Distinctive Phases in Immune Vulnerability of Infants? Insights from the Analysis of Mortality by Age and Season in Historic Scotland.

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The infant mortality rate (IMR) has long been used as a basic indicator of population health and quality of healthcare services. It is conventionally defined as the number of deaths to infants who die before reaching 1 year of age divided by the total number of live births. The first year of life is, however, a very dynamic period of human development and the epidemiology of mortality is changing very rapidly during this period, especially over the last 100 years. Decomposition of IMR into its age defined components can, therefore, improve our understanding of infant mortality decline that took place in the twentieth century. We focus especially on the relationship between various stages of the maturing immune system and infant's different susceptibility to infectious diseases during those phases. To identify distinctive phases in immune system vulnerability, we look at detailed age groupings that reflect that maturing rather than conventional groupings. We also contrast different time periods, seasons and parts of Scotland in order to assess the impact of different 'environments' on the vulnerability of the infant to different insults and health measures. Since early neonatal (0-6 days) deaths are linked mainly with congenital viability, they are not discussed in detail here and showed for comparative purposes only. We use information from the Scottish death and birth certificates (1901-1970) that have been recently transcribed within the ongoing Digitising Scotland project. The wealth of data that is going to be available soon will allow us an extension of the observation period till 1855 and the analysis of causes of death.

Development of the immune system in early life

During the last 3 months of pregnancy, the fetus receives maternal antibodies (immunoglobulin G, IgG) through the placenta. At term birth the baby has a level of IgG equivalent to that of its mother and the antibodies produced by her body when she was infected 20-30 years ago can protect her infant. The newborn may get an additional boost of antibodies (immunoglobulin A, IgA) from breast milk. Those antibodies are not absorbed from the gastrointestinal tract, but nonetheless they can protect the baby from diarrheal diseases and to some extent from respiratory diseases. The passive immunity in newborn babies is, however, only temporary. The transplacental IgG starts to fade away slowly after the first few weeks or months and it is essentially gone by about 6 months of age. Between 3 and 6 months all infants have low level of IgG and increased susceptibility to infections as a result of the disappearing maternal IgG and underdeveloped adaptive immunity of the baby. Later on babies must rely on its own immature immune system supported to some extent by IgA from breast milk.

We explore whether, in the twentieth century, the period before the widespread availability of antibiotics, living conditions and particularly poverty in the industrial cities of Scotland may be particularly important for infant mortality and that this effect was strongest for the age 3-6 months period when IgG is at its lowest.

National and regional infant mortality decline (or lack thereof)

Since the beginning of the twentieth century we observe constant improvement in infants' lives as measured by IMR. The most rapid changes took place between 1940s and early 1950s, then the progress slowed down. The decreasing trend in IMR reflects mostly changes in post-neonatal

mortality, i.e. in deaths of infants who survived at least 28 days. Disaggregation of post-neonatal deaths reveals, however, that the decline was driven mostly by decreasing number of deaths of those older than 6 months (see Figure 1). The share of those deaths in all infant deaths dropped from around 30% at the beginning of the twentieth century to about 5% by the sixties.

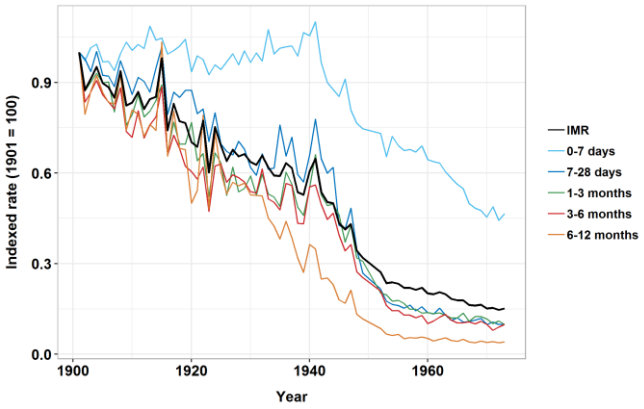

Figure 1 Indexed infant mortality rate (IMR) and its components over time

Late neonatal (7-28 days) mortality decline actually stagnated in 1930s. Geographically disaggregated time series show that in the cities of Glasgow and Edinburgh late neonatal mortality even increased in this period (see Figure 2). A very similar pattern was observed for a bit older infants, namely those younger than 6 months, living in the industrial city of Glasgow.

