Advanced maternal age is not an independent risk factor for low birth weight and preterm delivery: a within-family analysis using Finnish population registers

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Abstract

Importance Advanced maternal age at birth is considered a major risk factor for birth outcomes. It is unclear to what extent this association is confounded by maternal characteristics.

Objective To test whether advanced maternal age at birth independently increases the risk of low birth weight and preterm delivery.

Method We compare between (comparing children born to different mothers at different ages) and within-family (comparing children that are born to the same mother at different ages) models. The latter approach reduces confounding by unobserved parental characteristics that are shared by siblings.

Design Finnish population registers. The data includes children who were born between the years 1987-2000.

Setting Nationally representative 20% random sample of households with at least one child aged 0–14 at the end of 2000 with individual-level information on all household members.

Participants The sample size is 124,098 children. The sample is representative of mothers with at least two children. The analyses excluded children without siblings since the within-family model is identified from variation between siblings.

Exposure Born at an advanced maternal age (35 and over).

Main outcome and measures Low birth weight (less than 2500 g) and/or preterm (less than 37 weeks of gestation). A set of child and parental socio-demographic and health characteristics.

Results Between-family models document a robust association between advanced maternal age and the risk of LBW. Maternal age of 35-39 years is associated with increases in the probability of LBW by 1.1% (95% CI: 0.008-0.014) and in the group 40 and above by 2.2% (95% CI: 0.014 to 0.029). In contrast, the within-family models show that this association is negligible both statistically and substantively. Results for preterm delivery are qualitatively similar.

Conclusion and Relevance Advanced maternal age is not an independent risk factor for LBW and preterm delivery among mothers who have at least two live births. This finding is of great relevance both for women who are contemplating the postponement of childbearing and for physicians who are providing advice to patients about these risks.

INTRODUCTION

Advanced maternal age, defined as the mother being aged 35 or above at the time of birth, is considered a major risk factor for negative pregnancy and perinatal outcomes in both low income and high income countries. [1 2] In particular, advanced maternal age is associated with increased risk of low birth weight and preterm delivery[3-12] amongst both primigravidas [13] and multiparas.[14-16] Low birth weight children have more respiratory, cognitive and neurological problems than those born with normal birth weight.[23-26] Preterm babies have higher risk of heart defects, lung disorders, cerebral palsy, and delayed development.[27 28] Given current trends in delayed fertility,[22] it is important to know whether advanced maternal age at birth independently increases the risk of low birth weight and preterm delivery.

Although most research documents a positive association between advanced maternal age and risk of low birth weight and preterm delivery even after adjustment for parental characteristics [3-12], a subset of studies suggests that the association may be confounded by pre-existing medical conditions, obstetric history or maternal social characteristics. [17-21] This evidence questions whether an advanced maternal age at birth is an independent determinant for birth outcomes, and suggests that children born to older mothers may face higher risks due to parental characteristics that are unobserved in the data. No existing study has addressed this question.

Using data from the Finnish population register, this is the first study to directly test whether the association between advanced maternal age and the risk of low birth weight and preterm delivery is attributable to maternal age per se, or to other confounding factors. We compare the association between advanced maternal age and the risk of low birth weight and preterm delivery using two alternative approaches. First, we use the standard approach that compares children born to different mothers at different ages, while controlling for observed maternal characteristics. Second, we compare children that are born to the same mother at different ages, while controlling for factors that vary between siblings. This latter approach, which has not been used in the literature before, enables us to remove confounding by unobserved parental characteristics that are shared by siblings.

MATERIAL AND METHODS

Data

The study utilizes data from the Finnish population register and other administrative registers. The base data is a 20% random sample of households with at least one child aged 0–14 at the end of 2000 with individual-level information on all household members (n=415,000). Therefore, the data includes children who were born between the years 1987-2000. The individual level linkages between different registers, maintained by Statistics Finland, the National Institute for Health and Welfare and the Finnish Social Insurance Institution, were carried out by Statistics Finland using unique personal identification numbers.

Birth outcomes

Information on birth outcomes was extracted from the birth register. We use two dependent variables: whether the child was born low birth weight (LBW, less than 2500 g at birth) and whether the child was delivered preterm (less than 37 weeks of gestation).

