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Multiple births mortality by maternal age at birth: A within-family analysis of Demographic and Health Survey data on 42 low-income countries

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Title

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Running title: Multiple births mortality by maternal age at birth

Abstract

Background: Existing evidence suggests that children from multiple-births experience lower infant mortality with advanced maternal age, in contrast to what is observed for singletons. The role of unmeasured confounding, and whether this observation is also present in low-income countries where the infant mortality is higher than in Western countries, remain unknown.

Methods: Using the Demographic Health Surveys data of over 6 million live births reported from 42 low-income countries, we applied mother fixed-effects in linear probability models with and without parity.

Results: The infant mortality (as well as neonatal mortality) was highest among the twin offspring of younger mothers. Compared to infants of mothers age 24-25 at delivery, the infant mortality was highest (0.14 [0.13, 0.15]) among offspring of mothers younger than 18 years of age, and declined by around 0.01 until a mother reaches her late 30s. The overall pattern was robust to adjustment for parity to the model and estimation without mother fixed-effects. Similar patterns hold in Southern Asia and sub-Saharan Africa, and across different developmental settings.

Conclusions: We observed a lower infant mortality among children from multiple births when the mothers were in the 30s compared to when mothers are in the mid-20s or younger also in low-income countries. Unlike previous findings, the lower mortality associated with advanced maternal age is visible from the mid-20s.

Key words

Multiple pregnancy; maternal age; twin; child mortality; demographic health surveys; low-income countries

Introduction

There is a persistent higher mortality among children of multiple births compared to singletons [2–4]. This is concerning due to the dramatic increase in twinning rates globally over the recent decade [1]. In sub-Saharan Africa, an unequal decline in under-5 mortality between 1995 and 2014 has resulted in the increased share of twins in total under-5 mortality [5]. The mortality gap is alarming, given that both relative and absolute number of twins is higher and likely to increase in sub-Saharan Africa, due to the changing maternal age structure and increasing population size. One well-known risk factor for early life mortality is advanced maternal age at birth [6–9]. The association between maternal age at birth and infant mortality is usually found to be linear or J-shaped. Higher mortality of children born at advanced maternal age has been generally attributed to the higher incidence of chromosomal[10] or congenital[11] abnormalities, gestational complications[6], and placental dysfunction[12] as women age, which all can negatively affect child health and survival. The increasing parity as maternal age increases may also contribute to the heightened early life mortality in children born to older mothers, though recent evidence suggests that it is the maternal characteristics associated with high fertility rather than parity per se that may underlie the 'parity effect' [9,13].

Somewhat unexpectedly, existing evidence including recent meta-analyses suggests that children of multiple births born to older mothers do not necessarily experience higher mortality than those born to younger mothers [15,16]. In a study drawing on all live births records from the United States between mid-1980s and mid-1990s, maternal age and infant mortality were inversely related among twins, with those born to young mothers experiencing the highest mortality rates [17]. The authors attributed the finding to the higher risks of injuries or suboptimal care among relatively inexperienced younger mothers. More generally, multiple pregnancy could be particularly more challenging for younger mothers, who already face stronger reproductive trade-offs due to both biological and sociocultural constraints in resources available for optimal birth outcomes [18]. Another explanation highlights the possibility that multiple-birth mortality is actually lower at advanced maternal age compared to younger age. Specifically, based on the evolutionary theory, the terminal investment hypothesis suggests the adaptive value of allocating more maternal resources to multiple pregnancies when the chance of future reproduction is lower (e.g., advanced maternal age) [19]. Propensity for multiple pregnancy increases with maternal age even in spontaneously conceived pregnancies, a likely by-product of natural selection for

polyovulation towards the end of reproductive lifespan [20]. Twins born to older mothers also do not appear to be at higher risk of adverse neonatal outcomes [15,16] and of mortality across the lifespan [21,22], although the risk of obstetric complications may be high[23]. These observations are suggested as evidence of terminal investment, in the form of more multiple births and favorable outcomes therein, as maternal age becomes older.

However, it is currently unclear if the previous findings of lower mortality in multiple births born to older mothers are directly attributable to maternal age effect. First, existing evidence is based on studies that do not adequately adjust for common confounders, such as the method of conception and other maternal characteristics. For example, the chance that a woman gives birth to a twin is positively correlated with the indicators of better maternal health and prenatal environment [24]. It is thus possible that healthier mothers are selected into giving twin births at older age. Twins born to older mothers may also benefit from medical care that prevents adverse outcomes associated with twin pregnancies, if women of higher socioeconomic position delay childbearing and are more represented in the group of women giving twin births at older age. Second, most studies are based on data from high-income countries [15,16] where the twinning rate has increased dramatically with the uptake of *in vitro* fertilization (IVF) [25]. Since the use of IVF is higher among older mothers, any associations between maternal age and the mortality of multiple births can be further confounded by potential consequences of using assisted reproductive technology. Third, available studies did not examine the full maternal age distribution in relation to the early mortality of multiple births, and instead compared mortality from mothers older than certain age threshold (usually 35) to that from younger mothers. Doing so can underestimate the mortality risks associated with the far ends of maternal age continuum.

The present study aims to clarify whether advanced maternal age is associated with higher infant mortality among children of multiple births. We examine mortality outcomes of the siblings by applying mother fixed-effects (also known as sibling fixed-effects), to address the possible confounding by factors that are unobserved and largely consistent within mothers. These factors could include genetics, ethnicity, religion, and socio-economic characteristics, which comprise largely constant differences between mothers and could correlate both with the chance of multiple births and with offspring survival at advanced maternal age. We use Demographic Health Surveys (DHS) data from 42 low-income countries, where infant mortality

rates (IMR; number of children dying within the first year of life per 1,000 births) are currently amongst the highest[28] and where twinning rates are high, particularly in sub-Saharan Africa[1].

Materials and methods

Study population

The DHS is a household survey on a nationally representative sample of women aged 15-49 years old. The survey has been conducted several times depending on countries, and here we used 256 surveys conducted between 1986 and 2022. To minimize the possibility that multiple births observed in the data are attributable to the use of IVF, we excluded South Africa and all births after 2000 from India, based on the literature suggesting relatively active uptake of IVF in those countries [29,30]. From the birth histories data of DHS, we took 6,480,038 live births reported to have occurred within 10 years from the time of interview to 1,765,489 women. From here, 1,418,362 mothers contributed at least two cases of live births, a prerequisite for mother fixed-effects models (see below). Consequently a total of 6,132,911 births were eligible for the present analysis.

Each child was classified as being the result of a singleton or multiple birth. Vast majority (98%) of multiple births were twins. Although the DHS data does not distinguish monozygotic from dizygotic twins, the variation in twinning rates is largely driven by dizygotic twinning. Monozygotic twinning rates are constantly low at 3-4 per 1,000 deliveries across populations [31]. About 4.4% of mothers in the sample ever gave a multiple birth, and 90.5% of them gave a twin birth once.

Variables

Infant mortality, defined as death during the first year of life, was defined by maternal report through the surveys. [32]. We also examined neonatal mortality (the rate of children dying within the first month of life) to compare if its relation to maternal age at birth is similar to that with infant mortality. Our analytic sample excluded children who were born within 12 months (or 1 month) from the survey, as we cannot be certain about their survival status at the first year (or first month) of life, depending on which early life mortality outcome used. Finally, each child was paired with the information on maternal age at birth (<18 years, 2-year intervals from 19 until 40, >40 years), and parity (1, 2, 3, 4, and 5 or more). Children within one multiple birth were randomly assigned to the ascending number of parity, e.g., parity of 2 and 3 for each

siblings from a twin born after a first child who is singleton. This way, each child rather than each bout of childbearing is assigned a unique parity number. Another way of assigning the same parity number to all children within one multiple birth did not change our main findings, likely because multiple births are rare anyway.

