

Secular changes in the association between advanced maternal age and the risk of low birth weight: a cross-cohort comparison in the UK

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Running head: secular changes in the maternal age/child health association

Abstract

Existing studies provide contradictory evidence concerning the association between child well-being and advanced maternal ages. A potential explanation for the lack of consensus are changes over time in the costs and benefits of giving birth at advanced ages. This is the first study that investigates secular changes in the characteristics of older mothers and in the association between advanced maternal age and child health.

We use data from four UK cohort studies covering births from 1958-2001, and use low birth weight as a marker for child health. We find that across successive birth cohorts, the negative association between advanced maternal age and low birth weight becomes progressively weaker which is partially explained by secular changes in the characteristics of older mothers. The results suggest that the association between maternal age and child outcomes is tied to a specific population and point in time.

Introduction

Since the 1970s, there has been a marked increase in childbearing postponement in developed countries (Sobotka, 2004). This trend has in turn led to a sharp increase in the mean age at first birth and in births at advanced maternal ages (Billari, Kohler, Andersson, & Lundstrom, 2007). Yet even as childbearing postponement has become common across the entire developed world, whether and to what extent women should be advised against giving birth at advanced ages because of the associated health risks are issues that are still being debated (Tough et al., 2002). One reason why there is no general consensus on the question of “how old is too old” (Heffner, 2004) is the growing awareness that evidence from earlier periods might not accurately reflect the contemporary association between maternal age and child well-being. Whereas in earlier periods an advanced maternal age at birth was associated with high parity and low socio-economic status, today advantaged women are more likely than disadvantaged women to give birth at an older age (Prioux, 2005). It would therefore be reasonable to expect that older mothers and their children face lower risks of poor health outcomes today than they did two or more decades ago (Carolan, 2003). Up to now, however, no study has analyzed whether this is the case leaving a gap in the literature. There is a growing number of women giving birth at advanced maternal ages in the UK (Figure 1), as well as in other countries, and evidence on whether and why the association between maternal age and the risk of poor birth outcomes has changed over time is relevant both from a demographic and a medical perspective.

We use data from four birth cohort studies covering births that took place in different parts of the UK between 1958 and 2001. We find that across successive birth cohorts,

older mothers have become more advantaged, and that an advanced maternal age has become progressively less likely to be associated with low birth weight. Indeed, in the most recent birth cohort studied, the association is shown to be both statistically and substantively negligible. The decline in the association can be partially explained by secular changes in the characteristics of older mothers. Moreover, the overall improvement in the epidemiological context of childbearing may have contributed to the decline.

Background

The association between advanced maternal age and child health remains a highly controversial topic. The medical literature has expressed concerns about late childbearing, with many studies suggesting that in terms of pregnancy outcomes, the optimal age range for childbearing is 20-35 (Bewley, Davies, & Braude, 2005; Nwandison & Bewley, 2006). This argument is based on evidence that women who give birth after age 35, and especially after age 40, face increased risks of ante-partum, intra-partum, and post-partum complications. The risks range from a higher incidence of miscarriage, high blood pressure, preeclampsia, gestational diabetes, and chromosomal abnormalities; to problematic neonatal outcomes, such as preterm delivery and low birth weight (Aldous & Edmonson, 1993; Fretts, Schmittiel, McLean, Usher, & Goldman, 1995; J. P. Hansen, 1986; Jolly, Sebire, Harris, Robinson, & Regan, 2000; Kenny et al., 2013).

However, other studies have found no or limited evidence of increased risks of adverse pregnancy outcomes associated with advanced maternal age (Barkan & Bracken, 1987; Berkowitz, Skovron, Lapinski, & Berkowitz, 1990; Carolan &

Frankowska, 2011; Cunningham & Leveno, 1995; Kirz, Dorchester, & Freeman, 1985). For example, while older mothers face higher risks of operative delivery (e.g., C-section) and morbidity (e.g., gestational hypertension), neonatal outcomes do not appear to be affected (Bianco et al., 1996; Ziadeh & Yahaya, 2001).

One potential reason why there is no general consensus about the risks associated with giving birth at advanced maternal ages is that the association may be changing over time. It has been argued, but not tested empirically, that mothers who give birth at an advanced age today face lower risks of poor neonatal outcomes than their counterparts two or three decades ago (Carolan, 2003).

There are several mechanisms through which the risks associated with giving birth at an advanced maternal age could have declined. First, the risks may be lower today than they were several decades ago because the socio-demographic characteristics of older mothers have changed. In a contemporary developed country like the UK, the geographical focus of this study, older mothers are, on average, a particularly advantaged subsection of the population, as they tend to be highly educated and employed in professional occupations (Bray, Gunnell, & Davey Smith, 2006; Goisis, 2015; Hawkes, Joshi, & Ward, 2004). Conversely, in the past a child who was born to an older mother was more likely than average to have been a higher order birth, and to have been born into a family that was large and relatively poor (Prioux, 2005). Because there were fewer socio-economic incentives associated with giving birth at older ages, older mothers were a more heterogeneous group in the past than they are today. Moreover, knowledge about the link between health behaviours during pregnancy and birth outcomes has improved considerably over time. For example, in the UK, as in many developed contexts, knowledge about the detrimental effects of

smoking during pregnancy and birth outcomes was not widespread until the 1970s. Thus, we expect that smoking during pregnancy has become more selective of disadvantaged and younger mothers (Fertig, 2010).

