Commentary: Infectious diseases during infancy and mortality in later life

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Do the very first years of life determine old-age mortality? This question has stimulated an extensive debate since 1973, when Forsdahl published his first paper about the effect of very poor living conditions in childhood and adolescence on adult mortality. Further work by Barker and colleagues led to the formulation of the ‘fetal-origins’ hypothesis, which states that chronic disease later in life is caused by nutritional deficiencies in utero. While these theories are developed on the basis of studies of mortality in the 20th century, Fridlizius suggested that, in the 19th century, exposure to infectious disease in the first 5 years of life caused an increased risk of infectious disease later in life.

Bengtsson and Lindström set out to test whether the critical early-life period for old-age mortality is in utero or during the first year of life, and whether the underlying mechanism is related to nutrition or infectious disease. They use individual-level data based on church records from four parishes in southern Sweden for the time period 1766–1894. The high quality of the Swedish demographic data both in historical and contemporary times is well known. The time period in their study coincides with a period of mortality decline on a cohort basis, which implies that, in terms of life expectancy, the year of birth had more predictive power than the year of death.

The authors use infant mortality during the year of birth to measure the disease load in the first year of life and the crude death rate of women at ages 20–50 years 9 months prior to birth to measure the disease load in the first year of life and the crude death rate of women at ages 20–50 years. Similarly, they use rye prices at the time of birth to account for differences in nutrition in the first year of life and rye prices 9 months prior to birth to account for fetal differences in nutrition. They find that both long-term trends and short-term fluctuations in infant mortality significantly influence late life mortality. The effect of
the short-term fluctuations is mainly the result of years with particularly high infant mortality, primarily caused by smallpox or whooping cough. They did not find an effect of the crude death rate at ages 20–50 and of rye prices on late life mortality.

The study is convincing in demonstrating the effect of infant mortality, and thus the disease load in the first year of life, on old-age mortality. It is less convincing in the treatment of the measures that pertain to the environment in utero. Much depends on the time point that these measures are fixed to. For both measures Bengtsson and Lindström choose to fix them 9 months prior to birth. However, both rye prices and mortality are highly seasonal and this seasonality may have distorted their results.

In a footnote of their book about the population history of England, Wrigley and Schofield report seasonal mortality indices for Sweden (ref. 6, p. 296). Between 1749 and 1855 mortality in Sweden differed by 36%, reaching its peak in March and its minimum in July. On the basis of these indices one finds that the seasonal pattern of the mortality indices 9 months prior to birth is highly correlated with the seasonal pattern of the average mortality indices of the first trimester ($p = 0.83$, $P = 0.001$) and the third trimester ($p = -0.78$, $P = 0.002$) of pregnancy. There is little resemblance, however, with the seasonal pattern for the whole 9-month period ($p = 0.46$, $P = 0.131$). A better approach would have been to use the crude death rate for the whole 9-month period of pregnancy. This would also guarantee that the effect of extremely high mortality in only one of the 9 months of pregnancy is not missed. A similar argument pertains to rye prices.

Since the authors did not find any significant results for the crude death rate and the rye price in their first model they did not explore these variables in the same careful manner as they did with infant mortality. One would wish they had used the same threshold approach as they had used for infant mortality, i.e. exploring periods of extremely high rye prices or adult mortality.

The authors include the season of birth in their models and find an effect of borderline significance. Those born in spring and summer tend to have the highest mortality risk at ages 55–80, those born in autumn the lowest. This is consistent with the authors who had used for infant mortality, and thus the disease load in the first year of life, on old-age mortality. It is less convincing in the treatment of the measures that pertain to the environment in utero. Much depends on the time point that these measures are fixed to. For both measures Bengtsson and Lindström choose to fix them 9 months prior to birth. However, both rye prices and mortality are highly seasonal and this seasonality may have distorted their results.

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The authors include the season of birth in their models and find an effect of borderline significance. Those born in spring and summer tend to have the highest mortality risk at ages 55–80, those born in autumn the lowest. This is consistent with the results for contemporary populations in Austria and Denmark, 7,8 although the excess mortality in the historical Swedish population is much larger (Denmark: 3%, Sweden: 14%).

In their final model they find that the effect of infant mortality on late-life mortality is particularly large for the winter- and the summer-born. Historically, in Sweden, as in many other countries, infant mortality was highly seasonal with peaks in the winter and the summer months. 9 Respiratory diseases were mainly responsible for the mortality during the winter months, while water- and airborne infections were virulent during the summer months. 10 Also smallpox is a highly seasonal disease with large outbreaks occurring during the winter months, rarely during the summer. 11 Thus, extremely high infant mortality mainly occurred during winter and summer. The particularly large effect of infant mortality on old-age mortality for the summer- and winter-born has an important implication: in terms of infectious disease the critical time-period early in life is the very first months of life because those born during seasons with high infant mortality also experience increased old-age mortality.

The overall month-of-birth pattern in this study, however, indicates that the spring- and summer-born suffer from the highest mortality risk later in life, which suggests also that other factors than infectious disease play an important role. In terms of pre-natal nutrition the spring-born were particularly disadvantaged, because the last trimester of the pregnancy, which is the time of peak-growth in utero, falls into a season when nutritional deficiencies were most likely. This lends further support to the view that Bengtsson and Lindström do not find an effect of nutrition or infectious disease in utero because of the specification of their variables rather than because it does not exist.

References


