The Effects of Prenatal Exposure to Seasonal Influenza on Life Course Outcomes in the United States

Julia M. Dennett

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Abstract

Seasonal influenza is a common infectious disease that jeopardizes the health of pregnant women. Prenatal exposure to the flu likely disturbs fetal development and harms health at birth, but long run effects have been difficult to identify. I investigate the impact of *in utero* exposure to seasonal influenza over the life course in the U.S. by exploiting state and time variation in influenza-related mortality, a proxy for disease severity in the local environment. I first show adverse effects on birth weight and an increased risk of heart malformations, and then evaluate impacts on long term outcomes. Exposure to seasonal influenza while *in utero* increases disability and decreases childhood school attendance, adult high school completion, and labor force participation. I examine implications for influenza vaccination as a policy intervention and find that historical vaccine uptake accounted for economically meaningful improvements in life course outcomes. Furthermore, my estimates suggest substantial returns to future reductions in flu exposure due to vaccination expansions, including 10,000 fewer infants born each year with low birth weight, 54,000 more workers in the labor force, and 34,000 more adults without a disability.

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1. Introduction

Seasonal influenza infects and sickens an estimated three to 11 percent of the United States population every flu season (Tokars, Olsen, and Reed, 2018) and imposes an annual economic burden of approximately $87 billion (Molinari et al., 2007).[1] Exposure to this routine infectious disease is particularly dangerous for pregnant women, who face an elevated risk of health complications.[2] The hazard extends to *in utero* infants; researchers have speculated that prenatal exposure to the flu interferes with fetal development, potentially harming health at birth and long term outcomes. Studies of other adverse prenatal shocks support this hypothesis and document negative effects on health and human capital in the exposed population decades later.[3] If prenatal exposure to influenza is similarly harmful, then interventions that curb the disease may improve both infant health and adult outcomes. Only 50 percent of pregnant women currently receive the recommended flu vaccine, which suggests the potential for substantial health and economic returns to interventions that expand vaccination.[4]

Despite these potentially large public health consequences, the effects of prenatal exposure to seasonal influenza in the United States are not fully understood and difficult to identify. An experimental approach would compare the outcomes of children born to mothers sickened with the flu during pregnancy to the outcomes of unexposed children. However, this strategy contends with several sources of potential bias; catching the flu may be endogenous to maternal characteristics, selection into medical care may bias estimated effect sizes, and seasonal variation in other factors may confound results (Currie and Schwandt, 2013; Schwandt, 2018; Dorélien, 2019). Using the devastating 1918 influenza pandemic as a natural experiment provides some suggestive evidence. The prenatally exposed cohort experienced adverse impacts on socioeconomic status, educational attainment, income, entitlement payments, disability, and health outcomes later in life (Almond and Mazumder, 2005; Almond, 2006). However, more

[1] This estimate includes a cost of $72 billion associated with deaths (Molinari et al., 2007).
[2] CDC, "Pregnant Women & Influenza (Flu)," Available: https://www.cdc.gov/flu/highrisk/pregnant.htm; CDC, "People at High Risk for Flu Complications," Available: https://www.cdc.gov/flu/highrisk/index.htm
[3] Numerous studies document adverse effects from disasters, including famine and nuclear fallout, as well as routine occurrences like pollution. For a summary of this literature, see extensive reviews by Almond and Currie (2011a) and Almond, Currie, and Duque (2018).
[4] Centers for Disease Control and Prevention (CDC), "Results of CDC's 2016-2017 Internet panel survey of pregnant women," Available: https://www.cdc.gov/flu/pdf/partners/flu-pregnancy-infographic-updated.pdf; CDC, "Pregnant Women and Flu Vaccination, Internet Panel Survey, United States, November 2016," Available: https://www.cdc.gov/flu/fluvaxview/pregnant-women-nov2016.htm

recent research questions these findings and contends that accounting for paternal characteristics eliminates adverse long term economic impacts from the pandemic (Brown and Thomas, 2018). In any case, results from studies of the 1918 influenza pandemic may fail to generalize to the present disease or social environment in the United States. Advances in public health, medicine, and vaccination since the early 20th century decreased mortality (Cutler, Deaton, and Lleras-Muney, 2006), and potentially diminished the risk of harm from prenatal exposure to the flu. Moreover, rare and severe pandemics may pose a greater threat compared to the annual seasonal flu. Additional inquiry is needed to identify the magnitude of the prenatal danger posed by seasonal flu in the U.S. and if adverse effects at birth persist into adulthood. A greater understanding of these potential effects can also shed light on the value of preventative care policies like flu vaccination programs, as well as deepen our knowledge of health disparities and aging-related issues.

To address this gap, I investigate the effects of prenatal exposure to the seasonal flu on life course outcomes in the United States. My empirical strategy provides several advantages. First, I isolate causality by generating an intent-to-treat estimate of prenatal exposure to the flu. [5] I construct a granular time series of state-level influenza-related mortality between 1959 to 2004 to proxy for the intensity of the disease environment. The use of this measure provides a source of plausibly exogenous variation, as unpredictable viral mutations influence disease severity (Cox and Subbarao, 2000). I also incorporate state-date of birth fixed effects in my model to exploit variation in disease exposure across flu seasons within a specific state and period of time.[6] This approach overcomes potential endogeneity issues, selection biases, and seasonal confounding (Dorélien, 2019). In addition, my strategy detects small effects over a wide range of outcomes by using several large data sets pooled over multiple years.

I start by analyzing health at birth using 1971-2004 National Center for Health Statistics (NCHS) Vital Statistics Natality data (NCHS *Natality*). I model the effects of influenza exposure during each separate month *in utero* on outcomes including birth weight, gestation length, and congenital anomalies that the medical and epidemiology literature connects to flu or

[5] In an instrumental variables framework, I am identifying the reduced form effect of prenatal flu exposure on outcomes. I am unable to measure the first stage effect of the disease environment on maternal flu infection due to data limitations and the structural equation that captures the effect of a mother's influenza infection on their child's outcomes contends with the same potential sources of bias as the experimental approach.

[6] Dorélien (2019) follows a similar methodology and uses exposure to county-level influenza mortality with county-month fixed effects.

fever. Consistent with prior evidence, I find that prenatal exposure to seasonal flu later in pregnancy negatively impacts birth weight. Effect sizes suggest that maternal flu infection in a severe season is as harmful as smoking during pregnancy. Decreases in birth weight appear to result from restricted fetal growth as opposed to preterm birth. Prenatal flu exposure also increases the risk of heart malformations early in pregnancy, but does not consistently affect other birth outcomes.

I next examine long term outcomes using 2008-2017 IPUMS (Integrated Public Use Microdata Series) American Community Survey (ACS) data (Ruggles et al, 2019). I evaluate impacts from influenza exposure over the course of a pregnancy on economic outcomes and disability. I identify small, negative effects on education and labor force participation. In particular, prenatal exposure to a severe flu season statistically significantly decreases the probability of school attendance during childhood by 0.5 percentage points, the probability of high school completion by 0.1 percentage points, and the probability of labor force participation by 0.3 percentage points. I find similar effects on adult disability; exposure to a severe flu season while *in utero* increases the probability of any disability by 0.2 percentage points and particularly affects ambulatory and vision difficulties. While these effect sizes are small, they affect a large number of people and aggregate to a substantial economy-wide impact.

I use these findings to examine vaccination as a policy tool to reduce the harm of prenatal exposure to seasonal influenza. I simulate how historical expansions in flu vaccination diminished flu severity in the population and correspondingly improved outcomes. Increases in vaccine uptake account for an estimated 16 percent of the decline in low birth weight, roughly 0.5 to 1.5 percent of improvements in economic outcomes, and 0.2 percent of the decline in any disability across varying periods in the late 20th and early 21st centuries. I similarly estimate the effect of future vaccination expansions on further moderating *in utero* exposure to the seasonal flu. Policies that promote the Healthy People 2020 goal of vaccinating 70 percent of the adult population may decrease low birth weight by four percent, increase labor force participation by nearly 0.1 percent, and decrease any disability by nearly 0.3 percent from current levels. This translates to nearly 10,000 fewer infants born with low birth weight each year, 54,000 more workers in the labor force, and 34,000 more adults without any disability. As a result of these economically meaningful returns, cost-benefit analyses of vaccination interventions should consider the long-run benefits of flu vaccine uptake.

This study complements prior investigations into the effects of prenatal exposure to seasonal influenza on birth and long term outcomes (Currie and Schwandt, 2013; Schwandt, 2018; Dorélien, 2019). I support and expand on the health at birth findings by examining an extended time period of births in all states and identifying causal impacts on congenital anomalies. Furthermore, I provide, to my knowledge, the first causal estimates of the effects of prenatal exposure to the seasonal flu on long term economic outcomes and disability in the United States.

This paper is organized as follows: Section 2 presents background information on the epidemiology of seasonal influenza and human development. Section 3 describes data sources and variable construction. Section 4 evaluates the effects of prenatal exposure to the flu on health at birth and Section 5 analyzes the impacts on long term economic outcomes and disability. Section 6 simulates the influence of flu vaccination levels and discusses the policy implications of my findings. Section 7 concludes.

2. Background

2.1. Epidemiology of Influenza and Vaccination

The timing and intensity of influenza viral activity varies each year. Influenza infections generally emerge in October, peak between December and February, and can continue through May, although the virus is observed throughout the year. The flu sickens three to 11 percent of the United States population each season (Tokars, Olsen, and Reed, 2018), with symptoms that include fever, cough, sore throat, muscle aches, headaches, and fatigue. Although the majority of people fully recuperate within two weeks, influenza can trigger a cascade of severe complications including pneumonia, inflammation of the heart, muscle, and brain, or organ failure, which may lead to death. Deaths from the flu primarily occur in older age groups, but people with certain chronic conditions also face elevated risks of complications (Cox and Subbarao, 2000). Pregnant women are particularly susceptible to the adverse effects of influenza due to pregnancy-associated modifications to the immune system, heart, and lungs. Children under the age of five also face increased risks from infection.[7]

[7] Information on the flu season, flu symptoms, groups at high risk for complications, and viral types is available from the CDC: https://www.cdc.gov/flu/

Influenza types A and B cause seasonal illness in humans.[8] Random genetic mutations in the virus can generate new strains of the flu. The human immune system does not recognize the new variant, even if they were previously infected with or vaccinated against the flu (discussed in greater detail in *Appendix Section A1*). This process is referred to as antigenic variation (Cox and Subbarao, 2000; Rasmussen, Jamieson, and Bresee, 2012). The severity of an influenza outbreak depends on the interaction between several factors: the degree of antigenic variation, impacted demographic groups, and prior immunity to the virus (Cox and Subbarao, 2000).

The flu vaccine is a frontline defense against influenza. Evidence from a randomized controlled trial suggests that maternal vaccination against the seasonal flu may directly translate into improvements in infant health (Steinhoff et al., 2012). In the U.S., vaccination was initially recommended for pregnant women in their third trimester in 1995 and eventually expanded to include all trimesters by 2004 (CDC, 1995; CDC, 2004; Rasmussen et al., 2014) (discussed in *Appendix Section A2*). Unfortunately, uptake of the influenza vaccination amongst pregnant women is low. ***Figure 1*** compares the share of the population over the age of 18 and the share of pregnant women aged 18 to 44 reporting receipt of a flu shot in the previous 12 months. Vaccination levels of pregnant women increased substantially, from less than 10 percent of pregnant women in the mid-1990s to more than 40 percent by 2015. Nonetheless, recent vaccination estimates for both the adult population and pregnant women fall substantially short of the respective 70 and 80 percent targets set by Healthy People 2020 objectives.[9]

2.2. Developmental Implications of Prenatal Influenza Exposure

The influenza virus likely affects the fetus through harmful maternal symptoms, such as fever or hyperthermia, inflammation, or reduced nutritional uptake, as opposed to crossing the placental barrier (Kelly, 2011; Rasmussen, Jamieson, and Bresee, 2012; Kourtis, Read, and Jamieson, 2014). Exposure to the flu while *in utero* may interfere with fetal development, directly affecting health at birth and subsequent human capital accumulation (an applicable

[8] Other influenza types are influenza C and D. Influenza C is not associated with epidemics and influenza D mainly impacts cattle.

[9] U.S. Department of Health and Human Services. "Healthy People 2020" Objectives – IID-12.12 and IID-12.14. Available: https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives

conceptual framework is discussed in *Appendix Section A3*). This shock may also generate physiological changes associated with the fetal origins hypothesis, wherein a prenatal exposure alters developmental processes in ways that harm health later in life (Almond and Currie, 2011a). Exposure at different points of gestation may differentially affect outcomes due to the timing of fetal development. Shocks early in pregnancy may interfere with fetal structural development and cause congenital anomalies; shocks in mid-pregnancy may interfere with central nervous system development affecting brain and cognitive development (Kelly, 2011); and shocks late in pregnancy, when the fetus gains the majority of its weight, may negatively affect birth weight and gestation length outcomes (discussed in detail in *Appendix Section A4*).[10]

Effects from prenatal exposure to the flu may manifest over the life course (***Appendix Figure A1*** provides a summary of some of the literature). Studies of the impacts on health at birth use data from select states and large counties in the U.S. between approximately 1990 and 2010, as well as administrative data in Denmark (Currie and Schwandt, 2013; Schwandt, 2018; Dorélien, 2019).[11] These analyses find that prenatal exposure to seasonal influenza late in pregnancy decreases birth weight largely through decreased gestation length. Other work hypothesizes that male fetuses are less likely to survive a negative shock compared to female fetuses, potentially resulting in fewer male infants (Hansen, Møller, and Olsen, 1999; Bruckner et al., 2014). Medical and epidemiological research also suggests a possible association between fever or febrile illness early in pregnancy and congenital anomalies at birth, including neural tube defects, oral clefts, and heart defects (Botto et al., 2014; Dreier, Andersen, and Berg-Beckhoff, 2014; Kerr et al., 2017; Waller et al, 2018).

Despite the compelling evidence that seasonal influenza affects birth outcomes, few economic studies evaluate impacts over the long term. To my knowledge, no papers causally evaluate how prenatal flu exposure affects childhood outcomes, possibly because any effects are likely to be small in magnitude and identification would require large data sets.[12] The medical

[10] CDC, "Fetal Development Chart" in "An Alcohol-Free Pregnancy is the Best Choice for Your Baby" Brochure, Available:
https://www.cdc.gov/ncbddd/fasd/documents/FASDBrochure_final-508.pdf

[11] Specifically, Currie and Schwandt (2013) use Vital Statistics Natality birth data from New Jersey (1997 to 2006), Pennsylvania (2004 to 2010), and New York City (1994 to 2004); Dorélien (2019) uses NCHS Birth Cohort Linked Birth-Infant Death data for large U.S. counties from 1989 to 1991 and 1995 to 2004; and Schwandt (2018) uses administrative data on a cohort born between 1980 and 1993 in Denmark. Dorélien (2019) also suggests that an early pregnancy exposure increases mortality due to congenital abnormalities.

[12] The study of the Danish cohort finds suggestive evidence of prenatal exposure to seasonal influenza increasing the probability of death by age 18 (Schwandt, 2018). Another analysis evaluates the impacts of pandemic influenza on

and epidemiology literature points to a link between fever during the second trimester of pregnancy and adverse childhood behavioral outcomes (Dombrowski, Martin, and Huttunen, 2003) and autism spectrum disorders (Hornig et al., 2018), as well as an association between infection early in pregnancy and schizophrenia (Khandaker, Dibben, and Jones, 2012). However, only the study of Danish young adults provides causal evidence of the effects of prenatal exposure to the seasonal flu on adult economic outcomes (Schwandt, 2018). Exposure during the second trimester of pregnancy negatively affected educational attainment, labor market participation, wages, and welfare receipt for young adults aged 19 to 32. To my knowledge, outside of Denmark, there are no causal estimates on long term outcomes.

Although scant evidence is available on the consequences of exposure to seasonal flu, several influential papers evaluate the effects of the 1918 influenza pandemic on U.S. adults. Adverse impacts on socioeconomic status, educational attainment, income, entitlement payments, and disability were documented after roughly age 40 (Almond, 2006), and negative effects on health outcomes were identified after roughly age 65 (Almond and Mazumber, 2005). Similar studies were undertaken in other countries (Nelson, 2010; Neelsen and Stratmann, 2012; Lin and Liu 2014; Bengtsson and Helgertz, 2015). A recent paper in this literature proposes an alternative explanation: the cohort exposed to the 1918 influenza while *in utero* were born to fathers with lower socioeconomic status relative to comparison cohorts, potentially due to the deployment of fathers with higher socioeconomic status to Europe during WWI (Brown and Thomas, 2018).[13]

3. Data

3.1. Seasonal Influenza Exposure

I use influenza-related mortality rates to proxy for the severity of the flu and the magnitude of a pregnant woman's exposure in a given state and time period. I generate monthly and

children and finds negative effects on cognitive test scores and decreased height for the children of smokers from prenatal exposure to the 1957 H2N2 pandemic in the United Kingdom (Kelly, 2011). This analysis also found that this mainly second trimester exposure decreased birth weight for children of mothers with a height of 60 inches or less and mothers who smoke.

[13] The effects of prenatal exposure to the pandemic disappear when including controls that proxy for parent characteristics. Another study further examined these concerns with a methodology that uses geographic variation in the pandemic and directly links parents to children (Beach, Ferrie, and Saavedra, 2018). This analysis reaffirmed the negative impacts on educational attainment in the U.S.

quarterly state-level influenza-related mortality rates per 100,000 for the years 1959 to 2004 using NCHS Vital Statistics multiple cause of death data (NCHS *Multiple Cause-of-Death*). Influenza-related mortality focuses on deaths with an underlying cause of influenza (the construction of influenza-related mortality rates is discussed in detail in *Appendix Section A5*). As previously described, the magnitude of an influenza epidemic is influenced by random genetic mutations that unpredictably change the flu virus and hinder identification by the immune system (Cox and Subbarao, 2000). This process provides a source of plausibly exogenous variation in flu severity across seasons.

Figure 2 displays the monthly average state-level influenza-related mortality rates for my sample period and ***Table 1*** presents summary statistics. Seasonal spikes in influenza-related mortality are apparent and typically occur in January or February. The peaks of influenza-related mortality dampen over time, with comparatively low mortality rates occurring from the mid-1980s onwards. As an illustrative example of the available variation, ***Appendix Figure A2*** demonstrates influenza-related mortality spreading across the U.S. during a particularly severe flu season in 1975-1976.

I also construct other measures of flu exposure for comparison in an alternative analysis and robustness tests (construction and additional discussion of these measures is outlined in *Appendix Section A6*). ***Appendix Figure A3*** displays the monthly state-level average of these measures and ***Appendix Table A1*** provides summary statistics. First, I generate multiple cause influenza- and pneumonia-related mortality per 100,000 (referred to as multiple cause mortality), which includes deaths with an underlying or contributing cause of influenza or pneumonia. This measure attributes a larger number of deaths to influenza in comparison to my primary exposure variable. Other studies use this multiple cause variable as an exposure (Dushoff, 2005; Dorélien, 2019; White, 2019), as influenza is likely underreported as a cause of death. This is particularly true for older populations, where flu deaths may instead be attributed to complications like pneumonia.[14] Although influenza-related mortality appears to better capture variation from the seasonal flu and

[14] CDC. "How CDC Estimates the Burden of Seasonal Influenza in the U.S.," Available: https://www.cdc.gov/flu/about/burden/how-cdc-estimates.htm. Influenza may interact with multiple chronic conditions; as a result, excess deaths due to all causes may be attributable to influenza (Cox and Subbarao 2000).

avoids introducing noise from deaths unrelated to the flu, I use multiple cause mortality as the exposure variable in alternative analyses for comparison.[15]

In addition, the age distribution of a state has implications for my exposure variable. Elevated influenza-related mortality in a state may reflect an older population as opposed to greater disease severity, since deaths from influenza primarily occur in older age groups (Cox and Subbarao, 2000). This suggests that the exposure variable should be adjusted to account for the age distribution. On the other hand, older individuals also possess weaker immune systems (Montecino-Rodriguez, Berent-Maoz, and Dorshkind, 2013). This implies that states with an aged population represent a particularly dangerous environment where the flu spreads effectively and the exposure variable should not be age-adjusted. Following this logic, I do not adjust for age in my primary exposure variable. However, I include age-adjusted influenza-related mortality per 100,000 as a robustness test (referred to as age-adjusted mortality) to ensure that my results do not depend on this supposition.

