Association between birth weight and objectively measured sedentary time is mediated by central adiposity: data in 10,793 youth from the International Children’s Accelerometry Database

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Association between birth weight and objectively measured sedentary time is mediated by central adiposity: data in 10,793 youth from the International Children’s Accelerometry Database1–3

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ABSTRACT

Background: Birth weight is an early correlate of disease later in life, and animal studies suggest that low birth weight is associated with reduced activity and increased sedentary time. Whether birth weight predicts later sedentary time in humans is uncertain.

Objectives: We examined the relation between birth weight and sedentary time in youth and examined whether this association was mediated by central adiposity.

Design: We used pooled cross-sectional data from 8 observational studies conducted between 1997 and 2007 that consisted of 10,793 youth (boys: 47%) aged 6–18 y from the International Children’s Accelerometry Database. Birth weight was measured in hospitals or maternally reported, sedentary time was assessed by using accelerometry (<100 counts/min), and abdominal adiposity (waist circumference) was measured according to WHO procedures. A mediation analysis with bootstrapping was used to analyze data.

Results: The mean (±SD) time spent sedentary was 370 ± 91 min/d. Birth weight was positively associated with sedentary time (B = 4.04, P = 0.006) and waist circumference (B = 1.59, P < 0.001), whereas waist circumference was positively associated with sedentary time (B = 0.82, P < 0.001). Results of the mediation analysis showed a significant indirect effect of birth weight on sedentary time through waist circumference (B: 1.30; 95% bias-corrected CI: 0.94, 1.72), and when waist circumference was controlled for, the effect of birth weight on sedentary time was attenuated by 32% (B = 2.74, P = 0.06).

Conclusion: The association between birth weight and sedentary time appears partially mediated by central adiposity, suggesting that both birth weight and abdominal adiposity may be correlates of sedentary time in youth. Am J Clin Nutr 2015;101:983–90.

Keywords: abdominal adiposity, birth weight, sedentary time, youth, mediation, accelerometry

INTRODUCTION

The Developmental Origins of Health and Disease hypothesis suggests that nonoptimal growth and environmental conditions during fetal life may result in permanent changes in the body’s structure, function, and metabolism (1). These irreversible adaptations can increase risk of diseases later in life, and birth weight, which is used as an indicator of intrauterine growth and the prenatal environment (2), is inversely associated with increased risk of all-cause mortality (3), cardiovascular disease (4), and type 2 diabetes later in life (5). In addition, a low birth weight is associated with reduced muscle mass and strength (6, 7) as well as lower aerobic fitness later in life (7–9). A lower probability of undertaking leisure-time physical activity later in life in individuals born with low or high birth weight was also suggested (10).

Animal studies showed that the offspring of undernourished mothers are less active and more sedentary than offspring born within normal birth weights (11, 12). In humans, the current knowledge on whether birth weight is associated with behaviors such as sedentary time is limited. One study that used an objective

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2 The pooling of data was funded through grant G0701877 from the United Kingdom National Prevention Research Initiative (http://www.mrc.ac.uk/Ourresearch/Resourcervices/ NPRF/index.htm). Funding partners relevant to this award are as follows: the British Heart Foundation, Cancer Research UK, the Department of Health, Diabetes UK, the Economic and Social Research Council, the Medical Research Council, the Research and Development Office for the Northern Ireland Health and Social Services, the Chief Scientist Office, the Scottish Executive Health Department, The Stroke Association, and the Welsh Assembly Government and World Cancer Research Fund. This work was further supported by the Medical Research Council [MC_UU_12015/4; MC_UU_12015/7], Bristol University, Loughborough University, and the Norwegian School of Sport Sciences. This is an open access article distributed under the CC-BY license (http://creativecommons.org/licenses/by/3.0/).

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measure of sedentary time showed no associations with birth weight; however, analyses were limited to subjects born in the low-to-normal weight spectrum of birth weights (13). In addition, knowledge about the mechanisms that may underpin a potential association between birth weight and sedentary time is scant; in the current study, we hypothesized that central adiposity is one such mechanism.

