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Bengtsson, Tommy; Lindström, Martin

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Airborne infectious diseases during infancy and mortality in later life in southern Sweden, 1766–1894

Tommy Bengtsson[1] and Martin Lindström[2]

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Background The importance of early life conditions and current conditions for mortality in later life was assessed using historical data from four rural parishes in southern Sweden. Both demographic and economic data are valid.

Methods Longitudinal demographic and socioeconomic data for individuals and household socioeconomic data from parish registers were combined with local area data on food costs and disease load using a Cox regression framework to analyse the 55–80 year age group mortality (number of deaths = 1398).

Results In a previous paper, the disease load experienced during the birth year, measured as the infant mortality rate, was strongly associated with old-age mortality, particularly the outcome of airborne infectious diseases. In the present paper, this impact persisted after controlling for variations in food prices during pregnancy and the birth year, and the disease load on mothers during pregnancy. The impact on mortality in later life stems from both the short-term cycles and the long-term decline in infant mortality. An asymmetrical effect and strong threshold effects were found for the cycles. Years with very high infant mortality, dominated by smallpox and whooping cough, had a strong impact, while modest changes had almost no impact at all. The effects of the disease load during the year of birth were particularly strong for children born during the winter and summer. Children severely exposed to airborne infectious diseases during their birth year had a much higher risk of dying of airborne infectious diseases in their old age.

Conclusions This study suggests that exposure to airborne infectious diseases during the first year of life increases mortality at ages 55–80.

Keywords Early life, life course perspective, infant mortality, old-age mortality, airborne infectious disease

The decline in old-age mortality in Sweden and other Western countries started in the mid-19th century, several decades later than the decline in infant mortality.[1,2] Old-age mortality is determined by a number of factors, some of which relate to economic and social conditions during the old-age period of life (period determinants). Others are related to the long-term effects of conditions *in utero* or during early childhood (cohort determinants).

Period determinants of old-age mortality include long-term changes in hygiene and public health,[3] and nutrition and standards of living in general,[4] but also short-term insecurity in access to food, etc.[5,6]

Kermack, McKendrick, and McKinley proposed the cohort explanation in 1934. They studied age-specific mortality in England, Wales, Scotland, and Sweden. Their conclusion was that reductions attained at any particular time in the death rates of the various age groups depended primarily on the individuals' date of birth, and only secondarily on the current year. The essential effects on health and survival among adults and older people were mainly caused by beneficial effects and improvements achieved in these birth cohorts during childhood several decades earlier.[7] This life-course perspective has been given more attention in recent years.[8,9] The plausible causal relationship between early life experiences and old-age mortality has been discussed, particularly in relation to intrauterine

[1] Department of Economic History, Lund University, 5220-07 Lund, Sweden. E-mail: tommy.bengtsson@ekh.lu.se

[2] Department of Community Medicine, Lund University, Sweden. E-mail: martin.lindstrom@smi.mas.lu.se

cellular development and cellular development during early childhood. Robert Fogel has proposed several plausible causal mechanisms that connect malnutrition, whether due to a lack of nutrients or increased demands as a result of disease, *in utero* and during early life to chronic diseases in later life.[10] The propositions regarding the effects of conditions before birth are supported by the work of Barker, among others, who suggested that the preconditions for coronary heart disease, hypertension, stroke, diabetes, and chronic thyroiditis are initiated *in utero* without becoming clinically manifest until much later in life.[11,12] In contrast, Fridlizius suggested that the genesis of disease in later life could be due to exposure to certain infectious diseases, such as smallpox, in the first 5 years after birth, resulting in reduced immunity to other diseases throughout life and, consequently, a higher general risk of other infectious diseases in later life.[13] This notion is supported by some studies that have suggested that lower respiratory tract illness in the first year of life is associated with later cough, phlegm, and impaired ventilatory function, independently of smoking and social class. Illness after the first year of life was not associated with any risk, which supports the idea of a critical period of influence for infection.[14,15] The hypothesis implies that factors other than nutrition were important early life determinants of mortality in later life, because the outcome of smallpox infection as well as some other important infectious diseases is almost completely unrelated to the nutritional status of the infected individual.[16] It also implies that it is not the conditions *in utero* that are important but rather the situation during infancy and early childhood. Fridlizius does not, however, discuss the possible effect on later health of the nutritional loss due to having experienced a non-nutritional disease or any infectious disease. Thus the cohort hypothesis put forward so far involves whether low nutritional intake or increased nutritional demands due to disease affect mortality in later life and whether the conditions *in utero* or during the first years of life are of the most importance. The problem in historical analysis has been that these four hypotheses have never been confronted with each other.

