DEMOGRAPHIC RESEARCH
A peer-reviewed, open-access journal of population sciences

DEMOGRAPHIC RESEARCH

VOLUME 42, ARTICLE 28, PAGES 777–798
PUBLISHED 5 MAY 2020
https://www.demographic-research.org/Volumes/Vol42/28/
DOI: 10.4054/DemRes.2020.42.28

Reflection

Are sibling models a suitable tool in analyses of how reproductive factors affect child mortality?

Øystein Kravdal

Contents

Demographic Research: Volume 42, Article 28
Reflection

Are sibling models a suitable tool in analyses of how reproductive factors affect child mortality?

Øystein Kravdal[1]

Abstract

BACKGROUND
Several studies of how reproductive factors affect child mortality or other child outcomes have been based on sibling comparisons. With such models one controls for unobserved determinants of the outcome that are shared by the siblings and linked to the reproductive process. However, it has been shown mathematically that estimates from sibling models are biased when the outcome for one sibling affects the exposure for another, and this is precisely the situation when the outcome is child mortality and the exposure is aspects of the mother's reproductive behaviour. The goal of this analysis was to find out, by means of simulation, whether the bias really matters in practice.

RESULTS
All simulation experiments showed that, when there was an effect of infant mortality on subsequent fertility, the estimated effect of higher maternal age was considerably more adverse than the true effect, while the effects of higher birth order and very short or very long birth interval were biased in the opposite direction.

CONTRIBUTION
Although it is possible that the bias is unimportant in other situations than those examined here, a reasonable conclusion is that one should have serious doubts about sibling model estimates of effects of reproductive factors on infant or child mortality. Stated differently, we may know less about these effects than we tend to think and need other alternatives to a 'naïve' regression model than the sibling approach. Obviously, there may be problems also when analysing other child outcomes that affect subsequent fertility, through mortality or otherwise.

[1] Department of Economics, University of Oslo, and Centre for Fertility and Health, Norwegian Institute of Public Health, Norway. Email: okravdal@econ.uio.no.

1. Introduction

There has been much interest in the importance of reproductive factors for child outcomes. For example, strong concerns have been voiced in developing countries about the health implications of being born to very young mothers or shortly after the previous birth (Kravdal 2018), and the possible effects of high parental age on children's well-being have attracted increasing attention in low-fertility settings (Barclay and Myrskylä 2016). A key problem when analysing such effects is that several factors that are hard to measure affect both the mother's reproductive behaviour and the child outcomes under study. Many researchers have therefore estimated sibling models, and thus controlled for unobserved parental and environmental characteristics that are shared by the siblings, although it is a disadvantage that one-child families and families where all children have had the same outcomes do not contribute in the estimation. For example, sibling models have been used in several recent studies of the importance of birth intervals for the chance of preterm birth or low birth weight (Ball et al. 2014; Shachar et al. 2016; Hanley et al. 2017; Class et al. 2017; Regan et al. 2018), child mortality (Molitoris 2018; Molitoris, Barclay, and Kolk 2019), or socioeconomic outcomes (Barclay and Kolk 2017).

However, it has been explained mathematically (see elaboration below) that estimates from sibling models are biased if the outcome for one sibling affects the 'exposure' for another (Sjölander et al. 2016). This is apparently not well known to demographers and epidemiologists who analyse effects of reproductive factors on various child outcomes, but is highly relevant if infant or child mortality is the outcome, because the death of a child is widely believed to affect subsequent fertility (and therefore the reproductive factors of potential relevance for the next child). Indeed, several studies from contemporary poor settings have shown strongly elevated fertility after a child death, which probably reflects higher fecundity because of terminated breastfeeding and that many parents want to 'replace' their dead child (e.g., Bousmah 2017; van Soest and Saha 2018; Ewemade, Akinyemi, and DeWet 2019). A strong relationship between child death and subsequent fertility appears in Norwegian data as well (see below). Other outcomes very early in life may also affect subsequent fertility, via the probability of child death or otherwise.

The key issue is, of course, whether the bias really matters or is so small that it can be ignored. Purely mathematical arguments do not provide sufficient guidance, as the analytical expression for the bias can be complex even in quite simple situations (Sjölander et al. 2016). The goal of this study was to show by means of a simulation experiment how much the effects of reproductive factors on infant mortality may actually be distorted in different realistic situations. Maternal age, length of previous birth interval, and birth order were considered, as researchers may be interested in the separate effects of all of these (strongly correlated) variables.[2]

Constant unobserved determinants of infant mortality were assumed to be linked to the reproductive factors, which is a structure that typically would motivate a sibling analysis. More specifically, the simulation model included equations for first and higher-order birth rates (which, so to speak, generate the three reproductive variables) and an equation for infant mortality. An indicator of infant death of the most recently born child was included in the equation for higher-order births[3], and the reproductive factors were included in the equation for infant mortality. The equations also included fertility and mortality random terms representing time-invariant unobserved characteristics of the mother and her environment, and these were allowed to be correlated. Sibling models were then estimated from the simulated population, and the estimated effects of the reproductive variables were compared with the assumptions made about these effects in the simulation.

The parameters used in most of the simulations were derived from models estimated from Norwegian register data, and thus reflect the situation in a low-fertility/low-mortality setting. However, a variety of alternative assumptions were made – about the overall infant mortality level (which in some simulations was as in poor regions of the world), the effects of the reproductive factors on infant mortality, and other aspects of the fertility and mortality processes. The conclusions were always the same.