Finally, as an additional robustness check, I construct quarterly influenza-related mortality excluding a cohort potentially exposed to a pandemic flu (born between 1968Q4 and 1970Q1). Although I focus on seasonal flu in this analysis, one season in my sample represents a pandemic year: the 1968 H3N2 "Hong Kong flu", which emerged when an avian flu virus combined with a previously circulating human strain to form a new influenza A virus.[16] Mortality from this pandemic peaked in January, 1969, although other seasonal flu years in my sample demonstrated similar or greater mortality rates (***Figure 2***).

3.2. Health at Birth

I examine impacts on health at birth using public birth certificate data from NCHS Vital Statistics Natality Data for children born between 1971 and 2004 (NCHS *Natality*).[17] These data

[15] Compared to influenza-related mortality, which falls to zero outside of flu season (***Figure 2***), multiple cause mortality exhibits seasonality but remains elevated at around five deaths per 100,000 outside of flu season (***Appendix Figure A3***).

[16] CDC, "1968 Pandemic (H3N2 virus)," Available: https://www.cdc.gov/flu/pandemic-resources/1968-pandemic.html

[17] Data from the year 1968 onwards is available. However, data from 1968 is omitted due to a lack of control variables (such as paternal age) and data from 1969 and 1970 are also omitted as they don't provide information on birth plurality to identify singleton births. This data is available from the National Bureau of Economic Research (NBER): http://www.nber.org/data/vital-statistics-natality-data.html

include birth year, birth month, state of birth, and demographic information for both infants and their parents. I create the analytic data set by linking births to the influenza-related mortality rate in the state of birth at the time of conception using gestation length.[18] I limit the sample to infants born as singleton births with nine months of gestation or less.[19] I also exclude births from the beginning and end of the time period that would mechanically exaggerate the number of short and long gestation lengths (i.e. I only include conceptions in or after Sept., 1970 and in or before Mar., 2004).

I analyze the effects of prenatal exposure to seasonal flu on *birth weight* (grams), an indicator for *low birth weight* (less than 2500 grams), *gestation length* (weeks), an indicator for *preterm birth* (less than 37 weeks), an indicator for *low five minute APGAR score* (less than seven, which indicates poor infant health at birth and is available beginning in 1978), and an indicator for *male birth*. I also evaluate the risk of congenital anomalies highlighted in medical literature in data available beginning in 1989. Specifically, I include indicators for *neural tube defects* (anencephalus and spina bifida/meningocele), *heart malformations*, and *cleft lip/palate*.[20] As a summary outcome, I construct an indicator to represent *any congenital anomaly*. ***Tables 2A and 2B*** presents summary statistics of the resulting analytic data sets. The main sample of birth weight and gestation outcomes represents approximately 92 million births and the congenital anomaly sample represents approximately 55 million births.

3.3. Long Term Economic Outcomes and Disability

I investigate health and human capital development later in life using pooled IPUMS 2008-2017 ACS data (Ruggles et al., 2019). In addition to various education, labor market, socioeconomic, income, and disability measures, these data include birth year, birth quarter, state of birth, and demographic information.[21] I generate an analytic sample of native-born working-

[18] I calculate the month/year of conception from gestation weeks following the strategy in Currie and Schwandt (2013) and Dorélien (2019). I first convert gestation in weeks to a rounded number of gestation months, equal to gestation in weeks * (7 days/1 week) * (1 month/average of 30.5 days) = gestation in weeks * ((7/30.5). I then subtract this value from the month/year of birth to identify the month of conception. Births with missing data on gestation length are omitted from the analysis.

[19] I omit births with long gestations since most women are induced before gestation month 10 (42 weeks).

[20] This sample also represents singleton births with nine months of gestation or less with a mechanical correction (conceived between Sept. 1988 and Mar. 2004).

[21] Birth year is not directly reported in the IPUMS ACS. Instead, it is constructed as the survey year minus age, representing an estimate of the year of birth. However, ACS surveys occurs throughout each year; as a result, "the

age adults aged 25 to 58 by linking individuals to the influenza-related mortality rate in their birth states and birth quarters. I similarly create an analytic sample of children aged five to 17 to evaluate childhood education.[22]

I focus on two dimensions of health and human capital that prenatal seasonal influenza exposure may affect: economic outcomes and disability. ***Table 3*** presents summary statistics of my outcomes. Economic outcomes include measures related to education and the labor market. Specifically, I examine effects on an indicator for *child attended school during the last three months*, an indicator for *high school completion*, *educational attainment* in years, and an indicator for *labor force participation*.[23] I also analyze several secondary outcomes related to economic prosperity, including an indicator for *below 150 percent of the poverty threshold*, the *Duncan Socioeconomic Index*[24], *wage and salary income* in real $1999, and *entitlement income* (defined as the sum of welfare, social security, and SSI income) in real $1999.

To evaluate impacts on disability, I construct an indicator of *any disability* that identifies if an individual reports difficulty in any of the following six categories: *cognitive difficulty* (difficulty "remembering, concentrating, or making decisions" due to a "physical, mental, or emotional problem"); *ambulatory difficulty* (difficulty "walking or climbing stairs"); *independent living difficulty* (difficulty "doing errands alone such as visiting a doctor's office or shopping" due to a "physical, mental, or emotional problem"); *self-care difficulty* (difficulty "bathing or dressing"); *vision difficulty* (the individual is "blind or having serious difficulty seeing, even when wearing glasses"); or *hearing difficulty* (the individual is "deaf or having serious difficulty hearing").[25] I also look at impacts on these six categories separately.

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errors averaged across the entire sample will be close to zero." IPUMS USA "BIRTHYR – Comparability" Available: https://usa.ipums.org/usa-action/variables/BIRTHYR#comparability_section. In addition, an analysis using IPUMS ACS data to examine long run impacts from prenatal and child Medicaid coverage examined the robustness of using this calculated birth year (Miller and Wherry, 2016, described p.19 and p.32). The study constructed year of birth using the ACS method in National Health Interview Survey (NHIS) data, which includes information on actual year of birth, and found a correlation coefficient of roughly 0.99. Nonetheless, this introduction of measurement error may attenuate any findings in my analysis.

[22] This child sample does not reflect the working-age adult sample as children. A comparison across the two samples would need to disentangle confounded age effects, time effects, and cohort effects.

[23] Years of educational attainment is coded as follows: any schooling up to grade four is coded as four years; grades five to eight is coded as eight years; and any education after four years of college is top coded as 17 years. High school completion is coded as having at least grade 12 educational attainment.

[24] The generated socioeconomic index ranges from 1 to 96, with greater values indicating a higher socioeconomic standing based on occupational education and income. For more information, see: https://usa.ipums.org/usa-action/variables/SEI

[25] These disability questions have been consistently available beginning with the 2008 ACS. The United States Census Bureau, "How Disability Data Are Collected from the American Community Survey," Available:

I further explore specific activity and functional limitations associated with disability using pooled data from the IPUMS 2011 to 2017 NHIS, which includes the same six disability categories, demographic information, and causes of limitations (Blewett et al., 2019). ***Appendix Table A2*** provides summary statistics for the analytic samples of native-born, working-age adults that report causes of an activity limitation or functional limitation.

4. The Effects of Prenatal Exposure to Seasonal Influenza on Health at Birth

4.1. Empirical Strategy

In this section, I evaluate the impacts of seasonal flu exposure during each month *in utero* on birth outcomes. I use a fixed effects model that exploits variation in influenza-related mortality within a state and during a specific conception month across flu seasons. My approach is similar to the empirical strategy in Dorélien (2019). Using the analytic sample of infants with nine months of gestation or less born between 1971 and 2004, I estimate effects with the linear regression:

$$(1) \qquad Y_{iscM} = \alpha_0 + \sum_{m=0}^{9}(\beta_{\mathrm{m}} F_{s,c+m} + \alpha_1 N_{i,s,c+m}) + \boldsymbol{X}_{isc}\alpha_2 + \gamma_{sM} + \tau_c + \mu_s T_c + \varepsilon_{iscM}$$

where Y_{isc} represents a specific outcome for individual *i* born in state *s* with time (month/year) of conception *c* in calendar month *M*. F is a vector of state-level influenza-related mortality per 100,000 beginning with influenza in the time of conception ($F_{s,c}$) and continuing over the following nine months to represent monthly influenza during gestation.[26] In order to capture impacts on infants with a gestation period of eight months or less, I set influenza-related

https://www.census.gov/topics/health/disability/guidance/data-collection-acs.html. For additional information, see the IPUMS-USA disability variable documentation available: https://usa.ipums.org/usa-action/variables/group?id=disab.

[26] I assume that conception and all months of gestation occur in the state of birth, and the pregnant woman is exposed to the influenza environment of that state. Studies indicate that 11 to 25 percent of women move during pregnancy (Bond et al., 2019). However, moves tended to be over short distances; a study of pregnant women in Connecticut and Massachusetts from 1988 to 2008 found a median moving distance of 5.1 km (3.2 miles), with an interquartile range of 11.4 km (7.1 miles) (Bell, Banerjee, and Pereira, 2018). This suggests limited crossing of state borders. However, this study also found that roughly eight percent of moves were over 4000 km (2485.5 miles) suggesting that some measurement error may occur.

mortality equal to zero for months after the month of birth and include a vector of dummies, N, equal to one for months where the infant is not *in utero*. For instance, an infant born during month seven of gestation would experience influenza-related mortality equal to zero in months eight ($F_{s,c+8}$) and nine ($F_{s,c+9}$), with $N_{i,s,c+8}$ and $N_{i,s,c+9}$ both equal to one. This confines the estimates of the effects of prenatal exposure to apply only to months when the infant is *in utero*.

$\boldsymbol{X}_{isc}$ is a matrix of infant and parent characteristics.[27] I also include multiple fixed-effects. γ_{sM} represent state of birth-calendar month *M* of conception fixed effects (e.g. Colorado in February) to identify effects using variation within a state-month and to account for any time invariant state-month factors. τ_c are time (month/year) of conception (e.g. February, 1970) fixed effects to account for national time-specific factors. Finally, $\mu_s T_c$ represent state of birth-specific linear time trends, where T_c is a monthly time trend beginning at 1 for conceptions in Jan., 1967. These control for long-term trends in each state that may be associated with influenza and birth outcomes over time, including improvements in medical care and changes in the population structure. Standard errors are clustered by state of birth-month of conception, such that the error term ε_{iscM} allows for correlation between infants born in the same state within the same month. Regressions are frequency weighted as some states used 50 percent samples of birth certificates prior to 1985.

I similarly examine the effects of prenatal exposure to seasonal influenza on the relative risk of congenital anomalies using my analytic sample of infants with nine months of gestation or less born between 1989 and 2004. I employ the same empirical strategy except I estimate (1) as a log-binomial regression to obtain exponentiated coefficients that represent relative risk.

The coefficients of interest, β_0 through β_9, capture the effects of prenatal flu exposure in months zero through nine of gestation on birth outcomes or the relative risk of congenital anomalies. By incorporating state of birth-calendar month of conception fixed effects in my model, I identify based on random fluctuations in influenza-related mortality, a proxy for the

[27] Characteristics include dummies for sex of child, live birth order of child (top coded at 15), mother's age in single years (bottom coded at 14, top coded at 50), father's age in single years (bottom coded at 14, top coded at 65), mother's race (white, black, Native American, Asian, other), father's race (white, black, Native American, Asian, other), mother's education (less than high school, 12th grade/four years of high school, some college, four years of college/Bachelor's degree, five plus years of college/post-Bachelor's), and mother's marital status (married, unmarried), including dummies for unknown/missing for all variables. I include in $\boldsymbol{X}_{isc}$ dummies for maternal tobacco and alcohol use during pregnancy when analyzing the congenital anomaly outcomes in the 1989 to 2004 sample. Maternal tobacco and alcohol use controls are not available prior to 1989.

disease environment, within a state and specific month of conception across flu seasons. For example, I use variation in influenza exposure for infants conceived in Colorado in February across years to identify differences in birth outcomes for infants conceived in Colorado in February across years. The main identifying assumption is that there are no unaccounted for shocks within state-months that simultaneously impact my measure of influenza-related mortality and birth outcomes. One limitation of this analysis is that I cannot isolate the impacts of flu exposure from other pathways or health behaviors that may directly correspond to infection (e.g. the use of antipyretics to control a fever could theoretically drive the effects).

On the other hand, this empirical approach provides multiple benefits. By using a population-level exposure, I generate intent-to-treat estimates and avoid potential sources of bias from an analysis of individual maternal infections. The risk of influenza infection may be endogenous to unobserved maternal features or behaviors, and selection into health care or hospitalization may also bias estimates (Schwandt, 2018; Dorélien, 2019).[28] In addition, this identification strategy does not rely on the use of seasonal variation in influenza which may bias results due to seasonal variation in other factors (Schwandt, 2018; Dorélien, 2019). For example, women with lower socioeconomic status are more likely to conceive between January and June than women with higher socioeconomic status (Currie and Schwandt, 2013).[29]

4.2. Results

I first evaluate the effects of prenatal exposure to seasonal influenza in months zero to nine of gestation on birth weight and gestation length outcomes. ***Figure 3*** presents the coefficients of interest, which estimate the impact of one additional influenza-related death per 100,000 with a 95 percent confidence interval bar (***Appendix Table A3a*** also shows results in table form with all indicator variables scaled from 0 to 100 for readability). I find that prenatal exposure to influenza decreases birth weight and increases the probability of low birth weight. Negative impacts begin in mid-pregnancy at around months four to six of gestation and increase in

[28] For example, women with fewer financial resources may simultaneously face a greater risk of influenza infection and a reduced ability to access health care during pregnancy compared to women with greater resources. Similarly, women with severe influenza infections may be more likely to seek medical treatment, resulting in estimates that overstate the impacts of prenatal exposure to the flu.

[29] Currie and Schwandt (2013) suggest that any bias in this instance is likely to be small compared to the effects of external factors such as influenza.

magnitude with gestation length, although the effect of a month nine exposure appears to diminish and is not statistically significant. To understand the magnitude of these effects, I use influenza-related mortality data from the particularly severe 1975-76 flu season to calculate impacts from an intense exposure late in pregnancy. According to my results, an infant in months six of gestation in January, 1976 and born in April, 1976 would experience a lower birth weight of 20.3 grams and an increase in the probability of low birth weight of 0.6 percentage points.[30]

These findings represent an intent-to-treat estimate of the population average; the effect on an infant born to an infected mother would be substantially higher. I estimate that maternal infection from the severe flu exposure would decrease birth weight between 185 and 677 grams and increase the probability of low birth weight by 5.5 to 20 percentage points.[31] This approximation suggests that the harm from a maternal flu infection late in pregnancy in a severe season is similar to or even greater than the dangers of smoking during pregnancy, which is estimated to decrease birth weight by 182 grams and increase the probability of low birth weight by seven percentage points (Lien and Evans, 2005).

Adverse impacts on birth weight may be due to shortened gestation length, or influenza exposure may directly interfere with fetal weight gain (Currie and Schwandt, 2013; Schwandt, 2018). I find inconsistent impacts of prenatal influenza exposure on gestation length and the probability of preterm birth. For example, exposure in months two, four, six, and eight decrease gestation length while an exposure in month nine substantially increases gestation length. As a result, the negative impacts on birth weight likely operate through a pathway separate from decreased gestation length. To further evaluate this possibility, I examine the effects of prenatal flu exposure on birth weight controlling for gestation length using dummies for single weeks of gestation (Currie and Schwandt, 2013; Schwandt, 2018; Dorélien, 2019). The effects on birth weight persist at a similar magnitude, which points to fetal growth inhibition as the main mechanism causing decreased birth weight.

[30] Calculation shown in notes of ***Appendix Table A3a***.

[31] I roughly estimate a treatment-on-the-treated effect of infection late in pregnancy using an all ages population infection rate that ranges from approximately three to 11 percent (Tokars, Olsen, and Reed, 2018). My calculation assumes that the infection rate in pregnant women is the same as the rate in the overall population. The birth weight effect is calculated as -20.3/0.03=677 to -20.3/0.11=185 and the probability of low birth weight effect is calculated as 0.6/0.03=20pp to 0.6/0.11=5.5pp.

I next examine the effects of prenatal flu exposure on the probability of a low five-minute APGAR score and the probability of a male child. ***Figure 4*** shows a lack of consistent pattern for these outcomes. Finally, I estimate the relative risk of congenital anomalies that are potentially sensitive to *in utero* exposure to the flu. ***Figure 5*** demonstrates that prenatal exposure to influenza very early in pregnancy may increase the risk of any congenital anomaly, driven by an increase in heart malformations (***Appendix Table A3b*** shows the results in table form). An increase in exposure of one influenza-related death per 100,000 in month zero of gestation results in a relative risk of 1.1 for any congenital anomaly and nearly 1.2 for heart malformations. Exposure does not appear to cause impacts in later months, or affect other congenital anomalies.

My findings are generally consistent with models of human development, which suggest that exposure to influenza late in pregnancy harms birth weight and exposure early in pregnancy increases the risk of heart malformations. However, I do not find evidence for all hypothesized effects, including decreased gestation length, probability of a male birth, and other congenital anomalies. The impacts on birth weight also align with other findings in the literature (***Table 4***). Differences in sample periods and empirical strategies make an exact comparison difficult, but generally my effect sizes appear to be similar.[32] A few of my effect sizes are somewhat larger than those suggested by the literature; in particular, my low birth weight estimate in comparison to Dorélien (2019) and my estimates of a severe flu impact. One important difference is that these other studies generally find that exposure late in pregnancy shortens gestation length, and attribute at least some of the decline in birth weight to preterm birth. However, a randomized controlled trial in Bangladesh found that the infants of women that were vaccinated against influenza during the flu season were less likely to be small for gestational age in addition to having a higher average birth weight, suggesting influenza's impact on fetal growth as a potential mechanism (Steinhoff et al., 2012).

4.3. Alternative Measure of Influenza Exposure

As an exploratory step, I repeat this analysis using multiple cause mortality as the exposure variable instead of influenza-related mortality. While influenza-related mortality includes deaths

[32] Similarly, Schwandt (2018) does not find a statistically significant impact on the probability of a male infant.

where influenza is listed as the underlying cause, multiple cause mortality widely identifies an influenza death using any mention of influenza or pneumonia as an underlying or a contributing cause. ***Appendix Figure A4*** suggests that using multiple cause mortality does not detect effects on birth weight outcomes as effectively as my primary measure, although it does identify an increased risk of heart malformations (***Appendix Tables A4a and A4b*** presents the results in table form). The broad definition of flu deaths used by the alternative variable may drive these differences by less effectively representing disease severity in the environment. The annual flu season may trigger some pneumonia deaths in older populations regardless of flu intensity and introduce deaths in the measure that do not reflect the underlying severity of the exposure to pregnant women. Multiple cause mortality may also introduce noise from pneumonia deaths unaffiliated with the flu season. As a result, the primary measure may better represent disease severity and the extent of flu exposure in the population.

4.4. Robustness Checks

I also examine the robustness of my main results to several of my modeling decisions. First, I use the age-adjusted measure of influenza-related mortality (***Appendix Figure A5a*** and ***Appendix Tables A5a and A5b***). Second, I omit state-specific linear time trends from my main specification to evaluate if my findings for birth outcomes are sensitive to their inclusion (***Appendix Figure A5b*** and ***Appendix Tables A5c***). My findings are robust to these changes. Although the effects of an exposure in any given month may vary, the overall patterns and magnitudes are consistent with my primary results.

5. Long Term Economic Outcomes and Disability

5.1. Empirical Strategy

In this section, I analyze the effects of prenatal exposure to seasonal flu on long term economic outcomes and disability. Similar to the analysis of health at birth, I use a fixed effects model to exploit variation in influenza-related mortality within a state and quarter of birth across

flu seasons. Using the analytic samples constructed using ACS data, I estimate impacts with the linear regression:

$$(2) \qquad Y_{isbtQ} = \alpha_0 + \beta_1 F_{sb} + \boldsymbol{X}_{isbt}\alpha_1 + \gamma_{sQ} + \tau_b + \mu_s T_b + \delta_t + \varepsilon_{isbtQ}$$

where Y_{isbt} represents an outcome for individual *i* in current survey year *t* born in state *s* with quarterly time of birth *b* in calendar quarter *Q*. F represents state-level influenza-related mortality per 100,000 over the course of a typical pregnancy (the sum of deaths in the quarter of birth and previous three quarters divided by corresponding annual populations). This measure approximates influenza exposure during a nine-month gestation length, as additional months of influenza exposure may be included prior to conception or after birth.[33]

I include controls and fixed effects in equations (2) that are similar to those in equation (1). $\boldsymbol{X}_{isbt}$ is a matrix of demographic characteristics including dummies for sex, single year of age, and race/ethnicity (white, black, Hispanic, Asian, and other). γ_{sQ} represent state of birth-quarter *Q* of birth fixed effects (e.g. Colorado in Q1) to identify effects using influenza variation within a state-quarter of birth and account for time-invariant state-quarter factors. τ_b are time (year-quarter) of birth (e.g. Q1, 1970) fixed effects to account for national time-specific factors. $\mu_s T_b$ represent state of birth-specific linear time trends to account for long-term trends in each state that may be associated with influenza, such as secular increases in educational attainment. Finally, δ_t represent current year fixed effects to control for survey year factors. Standard errors are clustered by state of birth-quarter of birth, such that the error term ε_{isbtQ} allows for correlation between individuals born in the same state within the same quarter and regressions are weighted to adjust for the sampling design.

