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Exploring Educational Disparities in Risk of Preterm Delivery: A Comparative Study of 12 European Birth Cohorts

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Abstract

Background

An association between education and preterm delivery has been observed in populations across Europe, but differences in methodology limit comparability. We performed a direct cross-cohort comparison of educational disparities in preterm delivery based on individual-level birth cohort data.

Methods

The study included data from 12 European cohorts from Denmark, England, France, Lithuania, the Netherlands, Norway, Italy, Portugal, and Spain. The cohorts included between 2434 and 99 655 pregnancies. The association between maternal education and preterm delivery (22–36 completed weeks of gestation) was reported as risk ratios, risk differences, and slope indexes of inequality with 95% confidence intervals (CIs).

Results

Singleton preterm live delivery proportion varied between 3.7% and 7.5%. There were large variations between the cohorts in the distribution of education and maternal characteristics. Nevertheless, there were similar educational differences in risk of preterm delivery in 8 of the 12 cohorts with slope index of inequality varying between 2.2 [95% CI 1.1, 3.3] and 4.0 [95% CI 1.4, 6.6] excess preterm deliveries per 100 singleton deliveries among the educationally most disadvantaged, and risk ratio between the lowest and highest education category varying from 1.4 [95% CI 1.1, 1.8] to 1.9 [95% CI 1.2, 3.1]. No associations were found in the last four cohorts.

Conclusions

Educational disparities in preterm delivery were found all over Europe. Despite differences in the distributions of education and preterm delivery, the results were remarkably similar across the cohorts. For those few cohorts that did not follow the pattern, study and country characteristics did not explain the differences.

Socio-economic disparities in risk of preterm delivery have been observed in many countries and contexts.[1], [2] The causes of these disparities are poorly understood, and, apart from smoking during pregnancy, modifiable lifestyle factors, such as maternal alcohol consumption and overweight, have been shown only to be weak risk factors for preterm delivery.[3]

The European Perinatal Health Reports[4], [5] has documented a substantial variation in preterm delivery rates across Europe as well as differences in pregnancy management and characteristics of pregnant women across Europe. Comparisons of educational disparities in risk of preterm delivery across Europe may therefore provide insight in how health policies and population characteristics influence disparities. The European Perinatal Health Reports were mainly based on national birth registration systems and found that it was difficult to obtain comparable socio-economic measures from these sources, as there was no common standard for recording socio-economic measures.

As an alternative, the present study compares educational disparities in preterm delivery in European birth cohorts. The study is a part of the European Union-funded Developing a Child Cohort Research Strategy for Europe (CHICOS) project aimed to coordinate birth cohorts and to examine possibilities and limitations in combining European birth cohort data.[6] The aim of the present study is to compare the association between maternal education and risk of preterm delivery across 12 European birth cohorts.

Methods

Identification and eligibility of cohorts

Eligible birth cohorts were identified through the cohort inventories **www.birthcohorts.net**and **www.birthcohortsenrieco.net** (accessed August 2011) along with publications on preterm delivery. European birth cohorts of at least 3000 pregnancies were eligible for this study if women were recruited either during pregnancy or at delivery. Furthermore, sampling into the cohort should be independent of pregnancy complications or birth outcome. These criteria were chosen to exclude cohorts that focused on women at either high or low risk for preterm delivery.

The minimum sample size was based on power calculations, which showed that a sample of 3000 gives the statistical power of 0.6 to determine a risk ratio of 1.5 in a subgroup of 20% of the population at a 5% significance level. A total of 65 birth cohorts were identified; of these, 19 satisfied the eligibility criteria. The main cause of exclusion was sample size, although a few cohorts focused on specific birth outcomes or population subgroups. The cohorts were asked to provide an anonymised data set including variables on pregnancy and delivery, birth outcome, socio-economic markers, and pregnancy complications. Of the 19 eligible cohorts, two never responded, two declined, two failed to deliver data on time for statistical analyses, and one was excluded as recruitment to the cohort occurred in the last month of pregnancy that only few women in this cohort were at risk for preterm delivery. This left us with 12 participating birth cohorts: Aarhus Birth Cohort (ABC),[7] Amsterdam Born Children and Their Development (ABCD),[8] Born in Bradford (BIB),[34] The Danish National Birth Cohort (DNBC),[10] Generation R (Gen R),[11] Generation XXI (Gen 21),[12] INMA – Environment and Childhood Project,[13] Kaunas cohort (KANC),[14] The Norwegian Mother and Child Cohort (MoBa),[9] Nascita e INFanzia: gli Effetti dell'Ambiente (NINFEA),[15] Endocrine disruptors: longitudinal study on pathologies of pregnancy, infertility and childhood (PELAGIE),[16] and Prevention and Incidence of Asthma and Mite Allergy (PIAMA)[17] (see Figure 1).

