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1 Socioeconomic inequalities in weight, height and body mass index from birth to 5 years

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18 Short running title: Socioeconomic inequalities in early growth

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Abbreviations: Body Mass Index (BMI); Ponderal Index (PI); Overweight (OW)

40 Abstract

Background/Objectives: Studies in high income countries show that despite the positive association of weight with socioeconomic position at birth, an inverse socioeconomic gradient in overweight (OW) appears later in childhood. The objectives were to understand the natural history of socioeconomic inequalities in weight, height and body mass index (BMI), by investigating their associations with maternal educational level between birth and five years, separately in boys and girls.

47 Subjects/Methods: A published work of growth modelling between birth and 5 years allowed 48 us to calculate predicted weight, height and BMI at 1 month, 6 months, 1, 3 and 5 years for 49 1735 children from the French EDEN mother-child cohort. Associations between maternal 50 education and predicted measures of body size were analysed with marginal linear and 51 logistic models, stratified by sex.

Results: In girls, despite a positive association between maternal education and birthweight, an inverse socioeconomic gradient was observed as early as 1 month for BMI. Girls whose mothers had low education levels were shorter on the whole than their counterparts with better-educated mothers, despite their similar weights. In boys, no socioeconomic gradient in BMI was observed at any age, including birth, but positive associations were found as early as 1 month for both weight and height.

58 **Conclusion:** The emergence of an inverse socioeconomic gradient in BMI and OW 59 apparently results from a complex pattern of socioeconomic inequalities in weight and height 60 from 1 month onwards. The very start of life thus appears to be an important window of 61 opportunity for addressing socioeconomic inequalities in growth.

62

64 INTRODUCTION

65 Childhood overweight (OW) and obesity are an important public health concern worldwide 66 because of their relations to a range of short- and long-term health issues.¹⁻³ Moreover, OW 67 children are more likely to remain OW in adulthood.⁴ Childhood is therefore a critical 68 window for preventing the development of excessive adiposity and its associated negative 69 health outcomes, which are likely to accumulate across the life course.

The prevalence of OW in children has sharply increased worldwide since the 1970s, although 70 evidence suggests that it has stabilized in some industrialized countries in recent years.⁵⁻⁹ An 71 inverse association between socioeconomic position and child adiposity has been identified,^{10,} 72 and its gradient is reported to widen with age¹²⁻¹⁴ as well as with time, since stronger 11 73 gradients have been observed in more recent studies.¹⁵⁻¹⁷ This inverse socioeconomic gradient 74 in the body mass index (BMI) of children seems paradoxical in view of the positive 75 association between socioeconomic position and weight observed at birth.^{18, 19} Given the 76 switch from lower weight at birth to greater adiposity during childhood in more disadvantaged 77 children, growth history from birth, including the effects of changes in weight and height or 78 length on BMI gradient, is an interesting topic. Various studies have examined the age at 79 which this inverse socioeconomic gradient in BMI or OW appears, with findings of around 4 80 years in England,¹³ before 4-5 years in Australia,¹⁴ between 2 and 7 years in Germany²⁰, 81 before 7 years in Denmark²¹ and around 6 years in Holland.^{12, 22} This gradient may operate 82 differently according to sex, in view of the steeper socioeconomic inequalities in BMI and 83 OW^{13, 23, 24} or in length^{25, 26} that have been reported in girls. However, most of the studies that 84 have explored the age of onset of the inverse socioeconomic gradient in BMI or OW are 85 limited by both ages at data collection and the methods used, which do not take the non-linear 86 shape of the BMI or z-score BMI growth trajectories into account accurately. 87

In France, separate cross-sectional studies have demonstrated an inverse relation between socioeconomic position and OW at both 5-6 years²⁷⁻²⁹ and at 2 years.³⁰ Given this background, we hypothesised that this inverse relation with socioeconomic position was likely to be apparent by 2 years of age. Our objectives were to understand the natural history of socioeconomic inequalities in weight, height and BMI, by investigating their associations with maternal education levels between birth and five years, separately in boys and girls.