The coefficient of interest, β_1, captures the effects of prenatal influenza exposure on later life economic outcomes and disability. The identification strategy, key identifying assumption, limitations, and strengths are the same as those previously outlined for equation (1). This

[33] Like in the evaluation of health at birth, I assume that conception and all months of gestation occur in the state of birth, and that pregnant women are exposed to the influenza environment of that state. Using four quarters to estimate a nine-month gestation is an approximation, and will include excess months of influenza exposure before conception or after birth. For example, an infant conceived in January (or March) Q1 with nine-months gestation would be born in October (December) Q4. In the analysis, the infant conceived in January will face an excess two months of flu exposure after birth (November and December). Likewise, the infant conceived in March will face an excess two months of flu exposure before conception (January and February).

empirical approach also avoids confounding from later life seasonal factors like school entry laws (Schwandt, 2018).

5.2. Results

I first evaluate the long term economic impacts of exposure to flu while *in utero*. ***Table 5*** shows negative effects on school attendance during childhood, high school completion, and labor force participation, with no effects on educational attainment measured in years. All coefficients can be interpreted as the effect of an increase of one influenza-related death per 100,000 (indicator variables are scaled from 0 to 100 for readability). I also provide estimates of the impact of an intense influenza exposure equivalent to the harmful 1975-76 influenza season (representing approximately 4.55 deaths per 100,000 between January and April, 1976). Effect sizes suggest that prenatal exposure to this severe flu decreases the probability of childhood school attendance by 0.5 percentage points, high school completion by 0.1 percentage points, and labor force participation by 0.3 percentage points. Exposure does not appear to affect secondary economic measures presented in ***Appendix Table A6***.

I next examine impacts on long term disability. ***Table 6*** shows that prenatal influenza exposure increases disability as an adult; an intense flu increases the probability of any disability by 0.2 percentage points. Effects appear concentrated amongst ambulatory and vision difficulties, which both increase by roughly 0.1 percentage points with a severe flu exposure. As an exploratory step, ***Appendix Table A7*** conducts the same analysis on two different samples: the child analytic sample and a full population sample (aged four to 58). Prenatal influenza exposure increases disability in the full population sample, affecting cognitive, ambulatory, self-care, and vision difficulties, but does not appear to impact disability in children.

Although these effect sizes are small, they represent impacts on a sizable number of people with economy-wide consequences. For example, I use the current U.S. population to estimate that these findings translate to 32,140 fewer people with high school completion, 80,695 fewer workers in the labor force, and 50,965 more people with any disability.[34]

[34] I calculate these values as the percent change in outcome from prenatal flu exposure multiplied by the number of native-born people aged 25 to 58 with high school completion, in the labor force, or with any disability in 2016-2017 (calculated as the shares with these outcomes multiplied by the average number of corresponding people in 2016 and 2017).

5.3. Timing of Influenza Exposure

I investigate potential mechanisms by evaluating the impacts of flu exposure during each separate "quarter" of pregnancy. This captures the long term effects of exposure during different stages of pregnancy. I estimate a linear regression identical to (2), except influenza-related mortality is separated into its component quarters:

$$(3)\ Y_{isbt} = \alpha_0 + \beta_1 F_{s,b} + \beta_2 F_{s,b-1} + \beta_3 F_{s,b-2} + \beta_4 F_{s,b-3} + \boldsymbol{X}_{isbt}\alpha_1 + \gamma_{sQ} + \tau_b + \mu_s T_b + \delta_t + \varepsilon_{isbt}$$

where $F_{s,b}$ represents state-level influenza-related mortality per 100,000 in the quarter of birth b, $F_{s,b-1}$ represents the same measure in the quarter before birth, and $F_{s,b-2}$ and $F_{s,b-3}$ represent the same measure two and three quarters before the birth quarter, respectively. Like equation (2), this specification assumes a nine-month gestation period and includes potentially extraneous months of influenza exposures. I approximate $F_{s,b-3}$ and $F_{s,b-2}$ as exposures to influenza earlier in pregnancy, $F_{s,b-2}$ and $F_{s,b-1}$ as exposures during mid-pregnancy, and $F_{s,b-1}$ and $F_{s,b}$ as exposures in late pregnancy.[35]

Table 7 shows that influenza exposure late in pregnancy negatively impacts labor force participation, any disability, and ambulatory difficulties, with a borderline statistically significant impact on high school completion ($p<0.1$). Effects on childhood school attendance appear diluted throughout pregnancy. On the other hand, influenza exposure early in pregnancy increases the probability of vision difficulties.

5.4. Specific Limitations Associated with Long Term Disability

I further explore mechanisms linking *in utero* flu exposure and long term disability. I use the analytic samples from the NHIS to estimate a linear regression that examines how ambulatory

[35] An infant conceived in January (or March) Q1 would experience early pregnancy/first trimester from roughly January to April (March to June) Q1/Q2, a second trimester from May to July (July to September) Q2/Q3, and a third trimester of August to October (October to December) Q3/Q4.

and vision difficulties relate to distinct causes of activity and functional limitations.[36] ***Table 8*** presents estimates for the activity and functional limitations with the strongest relationships with ambulatory and vision difficulties (full results are available in ***Appendix Table A8***).[37] For example, reporting an "other developmental problem" (non-intellectual) increases the probability of ambulatory disability by 43.0 percentage points. Stroke, missing limb/finger, and chronic conditions like diabetes and nervous system, heart, and arthritis problems also increase the probability of ambulatory difficulty by at least 15 percentage points. Unsurprisingly, indicating a vision problem as the cause of a limitation increases the probability of a vision disability.

5.5. Previous Research and Mechanisms Causing Long Term Effects

I compare my findings to estimates from the literature in ***Table 9***. The magnitudes of my results are plausible, although the analyses differ in terms of empirical strategy and setting. Similar to my findings, maternal influenza infection decreased the probability of labor force participation by 2.8 percentage points amongst young Danish adults, although this is primarily the result of a second trimester exposure (Schwandt, 2018). Exposure during the third trimester impacts labor force participation to a lesser extent. On the other hand, prenatal exposure to the 1918 pandemic in the U.S. resulted in larger adverse impacts on adult men than my findings suggest. Compared to a cohort trend line, the pandemic decreased the probability of high school completion by roughly two percentage points and increased the probability of a physical disability that "limits work" and a physical disability that "prevents work" by roughly 0.5 percentage points (Almond, 2006).[38] These analyses also found effects on a wider range of

[36] Specifically, I regress indicators for disability (scaled from 0 to 100 for readability) on indicators for activity limitation causes or functional limitation causes in separate regressions, including dummies for sex, age, and race. I correct for variance estimation and weigh to account for survey design using the weight associated with disability questions adjusted for years of pooled data (divided by seven).

[37] Selected estimates possess a statistical significance of $p<0.01$ and a coefficient showing an association of at least 15 percentage points.

[38] Effect sizes for high school completion are -0.021, -0.020, and -0.014 using the 1960, 1970, and 1980 Census years, respectively. Effects sizes for disability "limits work" are 0.006 and 0.005 and for disability "prevents work" are 0.004 and 0.001 (last estimate not statistically significant) in the 1970 and 1980 Census years, respectively. A pandemic analysis of adults aged 60 and older also observes an increase in reporting a "trouble walking at all" functional limitation, which parallels my findings on ambulatory difficulty. However, there were no impacts on other relevant outcomes like "trouble climbing stairs" or "blindness" (Almond and Mazumber, 2005).

outcomes than my study, such as years of education, socioeconomic status, poverty, wage income, and entitlement payments.

Although I study the impacts of the seasonal flu, this analysis is relevant to the concern surrounding the impacts of the 1918 pandemic flu, which discusses if the pandemic adversely affected long term outcomes (Almond, 2006; Beach, Ferrie, and Saavedra, 2018) or if the results are actually driven by selection (Brown and Thomas, 2018). My findings imply that the pandemic likely had negative long term socioeconomic impacts. I identify effects from milder seasonal flu in a comparatively modern era, which provides a theoretical lower bound of any impacts from a severe historical pandemic.

My analysis cannot identify the mechanisms underlying the long term impacts from prenatal flu exposure; however, some results might contribute to future hypothesis generation. The effects on childhood school attendance are not concentrated within a single stage of pregnancy, suggesting that multiple mechanisms may impact this outcome. On the other hand, exposure late in pregnancy decreases high school completion (borderline, $p<0.1$) and labor force participation. This contradicts a common hypothesis in the literature; negative shocks in the second trimester interfere with brain development, potentially harming long term cognitive development, educational attainment, and labor market outcomes (Kelly, 2011; Schwandt, 2018). Any disability and ambulatory difficulties are also sensitive to a prenatal influenza exposure late in pregnancy, and the latter is associated with functional limitations from non-intellectual developmental problems and chronic conditions. These findings support the existence of one or more mechanisms that link seasonal influenza exposure during the third trimester with adverse economic outcomes and increased disability later in life. One conjecture is that these effects may operate through a decrease in birth weight resulting from exposure late in pregnancy. A large literature has found adverse long run impacts from low birth weight, including effects on education and labor market outcomes (Almond and Currie, 2011b).[39] Finally, an increase in the risk of vision difficulty due to an exposure early in pregnancy is consistent with models of human development, where an adverse shock may interfere with structural development of the eye. Overall, this analysis suggests that prenatal exposure to seasonal flu can impact multiple developmental pathways.

[39] However, Schwandt (2018) finds that impacts on labor market outcomes persist even when controlling for birth weight.

5.6. Alternative Measure of Influenza Exposure

I repeat the main analysis on long term outcomes using multiple cause mortality as the prenatal exposure. Whereas the primary exposure variable is narrowly defined and attributes a death to influenza only when influenza is reported as the underlying cause, multiple cause mortality is based on influenza or pneumonia listed as an underlying or contributing cause of death. Similar to the multiple cause analysis of birth outcomes, ***Appendix Tables A9*** suggests that multiple cause mortality fails to find some effects identified in the main analysis. Although the directions of the estimates are the same, the alternative measure does not identify statistically significant effects on school attendance during childhood or labor force participation. Using multiple cause mortality, however, does find larger impacts on adult educational attainment measures and some secondary labor market outcomes consistent with adverse impacts from a prenatal exposure to influenza. Finally, ***Appendix Tables A10*** demonstrates that multiple cause mortality fails to identify a statistically significant effects of prenatal influenza exposure on disability.

The difference between these results and the main findings may derive from multiple cause mortality acting as a comparatively poor proxy for disease severity in the environment relative to the primary measure. Multiple cause mortality may include deaths that are unrelated to the flu or reflect pneumonia deaths during the flu season in an older population that do not embody the intensity of exposure to pregnant women.

5.7. Robustness Checks

I next evaluate the robustness of my primary findings to three specification changes that I apply separately: I use age-adjusted mortality as the prenatal exposure variable, I exclude the cohort potentially exposed to the 1968 pandemic flu, and I omit state-specific linear time trends from my specification. The resulting effects on economic outcomes are presented in ***Appendix Table A11*** and impacts on disability are presented in ***Appendix Table A12***. These robustness checks suggest that my results are robust to my modeling decisions. Age-adjusting the exposure variable yields generally similar findings, although ambulatory difficulty becomes borderline statistically significant ($p<0.10$). Excluding the pandemic cohort also generates similar effects.

Omitting state-specific linear time trends strengthens effect sizes on all estimates except for childhood school attendance, which becomes borderline statistically significant ($p<0.10$).

6. Vaccination as a Policy Intervention

This analysis finds that prenatal exposure to seasonal flu negatively impacts birth weight, increases adult disability, and decreases later life education and labor force participation in the U.S. I examine the policy implications of the results by studying flu vaccination as an intervention to improve life course outcomes.

I begin by exploring how historical increases in vaccination levels over my sample years improved health at birth and long term outcomes. As a first step, I approximate the impact of changes in vaccination uptake on influenza-related mortality by using an estimate from White (2019) that reflects the causal effects of vaccination on flu mortality.[40] ***Appendix Table A13*** presents these calculations in detail, as well as any assumptions and sources on historical vaccination rates.[41] I then apply these declines in influenza-related mortality to the coefficients estimated in my models, simulating the corresponding improvements in outcomes due to vaccination.[42]

The top panel of ***Table 10*** reports these estimates as the share of the overall change in each outcome associated with historical adult vaccination increases (calculations are shown in the top panel of ***Appendix Table A14***). The increase in population vaccination between 1971 and 2004 accounts for roughly 19 percent of the improvement in birth weight and 16 percent of the improvements in the share of infants born with low birth weight. Vaccination improved a smaller, but still economically meaningful, share of later life outcomes. The increase in vaccination rates between 1991 and 2004 is responsible for 1.4 percent of the increase in childhood school attendance, and the increase between 1959 and 1992 accounted for 0.6 percent

[40] Specifically, White (2019) concludes that a one percentage point increase in the vaccination rate would decrease influenza- and pneumonia- multiple cause mortality by 0.246 deaths per 100,000, operating primarily through positive externalities.

[41] Briefly, I multiply the percentage point increase in historical vaccination rates over each sample period by the estimate from White (2019) to translate this value into a decrease in multiple cause mortality. I then scale multiple cause mortality to influenza-related mortality using the ratio of the two measures from the peak Jan. to Apr. 1975-1976 influenza epidemic.

[42] I use the sum of coefficients from all months of gestation for birth outcomes and the coefficient from the full pregnancy period for later life outcomes.

of the increase in high school completion and 0.5 percent of the increase in labor force participation. Finally, I estimate that this vaccination expansion is response for 0.2 percent of the decreases in any disability.

I next evaluate the role of future vaccination policy to further improve outcomes. I focus on reaching the Healthy People 2020 target of vaccinating 70 percent of the population aged 18 and over. I use the same strategy as the historical vaccination calculations; I estimate the impact of increasing vaccination levels from the current 2016-2017 baseline of 45.2 percent on influenza-related mortality (***Appendix Table A13***) and then apply this decline to the estimates from my models. This calculates the change in life course outcomes associated with reaching this public health vaccination target. As an additional exploratory step, I approximate an upper bound to the benefits of perfect flu vaccination. I apply a decline in the influenza-related mortality rate from its current levels to zero to my models.[43] This simulates the effect of entirely eliminating the circulation of the flu on future outcomes.

The bottom panel of ***Table 10*** reports the percent change in outcomes from the current baseline associated with reaching 70 percent vaccination and the elimination of influenza deaths (calculations are shown in the bottom panel of ***Appendix Table A14***). Reaching the Healthy People 2020 target would decrease the share of infants born low birth weight by an additional four percent from baseline, which translates to 9,908 fewer infants born with low birth weight each year. Eliminating influenza would decrease the share by almost nine percent, or 20,920 fewer infants born with low birth weight. Once again, the benefits to later life outcomes are smaller, but economically meaningful. For example, the Healthy People 2020 target would increase labor force participation by 0.06 percent (53,605 more workers in the labor force) and decrease any disability by 0.26 percent (33,862 more adults without any disability).[44] Eliminating the flu entirely would roughly double these percent changes, including a 0.12

[43] Current influenza-related mortality rates are as 1.4 influenza-related deaths per 100,000 (CDC Wonder Multiple Cause of Death Files). This value was calculated as the average of national influenza-related mortality per 100,000 for years 2013-2017.

[44] Numbers of infants or people estimated as the percent change in the outcome due to vaccination multiplied by the number of singleton infants with nine-month gestation or less, or native-born people aged 25 to 58 in the labor force or with a disability in 2016-17 (calculated as the percent of infants with low birth weight or people in the labor force or with a disability in 2016-17 multiplied by the average number of corresponding infants or people in 2016 and 2017, obtained using United States Department of Health and Human Services CDC Wonder Natality data and IPUMS ACS data).

percent increase in labor force participation (nearly 113,000 more workers in the labor force) and a 0.55 percent decrease in any disability (over 71,000 more adults without any disability).

This exercise suggests that historical increases in influenza vaccination made a meaningful improvement to life course outcomes. Likewise, policies that expand vaccinations demonstrate the potential to generate economically meaningful impacts on future outcomes. These benefits are in addition to the contemporaneous gains from increases in vaccination, including decreases in productivity loss, health care expenditures, and deaths. Cost-benefit analyses of vaccination interventions should include the economic benefits to children born to mothers at risk for influenza infection.

7. Conclusion

In this study, I evaluate the effects of prenatal exposure to the seasonal flu on life course outcomes in the United States. I confirm and expand on the results in the literature by showing that exposure late in pregnancy decreases birth weight and exposure early in pregnancy increases the risk of heart malformations. I also provide the first causal estimates of the long term economic and disability effects of prenatal exposure to seasonal flu in the U.S., including the first impacts on child or older adult outcomes in any nation. Prenatal exposure to the flu increases the probability of disability and decreases school attendance during childhood, high school completion, and labor force participation.

My results also highlight the role of vaccination policy to moderate adverse effects from an *in utero* exposure to influenza. Historical increases in vaccination levels account for economically important improvements in life course outcomes during the late 20th and early 21st centuries. Furthermore, reaching the Healthy People 2020 vaccination target and beyond may provide meaningful benefits for future Americans. Interventions that promote vaccination may improve long term outcomes in addition to the immediate gains from limiting infectious disease, and any cost-benefit analysis of vaccination policy should include these considerations.

Despite these advantages, estimates suggest that only 50 percent of pregnant women receive the recommended flu vaccination.[45] Reported barriers to flu vaccination during pregnancy

[45] Centers for Disease Control and Prevention (CDC), "Results of CDC's 2016-2017 Internet panel survey of pregnant women," Available: https://www.cdc.gov/flu/pdf/partners/flu-pregnancy-infographic-updated.pdf; CDC,

include incomplete or incorrect information, safety fears, vaccine unavailability, and lack of physician counseling (Fabry et al, 2011; Schindler et al., 2012; Meharry et al., 2013). Providing additional information to pregnant women and physicians on the life time risks of prenatal flu exposure and the protection offered by vaccination may help increase vaccine uptake. For example, my results imply that maternal flu infection late in pregnancy during a severe season impacts birth weight as much as smoking during pregnancy, and that the long term consequences are economically sizeable. Increasing vaccination rates may provide substantial returns over the next century.

This analysis is subject to several limitations that point to areas of future study. First, I am unable to identify whether the impacts from prenatal flu exposure derive from the disease itself or factors correlated with the disease, such as the use of antipyretics. In addition, I am unable to elucidate the precise mechanisms linking a negative *in utero* shock, health at birth, and long term outcomes. Suggestive evidence indicates that multiple pathways are at work, and that they likely differ by period of exposure. Future research could clarify these channels. A greater understanding of how to improve health and human capital in its earliest stages may translate into improved outcomes over the life course.

