Mother’s education and the risk of preterm and small for gestational age birth: a DRIVERS meta-analysis of 12 European cohorts


ABSTRACT

Background A healthy start to life is a major priority in efforts to reduce health inequalities across Europe, with important implications for the health of future generations. There is limited combined evidence on inequalities in health among newborns across a range of European countries.

Methods Prospective cohort data of 75 296 newborns from 12 European countries were used. Maternal education, preterm and small for gestational age births were determined at baseline along with covariate data. Regression models were estimated within each cohort and meta-analyses were conducted to compare and measure heterogeneity between cohorts.

Results Mother’s education was linked to an appreciable risk of preterm and small for gestational age (SGA) births across 12 European countries. The excess risk of preterm births associated with low maternal education was 1.48 (1.29 to 1.69) and 1.84 (0.99 to 2.69) in relative and absolute terms (Relative/Slope Index of Inequality, RII/SII) for all cohorts combined. Similar effects were found for SGA births, but absolute inequalities were greater, with an SII score of 3.64 (1.74 to 5.54). Inequalities at birth were strong in the Netherlands, the UK, Sweden and Spain and marginal in other countries studied.

Conclusions This study highlights the value of comparative cohort analysis to better understand the relationship between maternal education and markers of fetal growth in different settings across Europe.

INTRODUCTION

Prematurity and restricted fetal growth remain a crucial health risk for newborns in Europe. Poor fetal growth has been linked with not only impaired development throughout early childhood, but evidence supporting the ‘fetal origins of adult disease’ hypothesis has shown that these at-risk babies are more susceptible to a range of chronic diseases in later adulthood, such as cardiovascular disease, type 2 diabetes mellitus and adiposity, independent of environmental risk factors throughout the life course.

Methods

Participants Twelve European prospective birth cohorts provide data to this analysis: the European Longitudinal Programme and in recognition that ‘equity from the start’ of life is instrumental to reducing health inequalities in Europe.

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Study data

Study protocols were approved by ethics committees for each cohort. All participating mothers provided consent for themselves and their children. Data on maternal characteristics and health at birth were provided from each cohort in accordance with the ethical procedures approved for each site. Individual-level participant data are defined below.

Mother’s education was ascertained during pregnancy or at birth. Years of schooling were available in FR-EDEN, GR-GBC, NL-ABCD, NO-HUMIS and PT-G21. Levels of completed schooling were collected in CZ-ELSPAC, FI-NFBC8586, IT-GASPII, ES-INMA, SE-ABIS and UA-FCOU. Highest obtained qualifications were obtained in UK-MCS. The International Standard Classification of Education (ISCED) is an international categorisation managed by the United Nations Educational, Scientific and Cultural Organization (UNESCO) to facilitate comparison of educational data across countries. The country-specific coding scheme provided by ISCED-1997 was used to classify mothers into high (ISCED 4–6; postsecondary non-tertiary to second stage of tertiary education), medium (ISCED 3: upper secondary education) and low (ISCED 0–2; preprimary to lower secondary or second stage of basic education) categories, using the individual measures of education that were available for each cohort.

Preterm births were defined as live births occurring prior to the gestational age of 37 weeks. In CZ-ELSPAC, FI-NFBC8586, FR-EDEN, NL-ABCD, NO-HUMIS and PT-G21, gestational age was based on ultrasonound records, if available, or alternatively, using the date of the mother’s last menstrual period (LMP). In GR-GBC and IT-GASPII, this was determined only from LMP. In GR-GBC and FI-NFBC8586, gestational age was based on ultrasound records, if available, or alternatively, using the date of the mother’s last menstrual period (LMP). In GR-GBC and IT-GASPII, this was determined only from LMP. In GR-GBC and FI-NFBC8586, gestational age was based on ultrasound records, if available, or alternatively, using the date of the mother’s last menstrual period (LMP). In GR-GBC and IT-GASPII, this was determined only from LMP.

