## Multigenerational Effects of Early Life Health Shocks

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## Abstract

A large literature has documented links between harmful early life exposures and later life health and socioeconomic deficits. These studies, however, are typically unable to examine the possibility that these shocks are transmitted to the next generation. Our study traces the impacts of in utero exposure to the 1918 influenza pandemic on the outcomes of the children and grandchildren of those affected using representative survey data from the US. We find evidence of multigenerational effects on educational, economic, and health outcomes.

Key Terms*:*1918 influenza, Multigenerational effects, Wisconsin Longitudinal Study (WLS)

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Understanding persistent poverty and poor life outcomes has posed significant challenges for social science theories as well as crafting policy responses. Of particular interest is the so called “long arm” of childhood circumstances, where events and conditions early in an individual’s life (even in utero) may set in motion an accumulation of disadvantage. The Developmental Origins of Health and Disease theory (often referred to as the Barker hypothesis) suggests that in utero insults program the fetus in ways that lead to maladaptive responses to the environment that persist throughout the life course and explain poor long term outcomes (for a history of the Barker hypothesis, see Barker 2007). However, since the likelihood of experiencing an early insult is related to parental circumstances, there is an empirical challenge to causally examining the impacts of early insults. This issue ties into a key question of whether intergenerational persistence in poor outcomes may stem in part from genetic mechanisms that may be more resistant to policy efforts. In order to separate potential channels, some research has focused on exogenous (i.e. unrelated to genetics) health shocks during early life to explore long term outcomes.
 Indeed, a strong causal link between harmful early life / in utero shocks and lowered later life health and economic outcomes has been found in a number of clearly identified empirical studies. In addition to separating genetic and non-genetic mechanisms, many of these investigations are also able to uncover biological (i.e. fetal programming) explanations by studying specific insults, including the effects of prenatal nutritional status and exposure to infectious disease. Without the use of experimental (i.e. animal model) research designs, these studies use so-called quasi-experimental designs by leveraging striking demographic events such as the Dutch famine and the 1918 flu pandemic (Almond 2006, Lindeboom, Portrait et al. 2010). The results generally suggest large, lifelong impacts of in utero insults on economic and health outcomes.

With these results established, a next question is whether they might persist into the outcomes of future generations. We explore the question of multigenerational persistence of fetal insults by extending previous work that uses the 1918 influenza pandemic (Almond 2006) by adding multigenerational data. We document that in utero exposure to the pandemic can be seen in the educational attainments of multiple generations. More specifically, we find a reduction of approximately 1/5th a year of schooling for the second generation and 1/6th of a year of schooling for the third generation. We also show large effects on economic as well as health outcomes for the second generation. Our findings suggest the importance of in utero health insults that persist across multiple generations and allow a shift in our analytical frame from the “long arm of childhood circumstances” to the “long arm of previous generation’s circumstances,” or, alternatively, “the long reach of history” (Kuzawa and Eisenberg 2014). Our results can also be interpreted in the context of assessing benefits of policy and environmental conditions that reduce the likelihood of in utero health insults, where the full benefits may unfold over multiple generations.

**Background Literature**

Our research intersects several related literatures. There is a large literature that documents associations between early life insults and later life outcomes, following the original Barker Hypothesis. In addition, we draw on literature that explores multigenerational linkages of environmental exposures on life course outcomes. These literatures are rarely unified in a single analysis, largely due to data constraints. We overcome these limitations by leveraging a three-generational dataset that coincides with a key demographic event from the early 20th century—the 1918/1919 influenza epidemic.

The seminal work of the economist Douglas Almond (2006) was one of the first papers to exploit the 1918 flu pandemic as a natural experiment and to test whether in utero exposure to infectious disease influences later life outcomes. Using US census microdata to situate respondent births in both time (birth quarter) and place (exploiting geographic variation in the severity of the flu), Almond (2006) finds evidence of lower educational attainment, higher rates of physical disability, as well as lower income and socioeconomic status for cohorts exposed to the 1918/1919 flu while in utero (estimated using birth quarter, age, and timing of the flu) as compared to unexposed adjacent cohorts. In a related paper, Almond and Mazumder (2005) use a similar approach with the Survey of Income and Program Participation and find negative health effects for adults who were in utero (based on birth quarter) during the outbreak. Subsequent work has built on these outcomes, finding excess cardiovascular disease (Mazumder, Almond et al. 2010); increased likelihood of kidney disease, diabetes, circulatory, and respiratory problems in old age (Lin and Liu 2014); and increased old-age mortality in non-cancer related causes (Myrskylä, Mehta et al. 2013, Fletcher 2014).[[1]](#footnote-1)