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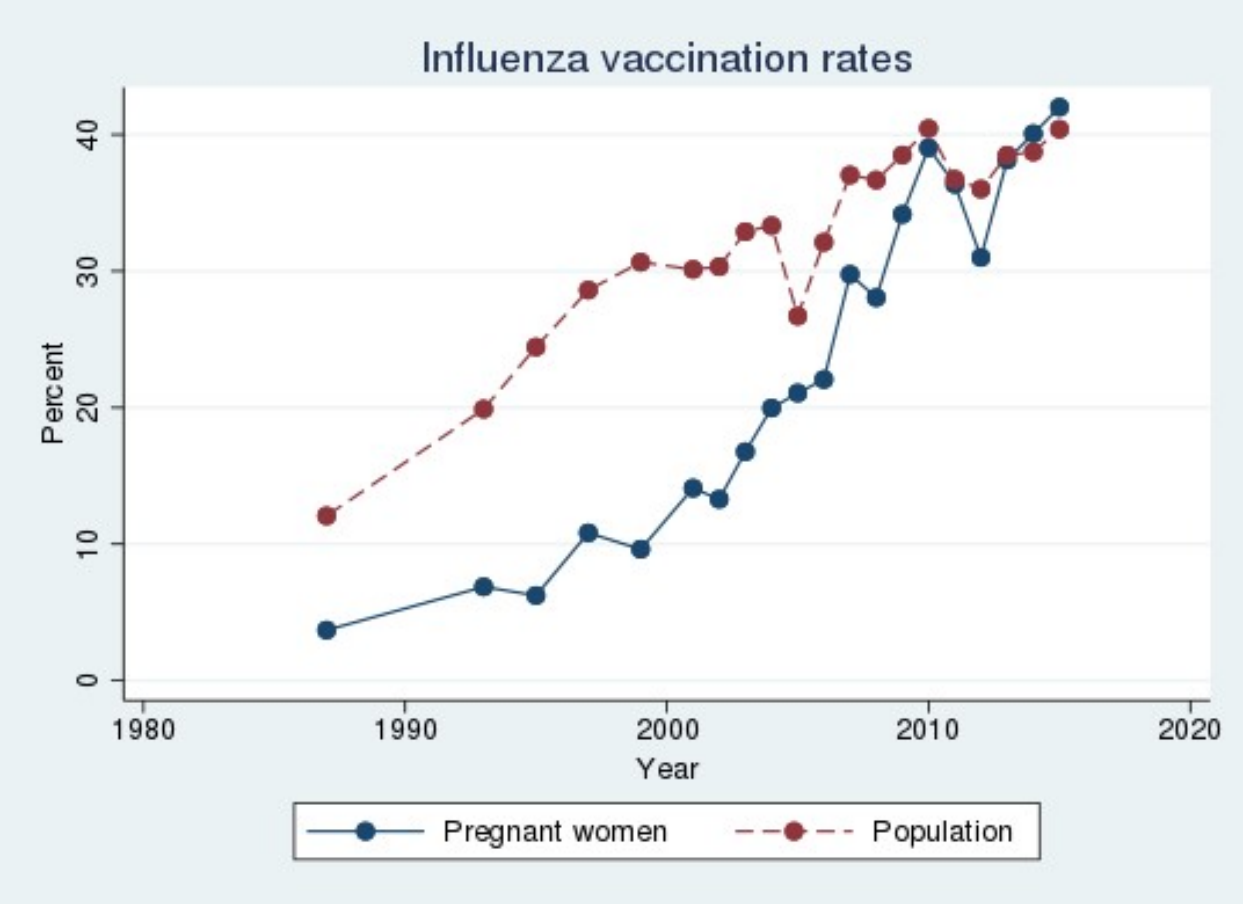
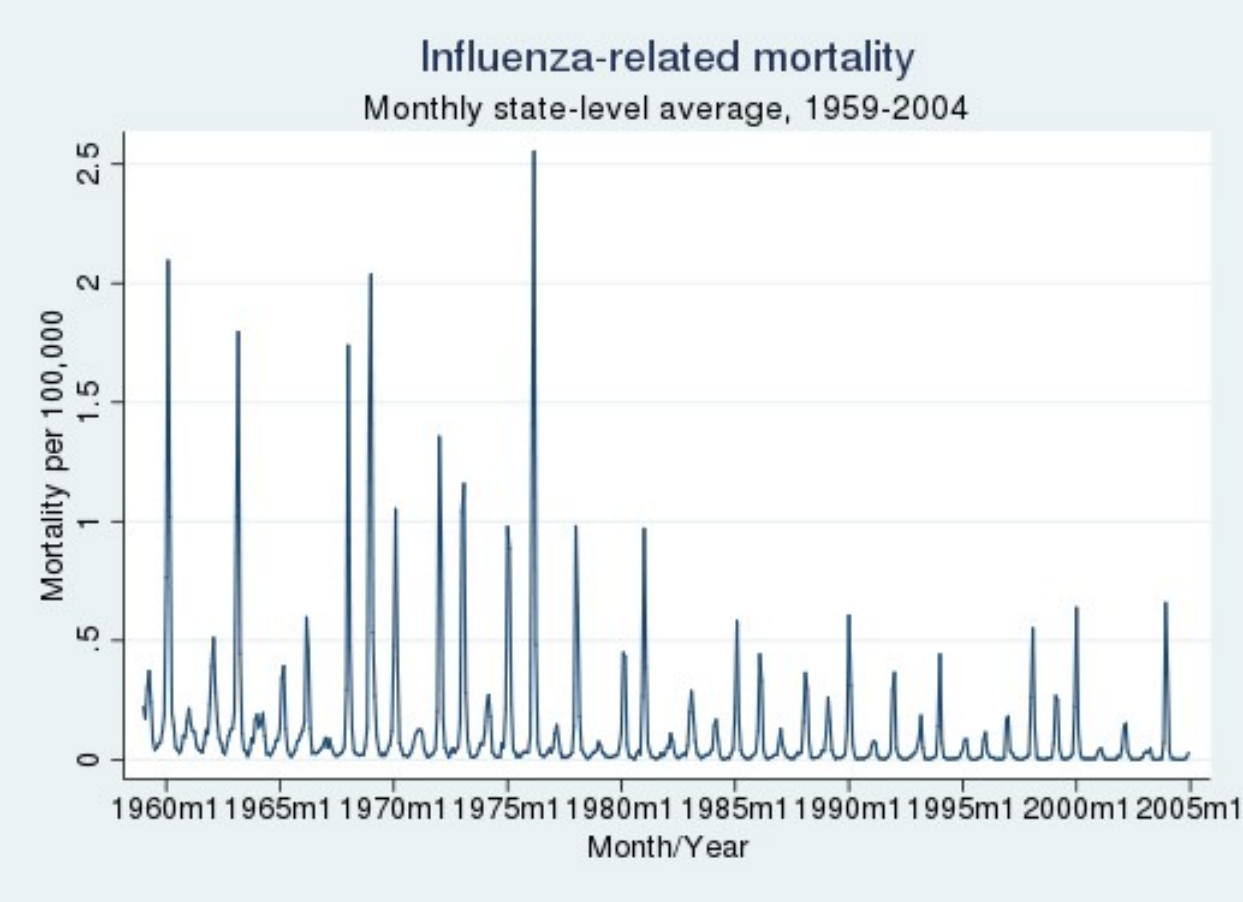
Figure 1: Percent with Influenza Vaccinations in the Previous 12 Months



Notes: Figure shows percent of the population aged 18+ and pregnant women aged 18 to 44 that reported receiving an influenza vaccine or nasal spray in the previous 12 months in the United States, 1987 to 2015. Data is from the Behavioral Risk Factor Surveillance System Annual Survey data and is weighted to adjust for sampling design (CDC BRFSS). Data is limited to core question years (1987, 1993, 1995, 1997, 1999, 2001-2015). Not all states are represented in earlier years: 32 states and the District of Columbia participated in 1987, Rhode Island did not participate in 1993, the District of Columbia did not participate in 1995, and Hawaii did not participate in 2004. Methodological updates occurred in 2011 and question wording may differ across some years.

Figure 2: Influenza-Related Mortality over Time



Source: National Center for Health Statistics (1959-2004)

Table 1: Summary Statistics of Monthly State Influenza-Related Mortality per 100,000, 1959-2004	
Mean:	0.12
Std. Dev:	0.37
Min:	0.00
Max:	8.93
Observations:	28,152

Source: National Center for Health Statistics (1959-2004)

Table 2A: Summary Statistics of U.S. Births - Outcomes

Birth weight and gestation sample		*Congenital anomaly sample*	
Birth weight (grams)	3332.2	Percent with any congenital anomaly	0.24
Percent with low birth weight (<2500g)	6.4	Percent with heart malformations	0.12
Gestation (weeks)	38.7	Percent with any neural tube defect	0.04
Percent with preterm birth (<37 weeks)	10.7	Percent with cleft lip/palate	0.08
Percent with five minute APGAR low (<7)	1.5		
Percent male	51.4		
Conception month influenza-related mortality per 100,000	0.059	*Conception month influenza-related mortality per 100,000*	0.038
Observations	92,283,912	Observations	55,051,399
Weighted Observations	97,291,162	Weighted Observations	55,051,399
Birth Year	1971-2004	Birth Year	1989-2004

Notes: Sample includes infants born as singleton births with available gestation information and nine months of gestation or less. Birth weight and gestation sample conceived between Sept. 1970 and Mar. 2004 and congenital anomaly sample conceived between Sept. 1988 and Mar. 2004. Five-minute APGAR score available beginning in 1978 (observations = 66,866,334). Source: National Center for Health Statistics (1971-2004)

Table 2B: Summary Statistics of U.S. Births - Demographic Characteristics

	Birth weight and gestation sample	*Congenital anomaly sample*
Infant Characteristics		
Percent female	48.6	48.6
Child live birth order, top coded 15	2.0	2.0
Percent unknown child live birth order	0.5	0.4
Parent Characteristics		
Mother's age, <14=14 50+=50	26.3	27.0
Percent unknown mother's age	0.0	0.0
Father's age, <14=14 65+=65	29.5	30.1
Percent unknown father's age	13.4	14.7
Percent white mother	79.0	77.6
Percent black mother	15.6	15.4
Percent Native American mother	0.9	1.0
Percent Asian mother	3.5	4.4
Percent other race mother	0.1	0.0
Percent race unknown mother	1.0	1.6
Percent white father	72.0	69.1
Percent black father	10.6	10.4
Percent Native American father	0.6	0.7
Percent Asian father	3.0	3.7
Percent other race father	0.1	0.0
Percent race unknown father	13.7	16.1
Percent mother less than high school education	19.9	21.4
Percent mother high school education	33.4	32.4
Percent mother some college education	18.2	20.8
Percent mother four-year college education	11.5	13.8
Percent mother post-four year college education	6.2	8.0
Percent mother unknown education	10.8	3.6
Percent mother married	69.2	68.2
Percent mother unmarried	25.3	31.8
Percent mother marital status unknown	5.5	0.0
Percent mother used tobacco during pregnancy		10.8
Percent mother did not use tobacco during pregnancy		68.4
Percent mother tobacco use status unknown		20.9
Percent mother used alcohol during pregnancy		1.3
Percent mother did not use alcohol during pregnancy		80.2
Percent mother alcohol use status unknown		18.5
Observations	92,283,912	55,051,399
Weighted Observations	97,291,162	55,051,399
Birth Year	1971-2004	1989-2004

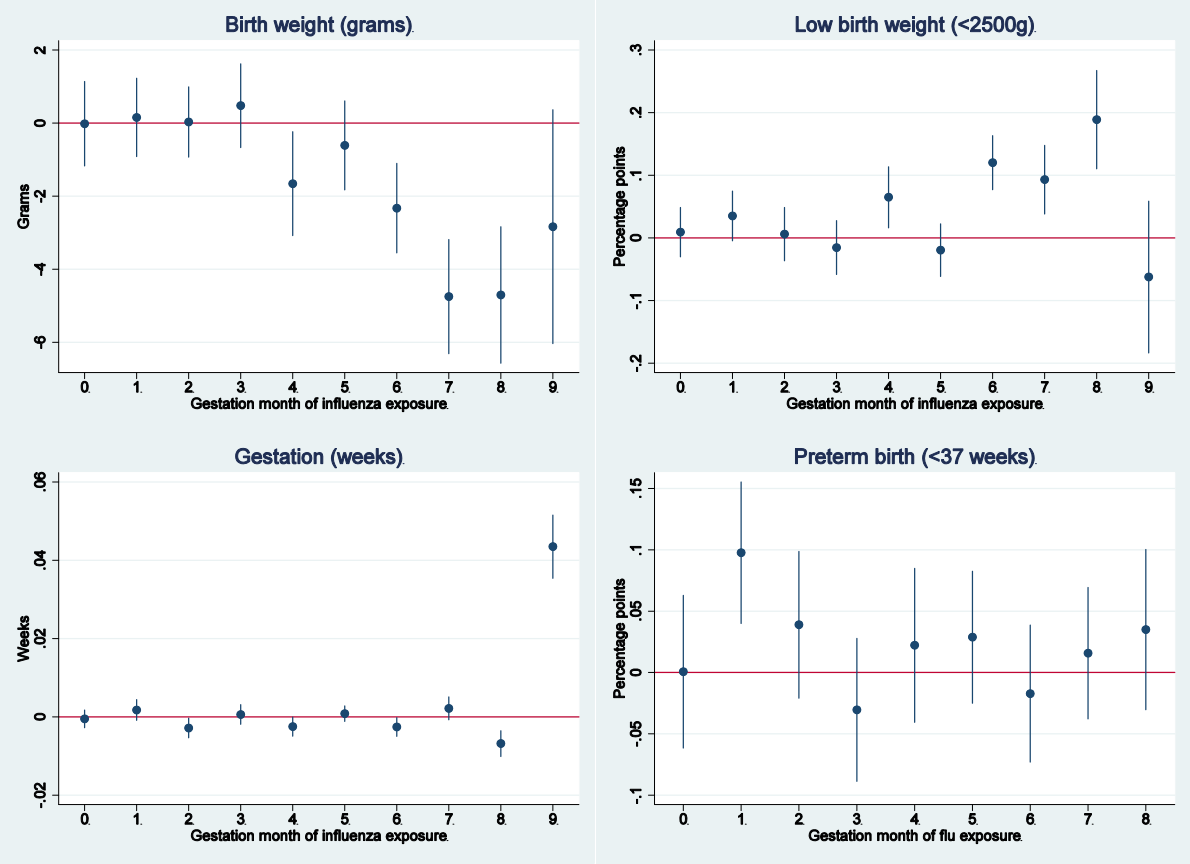
Notes: Sample includes infants born as singleton births with available gestation information and nine months of gestation or less. Birth weight and gestation sample conceived between Sept. 1970 and Mar. 2004 and congenital anomaly sample conceived between Sept. 1988 and Mar. 2004. Source: National Center for Health Statistics (1971-2004)

Table 3: Summary Statistics of Later Life Outcomes

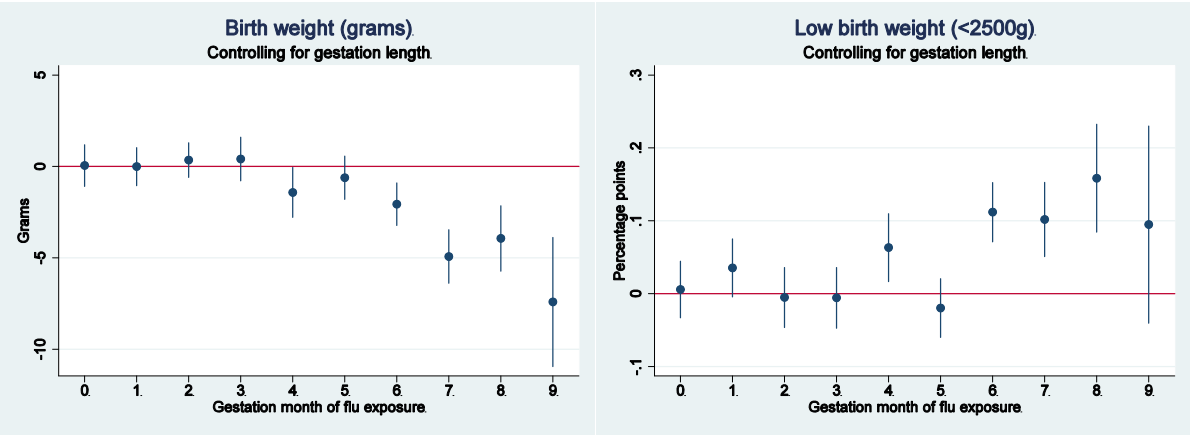
	Children	*Working-age adults*
Economic Outcomes		
Percent Attended School During Past 3 Months	97.6	
Percent with High School Completion		93.3
Educational Attainment (Years)		13.6
Percent in the Labor Force		82.2
Percent Below 150% of Poverty Threshold		18.7
Duncan Socioeconomic Index		46.1
Wage and Salary Income ($1999)		27849.0
Welfare, Social Security, and SSI ($1999)		429.8
Disability		
Percent with Any Disability Type		10.0
Percent with Cognitive Difficulty		4.8
Percent with Ambulatory Difficulty		4.5
Percent with Independent Living Difficulty		3.7
Percent with Self-Care Difficulty		1.8
Percent with Vision Difficulty		1.8
Percent with Hearing Difficulty		1.8
Demographic Characteristics		
Percent female	48.7	50.2
Age (years)	12.4	39.1
Percent White	57.1	72.7
Percent Black	14.2	13.9
Percent Asian	3.4	1.4
Percent Hispanic	20.6	9.3
Percent Other	4.8	2.6
Influenza-related mortality per 100,000	0.4	1.5
Observations	3,491,429	9,188,753
Birth Year	1991-2004	1959-1992

Notes: Analytic samples obtained from the pooled IPUMS ACS 2008-2017. Child sample includes aged five to 17 and working-age adults sample includes aged 25 to 58. Sample means weighted using the person weight. Income measures are in real $1999 dollars. Any disability type includes the subsequent six categories of disability.

Figure 3: Effects on Birth Weight and Gestation Length

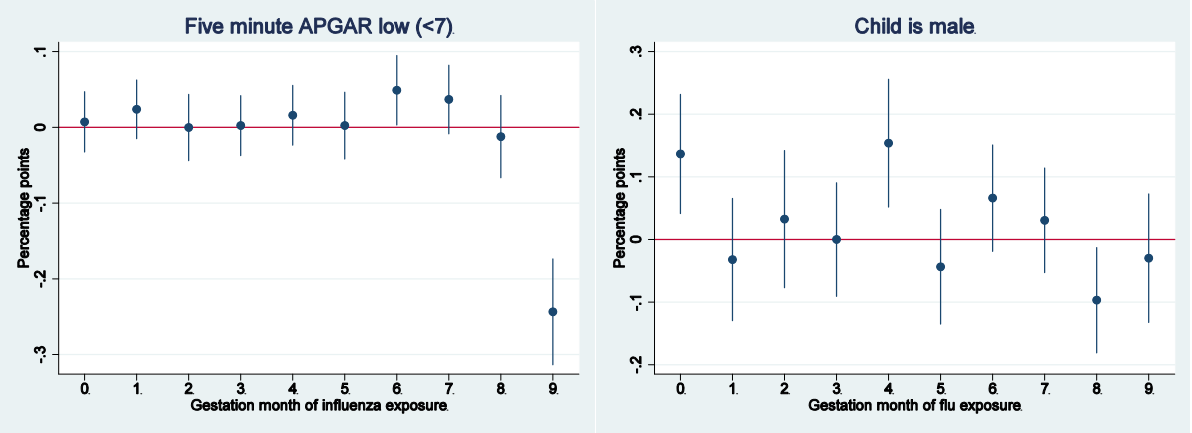


Effects on Birth Weight Controlling for Gestation Length



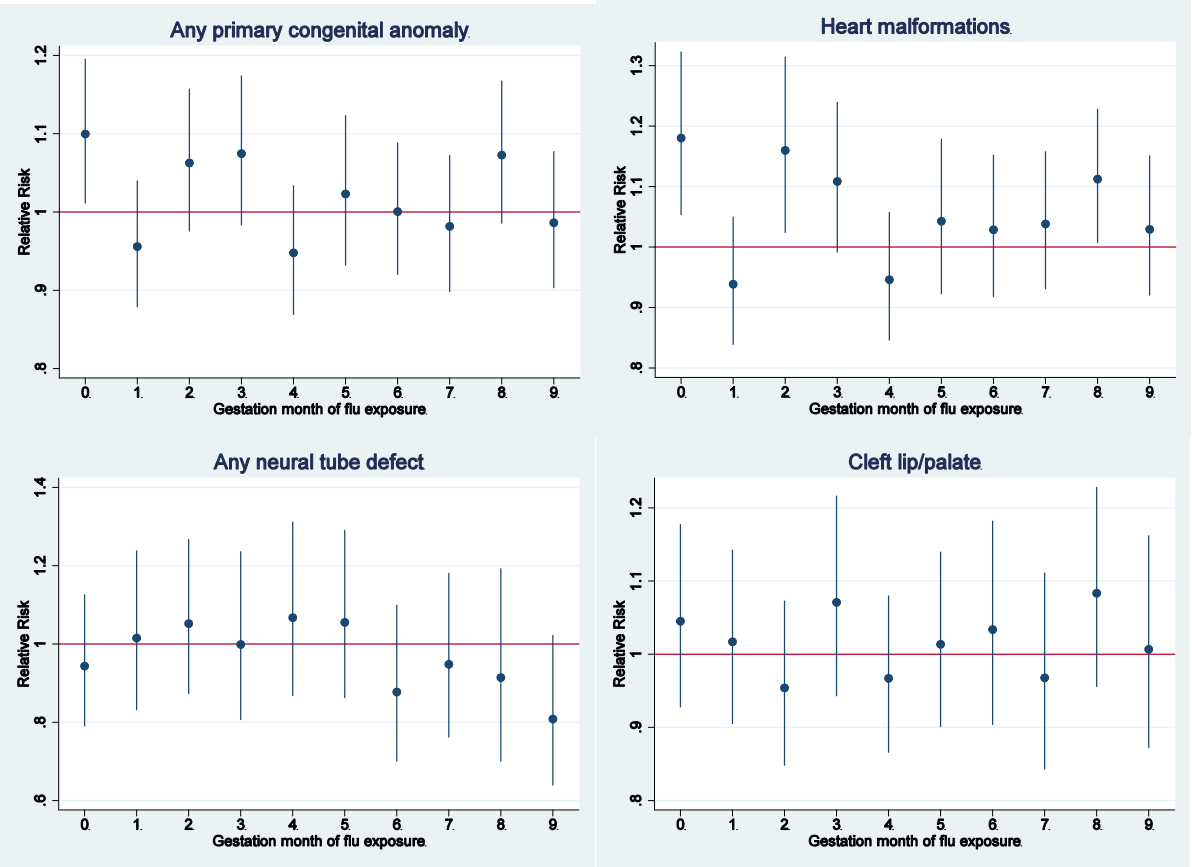
Notes: Figures display the effect of one additional influenza-related death per 100,000 on outcomes, with 95 percent confidence intervals around the estimate. All indicator outcomes are scaled from 0 to 100 for readability. For the preterm birth outcome, month nine gestation is omitted since all month nine births are considered full-term. In the bottom two figures, regressions include dummies for single weeks of gestation.