Second, the risks associated with giving birth at an advanced maternal age could have declined as a result of the changes in the medical and epidemiological contexts surrounding childbearing. The introduction of prenatal screenings has helped to reduce the number of negative birth outcomes associated with advanced maternal age (Myrskylä & Fenelon, 2012), as these screenings have made it easier to detect genetic abnormalities and identify problematic pregnancies in the early stages. There have been significant advancements in postnatal care as well. In the UK, for example, special baby care units were introduced in the 1960s, neonatal intensive care was introduced in the 1970s, and further technological and pharmacological advancements were made during the 1970s and 1980s (Dunn, 2006). Modern neonatal technology has contributed to the reduction in complications arising from poor health outcomes at birth (Hack, Klein, & Taylor, 1995). It therefore appears likely that these improvements in obstetric care have made the risks associated with giving birth at an advanced maternal age more manageable than they were in the past (Carolan, 2003). Moreover, overall improvements in medical practice and services may have helped to slow down the natural health deterioration and “reproductive ageing” processes. Thus, today’s older mothers may be healthier than they were in the past.

In sum, the association between maternal age and child health reflects a complex interaction between health and social processes, as illustrated in Figure 2. Over time, changes in the way an advanced maternal age is associated with these socio-demographic and health processes and in the context surrounding childbearing might

have resulted in systematic changes in the costs and benefits of giving birth at advanced ages. In this study, we aim to empirically test whether there have been secular changes in the socio-demographic and health (behaviours) of older mothers and thus in the association between advanced maternal age and giving birth to a LBW child.

Data

To examine the secular trends in the association between advanced maternal age and child health around the time of birth, we made use of four of the UK birth cohort studies¹ that cover individuals born in the UK over a 40-year time period. These surveys are longitudinal, but because our focus in this study is on the association between maternal age and child health at the time of birth, we include only the data collected in the first sweep. The focus of the analyses is on the cohort members' birth weight and their mother's age at birth.

1958 National Child Development Study (NCDS)

The 1958 NCDS is a nationally representative longitudinal cohort study of all children born (including stillborn) in England, Scotland, and Wales during one particular week of March 1958. The study has its origins in the Perinatal Mortality Survey, and later became known as the NCDS or the 1958 birth cohort study. The Perinatal Mortality Survey collected information on 17,416 babies. The birth survey was completed by a midwife who attended the delivery, and who interviewed the mother after the birth of

¹ The 1946 National Survey of Health and Development was not included in this study because of the selected characteristics of its sample (which excluded stillbirths, twins, and children born to unmarried mothers); the reduced level of covariates available for this cohort compared to the levels for the other cohorts; and the smaller sample size, which would have raised power issues in most of the analyses.

the cohort child. In the case of a stillbirth or a neonatal death, a clinical summary was also completed by the midwife and medical attendants. The response rate from the birth survey was 98.8%.

1970 British Cohort Study (BCS)

The 1970 BCS is a nationally representative longitudinal cohort study of all children born (including stillbirths) in England, Scotland, and Wales during one particular week of April 1970. The birth survey collected information on 16,571 babies. As in the NCDS, the birth survey was completed by the midwife who attended the birth, and was complemented with clinical information. The response rate for the birth survey was 95.9%.

1992 Avon Longitudinal Study of Parents and Children (ALSPAC)²

The ALSPAC is a longitudinal cohort study of children born in the county of Avon between April 1991 and 31 December 1992.³ The study targeted pregnant women who were living in the catchment area of the county of Avon (Boyd et al., 2013). The “eligible sample” consisted of 20,248 pregnant women, of whom 14,541 (71.8% of the eligible sample) were recruited. A total of 14,062 of these women had a live birth. Unlike the other cohort studies used in this study, the ALSPAC is not nationally representative. However, its inclusion in our analysis allows us to fill in a 30-year gap between the BCS and the MCS during which no nationally representative data were collected. The birth weight of each child is taken from obstetric records collected at

² Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees.

³ Please note that the study website contains details of all the data that are available through a fully searchable data dictionary which can be accessed on the following webpage: <http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/>

the time of birth. For ease of exposition, we refer to the ALSPAC as the 1992 cohort study, since the majority of the births in this sample occurred in 1992.

2001 Millennium Cohort Study (MCS)

The MCS is a nationally representative longitudinal cohort study of 19,244 children born in England, Scotland, Wales, and Northern Ireland in 2000-2001 (K. Hansen, 2008). It is the most recent representative cohort study collected in the UK. The first sweep was collected when the cohort children were around nine months old. In most cases, the main respondent was the cohort child's biological mother. Mothers' reports of birth weight tend to be reliable and in line with registration data (Tate, Dezateux, Cole, & Davidson, 2005). Throughout the analyses, we excluded cases in which the main respondent was not the biological mother. Selected wards were disproportionately sampled to over-represent areas of high child poverty, concentrations of ethnic minorities, and the three smaller countries of the UK (Scotland, Wales, and Northern Ireland). For this reason, weights were used in the analyses to rebalance the survey and to account for its complex structure. The response rate was 68%. For ease of exposition, we refer to the MCS as the 2001 cohort study, as the majority of the births in the sample occurred in 2001.

