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Decline in the negative association between low birth weight and cognitive ability

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Abstract
Low birth weight predicts compromised cognitive ability. We used data from the 1958 National Child Development Study (NCDS), the 1970 British Cohort Study (BCS), and the 2000–2002 Millennium Cohort Study (MCS) to analyze how this association has changed over time. Birth weight was divided into two categories, <2,500 g (low) and 2,500–4500 g (normal) and verbal cognitive ability was measured at the age of 10 or 11 y. A range of maternal and family characteristics collected at or soon after the time of birth were considered. Linear regression was used to analyze the association between birth weight and cognitive ability in a baseline model and in a model that adjusted for family characteristics. The standardized difference (SD) in cognitive scores between low-birth-weight and normal-birth-weight children was large in the NCDS [−0.37 SD, 95% confidence interval (CI): −0.46, −0.27] and in the BCS (−0.34, 95% CI: −0.43, −0.25) cohorts, and it was more than halved for children born in the MCS cohort (−0.14, 95% CI: −0.22, −0.06). The adjustment for family characteristics did not explain the cross-cohort differences. The results show that the association between low birth weight and decreased cognitive ability has declined between the 1950s and 1970s birth cohorts and the 2000-2002 birth cohort, despite a higher proportion of the low-birth-weight babies having a very low birth weight (<1,500 g) in the more recent birth cohort. Advancements in obstetric and neonatal care may have attenuated the negative consequences associated with being born small.

Significance statement
Many studies have shown that children with a low birth weight (less than 2.5 kg) have worse cognitive development that those with a normal birth weight. No existing study has analyzed whether, given the advances in neonatology and obstetric practice which occurred over the past 50 years in developed contexts, the association between low birth weight and cognitive development has changed over time. Using data from the 1958 National Child Development Study, the 1970 British Cohort Study, and the 2000-2002 Millennium Cohort Study, we show that the association between low birth weight and decreased cognitive ability has been more than halved between the 1950s-1970s birth cohorts and the cohort born around the year 2000.

Introduction

Birth weight is one of the most important birth outcomes because it is strongly associated with infant mortality,(1) and it is a predictor of social and health outcomes in childhood and adulthood.(2-4) Many studies have shown that children who have a reduced weight at birth, and especially children who are classified as having a low birth weight (less than 2.5 kg), have worse outcomes than children whose birth weight is in the normal range (2.5-4.5 kg).

One of the outcomes that has been linked with low birth weight is cognitive development.(5) Low weight at birth is negatively associated with cognitive development, even after family characteristics are taken into account.(6) Recent studies have shown that childhood cognitive ability scores are associated with various important outcomes in adulthood, such as educational attainment,(7, 8) occupational prestige,(9) and long-term sickness.(10)

A limitation of the existing literature is that some of these studies examined cohorts who were born more than half a century ago.(5, 11) Some studies that have analyzed the association between birth weight and cognitive ability in 1990s-2000s birth cohorts have found significant associations,(5, 12) but there are no studies that have analyzed whether the association between birth weight and cognitive ability has changed over time. Given the advances in neonatology and obstetric practice,(13) we hypothesize that the association between low birth weight and cognitive ability has declined over time.

We investigate the question of whether the association between birth weight and cognitive development has changed over time using data from three large and representative UK birth cohort studies: the 1958 National Child Development Study, the 1970 British Cohort Study, and the Millennium Cohort Study. The negative association between low birth weight and cognitive ability has been more than halved between the 1950s-1970s birth cohorts and the cohort born around the year 2000. The adjustment for family characteristics did not explain the cross-cohort differences. We comment on how advancements in obstetric and neonatal care may have attenuated the negative consequences associated with being born small.

Results

Table 1 shows the descriptive associations, which indicate that there were striking cohort differences in mean cognitive scores by birth weight status. In the earlier cohorts, the association between low birth weight and decreased cognitive ability was much stronger than in the most recent birth cohort. In the 1958 cohort study, the cognitive ability of children with a low birth weight was 0.32 standard deviations (SD) lower than that of children with a normal birth weight (95% CI: -0.41 -0.22). In the 1970 birth cohort, the difference was 0.29 SD (95% CI: -0.39,-0.19), and in the 2001 MCS the difference was 0.12 SD (95% CI: -0.22,0.03).