Figure 4: Effects on Probability of low APGAR and Male Infant



Notes: Figures display the effect of one additional influenza-related death per 100,000 on outcomes, with 95 percent confidence intervals around the estimate. All indicator outcomes are scaled from 0 to 100 for readability. Five-minute APGAR is only available beginning in 1978.

Figure 5: Effects on Relative Risk of Congenital Anomalies



Notes: Figures display the relative risk of one additional influenza-related death per 100,000 on outcomes, with 95 percent confidence intervals around the estimate. Congenital anomalies outcomes are only available beginning in 1989. In additional to the full set of covariates, regressions also include dummies for maternal use of tobacco and alcohol during pregnancy.

Table 4: Comparison of Effects of Prenatal Influenza Exposure with Birth Estimates in the Literature

	Primary results (effect of one-influenza related death per 100,000 in month eight)	Primary results (effect of an intense flu late in pregnancy)	Currie and Schwandt (2013) (effect of a May conception)	Dorélien (2019) (effect of a "moderate" to "extreme" exposure in January)	Schwandt (2018) (effect of a maternal influenza infection)
Birth weight (grams)					
Population exposure:	-4.7	-20.3	-3.1†	-1.4 to -6.8	
Exposure to maternal infection:	-43 to -157	-185 to -677			-113
Low birth weight (<2500g) (percentage points)					
Population exposure:	0.2	0.6		0.01 to 0.02	
Exposure to maternal infection:	1.8 to 6.7	5.5 to 20			3.8
Setting:	*All U.S. states in birth years 1971-2004 (birth outcomes) and 1959-1992 (long term outcomes)*		*New Jersey (birth years 1997-2006), Pennsylvania (2004-2010) New York City (1994-2004)*	*Large U.S. counties in birth years 1989-1991 and 1995-2004*	*Denmark in birth years 1980-1993*

Notes: Estimates across studies represent differences in empirical strategies and settings. Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976), equal to approximately 4.55 deaths per 100,000. † indicates effect was not statistically significant. Population exposure effects sizes translated to effects from exposure to a maternal infection by dividing by three to 11 percent population infection rate in Tokars, Olsen, and Reed (2018).

Table 5: Economic Outcomes

	Child Attended School Past 3 Months	High School Completion	Educational Attainment (years)	In the Labor Force
Influenza-related mortality per 100,000	-0.101**	-0.0280**	0.000836	-0.0703***
	(0.0453)	(0.0136)	(0.00128)	(0.0214)
Observations	3,491,429	9,188,753	9,188,753	9,188,753
Effect of an intense flu:	**-0.46**	**-0.13**	0.00	**-0.32**
Sample mean of dependent variable:	97.6	93.3	13.6	82.2

Notes: This table presents linear regression estimates of the long term effects of prenatal exposure to influenza. Standard errors in parentheses. * p<0.10, ** p<0.05, *** p<0.01. All indicator outcomes are scaled from 0 to 100 for readability. Analytic sample includes aged 25 to 58 (except child school attendance, which includes aged five to 17). Influenza-related mortality represents the sum of mortality per 100,000 during the course of a hypothetical pregnancy (current and previous three quarters). Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976), equal to approximately 4.55 deaths per 100,000. All regressions include dummies for sex, age, and race, as well as state of birth-quarter of birth fixed effects, birth year-quarter fixed effects, current year fixed effects, and state-specific linear time trends. Standard errors clustered by state of birth-quarter of birth. All regressions weighted using the person survey weight.

Table 6: Disability

	Any Disability Type	Cognitive Difficulty	Ambulatory Difficulty	Independent Living Difficulty	Self-Care Difficulty	Vision Difficulty	Hearing Difficulty
Influenza-related mortality per 100,000	0.0444***	0.0168	0.0269**	0.00797	0.00932	0.0191***	0.00566
	(0.0144)	(0.0114)	(0.0107)	(0.0104)	(0.00650)	(0.00638)	(0.00658)
Observations	9,188,753	9,188,753	9,188,753	9,188,753	9,188,753	9,188,753	9,188,753
Effect of an intense flu:	**0.20**	0.08	**0.12**	0.04	0.04	**0.09**	0.03
Sample mean of dependent variable:	9.95	4.81	4.55	3.67	1.76	1.77	1.78

Notes: This table presents linear regression estimates of the long term effects of prenatal exposure to influenza. Standard errors in parentheses. * p<0.10, ** p<0.05, *** p<0.01. All indicator outcomes are scaled from 0 to 100 for readability. Analytic sample includes aged 25 to 58. Influenza-related mortality represents the sum of mortality per 100,000 during the course of a hypothetical pregnancy (current and previous three quarters). Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976), equal to approximately 4.55 deaths per 100,000. All regressions include dummies for sex, age, and race, as well as state of birth-quarter of birth fixed effects, birth year-quarter fixed effects, current year fixed effects, and state-specific linear time trends. Standard errors clustered by state of birth-quarter of birth. All regressions weighted using the person survey weight.

Table 7: Select Outcomes by Stage of Pregnancy Exposure

	Child Attended School During Past 3 Months	High School Completion	In the Labor Force	Any Disability Type	Ambulatory Difficulty	Vision Difficulty
Influenza-related mortality per 100,000 during the:						
Birth quarter	-0.0830	-0.0580*	-0.117***	0.0763***	0.0645***	0.0250*
	(0.0873)	(0.0302)	(0.0381)	(0.0273)	(0.0246)	(0.0141)
Birth quarter-1	-0.0934	-0.0277	-0.0464	0.0415	0.0283	0.00540
	(0.101)	(0.0228)	(0.0414)	(0.0269)	(0.0244)	(0.0109)
Birth quarter-2	-0.127	-0.0265	-0.0603	0.0393	0.0134	0.0148
	(0.0784)	(0.0239)	(0.0403)	(0.0299)	(0.0183)	(0.0143)
Birth quarter-3	-0.0983	-0.000718	-0.0599	0.0220	0.00400	0.0319***
	(0.0808)	(0.0214)	(0.0435)	(0.0251)	(0.0196)	(0.0119)
Observations	3,491,429	9,188,753	9,188,753	9,188,753	9,188,753	9,188,753

Notes: This table presents linear regression estimates of the long term effects of prenatal exposure to influenza by different stage of pregnancy. Standard errors in parentheses. * p<0.10, ** p<0.05, *** p<0.01. All indicator outcomes are scaled from 0 to 100 for readability. Analytic sample includes aged 25 to 58 (except child school attendance, which includes aged five to 17). Influenza-related mortality represents deaths per 100,000 during the course of a hypothetical pregnancy separately by stage of pregnancy (birth quarter, quarter prior to birth, etc.). All regressions include dummies for sex, age, and race, as well as state of birth-quarter of birth fixed effects, birth year-quarter fixed effects, current year fixed effects, and state-specific linear time trends. Standard errors clustered by state of birth-quarter of birth. All regressions weighted using the person survey weight.

Table 8: Selected Associations Between Disability and Limitations

	Ambulatory Disability	Vision Disability		Ambulatory Disability	Vision Disability
Indicators for activity limitation from:			*Indicators for functional limitation from:*		
Missing limb/finger	21.17***		Other developmental problem	43.04***	
	(4.459)			(6.488)	
Arthritis/rheumatism	16.46***		Stroke	27.38***	
	(1.437)			(3.844)	
Other developmental problem	16.23***		Missing limb/finger	26.48***	
	(3.220)			(6.593)	
Musculoskeletal problem	15.74***		Diabetes	18.24***	
	(1.375)			(2.177)	
Stroke	15.73***		Nervous system problem	18.10***	
	(2.447)			(1.696)	
Vision problem		53.15***	Heart problem	17.02***	
		(1.926)		(2.607)	
			Lung/breathing problem	15.01***	
				(1.926)	
			Vision problem		47.63***
					(2.776)
Observations	14,181	14,176	Observations	16,236	16,237

Notes: This table presents linear regression estimates of the association between specific causes of limitations and disability. Standard errors in parentheses. All indicator outcomes are scaled from 0 to 100 for readability. Analytic samples obtained from the pooled IPUMS NHIS 2011-2017 and represent individuals aged 25 to 58 with an activity or functional limitation. Selected estimates represent coefficients with *** $p<0.01$ and a magnitude of a positive effect of at least 15 percentage points. All regressions include dummies for sex, age, and race and are corrected for variance estimation. Sample means weighted using the weight associated with disability adjusted for years of pooled data.

Table 9: Comparison of Effects of Prenatal Influenza Exposure with Long Term Estimates in the Literature

	Primary results (effect of one-influenza related death per 100,000 during pregnancy)	Primary results (effect of an intense flu)	Schwandt (2018) (effect of a maternal influenza infection)	Almond (2006) (effect of exposure relative to cohort trend line)
Labor force participation (percentage points)				
Population exposure:	-0.07	-0.32		
Exposure to maternal infection:	-0.6 to -2.3	-2.9 to -10.7	-2.8	
High School Educational Attainment (percentage points)				
Population exposure:	-0.03	-0.13		-0.2
Exposure to maternal infection:	-0.3 to -0.9	-1.2 to -4.3		
Ambulatory difficulty^ (percentage points)				
Population exposure:	0.0269	0.12		0.5
Exposure to maternal infection:	0.2 to 0.9	1.1 to 4.0		
Setting:	*All U.S. states in birth years 1971-2004 (birth outcomes) and 1959-1992 (long term outcomes)*		*Denmark in birth years 1980-1993*	*U.S. 1918 Influenza Pandemic*

Notes: Estimates across studies represent differences in empirical strategies and settings. Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976), equal to approximately 4.55 deaths per 100,000. ^Ambulatory difficulty is compared to approximate separate effects sizes for physical disability "limits work" and "prevents work" in Almond (2006). Population exposure effects sizes translated to effects from exposure to a maternal infection by dividing by three to 11 percent population infection rate in Tokars, Olsen, and Reed (2018).

Table 10: Estimated Effects of Population Vaccination on Outcomes

	Birth Weight (grams)	Low Birth Weight (<2500g) (percent)	Child Attended School Past 3 Months (percent)	High School Completion (percent)	In the Labor Force (percent)	Any Disability Type (percent)
Historical changes across birth years	*1971 to 2004*		*1991 to 2004*		*1959 to 1992*	
Share of change due to historical vaccination (percent)	19.23	15.95	1.41	0.64	0.54	0.23
Future interventions			*Baseline: 2016-2017*			
Percent change due to 70 percent vaccination	0.33	-4.13	0.07	0.02	0.06	-0.26
Percent change due to eliminating flu mortality	0.69	-8.73	0.15	0.04	0.12	-0.55

Notes: See ***Appendix Tables A13 and A14*** for all calculations and sources. Child school attendance represents children aged five to 17 and other later life outcomes represents adults aged 25 to 58.

Appendix

A1: Additional Background on the Epidemiology of Influenza

Mutations in the flu virus can result in new strains of the disease. Specifically, random genetic changes alter two surface proteins, hemagglutinin and neuraminidase, through a process called *antigenic drift*. As a result, the immune system of a previously infected or vaccinated person does not recognize the new variant of the virus, which potentially subjects the person to reinfection. This process is referred to as antigenic variation (Cox and Subbarao, 2000; Rasmussen, Jamieson, and Bresee, 2012).

Pandemic flu occurs when a novel influenza A virus infects human populations. A new influenza A virus surfaces through a process called *antigenic shift*, which involves the direct mutation of an animal virus, or an animal virus combining with a human virus (Cox and Subbarao, 2000; Rasmussen, Jamieson, and Bresee, 2012).[46] Four flu pandemics have occurred since 1900: the 1918 H1N1 "Spanish flu", the 1957-58 H2N2 "Asian flu", the 1968 H3N2 "Hong Kong flu", and the 2009 H1N1 "swine flu".[47] Deaths are not necessarily greater during pandemics compared to intense seasonal flu seasons, but are typically more harmful to younger ages (Cox and Subbarao, 2000). For instance, roughly half of all flu mortality occurred in individuals younger than age 65 during the 1968 H3N2 pandemic (Cox and Subbarao, 2000). This phenomenon may result from older age groups deriving immune protection from prior contact with a past version of the virus; while younger age groups demonstrated a limited antibody response to the 2009 H1N1 pandemic virus, almost one-third of individuals aged over 60 years possessed immunity.[48]

A2: The History of Influenza Vaccination for Pregnant Women

General vaccination to protect against the flu began in the 1940s (CDC, 2015). In 1960, the Surgeon General indicated that pregnant women should receive the flu vaccine due to the high death rate of this group during the 1957-58 H2N2 pandemic (Burney, 1960a; Omer et al., 2012). However, the Advisory Committee on Immunization Practices (ACIP) decided against flu

[46] CDC, "Pandemic Basics," Available: https://www.cdc.gov/flu/pandemic-resources/basics/index.html
[47] Ibid. "Past Pandemics."
[48] Ibid. "Past Pandemics: 2009 H1N1 Pandemic."

vaccination for pregnant women in 1966. The ACIP cited a lack of evidence of influenza-related mortality in pregnant women after the pandemic, and suggested that only pregnant women with specific chronic conditions receive vaccinations (CDC, 1966; Omer et al., 2012). In 1995, the ACIP indicated that pregnant women may face severe influenza complications in their third trimester and recommended that this group receive the vaccine (CDC, 1995; Rasmussen et al., 2014). This recommendation was updated to include women in the second and third trimester in 1997 (CDC, 1997; Rasmussen et al., 2014), and later all pregnant women in 2004 (CDC, 2004; Rasmussen et al., 2014).

A3: Conceptual Framework for Prenatal Exposures

Exposure to influenza while *in utero* may interfere with fetal development, affecting health and human capital accumulation over the life course. Based on evidence that early life exposures affect the trajectory of cognitive and non-cognitive development, Heckman (2007) describes a capability formation model across multiple stages of the life cycle. In this framework, individuals in each period possess a vector of cognitive, non-cognitive, and health capabilities, and an investment during a given stage improves capabilities in a subsequent time period. This model allows early life events to shape later outcomes, providing an advantageous theoretical framework to evaluate prenatal shocks over the life course (Almond and Currie, 2011a; Almond and Currie, 2011b). Applying this framework, a negative shock from the flu while *in utero* can theoretically impact multiple elements in the capability vector. These initial impacts may undermine cumulative development and harm long term health and human capital.

Economists traditionally use the classic Grossman (1972) model to examine health capital. In this framework, the initial endowment of health depreciates over each period of the life cycle, but agents can also invest in in health resources to increase health capital in accordance with their preferences. Almond and Currie (2011b) indicate that, in this setting, the impacts of a shock to early health capital would similarly depreciate with the stock of health, making the effects of prenatal exposures inconsequential relative to later actions that influence health.

A4: Prenatal Influenza Exposure and the Timing of Fetal Development

Insight into the mechanisms linking maternal influenza infection and fetal development is limited, but the virus is unlikely to pass through the placental barrier (Rasmussen, Jamieson, and

Bresee, 2012). Instead, adverse effects are potentially due to influenza symptoms in the mother, including fever or hyperthermia, inflammation, or reduced nutritional uptake (Kelly, 2011; Rasmussen, Jamieson, and Bresee, 2012; Kourtis, Read, and Jamieson, 2014). Suggestive evidence indicates that prenatal seasonal flu exposure may increase the possibility of miscarriage (Schwandt, 2018).

Adverse exposures that occur at different points during gestation may differentially affect outcomes due to the timing of fetal development (summarized in ***Appendix Figure A1***). The fetal structure forms early in pregnancy and during the first trimester (approximately week one to week 12). The manifestation of physical defects in the central nervous system, heart, palate, eyes, and ears are concentrated in this timeframe.[49] Studies find a link between maternal flu infection or fever in this period and congenital anomalies (Dreier, Andersen, and Berg-Beckhoff, 2014; Botto et al., 2014; Kerr et al., 2017; Waller et al, 2018; Dorélien, 2019). Prenatal exposure earlier in pregnancy may also increase the risk of developing schizophrenia (Khandaker, Dibben, and Jones, 2012).

Central nervous system development continues through the second trimester (approximately weeks 13 to 28), when both structural and functional defects are possible.[50] Brain development may be particularly vulnerable to adverse shocks, especially during weeks eight to 25 (Kelly, 2011). Evidence indicates that second trimester flu exposure may adversely affect cognition (Kelly, 2011), childhood behavioral outcomes (Dombrowski, Martin, and Huttunen, 2003), autism spectrum disorders (Hornig et al., 2018), and later life education and labor market outcomes (Schwandt, 2018). Functional ear and eye development also continues through the second trimester.[51]

Finally, negative shocks during the third trimester (weeks 29 to 40), when the fetus gains the majority of its weight, may negatively affect birth weight and gestation outcomes (Currie and Schwandt, 2013; Schwandt, 2018; Dorélien, 2019) and increase mortality by age 18 (Schwandt,

[49] CDC, "Fetal Development Chart" in "An Alcohol-Free Pregnancy is the Best Choice for Your Baby" Brochure, Available:
https://www.cdc.gov/ncbddd/fasd/documents/FASDBrochure_final-508.pdf
[50] Ibid.
[51] Ibid. Shocks in the second trimester may also adversely impact birth weight (Kelly, 2011; Dorélien, 2019) and childhood height (Kelly, 2011), in particular for certain mothers that face nutritional deficits, such as smokers (Kelly, 2011).

2018). Functional central nervous system and eye development also continues through the third trimester.[52]

A5: Constructing Influenza-Related Mortality per 100,000

I use data from the NCHS Vital Statistics multiple cause of death data, which is based on death certificates, to represent the severity of influenza in the environment (NCHS *Multiple Cause-of-Death*).[53] I generate monthly and quarterly state-level influenza-related mortality rates per 100,000 for the years 1959 to 2004. An influenza-related death is defined as a death with an underlying cause of influenza, identified using ICD-7, ICD-8, ICD-9, and ICD-10 codes. Specifically, influenza-related mortality is defined as deaths with an underlying cause of death of ICD-7 code (1959-1967): 480-483; ICD-8 code (1968-1978): 470-474; ICD-9 code (1979-1998): 487; ICD-10 code (1999-2004): J10-J11. I apply comparability ratios to maintain a consistent series over time.[54] Monthly mortality rates per 100,000 are obtained by dividing monthly death counts by annual estimates of the state population from the U.S. Census Bureau (U.S. Census Bureau).[55] Quarterly mortality rates per 100,000 are similarly obtained by summing monthly influenza deaths into quarters and dividing by annual estimates of the state population.