[2] For example, for women making decisions about when to have their next child, the birth order of that child is not a matter of choice, but by having the child after a shorter or longer interval – which will also have implications for their age when the child is born – they can influence the probability that the child dies (Kravdal 2018). For a woman aged A_0 when the previous child was born, prediction of that probability requires information about the effect of the birth interval D and the effect of her age A at next birth (which will be A_0+D). When estimating such effects one should control for birth order, as it is closely linked with maternal age. (One might consider estimating a model for infant mortality for these women aged A_0 at the time of last birth and include only birth interval along with birth order. The effect of birth interval would then pick up the sum of the effects of age and interval. However, if the age effect is not linear, this sum varies with A_0, which should therefore be an interacting variable if a model is estimated for all women. In that case, one could just as well include both age and interval in the model and predict mortality from the estimated effects of these two variables.)

[3] For simplicity, the possibility that a child can die after the first year was ignored. This has no fundamental implications for the arguments that are made, and actually also accords quite well with reality in Norway. For example, a life table for 2018 shows that, among 100000 newborn, 230 die within the first year, 252 within the first five years, and 291 within the first 10 years (Statistics Norway 2019).

2. A mathematical argument

A quite simple model was presented by Sjölander et al. (2016). They considered one individual exposure variable, X, and an outcome, Y, and assumed that X and Y were jointly influenced by an unobserved family-specific factor. More specifically, they assumed that the exposure for sibling 1 in family i was

$$X_{i1} = \alpha_i + \varepsilon_{i1},$$

where α_i is a family-level factor affecting both X and Y for all siblings and ε_{i1} is an error term, and that the outcome for sibling 1 was

$$Y_{i1} = \alpha_i + \beta X_{i1} + \varepsilon_{i2}.$$

For sibling 2, the exposure was supposed to be influenced by the outcome for sibling 1, so

$$X_{i2} = \alpha_i + \gamma Y_{i1} + \varepsilon_{i3,}$$

while the outcome was

$$Y_{i2} = \alpha_i + \beta X_{i2} + \varepsilon_{i4}.$$

The error terms and α_i were assumed to be independent with mean 0 and variance 1.

They then showed that the conditional likelihood estimator for β in this case converged to

$$(-\gamma + 2(\beta - \beta^2\gamma + \beta\gamma^2 + \beta^2\gamma^2 + \beta^3\gamma^2))/(2\ (1 - \beta\gamma + \gamma^2 + \beta\gamma^2 + \beta^2\gamma^2)),$$

which can be both larger and smaller than β.

3. Methods

3.1 Estimation of effect parameters to use in the simulation

Ideally, one should use realistic effects in the simulation, but what is actually realistic? The very motivation for this analysis was a suspicion that earlier investigations, even those using sibling models, may have given biased estimates. For simplicity, the simulation was based on effects in rather simple models estimated from the Norwegian Population Register for the years 1991–2015.

More specifically, discrete-time fertility hazard models were estimated for women born in 1947–1998, except that the few with twins were excluded for simplicity. For the analysis of first births, a series of one-month observations was constructed for each woman, starting in January 1991 or the month when she turned 17, whichever came last. The last month of observation was the month of first birth, December 2015 (the last month covered by the data), the month before she turned 45, or the month of death, whichever came first. If the woman lived outside Norway at the beginning of a year, all one-month observations for that year were excluded. Logistic regression models with age as the only variable were estimated from all remaining one-month observations. See estimates in the online appendix Table A-1.

A similar series of monthly observations was constructed to analyse higher-order births, except that the first observation was no earlier than the month after the previous birth, and the last observation was the month of the fifth birth (as larger families are very uncommon in Norway), if this occurred before the other limits mentioned. The model included age, time since last birth, parity, and a dummy indicating whether the previously born child had died within a year after birth and within nine months before the month under consideration. Note that the effect of the latter variable was 1.21, which means that the monthly birth probabilities are more than tripled after a child death.

Also a logistic model for the probability of infant death was estimated, for all children born to the included women. Because of the quite small number of deaths, the birth intervals could not be as finely categorized as in the fertility model. It was controlled for whether the father of the child was another person than the father of the mother's first child (which produced less adverse effects of long intervals), although this factor was disregarded in the simulation for simplicity. The estimates are shown in online appendix Table A-2. It seems reasonable to assume that the relationships between the reproductive variables and infant mortality are quite smooth in reality and (1) nonpositive over the entire range, (2) nonnegative over the entire range, or (3) first nonpositive and then nonnegative, or vice versa (i.e., something similar to U- or inverse U-shape). For example, if infant mortality decreases with increasing maternal age up to a certain age and then increases, it would be surprising to see a new decline at higher ages. Therefore, the effect parameters used in the mortality equation in the simulation (see e.g., Table 1, column 1) were not the estimated ones, but were a result of interpolation and extrapolation of the estimated effects (because of the finer categories in the simulation) followed by visual smoothing to obtain the mentioned patterns. This 'cosmetic' step had, of course, no implications for the conclusions.