Maternal age at birth

The key explanatory variable is maternal age at the birth of the child, divided into the following categories: <20, 20-24, 25-29, 30-34, 35-39, 40+. We use the 25-29 group as the reference category because this is the most common age range. We define mothers who give birth at an advanced age as those aged 35 and older.

Control variables

We consider a range of child and family characteristics that might be associated with both maternal age at birth and with the risk of giving birth to a LBW and/or preterm baby. The control variables are grouped according to whether they refer to the child, the socio-demographic and behavioural characteristics of the family, or health of the mother. The child characteristics are sex, birth order (1, 2, 3, 4 or more) and birth year (one-year indicator variables).

The socio-demographic and behavioural characteristics are deciles of family income (continuous), highest level of education in the household (basic, secondary, lower tertiary, higher tertiary), and whether the mother smoked during pregnancy. Income and smoking during pregnancy vary between siblings. Income was measured the year of each child's birth and varies between siblings. Education was measured the year of the first child's birth since there is little variation between siblings. Smoking during pregnancy was taken from the birth register and varies between siblings.

The health characteristics are the mother's number of previous miscarriages (continuous), whether she had any previous stillbirths, whether the child was born with a C-section and whether the mother experienced high blood pressure during pregnancy. With these variables, we intend to capture both the mother's previous obstetric history and her health during the observed pregnancy. Information on health characteristics was taken from the birth register and varies between siblings.

Statistical analyses

We compare the association between advanced maternal age and birth outcomes using two approaches. The standard approach used in the literature consists of analysing the association between maternal age and the risk of LBW or preterm delivery by comparing children born to different mothers. In order to account for potential confounders, these models include controls for observable parental characteristics. Throughout the study, we refer to these models as *between-family* comparisons since they compare children born to different mothers.

The alternative approach is based on a comparison of siblings that are born to the same mother at different ages, and throughout the study we refer to this as the *within-family* model. The *within-family* model, also known as sibling fixed effects, includes an indicator for each sibling group and identifies the association between maternal age and the risk of LBW/preterm from variation between siblings. [29] The main advantage of the *within-family* model (as opposed to a standard between-family model) is that unobserved maternal characteristics that are shared by siblings are fully accounted for. These unobserved characteristics may, for example, include health behaviours during pregnancy, the height of the mother, and health characteristics that are associated both with difficulty in conceiving – leading to births occurring at a later age – and the risk of LBW or preterm delivery. Observable characteristics that are not shared by siblings such as sex of the child, birth order and birth year, and all other observed and time-varying characteristics such as income and smoking during pregnancy that were discussed above, are adjusted for as in standard regression analyses.

We estimate 4 regression models using both the between- and within-family approaches. We estimate linear probability models (LPM) such that the coefficients of the models are directly interpretable as marginal effects and to enable comparability across the within and between-family models.[29] Model 1 documents the descriptive association between advanced maternal age and LBW/preterm and includes a control only for the child's sex. Subsequent models progressively include adjustment for child and parental characteristics. Model 2 introduces controls for the child's birth order and birth year. Model 3 introduces control for parents' socio-demographic and behavioural characteristics. Model 4 introduces control for health characteristics.

Inclusion criteria and exclusions

Multiple births were excluded from the analyses (3%) as were observations that had a missing value on any of the variables used in the analyses (7%). Since the sibling fixed-effect model is identified from variation between siblings, it is necessary to exclude only children. The resulting sample size for the sibling analytical sample was 124,098 children and 63,407 mothers. On average there are slightly less than 2 children per woman because we keep in the sample children who only have siblings that were born before 1987 and for whom we do not have information about birth outcomes. We use this study population for both the between-family and within-family comparison analyses.

RESULTS

Descriptive analyses

Table 1 shows the descriptive characteristics of the analytical sample. The most common maternal age group is 25-29 (37%). LBW and preterm births show a U-shaped association with maternal age. Mothers aged 40 and above have the highest prevalence of LBW and preterm delivery. Mean birth order increases with maternal age.

Mothers who give birth from age 30 onwards appear similar in terms of socio-economic status. Household income and education both increase with maternal age up to age 30-34, but then stabilize. Rates of smoking during pregnancy decrease with maternal age, but vary relatively little after age 30. Pregnancy complications and health issues increase with maternal age. Although the results suggest that older mothers are at higher risk of worse birth outcomes, they also indicate that older mothers face more health problems before and after delivery. This highlights the importance of accounting for parental characteristics, some of which might be unobserved in the data, when analysing the association between advanced maternal age and birth outcomes.