Statistical analyses

Given the low prevalence of multiple births, we pooled data across countries to estimate the association between maternal age at birth and risk of infant mortality. We estimated linear probability models (LPM), which, compared to logistic regression models, produces more accurate estimates and predicted probabilities that are closer to the observed distribution in case of rare binary events [33]. Coefficients from LPM also allow direct comparison between models estimated from different groups, a task we sought to do in supplementary analyses (see below). Although average marginal effects from logistic regression may be comparable across models, such comparison requires care when unobserved continuous response is of particular interest [34] as in our case.

$$y_{ij} = \beta_1 MAB_{ij} + \beta_2 Multiple_{ij} + \beta_3 MAB_{ij} \times Multiple_{ij} + \beta_2 Birth\ Order_{ij} + \alpha_j + \varepsilon_{ij},$$

where the dependent variable y_{ij} is infant mortality (or neonatal mortality) status of a child *i* of mother *j*, and can take a value of either 1 ("dead") or 0 ("survived".) The main independent variable is maternal age at the birth (MAB) of child *i* of mother *j*. Since the current literature suggests that the implication of maternal age at birth on early mortality differs between singletons and multiple births, we estimate the maternal age effect separately if a child is born as a singleton or as one of a multiple birth ($Multiple$). Birth order of child *i* of mother *j* was included as a control, as parity positively covaries with maternal age at birth especially in high-fertility settings. The error term is partitioned into a mother-specific term (α_j) and a individual child-specific term (ε_{ij}), such that children born to the same mother are compared with each other. In this way, the mother fixed-effects method allows us to effectively control for unobserved, time-invariant differences between mothers that correlate with the chance of giving a multiple birth at older age, such as genetic and physiological characteristics, as well as socio-economic and cultural backgrounds that operate at both micro- (e.g., lifestyle and health

behaviors, religion) and macro-levels (e.g., region, country) and underlie consistent differences in health and reproductive behaviors between mothers. Mother fixed-effects also adjust for the shared propensity for early life mortality (shared 'frailty') among children born to the same mother. We first specified Model 0 with only maternal age at birth and expanded it into Model 1 with parity added. Given the aim of this study to better understand maternal age effect, Model 1 that adjusts for parity is our preferred model. To see how the sibling fixed-effects make differences in maternal age effect, we also estimated ordinary least squares (OLS) as supplementary analyses.

We conducted four sensitivity checks, the first three of which were based on the same regression formula introduced above. First, we stratified the pooled sample by geographic regions – Sub-Saharan Africa and Southern Asia – to examine heterogeneous maternal age effects given the known differences in overall early mortality rate and the distribution of maternal age by regions [27]. Second, we stratified the pooled sample by national infant mortality rate (IMR) below 60, between 60 and 90, and above 90, to investigate if maternal age effects change as living standards and life expectancy improve. This exercise seeks to partly circumvent the challenge of distinguishing maternal age effect from period effect when estimating mother fixed-effects models[35]. The IMR data matched to each country in a given birth year was taken from the World Bank database. Third, we restricted the sample to 6,716 mothers who gave multiple births at least twice. This is to better approximate a within-mother comparison, which, given the rarity of multiple births, can be difficult even with the sibling comparison approach. Finally, we examined the composition of sibling deaths within the sample of multiple births. Specifically, we examined mortality risks by maternal age across different compositions of sibling deaths ("all dead", "some survived", and "all survived"), to better understand if maternal age exerts different impact on sibling deaths composition within multiple births. Since the outcome here is not binary but multiple, we used multinomial regression, in which we tested if moving between maternal age categories will make the risks of being in "some survived" (or "all dead") vs. "all survived" any different.

Results

Table 1 provides the country-level characteristics of key demographic variables examined in this study during the observed period (ranging between 1965 and 2020). Infant mortality rate (IMR) in 2020 varied across the studied countries, lower in most of the Southern Asian countries

(except for Pakistan) compared to sub-Saharan African countries. Although twinning rate also exhibits a considerable country-level variation, the rate is generally low, with more than 10 multiple births per 1,000 childbirths (or deliveries) in Sub-Saharan African countries, in comparison to below 10 in Southern Asian countries. In the global 'hot-spot' of twinning of West African countries, twinning rate is around 20 with the highest value of 24.4 observed in Benin according to the current data. Maternal age at birth in the analytic sample was on average 24.5 (Inter-quartile range: 19.9-28.3) years, with most births observed during early to mid-20s in all studied countries (Figure 1).

Table 1. Demographic characteristics of the analytic sample.

Country	Number of births	IMR [1] in 2020	Twinning rate[2]	Proportion of births in each maternal age category												
				<18	18-19	20-21	22-23	24-25	26-27	28-29	30-31	32-33	34-35	36-37	38-39	39>
Afghanistan	125715	44.8	9.4	0.103	0.111	0.134	0.133	0.119	0.101	0.084	0.066	0.052	0.039	0.027	0.016	0.015
Angola	42002	48.7	15.5	0.148	0.123	0.125	0.114	0.102	0.090	0.076	0.063	0.050	0.042	0.029	0.020	0.019
Bangladesh	295457	24.1	7.6	0.236	0.155	0.143	0.122	0.098	0.077	0.058	0.042	0.029	0.018	0.011	0.006	0.004
Benin	188994	56.6	24.4	0.113	0.108	0.124	0.126	0.118	0.101	0.086	0.068	0.053	0.040	0.028	0.017	0.017
Burkina Faso	189243	53	16.0	0.101	0.117	0.130	0.122	0.110	0.097	0.082	0.069	0.055	0.043	0.031	0.021	0.021
Burundi	81825	38.8	12.2	0.052	0.086	0.119	0.127	0.125	0.110	0.097	0.081	0.066	0.051	0.037	0.024	0.025
Cameroon	166542	48.5	19.3	0.150	0.125	0.128	0.123	0.108	0.094	0.077	0.061	0.048	0.035	0.023	0.015	0.013
Central African Republic	16936	77.2	13.3	0.162	0.126	0.130	0.118	0.106	0.088	0.076	0.059	0.046	0.035	0.023	0.015	0.017
Chad	116176	67.6	14.3	0.170	0.122	0.123	0.119	0.107	0.091	0.075	0.060	0.046	0.035	0.024	0.015	0.013
Comoros	19410	40.4	21.6	0.123	0.098	0.116	0.118	0.115	0.103	0.088	0.075	0.058	0.044	0.029	0.017	0.016
Congo Brazzaville	48635	32.9	20.4	0.146	0.127	0.124	0.117	0.105	0.091	0.075	0.065	0.049	0.039	0.028	0.017	0.016
Cote D'Ivoire	100635	57.5	19.2	0.146	0.117	0.123	0.118	0.107	0.092	0.080	0.064	0.050	0.039	0.028	0.018	0.017
Eswatini	11410	44.2	14.0	0.150	0.144	0.136	0.117	0.109	0.088	0.070	0.059	0.046	0.033	0.024	0.015	0.010
Ethiopia	170987	35.4	11.4	0.139	0.115	0.125	0.121	0.111	0.095	0.080	0.064	0.051	0.039	0.026	0.017	0.016
Gabon	39987	29.8	17.3	0.179	0.136	0.128	0.111	0.096	0.085	0.069	0.058	0.046	0.036	0.025	0.017	0.015
Gambia	26601	34.9	13.8	0.133	0.115	0.123	0.122	0.112	0.097	0.081	0.064	0.049	0.039	0.027	0.018	0.020
Ghana	114026	33.5	18.7	0.109	0.109	0.121	0.118	0.112	0.098	0.086	0.070	0.057	0.044	0.032	0.021	0.022
Guinea	106628	65.4	19.2	0.159	0.112	0.115	0.112	0.107	0.092	0.080	0.064	0.052	0.041	0.028	0.019	0.020
India	1193882	26.8	6.1	0.155	0.156	0.175	0.161	0.126	0.091	0.060	0.035	0.019	0.010	0.006	0.003	0.002
Kenya	278003	29	13.8	0.122	0.121	0.136	0.130	0.115	0.098	0.079	0.063	0.049	0.035	0.024	0.015	0.014
Lesotho	40847	58.4	13.9	0.084	0.138	0.155	0.138	0.116	0.093	0.076	0.061	0.047	0.035	0.026	0.017	0.016
Liberia	94956	58.2	19.2	0.159	0.123	0.123	0.112	0.102	0.087	0.075	0.062	0.051	0.039	0.028	0.020	0.021