Note that first-born children were assigned to the reference group for the birth interval variable.[4]

3.2 Simulation

The 'data generating model' included the equations (1), (2), and (3) below. More specifically, each simulation started with 100,000 women just turned 17. For each woman, fertility and mortality random terms – assumed to affect her fertility throughout her reproductive period and all her children's infant mortality – were drawn from a bivariate normal distribution with zero mean. In what is referred to below as the 'basic simulation,' both variances were 1 and the correlation 0.5. These values are close to those estimated from a similar model in an earlier study, based on African data (Kravdal 2018). At each month until the woman turned 45, first and higher-order birth probabilities were predicted from the effect parameters multiplied by the relevant demographic variables (updated monthly as the simulation 'proceeded'), plus the fertility random term. More precisely, the probabilities of first (f_1) and higher-order (f_2) births were given by:

$$\log (f_1/(1-f_1)) = \alpha_0 + \alpha_1 A + \sigma \qquad (1)$$

$$\log (f_2/(1-f_2)) = \beta_0 + \beta_1 A + \beta_2 D + \beta_3 P + \beta_4 G + \sigma \qquad (2),$$

where A, D, and P represent age, time since last birth, and parity, respectively, and are vectors of dummies corresponding to the same categories for these variables as used in the estimation reported above. G indicates whether the previously born child died in infancy and within nine months before the month under consideration, and σ is the fertility random term. The effect of earlier infant death (β_4) was set to 1 in the 'basic simulation.' This is quite close to the effect of 1.21 that was estimated.[5]

For each month, a number was drawn from a uniform distribution over [0,1], and if this number was smaller than the relevant predicted birth probability, a birth (up to a

---

[4] Thus, the intercept is the log-odds of death for a first-born child with a mother aged 30. The corresponding log-odds for, for example, a second-born child with a mother aged 30 and born after an interval of 28–36 months is 0.11 lower (–0.11 being the parameter for birth order 2). If the interval instead is 1–18 months, the figure is 0.57–0.11 higher (where 0.57 is the parameter for that interval).

[5] One might expect that the effect of the infant death of the previously born child varies with time since previous birth. For example, a biological effect of disrupted breastfeeding because of infant death is only relevant quite shortly after birth (and especially in settings with little contraceptive use). Furthermore, as time goes those who have been particularly eager to 'replace' the dead child have already done so. Such variation was indeed confirmed by supplementary estimation, but a constant effect was nevertheless assumed for simplicity.

fifth) was assigned to the woman that month. In that case, the probability that this child died within 12 months was predicted from the relevant demographic variables multiplied by – in the 'basic simulation' – the 'smoothed' estimates referred to above. The mortality random term was also added. In mathematical terms, the prediction equation was:

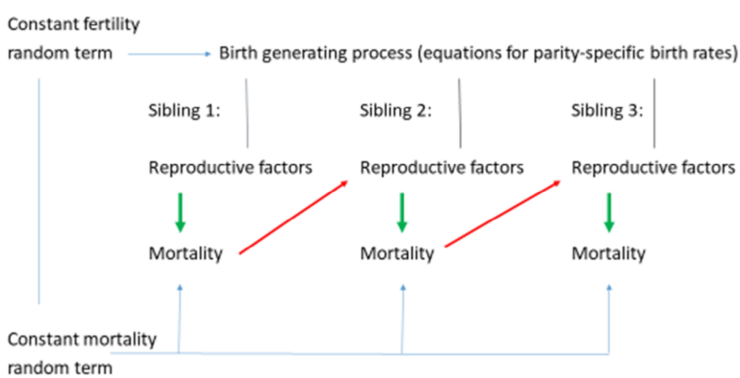
$$\log(m/(1\text{-}m)) = \gamma_0 + \gamma_1 A' + \gamma_2 D' + \gamma_3 O + \tau \quad (3),$$

where A' is the mother's age (primed because of finer categories than for A in the fertility equations), D' is time between current and previous birth (as finely categorized as in the fertility equation except that 0–9 and 10–18 months were pooled together, and the reference category includes the first-born), O is birth order (i.e., the mother's parity (P) the month after the child was born), and τ is the mortality random term.

Again, a number was drawn from a uniform distribution over [0,1], and if this was smaller than the predicted death probability, a death was assigned to the child. The timing of the death within the 12 months was assigned stochastically by drawing a number from another uniform distribution. 59% of the deaths were assumed to happen within the month of birth, and 16%, 6%, 4%, 3%, 2%, 2% 2%, 2%, 2%, 1%, and 1% in each of the subsequent months, in accordance with what was observed in the Norwegian register data. Several simulations were done in addition to this basic one. See details below.

The model is illustrated in Figure 1. The blue arrows symbolize the effects of the random terms, the green symbolize the effects that the analysis is aimed at identifying, and the red symbolize the potentially problematic effect of infant death on subsequent fertility.

Figure 1: Illustration of the simulation model



3.3 Estimation of mortality models from the simulated population

Mortality models were estimated from the simulated population. The equation was as equation (3) above, with the same finely categorized variables, except that the random term was substituted by sibling fixed effects (ν):

$$\log (m/(1-m)) = \lambda_0 + \lambda_1 A' + \lambda_2 D' + \lambda_3 O + \nu \qquad (4).$$

Previous analysis has shown that, because of the strong correlations between the reproductive variables, the estimated effects may be quite strongly biased if these variables – and especially maternal age and birth order – are not finely categorized (Kravdal 2019). In some models (referred to below as ‘naïve models’), the sibling fixed effects were left out.

3.4 Replications

Simulation followed by estimation was done 100 times, after which the averages over the 100 sets of estimates were calculated. These averages are shown in the tables along with the mortality effect parameters used in the simulation and the mean absolute bias and the root of the mean of the squared bias. The ‘bias’ refers the difference between an effect parameter used in the simulation and the average of the corresponding estimates, and the mean is taken over all 41 parameters (27 for maternal age, 10 for birth interval, and 4 for birth order). The CPU time for such a simulation-estimation experiment was typically about 90 minutes. Obviously, one would get ‘smoother’ average estimates with more replications, but that did not seem worthwhile given the goal of the study.