Definition of preterm delivery and gestational age

Preterm delivery was defined as delivery between 22 and 36 completed weeks of gestation. Generally, delivery variables such as gestational age and birthweight were extracted from medical records, although some cohorts relied on register data (DNBC, MoBa) and maternal report of gestational age (PIAMA, NINFEA). If more than one estimate of gestational age was available, gestational age estimates based on a combination of last menstrual period, ultrasound scans, and clinical assessment were preferred rather than estimates based on a single source. Otherwise, gestational age based on last menstrual period was used, unless it varied from ultrasound-based estimate by more than 2 weeks, in which case the ultrasound estimate was used. Implausible values of birthweight and gestational age were excluded based on the method given in Alexander *et al*.[18]

Maternal education

Data on maternal education were obtained through interviews or self-completed questionnaires with the exception of the DNBC cohort, which used linkage with population registers to obtain socio-economic data. Based on this information, and in accordance with the International Standard Classification of Education (ISCED-UOE 1997), education was categorised into three groups: (i) basic schooling (primary or lower secondary school) or less, (ii) further education (higher secondary school, lower vocational training, short further education, or other continued education not corresponding to a bachelor degree), and (iii) long education (tertiary education: university degree, further education, or vocational training corresponding to a bachelor degree).

Statistical methods

The analysis sample was restricted to liveborn singletons (gestational age 22¬43 weeks) and, for cohorts with recruitment during pregnancy, by women who had been recruited before 37 completed weeks of gestation.

Logistic regression was used to estimate odds ratio with 95% confidence intervals (CIs). As preterm delivery was fairly rare in all participating cohorts, the reported odds ratios can be interpreted as risk ratios. Risk differences were estimated by binomial regression with identity link function. The slope index of inequality (SII)[19] was calculated by ordering the education groups and assigning each group a value between 0 and 1 representing the midpoints of the cumulative distribution of education. For example, if the cumulative education distribution in one cohort were 20%, 70%, and 100%, the midpoints would be 0.1, 0.35, and 0.85. The proportion of preterm deliveries was then regressed on the assigned value by normal regression, indirectly taking the distribution of education in the population into account. The slope of the curve represents the difference between the educationally least and most deprived women, with higher SII values representing more unequal populations.

To take differences between cohort designs into account, three sensitivity analyses were performed. First, we restricted the sample to all non-immigrant women as education of women born in other countries can be difficult to classify and as associations between education and risk factors of preterm delivery may not be the same within ethnic subgroups. Secondly, three analyses restricted to women recruited before 22, 28, and 32 weeks of gestation were performed to consider differences in timing of recruitment. Finally, SII estimates were computed for the original education groups in each cohort to examine sensitivity to classification of education.

Data were analysed with SAS 9.3 (SAS Institute Inc., Cary, NC, USA) and R 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria; the ggplot2 package was used for figures).

Results

The 12 participating cohorts represented nine countries, covered the period 1990¬2012, and included between 2434 and 99 655 eligible observations (see Table **1**). Generally, the cohorts covered a single city or region with exception of the nationwide DNBC, MoBa and NINFEA cohorts, the INMA cohort, which was composed of seven smaller regional cohorts, and the PIAMA cohort, which covered 50 midwife clinics in different regions of the Netherlands. Most cohorts recruited women at first antenatal care visit or first ultraound scan (median gestational age at recruitment: 14 weeks), with exception of the NINFEA cohort which recruited women via the Internet throughout the pregnancy (median gestational age at recruitment: 26 weeks) and the Gen 21 cohort which recruited at delivery. Further, the PIAMA cohort did not collect data from the recruited women until third trimester (median gestational age at first interview: 33 weeks).

The percentage of singleton preterm deliveries varied between 3.7% and 7.5% (see Table **2**). Information about onset and method of delivery was available for nine cohorts; in these cohorts, the percentage of spontaneous preterm deliveries ranged from 2.0% in the INMA cohort to 4.9% in the ABCD cohort. Characteristics of mothers likewise varied between cohorts, both with respect to sociodemographic variables such as education and ethnicity as well as with respect to pregnancy characteristics such as gravidity and parity. For example, the proportion of women with basic education varied between 3% in the MoBa cohort and 57% in the Gen 21 cohort.