In a previous paper, Bengtsson and Lindström investigated these cohort hypotheses for four parishes in southern Sweden, 1766–1894.[17] They used a multivariate Cox regression model on longitudinal demographic data for individuals combined with household socioeconomic data, local area data on food prices, and disease load. While the focus was on cohort hypotheses, the analyses included both variables measuring period short-term economic stress and trends and cohort variables measuring the disease load on mothers during pregnancy and children during the first years of life and access to nutrition in early life. The hypothesis that access to nutrition was of primary importance was not supported by the results. Furthermore, no effects of conditions *in utero* were found. In contrast, the disease load experienced during the year of birth showed a consistent impact on mortality in later life, particularly on the outcome of airborne infectious diseases during old age. However, the previous study has some important limitations that we deal with in this paper. Firstly, different early-life indicators of stress were analysed in separate multivariate models, one at a time, due to technical constraints. Secondly, effects of long-term trends and short-term fluctuations in disease load during early life, threshold effects, and the patterns of disease load during the first year of life were not specified. Thirdly, possible seasonal effects of the date at birth were not taken into account. This is of potential importance as both diets and the exposure to disease vary seasonally. Mortality peaked in the winter season during the January–April period and was at its lowest from July to October.[18,19] It has also been shown that the season of birth has a strong influence on life expectancy.[20] The purpose of this paper is to eliminate these limitations so as to allow us to better understand the causal mechanisms of the previously observed effects of conditions in early life on old-age mortality, in particular on mortality from airborne infectious diseases.

Computer software development now allows us to analyse four or more time-varying community covariates simultaneously, which means that we can estimate the net effects of the disease load during the first year of life (infant mortality rate) and the disease load on the mother during pregnancy (measured indirectly by the crude death rates among adults aged 20–50 years), and the food prices during pregnancy and the first year of life will also be analysed as plausible determinants of old-age mortality. We are particularly interested in whether the large annual variations of food prices influence mortality in later life as one would expect it to reflect changes in nutrition. Variation in food prices also has a strong influence on current mortality. The effects of trends in infant mortality as opposed to fluctuations (cycles) from year to year on old-age mortality will be investigated by decomposing the infant mortality rate into two components using a Hodrick Prescott filter with a filtering factor of 100 (for a discussion of and references to this method, see ref. 21). The same filter is used to divide the crude death rates among adults aged 20–50 years into trend and cycle components. Furthermore, the cycle component of the infant mortality rate is divided into five categories to enable us to estimate potential threshold effects, and thus some years with a very high disease load have a proportionately stronger effect on old age mortality than other years. Furthermore, causes of death are identified for such years. The problem of seasonality is dealt with by including a season dummy (winter, spring, summer, autumn) as a covariate in the multivariate model, and also by analysing the season effect separately in four independent multivariate models. In addition, effects of sex, birth year, birthplace, present place of residence, present socioeconomic status (SES) (freeholders/crown tenants, tenants on nobility-owned land, semi-landless/crofters, landless), and current access to food (rye prices) are included in the model, based on both the variables available in this data collection[17] and in previous literature.[19]

Material and Methods

The sample consists of all married or previously married people aged 55–80 and living in Hög, Kevlinge, Halmstad, or Sireköpinge during any period between 1766 and 1894. Thus, it includes all those aged 55–80 in 1766, immigrants aged 55–80 and those who turned 55 years of age during the period. These people are considered exposed until they reach age 80, emigrate, are alive in 1894, or die (Figure 1). The data are from the Scanian Demographic Database and consist of records of births, marriages, deaths, and migrations for nine rural parishes and one town, while only the four parishes used in this paper are complete for analyses. The material for two parishes dates back

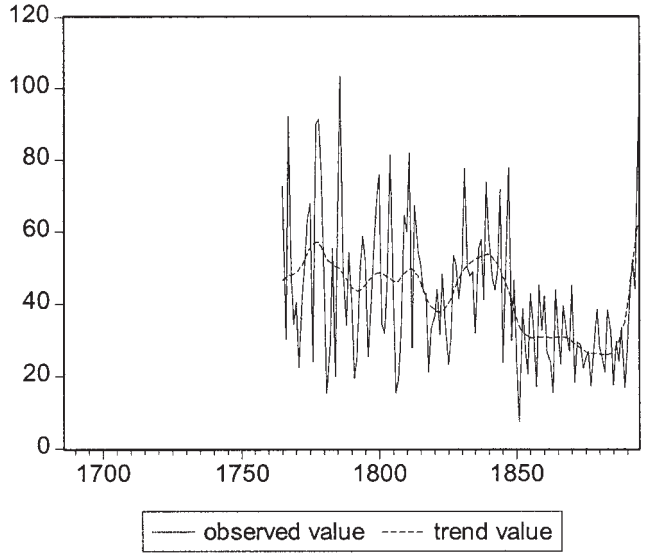

Figure 1 Crude death rate at ages 55–80 in four Scanian parishes, 1766–1894. Per thousand

to 1646 and for the others to the 1680s and continues until 1895. The parish register material is of high quality and shows few gaps in births, deaths, and marriages. Migration records are less plentiful, but continuous series exist from the latter part of the 18th century. Information concerning farm size, property rights, and various other items from the poll tax records and land registers are linked to the family reconstitutions based on the parish records of marriages, births, and deaths. The study period 1766–1894 was chosen because there is a gap in the information about landholdings prior to 1766 and the data on individuals are not available to us after 1895. We also have records throughout the study period on causes of death registered by the clergymen. For the period before the mid-18th century, we have, however, little information about causes of deaths, which we will come back to later.