4. Results

4.1 Assuming that there is no effect of earlier infant death on fertility

It was first assumed in the simulation that infant deaths have no impact on subsequent fertility, i.e., $\beta_4 = 0$ in equation (2). The simulation was otherwise as described above. In this case, the estimates from the sibling model (Table 1, column 2) were quite similar to those assumed in the simulation (column 1), which indicates that the simulation and estimation have been correctly done. To further strengthen that impression, note that addition of, for example, log(25) to the intercept in the mortality equation – which led to a much larger number of deaths – gave estimates even closer to the true values, as judged from the mean absolute bias and root mean square bias (column 3).[6] In contrast, the estimates from a 'naïve model' (i.e., no sibling fixed effects) were, as one would expect, far from the truth (column 4).[7]

Table 1: Estimated effects of reproductive factors on infant mortality when there was no effect of infant death on subsequent fertility in the simulation model

	Effects in simulation	Average of estimates from		
		sibling model	sibling model, when 25 times higher overall odds of infant death were assumed in the simulation	naïve model
Mother's age				
17	1.05	1.05	1.03	1.64
18	0.90	0.89	0.88	1.48
19	0.75	0.73	0.73	1.31
20	0.60	0.57	0.58	1.09
21	0.46	0.43	0.45	0.92
22	0.38	0.37	0.36	0.81
23	0.30	0.30	0.29	0.67
24	0.21	0.17	0.21	0.50
25	0.17	0.17	0.16	0.43
26	0.12	0.10	0.12	0.31
27	0.07	0.05	0.05	0.20
28	0.05	0.08	0.04	0.15
29	0.02	0.00	0.01	0.05
30 (ref)	0.00	0.00	0.00	0.00
31	0.01	0.03	0.01	–0.03
32	0.02	0.04	0.01	–0.05
33	0.04	0.06	0.04	–0.10
34	0.06	0.03	0.06	–0.13
35	0.08	0.16	0.09	–0.07
36	0.10	0.09	0.09	–0.13
37	0.12	0.15	0.12	–0.11
38	0.12	0.13	0.13	–0.15
39	0.12	0.10	0.08	–0.21
40	0.12	0.09	0.08	–0.21

[6] Alternatively, one could have expanded the simulated population correspondingly, or increased the number of replications, but that would have been more cumbersome.

[7] However, when the correlation between the fertility and mortality random terms was instead set to 0, the naïve model worked, of course, well (not shown).

Table 1: (Continued)

	Effects in simulation	Average of estimates from		
		sibling model	sibling model, when 25 times higher overall odds of infant death were assumed in the simulation	naïve model
41	0.12	0.16	0.13	–0.21
42	0.12	0.20	0.12	–0.21
43	0.12	0.09	0.12	–0.41
44	0.12	0.17	0.10	–0.30
Months since previous birth				
1–18	0.57	0.56	0.57	0.64
10–27	0.20	0.19	0.21	0.23
28–36 (ref)	0.00	0.00	0.00	0.00
37–48	–0.20	–0.23	–0.19	–0.24
49–60	–0.14	–0.19	–0.14	–0.23
61–72	–0.10	–0.17	–0.10	–0.18
73–84	–0.08	–0.09	–0.07	–0.10
85–96	–0.08	–0.08	–0.08	–0.09
97–108	–0.08	–0.14	–0.10	–0.09
109–120	–0.08	–0.09	–0.09	–0.04
121+	–0.08	–0.18	–0.09	–0.04
Birth order				
1 (ref)	0.00	0.00	0.00	0.00
2	–0.11	–0.10	–0.11	0.08
3	0.14	0.14	0.13	0.57
4	0.50	0.50	0.49	1.17
5	0.50	0.50	0.49	1.34
Mean absolute bias		0.026	0.010	0.259
Root of mean square bias		0.036	0.013	0.333

Note: The reference category for birth interval length includes first-born children.

4.2 What happens if there 'in reality' is an effect of earlier infant death on fertility?

With the 'basic simulation,' where it was assumed that the infant death of the previously born child increases the log-odds of a subsequent birth by 1 (which is realistic according to the fertility model estimated from Norwegian data), the sibling analysis no longer gave correct estimates (Table 2, column 2). The estimates of the effects of higher maternal age and higher birth order were particularly biased – the former being much more positive than the true effects and the latter more negative. However, the birth interval effects were also biased: The adverse effect of short interval (compared to the 28–36 month reference category) was underestimated, and a long interval appeared to be more advantageous than was actually the case.[8]

Table 2: Estimated effects of reproductive factors on infant mortality when there was an effect of infant death on subsequent fertility in the simulation

