Original Contribution

The Association of High Birth Weight With Intelligence in Young Adulthood: A Cohort Study of Male Siblings

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Initially submitted January 20, 2014; accepted for publication May 7, 2014.

We aimed to explore why, in population studies, the positive association between normal-range birth weight and intelligence becomes negative at the highest birth weights. The study population comprised 217,746 Norwegian male singletons born at term between 1967 and 1976. All had data on birth weight and intelligence quotient (IQ) score at the time of military conscription; 137,574 had data on sibling birth weights; and 62,906 had data on male sibling birth weights. We estimated associations between birth weight and IQ score by ordinary least squares regression for the total study population and by fixed-effects regression for comparisons of brothers. The crude mean IQ score was 1.2 points (95% confidence interval (CI): 0.3, 2.2) lower for those with birth weights of 5,000 g or more compared with the reference group (with birth weights of 4,000–4,499 g). This difference leveled off to 0.0 (95% CI: −0.8, 0.9) in multivariable ordinary least squares regression and reversed to 2.2 points (95% CI: 0.3, 4.2) higher in fixed-effects regression. Results differed mainly because, at a given birth weight, participants who had a sibling with macrosomia had a lower mean IQ score. Nevertheless, within families with 1 or more macrosomic siblings, as in other families, men with higher birth weights tended to have higher IQ scores. Thus, a family-level confounder introduces a cross-level bias that cannot be detected in individual-level studies. We suggest ways in which future studies might elucidate the nature of this confounder.

birth weight; cross-level bias; fetal macrosomia; intelligence; multilevel analysis; Norway; siblings

Abbreviations: CI, confidence interval; IQ, intelligence quotient; MBRN, Medical Birth Registry of Norway; OLS, ordinary least squares; SD, standard deviation.

Editor’s note: An invited commentary on this article appears on page 885, and the authors’ response appears on page 888.

On average, children of low birth weight tend to have low intelligence later in life (1). Evidence also supports an association between intelligence and birth weights in the normal range. The normal range includes the majority of births in a population, though its lower and upper bounds are defined differently across studies. A clear but moderate positive association between birth weights in the normal range and intelligence test scores was reported in 1969 (2). This relation has subsequently been observed in many studies (3–17), although in some studies associations were weak or nonsignificant.

There is still controversy as to what degree this association represents individual or contextual effects. It is well known that both birth weight and intelligence are associated with family socioeconomic position. The association could therefore be caused by a contextual family effect rather than a true birth weight effect (3). From a preventive point of view, both individual and contextual family effects could be of interest. Disentangling the two is a challenge that should be dealt with in study design and analysis (18). Sibling designs have proven fruitful in this regard (19, 20), in that they allow the separation of individual-level and family-level effects (3). Record et al. (2) found that the birth weight association, clearly present in
the whole cohort, nearly vanished when analyzed within sibships. Disentangling individual and contextual effects was later approached with more advanced analytical methods (3). Separate individual and contextual effects (3–5, 21, 22) or individual effects alone (6, 7, 23, 24) have been investigated in several sibling-based studies. Across all of these studies, the association between contextual family socioeconomic position and intelligence is strong. Although the relation between birth weight and intelligence at the individual level is weaker and less consistent across studies, the most rigorous designs suggest a relation at least up to the high birth weight range (18). Typically, high birth weight includes weights that are more than 2 standard deviations above the population mean, or it is set in terms of absolute birth weight.

The shape of the intelligence curve according to birth weight is still unsettled, particularly regarding high birth weights. Several studies have reported a lower mean intelligence score for those with the highest birth weights (4, 8, 9, 12, 13). This negative association seems to level off after adjustment for confounders in some (9, 12, 13) but not all (15, 21, 25) studies. Macrosomia could affect cognitive development because of the increased risk of birth trauma and asphyxia (26), but this has not been documented as an explanation for the lower intelligence associated with high birth weight in population studies. This apparent negative association has led some authors to make policy recommendations (27). A review article highlighted the need for studies that focus on the relation between intelligence and high birth weight (28). We are not aware of any sibling study that has responded to this call.