The mechanisms underlying these broad effects from in utero influenza exposure are not fully understood in humans. However, in studies of monkeys (Kobasa, Jones et al. 2007) and mice (Kash, Tumpey et al. 2006), it has been shown that the reconstructed 1918 flu virus triggers an exceptionally intense and prolonged innate immune response. More specifically, gene-expression analysis shows that proteins involved in the innate immune system have a higher and sustained expression when triggered by the 1918 reconstructed virus than when triggered by the contemporary flu of the same H1N1-type (Kobasa, Jones et al. 2007). While the specific 1918 flu strain cannot be studied in humans through purposeful exposure for ethical reasons, both animal and human studies have linked the maternal immune response during severe flu infection in pregnancy to offspring brain development as well as impaired adult behavior and cognitive outcomes (Fatemi, Earle et al. 2002, Brown and Derkits 2010, Canetta and Brown 2012, Miller, Zhu et al. 2013, Li, Chang et al. 2014).

Recent evidence suggests that in utero exposure to the 1918 flu may not only affect adult outcomes, but also the outcomes of subsequent generations. Richter and Robling (2013) were the first to identify an effect of prenatal exposure (using birth trimester) to the 1918 flu pandemic on the outcomes of the subsequent generation. The authors use historical influenza morbidity data matched to birth information to identify potential exposure to the 1918 flu and find that maternal in utero exposure in the second trimester lowers educational attainment for female offspring by 2-2.5 months, or by 1.5-1.8 percent, but not for male offspring. An analogous result is identified for paternal exposure and male outcomes; that is, exposure in the second trimester lowers educational attainment for male offspring by 2.4 to 3 months, or by 1.8-2.2 percent.[[2]](#footnote-2)

At least two major pathways exist for the intergenerational transmission of early life health shocks: socioeconomic and biological. Through socioeconomic channels, intergenerational persistence in poor outcomes could occur when a fetally insulted parent, marred by poorer health and socioeconomic outcomes, raises a child in a low-resource environment. Biologically, phenotype-to-phenotype transmission and epigenetic inheritance are hypothesized to be key mechanisms for intergenerational transmission (Kuzawa and Eisenberg 2014). In cases of in utero or very early life shocks, phenotype-to-phenotype transmission impacts the outcomes of the next generation through changes in parental biological systems that lead to altered gestational and/or lactation environments for offspring (e.g. pre-pregnancy hypertension is linked to low birthweight). Importantly, such effects may also extend to later generations through cumulative intergenerational phenotypic changes (Benyshek 2013); for example, stress experienced by a mother prenatally may alter stress regulation in offspring, which may in turn increase risk for the same adult phenotype in the offspring, as well as in subsequent generations. Epigenetic inheritance, in comparison, occurs when parental experiences alter gene expression, which may then be transmitted to offspring (and potentially grandoffspring) through the germ line.

Work extending effects of in utero exposure to the 1918 flu to the third generation (grandoffspring) in humans, to the best of the authors’ knowledge, does not exist. The strongest evidence for a potential biological channel across multiple generations comes from studies of historical data from Överkalix region in Northern Sweden that exploit variance in grandparental food supply during childhood. Bygren, Kaati et al. (2001), for example, find that an excess of food during the period just before adolescence, a time labeled the “slow growth period” (SGP), shortens the grandson’s longevity. A later study using the Överkalix data replicates the results of Bygren, Kaati et al. (2001) in a second cohort, and further extends the results to include an association between paternal grandmother’s food supply and granddaughter’s mortality risk (Pembrey, Bygren et al. 2006).[[3]](#footnote-3)