94 SUBJECTS AND METHODS

95 Study design and participants

The EDEN mother-child cohort aimed to assess pre- and post-natal determinants of child 96 growth, health and development. This cohort included 2002 pregnant women recruited in two 97 maternity hospitals (in Poitiers and Nancy, France) between 2003 and 2006. Exclusion criteria 98 were multiple gestation, known diabetes, illiteracy and intention to deliver outside the 99 maternity hospitals or to move outside the region within 3 years. Details of the study protocol 100 have been published elsewhere.³¹ Written consent was obtained from both parents. The study 101 102 was approved by the ethics committee of Kremlin-Bicêtre and declared to the national commission for data protection and liberties (CNIL). 103

104 Measurements

Data were collected from obstetric and paediatric records at birth and then from self-reported
questionnaires completed by the mothers and clinical examinations undertaken at different
stages of follow-up.

108

Socioeconomic position

109 Maternal education was used as a proxy for socioeconomic position, as it is the indicator most 110 consistently and strongly associated with child adiposity in the literature¹⁰ and is less likely to 111 be affected by childbearing – unlike income and occupation. Mothers were asked to self-112 report their highest educational attainment at inclusion. Educational level was categorized as low (failed to complete high school), intermediate (high school diploma to 2-year university
degree, reference category) and high (3-year university degree or more).

115

Weight and length or height

Weight was measured by previously trained midwives at birth, 1 year, 3, and 5 years using an 116 electronic scale (Seca Ltd or Terraillon SL-351). At 1 year, mothers were weighed both alone 117 and holding the child, whose weight was obtained by subtracting the two measurements. 118 Length was measured at birth and 1 year with a somatometer (Testut, NMMedical), and 119 height at 3 and 5 years with a stadiometer (Seca Ltd). For simplicity's sake, height will be 120 used to qualify length throughout the paper. Additionally, mothers filled in self-administered 121 questionnaires at 4 months, 8 months and 1, 2, 3, 4 and 5 years. They were asked to report 122 measured growth data available in their child's health booklet: one per month until one year, 123 and two or three per year until five year. Of note, the latter were measured by primary care 124 pediatricians or general practitioners during routine health monitoring. 125

126

Preliminary statistical treatment of growth data

127 Using all available collected data (on average 16 measurements per child, measured either by midwives or primary care pediatricians/general practitioners), predicted weight and height 128 were calculated using previously modelled trajectories from the Jenss-Bayley model.^{32, 33} 129 130 These trajectories were calculated in children with at least two measurements of weight (excluding birthweight) or two measurements of height.^{32, 33} In total, we were able to predict 131 weight and height between birth and 5 years for 1764 children. Predicted weight growth did 132 not include birthweight because the model assumes a monotonic shape and infants normally 133 lose weight immediately after birth. Instead, the minimum weight recorded during the first 4 134 days was used. Given that studies are not consistent regarding the use of either BMI or 135 ponderal index (PI) to identify fat mass differences,³⁴⁻³⁶ we calculated both predicted BMI and 136 PI as predicted weight (kg) divided by predicted height (m) squared and cubed, respectively. 137

Predicted weight, height, BMI and PI were calculated at 1 month and 6 months to characterise early growth and at 1 year, 3 and 5 years to facilitate sensitivity analysis between predicted and collected data (the latter coming from either the clinical examinations or the health booklets). OW was defined at 2, 3, 4, and 5 years according to the International Obesity Task Force (IOTF) definition, which provides thresholds from 2 years onwards.³⁷

143 *Other variables*

Gestational age and maternal age were reported at birth. Preterm birth (yes/no) was defined
based on gestational age <37 weeks of gestation.