We designed this study to examine the apparent lower intellectual performance of those in the highest birth weight range. Our study population was all Norwegian male singletons who were born at term in Norway between 1967 and 1976 and who were later conscripted into the military (29). We considered confounding primarily from birth order, family socioeconomic position, or shared but unidentified family factors. To disentangle the effects of birth weight from potential confounding caused by individual or contextual factors, we used a sibling design (18).

METHODS

Participants and study design

The study population was based on data in the Medical Birth Registry of Norway (MBRN), where all births occurring after 16 gestational weeks have been recorded since 1967 (30). We had data encompassing all singleton livebirths between 1967 and 1976. The national identification numbers of children and parents allowed us to identify and link data among the following national registers: the Norwegian Armed Forces Personnel Database, the National Education Database, and the income register of the Norwegian Labour and Welfare Administration.

We restricted the study to the 242,771 men born at term (gestational weeks 37–41). Men who were missing data on the study outcome—intellectual performance at military conscription—were excluded. Reasons for missing data were emigration ($n = 1,637$; 0.7%) or death ($n = 3,589$; 1.5%) before conscription. Also, 3,388 (1.4%) men were not conscripted, mainly because they were either disabled or seamen on ocean transport ships. Of those conscripted, 16,235 (6.7%) did not complete the intellectual performance test. In addition, we excluded 176 (0.1%) men with missing data on birth weight. The remaining 217,746 men made up the total study population.

We identified siblings on the basis of the mother’s identity. In total, 154,840 mothers had 1 participating son and 30,225 mothers had 2–6 participating sons (totaling 62,906 sons). Among mothers with only 1 participating son, we identified 74,668 mothers with additional singleton births during 1967–1976 of children of either sex and any gestational age. We were therefore able to study the total cohort of 217,746 men, as well as 2 subset populations: 1 sibling population and 1 fraternal population. The sibling population comprised the 137,574 men (of 104,893 mothers) with at least 1 sibling, and the fraternal population comprised 62,906 men who had at least 1 brother born at term.

Study outcome

We retrieved intellectual performance scores from the Norwegian Armed Forces Personnel Database. All male citizens were enlisted for compulsory military service after examinations and draft board assessment of duty fitness. Participants were examined between 1984 and 2003, when almost all participants (98.3%) were 18–19 years of age. The intellectual performance test is part of the examination and includes 3 timed components entitled Arithmetic, Word Similarities, and Figures. The test results are scaled using a composite stanine score in single digits from 1 (low) to 9 (high) (31). Scores are normally distributed with a mean of 5 and a standard deviation of 2 in the general population (31). The test results are highly correlated with intelligence quotient (IQ) scores on the Wechsler Abbreviated Scales of Intelligence (32). To make results more readily interpretable, we transformed the stanine test scores to an IQ scale with a mean of 100 and a standard deviation of 15 (31).

Independent variables

We obtained data on birth weight from the MBRN. Birth weight was ordered into 8 levels with less than 2,000 g as the lowest and 5,000 g or more as the highest. Birth weights of 4,500 g or higher were defined as macrosomic.

We derived most covariates from data in the MBRN, including year of birth, gestational age (completed weeks based on the date of the last menstrual period), birth order (5 categories), mother’s and father’s identities, sibship size (mother’s total number of offspring born before 1999, in 5 categories), maternal marital status at child’s birth (married, never married, previously married), maternal age at child’s birth (5 categories), and paternal age at child’s birth (5 categories). The MBRN records included medical diagnostic codes from the International Classification of Diseases, Eighth Revision. This allowed reliable identification of birth injury (code 772) and asphyxia (code 776). Some relevant maternal conditions, such as obesity and diabetes, could not be included in this analysis because they were not systematically recorded.