The sampled parishes are compact in their geographical location, showing the variations that could occur in peasant society with regard to size, topography, and socioeconomic conditions, and they offer good early source material. The entire area was open farmland, except northern Halmstad, which was more wooded. Halmstad and Sireköpinge were 'noble' parishes, in which the farmers rented the land from the estate owners, while freehold and crown land dominated in Kävlinge and Hög. The parishes had 200–500 inhabitants each in the latter part of the 18th century. Kävlinge rapidly expanded during the last decades of the 19th century due to the establishment of several factories.

Demographic data from Sweden dating from 1749 and onwards are generally highly valid and reliable both at the aggregated and individual level. The data are of much higher quality than, for example, those for England[22] covering the same historical period. Firstly, Sweden had a state church from 1527 to 2000, which means that the church books cover the entire population. Secondly, we have both census type information and records about migration and thus know the population at risk. Thirdly, we have occupational information and data on farm types and sizes. Fourthly, we have cause-of-death records. The quality of the death records in the parishes of this study is high, as indicated by the ratio of male to female births, the proportion of stillbirths, and the proportion of deaths during the first month.[23] The validity and reliability of historical data on causes of death in Sweden have been thoroughly discussed elsewhere.[17] In summary, changes in the nomenclature of medical diagnoses (in 1774, 1802, 1811, 1821, 1831, 1873, and 1891) and the succession of individual clergymen in the parishes seem to have had no effect on the validity and reliability of the medical diagnoses made by the clergymen.[24] Furthermore, some diseases, especially infectious diseases such as smallpox, were identified as the same diagnostic entities (based on distinct symptoms) and denoted by the same names as today.[17] The aetiology of infectious diseases, the most common cause of death during the whole study period, was not known; proper diagnosis was impossible, except for symptomatic diagnoses, until the end of the 19th century.[25] The system remained basically nosological during the whole period.[24]

The social structure of the agricultural sector is often difficult to analyse as differences in wealth between the various categories of farmers and occupations are unclear and subject to change with the passage of time. Data from land registers on types of tenure must therefore be combined with information from poll tax records concerning farm size in order to arrive at a better understanding of the social structure. From these sources we can conclude that the nobility was a rather small group and it has therefore been excluded from our sample. The peasants were divided into two categories: freeholders, tenants on crown land, and tenants on church land constituting the first group, while tenants on nobility-owned land constitute the second one. We only include peasants with farms larger than 1/16 *mantal* in these two categories as it has been argued that peasants with smaller farms could not support themselves. A *mantal* was not a measure of the actual size of the farm but a tax-assessment unit based on potential production. A third group, which we label semi-landless, includes farmers with land smaller than 1/16 *mantal* and crofters. The fourth group is the landless workers.

In estimating the parameters of the models, we use event-history analysis with time-varying external covariates, which makes it possible to run regressions on the change of life status, i.e. dying or giving birth to a child, measuring the effects of different explanatory variables (or covariates) on the hazard of the event. More specifically, we use the Cox proportional hazards model, which does not require specification of the underlying hazard function. The main interest in this case is to estimate the impact of different covariates on the hazard of death. The aggregated indicator of the food prices is included in the regressions as a communal, or external, covariate.[26,27] This means that the aggregate economic information is used as a time-varying covariate common to all individuals in the risk set at each point in calendar time.[27] Aggregated indicators—the infant mortality rate (Figures 2 and 3), the crude death rate at ages 20–50 years (Figure 4), and the food prices (Figure 5)—are also used as fixed community covariates. The value of the community covariate is then shared by all individuals with the same birth year or with the same year of conception, depending on which indicator it is. The infant mortality rate during the