SGA births were defined according to the Alexander fetal growth reference, which provides expected gender-specific distributions of birth weight (grams) according to gestational age for singleton live births in the USA. Babies were deemed cases if their weight fell below the 10th centile of this national reference projected for their gestational age and gender. This algorithm has been widely employed in various multicity studies. Birth weight was medically assessed in most cohorts, except in SE-ABIS and UK-MCS, which relied on parental reports. Child sex, maternal age and ethnicity at the time of birth, were potential confounders available in all participating cohorts and thus included in the present study. Mothers belonging to an ethnic minority group participated in 7 out of 12 cohorts. Maternal ethnicity was defined by country of birth in FR-EDEN, IT-GASPII, NL-ABCD and ES-INMA. In NO-HUMIS, mothers were classified as Caucasian, Asian, African, Hispanic, Inuit, Romanian or Oceanian. Mothers in PT-G21 were classified as Portuguese, Portuguese speaking, European migrant, Brazilian, or Other. In UK-MCS, mothers were classified as White, Mixed, Indian, Pakistani/Bangladeshi, Black/Black British or Other.

Statistical analysis

Analyses were restricted to singletons who made up between 95.9% and 100% of the total sample across cohorts. As NO-HUMIS oversampled preterm births in one of their sites, these participants were excluded and analyses were limited to 77.2% of the original sample.

Study characteristics of each cohort sample were analysed (table 1). The cohort-specific distribution of mother’s education was directly age-standardised using the WHO European Standard Population (ESP). The prevalence of preterm and SGA birth by mother’s education was calculated for each cohort, and the χ² test for trend assessed linearity across educational groups (table 2).

Associations between maternal education and birth outcomes were estimated to infer relative and absolute socioeconomic inequalities in each cohort sample using the Relative (and Slope) Index of Inequality (RII/SII). The regression-based indices consider both the size and distribution of socioeconomic groups across the population, by evaluating morbidity risk according to the specific proportions of the population within the socioeconomic hierarchy. Given the extent of cohort differences in maternal education, these indices account for such differences as a source of variation in the magnitude of health inequalities, and facilitate comparison of estimates between cohorts.

The RII is a summary measure of relative inequality, defined as the prevalence ratio of the child outcome between children at the lowest and those at the highest end of the maternal education hierarchy. The SII is the corresponding measure of absolute inequality, defined as the prevalence difference of the child outcome between the two ends of said hierarchy. A RII score greater than 1 (and a SII score greater than 0) indicates the presence of inequality between low and high positions. For both indices, higher scores denote a larger magnitude of inequality.

Generalised linear models were performed to obtain the RII and SII by, respectively, specifying a logarithmic or an identity link function. Educational categories were ranked from high to low and were each assigned a value between 0 and 1, based on the cumulative percentage of the midpoint of the ranges observed for each cohort. Models were adjusted for child sex, maternal age and ethnicity, as appropriate, for each outcome. All analyses of the UK-MCS employed survey weights to account for the cohort’s sampling design.

Cohort-specific scores were pooled together to obtain mean RII and SII scores at the European level using random effects meta-analysis procedures, given between-cohort heterogeneity (figures 1 and 2). The extent of heterogeneity was tested using the Q test and the I² measure, which confirmed the a priori expectation of heterogeneity between cohorts not attributable to within-cohort variation. Sensitivity analyses using fixed-effects meta-analysis techniques yielded estimates similar to those obtained by random-effects methods. All analyses were carried out using Stata V.13 (Stata Corp, College Station, Texas, USA).
Table 1  Overview and study characteristics of analytic cohort samples

<table>
<thead>
<tr>
<th>Country*</th>
<th>FR</th>
<th>NL</th>
<th>UK</th>
<th>CZ</th>
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<th>FI</th>
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<th>IT</th>
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<tr>
<td>Birth cohort</td>
<td>EDEN</td>
<td>ABCD</td>
<td>MCS†</td>
<td>ELSPAC</td>
<td>FCOU</td>
<td>NFBC8586</td>
<td>HUMIS</td>
<td>ABIS</td>
<td>GBC</td>
<td>GASPII</td>
<td>G21</td>
<td>INMA</td>
</tr>
<tr>
<td>N at birth</td>
<td>1903</td>
<td>7880</td>
<td>14 630</td>
<td>6933</td>
<td>4118</td>
<td>8993</td>
<td>2035</td>
<td>15 328</td>
<td>2044</td>
<td>636</td>
<td>8330</td>
<td>2466</td>
</tr>
<tr>
<td>Per cent boys (N)</td>
<td>52.6 (1000)</td>
<td>50.4 (3969)</td>
<td>51.0 (7467)</td>
<td>51.8 (3593)</td>
<td>52.7 (1066)</td>
<td>51.7 (7920)</td>
<td>52.4 (1066)</td>
<td>51.7 (7920)</td>
<td>52.7 (1066)</td>
<td>51.7 (7920)</td>
<td>52.7 (1066)</td>
<td>51.7 (7920)</td>
</tr>
<tr>
<td>Per cent girls (N)</td>
<td>47.5 (903)</td>
<td>49.6 (911)</td>
<td>49.0 (7163)</td>
<td>48.2 (3340)</td>
<td>47.3 (1498)</td>
<td>48.7 (4768)</td>
<td>47.6 (969)</td>
<td>48.3 (7408)</td>
<td>53.4 (1091)</td>
<td>49.2 (313)</td>
<td>48.9 (4071)</td>
<td>48.4 (1194)</td>
</tr>
</tbody>
</table>