Am J Epidemiol. 2014;180(9):876–884
We constructed family-specific variables by compiling data from the MBRN for all siblings of the 104,893 mothers who had more than 1 birth. Two variables were assigned to all 137,574 participants with at least 1 sibling born in 1967–1976: mean sibship birth weight and maximum sibship birth weight. Because this included all of the mother’s births, irrespective of sex and gestational age, we standardized both variables for sex and gestational age as z scores (standard deviations [SDs] above or below the mean) according to Norwegian population standards (33). Sibship mean birth weight was a continuous variable. The maximum sibship birth weight variable was categorized into 3 levels: less than 2 standard deviations above the mean, 2–3 standard deviations above the mean, and more than 3 standard deviations above the mean. Participants from families with at least 1 sibling birth weight that was 2 or more standard deviations above the mean were defined as having sibship macrosomia.

On the basis of the father’s identity in the MBRN, we constructed a fraternal relatedness variable, identifying sibships with full brothers, brothers with known different fathers, and brothers with at least 1 unknown father. We retrieved data on participant and parental educational attainment (Norwegian Standard Classification of Education, 9 levels) from the National Education Database (34), collapsing parental educational level when participants were 16 years of age into 5 categories according to the parent with the highest level.

Data on father’s income in the year of each participant’s birth were collected from the Norwegian Labour and Welfare Administration’s income register for identified fathers. Personal earnings are reported annually to estimate forthcoming retirement pension and are recorded in basic units that are adjusted annually in accordance with changes in the general income level. We classified father’s income into 5 categories, determined a priori. Independent variables and their categories are provided in Table 1 and Web Table 1, available at http://aje.oxfordjournals.org/.

### Data analysis and statistics

We used Stata/SE, version 13.1, software (StataCorp LP, College Station, Texas) for analysis. The main purpose was to estimate the individual-level associations (β coefficients) of macrosomic birth weight with IQ score. Throughout, the birth weight category of 4,000–4,499 g served as the referent. Specifically, we were interested in comparing results of ordinary least squares (OLS) regression in the total population (without any sibling information) with mixed model regressions in the sibling and fraternal subpopulations.

In the multivariable analysis, we included number of gestational weeks, year of birth, birth order, sibship size, mother’s and father’s ages at child’s birth, mother’s marital status, highest parental educational level, and father’s income level. Mean sibship birth weight, maximum sibship birth weight, and fraternal relatedness were added to the random-effects model. As shared family (contextual) factors, they were invariant in the fixed-effects regression. All covariates were included in the analyses on the basis of a priori assumptions about their confounding potential, with the exception of maximum sibship birth weight. The reason for including this variable was the discrepancy in high birth weight coefficients in the initial random-effects and the fixed-effects analyses. Upon examining this closer, we found that the main explanation was lower mean IQ scores among participants in the sibship macrosomia category. After including this variable, we

### Table 1. Selected Descriptive Characteristics and Distributions of Birth Weight and IQ Score at Military Conscription Among 217,746 Norwegian Male Singletons Born at Term From 1967 to 1976 and Conscripted Between 1984 and 2003

<table>
<thead>
<tr>
<th>Variable</th>
<th>%</th>
<th>Mean Birth Weight, g (SD)a</th>
<th>Mean IQ Score (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth order</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First</td>
<td>39.4</td>
<td>3,489 (471)</td>
<td>103.5 (13.7)</td>
</tr>
<tr>
<td>Second</td>
<td>33.1</td>
<td>3,640 (476)</td>
<td>101.4 (13.5)</td>
</tr>
<tr>
<td>Third</td>
<td>16.7</td>
<td>3,675 (476)</td>
<td>100.1 (13.7)</td>
</tr>
<tr>
<td>Fourth</td>
<td>6.7</td>
<td>3,703 (514)</td>
<td>99.9 (13.8)</td>
</tr>
<tr>
<td>Fifth or higher</td>
<td>4.1</td>
<td>3,738 (532)</td>
<td>97.6 (14.0)</td>
</tr>
<tr>
<td>Birth injury</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>99.7</td>
<td>3,594 (490)</td>
<td>101.7 (13.7)</td>
</tr>
<tr>
<td>Yes</td>
<td>0.3</td>
<td>3,825 (584)</td>
<td>102.0 (13.5)</td>
</tr>
<tr>
<td>Asphyxia at birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>99.0</td>
<td>3,595 (489)</td>
<td>101.7 (13.7)</td>
</tr>
<tr>
<td>Yes</td>
<td>1.0</td>
<td>3,548 (617)</td>
<td>101.9 (13.8)</td>
</tr>
<tr>
<td>Parental educational level</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Lower secondary or less</td>
<td>14.1</td>
<td>3,568 (505)</td>
<td>93.7 (12.8)</td>
</tr>
<tr>
<td>Upper secondary incomplete</td>
<td>39.6</td>
<td>3,590 (494)</td>
<td>99.4 (12.9)</td>
</tr>
<tr>
<td>Upper secondary complete</td>
<td>20.1</td>
<td>3,582 (486)</td>
<td>102.3 (12.8)</td>
</tr>
<tr>
<td>Lower tertiary</td>
<td>18.7</td>
<td>3,622 (479)</td>
<td>107.7 (12.5)</td>
</tr>
<tr>
<td>Upper tertiary</td>
<td>7.3</td>
<td>3,642 (469)</td>
<td>112.7 (11.9)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0.2</td>
<td>3,516 (498)</td>
<td>101.4 (14.3)</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>3,595 (490)</td>
<td>101.7 (13.7)</td>
</tr>
</tbody>
</table>