Measures

Our outcome is a binary variable indicating whether the cohort child was born low birth weight (LBW), which is defined as a birth weight below 2.5 kg. We chose this marker for three reasons. First, existing studies have shown that LBW is the most important determinant of neonatal and infant morbidity (Boardman, Boardman, Powers, Padilla, & Hummer, 2002), and, on average, that it appears to be an indicator

of the individual's chances later in life (Black, Devereux, & Salvanes, 2007; Figlio, Guryan, Karbownik, & Roth, 2014). Second, as many studies have shown that older women are more likely than younger women to give birth to a LBW baby (Aldous & Edmonson, 1993), birth weight is a relevant outcome given the scope of this study. Third, because birth weight data were collected in the four cohort studies, we are able to investigate the secular changes in the association between advanced maternal age and child health. Because we rely on LBW as a marker of chances later in life, stillbirths were excluded from the 1958 NCDS and the 1970 BCS samples.⁴ We excluded from the reference category children weighting more than 4.5 kg at birth as the later life outcomes for these children tend to be worse than outcomes of normal weight children (Van Lieshout & Boyle, 2011).⁵

In order to investigate the association between maternal age and LBW across cohorts, we have divided the mothers' ages at birth into six categories: under 20, 20-24, 25-29, 30-34, 35-39, and 40 and over. Throughout the analyses, 25-29 is used as the reference category since in all of the cohort studies this was the age group with the lowest prevalence of LBW. Because the social meaning of giving birth at this age is likely to have changed over time (Rindfuss & Bumpass, 1976), we replicated the analyses using 20-24 as the reference category which produces qualitatively similar results (see Appendix Figure A2). We define the mothers who gave birth at an advanced age as those aged 40 and above, as a large body of literature has indicated that the association between advanced maternal age and adverse birth outcomes becomes clinically relevant after this age threshold (Mills & Lavender, 2011).

⁴ In the ALSPAC, stillbirths were included in the original sample, but birth weight was not recorded for them. In the MCS, stillbirths were not part of the sample.

⁵ Although the prevalence of macrosomia increases with maternal age at birth, the number of children weighting more than 4.5 kg was too small to be able to analyze this outcome separately.

Throughout the analyses, we consider an extensive set of covariates that are used (as discussed in the next section) first to describe the characteristics of the mothers by the age when they gave birth, and then to explore how their inclusion in regression models modifies the estimated association between maternal age and the risk of giving birth to a LBW child. The evidence suggests that the older mothers who gave birth recently had, on average, a higher socio-economic status and better health behaviours than the younger mothers (Carolan, 2003; Martin, 2004; McLanahan, 2004). However, we do not know whether this was true to the same extent or at all for the mothers who gave birth at advanced ages in previous decades. Conversely, we expect to find that the older mothers in all of the cohorts had more complicated pregnancies than the younger mothers. Again, however, it is unclear whether complications occurred to the same extent across cohorts. Maternal age is a marker of both socio-demographic and health characteristics, and the interaction between these two sets of characteristics might determine whether mothers who give birth at advanced maternal ages are at higher risk of giving birth to a LBW child (Goisis, 2015). In other words, the social advantages of older mothers might compensate for or even outweigh the health risks associated with advanced age (Stein & Susser, 2000). For this reason, we analyse both the socio-demographic and health characteristics of mothers based on their age when they gave birth. Some of the covariates are identical or highly similar across the cohorts (e.g., social class), others are measured differently (e.g., the mother's education), and others have been collected in some of the cohorts and not in others (e.g., information on complications during pregnancy was collected in the MCS only). For each cohort study, we use all of the available and relevant variables. The variables are listed in Table 1.

We considered including additional covariates. For example, we adjusted for the region of residence as it might have captured variation in the quality of health services available where the mother gave birth, but the results were largely unchanged. Adjusting for mother's ethnicity in the MCS (in the other cohorts, the samples were predominantly white) also did not change the results.

Statistical analyses

The first step consists of comparing the socio-demographic characteristics, the health behaviours, and the health characteristics of the mothers by their age when they gave birth in the four cohort studies. The aim of this step is to show whether and how the profiles of the mothers who gave birth at advanced ages changed over time.

Next, in order to analyse the association between advanced maternal age and LBW, we estimate a series of logistic regression models. Since some of the variables had missing values, we have used multiple imputations to create 20 filled-in datasets for each birth cohort using the multivariate imputation by the chained equation method in Stata 13. Appendix Table A1 shows the sample size increase we obtain by imputing the datasets. The results on the non-imputed dataset are qualitatively similar. We impute all of the variables with the exception of the dependent variable (LBW) and birth order. We could not impute birth order since some of the regression models were run on first-order births only. Using the imputed datasets we estimate, for each birth cohort separately, a series of models that include varying sets of covariates. Analyses for the MCS are conducted using sample weighting and accounting for the complex survey design. All analyses are conducted in Stata 13.