 Our work builds off of this evidence to conduct novel examinations of multigenerational effects of *in utero* exposures in human populations. The current research leverages a unique survey to measure the multigenerational impacts of in utero exposure to the 1918 flu pandemic. Our hypothesis is that the previously documented direct effects of such shocks extend into the outcomes of the individual’s children. Going further, we also estimate whether these effects continue into the third generation. In other words, we ask whether the singular in utero shock has a multigenerational effect.
**Data and Empirical Methodology**

### *Data*

In order to examine multigenerational effects of an in utero exposure, we require multigenerational data. Very few datasets in the US have a multigenerational component and fit the relevant time period for our exposure (i.e. birth cohorts around 1918). Our data come from the Wisconsin Longitudinal Survey (WLS), which is a random one-third survey of graduating high school seniors in Wisconsin in 1957. The majority of these respondents (i.e. our “second generation”) were born in 1939. Thus, the parent (“first”) generation overlaps the 1918/1919 in utero exposure period. This allows for the creation of our primary measure for in utero exposure to the 1918 flu epidemic: an indicator for either parent being born during the 1918-1919 range[[4]](#footnote-4),[[5]](#footnote-5). Additional data are collected on the later life outcomes of the WLS graduates and a selected sibling, as well as a limited number of outcomes for the children (“third generation”) of the graduates/siblings, providing the structure for our multigenerational analysis.

 Summary statistics are presented in table 1. As shown, approximately 10 percent of WLS parents are born in either 1918 or 1919. On average fathers are born in 1907 and mothers are born in 1911; consequently, a birth year of 1918 or 1919 is closer to the right-tail of the distribution of births and the rate of 10 percent is driven primarily by relatively young mother exposures.[[6]](#footnote-6) This is seen in Figure 1. While not the primary focus of the WLS data collection, several parental (first generation) outcomes are available, including years of schooling, occupational prestige, and family socioeconomic status in 1957.[[7]](#footnote-7)

[insert table 1 here]

 The primary focus of the WLS data collection is high school seniors in 1957 Wisconsin, the second generation of our study. Given this focus on graduates (and their siblings), a large number of economic and health variables are available. In addition to examining years of schooling, several additional dependent variables in the second generation intend to capture broad differences in economic and health well-being. These include income during the peak earning years (i.e., family income collected when graduates are 53 years of age on average), net worth at initial retirement age (i.e., net worth collected when graduates are 65 years of age on average), and general indicators of health measured by body mass index and a count of doctor diagnosed illnesses (both collected in the wave when graduates are age 53 on average). Finally, the WLS data contains information that is collected from the second generation about the third generation; we focus on years of schooling as the main outcome of interest.

### *Empirical Methodology*

Our empirical strategy follows that of Almond (2006) by examining harmful effects of being exposed in utero on later life outcomes. We then extend this analysis by estimating multigenerational impacts on both the second and third generations. In so doing, the primary estimating equation is given by the following form:

Our primary focus is on the coefficient , which measures the effect of having a parent/grandparent born in 1918-1919 on a number of outcomes for individuals in families for generation . Parent year of birth time trends and their square are denoted by ; represents generation specific controls; and is representative of a family clustered error term.

 For the first generation, we control for birth year and its square, capturing age-specific trends that are tied to our first-generation outcomes of interest (e.g. years of schooling). For the analysis of second and third generations, birth years and squares for both first generation parents are included as controls along with generation-specific controls for sex, age, and birth order.

**Results**

### *First Generation*

Our initial analysis explores the direct effects of being born during the 1918 Influenza Epidemic. While health data are sparse for the WLS graduate’s parents (first generation), a number of economic outcomes are available, especially during the initial sample year of 1957. Table 2 explores the relationship between these economic variables and an indicator for birth during 1918/1919. Columns (1)-(3) of table 2 show the relationship between a WLS graduate’s father being born during 1918/1919 and the father’s years of schooling, the father’s occupational prestige, and the family’s index of socioeconomic status in 1957 (i.e. when the first generation members are approximately 40 years old). While statistically insignificant, a negative association is observed between years of schooling and being born in 1918 or 1919.[[8]](#footnote-8) This is carried over into father’s job prestige in column (2), from which the indicator of in utero exposure to the 1918 flu is associated with a roughly 25 point decline in the index of job prestige (approximately 0.1 standard deviations). These effects culminate in column (3), which shows a statistically significant negative effect of in utero exposure to the flu and later life economic well-being: a 1.25 decline in the SES index, which corresponds to a decline of roughly 10 percent of a standard deviation. The findings of table 2 corroborate past studies that show in utero exposure to the 1918 flu led to poorer economic outcomes later in life (Almond 2006).