Madagascar	157567	45.3	10.0	0.144	0.123	0.129	0.121	0.108	0.093	0.077	0.061	0.048	0.037	0.026	0.017	0.016
Malawi	233009	32.1	19.1	0.139	0.138	0.139	0.126	0.106	0.089	0.072	0.057	0.045	0.034	0.024	0.016	0.017
Maldives	34058	5.5	7.4	0.085	0.114	0.148	0.151	0.128	0.107	0.085	0.063	0.047	0.032	0.020	0.011	0.008
Mali	217902	63	15.2	0.147	0.118	0.122	0.116	0.107	0.093	0.079	0.063	0.051	0.040	0.028	0.018	0.018
Mozambique	101179	52.5	17.0	0.163	0.126	0.128	0.118	0.104	0.087	0.073	0.058	0.046	0.036	0.025	0.016	0.019
Namibia	65930	30	12.8	0.100	0.116	0.129	0.125	0.113	0.100	0.083	0.069	0.055	0.041	0.030	0.020	0.020
Nepal	164761	23.6	6.8	0.106	0.144	0.163	0.152	0.125	0.096	0.071	0.051	0.036	0.025	0.015	0.009	0.007
Niger	131290	59.9	15.2	0.160	0.122	0.124	0.117	0.106	0.090	0.076	0.061	0.048	0.038	0.026	0.018	0.016
Nigeria	402900	72.3	17.3	0.134	0.106	0.116	0.117	0.112	0.098	0.085	0.068	0.055	0.042	0.029	0.019	0.020
Pakistan	167151	54.4	9.5	0.079	0.097	0.127	0.136	0.131	0.115	0.096	0.074	0.055	0.039	0.024	0.015	0.013
Rwanda	170631	30.4	12.4	0.033	0.069	0.112	0.134	0.133	0.120	0.103	0.085	0.068	0.052	0.038	0.025	0.026
Sao Tome & Principe	7620	12.8	19.1	0.106	0.141	0.141	0.130	0.108	0.092	0.071	0.061	0.048	0.035	0.029	0.019	0.019
Senegal	301659	30	15.4	0.115	0.107	0.121	0.121	0.112	0.098	0.085	0.069	0.056	0.043	0.031	0.020	0.020
Sierra Leone	109071	80.5	17.0	0.159	0.117	0.120	0.116	0.108	0.093	0.077	0.062	0.050	0.039	0.025	0.017	0.018
Sri Lanka	17705	6	9.1	0.063	0.088	0.126	0.142	0.140	0.121	0.102	0.080	0.056	0.039	0.022	0.012	0.008
Tanzania	203882	34.9	16.9	0.115	0.125	0.132	0.124	0.109	0.094	0.078	0.064	0.052	0.040	0.029	0.019	0.020
Togo	63315	44.5	21.1	0.103	0.104	0.119	0.122	0.115	0.102	0.088	0.071	0.056	0.044	0.032	0.020	0.023
Uganda	178841	32.1	14.5	0.142	0.129	0.135	0.124	0.109	0.091	0.075	0.059	0.046	0.035	0.025	0.015	0.015
Zambia	179745	41.1	16.9	0.136	0.134	0.135	0.121	0.106	0.089	0.074	0.060	0.048	0.037	0.026	0.017	0.017
Zimbabwe	102925	36.6	16.3	0.114	0.136	0.144	0.131	0.114	0.093	0.075	0.060	0.046	0.034	0.024	0.015	0.014

1: Number of children dying within the first year of life, per 1,000 births. Taken from the World Bank database.
2: Number of multiple births, per 1,000 deliveries

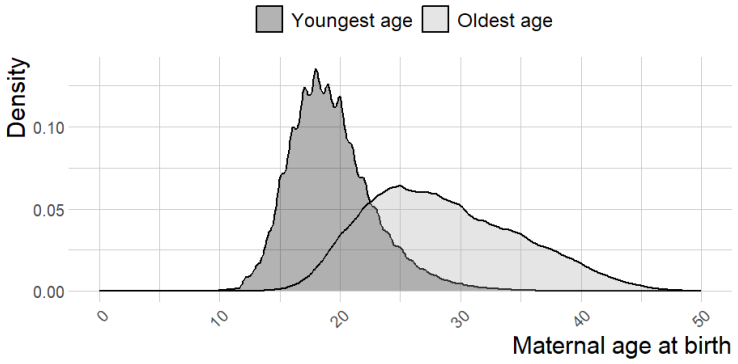

Figure 1. Maternal age at birth, one for the youngest age and the other for the oldest age within mothers. Each mother contributes at least two observed bouts of reproduction to our analytic sample, so that mother fixed-effects can be estimated. As such, for example, a mother can contribute one birth that occurred when she was 21 and the other that occurred when she was 35.

Figure 2 summarizes results from the mother fixed-effects models (Model 1). The results show that the association between maternal age at birth and early mortality differs between

children of multiple births (solid lines) and singletons (dashed lines). Children of multiple births (solid lines) are at the highest risk of early mortality if a mother was younger than 24-25 years old. For example, the probability of dying within a year steadily increased with decreasing maternal age, and was 0.013 [95% CI: 0.007, 0.018] if the mother was 22-23 years, 0.038 [95% CI: 0.032, 0.043] if the mother was 20-21 years, 0.078 [95% CI: 0.067, 0.079] if the mother was 18-19 years, and 0.14 [95% CI: 0.13, 0.15] if the mother was below 18, as compared to children of women age 24-25 years of age. However, after the reference age of 24-25, the probability of dying is lower by around 0.01 until a mother reaches her late 30s and beyond, when mortality is no longer different from that of the reference age group. In contrast to multiple births, the early mortality of singletons (dashed lines) showed a modest j-shaped relationship with maternal age, with a slightly heightened risk among offspring of mothers below 18. Lastly, the maternal age pattern for infant mortality (black line) is similar for neonatal mortality (grey line), except that the discrepancy in mortality between multiple births and singletons is larger for infant mortality (average mortality is lower in singletons by -0.222 [95% CI: -0.227, -0.217] for infant mortality compared to -0.168 [95% CI: -0.172, -0.165] for neonatal mortality).

We find an overall similar maternal age pattern in mother fixed-effects models without adjusting for parity (Supplementary Table S1) and the OLS results (Supplementary Table S2). In the former, absolute values of the estimates are larger if parity is not included, suggesting that the association between maternal age and early life mortality is partly explained by parity effect. In the subsample of women with at least two bouts of multiple births, the maternal age pattern for infant mortality indicates a clear increase of infant mortality as women are younger than 24-25 years and an overall lower infant mortality if maternal age at birth is older than 24-25 years (Supplementary Table S3).

In our analytic sample, which is restricted to women having had at least two births, the spread of births in terms of maternal age at birth is approximately 10 years within mothers, such that the youngest and oldest ages at birth are on average 19.3 and 28.6 years respectively (Figure 1, Supplementary Materials 4). For example, 67% of the women had given at least one birth before and after age 25. In the subsample of women whose youngest birth was before 25 and oldest birth was after 30, the association between maternal age and infant mortality in multiple births is similar (Supplementary Table S4) to the one identified from the pooled sample.

The pattern observed from the main/combined analysis was generally consistent when the sample was stratified by Southern Asian and Sub-Saharan countries (Figure 3 top) and by national IMR levels (Figure 3 below). That is, infant mortality was lower for children of multiple births born to older mothers compared to that of multiple births from younger mothers. Here we highlight notable differences. First, the lower twinning rates in Southern Asia meant that standard errors are larger compared to the estimates based on data from Sub-Saharan African countries (Supplementary Table S5). Nonetheless, the lower mortality of multiple births in mothers 40+ is evident in Southern Asia. Unlike in Sub-Saharan African countries, there was no increase in infant mortality at maternal age above 40 in Southern Asian countries (-0.04 [-0.08, 0]), and the higher infant mortality among children from multiple births to young mothers was more pronounced (e.g., relative increase of 0.23 [0.21, 0.25] in Southern Asia vs. 0.14 [0.13, 0.15] in Sub-Saharan Africa for maternal age at birth below 18 years). Second, the lower infant mortality with advanced maternal age up to 40 was consistently found across different IMR contexts (Supplementary Table S6). However, for births that occurred when IMR is below 60, the difference in mortality between younger and advanced maternal age groups was relatively smaller and only evident for the youngest age category (maternal age at birth below 18). As such, the maternal age effect is less dramatic for multiple births in contexts where national IMR is lower.