We begin by exploring the association between maternal age and LBW using a sample including all birth orders. We estimate four model specifications, illustrated in equations (1) to (4):

$$(1) \quad \text{Logit}(Y) = \alpha + \beta_1 \text{MAB} + \beta_2 \text{CHILDDDEM}$$

$$(2) \quad \text{Logit}(Y) = \alpha + \beta_1 \text{MAB} + \beta_2 \text{CHILDDDEM} + \beta_3 \text{BIRTHORD} + \beta_4 \text{MATSOCIODEM}$$

$$(3) \quad \text{Logit}(Y) = \alpha + \beta_1 \text{MAB} + \beta_2 \text{CHILDDDEM} + \beta_3 \text{BIRTHORD} + \beta_5 \text{MATHEALTH}$$

$$(4) \quad \text{Logit}(Y) = \alpha + \beta_1 \text{MAB} + \beta_2 \text{CHILDDDEM} + \beta_3 \text{BIRTHORD} + \beta_4 \text{MATSOCIODEM} \\ + \beta_5 \text{MATHEALTH}$$

where Y is child health (LBW), MAB are categories of maternal age at birth (maternal age 25-29 is the reference category), CHILDDDEM are cohort members' basic demographic characteristics (sex, multiplicity), BIRTHORD is the cohort member birth order in the family, MATSOCIODEM are the mothers' or the families' socio-demographic characteristics (e.g., level of education, marital status at the time of birth), and MATHEALTH is the mothers' health before or during pregnancy (e.g., previous miscarriages, C-section delivery). Model 1 is the baseline model. Model 2-4 include an adjustment for the child's birth order, which is not included in Model 1 since a large family size could be a marker for low socio-economic status in the family. In Model 2 we adjust for the mothers' or the families' socio-demographic characteristics, and in Model 3 we adjust for the mothers' health before or during pregnancy. Finally, Model 4 is a fully adjusted model. The models that include adjustments for covariates are only partially comparable across cohorts, since in each study we adjust for a different set of covariates and there might be differences within the same family characteristics across cohorts.

As a second step, we estimate the models on first-order births only. We estimate the same four models, although this time we do not control for birth order. Although excluding higher-order births comes at the cost of sample size, first-order births represent an important subsample. Existing studies have shown that the negative association between advanced maternal age and child health is particularly pronounced for first-order births (Lisonkova, Janssen, Sheps, Lee, & Dahlgren, 2010). Moreover, among the more recent cohorts the mothers who gave birth to their first child at an advanced age are likely to be particularly selected and advantaged (Martin, 2004), and their characteristics may have more than compensated for the increased health risks associated with giving birth at an advanced age. Therefore, if a secular decline in the association between advanced maternal age and LBW exists, we expect to find that it is more pronounced for first-order births than for all births.

Finally, in order to directly measure differences over time, we combine the data for the 1958 NCDS and the 2001 MCS studies (i.e., the least recent and the most recent birth cohorts), and estimate a pooled model that includes the baseline variables, as well as the interactions of the baseline variables with the MCS indicator variables. The pooled model enables us to estimate the coefficient and the statistical significance of the interaction of the 40+ age group with an MCS indicator. As with the analyses on each birth cohort separately, we obtain estimates for a sample that includes all order births, and for a second sample that includes first-order births only. Details on the pooling procedure are discussed in the Appendix.

Results

Descriptive associations

Figure 3 shows the unadjusted U-shaped association between LBW and maternal age by birth cohort for all births. The pattern we observe among young mothers is in line with our expectations given the socio-economic disadvantages of this group (McLanahan, 2004). The higher rates of LBW we observe among older mothers are consistent with the medical literature on the adverse health outcomes of fertility postponement (Nwandison & Bewley, 2006). The pattern for first births is qualitatively similar, but with some inconsistencies in the shape of the association, which may be due to the small sample size (Appendix Figure A1). Appendix Table A2 and A3 show how socio-demographic characteristics, health behaviours and health varied across maternal age categories across cohorts. Figures 4-6 show the results for selected indicators. Consistent with expectations, we find that the older mothers who gave birth in 1992 and 2001 were more advantaged than the younger mothers. For example, Figure 4 shows that among the mothers who gave birth in 1958 and 1970, the percentage of older mothers who belonged to a household of a high social class was lower than that of the mothers who gave birth in their mid-twenties. The reverse was true for the mothers who gave birth in 1992 and 2001. The results for other socio-economic indicators are qualitatively similar. For example, while, on average, in all of the cohort studies the older mothers were more likely to have been married when they conceived or gave birth than the younger mothers, the differences between the older and the younger mothers were much more pronounced in the more recent cohorts (see Appendix Table A2).