Plotting proportion of preterm delivery by maternal education showed similar gradients in most cohorts (see Figure **2**), although the slope varied between the cohorts and only a weak gradient was observed for the PELAGIE cohort. The exceptions were the NINFEA, BIB, and Gen 21 cohorts where the SII was not statistically different from zero. The SII varied between −1.2 in the NINFEA cohort and 4.0 in the INMA cohort. A SII of 4.0 means that the most educationally disadvantaged in the population have four more preterm deliveries per 100 singleton deliveries than the most educationally advantaged, while a negative SII of means that the educationally disadvantaged have fewer preterm deliveries. In the cohorts where educational disparities were observed, the basic education group had a 30–90% increased risk of preterm delivery compared with long education group (see Table **3**). In risk differences, this corresponded to 1–4 more preterm deliveries per 100 singleton live deliveries in basic education group. For the further education group, there was only a moderately increased risk of preterm delivery compared with the long education group, corresponding to less than 1 more preterm delivery per 100 deliveries.

To explore potential patterns in social inequality by characteristics of cohorts or countries, we compared SII by factors describing cohort design, study population, obstetric information, and country-level information. However, no clear patterns emerged with the exception that the three cohorts where no gradients were observed, all had markedly higher caesarean section rates than the other cohorts.

Results from sensitivity analyses are included in the online appendix. For the three cohorts ABCD, BIB, and Gen R, which all have large proportions of immigrant women, a sensitivity analysis stratifying by immigrant status revealed increased estimates in the native born groups and decreased association in the immigrant groups. However, in BIB, there were no educational differences in either group. Restricting the analyses to women recruited before 22, 28, and 32 completed weeks increased the proportions of preterm deliveries in cohorts with late recruitment, in particular in the PIAMA and NINFEA cohorts, and strengthened the observed associations. Using the original, more detailed, education categories did not change SII estimates.

Comment

In 8 of the 12 European cohorts, we found increasing risk of preterm delivery with shorter maternal education. In particular, cohorts from the Northern European countries Denmark, Norway, and the Netherlands showed strong gradients as have been observed before.[1, 2] The picture from Southern Europe was less clear; in the Portuguese Gen 21 and the Italian NINFEA cohorts, no differences were observed between the education groups whereas the Spanish INMA cohort had the highest SII of the 12 cohorts. The French cohort PELAGIE showed a weaker gradient, and in the British cohort BIB, we also found no educational differences. This is perhaps surprising as other British studies have found socio-economic disparities in preterm delivery[32, 33] but may be because of the population of BIB, which is very different from the general UK population.[34] Only one Eastern European cohort, the Lithuanian KANC cohort, satisfied our inclusion criteria, which highlights the scarcity of this type of data from Central and Eastern Europe. Other studies from Eastern Europe have found higher educational disparities in preterm delivery than studies from Western Europe,[20, 21] and we found that the results from KANC were similar to the Spanish INMA cohort. Compared with studies from outside Europe, we found educational disparities of similar or slightly lower magnitude than what have been observed in the United States and in Canada.[22, 23]

The proportions of preterm deliveries in the cohorts were in the range 3–5% with the exception of the Gen 21 cohort, which had 7.5% preterm deliveries. In the countries where more than one cohort was available, the proportions of preterm delivery were similar across the cohorts. A comparison with the 2004 European Perinatal Health Report[4] showed that with the exception of the Gen 21 and BIB cohorts, the percentages of preterm deliveries within the cohorts were similar, although slightly lower, than national figures.

Educational differences in birth outcomes may reflect differences in the way women utilise health care systems. We asked the cohorts to provide as much data as possible about mode and onset of delivery, complications during the index pregnancy, and previous pregnancy history. Eleven cohorts had information on caesarean section and nine on induction. However, only few cohorts were able to distinguish between emergency and planned caesarean section, and it was not possible to create a comparable definition of history of obstetric complications. We were not able to compare onset of delivery but could compare mode of delivery; this information was available for 9 of 12 cohorts. Notably, the three cohorts with no educational differences in risk of preterm delivery, the BIB, Gen 21, and NINFEA cohorts, all had high proportions of deliveries by caesarean section (respectively 22.0%, 37.0%, and 32.1% while the mean proportion of caesareans among the remaining cohorts were 13%).