	Effects in simulation	Average of estimates from sibling model when the effect of infant death on subsequent fertility in the simulation was				
		1.00 the 'basic simulation'	0.20	0.05	–0.05	–0.20
Mother's age						
17	1.05	–0.94	0.66	0.95	1.17	1.46
18	0.90	–0.89	0.54	0.81	0.98	1.26
19	0.75	–0.90	0.41	0.65	0.84	1.10
20	0.60	–0.91	0.27	0.50	0.66	0.90
21	0.46	–0.89	0.17	0.36	0.50	0.70
22	0.38	–0.78	0.14	0.32	0.44	0.62
23	0.30	–0.76	0.10	0.26	0.37	0.52
24	0.21	–0.67	0.01	0.14	0.22	0.36
25	0.17	–0.53	0.02	0.13	0.21	0.32
26	0.12	–0.45	0.00	0.08	0.13	0.21
27	0.07	–0.34	–0.04	0.03	0.06	0.12
28	0.05	–0.20	0.02	0.06	0.08	0.11
29	0.02	–0.12	–0.01	–0.01	0.00	0.02
30 (ref)	0.00	0.00	0.00	0.00	0.00	0.00
31	0.01	0.10	0.06	0.03	0.01	0.00
32	0.02	0.27	0.07	0.05	0.02	–0.02
33	0.04	0.35	0.14	0.08	0.03	0.00
34	0.06	0.43	0.08	0.03	–0.02	–0.05
35	0.07	0.62	0.25	0.19	0.11	0.03
36	0.10	0.62	0.19	0.12	0.05	0.00
37	0.12	0.76	0.25	0.12	0.10	0.01
38	0.12	0.82	0.27	0.17	0.08	0.02

[8] The estimates were biased also if a simpler 'reality' was assumed by including only one reproductive factor in the mortality equation in the simulation, and only this reproductive factor also in the model that was estimated. However, some of these biases were not in the same direction as when all reproductive variables were included (not shown). (If one of the variables was left out of the estimation in spite of being included in the simulation, the estimates of the other effects were, of course, biased even if there was not an effect of infant death on subsequent fertility.)

Table 2: (Continued)

	Effects in simulation	Average of estimates from sibling model when the effect of infant death on subsequent fertility in the simulation was				
		1.00 the 'basic simulation'	0.20	0.05	–0.05	–0.20
Mother's age						
39	0.12	0.80	0.21	0.12	0.06	–0.03
40	0.12	0.79	0.24	0.12	0.05	–0.06
41	0.12	0.76	0.17	0.20	0.09	–0.35
42	0.12	0.85	0.33	0.20	0.12	0.00
43	0.12	0.88	0.28	0.11	0.03	–0.15
44	0.12	0.96	0.11	0.19	–0.07	–0.14
Months since previous birth						
1–18	0.57	0.38	0.55	0.55	0.56	0.56
10–27	0.20	0.09	0.19	0.19	0.20	0.20
28–36 (ref)	0.00	0.00	0.00	0.00	0.00	0.00
37–48	–0.20	–0.17	–0.22	–0.23	–0.22	–0.23
49–60	–0.14	–0.12	–0.15	–0.19	–0.18	–0.18
61–72	–0.10	–0.14	–0.16	–0.16	–0.16	–0.15
73–84	–0.08	–0.18	–0.11	–0.10	–0.09	–0.06
85–96	–0.08	–0.12	–0.06	–0.06	–0.08	–0.04
97–108	–0.08	–0.36	–0.20	–0.16	–0.11	–0.10
109–120	–0.08	–0.28	–0.14	–0.08	–0.07	–0.01
121+	–0.08	–0.66	–0.22	–0.19	–0.15	–0.05
Birth order						
1 (ref)	0.00	0.00	0.00	0.00	0.00	0.00
2	–0.11	–0.47	–0.20	–0.13	–0.08	0.00
3	0.14	–0.72	–0.07	0.09	0.20	0.36
4	0.50	–0.82	0.19	0.43	0.60	0.82
5	0.50	–1.16	0.13	0.41	0.60	0.89
Mean absolute bias		0.659	0.138	0.049	0.045	0.146
Root of mean square bias		0.842	0.178	0.060	0.060	0.194

Notes: The reference category for birth interval length includes first-born children

As one would expect, the biases were smaller when the fertility effect of infant death was weaker (Table 2, columns 3 and 4). Furthermore, if this effect instead was assumed – very hypothetically – to be *negative*, there were biases in the opposite direction (columns 5 and 6).

The bias that appeared when infant death was assumed to affect subsequent fertility was, of course, not a result of the logit function in the mortality equation. There was a similar bias when a linear probability model was used for mortality both in the simulation and estimation (online appendix Table A-3).[9]

4.3 Generally higher fertility or mortality

If generally higher infant mortality was assumed in the simulation, by adding log(25) to the intercept in the mortality equation, the estimates were not only ’smoother’ (as when there was assumed to be no fertility effect of infant death and the number of deaths was increased; Table 1, column 3). The effects of higher maternal age and higher birth order were also slightly more positive and negative, respectively (Table 3, compare columns 2 and 3). The birth interval effects, however, were almost the same. Thus, the mean bias was somewhat larger.

Table 3: Estimated effects of reproductive factors on infant mortality when there was an effect of infant death on subsequent fertility in the simulation

	Effects in simulation	Average of estimates from sibling model when the following was assumed in the simulation		
		‘basic simulation’ (as Table 2 column 2)	25 times higher overall odds of infant death	25 times higher overall odds of infant death and 3 times higher overall odds of having a child
Mother’s age				
17	1.05	–0.94	–0.87	–1.09
18	0.90	–0.89	–0.94	–1.10
19	0.75	–0.90	–0.97	–1.08
20	0.60	–0.91	–0.95	–1.03
21	0.46	–0.89	–0.93	–1.00
22	0.38	–0.78	–0.85	–0.89
23	0.30	–0.71	–0.76	–0.78
24	0.21	–0.67	–0.69	–0.70
25	0.17	–0.53	–0.57	–0.58
26	0.12	–0.45	–0.47	–0.46
27	0.07	–0.34	–0.37	–0.36
28	0.05	–0.20	–0.23	–0.23
29	0.02	–0.12	–0.11	–0.12

[9] When it was assumed that infant death has no impact on subsequent fertility, the averages of the estimated effects were not as close to the true effects as in the corresponding set-up with the logit function. The reasons for this were not explored.