[insert table 2 here]

 Mirroring the results for males in the first generation, a negative but statistically weak association is observed between an indicator of birth in 1918/1919 and schooling for first generation females. This association however, becomes statistically significant at the 1 percent level for the index of family SES, the coefficient being nearly identical to that of a male’s in utero exposure to the flu, though it is unclear whether these effects flow from labor market and/or marriage market sources. The findings of table 2 are extended in table 3, which explores potential marriage market effects of early life exposure to the flu epidemic.

 Column (1) of table 3 regresses the indicator for male in utero exposure on an identical measure for spouse’s exposure. Females who were born in 1918/1919 were 5 percentage points more likely to marry men who were also born during the same period. Furthermore, as shown in columns (2) and (3), these women were more likely to marry men with fewer years of school and lower job prestige. These effects are significant at the 1 percent level. Similar effects are seen in columns (4)-(6) for 1918/1919 born males, who are 14 percentage points more likely to marry flu exposed females (p=0.00) and marry females with 0.27 fewer years of schooling (p=0.10) and lowered job prestige (p=0.61).

[insert table 3 here]

### *Second Generation*

Our hypothesis is that the direct effects observed in tables 2 and 3 extend into future generations. To address this hypothesis, we regress a number of economic and health outcomes of the WLS graduates and siblings, the offspring of the first generation examined in tables 2 and 3. These estimations are performed in tables 4 and 5. Column (1) in both tables focus on an indicator for *either* parent being born in 1918/1919; the primary regressor of column (2) is an indicator for *father’s* in utero exposure to the 1918 flu; column (3) considers *mother’s* exposure; and column (4) includes separate indicators for both mother and father’s exposure. Controls included in all columns include father’s year of birth and its square, mother’s year of birth and its square, an indicator for sex in the second generation, a measure of birth order in the second generation, and second-generation year of birth.

 Table 4 focuses on economic outcomes of the WLS graduates. To reiterate, our hypothesis is that in utero exposure to the 1918 influenza pandemic has effects that persist for multiple generations. Table 2 shows the direct, first generation effects, while table 4 begins to show the indirect effects that are transmitted to offspring. Panel A regresses years of schooling in the second generation on indicators of first generation exposure to the 1918 flu. From column (1), either parent being born in 1918/1919 is associated with a statistically significant decline of 0.20 years of schooling in the second generation. This estimate is likely understated because the sampling design of the WLS is a focus on high school seniors; thus, individuals with fewer than twelve years of schooling are underrepresented in the data.[[9]](#footnote-9) Columns (2)-(4) disambiguate this effect into the maternal and paternal lines. From which, the effect of column (1) seems to be driven by mother’s in utero exposure to the flu. Given the findings of table 3, however, we cannot rule out that this is a marriage market effect.[[10]](#footnote-10)

 The findings of Panel A are extended into Panel B, which replaces years of schooling as the dependent variable with the natural log of family income for the 1992 wave, a time when the second generation respondents are 53 years of age on average and represents a time of peak earning in the life course. As with years of schooling, a negative association is seen throughout the specifications of Panel B. Having either parent born in 1918/1919 is associated with a 23 percent decline in family income. Once again, this effect seems to be driven by mother’s, not father’s, exposure. Panel C replaces income with a measure of net worth for the 2004 wave. This measure of net worth is when the second generation respondents are on average 65 years of age and is representative of earnings throughout the life course. The dual indicator of column (1) is negative but statistically insignificant at conventional levels (p=0.18). When looking at the effect of mother exposure in column (3), however, a statistically significant negative association is estimated, implying those with mothers born during 1918/1919 have approximately $102,000 less in net worth by 2004.