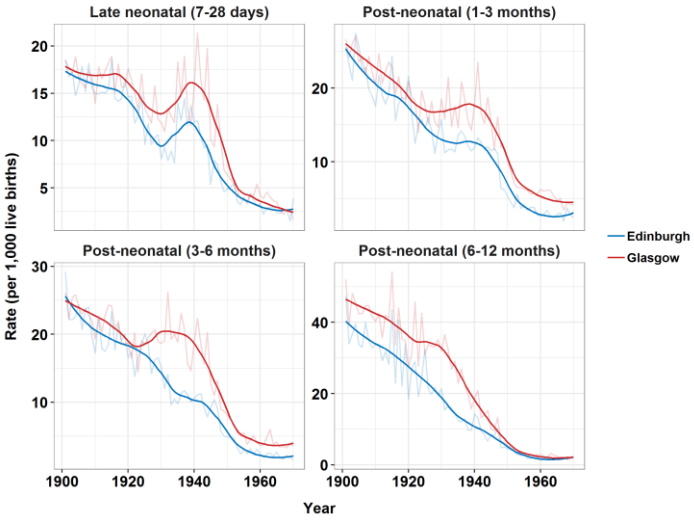

Figure 2 Components of infant mortality rate over time in Edinburgh and Glasgow

Seasonality

An excess winter mortality index (EWM) suggests a distinctive pattern of seasonality for infants older than 2 months and younger than 6 months, so those with relatively low immunity. The EWM mortality for them is lower compared with older infants and those slightly younger (see Figure 3).

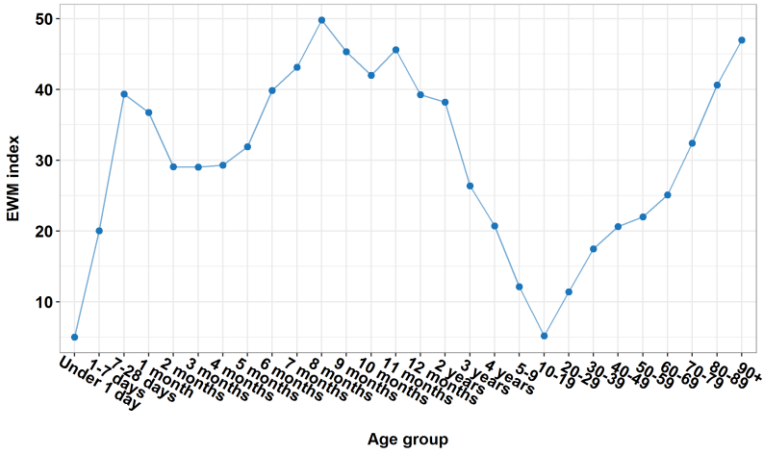

Figure 3 Excess winter mortality index (EWM) by age group, 1901-1970

Analysis of monthly mortality index reveals existence of very distinctive profiles for infants aged 2-6 months until around 1920 (see Figure 4). They had a distinct 'summer hump' which was not present in other age groups. Infants who are at least 6 months old were most vulnerable during spring and winter time, as evident also in EWM. Improving living conditions lead to the convergence of the age profiles by the seventies.