Table 2 shows the regression results for birth weight and cognitive ability, while Figure 1 displays the key results. The baseline model in Table 2 indicates that in all three birth cohort studies low birth weight children had significantly lower cognitive scores than normal birth weight children, after accounting for sex and for whether the cohort member was the first born. However, as in the descriptive results, there were marked differences across cohorts which suggests there was a secular decline in the association between low birth weight and low cognitive ability. The disparity in the mean cognitive scores between low birth weight and normal birth weight children was similar and more marked for children born in 1958 (-0.37 95% CI: -0.46,-0.27) and 1970 (-0.34 95% CI: -0.43,-0.25), but was about 50% lower for children born in 2001(-0.14 95% CI: -0.22, -0.06). The confidence intervals of the 1958 and 1970 coefficients were not overlapping with those of the 2001 cohort study.

Adjustments for the mother's and the family's characteristics attenuated the association between low birth weight and cognitive scores in all of the cohort studies to a similar extent; but importantly, the differences across cohorts remained (Model 1 in Table 2). The differences were attenuated by 24% in the 1958 cohort study, by 41% in the 1970 cohort study, and by 43% in the 2001 cohort study. Adjustments for additional controls in the 2001 cohort did not change the results (Model 2 in Table 2). After these adjustments, the differences between the confidence intervals of the 1958 and 2001 cohort studies coefficients were still not overlapping.

The pooled results (Table 3) for the baseline model show that the differences in the association between low birth weight and cognitive development were statistically significant at the 1% level between the 2001 and 1958/1970 cohort studies. After the adjustments for the mother's and the family's characteristics, the differences between the 2001 and 1958 cohort studies remained significant at the 1% level.

There were similarities across cohorts in the characteristics of families by birth weight categories (Appendix Table S1). Across all three cohort studies and compared to normal weight children, low birth weight children were more likely to have come from more disadvantaged families, from families in which the mother had poor health behaviors during pregnancy and did not breastfeed. Low birth weight children were more likely to have been a first born, and a girl (Table 4).

Table 4 shows that the percentage of very low birth weight children (<1500 g) – who have the worst outcomes at birth and later in life (2, 14) - increased across cohorts. In Appendix Table S5 we replicated the analyses by dividing the low birth weight group into very low birth weight (VLBW; <1500 g) and moderately low birth weight (1500 g - <2500 g). The results show a picture consistent with the main paper results. Although the results were not statistically significant, the magnitude of the association between being born VLBW (vs. normal weight) and cognitive ability decreased across cohorts. Appendix Table S1 shows the characteristics of families with very and moderately low birth weight children.

Discussion

In this study, we investigated the question of whether the association between birth weight and cognition in childhood has changed over time. To the best of our knowledge, this is the first study that has addressed this research question, although previous studies have shown that the survival and neurological outcomes of very low birth weight (<1500 g) children at two years of age have improved over time.(15, 16) Consistent with existing evidence,(6, 11) we show that low birth weight children had worse cognitive scores than normal birth weight children at age 10/11, but that the disparities have declined dramatically. The gap in the cognitive scores of low birth weight and normal birth weight children was around 50% smaller for children born in 2001 than for children born in 1958 and 1970. Adjustments for maternal and family characteristics attenuated the differences in the cognitive scores of low birth weight and normal weight children in all three cohort studies; but these adjustments did not explain the striking cross-cohort differences. (2, 14, 17)

The results suggest that having a low weight at birth was associated with more negative consequences for a child's cognitive well-being in the 1950s and 1970s than it did around the year 2000. One plausible explanation for this shift is that the introduction of and the advancements in obstetric and neonatal care have partially attenuated the negative consequences associated with being born with a low birth weight. This hypothesis is supported by evidence that health care for both mothers and babies has gradually improved in the UK. In particular, neonatal intensive care was introduced in the 1970s, and further technological and pharmacological advancements such as assisted ventilation, neonatal monitoring, and drugs to treat prematurity were made during the 1970s and 1980s.(5, 13) Therefore, low birth weight children born in 2001 would have benefited from a range of medical treatments that were not available to children born in 1958 and 1970. These advancements in medical care helped to prevent brain damage and other negative consequences often associated with low birth weight. This interpretation is consistent with the results showing no significant difference between the older cohorts. These statements are further supported by considering secular changes in the composition of low birth weight children. That is, the most healthy and resilient low birth weight children survived to age 10/11 in the 1958 NCDS/1970 BCS cohorts, whilst, because of the introduction of prenatal care, there is less selection in the most recent 2001 MCS cohort. This is also supported by our results which revealed that the percentage of very low birth weight children - who have the worst outcomes at birth and later in life (2, 14) - increased across cohorts.(5) (5)Differences in the composition of the LBW analytical samples used in this study should make the secular change less marked or non-existing. (2, 14)The fact that the results suggest that the negative association between low birth weight and cognitive development has declined dramatically over the considered period – also for very low birth weight children – makes our results more striking and supports the role of medical developments in explaining the results.