Abbreviations: IQ, intelligence quotient; SD, standard deviation.

a Recorded for only 137,574 sons of 104,893 mothers with more than 1 singleton birth between 1967 and 1976.
found that the birth weight coefficients in random-effects and fixed-effects regression were in better agreement according to the Hausman test (35).

The relation between birth weight and IQ score in the total study population was computed using OLS regression with robust standard error estimation and mother’s identity as a cluster variable. We used random-effects analysis for the sibling sub-population and fixed-effects analysis for the fraternal sub-population. We achieved this in Stata’s mixed model procedure with the xtrreg command. Mother’s identity served as a panel variable, and robust standard error estimation was applied.

The random-effects model includes individual within-family and contextual between-family factors simultaneously and can generally be expressed as

$$E(Y_{ij}) = \alpha + \beta X_{ij} + \gamma \bar{X}_i,$$

where $E(Y_{ij})$ is the expected IQ score for the person $j$ in sibship $i$ defined as all of the mother’s sons. $X_{ij}$ is the individual birth weight value, and $\bar{X}_i$ is the mean birth weight value for all siblings. $\beta$ is the coefficient for the individual, and $\gamma$ is the contextual family coefficient. This model is identical to model 2 in the article by Begg and Parides (3).

The fixed-effects approach is essentially a conditional analysis estimating differences between brothers, that is, the association between fraternal differences in birth weight and their differences in IQ score. Contrary to the random-effects model that controls only for contextual factors included in the model, all shared family factors are invariant and controlled for by design. This advantage of the fixed-effects approach is balanced by the considerably lower power in fixed-effects analysis compared with random-effects analysis. We therefore decided to run both.

To assess whether high birth weight associations could have been mediated through birth injury or asphyxia, we ran additional analyses restricted to participants without injury or asphyxia. We also analyzed birth weight–IQ score associations in separate maximum sibship birth weight strata.

We performed sensitivity analyses to assess potential bias from nonparticipation because of missing IQ scores. IQ score and educational attainment at age 25 years were strongly correlated ($r = 0.50$) among the participants, with mean IQ scores ranging from 91.9 points in the lowest level to 121.7 points in the highest level. We included nonparticipants who were singleton men born in 1967–1976 without IQ score at birth order could confound the exposure-outcome association, and furthermore, that macrosomic men with birth injury or asphyxia had low mean IQ scores. Figure 2 illustrates a pattern of relations among key variables that could be consistent with these results.

Table 2 shows associations between birth weight and IQ score in the 3 multivariable analyses. The $\beta$ coefficients in the high birth weight categories were different from those of the crude analysis. Coefficients leveled off for birth weights of 4,500 g or higher in the OLS analysis, mainly because of the influence of birth order and parental education. In fixed-effects analysis, the weight category of 5,000 g or more was $-1.2$ (95% confidence interval (CI): $-2.2$, $-0.3$) compared with the reference weight.