Figure 5 shows that there was no age gradient in smoking during pregnancy among the older cohorts, whereas the older mothers who gave birth in 1992 or 2001 were far less likely to have smoked during pregnancy than the younger mothers. The percentage of the mothers who used antenatal care for the first time after 12 weeks of pregnancy declined steadily across the cohorts (Appendix Table A2); on average, the older mothers were more likely than the younger mothers to have used antenatal care early in all of the cohorts. This pattern is not, however, entirely monotonic, as the mothers in the oldest age group were marginally less likely to have used antenatal care early than the mothers in the middle-aged group. However, the age gradient is clearer when we look at first births only. In the 1992 and 2001 cohorts, the older mothers were more likely than the younger mothers to have been drinking heavily during pregnancy, although the differences in 2001 were smaller than they were in 1992 (Appendix Table A2).

The results suggest that across the cohorts, the differences in the profiles of the mothers who gave birth at ages 40 and above and those of the mothers who gave birth in their early/mid-twenties grew, and became increasingly associated with socio-economic advantages and better health behaviours during pregnancy. In addition, the secular changes in the profiles of the older mothers appear to be more pronounced when we look at the characteristics of first-time mothers (Appendix Table A2).

Figure 6 shows the results for C-section deliveries. On average and in all of the cohorts, the older mothers were more likely than the younger mothers to have had a C-section delivery. Additional results (Appendix Table A3) also show that older mothers were more likely to have experienced stillbirths/miscarriages and

complications during pregnancy.. These results suggest that in all of the cohorts the older mothers were at higher risk of complications during pregnancy and delivery.

Table 2 shows marked changes in the distribution of all births and first-order births by maternal age categories. The percentage of births to mothers under age 20 remained fairly stable across the birth cohorts, while the percentage of births to mothers aged 20-24 halved. As expected, important changes occurred in the distribution of births at older maternal ages. The percentage of births (first births in particular) at ages 30-34 and 35-39 increased across birth cohorts. For example, 3% of first births in 1958 were to mothers aged 35-39, compared to 9% in 2001. The percentage of all order births to mothers aged 40 or older remained fairly stable across the birth cohorts but it increased for first-order births. These changes across cohorts reflect the process of childbearing postponement documented in the UK and other European countries since the 1970s (Sobotka, 2004).

Table 2 also shows that the overall prevalence of LBW babies who were born alive remained fairly stable across birth cohorts. This may be because (very) LBW children have higher survival rates today than they did in the past (Hack et al., 1995). This suggests that the more recent cohorts (1992 and 2001) include LBW children who were excluded in the less recent cohorts (1958 and 1970).

Regression results

Figure 7 shows the odds ratios for low birth weight among mothers aged 40 and above, relative to the ratios among mothers aged 25-29, from Model 1 (the baseline Model). Table 3 shows the parameter estimates (with 95% confidence intervals) for

mothers aged 40 and above for Models 1-4 for all births and for first-order births. Appendix Table A4 and A5 show the full model results.

As we can see in Figure 7, Model 1 (baseline model) for all births and first-order births shows a secular decline in the association between advanced maternal age and LBW. Appendix Figure A2 shows very similar results when maternal ages 20-24 are used as the reference category. It is worth highlighting that although the data enables us to cover a 40-years period, there is a large gap between the 1970 and 1992 cohort studies. This might explain why we don't always observe smooth transitions across the different surveys.

Table 3 shows that for all order births in Model 1 the mothers who were aged 40 and above at the time of birth in the 1958, 1970, and 1992 cohort studies had significantly higher odds of giving birth to a LBW child than the mothers in the reference category (25-29). The mothers who gave birth in the 2001 cohort had higher odds of having a LBW child, but the odds ratio was smaller than the odds ratio in the other cohort studies, and was not statistically significant. Although the secular decline is not monotonic, since the odds ratio of the 1992 cohort study is above the odds ratios of the 1958 and 1970 cohort studies, in the former the parameter is only significant at the 10% level while in the latter at the 1% level. Model 1 results for first-order births reveal that the mothers who were aged 40+ when they gave birth to their first child in 1958 had significantly higher odds of having a LBW child than the mothers in the reference category (25-29). The mothers who were aged 40+ when they gave birth in 1970 had higher odds of having a LBW child than the mothers aged 25-29, but the differences are not statistically significant, which could be because the small number of first births at ages 40+ result in an imprecise estimation of the parameters. The

mothers who were aged 40+ when they gave birth in 1992 or 2001 did not have significantly higher odds of having a LBW child than the mothers in the reference category. As we expected, the secular decline is more pronounced when we look at first-order births only. As we can see in the descriptive results, the mothers who gave birth to their first child at an advanced age in 1992 and 2001 are particularly selected and advantaged, and their characteristics could more than compensate for the increased health risks associated with giving birth at an advanced age.