Another potential explanation for the difference could be that the characteristics of families who have low birth weight children has changed over time, but the results fail to support this hypothesis.

An implication of the study's findings is that medical developments at least partly explain the secular change in the association between birth weight and cognition.

However, the results also suggest that despite substantial improvements in the association between birth weight and cognitive development, low birth weight children born in 2001 performed worse than normal weight children, even after accounting for family characteristics. Hence, despite medical advancements, a disadvantage associated with low birth weight remains that may be both social and biological, and that appears to be difficult to overcome.

This analysis has limitations. First, we were not able to account for gestational age, because in a significant proportion of the 1958 NCDS and the 1970 BCS subsamples used in this study it was either not reported or not reliable. As additional analyses have shown that the children with a missing or an uncertain gestational age tend to have the worst cognitive scores, excluding them from the analyses would have biased the results. Although we would have preferred to distinguish between children based on their gestational age, previous studies have shown that both pre- and full-term children with a reduced birth weight have more problems than those who are born (at term) with a normal birth weight.(17) Second, the analyses which distinguished very low birth weight (<1500 g) and a moderately low birth weight (1500 g to <2500 g) children need to be interpreted cautiously because of the small number of very low birth weight children. Third, the results suggest the existence of a secular trend in the association between birth weight and cognitive abilities using three data points; more data points are needed to fully test for the existence of a secular trend. Despite these limitations, this study is the first to investigate secular changes in the association between birth weight and cognitive development. A major strength of this study is that our data cover a 40-years' time period, are representative of the British population, and that the cognitive outcomes analyzed are comparable across cohorts.

To further analyze the implications of this study, future work should test whether similar results are found when considering a larger number of data points (in other contexts), and when other outcomes, both in childhood and adulthood, are investigated; and whether similar or different results are found in contexts that have/have not experienced advances in obstetric and neonatal care.

Methods

Data

The 1958 National Child Development Study (NCDS) is a longitudinal cohort study that followed the lives of around 17,500 individuals born during a single week of March 1958 in Britain. We used data from the birth survey (response rate 98.8%) and from the age 11 survey (response rate around 88%). The 1970 British Cohort Study (BCS) is a longitudinal cohort study that followed the lives of around 17,000 individuals born in Britain during one week of April 1970. We used data from the birth survey (response rate 95.9%) and the age 10 survey (response rate around 87%). The Millennium Cohort Study (MCS) is a longitudinal cohort study that followed the lives of around 19,000 children born in the UK from September 2000 to January 2002. The sample was selected from a random sample of electoral wards using a stratified sampling strategy to ensure the adequate representation of all four of the UK countries, and of disadvantaged and ethnically diverse areas. In the analyses, we used data from Sweep 1 (response rate 82%), which was collected when the children were around nine months old; and from Sweep 5, which was collected when the children were around 11 years old (response rate around 72%). For ease of exposition, we refer to the MCS as the 2001 cohort study, as the majority of the births in the sample occurred in 2001.

Birth weight

In the NCDS and in the BCS birth weight was recorded in the birth survey, which was completed by a midwife who attended the delivery. In the MCS, birth weight was reported by the main respondent in Sweep 1 (when the cohort child was around nine months), and evidence suggests that such reports are reliable and in accordance with registration data.(18) Birth weight was divided into two categories: low (<2500 g) and (19) normal (2500-4500 g). Heavy weight (4500 g and above)(20) children were excluded from the analyses since in all cohorts differences in cognitive outcomes between heavy and normal weight children were not statistically significant. In supplementary analyses, we divided the LBW group into two categories: very low birth weight (<1500 g) and moderately low birth weight (1500 g – <2500 g).