The higher infant mortality among children from multiple births to young mothers was largely driven by the cases in which all siblings from multiple births died. For most maternal age categories, the proportion of siblings surviving from a multiple birth did not differ (Figure 4, blue bars); however, the probability that all of the siblings from a multiple birth died was the highest in the youngest maternal age category and declined gradually up to the reference age category of 24 to 25 years (Figure 4, dark blue bars). This pattern is supported by the multinomial logit results, which suggest that the relative risk of all siblings dying (vs. all siblings surviving) declined gradually as maternal age reached mid-20s, whereas the relative risk of some siblings dying did not change much across maternal age categories (Supplementary Table S6).

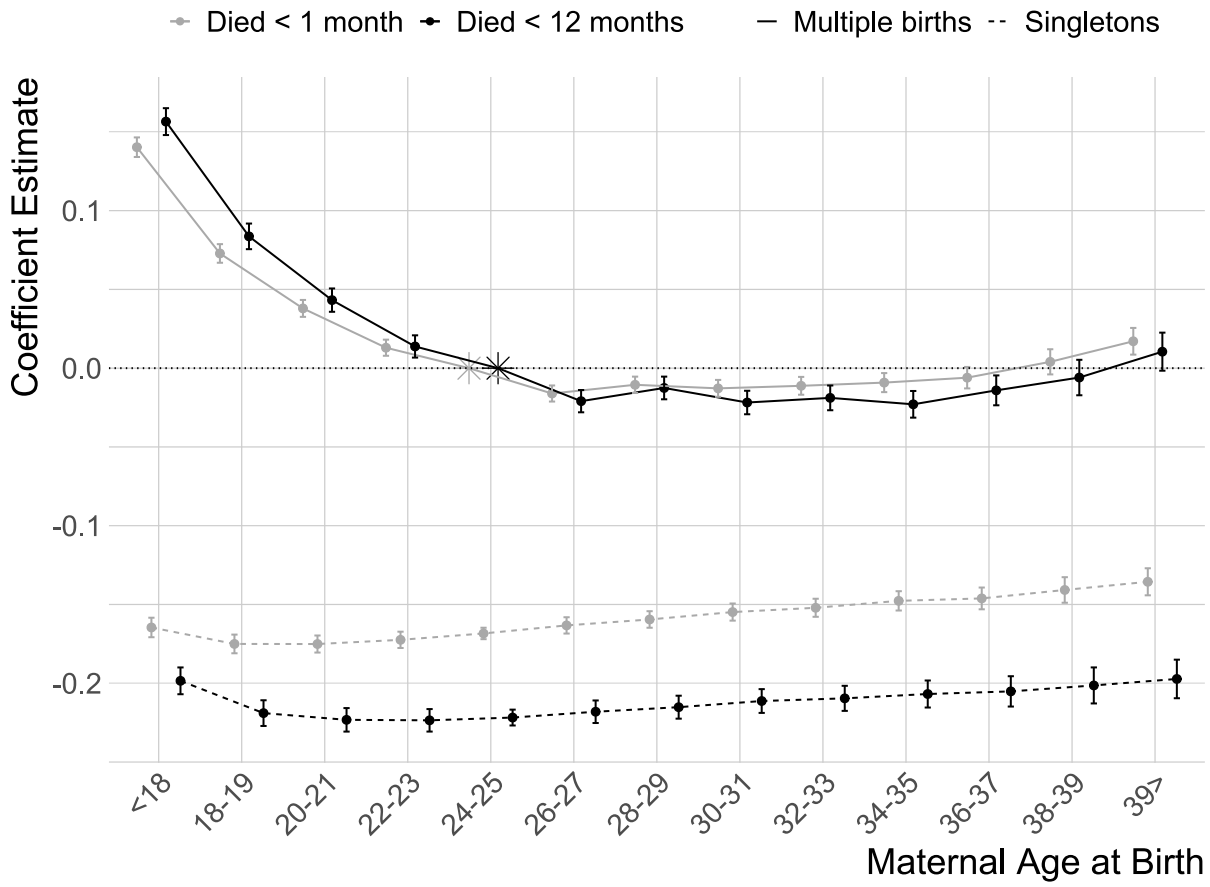

Figure 2. Mortality difference from the reference category (asterisks; children of multiple births born to women 24-25 years), for infant mortality (black) and neonatal mortality (grey). Coefficient estimates are from linear probability models with mother fixed-effects adjusted for parity effect. Error bars correspond to 95% confidence interval (CI). Data are pooled across 42 low-income countries for which data are available from Demographic Health Surveys. For full results, see Supplementary Table S1.

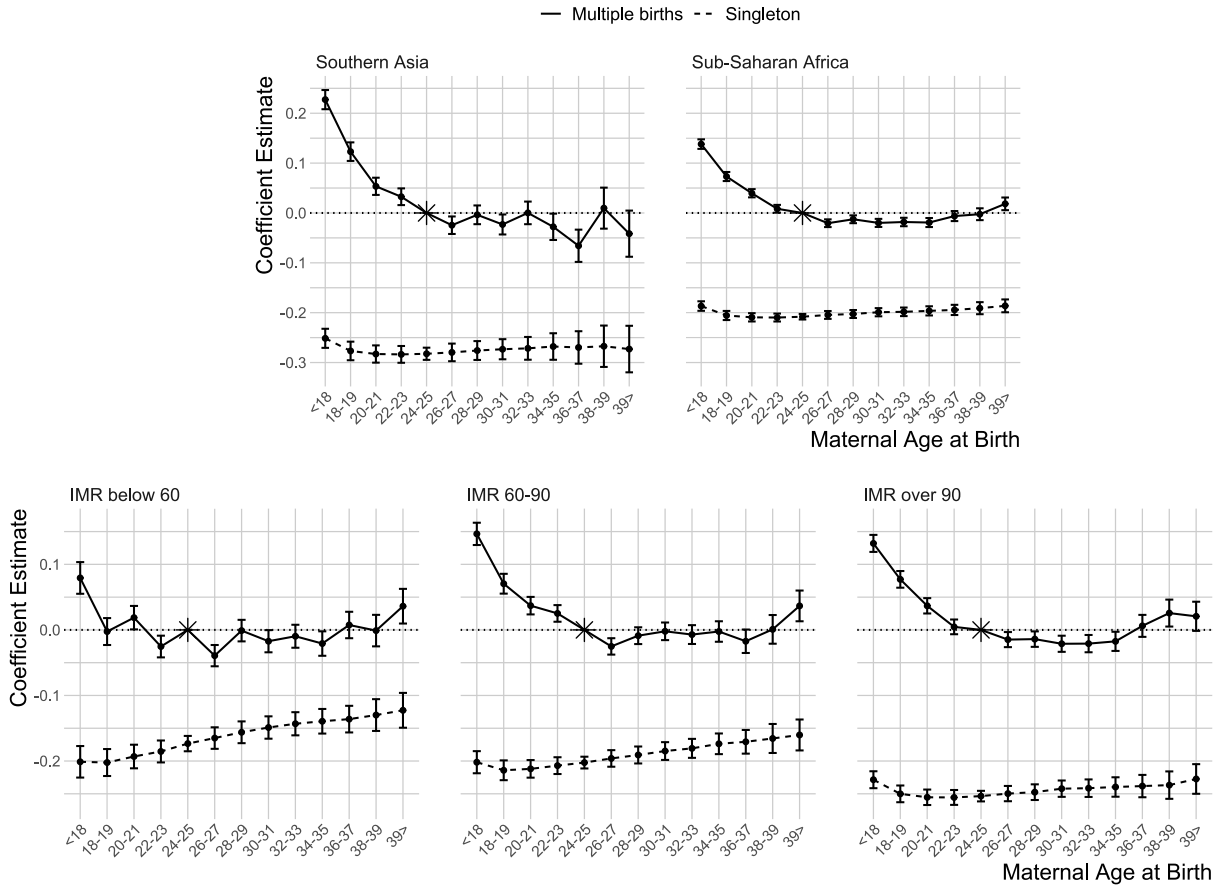

Figure 3. Infant mortality difference from the reference category (children of multiple births born to women 24-25 years). Results from the stratified analyses of linear probability models with mother fixed-effects adjusted for parity effect. Top: Samples are stratified by geographic regions. Below: Samples are stratified by the national infant mortality rate (IMR) in the years of birth. Error bars correspond to 95% confidence interval (CI), and coefficient estimates can be found in Supplementary Tables S5 and S6.