146

147 **Population studied**

Among the 1907 children included in the EDEN cohort, 143 were excluded because they had fewer than two weight or height measurements between birth and 5 years, and 29 more due to missing values for maternal education. The sample in this analysis thus includes 1735 children (838 girls and 897 boys).

152

153 Statistical analysis

154 Characteristics of the study population (namely, mother's age, child's weight, length, BMI, PI 155 and preterm birth) were described at birth according to maternal education and sex. Chi-156 square tests and ANOVA analyses were used for statistical comparisons as appropriate.

Linear and logistic marginal models were used to investigate the association between maternal education and repeated BMI, PI, weight and height data from 1 month to 5 years and OW from 2 years to 5 years, respectively. Child age was included as a categorical variable, defined based on 5 values in the linear models (i.e., 1 month, 6 months, 1 year, 3 and 5 years) and 4 values in the logistic model (i.e., 2, 3, 4 and 5 years). An interaction term involving child age and maternal education was included in each model to allow the association 163 between maternal education and BMI (or PI, OW, weight or height) to change according to 164 child age. Models were adjusted for centre (i.e., Nancy or Poitiers). Therefore, the model 165 equation for the ith subject at the jth measurement, with y the BMI (or PI, weight or height), k 166 the level of education and ε_{ij} the error measurement, can be written as follows:

(1)
$$y_{ij} = \beta_0 + \beta_1 \times \text{sex}_i + \beta_2 \times \text{centre}_i + \beta_{3j} \times \text{age}_{ij} + \beta_{4k} \times \text{education}_{ik} + (1)$$
$$\beta_{5jk} \times \text{age}_{ij} \times \text{education}_{ik} + \varepsilon_{ij}$$

167 A hypothesis underlying this model is that the pattern of association with age and education is 168 the same for both sexes. To test specifically whether the educational level was associated with 169 the different growth trajectories differently in boys and girls, we computed two nested models 170 (2 and 3), described below. The difference between these two models was assessed and tested 171 through the interaction terms $sex_i \times education_{ik}$ and $sex_i \times age_{ii} \times education_{ik}$.

$$y_{ij} = \beta_0 + \beta_1 \times sex_i + \beta_2 \times centre_i + \beta_{3j} \times age_{ij} + \beta_{4k} \times education_{ik} + \beta_$$

(2)
$$\beta_{5jk} \times age_{ij} \times education_{ik} + \beta_{6j} \times age_{ij} \times sex_i + \beta_{7k} \times sex_i \times education_{ik} + \beta_{6j} \times age_{ij} \times sex_i + \beta_{7k} \times sex_i \times sex_i + \beta_{7k} \times sex_i \times sex_i + \beta_{7k} \times$$

 $\beta_{8jk} \times sex_i \times age_{ij} \times education_{ik} + \varepsilon_{ij}$

(3)
$$y_{ij} = \beta_0 + \beta_1 \times sex_i + \beta_2 \times centre_i + \beta_{3j} \times age_{ij} + \beta_{4k} \times education_{ik} + \beta_{5jk} \times age_{ij} \times education_{ik} + \beta_{6j} \times age_{ij} \times sex_i + \epsilon_{ij}$$

We compared models (2) and (3) using the likelihood ratio test, or the quasi-likelihood under 172 the independence model criterion (QIC) for OW. Given that the tests were significant for 4 of 173 the 5 outcomes, all analyses were stratified by sex. The choice of the best matrix of 174 covariance of residuals, among the unstructured, autoregressive heterogeneous, Toeplitz and 175 compound symmetry matrices, relied on the convergence of the model and the minimization 176 of the Akaike Information Criterion (AIC) or the QIC. An unstructured matrix was chosen for 177 models of all continuous outcomes, except for models of height in girls, where a Toeplitz 178 matrix was chosen. For OW, the autoregressive heterogeneous (order 1) matrix was selected. 179

In a first sensitivity analysis, we investigated the impact of the 29 missing data items for maternal educational level on the results. Because these data were unlikely to be missing at random, we reran the analyses with two imputed databases, one with all missing data set at the low level of education, and the other with all missing data set at the high level of education. In a second sensitivity analysis, we used the observed values of BMI, PI, weight, and height (in place of the predicted ones) and further adjusted for exact age at clinical examination.