Distributions of population characteristics are provided in Table 1 and Web Table 1. In the total population, 7,826 births (3.6%) were macrosomic and 6,832 (4.9%) of the 137,574 participants with sibling information had sibship macrosomia. Birth weight and IQ score across categories of independent variables are also presented in Table 1 and Web Table 1. Mean differences in IQ scores were much larger for parental educational level and somewhat larger for birth order than for birth weight. Other covariates were more weakly associated with IQ score (Web Table 1).

We examined relations of potential confounders with exposure (macrosomia) and outcome (IQ score). Web Table 2 shows that sibship macrosomia, parental education, and birth order could confound the exposure-outcome association, and furthermore, that macrosomic men with birth injury or asphyxia had low mean IQ scores. Figure 2 illustrates a pattern of relations among key variables that could be consistent with these results.

Table 2 shows associations between birth weight and IQ score in the 3 multivariable analyses. The $\beta$ coefficients in the high birth weight categories were different from those of the crude analysis. Coefficients leveled off for birth weights of 4,500 g or higher in the OLS analysis, mainly because of the influence of birth order and parental education. In fixed-effects analysis, the weight category of 5,000 g or more was associated with an IQ score that was 2.2 points higher (95% CI: 0.3, 4.2). The corresponding random-effects estimate lay between the other 2 models. The adjusted difference between the OLS and fixed-effects estimates was 2.2
Familial macrosomia

Birth injury or asphyxia

First born or high parental educational level

Macrospomia

Figure 2. Relations of potential confounders and mediators on macrosomia at birth and intelligence quotient (IQ) score at military conscription among 217,746 Norwegian male singletons born at term between 1967 and 1976 and conscripted between 1984 and 2003. Solid lines represent positive associations; dashed lines represent negative associations.

Table 2. Associations Between Birth Weight and IQ Score at Military Conscription From 3 Analytical Models in Norwegian Male Singletons Born at Term Between 1967 and 1976 and Conscripted Between 1984 and 2003

<table>
<thead>
<tr>
<th>Variable</th>
<th>OLS Regression (n = 217,746)</th>
<th>Mixed Model Random-Effects Regression (n = 137,574)</th>
<th>Mixed Model Fixed-Effects Regression (n = 62,906)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IQ Score Coefficient</td>
<td>95% CI</td>
<td>IQ Score Coefficient</td>
</tr>
<tr>
<td>Birth weight category, g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>830–1,999</td>
<td>-4.8</td>
<td>-6.1, -3.5</td>
<td>-5.0</td>
</tr>
<tr>
<td>2,000–2,499</td>
<td>-3.7</td>
<td>-4.2, -3.1</td>
<td>-3.4</td>
</tr>
<tr>
<td>2,500–2,999</td>
<td>-2.5</td>
<td>-2.7, -2.2</td>
<td>-2.1</td>
</tr>
<tr>
<td>3,000–3,499</td>
<td>-1.6</td>
<td>-1.8, -1.5</td>
<td>-1.4</td>
</tr>
<tr>
<td>3,500–3,999</td>
<td>-0.6</td>
<td>-0.8, -0.5</td>
<td>-0.5</td>
</tr>
<tr>
<td>4,000–4,499</td>
<td>0.0</td>
<td>Referent</td>
<td>0.0</td>
</tr>
<tr>
<td>4,500–4,999</td>
<td>-0.0</td>
<td>-0.3, 0.4</td>
<td>0.1</td>
</tr>
<tr>
<td>5,000–6,660</td>
<td>0.0</td>
<td>-0.8, 0.9</td>
<td>1.0</td>
</tr>
<tr>
<td>Mean sibship birth weight (z score)</td>
<td>Not included</td>
<td>0.2</td>
<td>0.1, 0.4</td>
</tr>
<tr>
<td>Maximum sibship birth weight (z score)</td>
<td>Not included</td>
<td>Invariant</td>
<td></td>
</tr>
<tr>
<td>&lt;2 SDs above mean</td>
<td>0.0</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>2–3 SDs above mean</td>
<td>-0.5</td>
<td>-0.9, -0.1</td>
<td></td>
</tr>
<tr>
<td>&gt;3 SDs above mean</td>
<td>-1.5</td>
<td>-2.4, -0.7</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; IQ, intelligence quotient; OLS, ordinary least squares; SD, standard deviation.