The upper part of Table 3 shows how the odds ratios for all order births among the mothers aged 40+ changes when we adjust for socio-demographic and health characteristics. The results for Model 2 show that the adjustment for socio-demographic characteristics (variables listed in Table 1) results in opposite changes for the mothers in the 1958 and 1970 studies on the one hand, and for the mothers in the 1992 and 2001 cohort studies on the other. The odds ratio decreases among the mothers aged 40+ of the 1958 and 1970 cohort studies. In contrast, among the mothers aged 40+ in the 1992 and 2001 cohorts studies, the odds ratio increases, and for the mothers in the 2001 study the odds ratio becomes statistically significant. The results for the 2001 cohort suggest that the secular decline in the association between advanced maternal age and LBW is at least partially explained by the more advantaged profile of the women who recently gave birth at an advanced maternal age. The results for Model 3 show that adjustment for health characteristics reduces the odds ratios in all of the birth cohorts to a similar extent. In particular, for the 1992 cohort study the odds ratio for the mothers aged 40+ is no longer statistically significant. This suggests that in this cohort the older mothers faced a higher risk of having a LBW child because of increased health complications that were not compensated for by the advantaged profiles of older mothers to the same extent as

they were in the more recent 2001 cohort. Conversely, after health variables are adjusted for in the 1958 and 1970 cohort studies, the odds ratios are reduced, but are still statistically significant. The results for Model 4 (fully adjusted for both socio-demographic and health characteristics) show that only the odds ratio for the mothers aged 40+ in the 1958 cohort is statistically significant. In the fully adjusted model, the secular decline is attenuated compared to Model 1, but not entirely eliminated. However, one has to be cautious in comparing the fully adjusted models across cohorts since they adjust for different set of covariates. For example, in the 2001 cohort study, we were able to adjust for pregnancy planning - which has been found to be a risk factor for LBW (Flower, Shawe, Stephenson, & Doyle, 2013). In contrast, this variable was not available in the older cohort studies but could be integral to the advanced maternal age/LBW association since some of the births at older ages could have been unplanned because of lack of contraception.

The lower part of Table 3 shows that the odds ratios for the mothers aged 40+ for first-order births changes when the socio-demographic and health characteristics are adjusted for. The adjustment for socio-demographic variables results in a small increase compared to the baseline model of the odds ratio for the mothers aged 40+ in the 1958 cohort; for these mothers in the 1970 cohort, the odds ratio decreases compared to the baseline model. For the mothers aged 40+ in the 1992 and 2001 cohort studies, the odds ratios increases. However, for the mothers aged 40+ in the 2001 study, the odds ratio for first-order births, unlike for births of all orders, does not reach statistical significance and the levels observed in the unadjusted model of the older cohorts. The remaining differences can be attributed to the mothers' unobserved characteristics and/or changes in the medical context surrounding childbearing (e.g., introduction of prenatal screening and pharmacological advancements for treating

complicated pregnancies). Adjustments for health variables produce changes similar to those observed for all order births, since in all of the cohort studies they attenuate the association between giving birth at an advanced maternal age and the odds of having a LBW child. In the 1992 and 2001 cohort studies, the odds ratio for the mothers aged 40+ become smaller than one. The odds ratios for the mothers aged 40+ in Model 4 (fully adjusted) are lower compared to the baseline values, but the secular decline is not eliminated or reduced.

The results suggest that the increased odds of having a LBW child among the mothers aged 40+ in the older cohorts are at least partially (1958 cohort) or entirely (1970 cohort) explained by their relatively high health risks and their socio-economic profiles, which are not more advantaged than those of younger mothers. The results also indicate that in a contemporary context mothers who give birth at advanced maternal ages are at lower risk of giving birth to a LBW child than in the past, despite having a higher risk of pregnancy complications. This finding reinforces the hypothesis that the secular decline could be attributed to changes in mothers' characteristics and obstetric practices, which can compensate for and manage the health risks associated with giving birth at advanced maternal ages.

As a final step, we estimate the baseline model pooling data from the oldest (1958) and the most recent (2001) cohort studies. The aim is to directly compare differences across these cohorts and the secular change in the association between advanced maternal age and LBW. Appendix Table A6 reports the main coefficients of interest. The pooled model includes interaction terms between the 2001 cohort variable and the categorical maternal age variable. Of central interest is the estimate and the statistical significance of the interaction of the 40+ age group with the MCS indicator. The

exponentiated interaction coefficient estimate is a ratio of odds ratios, a factor by which the odds ratio corresponding to the 40+ age group changes when comparing the MCS to the NCDS. Appendix Table A6 reports both the 40+ odds ratio, as well as the modifier for the MCS. The results are in line with those in Figure 5. For all order births, the interaction term is substantially below one (0.80), but is statistically insignificant. When we look at first-order births only, we can see that the ratio of odds ratios is even smaller than the corresponding number for all order births (0.44), but again it fails to reach statistical significance. However, when we look at the results for first-order births with reference category 20-24, we observe differences that are statistically significant (exactly) at the 10% level.

Although the focus of this study is on mothers who gave birth at advanced maternal ages, we briefly comment on the results at young maternal ages. The unadjusted results show that mothers who gave birth at ages 20 and below experienced significantly higher odds of LBW compared to mothers who gave birth at ages 25-29 in all cohorts. However, the results show that the magnitude of this association has weakened across cohorts. On one side, these findings are consistent with the descriptive results showing that the young mothers group has remained a relatively disadvantaged subgroup of the population across the cohorts. On the other side, the fact that the magnitude of the association has decreased over time could be attributed to changes in medical and obstetric practices from which mothers of all ages have benefited.