Regression analyses

Table 2 and 3 show the maternal age coefficients for the between- (upper part) and within-family (lower part) models using, respectively, LBW and preterm as outcome variables. Mothers aged 25-29 are the reference category. Coefficients for the control variables included in the different model specifications are presented in Appendix Tables A1-A4.

Between-family models document a robust association between advanced maternal age and the risk of LBW. The unadjusted Model 1 shows that children born to older mothers experience significantly higher risk of LBW compared to children born to mothers aged 25-29. The association is similar in Model 2 where we adjust for birth order and birth year. The association is statistically significant but small in magnitude for mothers aged 30-34, but grows in magnitude with maternal age. For example, in Model 2 maternal age 35-39 is associated with a 1.1 percentage point increase in the probability of LBW (95% CI: 0.8-1.4) and in the group 40 and above a 2.2 percentage point increased probability (95% CI: 1.4 to 2.9). The size of these associations is large. The overall prevalence of LBW in our sample is 2% so the associations correspond to approximately 50% and 100% increases in the risk of low birth weight, respectively. Adjustment for socio-economic characteristics in Model 3 produces small changes in the advanced maternal age coefficients. Adjustment for maternal health characteristics in Model 4 reduces the magnitude of the coefficients by approximately half.

A different picture emerges when the association between maternal age and LBW is analysed using a within-family model (lower part of Table 2). Here each of the regressions suggest that children born to mothers aged 35-39 or 40 and above do not have a higher risk of LBW than the reference category (25-29). In Model 1 and Model 2, the size of the association is small both statistically and substantively. Adjustment for parental socio-economic and health characteristics not shared by siblings does not produce any significant change in the advanced maternal age coefficients. Figure 1 illustrates this key result using Model 2 from Table 2.

The results for preterm deliveries (Table 3) are qualitatively similar to those for LBW. The between-family analyses show that advanced maternal age significantly increases the risk of preterm delivery. For example, Model 2 shows that giving birth in the age group 35-39 is associated with a 1.4 percentage point increase in the probability of preterm delivery (95% CI: 1.0-1.8). In the age group 40 and above, the increase is 3.1 percentage points (95% CI: 2.1-4.0). The size of these associations corresponds to approximately a one-third to three-quarters increase in the probability of preterm delivery, as average prevalence in our sample is 4%. Adjustment for parental characteristics increases the age gradient slightly. Conversely, adjustment for health characteristics attenuates the age gradient.

As in the analyses for LBW, the within-family models show a different picture. In all of the model specifications, maternal age is neither significantly nor substantively associated with the risk of preterm delivery. Adjustment for characteristics not shared by siblings does not produce any significant change in the advanced maternal age estimates. Figure 2 illustrates this key result for Model 2 from Table 3.

DISCUSSION

In this study we investigated whether an advanced maternal age at birth has an independent effect on the risk of low birth weight and preterm delivery, or whether the association is explained by other observed or unobserved parental characteristics. We compared the association between advanced maternal age and the risk of low birth weight and preterm delivery using both a standard regression approach that compares children born to different mothers, and an approach that enables us to account for unobservable parental characteristics shared by siblings. The latter approach has not been used earlier in this context.

The standard between-family comparison analyses reproduce the results that are common in the literature [3-6]: advanced maternal age is associated with significantly higher risks of low birth weight and preterm delivery. Adjustment for parental socioeconomic, behavioural, and health characteristics attenuates but does not explain the maternal age gradient. In contrast, using the sibling-comparison approach we find no evidence that advanced maternal age is associated with increased risk of low birth weight or preterm delivery. This result is observed consistently through models that control or do not control for parental characteristics. The results suggest that advanced maternal age is not an independent risk factor for LBW or preterm delivery.

Our results that show that advanced maternal age is not an independent risk factor for low birth weight and preterm delivery clearly suggest that, in addition to the observed maternal health and pregnancy related problems, there are unobserved factors that are related to both the probability of giving birth at older ages, as well as to the probability of low birth weight and preterm delivery. These unobservable factors might vary between different women. One example could be unobserved maternal health factors that are associated both with difficulty in conceiving – leading to births occurring at a later age – and the risk of giving birth to a LBW or preterm infant. In addition, a later maternal age at birth could also be related to other social (e.g. partnership and employment patterns, etc.) and behavioural (e.g. alcohol consumption during pregnancy) factors that are unobserved but may be correlated with adverse birth outcomes.