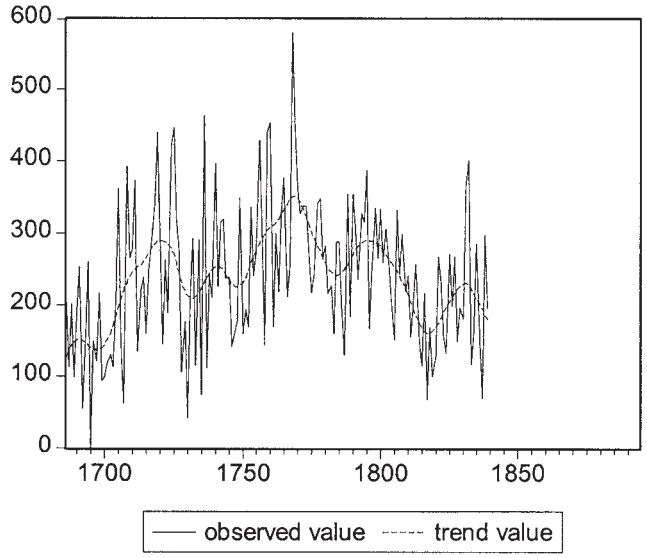

Figure 2 Infant mortality rate in four Scanian parishes, 1686–1839. Per thousand

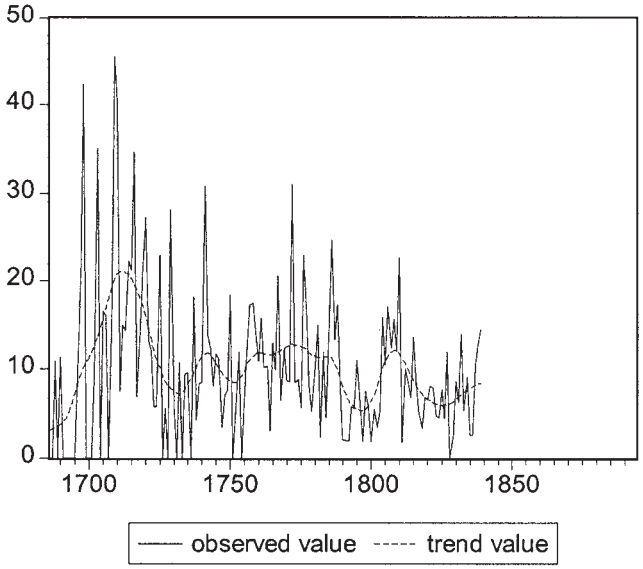

Figure 4 Crude death rate in ages 20–50 in four Scanian parishes, 1686–1839. Per thousand

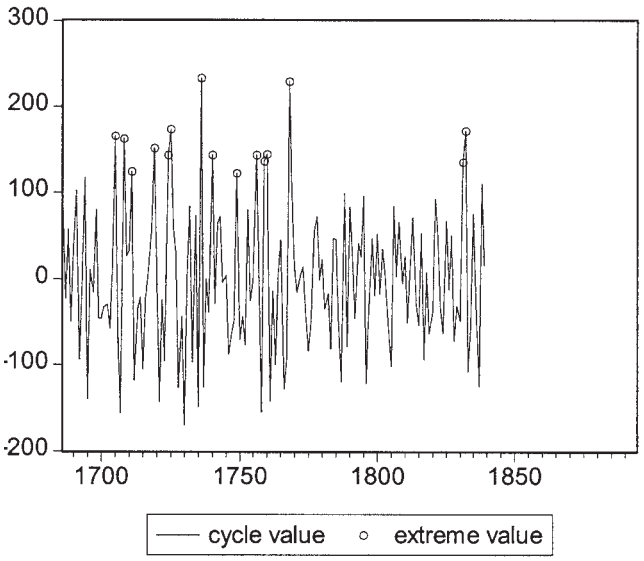

Figure 3 Cycles and extreme values in infant mortality rate in four Scanian parishes, 1686–1839. Per thousand

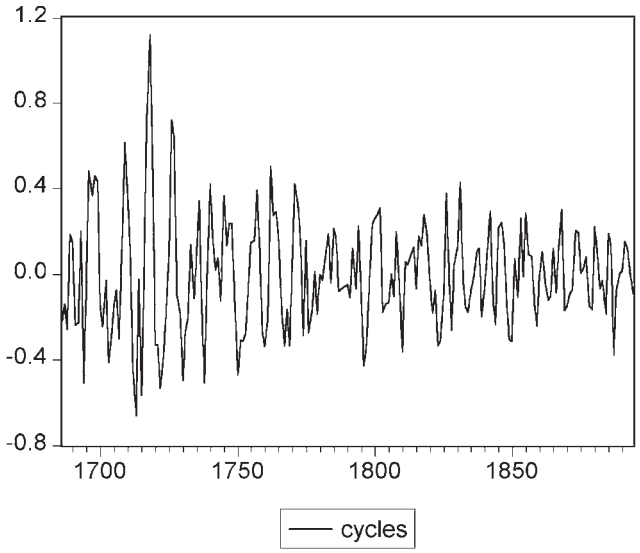

Figure 5 Cycles in the logarithm of local rye prices, 1686–1894

year at birth is shared by all individuals with the same birth year to indicate the disease load on infants. The crude death rate at ages 20–50 during the year of conception is shared by all individuals with the same year of conception to indicate the disease load on the mothers during the pregnancy. Food prices are likewise fixed to reflect the access to food during both the fetal stage and the birth year. We use the logarithm of local rye prices as an indication of the availability of food because grain dominated the diet and rye was the major crop. This indicator has been used in many previous studies and has been shown to have high validity.[27] The software program used is called MLIFE and was developed by Professor Göran Broström of Umeå University and Lund University. It is a GNI licence program and has specific features to facilitate the use of time-varying and fixed community covariates.[28]