Table 3: (Continued)

	Effects in simulation	Average of estimates from sibling model when the following was assumed in the simulation		
		'basic simulation' (as Table 2 column 2)	25 times higher overall odds of infant death	25 times higher overall odds of infant death and 3 times higher overall odds of having a child
30 (ref)	0.00	0.00	0.00	0.00
31	0.01	0.10	0.14	0.12
32	0.02	0.27	0.26	0.24
33	0.04	0.35	0.39	0.38
34	0.06	0.43	0.51	0.49
35	0.08	0.62	0.62	0.60
36	0.10	0.62	0.72	0.69
37	0.12	0.76	0.81	0.78
38	0.12	0.82	0.86	0.84
39	0.12	0.80	0.90	0.86
40	0.12	0.79	0.96	0.92
41	0.12	0.76	0.99	0.96
42	0.12	0.85	0.98	0.96
43	0.12	0.88	1.03	0.99
44	0.12	0.96	1.04	1.05
Months since previous birth				
1–18	0.57	0.38	0.42	0.40
10–27	0.20	0.09	0.10	0.11
28–36 (ref)	0.00	0.00	0.00	0.00
37–48	–0.20	–0.17	–0.17	–0.18
49–60	–0.14	–0.12	–0.12	–0.16
61–72	–0.10	–0.14	–0.12	–0.17
73–84	–0.08	–0.18	–0.15	–0.21
85–96	–0.08	–0.12	–0.23	–0.28
97–108	–0.08	–0.36	–0.28	–0.36
109–120	–0.08	–0.28	–0.37	–0.38
121+	–0.08	–0.66	–0.60	–0.66
Birth order				
1 (ref)	0.00	0.00	0.00	0.00
2	–0.11	–0.47	–0.51	–0.36
3	0.14	–0.72	–0.80	–0.58
4	0.50	–0.82	–0.94	–0.66
5	0.50	–1.16	–1.27	–0.98
Mean absolute bias		0.659	0.703	0.697
Root of mean square bias		0.842	0.888	0.889

Notes: The reference category for birth interval length includes first-born children.

If the birth rates were also assumed to be higher, by adding log(3) to the intercept in the fertility equations, while there was still a five-child limit, the average number of children per woman was almost doubled. In this situation, the effects of maternal age and birth interval were slightly more biased than when only a generally higher mortality was assumed, while the effect of birth order was somewhat less biased (column 4). The mean bias was almost the same.

These alternative assumptions, with 25 times higher death probabilities and almost twice as high fertility, correspond to a situation found in poor regions of the world today, except that fertility is often even higher in those settings. Thus, it can be concluded that the bias discussed in this paper is relevant for studies of both rich and poor countries.

4.4 Alternative assumptions about effects of maternal age, birth interval, and birth order in the simulation

Because there is meager knowledge about the true effects of maternal age, birth interval and birth order, simulations with a variety of assumptions about these effects were carried out. First, a linear negative effect of maternal age was assumed (as opposed to the decline and then modest upturn in the 'basic simulation'). The two other effects were as in the 'basic simulation.' Again, the effects of higher maternal age and higher birth order were too positive and too negative, respectively, while the adverse effect of short interval was underestimated and a long interval appeared as too much of an advantage (online appendix Table A-4). The conclusion was the same when a linear positive effect of maternal age was assumed instead.

Second, it was assumed that further lengthening of the birth interval beyond four years had no impact on mortality (as opposed to a moderately adverse effect of further lengthening in the 'basic simulation'), or that it had a more sharply adverse linear effect. In both cases the conclusion was the same as above (online appendix Table A-5). Third, birth order was assumed to have a generally negative effect on mortality (as opposed to the small decline and then stronger increase in the 'basic simulation'), or a general and more strongly positive effect. Again, both assumptions gave the same conclusion as above (online appendix Table A-6).

In all these cases, the mean bias in the estimates was quite similar to that appearing with the 'basic simulation.'

4.5 Alternative assumptions about other relationships

In the next step, the assumptions about the standard deviations of the fertility and mortality random terms and the correlation between them were changed, while everything else was as in the 'basic simulation.' The patterns were the same as above in all four sets of assumptions (online appendix Table A-7): In fact, reducing the correlation from 0.50 to 0.25 or increasing it to 0.75 did not change the bias much. Changing the standard deviation of the mortality random term from 1 to 0.5 did not have much impact either, but if also the standard deviation of the fertility random term was reduced from 1 to 0.5, the effects of maternal age and birth order became stronger, and the mean bias was larger.

The patterns in the estimates were actually quite similar also if the correlation was set as low as 0.05 or even at exactly 0 (absolute bias 0.682 or 0.693, and root mean square bias 0.882 or 0.894, respectively; not shown in tables). In such a situation, where there are (essentially) no common unobserved determinants of fertility and mortality, a naïve model would give correct estimates – regardless of whether there is an effect of child deaths on subsequent fertility. However, a researcher would typically not know that there are no common unobserved determinants, and may therefore estimate sibling models – which will give biased estimates.