The population included in the analysis was compared to the population not included using chi-square tests and ANOVA analyses as appropriate. All analyses were conducted with SASv9.3 (SAS, Cary, NC, US). Graphics were plotted with R software. The level for significance of two-sided test was set at $P \le 0.05$.

191 **RESULTS**

192 Population characteristics

The more highly educated mothers were older than the less educated mothers (**Table 1**). Girls born to mothers with high educational levels had higher measured birth weights and birth lengths than girls whose mothers had low educational levels, while no significant difference was observed in boys. A trend towards a positive association between maternal education and BMI and PI at birth was observed in boys only (P < 0.10).

198 Maternal education and BMI and PI

In girls, an inverse socioeconomic gradient in BMI was observed from 1 month to 5 years (**Figure 1**). Consistent results were found with PI. In boys, the association between education and BMI changed along the age range in a non-monotonic fashion (*P* for age \times education interaction = 0.02), but no significant socioeconomic gradient in BMI was observed at any age (**Figure 1**). A significant negative association was however observed with PI at 1 month and at 5 years (**Supplementary Figure 1**).

205 Maternal education and OW

At 2 years, the risk of OW in girls was already inversely associated with maternal education (**Figure 2**). This inverse gradient was consistent across all ages studied, as reflected by the non-significant interaction between age and maternal education (P for age \times education interaction = 0.28). In boys, the risk of OW did not differ according to maternal education from 2 to 5 years and there was no interaction between age and maternal education (P for age \times education interaction = 0.68, **Figure 2**).

212 Maternal education and weight

Girls born to mothers with a low educational level had a lower birthweight (Table 1) but the 213 pattern of the relation between maternal education and children's postnatal weight then 214 seemed to shift. This change had already started at 1 month and was also observed at 215 subsequent ages but we did not observe any significant gradient in weight at any age (Figure 216 217 **3**, P for age \times education interaction <0.01). In boys, there was no significant gradient at birth or at 1 month, but a positive socioeconomic gradient in weight was observed between 6 218 219 months and 3 years. The change in the association across ages was reflected by the 220 significance of the interaction test (P for age \times education interaction < 0.01, Figure 3).

221 Maternal education and height

Girls whose mothers had low educational levels were significantly shorter than their counterparts whose mothers had more education at birth, 1 month and 5 years (**Figure 4**). In boys, this association remained significant as early as 1 month through 5 years (**Figure 4**, *P* for age \times education interaction = 0.06 for both girls and boys).

226 Sensitivity analyses

Results were on the whole consistent when analyses were performed on the databases with imputed maternal education as low or high (results not shown but available on request). When we used observed instead of predicted data, the overall pattern of the relations between maternal education and continuous outcomes (BMI, PI, weight or height) was consistent
regarding effect size, in both sexes (results not shown but available on request).

232 Comparison of included to excluded population

Mothers excluded from the analysis (n=172) were younger and less educated than those included (mean age (SD): 27.6 (5.3) vs. 29.7 (4.8) years; low education level: 52.2% vs. 26.9%). The proportion of boys and preterm births was higher in children excluded from the analysis (boys: 61.3% vs. 51.7%; preterm: 9.4% vs. 5.4%). No significant difference was observed in length and weight measured at birth among those included and excluded respectively (length: 49.3 (2.7) vs. 49.6 (2.3) cm; weight: 3.23 (0.57) vs. 3.28 (0.51) kg).

239 **DISCUSSION**

Using a large French mother-child cohort with repeated measurements of height and weight on 1735 children between birth and 5 years, this study provides original and comprehensive insights into the socioeconomic patterning of BMI and OW, in light of the socioeconomic inequalities in weight and height growth.