Cognitive ability

We used a measure of verbal cognitive ability in childhood. One of the strengths of this study is that we relied on measures of cognitive ability that are comparable across the three cohorts because they were collected at around the same age in each cohort (age 11 in the 1958 NCDS and 2001 MCS; age 10 in the 1970 BCS), they tested the same dimension of cognitive well-being, namely verbal ability and they were found to serve as a good proxy for general cognitive ability scores.(21-24) In the 1958 NCDS, cognition was assessed based on the verbal score of the General Ability Test (National Foundation for Educational Research) which consisted of 40 items.(23) The children were tested individually by teachers, who recorded the answers for the tests. In the

1970 BCS, the cognition of each child was assessed using the 21 items Word Similarity subscale of the British Ability Scales (First Edition), which was administered by a teacher.(24) The scores were standardized from a normed pool of scores within 3 month age ranges. In the 2001 MCS, the cognition of each child was assessed using the 37 items Verbal Similarity subscale from the British Ability Scale (Second Edition), which was administered by the interviewer. (25) The scores were standardized from a normed pool of scores within 3 months age ranges.

Since different tests were administered in each cohort, regression results based on the raw test scores would not be directly comparable across cohorts. We therefore standardized the cognitive scores to a mean of zero and a standard deviation of one within each cohort, which means that children were ranked within their respective cohorts. The standardization procedure ensured that the regression coefficients on the association between low birth weight and cognitive ability – obtained by estimating separate models within each cohort - could be compared across cohorts.

Family characteristics

We selected the maternal and the family characteristics that were hypothesized to attenuate the association between birth weight and cognition in childhood,(19, 26) and that were collected in all three cohort studies. To capture the socio-economic status in the family, we adjusted for the mother's level of education (in the 1958 NCDS and the 1970 BCS, whether the mother stayed in school beyond the minimum age; in the MCS, whether the mother had degree-level education), and for either the father's (1958 NCDS) or the household's (1970 BCS and 2001 MCS) registrar general social class. As socio-demographic variables, we considered the age of the mother at the birth of the cohort child and her marital status at conception or at the time of birth (in the 1958 NCDS and the 1970 BCS whether she was or was not married; and in the 2001 MCS whether she was married, cohabiting, or single). We considered three markers of the mother's health behavior: whether she smoked during pregnancy, whether she used antenatal care for the first time after 12 weeks of pregnancy or did not use it at all, and whether she breastfed the child. Finally, we adjusted for the mother's height, which is a marker of both socio-economic status and health.(27) Since the MCS provides a richer set of variables, we also showed in this cohort study how the results change after we controlled for the mother's heavy drinking during pregnancy, for the quintile of household income, and for the mother's ethnicity.

Inclusion criteria and exclusions

We dropped observations with missing values on cognitive scores at age 10 or 11 (1958 NCDS=1226; 1970 BCS=2267; 2001 MCS=297). From this subsample, we dropped observations with missing values on birth weight (1958 NCDS=1128; 1970 BCS=965; 2001 MCS=488) and observations with missing values on any of the covariates measured around the time of the cohort child's birth. We also excluded multiple births from the analytical samples. These exclusions reduced the 1958 NCDS sample to 10,341, the 1970 BCS sample to 9,116 observations, and the 2001 MCS sample to 11,231 observations.

Statistical analyses

We used linear regression models to estimate, within each cohort, the association between the cohort children's birth weight and verbal cognition at age 10/11. Two sets of models were estimated for each cohort study. The baseline model included an adjustment for the basic characteristics of each child: namely, the child's gender, , and whether the child was a first or a higher order birth. Model 1 included adjustments for the basic characteristics of the child, of the mother, and of the family. For the 2001 cohort, Model 2 was adjusted for additional covariates, which were not collected in the 1958 and 1970 cohort studies. To test directly whether the association between birth weight and cognition varied across cohorts, we pooled the three cohort studies and estimated a unique model in which we interacted each regressor by a cohort dummy.

All of the analyses were conducted in Stata version 13. In the analyses of the 2001 MCS, we used weights to account for non-response and for the overrepresentation of disadvantaged and ethnically diverse areas, and the survey command to account for the clustering of samples within strata. No weighting was used in the analyses of the 1958 NCDS and the 1970 BCS, as these surveys were not based on a complex design and weights for non-response were not available.

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Contributors: AG, BO, and MM were involved in the design of the study. AG conducted the statistical analyses and wrote the first draft of the paper. All of the authors were involved in the writing and made contributions to the drafts of the paper.

Conflict of interest: none

Ethics committee approval: The cohort studies were approved by the London Multicentre Research Ethics Committee.

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Figure legend: Figure 1 Linear regression estimates (with 95% confidence intervals) for the Baseline Model and Model 1 by birth cohort.