a OLS linear regression in a model including birth weight, gestational age, year of birth, birth order, sibship size, mother’s and father’s ages at child’s birth, maternal marital status at child’s birth, highest parental educational level, and father’s income level.

b Random-effects mixed model regression including birth weight, mean sibship birth weight, maximum sibship birth weight, gestational age, year of birth, birth order, sibship size, mother’s and father’s ages at child’s birth, maternal marital status at child’s birth, fraternal relatedness, highest parental educational level, and father’s income level.

c Fixed-effects mixed model regression including birth weight, gestational age, year of birth, birth order, mother’s and father’s ages at child’s birth, maternal marital status at child’s birth, and father’s income level. Shared family factors (mean sibship birth weight, maximum sibship birth weight, sibship size, fraternal relatedness, and highest parental educational level) were invariant.

Am J Epidemiol. 2014;180(9):876–884
points (95% CI: 0.0, 4.3). Results for all factors in the models are provided in Web Table 3. Fixed-effects regression restricted to full brothers (n = 58,378) provided almost identical results (data not shown).

Including participants with injury or asphyxia in the analysis altered associations between birth weight and IQ score only marginally (data not shown). Analysis restricted to births without injury or asphyxia showed that the IQ score associations for birth weights of 5,000 g or more were somewhat stronger in all 3 models (Table 3). The adjusted difference between the OLS and fixed-effects estimates was 2.9 IQ points (95% CI: 0.7, 5.1).

Random-effects analysis showed a relatively consistent pattern with higher IQ scores for higher birth weights, irrespective of sibship macrosomia category (Figure 3). Furthermore, IQ scores were lower for persons of any birth weight in sibships with macrosomic births. As an example, the adjusted IQ score for those with birth weights of 3,500–3,999 g was 1.4 (95% CI: 0.4, 2.5) points lower for participants with sibship macrosomia compared with other participants.

Men with missing IQ data had slightly lower mean birth weight and lower educational attainment than the participants (data not shown). Sensitivity analyses comprising all men with either measured or imputed data on IQ yielded almost identical results as the estimates in Table 2 (Web Tables 4 and 5).

**DISCUSSION**

We have, for the first time, shown in a sibling analysis that the major part of the apparent association between high birth weight and lower educational attainment is due to the effect of macrosomia itself. The importance of macrosomia as a risk factor for low IQ scores among Norwegian men was similar in all 3 analytical models. These findings are consistent with previous reports from Danish, British, and Japanese cohorts. These studies also found that birth weights above 4,000 g were associated with lower IQ scores. The association between birth weight and IQ score varied according to sibship macrosomia status, meaning that the effect of birth weight on IQ score was stronger in sibships with macrosomic births. As an example, the adjusted difference in IQ score for births of 3,500–3,999 g was 1.4 (95% CI: 0.4, 2.5) points lower for participants with sibship macrosomia compared with other participants. These results are consistent with the findings from previous studies, which have shown that macrosomia is associated with lower IQ scores. These findings suggest that macrosomia, rather than birth weight per se, is the main risk factor for lower IQ scores among Norwegian men.

**Figure 3.** Differences in intelligence quotient (IQ) scores at military conscription in association with birth weight and sibship macrosomia category among 135,909 Norwegian male singletons born without injury or asphyxia, at term, between 1967 and 1976 and conscripted between 1984 and 2003. Bars, 95% confidence intervals. Results of random-effects mixed model regression analyses adjusted for sibship mean birth weight, gestational age, year of birth, birth order, mother’s and father’s ages at child’s birth, fraternal relatedness, highest parental educational level, and father’s income level.