Results

Table 1 shows the average of each covariate, or category, the likelihood ratio *P*-value test for the covariate, the relative risk, and the Wald *P*-value for each covariate or category. The 'average' depicts the mean value of the covariate or category. In the case of sex, it shows the proportion of men and women in percentage at risk (similarly to birth season, parish, socioeconomic group, and birthplace). The average birth year is 1775.2 and infant mortality is 20% on average, while crude death rate in

Table 1 Estimation of effects of sex, birth year, birth season, birthplace, parish of residence, socioeconomic status, infant mortality rate at birth, crude death rate at ages 20–50 years at conception, and cycles in the logarithm of rye prices at conception, at birth and currently in four Scanian parishes, 1766–1894. The number of deaths is 1398

Covariate	Average	LR[a] *P*-value	Relative risk	Wald *P*-value
Sex		0.857		
Male	54.1%		1	(ref.)
Female	45.9%		1.010	0.857
Birth season		0.119		
Winter	26.6%		1	(ref.)
Spring	21.5%		1.104	0.193
Summer	22.1%		1.091	0.259
Autumn	29.8%		0.942	0.413
Parish		0.448		
Hög	13.7%		1	(ref.)
Kävlinge	16.6%		0.927	0.391
Halmstad	46.8%		1.013	0.877
Sireköpinge	22.9%		1.056	0.504
Socioeconomic group		0.013		
Freeholders/crown tenants	7.8%		1	(ref.)
Tenants on nobility-owned land	9.9%		0.870	0.440
Semi-landess/crofters	15.1%		0.759	0.067
Landless	67.2%		0.994	0.965
Birthplace		0.363		
In parish	29.3%		1	(ref.)
Other parish	70.7%		1.056	0.365
Birth year	1775.2	0.000	0.997	0.000
Infant mortality rate, at birth	0.20	0.000	2.925	0.000
cdr, ages 20–50, at conception	0.01	0.911	0.669	0.911
Log of rye prices				
At conception	0.00	0.604	1.065	0.604
At birth	0.00	0.860	1.021	0.860
Current	0.00	0.420	1.128	0.420
Overall *P*-value: 0.0000				

[a] Likelihood ratio.

ages 20–50 years is about 1%. The likelihood ratio test compared the full model with one in which the covariate is excluded, whether it is a nominal covariate or categorized. It is known to be a very robust test. The relative risk gives the risk relative to a reference category, such as the risk for mortality among females relative to men. In the case of nominal covariates, it shows the change in risk associated with a one-unit change in the covariate. For example, the relative risk for birth year is the value associated with being born one year later. The final column shows the Wald test *P*-value for each category. This test is less robust than the likelihood ratio test, particularly for small samples.

Table 1 shows that the disease load in the year of birth, measured by the period infant mortality rate for that year, had a strong impact on mortality among the elderly when also considering other conditions close to birth simultaneously. The effects of the disease load on the mother during pregnancy, measured by the crude death rate among adults 20–50 years of age and food prices during the pregnancy as well as during the first year of life, are minor. This holds true also when trend and cycle effects are analysed separately (not shown here). The likelihood ratio tests in Table 1 show that each of these variables can be excluded and the same is true of the current time effect of food prices. A likelihood ratio test comparing the estimations of a reduced model, in which neither of these variables is included, with the full model shows that they can be excluded as a group. The χ^2 value only decreases from 58.69 to 57.48 when the degrees of freedom go down by 4.

The effect of the disease load during the year of birth is strong and highly significant. A one-unit change in the disease load increased the mortality risk by approximately 50%, from an average of 0.042 to about 0.06. The effects of birth year and SES are also significant. Being born one year later is associated with a 0.3% lower death risk. The finding regarding SES seems at first paradoxical as the semi-landless—crofters and people with very small farms—have lower death risks than the better-off freeholders and tenants. They have, on the other hand, lower mortality than the landless, which is what one would expect from an economic point of view. A possible explanation is that the size and composition of the semi-landless group changes over time, partly as a result of the agricultural reforms at the beginning of the 19th century. We have therefore estimated the model similarly to the one shown in Table 1 with controls for various time periods. While we are not reporting these details in this paper, we did find that the results are stable throughout the 19th century. Thus, the lower mortality for the semi-landless group relative to the better-off groups is not a result of its increase in size in a period with lower mortality but is genuine. A possible explanation of the lower mortality among the semi-landless is the fact that they often lived in cottages outside the villages and that they were therefore less exposed to infectious diseases. Furthermore, we did not find effects of gender, the time of the year when the birth occurred, which parish the elderly lived in, and whether people were living in their native parish or not.