*Country abbreviations represent France (FR), the Netherlands (NL), the UK (UK), the Czech Republic (CZ), Ukraine (UA), Finland (FI), Norway (NO), Sweden (SE), Greece (GR), Italy (IT), Portugal (PT) and Spain (ES).
†Descriptive data of the MCS sample use survey weights to account for the cohort study’s sampling design.
‡Approximate sample sizes from which health outcome data for the present analysis were ascertained.
§Educational levels in each country have been age-standardised to the WHO European Standard Population.
MCS, Millennium Cohort Study.

Table 2  Cohort-specific prevalence of preterm and SGA births by maternal education

<table>
<thead>
<tr>
<th>Country*</th>
<th>FR</th>
<th>NL</th>
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<th>CZ</th>
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<td>Birth cohort</td>
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<td>ELSPAC</td>
<td>FCOU</td>
<td>NFBC8586</td>
<td>HUMIS</td>
<td>ABIS</td>
<td>GBC</td>
<td>GASPII</td>
<td>G21</td>
<td>INMA</td>
</tr>
<tr>
<td>Preterm birth, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>5.2</td>
<td>4.9</td>
<td>6.0</td>
<td>1.7</td>
<td>4.4</td>
<td>4.0</td>
<td>5.9</td>
<td>3.3</td>
<td>8.9</td>
<td>4.4</td>
<td>7.4</td>
<td>3.3</td>
</tr>
<tr>
<td>Medium</td>
<td>6.0</td>
<td>6.3</td>
<td>6.9</td>
<td>1.1</td>
<td>6.1</td>
<td>4.0</td>
<td>9.2</td>
<td>3.5</td>
<td>3.3</td>
<td>3.4</td>
<td>6.4</td>
<td>4.3</td>
</tr>
<tr>
<td>Low</td>
<td>8.6</td>
<td>7.0</td>
<td>8.2</td>
<td>1.5</td>
<td>7.3</td>
<td>5.4</td>
<td>9.7</td>
<td>4.3</td>
<td>4.7</td>
<td>8.3</td>
<td>8.1</td>
<td>6.3</td>
</tr>
<tr>
<td>p for trend</td>
<td>0.146</td>
<td>0.001</td>
<td>0.014</td>
<td>0.004</td>
<td>0.001</td>
<td>0.002</td>
<td>0.009</td>
<td>0.012</td>
<td>0.178</td>
<td>0.003</td>
<td>0.012</td>
<td>&lt;0.005</td>
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<tr>
<td>SGA birth, %</td>
<td></td>
<td></td>
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<tr>
<td>High</td>
<td>9.7</td>
<td>5.4</td>
<td>7.6</td>
<td>10.5</td>
<td>6.7</td>
<td>3.9</td>
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<td>8.9</td>
<td>6.6</td>
<td>11.8</td>
<td>11.9</td>
</tr>
<tr>
<td>Medium</td>
<td>13.5</td>
<td>9.1</td>
<td>11.1</td>
<td>10.9</td>
<td>7.7</td>
<td>4.7</td>
<td>7.5</td>
<td>4.2</td>
<td>8.2</td>
<td>10.8</td>
<td>11.4</td>
<td>15.3</td>
</tr>
<tr>
<td>Low</td>
<td>12.9</td>
<td>10.8</td>
<td>17.2</td>
<td>11.2</td>
<td>12.2</td>
<td>5.3</td>
<td>8.1</td>
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<td>8.4</td>
<td>9.5</td>
<td>13.7</td>
<td>18.5</td>
</tr>
<tr>
<td>p for trend</td>
<td>0.026</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.005</td>
<td>0.024</td>
<td>0.006</td>
<td>0.165</td>
<td>0.003</td>
<td>0.912</td>
<td>0.203</td>
<td>0.012</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Country abbreviations represent France (FR), the Netherlands (NL), the UK (UK), the Czech Republic (CZ), Ukraine (UA), Finland (FI), Norway (NO), Sweden (SE), Greece (GR), Italy (IT), Portugal (PT) and Spain (ES).
†Descriptive data of the MCS sample use survey weights to account for the cohort study’s sampling design.
MCS, Millennium Cohort Study; SGA, small for gestational age.
RESULTS
Mothers were primarily representative of the ethnic majority of their cohort, and aged between 23.8 and 31.4 years at the time of birth (Table 1). Substantially more mothers with low education were present in ES-INMA (44%), and in GR-GBC and PT-G21 (65%+). Conversely, the proportion of lowly educated mothers were very few (<5%) in UA-FCOU. Mothers with high education were greater (50%+) in FR-EDEN and NO-HUMIS and lower