I explore this variable further by comparing it to other CDC measures of flu activity only available for recent years. In particular, the CDC provides data on the geographic spread of influenza beginning with the 2003-04 flu season.[56] I examine the correlation between my measure of state-level influenza-related mortality and CDC state geographic spread of the flu for the 16 month period of data overlap between October, 2003 and December, 2004. Influenza-related mortality rates are highly correlated with both the number of weeks of "regional or

[52] CDC, "Fetal Development Chart" in "An Alcohol-Free Pregnancy is the Best Choice for Your Baby" Brochure, Available:
https://www.cdc.gov/ncbddd/fasd/documents/FASDBrochure_final-508.pdf.
[53] This data was obtained from the NBER: https://www.nber.org/data/vital-statistics-mortality-data-multiple-cause-of-death.html. The final year that geographic identifiers are publically available is 2004. As noted, some of the 1959 to 1967 data was reconstructed and their accuracy cannot be verified.
[54] Comparability ratios are obtained from the CDC, "Comparability of Cause-of-death Between ICD Revisions," Available: https://www.cdc.gov/nchs/nvss/mortality/comparability_icd.htm
[55] Population data was obtained from the Federal Reserve Bank of St. Louis FRED Economic Data, "U.S. Census Bureau," "Annual Estimates of the Population for the U.S. States, and for Puerto Rico," "Resident Population by State, Annual".
[56] For geographic spread data, I convert weekly data to monthly data by summing weeks of influenza into months (with week assigned to month on the "week end" date). Geographic spread in New York City data is omitted. CDC, "FluView Interactive: Geographic Spread," Available:
https://www.cdc.gov/flu/weekly/fluviewinteractive.htm

widespread" flu activity in a month (correlation coefficient of 0.68) and weeks of only "widespread" flu activity in a month (correlation coefficients of 0.70) for 765 observations.[57]

A6: Constructing Alternative Mortality Rates

Multiple cause mortality: Multiple cause influenza- and pneumonia-related mortality per 100,000 (multiple cause mortality) includes deaths where influenza or pneumonia is reported as an underlying cause or contributing factor.[58] This compares to my primary independent variable, influenza-related mortality, which includes deaths with an underlying cause of influenza. I construct multiple cause mortality rates per 100,000 using NCHS Vital Statistics multiple cause of death data from 1968 to 2004 (years prior to 1968 do not provide multiple cause information) (NCHS *Multiple Cause-of-Death*). Influenza deaths are identified using the ICD codes outlined in *Appendix Section A5*. Pneumonia deaths are identified using ICD-7 code (1959-1967): 490-493; ICD-8 code (1968-1978): 480-486; ICD-9 code (1979-1998): 480-486; ICD-10 code (1999-2004): J12-J18.[59]

The CDC reports that influenza is underreported as a cause of death on death certificates. This is due to delayed tests or a failure to test, and some flu mortality corresponds to deaths from complications like pneumonia, especially in older populations.[60] As a result, the CDC uses influenza- and pneumonia-related mortality in their model of flu deaths and suggests that the use of only influenza would understate the extent of influenza.[61] Similarly, other studies use multiple cause mortality in their analyses (Dushoff, 2005; Dorélien, 2019; White, 2019).

[57] Regional influenza is defined as "[o]utbreaks of influenza or increases in ILI [influenza-like illness]and recent laboratory confirmed influenza in at least two but less than half the regions of the state with recent laboratory evidence of influenza in those regions." Widespread influenza is identically defined except that influenza occurs in "in at least half the regions of the state." CDC, "Overview of Influenza Surveillance in the United States," Available: https://www.cdc.gov/flu/weekly/overview.htm

[58] Specifically, influenza or pneumonia are listed as the underlying cause of death or a contributing cause in the record axis. The record axis includes up to 14 possible records between 1968-1978 and 20 possible records between 1979-2004.

[59] Comparability ratios are not applied due to the use of multiple causes of death.

[60] CDC. "How CDC Estimates the Burden of Seasonal Influenza in the U.S.," Available: https://www.cdc.gov/flu/about/burden/how-cdc-estimates.htm. Influenza may interact with multiple chronic conditions, resulting in death. As a result, influenza-related mortality may not only be captured by pneumonia- and influenza-related mortality, but also excess deaths due to all causes (Cox and Subbarao 2000).

[61] Ibid. The CDC also includes deaths from "other respiratory and circulatory causes" and "other non-respiratory, non-circulatory causes."

Influenza-related mortality and multiple cause mortality both exhibit a seasonal pattern and are correlated (correlation coefficient of 0.60). However, the use of influenza-related mortality in this analysis may provide empirical advantages compared to multiple cause mortality. First, influenza-related mortality appears to better represent variation in flu severity and the disease exposure facing pregnant women. While influenza-related mortality per 100,000 falls to zero outside of flu season as expected (***Figure 2***), multiple cause mortality remains elevated at around five deaths per 100,000 (***Appendix Figure A3***). Using only deaths where influenza is the underlying cause in an analyses that quantifies the number of influenza deaths may underestimate the true number; however, this study exploits variation in flu severity as opposed to calculating the mortality burden of the disease. Similarly, excluding pneumonia-related deaths may also avoid introducing noise that is unrelated to the flu; a study of individuals hospitalized for pneumonia identified a specific causal pathogen for fewer than 40 percent of cases, and influenza was identified in only six percent of cases (Jain et al., 2015).[62] Finally, influenza-related mortality is available over a longer time period beginning in 1959, whereas multiple cause records are not available until 1968.

Age-adjusted mortality: Age-adjusted influenza-related mortality per 100,000 (age-adjusted mortality) accounts for differences in the age distribution across states. This measure is based on NCHS Vital Statistics multiple cause of death data from 1959 to 2004 (NCHS *Multiple Cause-of-Death*). First, I obtain death counts by age groups: aged 0 to 14, aged 15 to 24, aged 25 to 34, aged 35 to 44, aged 45 to 54, aged 55 to 64, aged 65 to 74, aged 75 to 84, and aged 85 plus (unknown age is omitted from calculations). I obtain population counts for the same age groups by (1) calculating the age distribution for each state/year from the Survey of Epidemiology and End Results (SEER) beginning in 1969, (2) calculating the age distribution for 1959 to 1968 by projecting backwards via subtracting the average percentage point change in each age group between 1969-70 and 1970-71 for each prior year, and (3) applying these age distributions to U.S. Census Bureau population data to obtain the population counts for each age group, state,

[62] Rhinovirus was the leading pathogen detected at nine percent, followed by influenza at six percent and *Streptococcus pneumoniae* at five percent.

and year (SEER; U.S. Census Bureau).[63] Age-adjustment proceeds using direct standardization.[64]

Age-adjusted mortality is used as the exposure variable in a robustness test and not in the primary empirical strategy. The immune systems of older individuals do not respond to antigens as effectively as the immune systems of younger individuals due to age-related changes (Montecino-Rodriguez, Berent-Maoz, and Dorshkind, 2013). As a result, older individuals may be more susceptible to catching and spreading influenza. My primary independent variable, influenza-related mortality, reflects that a state with a greater percentage of older people represents a more dangerous disease environment than states with a lower percentage of older people. Age-adjusted mortality is highly correlated with influenza-related mortality (correlation coefficient of 0.95).

[63] All SEER data is available from the NBER: http://www.nber.org/data/seer_u.s._county_population_data.html (I use "all states combined", "county", "19 age groups", "1969-", "White, Black, Other"). U.S. Census Bureau data is described in Appendix Section A5.

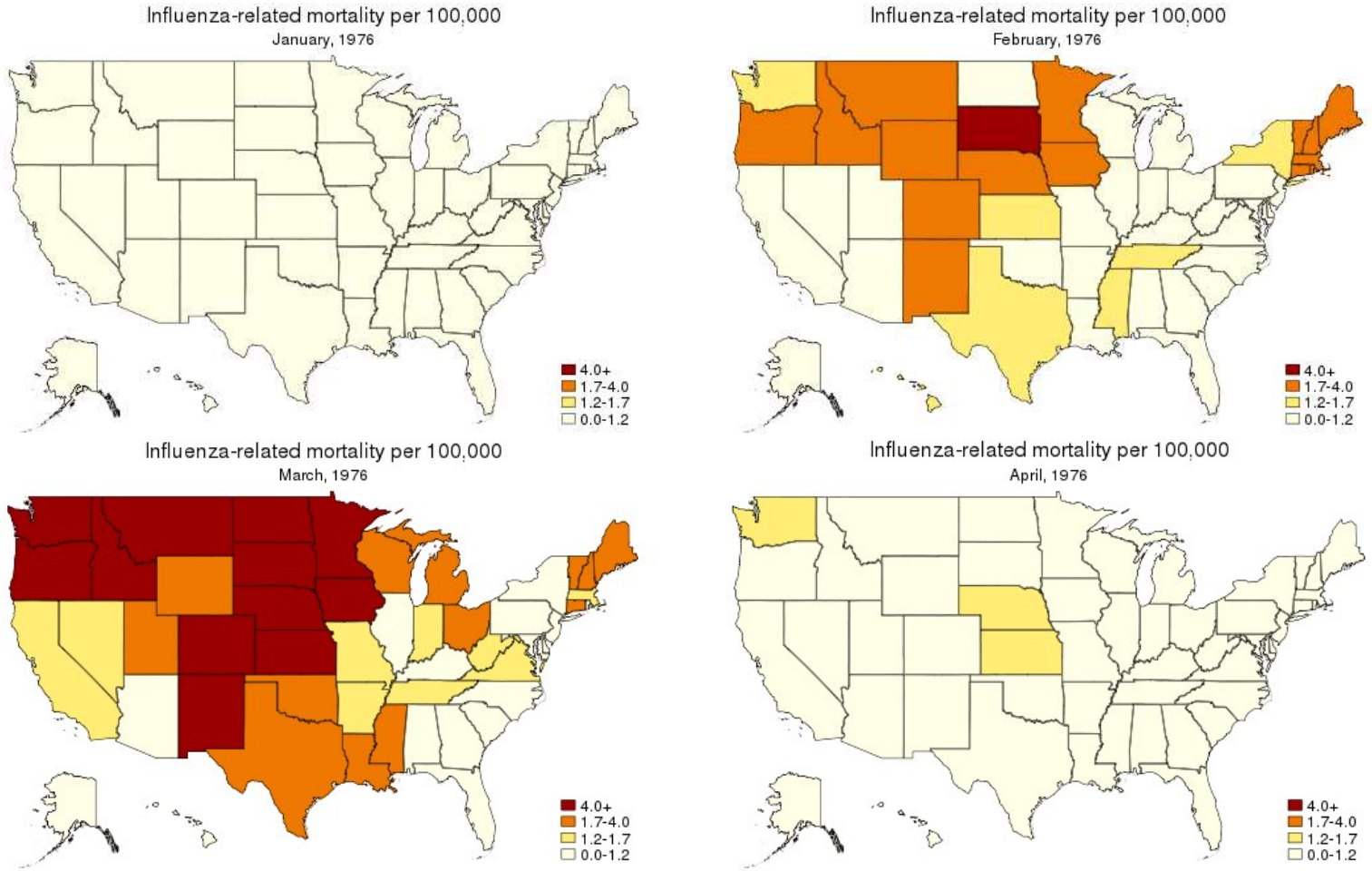
[64] Death counts are divided by population for each age group to obtain the crude rate per 100,000 for each age group, and the crude rate for each age group is multiplied by a weight for each age group equivalent to the age group share of the population from 2000 SEER data. These weighted values are then summed to obtain the age-adjusted influenza-related mortality rate per 100,000.

Appendix Figure A1: Empirical Evidence on Some Life Course Effects of Prenatal Exposure to Seasonal Influenza

Impact of In Utero Seasonal Influenza Exposure or Fever by Trimester	Health at Birth	Childhood Outcomes	Adult Outcomes
Conception and First Trimester • Fetal structural development occurs *(CDC℘)*	• Increased infant mortality and mortality due to congenital abnormalities (*Dorélien, 2019*) • Associated with increased risk of birth defects, including neural tube defects, oral clefts, and congenital heart defects (*Botto et al., 2014*; *Dreier et al, 2014*; *Kerr et al., 2017*; *Waller et al, 2018*) • Lower proportion of male infants (*Hansen, Møller, and Olsen, 1999*)		• Associated with schizophrenia risk (*Khandaker, Dibben, and Jones, 2012*)
Second Trimester • Central nervous system development (*Kelly, 2011*; *CDC℘*)	• Increased probability of low birth weight (*Dorélien, 2019*)	• Associated with adverse temperament and reduced educational achievement (*Dombrowski* et al, 2003) • Associated with increased risk of autism spectrum disorders (*Hornig et al, 2018*)	• Associated with schizophrenia risk (*Khandaker, Dibben, and Jones, 2012*) • Decreased educational attainment, labor force participation and wage/earnings, increased welfare aged 19 to 32 (*Schwandt, 2018*)
Third Trimester • Fetal weight gain	• Shortened gestation length resulting in decreased birth weight (*Currie and Schwandt, 2013*; *Schwandt, 2018*) and increased probability of low birth weight (*Dorélien, 2019*) • Increased probability of preterm birth, decreased birth weight (*Dorélien, 2019*)	• Potential increase in mortality by age 18 (*Schwandt, 2018*)	

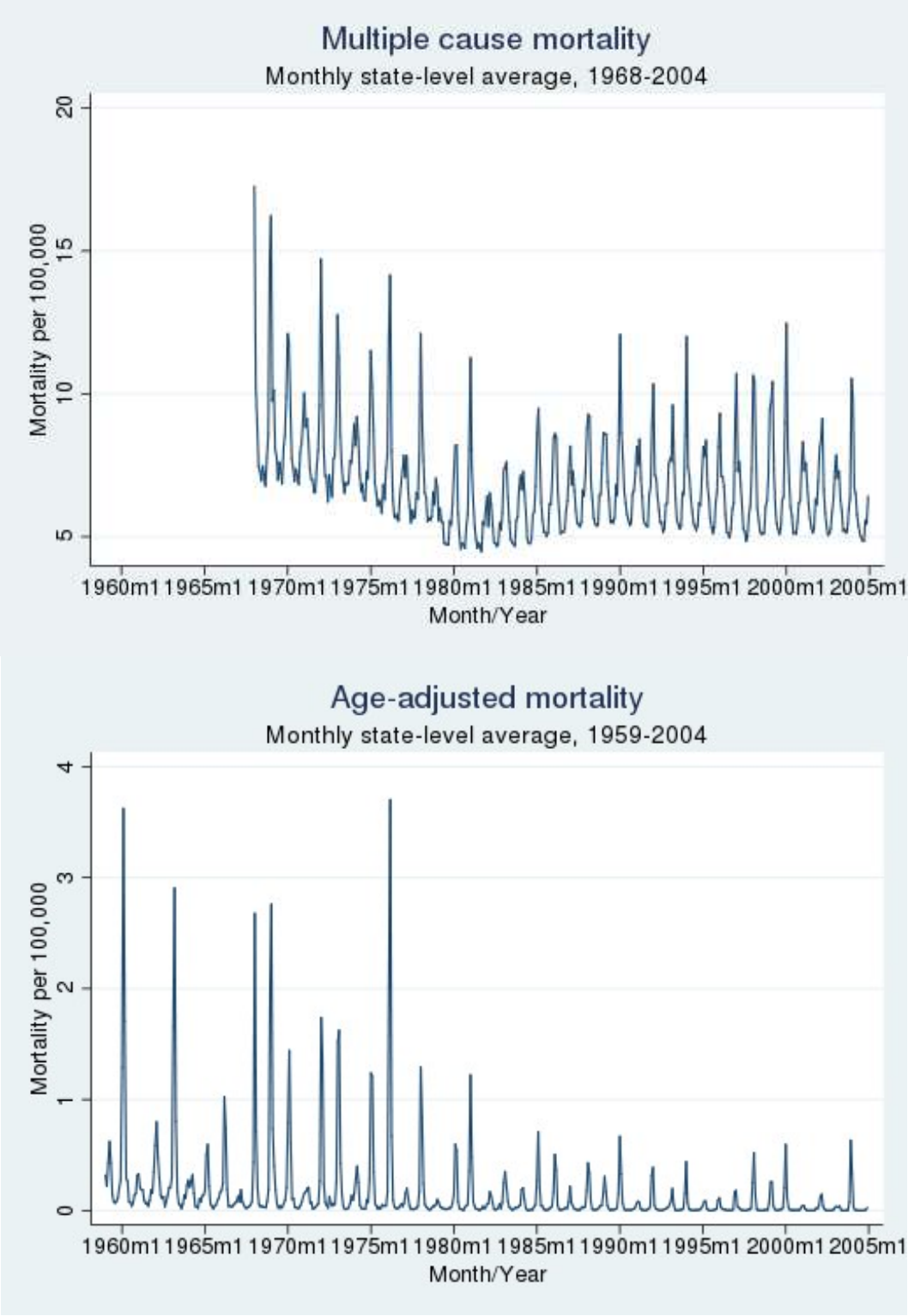
Notes: *CDC℘*, "Fetal Development Chart" in "An Alcohol-Free Pregnancy is the Best Choice for Your Baby" Brochure, Available: https://www.cdc.gov/ncbddd/fasd/documents/FASDBrochure_final-508.pdf

Appendix Figure A2: Spread of the 1975-1976 Seasonal Influenza Epidemic Across States



Source: National Center for Health Statistics (1976)

Appendix Figure A3: Alternative and Robustness Test Measures of Influenza Exposure



Source: National Center for Health Statistics (1959-2004)

Appendix Table A1: Comparison of Monthly State-Level Influenza Measures per 100,000

	Influenza-Related Mortality	Alternative Influenza Measure: Multiple Cause Influenza- and Pneumonia-Related Mortality	Age-Adjusted Influenza-Related Mortality	Influenza-Related Mortality Pandemic Cohort Excluded
Mean:	0.12	6.88	0.16	0.11
Std. Dev:	0.37	2.57	0.54	0.35
Min:	0.00	0.00	0.00	0.00
Max:	8.93	36.28	12.29	8.93
Observations:	28,152	22,644	28,152	27,234
Years:	1959-2004	1968-2004	1959-2004	1959-2004

Source: National Center for Health Statistics (1959-2004)

Appendix Table A2: Summary Statistics of Limitation Samples

	Activity Limitation Sample	Functional Limitation Sample
Percent any disability type	68.0	37.3
Percent cognitive disability	33.9	16.8
Percent ambulatory disability	43.2	23.2
Percent independent living disability	31.5	14.4
Percent self-care disability	14.7	6.9
Percent hearing disability	10.2	6.7
Percent vision disability	12.6	7.3
Percent female	53.3	58.2
Age (years)	45.8	45.2
Percent White	72.3	75.2
Percent Black	18.1	16.1
Percent Asian	0.8	0.7
Percent Hispanic	6.9	6.3
Percent Other	2.0	1.7
Observations	14,222	16,240

Notes: Analytic samples obtained from the pooled IPUMS NHIS 2011-2017 and represent individuals 25 to 58 with an activity or functional limitation. Sample means weighted using the weight associated with disability adjusted for years of pooled data. Any disability type includes subsequent six categories of disability.