It was then assumed in the simulation that infant death of the most recently born sibling had a direct effect on the mortality of the index child: $\gamma_4 G$ was added to equation (3), with γ_4 set to 0.5. Such an effect would not be unreasonable. For example, grief because of the loss of an older child may make the parents less able to care for the newborn. The biases in the effects of maternal age, birth interval, and birth order were not changed as a result of this alternative assumption (online appendix Table A-8, column 3).

As another alternative it was assumed in the simulation that the birth rate was influence not only by whether the most recently born child had died, but also by whether children born earlier had died – which makes good sense theoretically. More specifically, it was assumed that the log-odds of higher-order births were raised by 0.2 if a child born before the most recently born child had died in infancy. As one would expect, the bias was quite similar to that observed without this additional effect on fertility (online appendix Table A-8, column 5).

In the last step, two different fertility random terms – one for first births and one for higher-order births – were included instead of only one. Both were assumed to have a variance of 1, and the correlation between them was set to 0.5. The correlation between the random term for first births and that for mortality was 0.50, and the correlation between the random term for higher-order births and that for mortality was 0.25. Especially the effect of maternal age was then less biased than with the other assumptions, but the directions of the biases were the same (online appendix Table A-8, column 6).[10]

4.6 Steps one might consider taking to solve the problem

It is possible that some researchers could be tempted to try to solve the problem by controlling for the infant death of the most recently born sibling, i.e. adding a term $\lambda_4 G$ to the sibling model that is estimated (Equation 4). However, this does not work (online appendix Table A-9, column 3). Nor does it work if a direct effect of the death of the most recently born child is assumed in the simulation (online appendix Table A-8, column 4).

Furthermore, one might consider including only every second child in the estimation, because in that case the death of a child does not have such a direct effect on the reproductive factors for the younger sibling included. This was examined in a simple way by focusing on women with five children. In order to get a larger number of women with five children in the simulated population and a larger number of child deaths, log(25) was added to the intercept in the mortality equation in the simulation, and log(3) was added to the intercepts in the fertility equations.

It was first assumed in the simulation, for comparison, that there was no effect of infant deaths on subsequent fertility. As one would expect, correct estimates were then obtained both when all the children of the five-child mothers were included, and when only the first, third, and fifth child were included (online appendix Table A-10, columns 3 and 4). However, when the effect of infant death on subsequent fertility was set to 1 as usual, and when all the children of the five-child mothers were included, there were biases such as in the other simulation experiments. When the second and fourth child were then excluded, the estimates did, on the whole, not become more correct (columns 5 and 6): While the effect of maternal age was somewhat less biased, the effect of the birth interval length was more biased, and the mean bias was essentially the same.

The results were similar if the five-child mothers' second and fourth child were included instead, or if every second child of mothers with fewer than five children were included (not shown). Thus, the conclusion is that exclusion of every second child does not solve the problem either.

One might also consider including only the families where the last child has died, as there would then not be a younger sibling whose reproductive factors are influenced by that death. However, those who do not respond to a child death by having another child are not representative of the population. Furthermore, there may be deaths also

[10] In the absence of an effect of infant death on subsequent fertility, a sibling model also works well, of course, with such assumptions about the fertility and mortality random terms.

among the older siblings, and if one tries to solve that problem by excluding these families, further selectivity is introduced. More importantly, it would not be meaningful – and in some situations not technically possible either – to estimate effects of birth order and maternal age when the youngest sibling is bound to have died.

Sjölander et al. (2016) showed that one at least would be able to test the null-hypothesis of zero effect of the exposure on the outcome – but not get an estimate of the effect – by swapping exposure and outcome. However, their argument was based on a linear model and, more importantly, there was only one exposure variable. In the present study, there are three exposure variables (maternal age, birth interval length, and birth order), which are even categorical, and the intention is to find out how they affect infant mortality net of each other. Thus, although one could estimate a model for a continuous version of each of these variables separately, with child death as a regressor, that would not be very helpful.

5. Conclusion

A major problem when effects of reproductive factors on child mortality are analysed is that many inadequately measured factors may affect both the mother's reproduction and the children's mortality. Using sibling models, which means that one controls at least for unobserved mortality determinants that are time-invariant (i.e., affecting the siblings similarly) and somehow linked to the reproductive behaviour, would therefore appear to be a good strategy. However, it has been argued mathematically that such models may give biased estimates when the outcome for one sibling affects the exposure for another, and this is precisely the situation when the exposure is reproductive factors and the outcome is infant or child death.

By doing a series of simulation experiments one may get an idea of whether the bias actually matters in practice. The conclusion from the experiments reported above is that, given a variety of presumably quite realistic assumptions about fertility, mortality, and their determinants – which should mimic the situation in both rich and poor settings – the effects of maternal age, birth order, and birth intervals are substantially biased: The estimated effects of higher maternal age were less negative (beneficial) or more positive (adverse) than the true effects, while the effects of higher birth order and very short or very long birth intervals were biased in the opposite direction. One cannot, however, rule out the possibility that the biases would have been negligible or taken another direction with certain other assumptions.

These results mean that one should be very careful to draw conclusions from earlier studies were sibling models have been used, and estimates from more 'naïve' analyses are, of course, no more trustworthy. In other words, we may know less about the effects of reproductive factors on child mortality than we tend to believe.