Sensitivity analyses

Because comparing logit coefficients across model specifications and cohorts can be misleading (Mood, 2010) we also estimated linear probability models. The results in Appendix Table A7 show a consistent story. We also replicated the analyses using a continuous measure of birth weight and using maternal age continuous (rather than categorical). The results, available upon request, show a qualitatively similar story compared to the main results of the paper. Since the proportion of multiple births has increased across cohorts (Table 2), a pattern explained by medical advancements that have increased the survival rates in multiple pregnancies as well as an increase in the use of assisted reproductive technologies we replicated the analyses excluding the multiple births from all the cohorts. The results (available upon request) are qualitatively similar to the main paper results and they show a clear secular trend.

Conclusions

The association between maternal age and child well-being remains a highly controversial issue, as maternal ages at birth continue to increase across the developed world. The existing literature has not reached a consensus on the question of to what extent giving birth at advanced maternal ages should be avoided. In this literature and in the current debates, one issue that has not received attention until now is the question of whether the association between advanced maternal age and child well-being is systematically changing over time. A secular change in the association between advanced maternal age and child health may occur as a result of changes in the characteristics of older mothers, as well as of improvements in medical and obstetric practices. This study investigates the question of whether the characteristics of older mothers and, possibly as a consequence, the association between advanced

maternal age and LBW has changed over time. We analysed four large UK birth cohort studies, and found that, across successive cohorts, but particularly when the 2001 cohort was compared with the 1958 cohort, giving birth at an advanced maternal age (i.e., at age 40 or above) was less likely to be associated with giving birth to a low birth weight child. The secular decline in the association between advanced maternal age and birth weight was more pronounced for first-order births. In all of the cohorts older mothers tended to be more advantaged than their younger counterparts, but this gap widened considerably over successive cohorts. Still, in all of the cohorts studied, older mothers were at higher risk than younger mothers of having complicated pregnancies and deliveries.

Adjusting the association between advanced maternal age and low birth weight separately and then jointly for socio-economic characteristics and health of the mother proved to be helpful for understanding the process through which the association declined over birth cohorts. When we included in the models adjustments for the mothers' socio-demographic characteristics, the risk of low birth weight associated with advanced maternal age increased in the more recent cohort. This shows that an important mechanism through which the risk of low birth weight has declined among older mothers is that they have become more socio-economically advantaged over time, and this accumulation of social resources might offset the otherwise negative effect of advanced maternal age on birth weight. When we included in the models an adjustment for the mothers' health, the risk of low birth weight associated with advanced maternal age decreased in all of the cohorts. But the health-adjusted results in particular contribute to our conclusion that the increased health risks experienced by the mothers who gave birth at advanced maternal ages in the 1958 and 1970 cohort studies (and, to some extent, in the 1992 cohort study) – which were not compensated

for by the increased socio-economic status of the older mothers, as was the case in the more recent cohort – are important mechanisms for explaining the increased odds of having a LBW child among this group. Despite the fact that one cannot directly compare the fully adjusted results across cohorts since a different set of covariates were used in each cohort⁶ and the same variables could have different meanings across cohorts, a possible explanation for the remaining secular trend is that there were changes in the epidemiological context. Indeed, it is plausible to expect that having access to modern obstetric care could make the risks associated with giving birth at an advanced maternal age more manageable than they were in the past. Although the data do not allow us to test for the latter effects directly, we think it is reasonable to hypothesise that the explanation for the secular decline lies at the intersection of the changes in the mothers' characteristics and in the surrounding epidemiological context. In the UK, important advancements in antenatal care were introduced after the 1970s, and these improvements may have made it easier than it was in the past for women to manage the risks associated with giving birth at an advanced age. Changes in the epidemiological context have also made it more likely for very low birth weight children to survive and therefore to inflate the prevalence of LBW amongst mothers who give birth in the mid-late twenties (i.e. the reference category). Excluding VLBW children from the 2001 cohort study partially increases the association between advanced maternal age at LBW (results not shown), and hence the increased survival of VLBW children might have also contributed to make the maternal age/LBW association flatter in the more recent cohort.

⁶ For example, in the 2001 MCS cohort study we adjusted for whether the pregnancy was planned whilst this variable was not available in the earlier cohorts. Adjustment for this variable in the previous cohorts could potentially further attenuate the positive association between advanced maternal age and LBW – older childbearing could have been the result of unintended pregnancies due to lack of effective contraception.