 The economic effects of table 4 are replaced with health measures in table 5. The structure of the table is otherwise identical. Panel A considers the effect of a parent being in utero during the 1918 Flu Epidemic on second generation BMI. From column (1), having either parent being born in 1918/1919 is associated with a statistically significant increase in the offspring’s BMI of 0.4 points. As with the economic effects of table 4, this increase in BMI appears to be driven by mother’s exposure. This is seen in columns (2)-(4), which estimate a statistically significant positive coefficient for mother’s exposure but a coefficient that is statistically indistinguishable from zero for father’s exposure. Panel B of table 5 examines the effect of first generation exposure on the number of doctor diagnosed illnesses in the second generation. This measure comes from the 1992 wave of the WLS, a time when the graduates are 53 years of age on average. As with BMI in Panel A, first generation exposure to the 1918 Flu has a statistically positive association with the number of illnesses, increasing this count by 0.12 when considering either parent and 0.15 when considering mother’s exposure.[[11]](#footnote-11)

 A persistent effect of in utero exposure to the 1918 Flu is seen in tables 4 and 5. First generation exposure consistently has a statistically significant and economically meaningful effect on second generation health and economic outcomes. And this effect appears to be driven solely by mother’s exposure; although, due to marriage market associations, we cannot determine definitively that mother’s exposure produces this multigenerational effect through biological mechanisms.

*Third Generation*As mentioned previously, the focus of the WLS data collection is high school graduates in 1957, but additional samples have been collected for a number of variables on the children of these graduates. Table 6 explores the effects of the WLS parents on the years of schooling for WLS children, estimating the effect of flu exposure across three generations.[[12]](#footnote-12)

 Consistent with the second-generation estimations, a persistent effect of the in utero flu exposure is observed, and this effect seems to be driven by grandmother exposure. The joint indicator for either parent is negative and significant at the 10 percent level, suggesting that exposure in the first generation is associated with 0.14 years of schooling less in the third generation. The effect of grandfather exposure is insignificantly different than zero, while the coefficient of grandmother exposure is similar in magnitude and statistical significance to the joint indicator of column (1). Furthermore, the decline in schooling seen in the third generation is similar, but slightly smaller in magnitude compared to the second generation effects seen in Panel A of table 4 (for column (1), p=0.32). This again indicates a persistent effect that may be attenuating over time. Importantly, while the estimate for grandfather exposure is insignificant, it is consistent with intergenerational inheritance (Kuzawa and Eisenberg 2014). To say the same for grandmother exposure would require effects to persist into the fourth generation (due to the differences in gametic development), and this data is not available in the WLS.

**Conclusion**

This paper presents novel evidence of multigenerational effects of in utero health insults. We use the sudden and unexpected influenza pandemic in 1918/1919 to trace out the effects of in utero exposure to infectious disease on own outcomes, children’s outcomes, and grandchildren’s outcomes. We find that this exposure reduces educational attainment and related economic outcomes across three generations; for example, individuals who have grandmothers who were exposed to the pandemic in utero complete 1/6 fewer years of schooling than individuals without affected grandmothers.
 There are at least two key mechanisms for the persistence of poor outcome across three generations we find in our data. As previously outlined, the intergenerational persistence in poor outcomes could occur through socioeconomic channels, where a person with low educational attainment raises a child in a low-resource environment that reduces opportunities for high educational attainment of the child. In order to see multigenerational effects, the reduced opportunities for high educational attainment of the child must then reduce opportunities for their own children. Alternatively, intergenerational as well as multigenerational transmission may occur through biological channels such as epigenetic inheritance through the germ line, a distinct possibility based on findings of the Överkalix studies, or phenotype-to-phenotype transmission and cumulative intergenerational phenotypic change.

Our analysis is unable to fully distinguish between the two proposed intergenerational channels, the socioeconomic and biological, but it is important to note that the channels are by no means mutually exclusive. Further analysis (appendix tables 4-6) that is intended to partially account for the socioeconomic mechanism leads to mixed results in which the coefficient of first generation flu exposure is attenuated to insignificance for some outcomes but not others. This provides evidence for a socioeconomic channel, but does not eliminate the possibility of epigenetic mechanisms or other biological channels through which socioeconomic status “gets under the skin” to influence outcomes of subsequent generations (e.g. the socioeconomic circumstances of one generation may “get under the skin” of the next and subsequently be passed via biology and/or socioeconomics to other generations). Likewise, the estimates of grandfather effects on grandchildren are imprecise but consistent with transgenerational inheritance (Kuzawa and Eisenberg 2014). Additionally, while the WLS provides a unique framework to analyze multiple generations, the measurement of flu exposure is somewhat crude (from self-reported parents’ year of birth) and is in the right-tail of the distribution of parent birth years, suggesting the possibility of confounding from resource-poor younger mothers.[[13]](#footnote-13) That is, exposure to influenza in the first generation is mechanically tied to mother’s ages of 20 and 21 because the WLS sample is drawn based on having a child who was born in 1939 (and thus graduating high school in 1957). While we cannot definitively separate these two effects, our ability to compare outcomes of slightly older mothers (ages 22 and 23, born in 1917 or 1916) provide evidence more consistent with in utero exposure to influenza than impacts of having a mother who is 20/21 years old.

