In Utero Exposure to the 1918 Pandemic and Old-Age Mortality by Cause: Evidence from the NHIS Data

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Abstract

Accumulating evidence suggests that early life disease exposure has long-lasting negative negative effects on health. However, existing research on the deadliest pandemic of the 20th century, the 1918 Pandemic, has failed to find any long-term effects on mortality. We use a large population based U.S. panel data to reassess whether those who were exposed *in utero* to the 1918 Pandemic have elevated old-age mortality. Preliminary results indicate that cohorts born right after the peak of the epidemic have up to excess mortality when compared to the neighboring cohorts. The effects are larger for men than for women and for cardiovascular and respiratory diseases than for other causes of death. Overall, the results suggest that *in utero* disease exposure increases mortality decades later, and that the third trimester of pregnancy may be the most sensitive period for long-term outcomes. The results indicate that part of the secular old-age mortality decline may be attributable to improved early life conditions.

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MOTIVATION

Accumulating evidence suggests that early life, especially *in utero*, disease exposure has a long-lasting negative impact on health (for example, Barker 1990; Bengtsson and Lindstrom 2003). The implications of such a link reach beyond understanding specific disease risk factors, as it has been suggested that secular mortality declines are driven by decreased early life disease exposure (Finch and Crimmins 2004). Existing research, however, has not found long-lasting effects on mortality for those who were exposed early in life or *in utero* to the deadliest epidemic of the 20th century, the 1918 Influenza Pandemic (Cohen et al. 2009). This is surprising especially in the light of other papers which document that those who were exposed to the 1918 Pandemic in 3rd trimester of pregnancy have worse educational and job-market outcomes and are shorter and have higher cardiovascular disease prevalence than the neighboring cohorts (Almond 2006; Mazumder et al. 2009). It is possible that some of the negative findings regarding long-term mortality effects are due to countervailing forces such scarring, selection and immunity canceling each other, or due to methodological issues such as lack of statistical power or aggregation of birth cohorts. This study assesses the link between early life exposure to the 1918 Pandemic and later mortality using a large, U.S. population based panel data which allows accurate identification of the exposure timing and cause-specific mortality analysis.

DATA AND METHODS

We base our study on all available waves of the National Health Intheview Surveys (NHIS). NHIS is a continuing nationwide survey of the U.S. civilian noninstitutionalized population conducted in households. Each week a probability sample of households is interviewed by

trained personnel of the U.S. Bureau of the Census to obtain information about the health and other characteristics of each living member of the sample household. The data contains information on month and year of birth, adult socio-demographic characteristics, health and disability, and date and cause of death. The cause-specific mortality follow-up is from August 1989 to the end of year 2002.

We use all available waves of the National Health Interview Surveys. We restrict the data to cohorts born between 1916 and 1922 (inclusive), this window allows us to compare the 1918 Influenza cohorts with respect to the neighboring cohorts. The follow-up is from August 1989 to the end of year 2002. The sample size is 45,191 persons with 16,149 deaths. We use Cox proportional hazard models to estimate the effect of being exposed to the 1918 Influenza Pandemic *in utero* or early in life on disability and cause-specific mortality. We control for a linear trend in mortality over cohorts, age at entry, season of birth, and sex, and estimate the early life and *in utero* exposure to the the 1918 Pandemic using birth quarter dummies.

PRELIMINARY RESULTS

The preliminary results indicate that among the U.S. birth cohorts from 1916 to 1922, those born in January through March of 1919 have mortality 80 years later. These cohorts were exposed to the 1918 Pandemic during the third trimester of pregnancy, and partially during the first months of post-birth life. This cohort is approximately the same for which Almond (2006) finds decreased educational and job market outcomes, and Mazumder et al. (2009) increased cardiovascular disease prevalence. We find that the excess mortality is larger for men than for women, and is mostly attributable to cardiovascular disease and respiratory disease mortality. The effects on cardiovascular disease mortality is not surprising, as it has

been suggested that early life disease exposure may lead to chronically increased inflammation levels, which in turn predispose to cardiovascular disease. Likewise, the effects on respiratory disease mortality are not surprising as the third trimester is critical for lung development. However, our preliminary results also suggest that women born right after the peak of the epidemic may have lower cancer mortality than the neighboring cohorts. This result is surprising and warrants further research.

Our results suggest that the effect of disease exposure is largest if exposure happens during the third trimester of pregnancy. This may be because of two different mechanisms, one operating through scarring and one through selection. First, during earlier stages of pregnancy shocks in the environment are more likely to lead to miscarriage and/or stillbirth than at alter stages of pregnancy, so selection may mask scarring. Second, the third trimester may be most sensitive as during this period growth is fastest, and for example the development of lungs is in critical stage. For first and second trimesters (especially first) it may be that shocks lead to spontaneous abortion, which, while obviously being an important effect, would not show up in adult mortality.

Taken together, the results suggest that *in utero* disease exposure increases mortality decades later, and that the third trimester of pregnancy may be the most sensitive period for long-term outcomes. These results are in line with the hypothesis that part of the secular old-age mortality decline may be attributable to improved early life conditions.

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