This study has several strengths. First, the data is large and allows us to compare siblings. Second, the data is not prone to self-selection as it is drawn directly from administrative registers. Third, we rely on a methodological approach that enables us to account for unobserved parental traits that are shared by siblings. No existing study has analysed the association between advanced maternal age at birth and birth outcomes using this approach.

This study also has limitations. First, the results from the within-family sibling comparison model are based upon the sub-set of women who have had at least two live births. Although this approach minimizes the bias in our estimates to a great extent, it does reduce our ability to generalize the results to mothers who have only given birth to one child. Nevertheless, sibling groups with two or more children are far more common than one-child sibling groups in most high income countries, so our results may well generalize to the majority of the population. A second limitation is that our analysis only considers women who successfully conceived and had at least two live births. Maternal age at birth is related to a woman’s ability to conceive as well as the risk of miscarriage and stillbirth. Third, we study Finland, a country with a highly advanced health care system and world-leading low rates of infant mortality. The results may not generalize to contexts in which antenatal care is poor or unavailable. Fourth, we are unable to identify which unobserved parental characteristics are accounted for in the within-family comparison. Despite these limitations, this study is the first to show that when unobserved parental characteristics are accounted for, advanced maternal age does not have an independent effect on the risk of low birth weight and preterm delivery.

The question of whether delaying childbearing increases the risk of adverse pregnancy outcomes is important given the remarkable increase in the mean age at first birth. Knowledge about these risks is of great relevance both for women who are contemplating the postponement of childbearing and for physicians who are providing advice to patients about risks. Our findings suggest that an advanced maternal age at birth is not an independent risk factor for birth outcomes such as low birth weight and preterm delivery. Our result indicate that while older mothers more commonly give birth to a low birth weight or premature child, this is because of the characteristics of the mothers who delay childbearing to advanced maternal ages, and is not a consequence of reproductive ageing. Women who are pregnant at advanced ages may still be considered a group that is at risk of giving birth to a low birth weight or preterm infant, but this is due to factors other than their age.

Given that these findings challenge long-held conclusions about the relationship between advanced maternal age and the risk of LBW and preterm delivery, it is important that their robustness is tested in contexts that are both similar and dissimilar to contemporary Finland. Moreover, using different data, future research should identify unobserved confounding factors that explain the link between advanced maternal age and negative birth outcomes, which is ultimately important for the design of prevention programs to reduce negative birth outcomes. Furthermore, the sibling fixed effect approach should be applied to study the relationship between maternal age and other outcomes, which will shed light on both the costs and benefits of postponing childbearing.

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TABLES

Table 1: Descriptive statistics by Maternal age, for siblings born between 1987-2000

Maternal age in years	LBW (%)	Preterm (%)	Birth year (mean)	Birth order (mean)	Household income decile (mean)	Mother smoked during pregnancy (%)	Household high education (%)	Number of miscarriages	Any previous stillbirth (%)	C-section delivery (%)	High blood pressure (%)	N	%
10-19	3.1	4.2	1992.2	1.2	2.9	37.3	0.2	0.1	0.2	9.2	2.4	2183	1.8
20-24	2.6	4.0	1992.4	1.5	4.2	20.2	2.0	0.1	0.4	10.3	2.2	20562	16.6
25-29	1.9	3.3	1992.7	1.9	5.5	11.4	12.7	0.2	0.7	12.1	2.3	45946	37.0
30-34	2.0	3.3	1993.4	2.3	6.2	10.2	20.3	0.3	1.1	14.4	2.4	37580	30.3
35-39	2.7	4.4	1993.9	2.7	6.3	10.0	20.5	0.4	1.8	17.0	3.1	14924	12.0
40+	3.6	5.9	1994.0	3.6	6.3	8.1	19.2	0.7	2.8	19.4	4.9	2903	2.3
Average	2.2	3.7	1993.0	2.1	5.6	12.7	14.1	0.2	0.9	13.2	2.5	124098	

Table 2: Between-family and within-family fixed effects models for low birth weight, with 95% CI (Linear models)