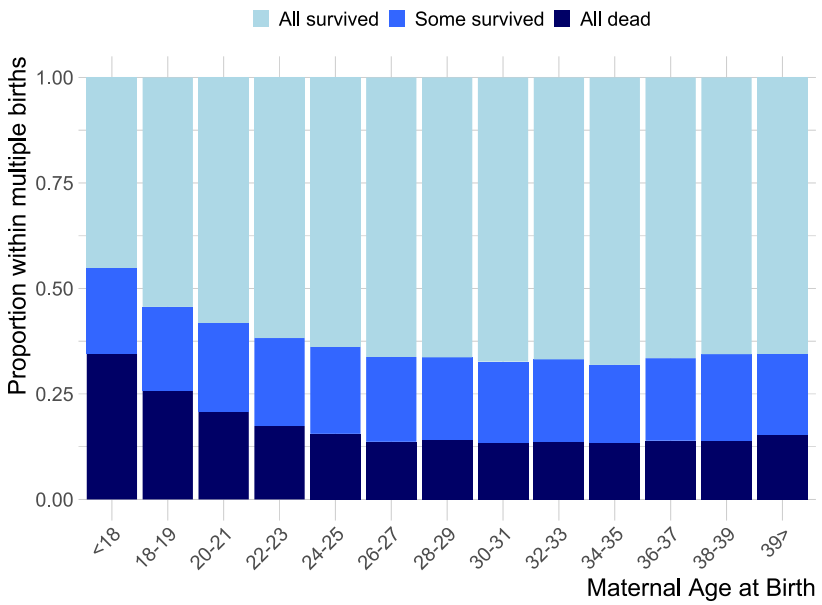

Figure 4. The proportion of multiple births that result in the death of all children within the first year of life (dark blue) is high when maternal age is younger. There is no big difference by maternal age in the proportion of multiple births that result in the death of some children (blue).

Discussion

The present study used a sibling comparison approach to clarify the association between maternal age and early mortality for children of multiple births in 42 low-income countries. Our results based on the pooled DHS data show that the probability of dying within the 1st year of life (as well as the 1st month of life) for children born from multiple births decreases with increasing maternal age until the mid-20s, then plateaus, before increasing again slightly at very advanced maternal ages (above 39). This pattern was largely consistent in Southern Asia and Sub-Saharan Africa, and across different level of national infant mortality rates.

Child outcomes associated with advanced maternal age are multifaceted and may not be always negative [14,36]. This appears to be the case for multiple births, for which previous works have shown that, in contrast to singletons, infant life mortality among children from multiple births is lower when mothers are older than 35 years of age compared to when mothers are younger [15,16]. However, these findings were based on cross-sectional comparisons of mothers with a fixed cut-off for advanced maternal age, and the studies have so far been restricted to samples from mostly high-income countries. Our results based on data from low-income countries show a lower infant mortality among children of multiple births with increasing maternal age, thereby suggesting that later motherhood does not always have more negative

consequences than young motherhood, at least in terms of early life mortality of children from multiple births.

In the present study, the examination of maternal age pattern across the full distribution of age (Figure 2), and the application of mother fixed-effects, help better assessment of different explanations for age-dependent outcomes of multiple births. For instance, under the terminal investment hypothesis, which posits that more resources are allocated to reproduction when the chance of future reproduction is lower (e.g., advanced maternal age), child mortality would decline as maternal age increases. We found no evidence of a steady decline in mortality with increasing age amongst multiple-birth-children born to women in their 30s. Mortality even increased slightly at very advanced maternal ages (above 39), consistent with previous research [23]. And yet, compared to multiple-birth-children born to mothers in their teens or early 20s, mortality was consistently lower amongst multiple-birth-children born to mothers in their 30s, supporting that there is relative increase in resources allocated to multiple births beyond young motherhood as the terminal investment posits.

Exact mechanisms – behavioral or physiological – underlying the higher child mortality for multiple births in young mothers remains to be clarified in future research. As an example of a behavioral mechanism, previous research has proposed that the relative inexperience of younger mothers can lead to higher risks of injuries or suboptimal care for children born from multiple births [17]. Our finding that the probability of both twins dying is much higher at younger maternal ages (Figure 4) suggests larger consequence of inexperience and lower childrearing skills in younger mothers if they give multiple births. This explanation may be likely more relevant in societies where social networks to support young motherhood are limited, whereas in many low-income countries today, kinship support in childrearing is prevalent, and many first-time mothers have prior experience of taking care of younger siblings or relatives [18]. Nevertheless, raising children from multiple births may be a greater challenge for younger mothers who are relatively lacking in those skills that are acquired with age. Infanticide of multiple births [37] is another behavioral mechanism by which child mortality in multiple births could differ. However, recent evidence suggests that this tradition is no longer practiced [38], though whether there was ever maternal-age-based variation in the practice of infanticide is unknown to the best of our knowledge.

In addition to behavioral mechanisms, adverse pregnancy and birth outcomes associated with young motherhood[39] may reflect physiological mechanisms that underlie the high child mortality of multiple births in young motherhood. As young mothers have typically not attained complete growth and development, somatic resources available to them are predicted to be traded off with reproduction [18], a trade-off that would be even steeper in case of multiple births. Since studies examining adverse pregnancy and birth outcomes by maternal age in multiple births have so far employed a single maternal age cut-off set in late 30s [15,16], it is currently unknown if the maternal age pattern of adverse pregnancy and birth outcomes would follow that of child mortality as observed in the present study. If so, that would provide at least partial evidence that the physiological underpinnings of adverse pregnancy and birth outcomes contribute to our findings. Clarifying this point is also important for assessing another alternative explanation, namely the higher mortality selection of mothers giving multiple births at older age. Specifically, the present finding could be the byproduct of our sample not having women who either lost their lives or lost fetuses during multiple pregnancy, because the DHS births history data only include live births self-reported by mothers. However, this explanation is plausible if such mortality selection is particularly stronger when maternal age at birth is older. Whether and why it should be such a case is currently unclear, due to the gap in the literature on birth complications and maternal mortality by maternal age in multiple births [23].

The present study is not without limitations. First, our sample is restricted to mothers who reported at least two live births, as mother fixed-effects is based upon comparison of cases within mothers. Although doing so limits the generalizability of our findings to only-child families, we believe that the impact of this limitation is likely small in many of the studied countries where one-child families are still the minority. Moreover, present study and previous studies reach a generally similar conclusion, although the latter would not have excluded only-child families due to their cross-section design. This means that our findings have implications for assessing the risk of child mortality in multiple births across different populations. Second, mother fixed-effects models do not adjust for unobserved time-varying factors. For example, our findings of heightened child mortality in younger mothers may reflect the improvement of childrearing skills within mothers, a possible explanation even if social support for childcare is generally available within kinship to 'buffer' the relative immature skills of young mothers. Our fixed-effects design cannot rule out such within-mother changes beyond what would be captured by maternal age or

parity. However, even though improvement in childrearing skills is a possible mechanism, it cannot satisfactorily explain why similar pattern with advanced maternal age is not observed in singletons, as well as why there is a slight increase in child mortality for multiple births from very advanced maternal age. Third, related to the second limitation, we cannot be certain about the degree to which the maternal age estimates from the mother fixed-effects models reflect birth year effects[35]. We attempted to circumvent this challenge in a sensitivity analysis, where we stratified the sample into three periods with different levels of IMR. Fourth, sibling model estimates could be biased if there is a carry-over effect on the chance of survival among siblings [40]. For instance, mothers who experienced the death of a twin at younger age might increase attention and care when they later have a twin to reduce their mortality. However, the possibility that this mechanism biases our estimates is low, given that the vast majority of mothers in our sample had only one multiple birth.