A higher birth weight is associated with increased risk of obesity (14), greater overall fat mass (15), and higher BMI (16), whereas a lower birth weight is related to a higher percentage of body fat (17) and central adipose tissue in youth (16, 18, 19). Therefore, it was suggested that both overnutrition and undernutrition during fetal life can trigger pathways responsible for obesity later in life (19). In addition, obesity appears to be associated with and shares the same pathophysiologic mechanisms as low cardiorespiratory fitness and muscle mass (20), and although studies that used both objective (21–24) and subjective (25) measures suggested that higher amounts of sedentary time may not predict central adiposity, the reverse was reported in young people (21, 23, 24). Therefore, it is plausible that central adiposity may mediate a potential association between birth weight and sedentary time in youth.

Because of the high amount of time spent sedentary in youth (26, 27) and the potential independent harmful effects of excessive sedentary behavior on numerous health outcomes later in life (25, 28, 29), an understanding of potential correlates and determinants of this behavior is important to provide evidence for public health interventions aimed at reducing sedentary time. Thus, the aims of this study were to examine the relation between birth weight and objectively measured sedentary time and whether this association is mediated by central adiposity.

METHODS

Study design and participants

The International Children’s Accelerometry Database (ICAD)4 (http://www.mrc-epid.cam.ac.uk/Research/Studies/) was established to pool data on objectively measured physical activity and sedentary time from observational studies in youth worldwide. Aims, design, inclusion criteria, and methods of the ICAD project have been described in detail previously (30). Briefly, the ICAD consists of re-analyzed and pooled accelerometer data combined with phenotypic information in ~32,000 young people aged 3–18 y. Ethical approval was granted for each individual study, and all participants have provided informed parental consent. Formal data-sharing agreements were established, and all partners consulted with their individual research boards to confirm sufficient ethical approval had been attained for contributing data. For this study, data from 8 studies conducted between 1997 and 2007, in which measured or maternally reported birth weight, measured waist circumference, and sedentary time were available (n = 10,793) were included (31–40). This subsample (aged 6–18 y) differed slightly from the whole ICAD sample in terms of time spent sedentary (+16 min/d; 4.3%; P < 0.001) and waist circumference (+1 cm; 1.5%; P < 0.001).

Measurements

A detailed description of the assessment of sedentary time and physical activity is available elsewhere (30). Accelerometer data in the ICAD were re-analyzed centrally in a standardized manner with specialist software (KineSoft Software, version 3.3.20; Kinesoft.org) (30) and processed in 60-s epochs to provide comparable physical activity outcomes across studies.

The Pelotas study used a 24-h wear protocol (34, 35), whereas the other studies asked participants to wear the accelerometer during waking hours only. To avoid accelerometer data being influenced by the increased wear time, accelerometer data were excluded for the overnight period between 2400 and 0700 in the Pelotas study. Children with ≥3 d with 600 min of measured monitor wear time between 0700 and midnight were included. Nonwear time was defined as 60 min of consecutive zeroes, with the allowance for 2 min of nonzero interruptions, terminated at the third nonzero interruption (41, 42). Overall physical activity was calculated as total counts over the wear period and expressed in counts per minute. The time spent sedentary was defined as all minutes with <100 counts/min (43), whereas the time spent in moderate-to-vigorous physical activity (MVPA) was defined as minutes with >3000 counts/min (44). Both sedentary time and time spent in MVPA are expressed in minutes per day.

Height and weight were measured by using a standardized procedure across studies. BMI (weight divided by height squared) was calculated for each participant, and age- and sex specific BMI cutoffs were used to categorize participants as normal weight, overweight, or obese (45). Waist circumference was used as a surrogate measure for abdominal adiposity and measured according to WHO procedures by using a metal anthropometric tape midway between the lower rib margin an iliac crest at the end of a gentle expiration (46). Birth weight was directly measured (Pelotas study) or maternally reported, which has been shown to be highly correlated with measured birth weight (47).

Statistical analyses

Means (±SDs) are shown for descriptive variables. An independent t test was used to compare descriptive data between sexes.

We used resampling strategies and the macro presented by Preacher and Hayes (48) to assess whether waist circumference (cm) acts as a potential mediator of the association between birth weight (kg) and sedentary time (min/d). Bootstrapping is a nonparametric resampling procedure that does not require the assumption of normality of the sampling distribution and is a recommended method of obtaining confidence limits for indirect effects. The method involves repeated sampling from the data set, and the indirect effect is estimated in each resampled data set (48). In the unstandardized regression equation (ordinary least-squares regression), birth weight was modeled as the predictor, sedentary time was modeled as the outcome, waist circumference was modeled as the mediator, and sex, age, study, and monitor wear time were modeled as covariates. Analyses were used to determine the total (c path) and direct effect (c’ path) of birth weight on sedentary time and estimate the mediating role.