**Table 3.** Associations Between Birth Weight and IQ Score at Military Conscription From 3 Analytical Models in Norwegian Male Singletons Born Without Injuries or Asphyxia, at Term, Between 1967 and 1976 and Conscripted Between 1984 and 2003

<table>
<thead>
<tr>
<th>Birth Weight Category, g</th>
<th>OLS Regressiona (n = 214,928)</th>
<th>Mixed Model Random-Effects Regressionb (n = 135,909)</th>
<th>Mixed Model Fixed-Effects Regressionc (n = 62,078)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IQ Score Coefficient 95% CI</td>
<td>IQ Score Coefficient 95% CI</td>
<td>IQ Score Coefficient 95% CI</td>
</tr>
<tr>
<td>830–1,999</td>
<td>−4.8 (−6.2, −3.5)</td>
<td>−5.0 (−6.7, −3.3)</td>
<td>−4.0 (−7.2, −0.8)</td>
</tr>
<tr>
<td>2,000–2,999</td>
<td>−3.7 (−4.3, −3.2)</td>
<td>−3.4 (−4.1, −2.6)</td>
<td>−3.9 (−5.2, −2.6)</td>
</tr>
<tr>
<td>2,500–2,999</td>
<td>−2.5 (−2.7, −2.2)</td>
<td>−2.1 (−2.5, −1.7)</td>
<td>−2.4 (−3.0, −1.8)</td>
</tr>
<tr>
<td>3,000–3,499</td>
<td>−1.6 (−1.8, −1.5)</td>
<td>−1.4 (−1.6, −1.1)</td>
<td>−1.4 (−1.9, −1.0)</td>
</tr>
<tr>
<td>3,500–3,999</td>
<td>−0.6 (−0.8, −0.4)</td>
<td>−0.5 (−0.7, −0.3)</td>
<td>−0.6 (−0.9, −0.2)</td>
</tr>
<tr>
<td>4,000–4,499</td>
<td>0.0 Referent</td>
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</tr>
<tr>
<td>4,500–4,999</td>
<td>0.1 (−0.3, 0.4)</td>
<td>0.1 (−0.3, 0.5)</td>
<td>−0.3 (−1.0, 0.4)</td>
</tr>
<tr>
<td>5,000–6,660</td>
<td>0.2 (−0.7, 1.1)</td>
<td>1.4 (−0.2, 2.5)</td>
<td>3.1 (1.1, 5.1)</td>
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</tbody>
</table>

Abbreviations: CI, confidence interval; IQ, intelligence quotient; OLS, ordinary least squares.
a Model including birth weight, gestational age, year of birth, birth order, sibship size, mother’s and father’s ages at child’s birth, maternal marital status, and highest parental educational level.
b Model including birth weight, mean sibship birth weight, maximum sibship birth weight, gestational age, year of birth, birth order, sibship size, mother’s and father’s ages at child’s birth, maternal marital status at child’s birth, fraternal relatedness, highest parental educational level, and father’s income level.
c Model including birth weight, gestational age, year of birth, birth order, mother’s ages at child’s birth, maternal marital status, and highest parental educational level, shared family factors (mean sibship birth weight, maximum sibship birth weight, sibship size, fraternal relatedness, and highest parental educational level) were invariant.

*Am J Epidemiol.* 2014;180(9):876–884
weight and low IQ score was caused by confounding from shared family factors. The main explanation was that participants from families with a tendency to have macrosomic babies had, on average, lower IQ scores than other participants; nevertheless, within these families (as in other families), men with higher birth weights tended to have higher IQ scores (Figure 3). Confounding from birth order and parental education had some additional influence in the same direction.

**Strengths and weaknesses of the study**

We based this exploratory study on a large cohort with data collected from birth onward. Our ability to apply a sibling design that identified and controlled for shared family factors is the main strength. Both the exposure and outcome measures have acceptable reliability and validity (30–32). Also notable, exposure and outcome data were collected independently from different registries, each of which has virtually complete nationwide coverage. These features lend considerable strength to the study.

Nonetheless, it is important to consider the potential for bias. Men without IQ scores tended to have lower educational attainment and lower mean birth weight. However, the sensitivity analyses suggested that exclusion of those missing IQ scores had only marginal impact on the birth weight–IQ score association.

