; p > 0.05, data not shown). The causal relationships between BMI and activity behaviours were tested using two-stage least squares regression analyses implemented in the ‘AER’ package in R (version 3.3.3). We used the Durbin-Wu-Hausman (DWH) test for endogeneity and calculated the F-statistic for the PANIC cohort (F-statistic_{PANIC}) to compare effect estimates between the instrumental and observational analyses (14). To test for potential directional pleiotropy in the genetic instrument, we used Egger regression, implemented in the ‘MendelianRandomization’ package in R (version 3.3.3), where the deviation of the intercept from zero provides evidence of pleiotropy (15). The associations of the BMI-increasing GRS, two-stage least squares regression and Egger regression analyses were additionally adjusted for the first three genome-wide principal components of the respective study.
We pooled the results from the SKOT I, SKOT II and PANIC studies by fixed effects meta-analyses using the ‘meta’ package in R (version 4.6.0).

Results

The characteristics of children from the SKOT I, SKOT II and PANIC studies are summarized in Supplementary Table 2. The average age of the children was 3.0 years (range 2.9-3.3 years) in SKOT I; 3.0 years (range 2.9-3.2 years) in SKOT II; and 7.6 years (range 6.6-9.0 years) in PANIC. The GRS was normally distributed in all three cohorts, with a mean (range) of 8.6 (3.8-14.7), 9.0 (5.0-17.8) and 9.3 (3.7-16.1) BMI-increasing alleles in SKOT I, SKOT II and PANIC, respectively.

A higher BMI z-score was associated with increased sedentary time (β=0.22 SD, P=7.6x10^{-9}) and reduced MVPA (β=-0.17 SD, P=1.1x10^{-5}), but not with total physical activity (β=0.003 SD, P=0.94) (Figure 1). Heterogeneity was observed in the association of BMI z-score with sedentary time and MVPA (p_{het}<0.05).

A higher BMI-increasing GRS was associated with a higher BMI z-score (β=0.056 SD/allele, P=0.003) and longer sedentary time (β=0.040 SD/allele, P=0.019), suggesting a causal effect of BMI z-score on sedentary time.
behavior (Figure 2). In two-stage least squares analyses, each genetically instrumented one unit increase in BMI z-score increased sedentary time by 0.47 SD (P=0.072, F-statistic\textsubscript{PANIC}=8.2), and no difference was found between the observational and genetically instrumented estimates in the DWH test (P>0.05). We found no evidence of directional pleiotropy in the genetic instrument using the Egger intercept test (P\textsubscript{INTERCEPT}=0.28), and the causal estimate from Egger regression was directionally consistent with that derived from the two-stage least squares method.

There was no significant association between the BMI-increasing GRS and MVPA (β=0.001, P=0.96) or total physical activity (β=0.011, P=0.58), and two-stage least squares analyses were not suggestive of a causal effect of BMI on MVPA (β=-0.026, P=0.94, F-statistic\textsubscript{PANIC}=7.5) or physical activity (β=0.22, P=0.55, F-statistic\textsubscript{PANIC}=7.5) (Figure 1).

Figure 2.

Mendelian randomization analysis to test the causal effect of childhood BMI on sedentary time. Beta values are expressed in units of standard deviation (SD) of the inverse-normally transformed traits. GRS = Genetic risk score, BMI z-score = age- and sex-specific BMI standard deviation score, N\textsubscript{TOTAL} = number of individuals included in meta-analysis.

Discussion

In the present study, a GRS for childhood BMI was nominally significantly associated with BMI and sedentary time, but not with total physical activity or MVPA. Our results may suggest that higher adiposity is causally associated with longer sedentary time but not with decreased physical activity in young children. Consistent with our findings, Richmond et al. (5) found that a higher GRS for BMI was positively associated with longer daily sedentary time in 11-year old children from the UK. However, they also reported that a higher GRS was associated with lower levels of total physical activity and MVPA, whereas we found no
association between the GRS and total physical activity or MVPA. While the sample sizes for the present analyses were smaller than in the study by Richmond et al., we observed an effect close to zero for the association of the GRS with physical activity and MVPA, and with confidence intervals suggesting that little or no effect is present in 3-8 year old children. Nevertheless, our findings should ideally be validated in further studies including large samples of young children with objectively measured activity behaviour.