This research has limitations. First, sample size issues meant that some parameters were not precisely estimated, especially in the analyses of first-order births. Nonetheless, the analyses of all births, which were less affected by problems with sample size, showed a secular decline in the association between advanced maternal age and LBW. It was not possible to account for gestational age, as this information was missing or not reliable in 10% and 18% of cases in, respectively, the 1958 and 1970 analytical samples used in this analysis. Moreover, since in the earlier cohorts ultrasound scans⁷ were largely not available, we expect that the measurement of gestational age varies across cohorts and in a way that would prevent us from meaningfully comparing this variable across cohorts. Nonetheless, LBW is considered an important marker of neonatal outcomes, as many existing studies have found that LBW, for both babies born preterm and at term, is associated with important markers measured at different stages of the life course (Black et al., 2007; Hack et al., 1995; Richards, Hardy, Kuh, & Wadsworth, 2001). Second, the ALSPAC 1992 cohort study is, in contrast to the other cohort studies, not nationally representative since based in the Avon region and the majority of participants were of White ethnicity. While validation studies have shown that ALSPAC has a shortfall of ethnic minority mothers, it only has a slight shortfall of more disadvantaged families and the mean birth weights are in remarkable accord with UK 1990 national estimates.⁸ Hence we expect that bias caused by the lack of national representativeness of ALSPAC is limited. Moreover, this cohort study enabled us to fill in a 30 years gap between the 1970 and 2001 cohort studies. Third, we were unable to establish to what extent secular changes in the association between advanced maternal age and LBW were

⁷ It was only during the 1970s that ultrasound use became an almost essential part of the care rendered to pregnant women and their fetuses.

⁸ <http://www.bristol.ac.uk/alspac/researchers/cohort-profile/representativeness/>

driven by changes in the overall epidemiological context. On one side, we can expect that improvements in medical and obstetric practice might have contributed to reduce the risks associated with giving birth at advanced maternal ages. On the other, there is evidence that the prevalence of gestational diabetes has increased across cohorts (Ferrara, 2007), a condition associated with higher birth weights. To reduce the possibility that our results could reflect these secular changes, we have excluded children weighting more than 4.5 kg at birth. Fourth, this study focuses on the UK only, and it is unclear to what extent the results are generalizable to other countries. We think it is likely that we would observe similar results in other developed countries in which the trends in the postponement of childbearing and the changes in the epidemiological context surrounding childbearing are similar to those in the UK. To overcome these limitations, it would be necessary to conduct similar analyses using different data, and for countries that have—and, importantly, for countries that have not—experienced improvements in the context. Finally, the most recent cohort was born in 2000-2002 and there is evidence that the percentage of mothers giving birth at advanced maternal ages has been increasing since then (ONS, 2011). While we expect that the social selection into advanced maternal ages has remained similar or has become more marked, women postponing to older maternal ages are increasingly often resorting to assisted reproductive technologies, which the literature finds to be associated with increased risks of poorer birth outcomes (Schmidt, Sobotka, Bentzen, & Nyboe Andersen, 2012; Sutcliffe & Ludwig, 2007). Therefore, we are unable to say whether the trends observed between 1958 and 2001 have continued, stabilized or potentially reversed. Additional analyses which excluded from the 2001 MCS children born through ART showed very similar results, which

could suggest that it is unlikely that the patterns would revert because of the increased use of ART.

Despite the limitations, these findings have implications that are relevant for both theory and research. First, the intersection of the changing selection into older maternal ages and the improvements in the context over time might modify the association between maternal age and child well-being. As a consequence, the direction and the strength of the association between maternal age and child outcomes are tied to a specific population and point in time. This indicates that studies that investigate the association between maternal age and child well-being must reflect on and situate the meaning of maternal age in the context, the groups, and the historical period under consideration; while paying particular attention to the selection process that underlies the individual differences in the timing of childbearing (Geronimus, 1996). Second, since the link between advanced maternal age and LBW has loosened over time, the children of older mothers are at lower risk of poor health outcomes today than they were 50 years ago. The results of study are informative not only from a demographic but also from a public health/medical perspective whereby the view has largely been that an advanced maternal age is one of the relevant risk factors for poorer birth outcomes (Bewley et al., 2005; Gynaecologists, 2009; Nwandison & Bewley, 2006). The results suggest that the balance of the costs and benefits of childbearing at older ages varies over time since it is tied to the characteristics of the groups who experienced it. Therefore, although an advanced maternal age should not be discarded as a risk factor for poorer birth outcomes, its relevance should be weighted since it is not static but rather shaped by the characteristics of older mothers and the surrounding epidemiological context. This argument is further supported by evidence showing that the negative association between having a low birth weight and

subsequent well-being has declined across cohorts (Goisis, Özcan, & Myrskylä, 2017). It therefore appears that, compared to previous generations, today's children of older mothers are not only less likely to be born LBW; when they are born LBW, the negative consequences are less severe.

This is the first study that has investigated how secular changes in the characteristics of older mothers are linked to the association between advanced maternal age and child health around the time of birth. This topic remains controversial, and our results suggest that the period under consideration might be an important source of variation between studies, which needs to be taken into account both before and after adjustment for covariates. Our results show that across successive birth cohorts, the association between advanced maternal age and low birth weight became progressively weaker, and is negligible, both statistically and substantively, for the most recent birth cohort. The decline in the association is at least partially explained by the socio-economic advantages of older mothers in the more recent cohorts. Moreover, the results suggest that if selection into older maternal ages had not changed in the more recent cohorts, an advanced maternal age would be likely to still be associated with a higher risk of LBW. Future research should enrich our understanding of these time trends by replicating the analyses of this study through the investigation of other markers of child outcomes, geographical contexts, and time periods.

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