Appendix Table A3a: Effect of Prenatal Influenza Exposure by Month on Outcomes at Birth

Influenza-related mortality per 100,000 in month:	Birth weight (grams)	Low birth weight (<2500g)	Gestation (weeks)	Preterm birth (<37 weeks)	Birth weight (grams)†	Low birth weight (<2500g)†	Five minute APGAR low (<7)	Child is male
0	-0.0176	0.00916	-0.000520	0.000621	0.0516	0.00564	0.00725	0.137***
	(0.588)	(0.0201)	(0.00114)	(0.0317)	(0.579)	(0.0197)	(0.0202)	(0.0485)
1	0.155	0.0350*	0.00175	0.0976***	-0.00949	0.0353*	0.0238	-0.0321
	(0.547)	(0.0202)	(0.00135)	(0.0294)	(0.529)	(0.0203)	(0.0197)	(0.0498)
2	0.0287	0.00604	-0.00284**	0.0389	0.348	-0.00524	-0.000255	0.0325
	(0.489)	(0.0217)	(0.00128)	(0.0305)	(0.483)	(0.0209)	(0.0222)	(0.0558)
3	0.477	-0.0155	0.000608	-0.0305	0.410	-0.00581	0.00231	-0.000164
	(0.584)	(0.0219)	(0.00127)	(0.0297)	(0.607)	(0.0212)	(0.0202)	(0.0462)
4	-1.657**	0.0648***	-0.00251**	0.0222	-1.421**	0.0631***	0.0159	0.154***
	(0.725)	(0.0248)	(0.00124)	(0.0319)	(0.696)	(0.0238)	(0.0201)	(0.0520)
5	-0.611	-0.0196	0.000826	0.0288	-0.617	-0.0198	0.00229	-0.0436
	(0.619)	(0.0214)	(0.00100)	(0.0274)	(0.604)	(0.0206)	(0.0224)	(0.0466)
6	-2.328***	0.120***	-0.00258**	-0.0172	-2.065***	0.112***	0.0491**	0.0660
	(0.624)	(0.0220)	(0.00121)	(0.0284)	(0.592)	(0.0207)	(0.0234)	(0.0433)
7	-4.750***	0.0931***	0.00216	0.0157	-4.928***	0.102***	0.0368	0.0305
	(0.795)	(0.0279)	(0.00149)	(0.0273)	(0.746)	(0.0259)	(0.0231)	(0.0426)
8	-4.703***	0.189***	-0.00684***	0.0350	-3.940***	0.158***	-0.0123	-0.0969**
	(0.951)	(0.0400)	(0.00167)	(0.0332)	(0.912)	(0.0376)	(0.0276)	(0.0428)
9	-2.835*	-0.0625	0.0435***		-7.417***	0.0948	-0.243***	-0.0300
	(1.628)	(0.0617)	(0.00411)		(1.796)	(0.0689)	(0.0356)	(0.0522)
Observations	97,205,009	97,205,009	97,291,162	97,291,162	97,205,009	97,205,009	66,866,334	97,291,162
Effect of an intense flu:	**-20.31**	**0.60**	0.01	0.11	-20.79	0.61	-0.09	-0.21

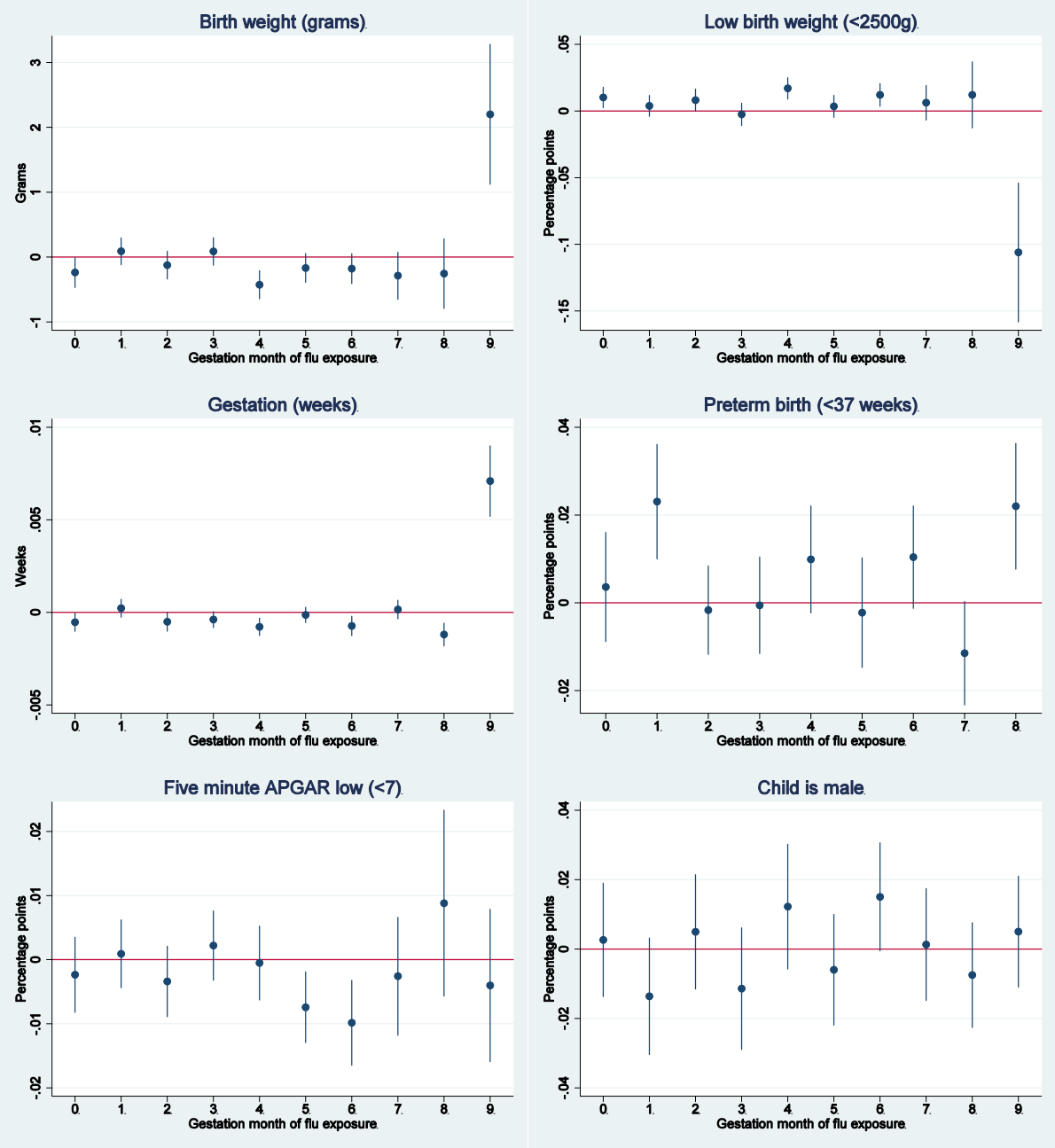
Notes: This table presents linear regression estimates of the effects of prenatal exposure to influenza on birth outcomes. * p<0.10, ** p<0.05, *** p<0.01. Standard errors in parentheses. All indicator outcomes are scaled from 0 to 100 for readability. † includes dummies for length of gestation in weeks. Sample is limited to singleton births born between 1971 and 2004 and conceived between September, 1970 and in or before March, 2004, with nine months of gestation or less. Month 0 is month of conception, month 1 is the first month of gestation, etc. Influenza-related mortality is set equal to zero if the infant was born in a prior month and regression includes dummy variables for "month not in utero" if born prior to that month (e.g. an infant born in month 7 of gestation would have "not in utero month 8" dummy = 1, "not in utero month 9" dummy = 1, etc.). Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976) beginning in month six of gestation, equal to a month six exposure of approximately 0.1 deaths per 100,000, month seven exposure of 1.4, month eight exposure of 2.6, and month nine exposure of 0.5. All regressions include full demographic controls: dummies for sex of child, live birth order of child, mother's single year of age, father's single year of age, mother's race, father's race, mother's education, and mother's marital status (including dummies for unknown/missing). All regressions also include state of birth-month of conception fixed effects (e.g. January in Alabama), year-month of conception fixed effects (e.g. January, 1985), and state of birth-specific linear time trends. Month 9 influenza exposure is omitted for the preterm birth specification, since all births in month 9 are full-term. Five-minute APGAR is available beginning in 1978. Standard errors clustered by state of birth-month of conception. All regressions are frequency weighted due to 50 percent birth certificate sampling in some years and states.

Appendix Table A3b: Relative Risk of Prenatal Influenza Exposure by Month on Congenital Anomalies

Influenza-related mortality per 100,000 in month:	Any congenital anomaly	Heart malformations	Any neural tube defect	Cleft lip/palate
0	1.099**	1.180***	0.943	1.045
	(0.0468)	(0.0685)	(0.0851)	(0.0634)
1	0.956	0.938	1.015	1.017
	(0.0409)	(0.0536)	(0.103)	(0.0604)
2	1.063	1.160**	1.052	0.954
	(0.0461)	(0.0739)	(0.0999)	(0.0571)
3	1.074	1.109*	0.998	1.071
	(0.0486)	(0.0631)	(0.109)	(0.0695)
4	0.948	0.946	1.067	0.967
	(0.0419)	(0.0538)	(0.112)	(0.0544)
5	1.023	1.043	1.055	1.013
	(0.0487)	(0.0650)	(0.108)	(0.0607)
6	1.001	1.029	0.877	1.034
	(0.0428)	(0.0596)	(0.101)	(0.0707)
7	0.982	1.038	0.948	0.968
	(0.0442)	(0.0578)	(0.106)	(0.0681)
8	1.073	1.112**	0.914	1.083
	(0.0463)	(0.0561)	(0.124)	(0.0692)
9	0.986	1.029	0.808*	1.007
	(0.0443)	(0.0587)	(0.0967)	(0.0735)
Observations	51,261,222	51,379,510	52,053,976	52,231,970

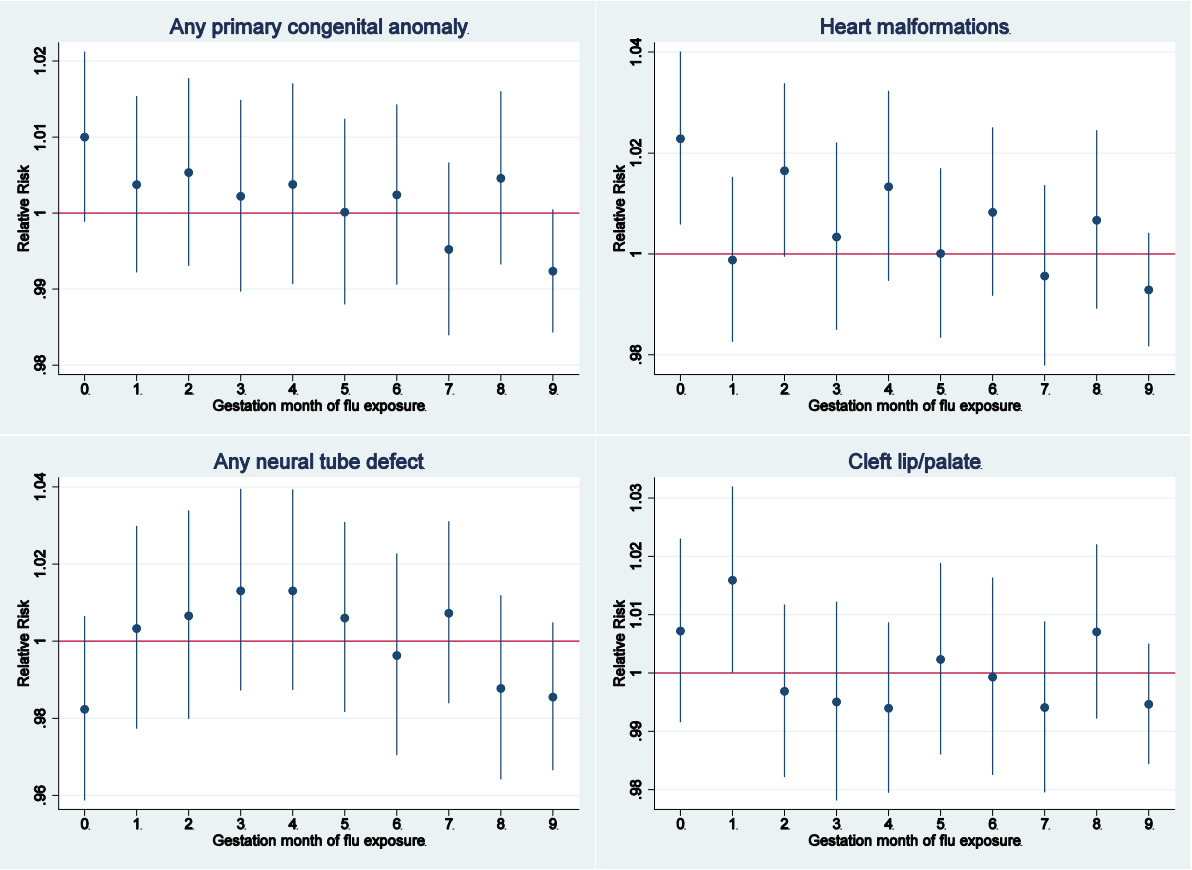
Notes: This table presents exponentiated log-binomial regression estimates of the relative risk of congenital anomalies from prenatal exposure to influenza. * p<0.10, ** p<0.05, *** p<0.01. Standard errors in parentheses. Sample is limited to singleton births born between 1989 and 2004 and conceived between Sept. 1988 and Mar. 2004, with nine months of gestation or less. Month 0 is month of conception, month 1 is the first month of gestation, etc. Influenza-related mortality is set equal to zero if the infant was born in a prior month and regression includes dummy variables for "month not in utero" if born prior to that month (e.g. an infant born in month 7 of gestation would have "not in utero month 8" dummy = 1, "not in utero month 9" dummy = 1, etc.). All regressions include full demographic controls: dummies for sex of child, live birth order of child, mother's single year of age, father's single year of age, mother's race, father's race, mother's education, and mother's marital status (including dummies for unknown/missing). All regressions also include state of birth-month of conception fixed effects (e.g. January in Alabama), year-month of conception fixed effects (e.g. January, 1985), and state of birth-specific linear time trends. Month 9 influenza exposure is omitted for the preterm birth specification, since all births in month 9 are full-term.

Appendix Figure A4: Effects on Health at Birth – Alternative Flu Measure



Notes: Figures display the effect of one additional multiple cause death per 100,000 on outcomes, with 95 percent confidence intervals around the estimate. All indicator outcomes are scaled from 0 to 100 for readability. For the preterm birth outcome, month nine gestation is omitted since all month nine births are considered full-term.

Appendix Figure A4: Effects on Health at Birth – Alternative Flu Measure (continued)



Notes: Figures display the relative risk of one additional multiple cause death per 100,000 on outcomes, with 95 percent confidence intervals around the estimate. Congenital anomalies outcomes are only available beginning in 1989. In addition to the full set of covariates, regressions also include dummies for maternal use of tobacco and alcohol during pregnancy

Appendix Table A4a: Effect of Prenatal Influenza Exposure by Month on Outcomes at Birth - Alternative Flu Measure

Multiple cause mortality per 100,000 in month:	Birth weight (grams)	Low birth weight (<2500g)	Gestation (weeks)	Preterm birth (<37 weeks)	Five minute APGAR low (<7)	Child is male
0	-0.239**	0.0101***	-0.000534**	0.00361	-0.00236	0.00262
	(0.117)	(0.00389)	(0.000251)	(0.00633)	(0.00298)	(0.00833)
1	0.0893	0.00385	0.000223	0.0231***	0.000912	-0.0136
	(0.106)	(0.00400)	(0.000246)	(0.00666)	(0.00270)	(0.00855)
2	-0.125	0.00811*	-0.000513**	-0.00168	-0.00340	0.00496
	(0.109)	(0.00425)	(0.000260)	(0.00514)	(0.00280)	(0.00838)
3	0.0862	-0.00253	-0.000390*	-0.000569	0.00220	-0.0114
	(0.108)	(0.00427)	(0.000219)	(0.00560)	(0.00275)	(0.00892)
4	-0.427***	0.0170***	-0.000781***	0.00989	-0.000515	0.0122
	(0.111)	(0.00409)	(0.000240)	(0.00621)	(0.00294)	(0.00916)
5	-0.169	0.00351	-0.000138	-0.00224	-0.00742***	-0.00597
	(0.113)	(0.00421)	(0.000212)	(0.00636)	(0.00281)	(0.00812)
6	-0.178	0.0121***	-0.000730***	0.0104*	-0.00985***	0.0151*
	(0.117)	(0.00432)	(0.000265)	(0.00595)	(0.00337)	(0.00792)
7	-0.288	0.00619	0.000155	-0.0115*	-0.00259	0.00131
	(0.185)	(0.00662)	(0.000256)	(0.00600)	(0.00469)	(0.00820)
8	-0.255	0.0121	-0.00120***	0.0220***	0.00881	-0.00750
	(0.273)	(0.0126)	(0.000310)	(0.00730)	(0.00738)	(0.00769)
9	2.201***	-0.106***	0.00710***		-0.00403	0.00502
	(0.549)	(0.0265)	(0.000971)		(0.00605)	(0.00814)
Observations	97,205,009	97,205,009	97,291,162	97,291,162	66,866,334	97,291,162
Effect of an intense flu:	9.20	-0.51	0.04	0.26	-0.02	0.07

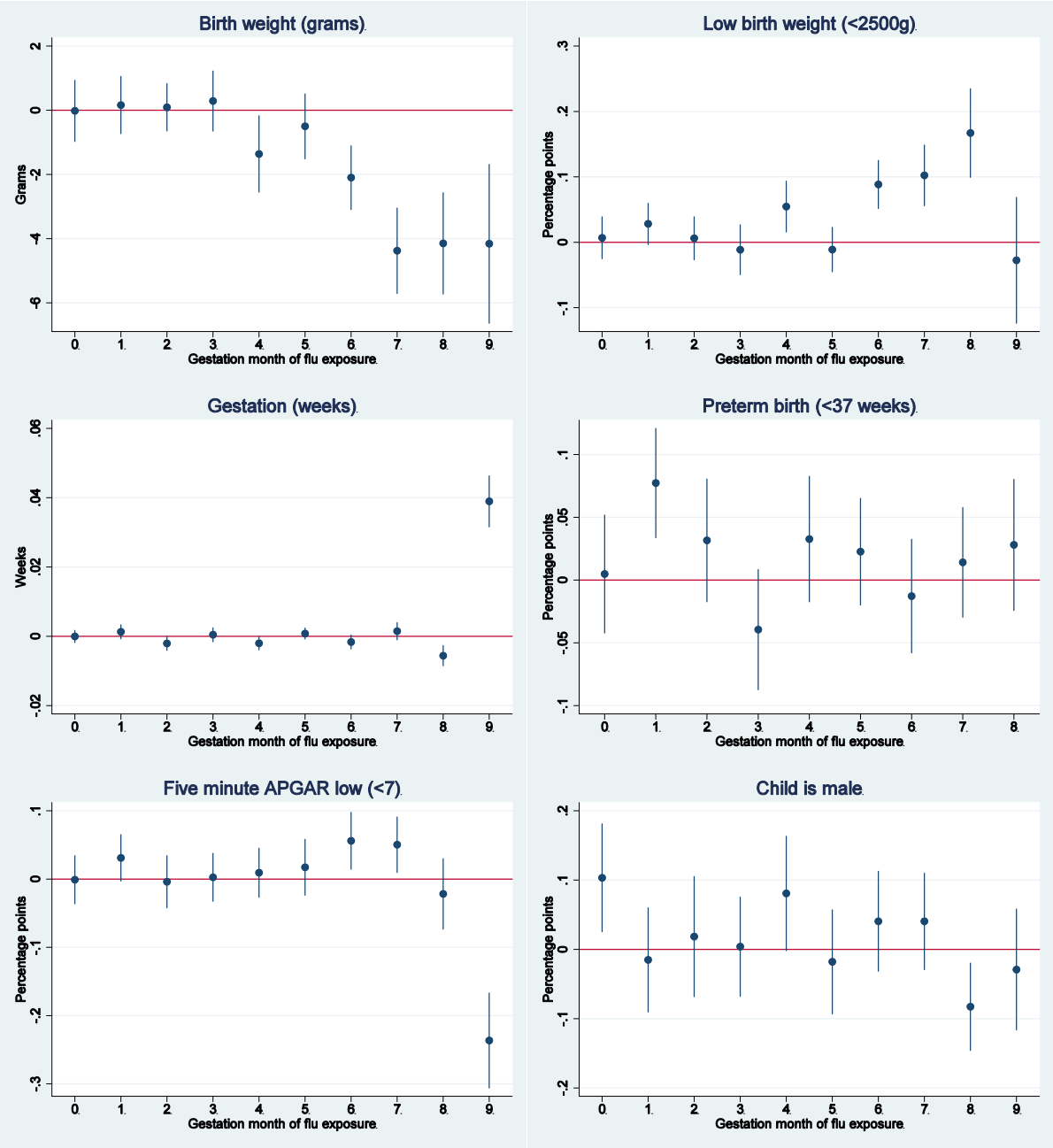
Notes: This table presents linear regression estimates of the effects of prenatal exposure to influenza on birth outcomes using multiple cause mortality. * p<0.10, ** p<0.05, *** p<0.01. Standard errors in parentheses. All indicator outcomes are scaled from 0 to 100 for readability. Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976) beginning in month six of gestation equal to approximately 41.8 deaths per 100,000 for multiple cause measure. Sample is limited to singleton births born between 1968 and 2004 with nine months of gestation or less. Additional notes available in ***Appendix Table A3a***.