In as much as the disease load during the birth year had such a strong effect on mortality at later ages, we have tried to specify it better. The infant mortality rate between 1686 and 1839, when the elderly people were born, fluctuated substantially. Figure 2 shows that the infant mortality rate changes annually, but also a secular trend. The estimated effect shown in Table 1 could either be a result of the short-term changes or the long-term ones. This infant mortality rate was therefore divided into two components using a Hodrick Prescott filter with 100 as the filter term, which resulted in the short-term component called cycle, shown in Figure 3, and the long-term component shown as the broken line in Figure 2. For a discussion of the method in this context see ref. 21. Table 2 shows that not only the long-term development of the infant mortality rate but also annual changes influenced mortality in later life.

In order to estimate potential non-linear effects in the short-term response, we categorized the cycles of the infant mortality rate into five spells, using the values –120, –60, +60, and +120 per thousand as limits. Fifteen years have an infant mortality rate above 120 after the trend removal. They are marked with rings in Figure 3. As shown in Table 3, these years have a very strong impact on mortality among the elderly. Thus the effect of the disease load during the birth year is neither symmetrical nor linear. Since they have such a strong influence, we have tried to find out what they are characterized by. Unfortunately, we have no record of causes of death for the four parishes before 1740,

Table 2 Estimation of effects cycles and trend in infant mortality rate at birth, sex, birth year, birth season, birthplace, parish of residence, and socioeconomic status in four Scanian parishes, 1766–1894. The number of deaths is 1398

Covariate	Average	LR[a] *P*-value	Relative risk	Wald *P*-value
Sex		0.849		
Male	54.1%		1	(ref.)
Female	45.9%		1.010	0.849
Birth season		0.118		
Winter	26.6%		1	(ref.)
Spring	21.5%		1.102	0.204
Summer	22.1%		1.087	0.277
Autumn	29.8%		0.938	0.385
Parish		0.415		
Hög	13.7%		1	(ref.)
Kävlinge	16.6%		0.925	0.380
Halmstad	46.8%		1.014	0.868
Sireköpinge	22.9%		1.059	0.481
Socioeconomic group		0.013		
Freeholders/crown tenants	7.8%		1	(ref.)
Tenants on nobility-owned land	9.9%		0.865	0.422
Semi-landess/crofters	15.1%		0.752	0.059
Landless	67.2%		0.983	0.899
Birthplace		0.294		
In parish	29.3%		1	(ref.)
Other parish	70.7%		1.066	0.296
Birth year	1775.2	0.001	0.997	0.001
Infant mortality rate, at birth				
Trend	0.20	0.006	4.849	0.006
Cycle	0.00	0.014	2.348	0.014
Overall *P*-value: 0.0000				

[a] Likelihood ratio.

Table 3 Estimation of non-linear effects of cycles in infant mortality rate at birth, sex, birth year, birth season, birthplace, parish of residence, and socioeconomic status in four Scanian parishes, 1766–1894. The number of deaths is 1398

Covariate	Average	LR[a] *P*-value	Relative risk	Wald *P*-value
Sex		0.801		
Male	54.1%		1	(ref.)
Female	45.9%		1.014	0.801
Birth season		0.204		
Winter	26.6%		1	(ref.)
Spring	21.5%		1.091	0.253
Summer	22.1%		1.102	0.205
Autumn	29.8%		0.961	0.585
Parish		0.515		
Hög	13.7%		1	(ref.)
Kävlinge	16.6%		0.929	0.408
Halmstad	46.8%		1.015	0.853
Sireköpinge	22.9%		1.048	0.563
Socioeconomic group		0.013		
Freeholders/crown tenants	7.8%		1	(ref.)
Tenants on nobility-owned land	9.9%		0.856	0.389
Semi-landess/crofters	15.1%		0.753	0.060
Landless	67.2%		0.985	0.906
Birthplace		0.406		
In parish	29.3%		1	(ref.)
Other parish	70.7%		1.051	0.407
Birth year	1775.2	0.000	0.997	0.000
Infant mortality rate, at birth				
Very low	6%	0.896	1.028	0.896
Low	11%	0.926	1.010	0.926
Normal	63%		1	(ref.)
High	13%	0.280	0.912	0.285
Very high	7%	0.019	1.508	0.013
Overall *P*-value: 0.0000				

[a] Likelihood ratio.

so we have to use information from neighbouring parishes for the first part of the period. Table 4 shows the results. For two years, 1708 and 1724, we have no information on neighbouring parishes either. The mortality peaks for all other years prior to 1740 are associated with smallpox in the neighbouring parishes. It is therefore likely that the peaks in the four parishes we use in this analysis, prior to 1740, are also due to smallpox since it was easily spread. Taken together with the information for the four parishes after 1740, we find that smallpox and/or whooping cough occurred in 13 out of the 15 years.