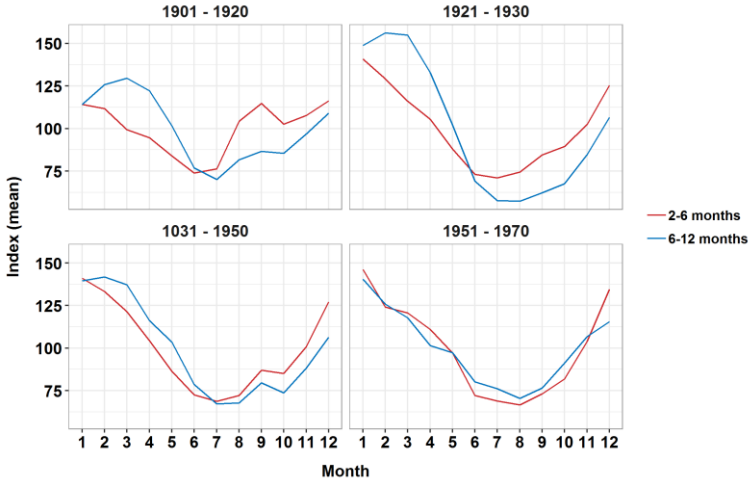

Figure 4 Monthly seasonality index by age in subperiods

The monthly index for years with especially hot summer with the increased risk of infections, emphasize the vulnerability of infants between 3 and 6 months old (see Figure 5). Years with outbreaks of severe seasonal influenza illustrate high mortality risk for older infants (more than 6 months old) that do not have protection in the form of maternal IgG (see Figure 6).

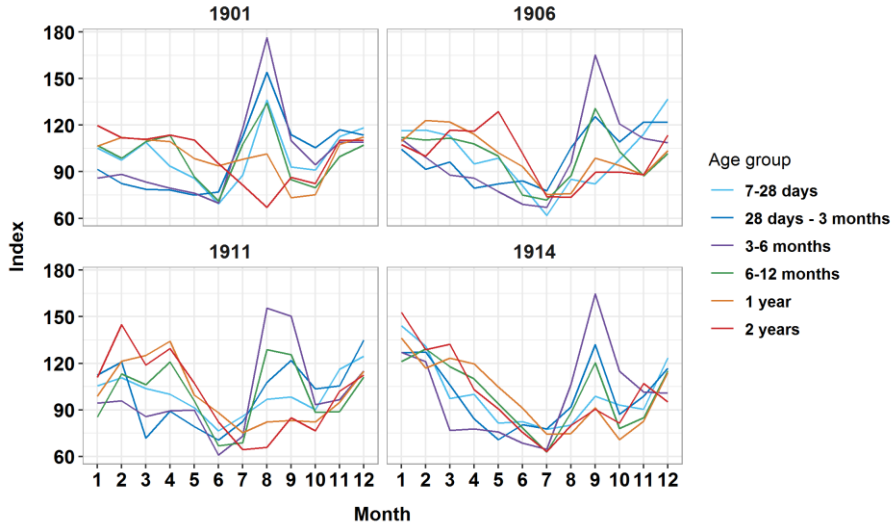

Figure 5 Monthly seasonality index by age group for years with especially hot summer.

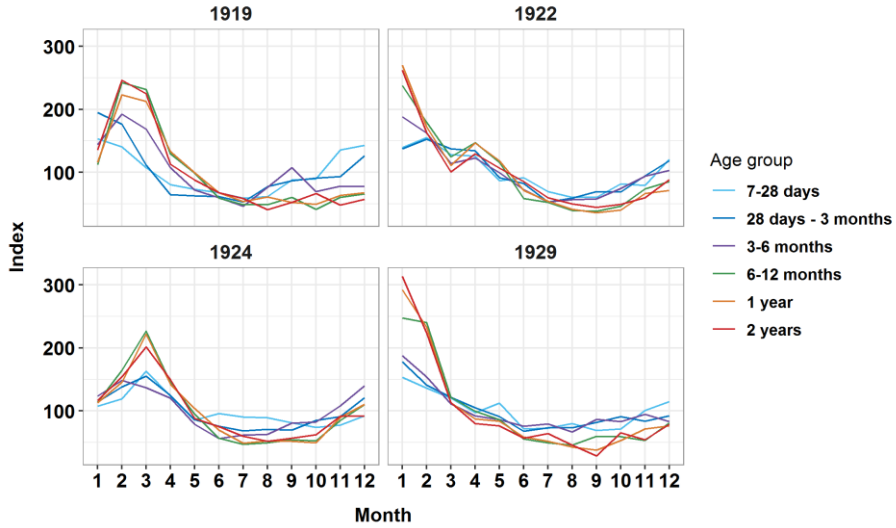

Figure 6 Monthly seasonality index by age group for years with flu outbreaks.

Final remarks

The exploration of infant mortality by age and its seasonality, geography and period provides some evidence for distinctive stages in early life. The most pronounced markers are 2nd/3rd month and 6th month, which can be connected, at least partially, to the development of immune system in infants. To complete the investigation we aim to analyse infant mortality components by causes of death.