Lastly, in the main analyses employing mother fixed-effects, each sibling from multiple births was treated as independent observation points, so that early mortality could be examined as a binary event consistently as for singletons. In a multiple birth, one sibling might die while the other(s) survives, and their survival is likely correlated given the known shared health risks (such as small for gestational age at birth [41]) among siblings born from the same pregnancy. Thus, the assumption of independent mortality risk may not be realistic. However, such assumption may still be reasonable, given that the degree of shared fate among these siblings appears to decline with time. For instance, a study based on the Norwegian birth registry has shown no correlation in the risk of dying within a year (conditional on surviving the first month of life) among twins [42]. The risk of biased estimates for coefficients would also be small due to the overall low prevalence of multiple births. Nonetheless, we conducted and presented results from a sensitivity analysis, in which we used multinomial regression to compare the relative risks by maternal age across different compositions of sibling deaths (“all dead”, “some survived”, and “all survived”).

Conclusion

The present sought to refine the existing literature on the maternal age pattern in infant mortality, by 1) applying mother fixed-effects to adjust for any unobserved between-mother differences that may predict both maternal age at multiple birth and the early life mortality, 2) examining maternal age across the full distribution of observed age, and 3) using a large sample from low-

income countries. Similar to the previous findings, our results highlight the lower mortality of children from multiple births amongst mothers in their mid-to-late 20s compared to mothers in the mid-20s or younger. Unlike the previous findings, the lower mortality associated with advanced maternal age is visible from the mid-20s. Since the majority of births are from mothers younger than 30 in the low-income countries studied here, the present study has broader implication for public health investments in early life in low-income countries. For example, these investments would benefit young mothers expecting multiple births more than mothers with advanced age. This, in turn, could help reduce the already large discrepancy in early life mortality between multiple births and singletons.

Author's roles

D.S.L. conceived the idea. D.S.L. designed the study and analyzed the data with K.B. D.S.L. wrote the manuscript with continuous input from K.B. and M.M., K.B. and M.M. read and edited the manuscript. All authors approved the final version of the manuscript.

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Conflict of interest

We declare no conflict of interest.

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Supplementary materials for the study:

Multiple births mortality by maternal age at birth: A within-family analysis of Demographic and Health Survey data on 42 low-income countries

Contents

1. Mother fixed-effects model results

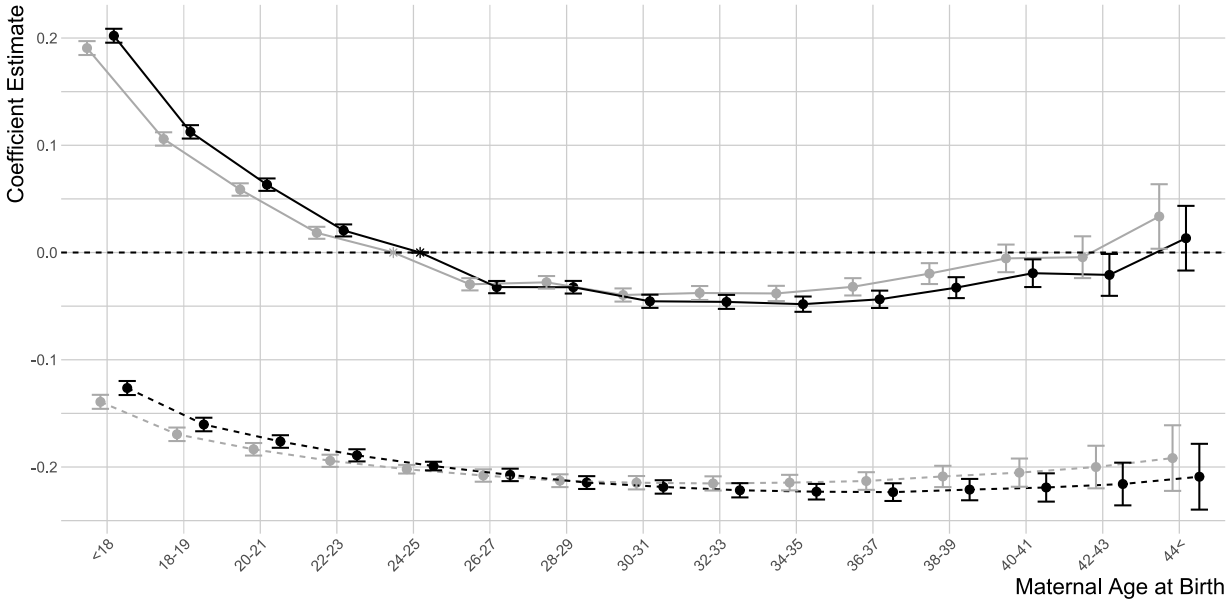
The results are estimated from linear probability models with mother fixed-effects. More details on the model specification are described in the 'Statistical analyses' section of the study.

$$y_{ij} = \beta_1 MAB_{ij} + \beta_2 Multiple_{ij} + \beta_3 MAB_{ij} \times Multiple_{ij} + \beta_2 Birth\ Order_{ij} + \alpha_j + \varepsilon_{ij},$$

	Neonatal mortality				Infant mortality			
	Model 0 (No parity)		Model 1 (Parity added)		Model 0 (No parity)		Model 1 (Parity added)	
Covariate	Estimate	S.E.	Estimate	S.E.	Estimate	S.E.	Estimate	S.E.
Multiple births								
18 < (ref. maternal age 24-25)	0.179	0.003	0.140	0.003	0.202	0.004	0.157	0.004
18-19	0.100	0.003	0.073	0.003	0.114	0.004	0.084	0.004
20-21	0.054	0.003	0.038	0.003	0.063	0.004	0.043	0.004
22-23	0.020	0.003	0.013	0.003	0.023	0.004	0.014	0.004
26-27	-0.024	0.003	-0.016	0.003	-0.028	0.004	-0.021	0.004
28-29	-0.021	0.003	-0.011	0.003	-0.026	0.004	-0.013	0.004
30-31	-0.028	0.003	-0.013	0.003	-0.039	0.004	-0.022	0.004
32-33	-0.029	0.003	-0.011	0.003	-0.039	0.004	-0.019	0.004
34-35	-0.029	0.003	-0.009	0.003	-0.046	0.004	-0.023	0.004
36-37	-0.027	0.004	-0.006	0.003	-0.038	0.005	-0.014	0.005
38-39	-0.016	0.004	0.004	0.004	-0.032	0.006	-0.006	0.006
40>	-0.006	0.005	0.017	0.004	-0.017	0.006	0.010	0.006
Singletons								
Singleton (maternal age 24-25)	-0.167	0.002	-0.168	0.002	-0.218	0.003	-0.222	0.003
18 <	-0.133	0.003	-0.136	0.003	-0.134	0.004	-0.133	0.004
18-19	-0.078	0.003	-0.079	0.003	-0.082	0.004	-0.081	0.004
20-21	-0.044	0.003	-0.045	0.003	-0.045	0.004	-0.045	0.004
22-23	-0.016	0.003	-0.017	0.003	-0.016	0.004	-0.016	0.004
26-27	0.022	0.003	0.021	0.003	0.024	0.004	0.025	0.004
28-29	0.018	0.003	0.019	0.003	0.018	0.004	0.019	0.004
30-31	0.026	0.003	0.026	0.003	0.030	0.004	0.032	0.004
32-33	0.027	0.003	0.027	0.003	0.028	0.004	0.031	0.004
34-35	0.029	0.003	0.030	0.003	0.035	0.004	0.038	0.004
36-37	0.027	0.004	0.028	0.004	0.027	0.005	0.031	0.005
38-39	0.021	0.004	0.024	0.004	0.023	0.006	0.026	0.006
40>	0.014	0.005	0.016	0.004	0.010	0.006	0.014	0.006
Parity								
Parity: 2 (ref. Parity 1)			-0.02				-0.02	0.000
Parity: 3			-0.03				-0.03	0.001
Parity: 4			-0.04				-0.04	0.001
Parity: 5			-0.06				-0.06	0.001

2. OLS estimation results

Ordinary least squares were estimated to examine how results differ from those obtained from mother fixed-effects. Same as mother fixed-effects, parity was included in the model. Only for OLS, we additionally included birth years (as dummies) to see if temporal improvement in life expectancy (including declining early life mortality) makes differences in our estimates. Doing this is not possible for mother fixed-effects, because maternal age and birth year are collinear in a mother fixed-effects models. Figure below show results when birth years were included (black) and not included (grey). The comparison shows the attenuation of maternal age effect in advanced age categories when birth years are included, but the overall maternal age pattern remains similar. Next page shows coefficient estimates from the OLS that included birth years. Birth years are not shown.