The age of the children and country-specific differences in the education system may partly explain the observed differences in the results of the study by Richmond et al (5) and our study. In our study, we also found heterogeneity in the association of the BMI z-score with sedentary time and MVPA, and visual observation of the forest plots indicated that the two SKOT cohorts show consistent results which differ from those seen for the PANIC cohort, which may be due to the different age range of children included in these cohorts. Most 3-year-old Danish children attend kindergarten where physical activity typically consists of play-oriented activities (16) and the children are free to choose whether to play passively or actively. The Finnish children 6-8 years of age were first graders in primary schools when they were invited to participate in the PANIC study. They were thus more likely to engage in play-oriented physical activity because of their recent pre-school times than the 11-year-old children from the UK, although they also spent longer periods of time in sedentary and non-sedentary activities during school hours. The tendency to engage in voluntary and play-oriented activities in younger children could explain the lack of association between the GRS for childhood BMI and physical activity in the present study.

While our results are suggestive of an effect of adiposity on sedentary behaviour, we could not investigate whether a genetic predisposition to sedentary behaviour reciprocally results in higher BMI, because no genetic variants associated with sedentary behaviour have yet been robustly identified (17). Similarly, we could not examine whether MVPA has a causal effect on BMI in young children, and whether such an effect explains the observed association between higher BMI and lower MVPA. Furthermore, we cannot fully
exclude the possibility of residual pleiotropy, i.e. that the selected genetic variants act not only on BMI but also on other phenotypes related to sedentary time.

In conclusion, we showed that young children with higher genetic risk for obesity have increased objectively measured sedentary time but not decreased physical activity, suggesting that obesity may be causally associated with longer time spent in sedentary pursuits at this age. Reducing BMI may thus be an effective strategy to reduce sedentariness in overweight children. While the mechanisms underlying the potential causal relationship between BMI and sedentary time remain unclear, they are likely to involve both physiological factors and factors related to the family environment (18). Our findings provide novel insights into the regulation of movement behaviour in childhood and suggest that more attention should be given to the sedentary-time increasing effect of obesity in young children.

Supplementary information is available at the International Journal of Obesity’s website.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

We specially want to express our thanks to the participant children and their parents that were part of the SKOT I, SKOT II and PANIC studies. This project was carried out as part of the research programme "Governing Obesity" funded by the University of Copenhagen Excellence Programme for Interdisciplinary Research (www.go.ku.dk) and was supported by the Danish Diabetes Academy supported by the Novo Nordisk Foundation. The SKOT studies were supported by grants from The Danish Directorate for Food, Fisheries and Agri Business as part of the ‘Complementary and young child feeding (CYCF) – impact on
short- and long-term development and health’ project. The PANIC study was funded by grants from Ministry of Social Affairs and Health of Finland, Ministry of Education and Culture of Finland, Finnish Innovation Fund Sitra, Social Insurance Institution of Finland, Finnish Cultural Foundation, Juho Vainio Foundation, Foundation for Paediatric Research, Doctoral Programs in Public Health, Paavo Nurmi Foundation, Paulo Foundation, Diabetes Research Foundation, Yrjö Jahnsson Foundation, Finnish Foundation for Cardiovascular Research, Research Committee of the Kuopio University Hospital Catchment Area (State Research Funding), Kuopio University Hospital (previous state research funding (EVO), funding number 5031343), and the city of Kuopio. The Novo Nordisk Foundation Center for Basic Metabolic Research is an independent research center at the University of Copenhagen partially funded by an unrestricted donation from the Novo Nordisk Foundation (http://metabol.ku.dk). The work of Soren Brage was funded by the UK Medical Research Council [MC_UU_12015/3]. Tuomas O. Kilpeläinen was supported by the Danish Council for Independent Research (DFF – 1333-00124 and Sapere Aude program grant DFF – 1331-00730B).