244

BMI, PI and OW

Our results show that, in girls, whereas birthweight was lower in newborns of women with 245 low educational levels, an inverse socioeconomic gradient in BMI and PI was already visible 246 247 at 1 month of age. Similarly, a socioeconomic gradient was observed for OW from 2 years, the earliest age for which cut-off points are available. Socioeconomic inequalities in BMI, 248 OW and PI in girls were therefore observed even earlier than in previous studies.^{12, 14, 20-22, 38} 249 Although an inverse association with PI was observed in boys at 1 month and 5 years, we did 250 not find any significant association between maternal education and their BMI or OW during 251 252 the first 5 years of life.

Other studies have also suggested stronger or earlier associations between socioeconomicposition and adiposity measures in girls compared to boys. Apouey et al. showed an inverse

socioeconomic gradient in OW from 2-3 years in girls and only from 4-5 years in boys,²⁴
while Howe et al. found an inverse socioeconomic gradient in BMI at 8 years and fat mass at
9 years in girls but nothing in boys.^{13, 25} Differences in body composition between sexes have
been described from infancy,^{36, 39, 40} with a higher proportion of BMI (or PI) variability
explained by fat mass in girls. This relatively better reflection of body fat mass variability by
BMI (or PI) in girls could partly explain the sex differences found in all these studies.

261

Weight and height

Socioeconomic gradients in weight and height were also observed very early in life. In girls, 262 although weight did not differ according to maternal education from 1 month of age onwards, 263 we observed that those born to mothers with low educational levels were shorter on the 264 whole. This difference in height but not in weight seemed to drive the inverse socioeconomic 265 gradient in both BMI and OW from 1 month and 2 years onwards, respectively. In boys, while 266 267 height was related to maternal education at each age, the parallel positive relation between maternal education and weight meant that neither BMI nor OW varied according to maternal 268 269 education at any age.

270 Although the emergence of socioeconomic inequalities in BMI across childhood has so far mainly been addressed with a focus on weight, our findings shed light on the potential 271 importance of height in the early development of such disparities. Socioeconomic patterning 272 273 of height in childhood was also observed by Howe et al. in the Avon Longitudinal Study of Parents and Children (ALSPAC),^{25, 26} Finch et al. in US children⁴¹ and Matijasevich et al. in 274 Brazilian children.⁴² This trend has not, however, been observed in all studies.^{43, 44} Besides the 275 methodological differences between studies (e.g. cross-sectional vs. longitudinal design, 276 statistical models used, ages studied), discrepancies between findings could come from 277 278 differences in the choice of the proxy of socioeconomic position or in the way that socioeconomic position affects weight-related behaviours in different populations. It is also 279

possible that socioeconomic patterning of growth and BMI takes place earlier in life in the
 most recent generations, given the increase of adiposity³ and socioeconomic inequalities in
 recent decades.⁴⁵

283 Potential explanations for socioeconomic inequalities in growth

Although our focus was a description of the socioeconomic gradient in growth over time, it is 284 worth considering the biological mechanisms that may underpin our findings. Weight and 285 height may be transmitted across generations through both genetic and environmental 286 influences.⁴⁶⁻⁴⁹ Smaller babies, exposed to an obesogenic environment, are perhaps more 287 vulnerable to overconsumption (and thus energy imbalance), than their taller counterparts. It 288 has also been suggested that babies born in disadvantaged backgrounds are more often 289 exposed to suboptimal parental feeding styles. In particular, mothers of smaller infants are 290 more likely to use pressuring styles, which could also contribute to overfeeding.⁵⁰ There is 291 292 also evidence showing a positive socioeconomic gradient in breastfeeding at the population level in industrialized countries,⁵¹ along with a slower growth during the first year of life in 293 breastfed babies⁵² and lower risk for overweight or obesity later in childhood.⁵³ Overall, 294 295 suboptimal health, diet and growth from birth could be considered to be indicators of a more global vulnerability transmitted from the mother to the child. 296