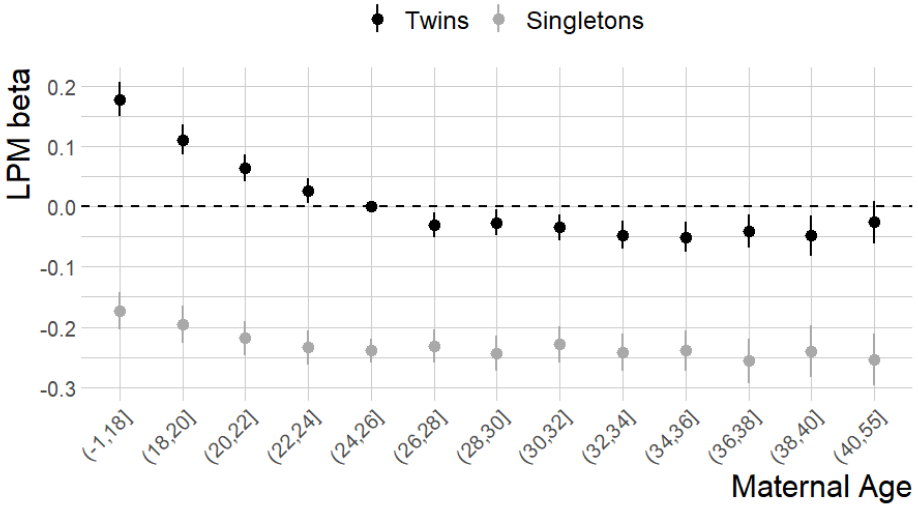
Infant mortality, with (black) and without (grey) birth years included in OLS.

	Neonatal mortality		Infant mortality	
Covariate	Estimate	S.E.	Estimate	S.E.
Intercept: maternal age 24-25, parity 1	0.119	0.210	0.139	0.281
18 <	0.164	0.002	0.191	0.003
18-19	0.088	0.002	0.106	0.003
20-21	0.049	0.002	0.059	0.003
22-23	0.016	0.002	0.018	0.003
26-27	-0.022	0.002	-0.03	0.003
28-29	-0.019	0.002	-0.028	0.003
30-31	-0.025	0.002	-0.04	0.003
32-33	-0.026	0.002	-0.038	0.003
34-35	-0.022	0.003	-0.038	0.004
36-37	-0.021	0.003	-0.032	0.004
38-39	-0.011	0.004	-0.02	0.005
40>	0.001	0.004	-0.001	0.005
Singletons				
Singleton (maternal age 24-25)	-0.153	0.001	-0.202	0.002
18 <	-0.130	0.002	-0.128	0.003
18-19	-0.072	0.002	-0.073	0.003
20-21	-0.041	0.002	-0.04	0.003
22-23	-0.013	0.002	-0.011	0.003
26-27	0.020	0.002	0.024	0.003
28-29	0.015	0.002	0.017	0.003
30-31	0.021	0.002	0.027	0.003
32-33	0.022	0.002	0.024	0.003
34-35	0.020	0.003	0.026	0.004
36-37	0.019	0.003	0.021	0.004
38-39	0.013	0.004	0.013	0.005
40>	0.005	0.004	0.001	0.005
Parity				
Parity: 2 (ref. Parity 1)	-0.007	0.000	0.001	0.000
Parity: 3	-0.004	0.000	0.013	0.000
Parity: 4	0.002	0.000	0.025	0.000
Parity: 5	0.012	0.000	0.048	0.000

3. Mother fixed-effects model outputs based on sub-sample of mothers who gave multiple births at least twice

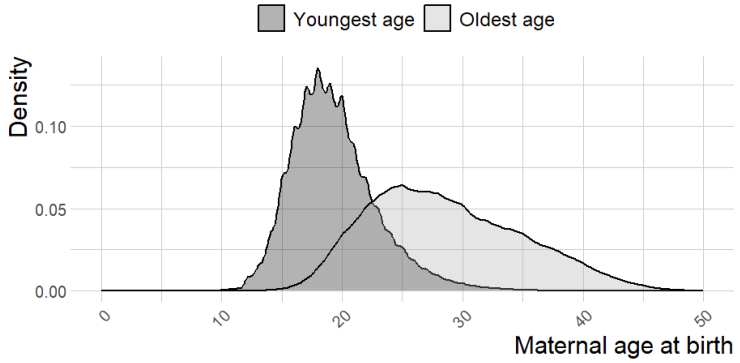
We re-estimated the same mother fixed-effects model based on subsample of women (n = 6,716) who have given at least two multiple births. Infant mortality difference from the reference category is visualized in the figure below.

Covariate	Estimate	S.E.
18 < (ref. maternal age 24-25)	0.177	0.014
18-19	0.111	0.013
20-21	0.063	0.011
22-23	0.026	0.011
26-27	-0.030	0.011
28-29	-0.027	0.011
30-31	-0.035	0.011
32-33	-0.047	0.012
34-35	-0.051	0.012
36-37	-0.040	0.014
38-39	-0.049	0.017
40>	-0.026	0.018
Singleton (maternal age 24-25)	-0.239	0.010
18 <	-0.111	0.016
18-19	-0.068	0.016
20-21	-0.042	0.015
22-23	-0.021	0.014
26-27	0.038	0.014
28-29	0.023	0.015
30-31	0.045	0.015
32-33	0.044	0.016
34-35	0.051	0.017
36-37	0.024	0.019
38-39	0.047	0.022
40>	0.011	0.022
Parity: 2 (ref. Parity 1)	-0.011	0.006
Parity: 3	0.004	0.007
Parity: 4	0.006	0.008
Parity: 5	0.004	0.009


Twins
Singletons
LPM beta
0.2
0.1
0.0
-0.1
-0.2
-0.3
(-1,18]
(18,20]
(20,22]
(22,24]
(24,26]
(26,28]
(28,30]
(30,32]
(32,34]
(34,36]
(36,38]
(38,40]
(40,55]
Maternal Age

4. Distribution of maternal age at birth in the analytic sample

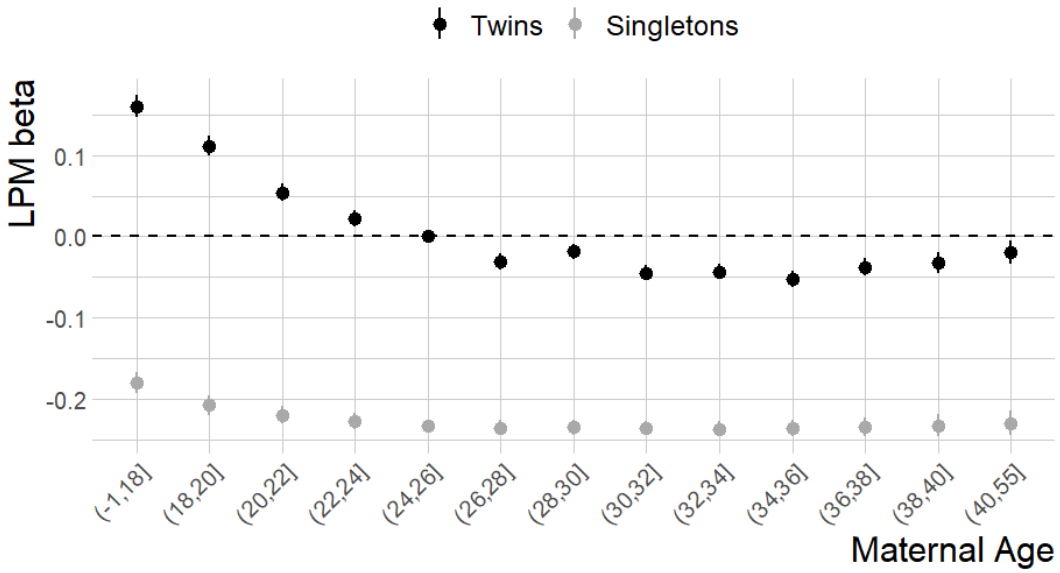
The figure below shows the density plots for maternal age at birth, one for the youngest age and the other for the oldest age within mothers. Each mother contributes at least two observed bouts of reproduction to our analytic sample, so that mother fixed-effects can be estimated. As such, for example, a mother can contribute one birth that occurred when she was 21 and the other that occurred when she was 35.