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4 Abbreviations used: bCI, bias-corrected CI; ICAD, International Children’s Accelerometry Database; MVPA, moderate-to-vigorous physical activity.
RESULTS

Descriptive statistics by study and sex are summarized in Tables 1 and 2, respectively. Overall, 79.3% of children were categorized as normal weight, 15.9% of children were categorized as overweight, and 4.8% of children were categorized as obese. The mean birth weight differed by 0.33 kg between studies, and the lowest mean (±SD) birth weight (3.22 ± 0.54 kg) was observed from the cohort who represented a low- and middle-income country (Brazil). Children’s sedentary time and physical activity were monitored for an average of 5.3 ± 1.3 d. Overall, the average time spent sedentary was 370 ± 91 min/d, whereas, on average, 56 ± 30 min/d were spent in MVPA. Boys spent, on average, significantly more time in MVPA than did girls (66 compared with 46 min/d, respectively; P < 0.001) and less time sedentary than did girls (360 compared with 380 min/d, respectively; P < 0.001).

Figure 1 shows the separate regression analyses conducted to assess each component of the proposed mediation model among variables. Birth weight was associated with sedentary time, and a 1-kg increase in birth weight was associated with 4 more minutes spent sedentary per day (c path; B = 4.04, P = 0.006). When this association was modeled graphically, the association seemed to be mainly driven by individuals in the extreme categories of birth weight (<2.75 kg and >4.75 kg) (Figure 2). In addition, birth weight was positively associated with waist circumference (a path; B = 1.59, P < 0.001), and waist circumference was positively associated with sedentary time (b path; B = 0.82, P < 0.001). Results of the mediation analysis confirmed the mediating role of waist circumference in the association between birth weight and sedentary time (a × b path; B: 1.30; 95% bCI: 0.94, 1.72). Furthermore, our results showed that the direct effect of birth weight on sedentary time was attenuated by 32% (c’ path; B = 2.74, P = 0.06) when controlling for waist circumference, which suggested partial mediation.

In sensitivity analyses, with the exclusion of individuals with birth weight <2.5 kg, results were mainly unchanged. Birth weight was associated with sedentary time (c path; B = 4.66, P = 0.01) and waist circumference (a path; B = 2.15, P < 0.001), and waist circumference was positively associated with sedentary time (b path; B = 0.81, P < 0.001). In addition, results of the mediation analysis confirmed the mediating role of waist circumference in the association between birth weight and