Our results add to the evidence that socioeconomic inequalities take root before birth, before and during pregnancy, and continue into childhood. In the background of this intergenerational transmission of inequality, our findings confirm that the window of opportunity for combatting non-optimal growth and/or OW begins very early in life. Future research into the early and modifiable risk factors involved in the socioeconomic patterning of both height and weight growth in girls and boys is clearly a priority.

303 *Limitations and strengths*

Limitations of the study include the fact that the predicted data were based on a mixture of 304 measured data and data collected from health booklets. The latter, likely more subject to 305 measurement errors, may have affected the accuracy of the predicted data and decreased the 306 307 statistical power. Modelling was performed on the assumption that children lost to follow-up had experienced the same growth curve compared to children with a complete follow-up and 308 a similar initial growth. This hypothesis, although possible, could not be verified, and we 309 cannot be certain of the validity of the growth modelling of children who dropped out. In 310 addition, prevalence of OW at 5 years was rather low in the Eden cohort, especially in boys 311 (5.7% vs. 9.8% in girls),⁵⁴ compared to findings from the 2006-07 INCA2 national dietary 312 survey, which reported a prevalence of 13.5% in children aged 3-6 years.⁵⁵ The presence of 313 selection bias at inclusion, as is often the case in cohort studies, is therefore possible and may 314 have implications for generalisation of the findings. Specifically, only including literate 315 316 women at baseline may have resulted in an underrepresentation of disadvantaged families, which might have weakened our ability to compare mothers according to their education 317 318 level. We also acknowledge that, consistent with the literature, we used maternal education 319 level as a proxy for socioeconomic position. Given the complexity in accurately assessing socioeconomic position, we cannot be certain that the results relating to disadvantage in our 320 analysis would not change if a different indicator were used. It is also possible that BMI is not 321 the most appropriate indicator of adiposity as it has been shown to underestimate the 322 socioeconomic gradient in obesity and body fatness. 56, 57 Under these circumstances, 323 however, our findings, which suggest early socioeconomic inequalities in weight, height and 324 325 BMI even in this rather low-risk sample, make the public health arguments even stronger. A clear strength of our study is that data are from a birth cohort, making it possible to address 326 the link between maternal education and the various outcomes prospectively, using marginal 327 models to account for repeated measurements. Growth modelling was the preferred method as 328

it allowed us to estimate accurate predicted weight and height at any age despite measurement error and missing values across the follow-up and thus reducing mis-classification and attrition biases.

332

In conclusion, these findings showed that the emergence of an inverse socioeconomic gradient in BMI and OW apparently results from a complex pattern of socioeconomic inequalities of weight and height from 1 month onwards. The very start of life thus appears to be an important window of opportunity for addressing socioeconomic inequalities in growth.

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350 **Contributors**: MB, SL, BH and JB conceived and designed the work, with advice from 351 MAC. MB analyzed the data with advice from BH, JB and SL. MB, BH and SL drafted and 352 revised the manuscript. All authors interpreted the data and criticized the manuscript for 353 important intellectual content. MAC and BH designed and led the EDEN mother-child cohort.

AF is responsible for the EDEN data management. JB and SC have fitted weight and height 354 growth trajectories using the Jenss-Bayley nonlinear model and provided the relevant data. 355 All authors have read and approved the final version of the manuscript. This article is the 356 work of the authors. MB serves as guarantor for the contents of this article. All authors had 357 358 full access to all of the data (including statistical reports and tables) in the study and take the responsibility for the integrity of the data and the accuracy of the data analysis. All 359 researchers are independent of the funding bodies. All members in the EDEN mother-child 360 361 cohort study group designed the study and revised the draft manuscript.

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