The table below shows coefficient estimates of a linear probability model based on subsample of women (n = 464,373) whose youngest birth was before 25 and oldest birth was after 30. Infant mortality difference from the reference category is visualized in the figure below.

0.160407	0.006669
0.111425	0.006204
0.054009	0.005465
0.02224	0.005072
-0.03089	0.004833
-0.01851	0.004801
-0.04496	0.004608
-0.04341	0.004822
-0.05242	0.005157
-0.03745	0.005702
-0.0325	0.00668
-0.01893	0.007281
-0.23363	0.003506
-0.01075	0.000675
-0.01021	0.000845
-0.01028	0.001016
-0.01943	0.001239
-0.10713	0.006677
-0.08551	0.00624
-0.04014	0.005515
-0.01658	0.005132
0.028747	0.004899
0.017209	0.004866
0.042397	0.004666

0.040196	0.004883
0.050388	0.005227
0.035894	0.005787
0.033618	0.006789
0.022817	0.007385



5. Mother fixed-effects separately by region

	Sub-Saharan Africa		Southern Asia	
	Estimate	S.E.	Estimate	S.E.
18 < (ref. maternal age 24-25)	0.138	0.005	0.227	0.010
18-19	0.073	0.005	0.123	0.009
20-21	0.040	0.004	0.053	0.009
22-23	0.008	0.004	0.033	0.009
26-27	-0.021	0.004	-0.025	0.009
28-29	-0.013	0.004	-0.004	0.010
30-31	-0.020	0.004	-0.023	0.010
32-33	-0.018	0.004	0.000	0.012
34-35	-0.019	0.005	-0.028	0.013
36-37	-0.006	0.005	-0.066	0.016
38-39	-0.003	0.006	0.010	0.021
40>	0.018	0.006	-0.042	0.024
Singleton (maternal age 24-25)	-0.208	0.003	-0.282	0.006
18 <	-0.117	0.005	-0.196	0.010
18-19	-0.071	0.005	-0.117	0.010
20-21	-0.041	0.004	-0.054	0.009
22-23	-0.010	0.004	-0.034	0.009
26-27	0.024	0.004	0.027	0.009
28-29	0.018	0.004	0.010	0.010
30-31	0.029	0.004	0.032	0.010
32-33	0.028	0.004	0.011	0.012
34-35	0.031	0.005	0.042	0.014
36-37	0.020	0.005	0.078	0.017
38-39	0.020	0.006	0.005	0.021
40>	0.004	0.007	0.051	0.024
Parity: 2 (ref. Parity 1)	-0.033	0.001	-0.027	0.001
Parity: 3	-0.056	0.001	-0.044	0.001
Parity: 4	-0.074	0.002	-0.058	0.001
Parity: 5	-0.095	0.002	-0.074	0.002

6. Mother fixed-effects separately by infant mortality rate (IMR) of birth year

	IMR < 50		IMR between 60-90		IMR > 90	
	Estimate	S.E.	Estimate	S.E.	Estimate	S.E.
18 < (ref. maternal age 24-25)	0.079	0.012	0.147	0.009	0.132	0.007
18-19	-0.002	0.010	0.070	0.008	0.077	0.006
20-21	0.019	0.009	0.037	0.007	0.037	0.006
22-23	-0.025	0.008	0.025	0.006	0.005	0.006
26-27	-0.039	0.008	-0.025	0.006	-0.015	0.006
28-29	-0.001	0.008	-0.009	0.007	-0.014	0.006
30-31	-0.017	0.009	-0.002	0.007	-0.021	0.006
32-33	-0.010	0.009	-0.007	0.007	-0.021	0.007
34-35	-0.021	0.010	-0.002	0.008	-0.017	0.007
36-37	0.007	0.010	-0.017	0.009	0.006	0.009
38-39	-0.001	0.012	0.001	0.011	0.026	0.010
40>	0.036	0.013	0.037	0.012	0.021	0.011
Singleton (maternal age 24-25)	-0.173	0.006	-0.202	0.005	-0.254	0.004
18 <	-0.107	0.012	-0.146	0.009	-0.107	0.007
18-19	-0.026	0.010	-0.082	0.008	-0.074	0.007
20-21	-0.038	0.009	-0.047	0.007	-0.039	0.006
22-23	0.013	0.009	-0.030	0.007	-0.007	0.006
26-27	0.048	0.008	0.031	0.006	0.019	0.006
28-29	0.018	0.008	0.020	0.007	0.020	0.006
30-31	0.042	0.009	0.020	0.007	0.033	0.006
32-33	0.040	0.009	0.029	0.007	0.033	0.007
34-35	0.055	0.010	0.031	0.008	0.031	0.008
36-37	0.030	0.010	0.049	0.009	0.009	0.009
38-39	0.045	0.012	0.036	0.011	-0.009	0.011
40>	0.015	0.014	0.006	0.012	0.005	0.012
Parity: 2 (ref. Parity 1)	-0.033	0.001	-0.027	0.001	-0.025	0.001
Parity: 3	-0.056	0.001	-0.044	0.001	-0.037	0.001
Parity: 4	-0.074	0.002	-0.058	0.001	-0.046	0.001
Parity: 5	-0.095	0.002	-0.073	0.002	-0.064	0.001

7. Multinomial regression results

	Outcome "All dead"				Outcome "Some survived"			
	(Reference outcome "All survived")							
	Model 1		Model 2		Model 1		Model 2	
	Estimate (S.E.)	Exp.	Estimate (S.E.)	Exp.	Estimate (S.E.)	Exp.	Estimate (S.E.)	Exp.
18 < (ref. maternal age 24-25)	1.15 (0.04)	3.14	1.39 (0.05)	4.01	0.34 (0.04)	1.4	0.55 (0.05)	1.74
18-19	0.67 (0.04)	1.95	0.89 (0.04)	2.42	0.12 (0.04)	1.13	0.29 (0.04)	1.34
20-21	0.38 (0.04)	1.47	0.55 (0.04)	1.74	0.12 (0.04)	1.13	0.25 (0.04)	1.28
22-23	0.15 (0.04)	1.16	0.24 (0.04)	1.27	0.04 (0.04)	1.04	0.11 (0.04)	1.12
26-27	-0.17 (0.04)	0.85	-0.27 (0.04)	0.76	-0.06 (0.04)	0.94	-0.13 (0.04)	0.88
28-29	-0.14 (0.04)	0.87	-0.34 (0.04)	0.71	-0.09 (0.04)	0.92	-0.20 (0.04)	0.82
30-31	-0.19 (0.04)	0.82	-0.47 (0.05)	0.63	-0.13 (0.04)	0.88	-0.29 (0.04)	0.75
32-33	-0.18 (0.05)	0.84	-0.50 (0.05)	0.61	-0.10 (0.04)	0.91	-0.29 (0.04)	0.75
34-35	-0.21 (0.05)	0.81	-0.58 (0.05)	0.56	-0.18 (0.05)	0.84	-0.39 (0.05)	0.67
36-37	-0.15 (0.06)	0.86	-0.54 (0.06)	0.58	-0.09 (0.05)	0.91	-0.32 (0.05)	0.72
38-39	-0.1 (0.07)	0.87	-0.56 (0.07)	0.57	-0.03 (0.06)	0.97	-0.28 (0.06)	0.76
40>	-0.04 (0.07)	0.96	-0.46 (0.07)	0.63	-0.10 (0.07)	0.90	-0.35 (0.07)	0.70
Parity 2			-0.03 (0.03)	0.98			0.05 (0.03)	1.05
Parity 3			0.15 (0.04)	1.16			0.22 (0.03)	1.25
Parity 4			0.31 (0.04)	1.37			0.35 (0.04)	1.42
Parity 5			0.72 (0.04)	2.05			0.41 (0.04)	1.68