Data availability

Relevant data for the present study are within the paper and its Supporting Information files. If you wish to see additional data, the authors confirm that, for approved reasons, some access restrictions apply to the data underlying the findings. Data is available from the Novo Nordisk Foundation Center for Basic Metabolic Research, section of Metabolic Genetics whose authors may be contacted at torben.hansen@sund.ku.dk.


Figure 1. Forest plots showing the associations of BMI z-score (left column), childhood BMI-increasing GRS (middle column) and genetically predicted BMI z-score (right column) with A. sedentary time, B. total physical activity, and C. moderate-to-vigorous physical activity (MVPA). For the GRS associations, the results are aligned according to the BMI-increasing allele of the GRS. All analyses are adjusted for age, gender, monitor wear-time and first three principal components. The effects were pooled using fixed effects models. The estimated per-BMI z-score, per-allele and per-genetically predicted BMI z-score effect sizes are reported in SD units based on inverse normally transformed outcome trait. Heterogeneity statistics include the $I^2$ value that describes the percentage of variation across the meta-analysis that is due to heterogeneity, and $p_{	ext{het}}$, the p-value for the $\chi^2$ test of heterogeneity.
Figure 2. Mendelian randomization analysis to test the causal effect of childhood BMI on sedentary time. Beta values are expressed in units of standard deviation (SD) of the inverse-normally transformed traits. GRS = Genetic risk score, BMI z-score = age- and sex-specific BMI standard deviation score, \( N_{\text{TOTAL}} \) = number of individuals included in meta-analysis.
Supplementary Material

Methods

Ethics statement

Prior to participation, written informed consent was obtained from all parents of the children included in SKOT I and SKOT II; and from all children and parents participating in the PANIC study. The Committees on Biomedical Research Ethics for the Capital Region of Denmark approved the study protocol of SKOT I (H-KF-2007-0003) and SKOT II (H-3-2010-122). The Research Ethics Committee of the Hospital District of Northern Savo, Finland approved the study protocol of the PANIC study. The PANIC study is registered under ClinicalTrials.gov with registration number NCT01803776. All studies were conducted in accordance with the principles of the Declaration of Helsinki.

Study population

SKOT I and SKOT II

As opposed to SKOT I, SKOT II children were all born from overweight mothers (with a pre-pregnancy BMI above 30kg/m^2). Recruitment and inclusion criteria have been described in detail previously (1, 2). In short, the 329 children included in SKOT I were healthy singletons randomly recruited from the National Civil Registry and living in Copenhagen or Frederiksberg municipality, Denmark, in 2006-2007 (3). The included children were born at term and had Danish-speaking parents. The 184 children included in SKOT II met all above criteria with the exception that they were recruited in 2010-2012 and were offspring of women who had participated in the Treatment of Obese Pregnant Women intervention study at Hvidore Hospital, Hvidovre (Denmark) (4).

Physical activity

SKOT I and SKOT II

The children were asked to wear the ActiGraph GT3X in an elastic belt tightly at the right hip for seven days and seven nights, besides when performing water-based activities (i.e. taking a bath or swimming). Only the data from children who wore the ActiGraph for at least eight hours per day for four days were included in the analyses. The processing of data was conducted using Actilife software, Version 6.7.3 (ActiGraph LLC,
Pensacola, FL, USA). Activity was recorded with a sample rate (epoch length) of 2 seconds and was reintegrated into 60-second epochs. Non-wear time during the day was defined as periods of 20 minutes or more of consecutive zeroes and was excluded prior to data analysis. Usual night time sleep from parent report questionnaire was used to exclude night time as non-wear time prior to data analysis. Eight children in SKOT I and five children in SKOT II did not have parent report questionnaire information available. For these children, usual night time sleep was defined individually for each child as the average sleep time based on manual inspection of the activity graphs produced by the sleep analysis module integrated into the Actilife software. We applied cut-offs based on Vector Magnitude settings: <819 counts per minute (cpm) to define sedentary time and ≥3908 cpm to define MVPA, based on a validation study in preschool-aged children (5). For the present study, total physical activity, expressed in counts per minute (cpm) averaged over the period of valid wear time recording, and time spent in sedentary and MVPA intensities, expressed as minutes per day (min/day).