<table>
<thead>
<tr>
<th>Study, country (reference)</th>
<th>n (%) boys</th>
<th>Age, y</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>BMI, kg/m²</th>
<th>Birth weight, kg</th>
<th>Total physical activity, counts/min</th>
<th>Sedentary time, min/d</th>
<th>MVPA, min/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALSpac, United Kingdom (32)</td>
<td>2003–2004</td>
<td>5808 (48)</td>
<td>11–15</td>
<td>151.8 ± 8.1</td>
<td>44.4 ± 10.5</td>
<td>19.1 ± 3.4</td>
<td>3.41 ± 0.55</td>
<td>588 ± 191</td>
<td>371 ± 75</td>
</tr>
<tr>
<td>EYHS, Denmark (31, 33)</td>
<td>1997–1998</td>
<td>1162 (45)</td>
<td>8–18</td>
<td>148.5 ± 15.3</td>
<td>41.8 ± 14.3</td>
<td>18.4 ± 3.1</td>
<td>3.40 ± 0.59</td>
<td>562 ± 253</td>
<td>384 ± 125</td>
</tr>
<tr>
<td>EYHS, Estonia (31)</td>
<td>1998–1999</td>
<td>557 (44)</td>
<td>8–17</td>
<td>151.8 ± 17.1</td>
<td>44.0 ± 15.6</td>
<td>18.4 ± 3.1</td>
<td>3.55 ± 0.59</td>
<td>631 ± 251</td>
<td>352 ± 111</td>
</tr>
<tr>
<td>EYHS, Norway (31, 40)</td>
<td>1999–2000</td>
<td>350 (51)</td>
<td>9–10</td>
<td>139.3 ± 6.3</td>
<td>33.3 ± 5.9</td>
<td>17.1 ± 2.3</td>
<td>3.46 ± 0.59</td>
<td>709 ± 305</td>
<td>339 ± 108</td>
</tr>
<tr>
<td>EYHS, Portugal (31, 36)</td>
<td>1999–2000</td>
<td>507 (41)</td>
<td>9–18</td>
<td>147.1 ± 14.6</td>
<td>43.3 ± 14.4</td>
<td>19.5 ± 3.7</td>
<td>3.39 ± 0.52</td>
<td>553 ± 233</td>
<td>390 ± 109</td>
</tr>
<tr>
<td>KISS, Switzerland (39)</td>
<td>2005–2006</td>
<td>307 (46)</td>
<td>6–13</td>
<td>136.4 ± 13.0</td>
<td>33.0 ± 10.1</td>
<td>17.3 ± 2.8</td>
<td>3.36 ± 0.57</td>
<td>576 ± 212</td>
<td>307 ± 112</td>
</tr>
<tr>
<td>Pelotas, Brazil (34, 35)</td>
<td>2006–2007</td>
<td>426 (53)</td>
<td>13–14</td>
<td>157.9 ± 8.4</td>
<td>50.9 ± 12.1</td>
<td>20.3 ± 8.3</td>
<td>3.22 ± 0.54</td>
<td>320 ± 118</td>
<td>389 ± 132</td>
</tr>
<tr>
<td>SPEEDY, United Kingdom (37, 38)</td>
<td>2007</td>
<td>1636 (44)</td>
<td>10–11</td>
<td>141.1 ± 6.7</td>
<td>36.5 ± 8.3</td>
<td>18.2 ± 3.1</td>
<td>3.35 ± 0.58</td>
<td>594 ± 190</td>
<td>371 ± 69</td>
</tr>
</tbody>
</table>

1 ALSpac, Avon Longitudinal Study of Parents and Children; EYHS, European Youth Heart Study; KISS, Kinder Sportstudie; MVPA, moderate-to-vigorous physical activity; SPEEDY, Sport, Physical Activity and Eating Behavior: Environmental Determinants in Young People.
2 All values are ranges.
3 BMI is calculated as weight divided by height squared.
4 The cutoff for sedentary time was <100 counts/min.
5 The cutoff for MVPA was >3000 counts/min.
6 Mean ± SD (all such values).
TABLE 2
Baseline descriptive statistics of the sample stratified by sex (n = 10,793)

|                  | Boys (n = 5092) | Girls (n = 5701) | P
|------------------|-----------------|-----------------|-----
| Age, y           | 11.5 ± 1.6      | 11.5 ± 1.7      | 0.63
| Weight, kg       | 42.0 ± 12.1     | 42.8 ± 11.6     | 0.001
| Height, cm       | 149.1 ± 11.9    | 148.8 ± 10.7    | 0.13
| Waist circumference, cm | 66.7 ± 9.2   | 65.7 ± 9.2      | <0.0001
| BMI3,4           | 18.6 ± 3.2      | 19.0 ± 3.4      | <0.0001
| Normal weight, n (%) | 4109 (80.8) | 4432 (77.9)     | —
| Overweight, n (%) | 767 (15.1)      | 946 (16.6)      | —
| Obese, n (%)     | 207 (4.1)       | 312 (5.5)       | —
| Birth weight, g   | 3459 ± 584      | 3345 ± 535      | <0.0001
| Total physical activity, counts/min | 637 ± 231 | 528 ± 186      | <0.0001
| Sedentary time5, min/d | 360 ± 91   | 380 ± 90       | <0.0001
| MVPA6, min/d     | 66 ± 33         | 46 ± 23        | <0.0001
| Wear time, d     | 5.4 ± 1.4       | 5.3 ± 1.3      | 0.96

1P values denote differences between sex and were determined by using a t test for normally distributed continuous variables.
2Mean ± SD (all such values).
3n = 5083 and 5690 for boys and girls, respectively.
4Age- and sex-specific BMI cutoffs proposed by Cole et al. (45) were used.
5The cutoff for sedentary time was <100 counts/min.
6MVPA, moderate-to-vigorous physical activity. The cutoff for MVPA was >3000 counts/min.

sedentary time (a × b path; B: 1.74; 95% bCI: 1.26, 2.30) and supported partial mediation (c’ path; B = 2.92, P = 0.11).