The interaction effects between the disease load in the first year of life and sex, birth season, parish, and socioeconomic group were estimated by adding the interaction to a model similar to the basic model shown in Table 1. The only difference was that the infant mortality rate was the only early-life indicator included, since the likelihood ratio test showed that the other ones could be excluded. The size of the data set does not allow us to estimate all interaction effects simultaneously. Separate models were therefore used. Using the likelihood ratio test to evaluate the results, we cannot show any interaction effects between infant mortality rates and sex, parish, socioeconomic group, and birthplace (not reported here). The coefficients for the interaction with birth season are quite strong, but still not significant (likelihood ratio *P*-value, 0.285). Children born during the winter and summer seem to be much more affected by diseases than those born during the spring and autumn. To release the models from the assumptions regarding proportionality between the other covariates and from sharing the same baseline hazard function, separate models for each birth season were estimated. Table 5 shows the results of the four estimations. It shows that the effect is particularly strong for children born during the first 3 months of the year, but it is also strong for those born during the summer. This indicates that our choice of measure of the disease load during the first period of life after birth (the infant mortality rate during the birth year) might possibly be improved. Such improvement would most likely lead to even stronger results. Thus we are on the safe side in terms of measurement using the infant mortality rate in the birth year as the indicator of health at the beginning of life.

Discussion

Old-age mortality during the study period was affected by both long-term changes in the disease load during the years of birth and variation in the disease load from one year to another, even after controlling for variations in food prices and the disease load at ages 20–50. The effects of the changes in the disease load from one year to another were mainly due to outbreaks of

Table 4 Prevalence of smallpox and whooping cough in years with extremely high mortality compared with years before and after in four Scanian parishes and their surroundings

1705	smallpox in Scania and in neighbouring parishes (Lackalänga, Stävie, V Karaby) in 1706
1708	no information available
1711	smallpox in Scania
1719	smallpox in a neighbouring parish (V Karaby) in 1718
1724	no information available
1725	smallpox in a neighbouring parish (Reslöv) in 1726
1736	smallpox in neighbouring parishes (Lackalänga, Stävie)
1740	smallpox
1749	whooping cough
1756	smallpox
1759	smallpox
1760	smallpox
1768	smallpox, whooping cough
1831	whooping cough
1832	whooping cough

Sources: 1740–1832 cause of death records from Hög, Kävlinge, Halmstad, and Sireköping (Scanian Demographic Database), 1706 and 1719–1736 church books for Lackalänga, Stävie, V Karaby, and Reslöv parishes, which are located very close to the parishes in our sample, 1705 and 1711 Persson (2001:135).

Table 5 Estimations of effects of infant mortality rate at birth for birth season cohorts after controlling for sex, parish, socioeconomic group, birthplace, and birth year in four Scanian parishes, 1766–1894

Covariate	No. of deaths	LR[a] *P*-value	Relative risk	Wald *P*-value
Infant mortality rate, at birth for				
Winter cohort	379	0.002	5.940	0.002
Spring cohort	320	0.504	1.527	0.504
Summer cohort	309	0.025	3.957	0.024
Autumn cohort	390	0.257	1.802	0.254

[a] Likelihood ratio.

infectious diseases such as smallpox, whooping cough, pneumonia, measles, etc. Moderate changes in the disease load during the birth year had no significant impact on old-age mortality. The other hypothesized causal cohort mechanisms, i.e. that the disease load on the mother during pregnancy (crude death rates among adults aged 20–50) and the food prices during both pregnancy and the first year of life would affect old-age mortality among those aged 55–80 years, could not be confirmed. Thus we find no effect of external conditions during the fetal stage, either of nutritional access or of the disease load on mothers, and no effect of nutritional access during the first year of life. But the disease load during the birth year mattered a lot regarding mortality among the elderly.

The results agree to some extent with those of Fridlizius,[13] who proposed that adult and old-age mortality was mainly affected by the disease load during the first 5 years of life. Fridlizius also suggested that exposure to especially infectious diseases, e.g. smallpox, but also, to some extent, other infectious diseases during the first years of life would affect survival during adulthood through an irreversible damaging effect on the immunological system. There is, however, no medical evidence to account for such a causal mechanism. Furthermore, our findings regarding the long-term component of the infant mortality influence on old-age mortality are in agreement with those of Fridlizius, since he filters out the short-term components by estimating the effects of the disease load during the first 5 years of life. The short-term fluctuations in infant mortality are also of great importance during the first year of life, as shown in this paper.