Figure 1

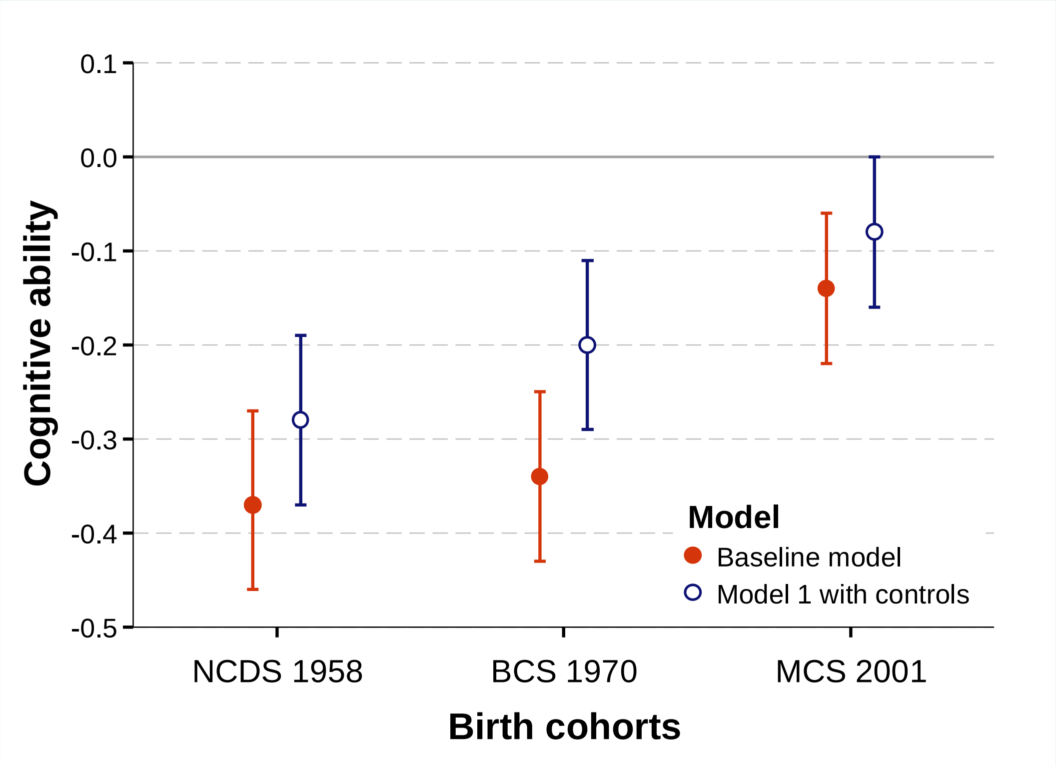

Table 1: Cohort members (CM) cognitive verbal ability z-scores (with 95% confidence intervals) by birth weight categories and birth cohort

	CM birth weight		
	below 2500 g	**2500 g - 4500 g**	**Average**
NCDS 1958 CM verbal ability at age 11	-0.32 (-0.41 to -0.22)	0.01 (-0.01 to 0.03)	0.00 (-0.02 to 0.02)
% of observations	4.41	95.59	
Test for difference (p-value reported)	0.000	reference	
Number of observations	456	9,885	10,341
BCS 1970 CM verbal ability at age 10	-0.29 (-0.39 to -0.19)	0.02 (-0.01 to 0.04)	0.00 (-0.02 to 0.02)
% of observations	5.06	94.94	
Test for difference (p-value reported)	0.000	reference	
Number of observations	461	8,655	9,116
MCS 2001 CM verbal ability at age 11			
% of observations	-0.12(-0.22 to -0.03)	0.01 (-0.04 to 0.06)	0.00 (-0.05 to 0.05)
Test for difference (p-value reported)	0.001	reference	
Number of observations	663	10,550	11,213

Note: results for the MCS are weighted to account for its complex survey design

Table 2: OLS model results (with 95% confidence intervals) of cohort members' verbal ability on birth weight categories by birth cohort. Reference category birth weight 2500 g -4500 g

	NCDS 1958	**BCS 1970**	**MCS 2001**
	Birth weight: below 2500 g	Birth weight: below 2500 g	Birth weight: below 2500 g
Baseline model[a]	-0.37 (-0.46 to -0.27)	-0.34 (-0.43 to -0.25)	-0.14 (-0.22 to -0.06)
Model 1: Baseline model+ family characteristics[b]	-0.28 (-0.37 to -0.19)	-0.20 (-0.29 to -0.11)	-0.08 (-0.16 to -0.00)
Model 2: Model 1+additional family characteristics[c]			-0.08 (-0.16 to -0.00)
Number of observations	10,341	9,116	11,213

Note: [a] adjustment made for CM sex and first birth. [b] adjustment made for CM sex, first birth, maternal age at CM birth, mother's education, family social class, marital status at the time of birth, mother smoking during pregnancy, mother's height, mother used antenatal care after 12 weeks of pregnancy, mother breastfed CM. [c] Just for the MCS, in addition to all the other control variables, we also adjusted for household income, whether the mother drank during pregnancy and mother's ethnic group. Results for the MCS are weighted to account for its complex survey design.