Figure 1 (A/B)—Cohort-specific, and pooled Relative/Slope Index of Inequality, RII and SII scores, in the meta-analysis of the association between maternal education and preterm birth.

elsewhere. Preterm births ranged from 1.7% in CZ-ELSPAC to 6.8% in UK-MCS. SGA births showed wider differences, as prevalence was lowest in FI-NFBC8586, NO-HUMIS and SE-ABIS (4.6–5.4%), and highest in ES-INMA and PT-G21 (12.7–15.3%).

Educational gradients in preterm and SGA births were palpable in NL-ABCD, UK-MCS, FI-NFBC8586, SE-ABIS and ES-INMA (table 2). Similar gradients were found in prevalent SGA, but not in preterm births, in FR-EDEN, UA-FCOU and

Figure 2 (A/B)—Cohort-specific, and pooled Relative/Slope Index of Inequality, RII and SII scores, in the meta-analysis of the association between maternal education and small for gestational age birth.
PT-G21. The gradient in NO-HUMIS was apparent for preterm birth only. Trends were inconclusive in CZ-ELSPAC, GR-GBC and IT-GASPII for either birth outcome.

Figure 1 displays the magnitude of inequalities in preterm birth. Cohort-specific scores ranged from 0.67 in CZ-ELSPAC to 3.26 in ES-INMA, and from −0.20 to 5.00 in the aforementioned cohorts, respectively, for the RII and SII. The mean RII and SII score indicated a heightened relative and absolute risk, in preterm birth, of 48% and 84% for babies born to mothers with low education (RII=1.48, 95% CI 1.29 to 1.69, SII=1.84, 95% CI 0.99 to 2.69) combined for all cohorts. No observed heterogeneity was found for relative inequalities, as shown by the Q test of 9.61 (df=11, p=0.566) and the I² statistic of 0%. Low to moderate heterogeneity was estimated for absolute inequalities given the I² statistic of 38.4%, although the Q test of 17.83 did not approach significance (df=11, p=0.085). Cohort-specific findings revealed significant associations in NL-ABCD, UK-MCS, FI-NFBC8586, SE-ABIS and ES-INMA, but not in FR-EDEN, UA-FCOU, NO-HUMIS, IT-GASPII and PT-G21. A positive, although insignificant, association between high maternal education and greater risk of preterm birth was observed in CZ-ELSPAC and PT-G21.

Equivalent estimates of inequalities in SGA births ranged from 0.97 in CZ-ELSPAC to 2.62 in NL-ABCD, and from −0.47 in GR-GBC to 8.75 in UK-MCS (figure 2). The mean RII and SII score pooled for all cohorts yielded a 55% increase in the role of residual confounding by factors that were not available for this study. Adjustment procedures do not eliminate the role of residual confounding by factors that were not available for this analysis. Completeness of gestational age and birth weight data was generally achieved in all cohorts, as these data are customarily collected for all newborns. However, data were more commonly missing among babies born to mothers with low education in the Czech Republic, Greece, Portugal and Sweden. A reverse pattern was found in France, Italy, the Netherlands and Spain. No evident pattern of missingness by maternal education was found in the UK or Ukraine.