**PANIC**

The children were instructed to wear the Actiheart device continuously for a minimum of four consecutive days and nights. The monitor was attached to the chest with two standard electrocardiogram electrodes (Bio Protech Inc, Seoul, South Korea) and data were recorded in 60-second epochs. The cleaning and calibration of these data in the PANIC study has been described in detail previously (6). For the present analyses, physical activity and time spent in sedentary and MVPA intensity records were included if they contained at least 48 hours (32 hours during week-days, 16 hours during weekend days) of wear data in total and at least 12 hours of morning, noon, afternoon, and evening wear data (7). Sedentary time was defined as time spent at intensity of at least 1.5 metabolic equivalents, excluding sleep time. MVPA was defined as time spent at intensity of at least 3 metabolic equivalents. We used the acceleration data from Actiheart to define total physical activity as movement intensity.

**Genotyping – quality control**

**SKOT I and SKOT II**

Genotypes were called using the Genotyping module, Version 1.9.4 of GenomeStudio software, Version 2011.1 (Illumina). We excluded closely related individuals and samples with extreme inbreeding coefficients, mislabelled gender or call rate < 95%, duplicates and individuals identified as ethnic outliers, leaving 275 individuals of SKOT I and 116 individuals of SKOT II individuals who passed all quality control criteria. We applied a >95% genotype call rate filter for the inclusion of SNPs. Additional genotypes were
imputed into 1000 Genomes Phase 1 (8) using Impute 2 (9). The imputation quality was high (proper_info > 0.95) for all imputed variants included in the current study. All variants obeyed Hardy Weinberg equilibrium (p > 0.05).

**PANIC**

Genotypes were called using Illumina BeadStudio, Version 3.3.7 (Cardio-Metabochip) and GenomeStudio (HumanCoreExome Beadchip) softwares using GenCall and zCall algorithms. The final quality control was done using the PLINK software, Version 1.07. Samples successfully genotyped with both Cardio-Metabochip and HumanCoreExome Beadchip were merged prior to quality control. We excluded closely related individuals, ethnic outliers, samples with mislabelled gender and call rate < 95%. A 95% genotype call rate criterion for inclusion of SNPs was applied and SNPs with Hardy Weinberg equilibrium p<1x10^-6 or MAF <1% were excluded. Additional genotypes were imputed into 1000 Genomes reference panel (Phase 1 integrated variant set release v3) using SHAPEIT v2 for haplotyping and Impute 2 for imputing genotype dosages.

**Genetic Risk score construction**

In SKOT I and SKOT II, eight of the 15 SNPs for childhood BMI identified by a GWAS were directly genotyped (rs7550711, rs543874, rs13130484, rs987237, rs7132908, rs12429545, rs1421085, rs11676272). The remaining genotypes (rs3829849, rs4854349, rs6567160, rs8092503, rs12041852, rs13253111, rs13387838) were retrieved from imputed data and the estimated risk-allele dosage was used in place of the unavailable risk-allele count when calculating the GRS (*Supplementary Table 1*).

In PANIC, 14 of the 15 BMI variants were directly genotyped. The remaining rs13253111 SNP was retrieved from the imputed data. For six children, rs13253111 imputations were not available and could be assumed to be missing at random. We imputed these to the mean allelic dosage of rs13253111 in the PANIC cohort (*Supplementary Table 1*).
References


## Supplementary Tables

### Supplementary Table 1.

Overview about the 15 BMI increasing genetic variants that were included in the GRS.