Table 3: Difference (with 95% confidence intervals) in the association between birth weight and cognitive development across cohorts. Results obtained from a pooled model

Birth weight: below 2500 g	BCS 1970 to NCDS 1958	MCS 2001 to NCDS 1958	MCS 2001 to BCS 1970
Baseline model[a]	0.05 (-0.08 to 0.17)	0.22 (0.12 to 0.33)	0.18 (0.06 to 0.30)
Baseline model+ family characteristics[bc]	0.10 (-0.02 to 0.21)	0.19 (0.07 to 0.29)	0.09 (-0.03 to 0.22)

Note: [a] adjustment made for CM sex and first birth. [b]adjustment made for CM sex, first birth, maternal age at CM birth, mother's education, family social class, marital status at the time of birth, mother smoking during pregnancy, mother's height, mother used antenatal care after 12 weeks of pregnancy, mother breastfed CM. [c] Just for the MCS, in addition to all the other control variables, we also adjusted for household income, whether the mother drank during pregnancy and mother's ethnic group. Results for the MCS are weighted to account for its complex survey design.

Table 4: Cohort members (CM) characteristics by birth weight categories and birth cohort. Results shown for the overall LBW group and for the subgroups of VLBW (below 1500 g) and MLBW (1500 g - below 2500 g)

	VLBW	**MLBW**	**LBW**	**Normal weight**	
	below 1500 g	*1500 g - below 2500 g*	below 2500 g	2500 g - 4500 g	Average
NCDS 1958					
CM girl	85.7	57.9	58.3	49.0	49.4
CM first birth	57.1	41.9	42.1	37.0	37.2
%	0.1	4.3	4.4	95.6	
Number of observations	7	449	456	9,885	10,341
BCS 1970					
CM girl	57.9	50.0	50.3	48.9	48.94
CM first birth	63.2	53.4	53.8	37.6	38.44
%	0.2	4.9	5.06	94.94	
Number of observations	19	442	461	8,655	9,116
MCS 2001					

CM girl	45.5	55.0	53.9	48.8	49.1
CM first birth	60.0	48.7	50.0	42.1	42.6
%	0.7	5.2	5.9	94.1	
Number of observations	76	587	663	10,550	11,213

Table S5 Ordinary least square model results (with 95% CIs) of CM cognitive ability on birth weight categories by birth cohort

Model specifications	NCDS 1958	BCS 1970	MCS 2001
	Birth weight: Below 1,500 g	Birth weight: Below 1,500 g	Birth weight: Below 1,500 g
Baseline model[a]	-0.34 (-1.06 to 0.39)	-0.24 (-0.69 to 0.20)	-0.12 (-0.44 to 0.20)
Model 1: Baseline model+ family characteristics[b]	-0.27 (-0.96 to 0.41)	-0.14 (-0.56 to 0.28)	-0.11 (-0.44 to 0.21)
	Birth weight: 1,500 g – below 2,500 g	Birth weight: 1,500 g – below 2,500 g	Birth weight: 1,500 g – below 2,500 g
Baseline model[a]	-0.37 (-0.46 to -0.27)	-0.34 (-0.44 to -0.25)	-0.14 (-0.22 to -0.06)
Model 1: Baseline model+ family characteristics[b]	-0.28 (-0.37 to -0.19)	-0.2 (-0.29 to -0.11)	-0.08 (-0.16 to 0.00)
Number of observations	10,341	9,116	11,213

Reference category: birth weight 2,500 g – 4,500 g.
[a] adjustmnent made for CM sex and first birth. [b]adjustment made for CM sex, first birth, maternal age at CM birth, mother's education, family social class, marital status at the time of birth, mother smoked during pregnancy, mother's height, mother used antenatal care after 12 weeks of pregnancy, mother breastfed CM. [c] Just for the MCS, in addition to all the other control variables, we also adjusted for household income, whether the mother drank during pregnancy and mother's ethnic group. Results for the MCS are weighted to account for its complex survey design.