The distribution of education within a country may be of importance for how education influences health. For example, educationally disadvantaged women could be more marginalised and vulnerable in societies where the majority is well educated than in societies where many women do not continue education. An example of such dynamic was observed in a multinational European case-control study where delivery outside marriage was associated with increased risk of preterm delivery only in countries where delivery outside marriage was rare.**24** However, although the included studies had very different educational distributions, no such pattern emerged. For example, in the NINFEA and MoBa cohorts only a few per cent had not completed secondary school; yet a SII of 2.6 was observed in the MoBa cohort, while no association was observed in the NINFEA cohort.

Cohort differences in risk factors for preterm delivery, such as maternal smoking, could potentially explain some educational differences. However, although smoking is known to be a risk factor of preterm delivery at individual level, the prevalence of smoking within the cohorts was not correlated with SII for preterm delivery at an ecological level. Another risk factor for preterm delivery could potentially be pregnancy after fertility treatment. Fertility treatment is more common in educationally advantaged women, and cohorts with high proportions of fertility treatments could be hypothesised to have smaller educational differences than cohorts with low prevalence of fertility treatment; however, such a pattern was not observed.

Strengths and limitations

Other studies have looked at socio-economic disparities in risk of preterm delivery, among them some of the cohorts participating in this study.[25-27] However, in this study, we had the opportunity to work on individual-level data and harmonise variables, which made it possible to compare results across cohorts. The advantages of using birth cohort data to study socio-economic inequality in perinatal health are many; most importantly, birth cohorts can provide more detailed information than what is available in national birth registries and make it possible to study potentially mediating factors of socio-economic inequality.[25, 27] Birth cohorts are typically designed to cover a region or city and can be designed to tackle special sub-populations, as is the case with the BIB cohort, which is designed to examine the Asian minority population in Bradford.[34] However, the restricted areas covered by the cohorts combined with selective participation may imply that one should be cautious not to generalise results from one cohort to the entire country and to make between-country comparisons. We have tried to take this into account by comparing results with national statistics and to examine how study design characteristics influence results; however, it is possible that some differences between cohorts may represent study design characteristics, such as selective participation, timing of enrolment, classification of maternal education, and source of delivery information.

Selection mechanisms may result in differences between the cohort populations and the source populations, for example, by having more years of education[28] or having lower preterm delivery rates.[29] Selection is particularly worrisome (i.e. bias-inducing) if it depends on both education and preterm delivery.**30** Because the SII is affected by the distribution of education, selection on education may bias this estimands in particular. The included cohorts used different study designs and sampling schemes, and selection may have different impact within the different cohorts.

In most cohorts, recruitment occurred in first trimester or first part of second trimester. Nevertheless, women recruited later in pregnancy would have a lower risk of preterm delivery, given that they had shorter time at risk in the study. None-differential timing of enrolment could be a potential source of error. We have dealt with this problem by restricting analyses to women recruited before 37 weeks rather than using a survival analysis approach because some of the cohorts only recruited at delivery or did not provide data on time of recruitment. However, sensitivity analyses showed that our results might have been influenced by timing of enrolment, in particular in the PIAMA and NINFEA cohorts.

Our primary socio-economic indicator of interest was maternal education, and this turned out to be the only socio-economic indicator that was available in all cohorts. Income was only available in a few cohorts while some version of occupation or labour market status was available in most cohorts. These socio-economic indicators capture different aspects of deprivation and advantage than education does, and it is possible that we might have found other patterns if these indicators had been available in all cohorts. For all socio-economic indicators, a main limitation was differences in coding systems and questionnaire designs. Although there are international standards such as the ISCED, there was no standard for how maternal education was assessed, even for cohorts from the same country. In addition, information about educational attainment in immigrants may be less valid than in the native born population. As the classification of maternal education will depend on the education system and the method of collecting data, we used the SII, which is less sensitive to differences between classifications because it takes distribution of education within a cohort into account. We examined how sensitive the results were to reclassification of education into three groups by estimating SII using the finest available grouping of education, and we found that these estimates did not differ much from the presented estimates.

Differences in the method of estimating gestational age and subsequent data cleaning may have resulted in differential outcome misclassification between the cohorts. Cohorts mainly using last menstrual period may overestimate preterm rate compared with cohorts with US-based gestational age estimates,**31**, **35** which would weaken the observed associations.

Conclusion

Educationally disadvantaged women were found to be at increased risk of preterm delivery in birth cohorts from all over Europe. Despite differences in the distribution of education and level of preterm delivery, the results were remarkably similar across cohorts.

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