DISCUSSION

This study examined whether birth weight acts as a correlate of sedentary time in youth and whether this association is mediated by waist circumference. The results suggested that the association between birth weight and sedentary time was partially mediated by waist circumference in young people aged 6–18 y.

We proposed that central adiposity could be an underlying mechanism of the association between birth weight and sedentary time for several reasons. Birth weight appears to be associated with several measures of adiposity (15, 17, 19), muscle mass (6), and aerobic fitness later in life (9), which are factors that are potentially related to sedentary time. In addition, obesity has been related to aerobic fitness, muscle mass (20), and objectively measured sedentary time in youth (21). Our participants covered a wide range of the birth-weight spectrum (645–5750 g), and even though we showed significant differences in weight and birth weight between sexes, differences were small (<0.8 kg or 115 g) and may not have been clinically important. The results showed that the association was partially mediated by waist circumference, and the effect of birth weight on sedentary time was reduced by 32% when controlling for the suggested mediator. In addition, controlling for waist circumference made the association between birth weight and sedentary time non-significant. This result could have been due to multicollinearity between birth weight and waist circumference, and with a larger sample size, this result could have reached significance. However, when the significance was disregarded, the magnitude of the association was small, and a 1-kg increase in birth weight was associated with only 2.7 more minutes spent sedentary per day. This observation was opposite to some previous observations in animal models (11, 12) but consistent with the results of a previous study in subjects born with low to normal birth weights; these results were also unable to show an association between birth weight and sedentary time (13). Although sedentary behavior is different from not performing enough physical activity (49), studies that used objectively measured physical activity were also unable to show an association between birth weight and later levels of physical activity in youth (13, 50–53), and it has been suggested that, across the normal birth weight spectrum, physical activity and sedentary time in youth are more influenced by environmental and behavioral factors than birth weight (50). In contrast, the magnitude of the association between birth weight and sedentary time (and physical activity) could have been underestimated because of the inherent variability of youth’s sedentary time and physical activity. A few days of measurement may not have been representative of the true durations of sedentary time in our participants (54, 55). It is also unknown whether the magnitude of the association between birth weight and sedentary time changes by age and may become apparent in adulthood.

A limitation regarding the mediating role of abdominal adiposity in the current study was that waist circumference was measured at the same point in time as sedentary time. Thus, the temporal sequence between waist circumference and sedentary

![FIGURE 1](image_url) Unstandardized regression coefficients (±SEs) in regression analyses included in the mediator model between birth weight, waist circumference, and sedentary time (n = 10,793). Analyses were performed by using ordinary least-squares regression and adjusted for sex, age, study, and monitor wear time. The paths represent the difference in waist circumference (cm) per 1-kg increase in birth weight (path a), difference in sedentary time (min/d) per 1-cm increase in waist circumference (path b), and differences in sedentary time (min/d) per 1-kg increase in birth weight with (path c’) and without (path c) adjustment for waist circumference.
time was not possible to establish. However, it was previously shown that higher waist circumference predicted higher amounts of sedentary time in youth (21, 23), whereas sedentary time did not predict adiposity (21–23, 56–58). In addition, a re-analysis of the data modeling sedentary time as the mediator and waist circumference as the outcome showed that, although significant, sedentary time attenuated the effect of birth weight on waist circumference by only 2% (compared with 32% when waist circumference was the mediator; data not shown), which supported the use of waist circumference as a mediator in our analyses. Nevertheless, our results did not dismiss the possibility of a reverse causation (i.e., a bidirectional association between sedentary time and abdominal adiposity).

Previous studies showed that lower birth weight is associated with central adipose tissue in childhood (16, 18, 19). In the current study, higher birth weight was associated with higher waist circumference; however, this association was attenuated by current BMI (results not shown). The interpretation of associations between birth weight and obesity later in life, which were substantially attenuated after adjustment for current body size (e.g., BMI), suggested that postnatal growth and the change in size (e.g., weight percentile crossing) between time points may be more-important factors on the causal pathway leading to abdominal adiposity than birth weight per se (59). As a result, public health strategies intended to influence the biology of fetal growth are most likely not the most essential approaches, maybe with the exception for obese pregnant women and those who have gestational diabetes, because both obesity during pregnancy and gestational diabetes are associated with large-for-gestational-age infants (60, 61). Rather, strategies that aim to affect other factors such as postnatal weight gain are likely to be more successful to moderate risk of obesity and metabolic diseases later in life because rapid infant weight is associated with childhood obesity (62).