<table>
<thead>
<tr>
<th>SNP reported in meta-analysis*</th>
<th>Chromosome</th>
<th>Position</th>
<th>Nearest Gene</th>
<th>EA/Non-EA*</th>
<th>EAF*</th>
<th>Effect size on BMI*</th>
<th>Directly genotyped = CHIP/ imputed = IMP</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs13387838</td>
<td>2</td>
<td>206989692</td>
<td>ADAM23</td>
<td>A/G</td>
<td>0.04</td>
<td>0.139</td>
<td>IMP/IMP</td>
</tr>
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<td>rs7550711</td>
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<td>109884409</td>
<td>GPR61</td>
<td>T/C</td>
<td>0.04</td>
<td>0.105</td>
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</tr>
<tr>
<td>rs4854349</td>
<td>2</td>
<td>637861</td>
<td>TMEM18</td>
<td>C/T</td>
<td>0.83</td>
<td>0.090</td>
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<td>rs543874</td>
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<td>176156103</td>
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<td>0.20</td>
<td>0.077</td>
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</tr>
<tr>
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<td>A/G</td>
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<td>0.076</td>
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<td>rs11676272</td>
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<td>G/A</td>
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<td>0.068</td>
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<td>A/G</td>
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<td>0.066</td>
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<td>52358455</td>
<td>FTO</td>
<td>C/T</td>
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<td>0.059</td>
<td>CHIP/CHIP</td>
</tr>
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<td>rs6567160</td>
<td>18</td>
<td>55980115</td>
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<td>rs12041852</td>
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<td>0.041</td>
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</table>

An overview of the SNPs presented in the report by Felix et al. and the SNPs investigated in the SKOT I, SKOT II and PANIC cohorts, sorted by effect size on BMI. *EA (BMI increasing allele)/Non-EA, EAFs (effect allele frequencies) and effect sizes are from the SNPs reported by Felix et al. (joint analyses). EA=Effect allele, EAF=Effected allele frequency.
## Supplementary Table 2.

### Cross-sectional study characteristics of children in the SKOT I, SKOT II and PANIC cohorts.

<table>
<thead>
<tr>
<th>Trait</th>
<th>SKOT I</th>
<th>SKOT II</th>
<th>PANIC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>all boys</td>
<td>girls</td>
<td>all boys</td>
</tr>
<tr>
<td><strong>n</strong></td>
<td>208</td>
<td>104</td>
<td>104</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>3.0 (0.1)</td>
<td>3.0 (0.1)</td>
<td>3.0 (0.1)</td>
</tr>
<tr>
<td><strong>Height (m)</strong></td>
<td>95.8 (3.4)</td>
<td>96.7 (3.4)</td>
<td>94.9 (3.2)</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>14.6 (1.5)</td>
<td>14.9 (1.5)</td>
<td>14.3 (1.5)</td>
</tr>
<tr>
<td><strong>BMI (kg/m(^2))</strong></td>
<td>15.9 (1.2)</td>
<td>15.9 (1.1)</td>
<td>15.8 (1.2)</td>
</tr>
<tr>
<td><strong>BMI z-score</strong></td>
<td>0.3 (0.9)</td>
<td>0.3 (0.8)</td>
<td>0.3 (0.9)</td>
</tr>
<tr>
<td><strong>Total physical activity (cpm)</strong></td>
<td>1321 (230)</td>
<td>1381 (213)</td>
<td>1261 (233)</td>
</tr>
<tr>
<td><strong>Sedentary time (min/day)</strong></td>
<td>300 (53)</td>
<td>301 (47)</td>
<td>315 (58)</td>
</tr>
<tr>
<td><strong>MVPA time (min/day)</strong></td>
<td>36 (17)</td>
<td>41 (18)</td>
<td>30 (15)</td>
</tr>
<tr>
<td><strong>GRS (Number of BMI increasing risk alleles)</strong></td>
<td>8.6 (2.1)</td>
<td>8.7 (2.0)</td>
<td>8.5 (2.1)</td>
</tr>
</tbody>
</table>

GRS = genetic risk score, MVPA = moderate-to-vigorous physical activity, cm=centimetre, kg=kilogram, BMI=body mass index, BMI z-score = age- and gender-specific BMI standard deviation score, cpm=counts per minute, min/day=minutes per day. * for PANIC, we used the uniaxial acceleration data from Actiheart and applied a previously derived conversion factor of 5 (Actigraph counts=Actiheart counts x 5) to express total physical activity in cpm (10).