This meta-analysis leads us to consider whether we may anticipate differences in the relationship between maternal education and health at birth, both between and within the selected 12 European countries. Very few multicountry studies on educational inequalities in preterm and SGA births have been performed across Europe; and have been limited to Northern and Western populations.5 Notwithstanding, extensive research on adult health inequalities has elucidated how national structures with particular income and welfare contexts, healthcare and social care systems, among others, differ between countries of Europe. These may also differentially impact inequalities in newborn health.

Country differences reported in this meta-analysis may be consequent to national differences in maternal education, the overall level of newborn health, as well as plausible mediating pathways, such as women’s participation in the labour market, gender-specific income and work life-related programmes, social norms that influence women’s health and child-rearing behaviours and family arrangements, among other societal, political and cultural factors. While data on such factors are not readily available for this investigation, future DRIVERS work will comprise comparative analysis to assess potential mediators in the relationship between maternal education, and preterm and SGA
birth. Such evidence may shed light on country differences observed in different European settings.

CONCLUSIONS
Poor health at birth is greater among babies of mothers with low education across all cohorts combined from 12 European countries. Inequalities were strongest in the Netherlands, the UK, Sweden and Spain. The study illustrates the need to improve newborn health and to reduce these inequalities across distinct European populations. The period of infancy is crucial to children’s immediate and subsequent health and development, and in generating social and health inequalities across the life course and between generations.

What is already known on this subject
Low levels of maternal education have been found to be associated with adverse neonatal outcomes in offspring. However, few studies have systematically assessed this at the European level, and it is unclear whether associations are consistent between European countries.

What this study adds
This study showed that children born to mothers with low education were more likely to be born preterm and small for gestational age at the regional level, but associations were not consistent between selected cohorts in 12 European countries.

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Acknowledgements The authors are grateful to participating members of the European birth cohort studies included in the present paper. The authors would like to acknowledge Marie-Aline Charles, Anne Forhan and Barbara Heude from the EDEN Mother-Child Cohort Study. In addition, the authors would like to acknowledge Alexander Zvinchuk for his work on preparing the UA-FCOU data for this collaborative paper. He is the Director of the Louis Hamilton Data Management Center in Ukraine, which is housed in the Institute of Pediatrics, Obstetrics and Gynecology in Kyiv. The authors are very grateful for constructive review to an earlier version of the manuscript given by the following members of the DRIVERS Consortium: Linden Farrer, EuroHealthNet; Olle Lundberg, Stockholm University; and Diego Montano and Johannes Siegrist, University of Duesseldorf.

Contributors MR designed the study, carried out all analyses, drafted the initial manuscript and approved the final manuscript as submitted. HP conceptualised and designed the study, oversaw all analyses and approved the final manuscript as submitted. PG, JM and MM reviewed and revised the manuscript, and approved the final manuscript as submitted. LK, JS, MR-J, AT, M-JS-C, SL, CB, AV, DP, FF, MvE, TGMV, MAE, RAIV, HB, SC, MV, MT, MR, IL, JLF, DH and YA procured and coordinated data for this study, critically reviewed the manuscript and approved the final manuscript as submitted.

Funding All phases of this study were supported by a European Union’s Seventh Framework Programme grant, 278350, as part of The Determinants to Reduce Health Inequality Via Early Childhood, Realising Fair Employment, and Social Protection (DRIVERS) research programme. The Czech ELSPAC Study was supported by the Ministry of Education of the Czech Republic (LM20120118, LD1214) and the Grant Agency of the Masaryk University (MUNI/M1075/2013). The Northern Finland Birth Cohort (NFBC8586) received financial support from the Academy of Finland, Biocenter, University of Oulu, Finland, the European Commission (EURO-BLCS, Framework 5 award QLG1-CT-2000-01643), EU FP7 EurHEALTHAgeing -277849, the Medical Research Council, UK ( PrevMetSyn/SALVE) and the MRC Centenary Early Career Award.

Competing interests None declared.

Ethics approval Study protocols of participating birth cohorts were approved by ethics committees for each respective cohort.

Provenance and peer review Not commissioned; externally peer reviewed.

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J Epidemiol Community Health published online April 24, 2015

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