There were several strengths of this study, including objectively measured sedentary time, a wide range of birth weights, and a large and diverse sample representing different geographical and cultural locations. Even though accelerometer data were re-analyzed in a standardized manner, and all analyses were adjusted for wear time, it was possible that differences in accelerometer wear protocol influenced the results. One of the included studies used a 24-h monitor wear protocol (34, 35), and even if this difference was accounted for by excluding time between 2400 and 0700, this protocol may have influenced the amount of time defined as sedentary time in this specific study. However, when the data were re-analyzed after the exclusion of this study, findings were largely unchanged (data not shown).

There were some limitations that warrant consideration in interpreting the results of the current study. The accelerometer is regarded as a valid tool for measuring physical activity and sedentary time (43, 63); however, a hip-placed monitor can be less effective in distinguishing sedentary postures, such as lying and sitting, from other light-intensity activities performed while standing and do not accurately capture upper-body movement, cycling (64), or other activities when the monitor is removed (e.g., water-based activities). Finally, nonwear time was subtracted from wear time and, consequently, prolonged quiet sitting could potentially have been considered nonwear time, thereby leading to an underestimation of sedentary time. The amount of time spent sedentary may have differed between weekdays and weekend days. However, >85% of participants in our data set had ≥1 d of valid accelerometer data during a weekend day, and therefore, we believe it was unlikely that this difference affected our analyses of associations between birth weight and sedentary

FIGURE 2  Mean (95% CI) differences expressed in sedentary min/d stratified by birth-weight categories compared with the reference group (birth weight: 3.26–3.75 kg; n = 10,793; P-trend = 0.003) adjusted for sex, age, study, and monitor wear time (ordinary least-squares regression). REF, reference.
time. With the exception of one study, birth weight was reported retrospectively. However, it has been suggested that maternally recalled birth weight is highly correlated with measured birth weight and is sufficiently accurate to use in epidemiologic studies (47). Waist circumference was used as the outcome for abdominal adiposity. Despite abdominal adiposity being recognized as an important determinant for disease and mortality (65), a more-detailed measure of body composition may be preferred. Finally, we could not exclude that other unmeasured confounding variables including genotype, infant rapid weight gain, socioeconomic status, and mothers’ BMI might explain our findings. Future prospective studies with several measures of the mentioned confounder variables are needed to examine the potential mediating or modifying effects on the relation between birth weight and later sedentary time at different ages.

In conclusion, the prevalence of sedentary time in youth is of public health concern, and therefore, it is important to understand potential biological and behavioral correlates of this behavior. The results suggest that birth weight is positively associated with sedentary time; however, the association appears partially mediated by central adiposity. Therefore, the targeting of both birth weight and obesity may be an important public health strategy to prevent excessive sedentary time in youth.

ICAD Collaborators include the ICAD Steering Committee [Ashley Cooper and Angie Page (Bristol University, Bristol, United Kingdom), Ulf Ekelund (Norwegian School of Sport Sciences, Oslo, Norway), Dale Elsiger and Lauren B Sherar (Loughborough University, Loughborough, United Kingdom), and Esther MF van Sluijs (Medical Research Council Epidemiology Unit, University of Cambridge, Cambridge, United Kingdom)] and the following ICAD data contributors—the Avon Longitudinal Study of Parents and Children: K Kordas; the BALLABEINA Study: J Puder; the Belgium Unit, University of Cambridge, Cambridge, United Kingdom)] and the following ICAD data contributors—the Avon Longitudinal Study of Parents and Children: K Kordas; the BALLABEINA Study: J Puder; the Belgium Unit, University of Cambridge, Cambridge, United Kingdom)] and the following ICAD data contributors—the Avon Longitudinal Study of Parents and Children: K Kordas; the BALLABEINA Study: J Puder; the Belgium Unit, University of Cambridge, Cambridge, United Kingdom)] and the following ICAD data contributors—the Avon Longitudinal Study of Parents and Children: K Kordas; the BALLABEINA Study: J Puder; the Belgium Unit, University of Cambridge, Cambridge, United Kingdom)] and the following ICAD data contributors—the Avon Longitudinal Study of Parents and Children: K Kordas; the BALLABEINA Study: J Puder; the Belgium Unit, University of Cambridge, Cambridge, United Kingdom]

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