An additional problem is that bias from nonshared confounders or random exposure error could be more serious in a sibling design than in an unpaired design (36). Random error in birth weight probably has little impact, but unidentified nonshared confounders are not so easily dismissed. We are, however, not aware of any such factors.

The study was large but had obvious power limitations. The main exposure constituted a small upper tail of the birth weight distribution. Sibling analysis was feasible only in subsets of the study population, and the fixed-effects regression and stratified analysis of subgroups particularly suffered from this. The consequence was rather low robustness in coefficients for macrosomic weights, which could possibly explain the deviation from a linear pattern in these 2 categories.

The study was restricted to male singletons born at term. The generalizability to women, twin births, or preterm births could therefore be questioned. Another uncertainty relates to the outcome measure, which was based on 1 specific test battery completed at a fixed age.

**Comparison with other studies**

The relation we found between birth weights in the low and normal ranges and IQ score is generally in accord with most recent and large studies, including sibling studies (2–7, 21–24). Most of these studies examined intelligence at younger ages, including singleton preterm births in both sexes (2, 3, 5, 6, 22, 24). Similar results have also been found in some twin studies (37, 38).

Several reports have described lower intelligence among those in the high birth weight range (8, 9, 12, 13, 27). This decline seems to level off after adjustment for parental socioeconomic position and birth order (9, 12, 13), which is in accord with our study. Others have reported no change (21) or a stronger decline (15) after adjustment. As far as we know, a continued increase in intelligence into the high birth weight range has not been reported earlier. We believe the main reason could be that high birth weights have not been examined in sibling designs.

**Possible explanations and implications**

The main factors explaining our high birth weight results were confounding from unknown shared family factors, parental educational level, and birth order. The higher risk of birth complications for macrosomic infants is well known (26), and in our data, macrosomic men with birth injury or asphyxia had lower IQ scores. Plausibly, this could explain low intellectual function later in life as a sequela of brain injury. Still, even in macrosomic families, birth weight or a factor associated with birth weight has a beneficial effect. The strongest impact came from unknown shared family factors, illustrated by the different IQ coefficients for high birth weights between OLS and fixed-effects regression. This discrepancy suggests that individual-level data analysis could be subject to cross-level bias (39, 40). Sons of mothers with a tendency to have macrosomic births had, on average, lower IQ scores compared with equally weighted sons of mothers without this tendency. This might be because, at any given birth weight, the former group are further below (or less above) their “expected” or “potential” birth weights than the latter group. Individual data alone will not be able to take sibship birth weight into consideration (39–41).

There is a continuing debate as to whether associations between birth weight and subsequent health outcomes are due to causality or confounding. This controversy has been clearly expressed for birth weight and postnatal death (42, 43). The importance of reproductive history (sibling birth weight) in our study could have its parallel in the influence of sibling birth weight on the relation between birth weight and perinatal survival (44) or maternal overweight and offspring mental health (45).

The distinction between causation and confounding is not a trivial matter. Given that birth weight is on the causal pathway, intervention aimed at gestational growth might be sensible, but if the explanation is confounding from some common cause, intervention should be directed at the confounder and not birth weight (42). Directing prevention of the apparent decline in IQ scores toward reducing high birth weight (27) will therefore not be the proper measure. It is plausible to relate the nature of the shared family factor(s) to fetal nourishment. However, we have no data that allow us to separate genetic and shared environmental factors. Maternal diabetes and obesity could give clues to mechanisms because they have both been associated with high birth weight and low offspring intelligence (46–49), but these diagnoses were not systematically registered in the MBRN between 1967 and 1976.

**Future research**

Uncovering the nature of the relation between birth weight and intellectual performance is a challenging enterprise. Future research should be directed at identifying the shared family factor(s) that contribute to the association. The
establishment of large prospective birth cohorts (50) that enable sibling designs and application of multilevel analysis could perhaps provide a frame for this.

ACKNOWLEDGMENTS

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This work was supported by the Research Council of Norway (grant 201334).

Conflict of interest: none declared.

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