The influence of the short-term variations in infant mortality on old-age mortality was mostly due to peaks in infant mortality caused by different infectious diseases, particularly by smallpox and whooping cough. These infectious diseases are so virulent that they must have penetrated the entire area. Smallpox is one example. It was mainly a childhood disease during the 18th century.[29,30] Approximately 95% of all deaths due to smallpox in Sweden during the 18th century occurred under age 10.[29,31] The 18th century patterns of total childhood dominance in smallpox mortality indicate that most of the adult population during this period had already been exposed to smallpox as children but had survived. Those cohorts exposed to such infectious diseases during infancy may also be much more susceptible to high morbidity and mortality rates even in old age as an effect of this exposure than cohorts exposed to epidemics of smallpox and other infectious diseases later in childhood. The causal biological mechanisms in early life that might explain these significant associations are only partly understood, although long-term effects on morbidity and mortality seem to have some support in the literature.[32] The pathways that have been discussed mostly concern infectious diseases of the respiratory tract. Respiratory infections, atopy, reversible airway obstruction, chronic mucus hypersecretion, and irreversible airflow obstruction are interconnected by a complex web of associations and putative causal relationships.[8] Respiratory infectious diseases in infancy (ages 0–1 year) have been suggested to be one cause of a chronic wheezing tendency,[33,34] chronic cough and phlegm,[33,35] irreversible impaired ventilatory function,[33,36] and the related mortality.[37] Two historical cohort studies in England suggest that respiratory infectious diseases in the first year of life are associated with later cough, phlegm, and impaired ventilatory function, independently of smoking habits and social class. Infectious respiratory diseases after the first year of life did not seem to be a risk, which supports the idea of a critical period of influence for infection. Mortality from chronic respiratory diseases was also associated with early bronchitis and pneumonia.[14,15] These studies have been interpreted as evidence of persistent lung damage from respiratory infectious diseases during the first year of life.[8]

This study deals with exposure to smallpox and other airborne infectious diseases during the latter part of the 18th century and whether this exposure during infancy affected mortality later in life. The results and conclusions of this study could most probably be generalized to other geographical areas and countries than Sweden, and also to the 20th century. As smallpox was eradicated in human populations as late as in the late 1970s, long-term effects of smallpox on morbidity and mortality are still highly interesting and will remain so for many years to come.[33]

Several studies on more recent 20th century data series show that there is a strong association between low SES and both mortality and general practice consultations for adult respiratory

disease.[38] Although most of these socioeconomic differences are probably due to socioeconomic differences in smoking behaviour, independent associations between SES and symptoms of mucus hypersecretion[39,40] and ventilatory function[41] have been demonstrated. A significant socioeconomic gradient in bronchitis mortality was observed before the occurrence of socioeconomic differences in smoking behaviour.[42] However, the present study on an older historical data series does not demonstrate the same results. We find no effects of rye prices experienced in early life, an indicator of economic hardship, the consequences of which varied greatly in different socioeconomic strata, on old-age mortality. In contrast, highly contagious infectious diseases such as smallpox, which affected different socioeconomic strata similarly, had this effect on old-age mortality.

This study suggests that airborne infectious diseases are important for the causal mechanisms linking infant mortality to old-age (55–80 years) mortality. The variations in infant mortality that affected old-age mortality were mainly caused by both trends and short-term cycles in infant mortality from airborne infectious diseases. Furthermore, old-age mortality was mainly affected by these cohort mechanisms through an increase in old-age mortality from infectious diseases.[17] The combination of these two patterns may seem paradoxical, as exposure to airborne infectious diseases during the first year of life might be expected to result in lesser susceptibility to such diseases in later life because of stronger immunity. However, the results may instead indicate a more general vulnerability throughout life caused by weakening effects in other aspects of the airborne infectious diseases of infancy. In fact, Bengtsson has also shown that the negative impact is not found only at ages 55–80, but also at ages 20–55.[43]

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Commentary: Infectious diseases during infancy and mortality in later life

G Doblhammer

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[1] 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*.[2] While these theories are developed on the basis of studies of mortality in the 20th century, Fridlizius[3] suggested that, in the 19th century, exposure to infectious disease in the first 5 years of life causes 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.[4] 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.[5]

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 utero*. 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

Max Planck Institute for Demographic Research, Konrad-Zuse Str. 1, 18055 Rostock, Germany. E-mail: doblhammer@demogr.mpg.de

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 ($\rho = 0.83$, $P = 0.001$) and the third trimester ($\rho = -0.78$, $P = 0.002$) of pregnancy. There is little resemblance, however, with the seasonal pattern for the whole 9-month period ($\rho = -0.46$, $P = 0.131$). 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 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.

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