	Model 1: unadjusted		Model 2: birth order and birth year		Model 3: Model 2 + socio-demographic variables[a]		Model 4: Model 3 + health variables[b]	
Between-family model on sibling sample								
	β	**95% CI**	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
Maternal age 10-19	0.012***	(0.005 - 0.020)	0.007*	(-0.001 - 0.015)	0.002	(-0.006 - 0.010)	0.004	(-0.004 - 0.012)
Maternal age 20-24	0.007***	(0.005 - 0.010)	0.005***	(0.003 - 0.008)	0.003***	(0.001 - 0.006)	0.005***	(0.002 - 0.008)
Maternal age 25-29	0.000		0.000		0.000		0.000	
Maternal age 30-34	0.002**	(0.000 - 0.004)	0.004***	(0.002 - 0.006)	0.005***	(0.003 - 0.007)	0.002**	(0.000 - 0.004)
Maternal age 35-39	0.008***	(0.005 - 0.011)	0.011***	(0.008 - 0.014)	0.012***	(0.009 - 0.015)	0.006***	(0.003 - 0.009)
Maternal age 40+	0.018***	(0.011 - 0.025)	0.022***	(0.014 - 0.029)	0.023***	(0.015 - 0.030)	0.012***	(0.005 - 0.019)
Number of observations	124,098		124,098		124,098		124,098	
AIC	-124,986		-125,137		-128,167		-153,237	
Within-family model on sibling sample								
	β	**95% CI**	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
Maternal age 10-19	0.020***	(0.011 - 0.028)	0.009*	(-0.001 - 0.020)	0.009*	(-0.001 - 0.020)	0.009*	(-0.001 - 0.019)
Maternal age 20-24	0.008***	(0.005 - 0.012)	0.005**	(0.000 - 0.009)	0.005**	(0.000 - 0.009)	0.005**	(0.000 - 0.009)
Maternal age 25-29	0.000		0.000		0.000		0.000	
Maternal age 30-34	-0.004***	(-0.007 - -0.001)	-0.002	(-0.006 - 0.002)	-0.002	(-0.007 - 0.002)	-0.002	(-0.006 - 0.002)
Maternal age 35-39	-0.001	(-0.006 - 0.003)	-0.001	(-0.008 - 0.007)	-0.001	(-0.008 - 0.007)	-0.002	(-0.009 - 0.006)
Maternal age 40+	-0.003	(-0.012 - 0.007)	-0.004	(-0.018 - 0.009)	-0.004	(-0.018 - 0.009)	-0.009	(-0.022 - 0.005)
Number of observations	124,098		124,098		124,098		124,098	
Number of sibling groups	63,407		63,407		63,407		63,407	

AIC	-234,593	-234,859	-234,857	-237,704

Note: *** p<0.01, ** p<0.05, * p<0.1 [a] household income deciles, mother smoked during pregnancy, household level of education (only in the between-family analyses) [b] Number of previous miscarriages, any previous stillbirth, high blood pressure, C-section delivery. In the between-family analyses, standard errors are clustered at the family level.

Table 3: Between-family and within-family fixed effects models for preterm, with 95% CI (linear models)