From a policy perspective, our evidence may suggest a novel source of intergenerational persistence in poverty through biosocial factors and suggest a need to consider evidence of transgenerational social and/or biological mechanisms. We document the extent to which harmful early life environments cascade through generations, promoting a disadvantaged start for those whose grandparents exposed to a hazardous early life environment.

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1. Though Cohen, Tillinghast, and Canudas-Romo (2010) and Fletcher (2014) found no effects on overall mortality. [↑](#footnote-ref-1)
2. Our analysis does not find a consistent difference by sex; see appendix tables 10A-10F. [↑](#footnote-ref-2)
3. Van den Berg and Pinger (2014) externally validated the potential for transmission across three generations by analyzing the impact of the German famine of 1916-1918 on the mental health outcomes of the children and grandchildren of those exposed to the famine during their SGP. The authors find that paternal (maternal) grandfather (grandmothers) exposure during their SGP is associated with higher mental health in grandsons (granddaughters). [↑](#footnote-ref-3)
4. Parent year of birth is recorded from the WLS graduates. This self-reported measure is used to create the indicator of flu exposure: those parents born in 1918 or 1919. We also use a second variable (age of oldest sibling of the WLS graduate respondent) to construct parent year of birth in cases where parental year of birth is not reported by the graduate, we exclude cases where the constructed age at first birth of the mother is ten years or younger (a sample reduction of 67 individuals, or parents, for the first generation.) [↑](#footnote-ref-4)
5. The 1918 flu epidemic in Wisconsin peaked October 1918 through December 1918, but did not reach the severity experienced in many other states. According to historical records, Wisconsin had the fourth lowest numbers of deaths out of 25 reporting states (Burg 2000, Shors and McFadden 2009). [↑](#footnote-ref-5)
6. Appendix tables 8 and 9 provide evidence that our results are not driven solely by confounding between exposure to the influenza pandemic and being a young mothers. [↑](#footnote-ref-6)
7. The index of socioeconomic status is a factor weighted score combining data on father and mother’s years of schooling, father’s occupational prestige, and average parental income. Replacing this measure with average parental income (see appendix table 1) does not change the effect of the flu indicator. Job prestige measures for both mother and father are based on Duncan’s Socioeconomic Index. [↑](#footnote-ref-7)
8. First generation years of schooling are reported by the second generation WLS graduates. Measurement error is likely, which may result in the insignificant coefficients of table 2. [↑](#footnote-ref-8)
9. Table 3 includes selected siblings of the WLS graduates. These siblings do not have to be high school graduates. [↑](#footnote-ref-9)
10. Appendix table 2 repeats the estimation of table 3 while also controlling for an indicator of own-flu exposure and own year of birth measures. [↑](#footnote-ref-10)
11. These associations hold when considering non-linear estimators that are better suited for the count of illnesses. This is given in Appendix Table 3. [↑](#footnote-ref-11)
12. Analysis of the WLS grad/sibling children (i.e. the third generation) restricts the sample to those children that are biological children and that are 35 years of age and older by the 2003/2004 wave of the WLS. [↑](#footnote-ref-12)
13. We specifically explore the confounding effects of younger mothers in appendix tables 8 and 9. These tables show that younger mothers are indeed initially disadvantaged (i.e. less years of schooling); however, this young-mother disadvantage does not persist in subsequent generations. Rather, only those mothers born in the 1918-1919 range have significant negative effects on later generations. [↑](#footnote-ref-13)