In principle, analysis based on an exogenous variation in the reproductive factors – for example a policy reform or intervention affecting birth interval lengths but otherwise not mortality – would have the potential to add considerably to our knowledge (Baqui et al. 2018). However, in most settings it is difficult to find good sources of such variation. One might also consider estimating a multilevel-multiprocess model, and include an effect of child mortality in the fertility equation (Kravdal 2018), but it is not obvious that the model can actually be correctly estimated when there are effects *of* mortality *on* fertility in addition to the effects in the opposite direction (that we are primarily interested in). That needs to be checked, for example, with the same type of simulation experiments as here. Also, these models rest on certain assumptions about the association between the unobserved mortality determinants and the reproductive process that are not necessarily reasonable, while there are no such assumptions behind the siblings models.

Although the problem discussed here is particularly large when the focus is on mortality, since it strongly affects later fertility, it may also be relevant when the attention is directed towards other child or pregnancy outcomes. The important message to researchers doing sibling analysis to learn about effects of reproductive factors on child outcomes is that, whenever there is a possibility that the outcome influences subsequent fertility or pregnancy rates, conclusions should be drawn very cautiously.

6. Acknowledgements

The advice from two reviewers is greatly appreciated. The research has been supported by the Norwegian Research Council through its Centres of Excellence funding scheme, project number 262700.

References

Ball, S.J., Pereira, G., Jacoby, P., De Klerk, N., and Stanley, F.J. (2014). Re-evaluation of link between interpregnancy interval and adverse birth outcomes: Retrospective cohort study matching two intervals per mother. *British Medical Journal* 349: g4333. doi:10.1136/bmj.g4333.

Baqui, A.H., Ahmed, S., Begum, N., Khanam, R., Mohan, D., Harrison, M., ... and Ahmed, S. (2018). Impact of integrating a postpartum family planning program into a community-based maternal and newborn health program on birth spacing and preterm birth in rural Bangladesh. *Journal of Global Health* 8(2): 020406. doi:10.7189/jogh.08.020406.

Barclay, K. and Kolk, M. (2017). The long-term cognitive and socioeconomic consequences of birth intervals: A within-family sibling comparison using Swedish register data. *Demography* 54(2): 459–484. doi:10.1007/s13524-017-0550-x.

Barclay, K. and Myrskylä, M. (2016). Advanced maternal age and offspring outcomes: Reproductive ageing and counterbalancing period trends. *Population and Development Review* 42(1): 69–94. doi:10.1111/j.1728-4457.2016.00105.x.

Bousmah, M.A.Q. (2017). The effect of child mortality on fertility behaviors is non-linear: New evidence from Senegal. *Review of Economics of the Household* 15: 93–113. doi:10.1007/s11150-014-9264-7.

Class, Q.A., Rickert, M.E., Oberg, A.S., Sujan, A.C., Almqvist, C., Larsson, H., ... and D'Onofrio, B.M. (2017). Within-family analysis of interpregnancy interval and adverse birth outcomes. *Obstetrics and Gynecology* 130(6): 1304–1311. doi:10.1097/AOG.0000000000002358.

Ewemade, J., Akinyemi, J., and DeWet, N. (2019). The effect of child death on birth spacing in Nigeria. *Journal of Biosocial Science* 52(3): 1–8 doi:10.1017/S0021932019000464.

Hanley, G.E., Hutcheon, J.A., Kinniburgh, B.A., and Lee, L. (2017). Interpregnancy interval and adverse pregnancy outcomes. *Obstetrics and Gynecology* 129(3): 408–415. doi:10.1097/AOG.0000000000001891.

Kravdal, Ø. (2018). New evidence about effects of reproductive variables on child mortality in sub-Saharan Africa. *Population Studies* 72(2): 139–156. doi:10.1080/00324728.2018.1439180.

Kravdal, Ø. (2019). Taking birth year into account when analysing effects of maternal age on child health and other outcomes: The value of a multilevel-multiprocess model compared to a sibling model. *Demographic Research* 40(43): 1249–1290. doi:10.4054/DemRes.2019.40.43.

Molitoris, J. (2018). Heterogeneous effects of birth spacing on neonatal mortality risks in Bangladesh. *Studies in Family Planning* 49(1): 3–21. doi:10.1111/sifp.12048.

Molitoris, J., Barclay, K., and Kolk, M. (2019). When and where birth spacing matters for child survival: An international comparison using the DHS. *Demography* 56: 1349–1370. doi:10.1007/s13524-019-00798-y.

Regan, A.K., Ball, S.J., Warren, J.L., Malacova, E., Padula, A., Marston, C., ... and Pereira, G.A. (2018). Population-based matched-sibling analysis estimating the associations between first interpregnancy interval and birth outcomes. *American Journal of Epidemiology* 188(1): 9–16. doi:10.1093/aje/kwy188.

Shachar, B.Z., Mayo, J.A., Lyell, D.J., Baer, R.J., Jeliffe-Pawlowski, L.L., Stevenson, D.K., and Shaw, G.M. (2016). Interpregnancy interval after live birth or pregnancy termination and estimated risk of preterm birth: A retrospective cohort study. *BJOG: An International Journal of Obstetrics and Gynaecology* 123(12): 2009–2017. doi:10.1111/1471-0528.14165.

Sjölander, A., Frisell, T., Kuja-Halkola, R., Öberg, S., and Zetterqvist, J. (2016). Carryover effects in sibling comparison designs. *Epidemiology* 27(6): 852–858. doi:10.1097/EDE.0000000000000541.

Statistics Norway (2019). Life table 2018. Available at https://ssb.no/befolkning/statistikker/dode.

van Soest, A. and Saha, U.R. (2018). Relationships between infant mortality, birth spacing and fertility in Matlab, Bangladesh. *PloS One* 13(4). doi:10.1371/journal.pone.0195940.