	Model 1: unadjusted		Model 2: birth order and birth year		Model 3: Model 2 + socio-demographic variables[a]		Model 4: Model 3 + health variables[b]	
Between-family model on sibling sample								
	β	**95% CI**	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
Maternal age 10-19	0.009*	(-0.000 - 0.018)	0.003	(-0.006 - 0.012)	-0.002	(-0.011 - 0.007)	0.003	(-0.007 - 0.012)
Maternal age 20-24	0.006***	(0.003 - 0.010)	0.004**	(0.001 - 0.007)	0.002	(-0.002 - 0.005)	0.004**	(0.001 - 0.008)
Maternal age 25-29	0.000		0.000		0.000		0.000	
Maternal age 30-34	0	(-0.002 - 0.003)	0.003**	(0.000 - 0.005)	0.003**	(0.001 - 0.006)	0	(-0.002 - 0.003)
Maternal age 35-39	0.011***	(0.007 - 0.014)	0.014***	(0.010 - 0.018)	0.015***	(0.011 - 0.019)	0.009***	(0.005 - 0.013)
Maternal age 40+	0.026***	(0.017 - 0.035)	0.031***	(0.021 - 0.040)	0.031***	(0.022 - 0.040)	0.020***	(0.011 - 0.029)
Number of observations	124,098		124,098		124,098		124,098	
AIC	-63444.67		-63539.1		-63570.43		-65254.76	
Within-family model on sibling sample								
	β	**95% CI**	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
Maternal age 10-19	0.019***	(0.008 - 0.031)	0.006	(-0.007 - 0.020)	0.007	(-0.006 - 0.020)	0.007	(-0.006 - 0.020)
Maternal age 20-24	0.010***	(0.006 - 0.015)	0.005*	(-0.000 - 0.011)	0.006*	(-0.000 - 0.011)	0.006**	(0.000 - 0.011)
Maternal age 25-29	0.000		0.000		0.000		0.000	
Maternal age 30-34	-0.007***	(-0.010 - -0.003)	-0.004	(-0.009 - 0.002)	-0.004	(-0.009 - 0.001)	-0.004	(-0.009 - 0.001)
Maternal age 35-39	-0.001	(-0.007 - 0.005)	0.002	(-0.007 - 0.012)	0.002	(-0.007 - 0.012)	0.002	(-0.008 - 0.011)
Maternal age 40+	-0.002	(-0.015 - 0.010)	0.000	(-0.017 - 0.018)	0.001	(-0.016 - 0.018)	-0.003	(-0.020 - 0.014)
Number of observations	124,098		124,098		124,098		124,098	
Number of sibling groups	63,407		63,407		63,407		63,407	
AIC	-176368.6		-176555.9		-176563.4		-178160.5	

Note: *** p<0.01, ** p<0.05, * p<0.1 [a] household income deciles, mother smoked during pregnancy, household level of education (only in the between-family analyses) [b] Number of previous miscarriages, any previous stillbirth, C-Section delivery. In the between-family analyses, standard errors are clustered at the family level.

Figure 1 Between- and within-family models for LBW with 95% CI (Model 2, Table 2)

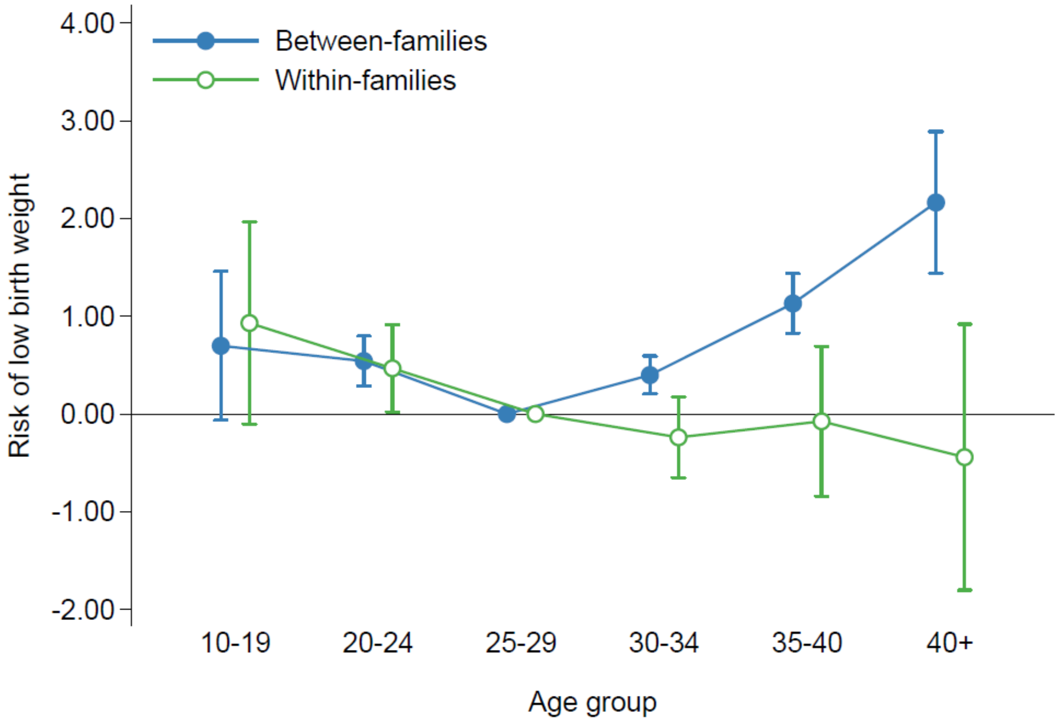

Figure 2 Between- and within-family models for preterm with 95% CI (Model 2, Table 3)