Appendix Table A4b: Relative Risk of Prenatal Influenza Exposure by Month on Congenital Anomalies - Alternative Flu Measure

Multiple cause mortality per 100,000 in month:	Any congenital anomaly	Heart malformations	Any neural tube defect	Cleft lip/palate
0	1.010*	1.023***	0.982	1.007
	(0.00568)	(0.00870)	(0.0121)	(0.00801)
1	1.004	0.999	1.003	1.016**
	(0.00589)	(0.00830)	(0.0134)	(0.00811)
2	1.005	1.017*	1.007	0.997
	(0.00628)	(0.00874)	(0.0137)	(0.00751)
3	1.002	1.003	1.013	0.995
	(0.00641)	(0.00943)	(0.0133)	(0.00866)
4	1.004	1.013	1.013	0.994
	(0.00670)	(0.00957)	(0.0132)	(0.00742)
5	1.000	1.000	1.006	1.002
	(0.00620)	(0.00853)	(0.0125)	(0.00834)
6	1.002	1.008	0.996	0.999
	(0.00602)	(0.00848)	(0.0133)	(0.00860)
7	0.995	0.996	1.007	0.994
	(0.00577)	(0.00908)	(0.0120)	(0.00745)
8	1.005	1.007	0.988	1.007
	(0.00579)	(0.00899)	(0.0121)	(0.00759)
9	0.992*	0.993	0.986	0.995
	(0.00411)	(0.00570)	(0.00973)	(0.00524)
Observations	51,261,222	51,379,510	52,053,976	52,231,970

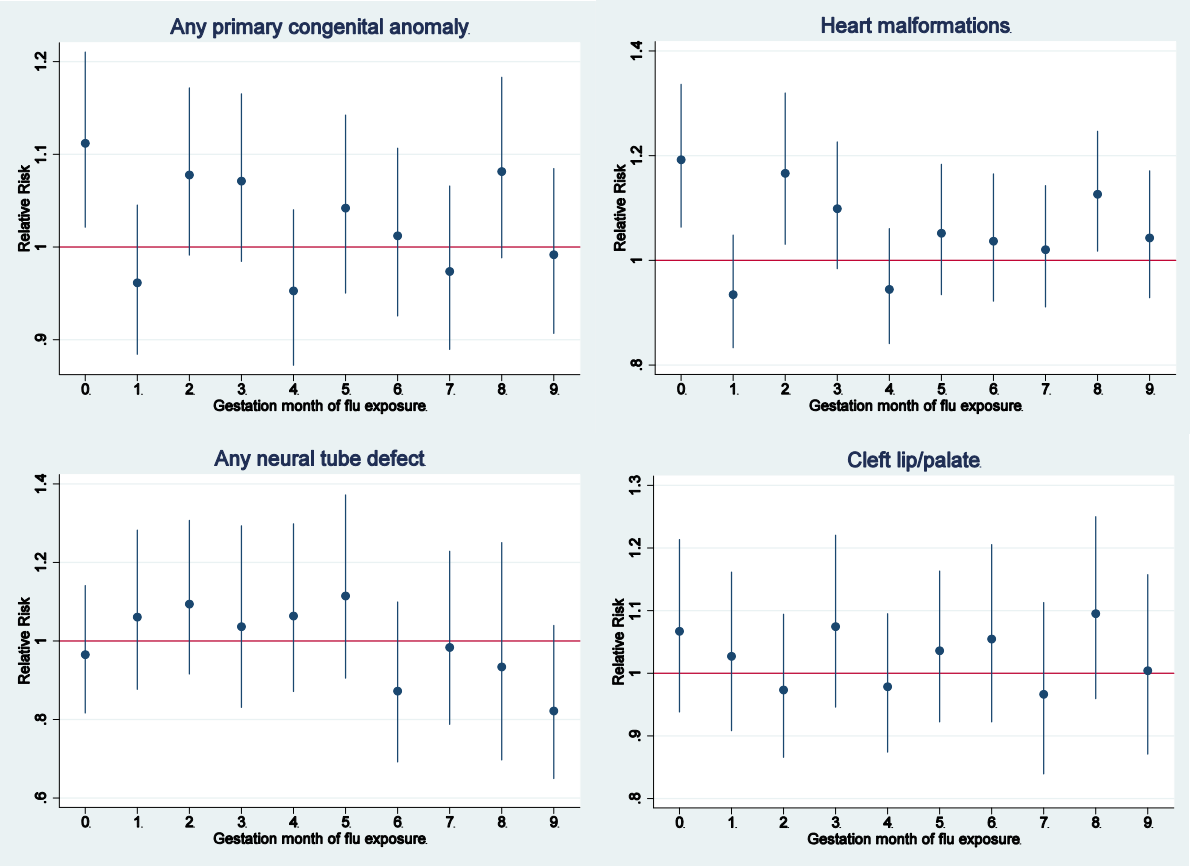
Notes: This table presents exponentiated log-binomial regression estimates of the relative risk of congenital anomalies from prenatal exposure to multiple cause mortality * p<0.10, ** p<0.05, *** p<0.01. Standard errors in parentheses. Additional notes available in ***Appendix Table A3b***.

Appendix Figure A5a: Effects on Health at Birth – Age-Adjusted Robustness Check



Notes: Figures display the effect of one additional age-adjusted death per 100,000 on outcomes, with 95 percent confidence intervals around the estimate. All indicator outcomes are scaled from 0 to 100 for readability. For the preterm birth outcome, month nine gestation is omitted since all month nine births are considered full-term.

Appendix Figure A5a: Effects on Health at Birth – Age-Adjusted Robustness Check (continued)



Notes: Figures display the relative risk of one additional age-adjusted death per 100,000 on outcomes, with 95 percent confidence intervals around the estimate. Congenital anomalies outcomes are only available beginning in 1989. In addition to the full set of covariates, regressions also include dummies for maternal use of tobacco and alcohol during pregnancy

Appendix Table A5a: Effect of Prenatal Influenza Exposure by Month on Outcomes at Birth - Age-Adjusted Robustness Check

Age-adjusted mortality per 100,000 in month:	Birth weight (grams)	Low birth weight (<2500g)	Gestation (weeks)	Preterm birth (<37 weeks)	Five minute APGAR low (<7)	Child is male
0	-0.0156	0.00688	-0.0000548	0.00485	-0.000968	0.103***
	(0.485)	(0.0163)	(0.000884)	(0.0239)	(0.0179)	(0.0396)
1	0.163	0.0282*	0.00128	0.0773***	0.0311*	-0.0151
	(0.453)	(0.0161)	(0.00104)	(0.0222)	(0.0173)	(0.0383)
2	0.0929	0.00607	-0.00207**	0.0317	-0.00392	0.0184
	(0.375)	(0.0167)	(0.00101)	(0.0249)	(0.0194)	(0.0441)
3	0.288	-0.0114	0.000438	-0.0395	0.00260	0.00385
	(0.476)	(0.0194)	(0.00102)	(0.0244)	(0.0179)	(0.0365)
4	-1.361**	0.0546***	-0.00203**	0.0327	0.00936	0.0806*
	(0.606)	(0.0198)	(0.000966)	(0.0254)	(0.0183)	(0.0420)
5	-0.501	-0.0111	0.000795	0.0226	0.0173	-0.0180
	(0.514)	(0.0173)	(0.000803)	(0.0217)	(0.0209)	(0.0382)
6	-2.096***	0.0884***	-0.00166	-0.0128	0.0560***	0.0406
	(0.505)	(0.0188)	(0.00102)	(0.0231)	(0.0212)	(0.0367)
7	-4.375***	0.102***	0.00145	0.0141	0.0504**	0.0404
	(0.678)	(0.0236)	(0.00126)	(0.0222)	(0.0207)	(0.0355)
8	-4.147***	0.167***	-0.00560***	0.0280	-0.0217	-0.0828**
	(0.803)	(0.0345)	(0.00149)	(0.0266)	(0.0262)	(0.0321)
9	-4.158***	-0.0275	0.0390***		-0.236***	-0.0292
	(1.259)	(0.0490)	(0.00374)		(0.0354)	(0.0445)
Observations	97,205,009	97,205,009	97,291,162	97,291,162	66,866,334	97,291,162
Effect of an intense flu:	-27.32	0.82	0.01	0.13	-0.13	-0.24

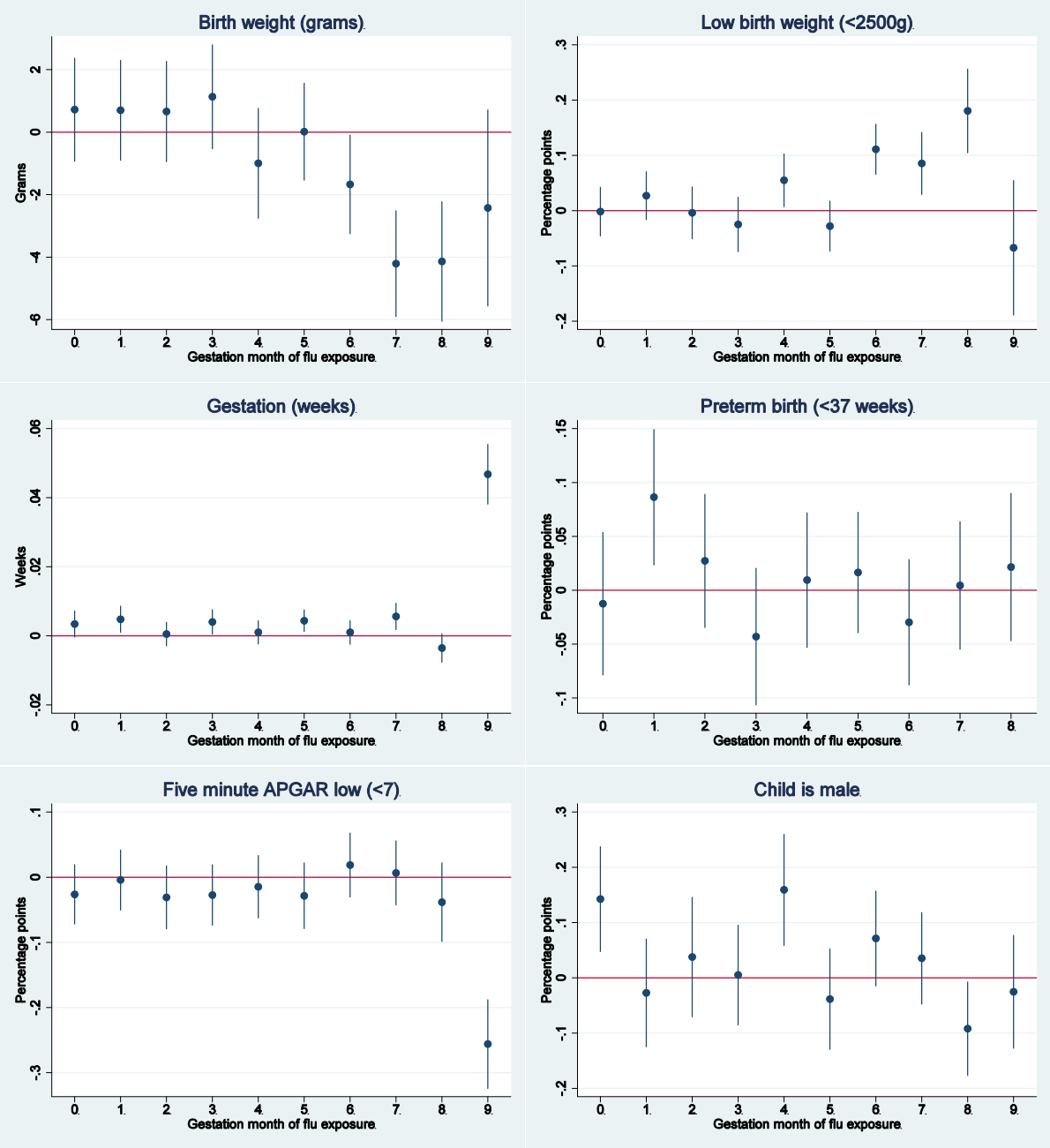
Notes: This table presents linear regression estimates of the effects of prenatal exposure to influenza on birth outcomes using age-adjusted mortality. * p<0.10, ** p<0.05, *** p<0.01. Standard errors in parentheses. Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976) beginning in month six of gestation equal to approximately 6.56 age-adjusted deaths per 100,000. Additional notes available in ***Appendix Table A3a***.

Appendix Table A5b: Relative Risk of Prenatal Influenza Exposure by Month on Congenital Anomalies - Age-Adjusted Robustness Check

Age-adjusted mortality per 100,000 in month:	Any congenital anomaly	Heart malformations	Any neural tube defect	Cleft lip/palate
0	1.112**	1.192***	0.965	1.067
	(0.0481)	(0.0695)	(0.0825)	(0.0701)
1	0.961	0.934	1.061	1.027
	(0.0410)	(0.0548)	(0.103)	(0.0645)
2	1.078*	1.166**	1.094	0.973
	(0.0460)	(0.0736)	(0.0993)	(0.0582)
3	1.071	1.099*	1.037	1.075
	(0.0460)	(0.0616)	(0.117)	(0.0698)
4	0.953	0.944	1.064	0.978
	(0.0427)	(0.0559)	(0.108)	(0.0563)
5	1.042	1.052	1.115	1.036
	(0.0490)	(0.0634)	(0.118)	(0.0613)
6	1.012	1.037	0.872	1.054
	(0.0461)	(0.0618)	(0.103)	(0.0721)
7	0.974	1.020	0.984	0.966
	(0.0449)	(0.0590)	(0.112)	(0.0696)
8	1.081*	1.126**	0.934	1.095
	(0.0496)	(0.0583)	(0.139)	(0.0740)
9	0.992	1.043	0.822	1.004
	(0.0453)	(0.0618)	(0.0985)	(0.0729)
Observations	51,261,222	51,379,510	52,053,976	52,231,970

Notes: This table presents exponentiated log-binomial regression estimates of the relative risk of congenital anomalies from prenatal exposure to age-adjusted mortality. * p<0.10, ** p<0.05, *** p<0.01. Standard errors in parentheses. Additional notes available in ***Appendix Table A3b***.

Appendix Figure A5b: Effects on Health at Birth – State-Specific Linear Time Trends Excluded Robustness Check



Notes: Figures display the effect of one additional influenza-related death per 100,000 on outcomes omitting state-specific linear time trends, with 95 percent confidence intervals around the estimate. All indicator outcomes are scaled from 0 to 100 for readability. For the preterm birth outcome, month nine gestation is omitted since all month nine births are considered full-term.

Appendix Table A5c: Effect of Prenatal Influenza Exposure by Month on Outcomes at Birth - State-Specific Linear Time Trends Excluded

Influenza-related mortality per 100,000 in month:	Birth weight (grams)	Low birth weight (<2500g)	Gestation (weeks)	Preterm birth (<37 weeks)	Five minute APGAR low (<7)	Child is male
0	0.719	-0.00184	0.00339*	-0.0125	-0.0264	0.143***
	(0.840)	(0.0224)	(0.00192)	(0.0336)	(0.0232)	(0.0482)
1	0.699	0.0269	0.00478**	0.0863***	-0.00420	-0.0274
	(0.814)	(0.0222)	(0.00193)	(0.0320)	(0.0235)	(0.0496)
2	0.659	-0.00391	0.000494	0.0273	-0.0310	0.0376
	(0.818)	(0.0239)	(0.00174)	(0.0315)	(0.0247)	(0.0550)
3	1.131	-0.0250	0.00401**	-0.0430	-0.0273	0.00507
	(0.846)	(0.0251)	(0.00181)	(0.0322)	(0.0237)	(0.0459)
4	-0.998	0.0549**	0.001000	0.00939	-0.0146	0.159***
	(0.895)	(0.0243)	(0.00172)	(0.0318)	(0.0244)	(0.0512)
5	0.0132	-0.0282	0.00438***	0.0165	-0.0286	-0.0385
	(0.790)	(0.0231)	(0.00160)	(0.0284)	(0.0256)	(0.0462)
6	-1.673**	0.111***	0.000990	-0.0297	0.0187	0.0711
	(0.804)	(0.0230)	(0.00175)	(0.0296)	(0.0250)	(0.0437)
7	-4.211***	0.0853***	0.00558***	0.00449	0.00652	0.0353
	(0.862)	(0.0286)	(0.00194)	(0.0301)	(0.0250)	(0.0422)
8	-4.138***	0.180***	-0.00354*	0.0215	-0.0383	-0.0920**
	(0.973)	(0.0385)	(0.00210)	(0.0348)	(0.0307)	(0.0430)
9	-2.426	-0.0674	0.0468***		-0.256***	-0.0253
	(1.596)	(0.0619)	(0.00440)		(0.0346)	(0.0520)
Observations	97,205,009	97,205,009	97,291,162	97,291,162	66,866,334	97,291,162
Effect of an intense flu:	-17.85	0.56	0.02	0.06	-0.21	-0.19

Notes: This table presents linear regression estimates of the effects of prenatal exposure to influenza on birth outcomes omitting state-specific linear time trends. * p<0.10, ** p<0.05, *** p<0.01. Standard errors in parentheses. All indicator outcomes are scaled from 0 to 100 for readability. Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976) beginning in month six of gestation equal to approximately 4.55 age-adjusted deaths per 100,000. Additional notes available in ***Appendix Table A3a***.

Appendix Table A6: Secondary Economic Outcomes

	Below 150% of Poverty Threshold	Duncan Socioeconomic Index	Wage and Salary Income ($1999)	Welfare, Social Security, and SSI ($1999)
Influenza-related mortality per 100,000	0.0170	0.0142	20.63	1.773
	(0.0198)	(0.0124)	(19.51)	(1.110)
Observations	8,931,557	8,226,222	9,188,753	9,188,753
Effect of an intense flu:	0.08	0.06	93.78	8.06

Notes: This table presents linear regression estimates of the long term effects of prenatal exposure to influenza. Standard errors in parentheses. * p<0.10, ** p<0.05, *** p<0.01. All indicator outcomes are scaled from 0 to 100 for readability. Analytic sample includes aged 25 to 58. Influenza-related mortality represents the sum of mortality per 100,000 during the course of a hypothetical pregnancy (current and previous three quarters). Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976), equal to approximately 4.55 deaths per 100,000. All regressions include dummies for sex, age, and race, as well as state of birth-quarter of birth fixed effects, birth year-quarter fixed effects, current year fixed effects, and state-specific linear time trends. Standard errors clustered by state of birth-quarter of birth. All regressions weighted using the person survey weight.

Appendix Table A7: Disability for Children and Full Sample

	Any Disability Type	Cognitive Difficulty	Ambulatory Difficulty	Self-Care Difficulty	Vision Difficulty	Hearing Difficulty
Children:						
Influenza-related mortality per 100,000	-0.0901	-0.0354	-0.0218	-0.00705	-0.0426*	-0.0317
	(0.0650)	(0.0585)	(0.0206)	(0.0237)	(0.0254)	(0.0211)
Observations	3,491,429	3,491,429	3,491,429	3,491,429	3,491,429	3,491,429
Effect of an intense flu:	-0.41	-0.16	-0.10	-0.03	-0.19	-0.14
Full Sample:						
Influenza-related mortality per 100,000	0.0963***	0.0312***	0.0799***	0.0215***	0.0335***	0.0116*
	(0.0143)	(0.0107)	(0.0113)	(0.00581)	(0.00647)	(0.00625)
Observations	15,116,969	15,116,969	15,116,969	15,116,969	15,116,969	15,116,969
Effect of an intense flu:	0.44	0.14	0.36	0.10	0.15	0.05

Notes: This table presents linear regression estimates of the long term effects of prenatal exposure to influenza. Standard errors in parentheses. * p<0.10, ** p<0.05, *** p<0.01. All indicator outcomes are scaled from 0 to 100 for readability. Analytic sample includes aged 25 to 58. Child analytic sample includes aged five to 17 and full analytic sample includes aged 5 to 58. Any disability does not include independent living difficulty, which is only available beginning at age 16. Influenza-related mortality represents the sum of mortality per 100,000 during the course of a hypothetical pregnancy (current and previous three quarters). Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976), equal to approximately 4.55 deaths per 100,000. All regressions include dummies for sex, age, and race, as well as state of birth-quarter of birth fixed effects, birth year-quarter fixed effects, current year fixed effects, and state-specific linear time trends. Standard errors clustered by state of birth-quarter of birth. All regressions weighted using the person survey weight.

Appendix Table A8: All Associations Between Disability and All Limitations

	Ambulatory disability	Vision disability		Ambulatory disability	Vision disability
Indicators for activity limitation from:			*Indicators for functional limitation from:*		
Alcohol/drug problem	-5.674	-4.980**	Alcohol/drug problem	21.19	-2.830
	(8.616)	(2.205)		(20.83)	(2.057)
First unclassified problem for adults	3.422	3.231*	Arthritis/rheumatism	10.64***	0.199
	(2.930)	(1.899)		(0.944)	(0.570)
Second unclassified problem for adults	10.62	16.55	Back/neck problem	9.365***	-0.211
	(13.01)	(21.81)		(0.856)	(0.513)
Arthritis/rheumatism	16.46***	-0.380	Benign tumor	9.670	3.862
	(1.437)	(0.926)		(6.918)	(4.232)
Back/neck problem	10.98***	-0.612	Birth defect	14.75***	0.237
	(1.055)	(0.713)		(5.052)	(2.262)
Benign tumor	-8.164	4.260	Blood problem	-5.323	1.973
	(5.179)	(3.525)		(8.998)	(5.286)
Birth defect	13.11***	1.458	Cancer	14.55***	7.582***
	(3.613)	(2.522)		(4.218)	(2.723)
Blood problem	-12.12	0.835	Circulatory problem	8.866***	2.374
	(7.576)	(6.273)		(3.134)	(2.189)
Cancer	3.533	3.380**	Depression/anxiety/emotional problem	7.599***	1.805**
	(2.413)	(1.672)		(1.218)	(0.862)
Circulatory problem	7.799***	-2.541	Diabetes	18.24***	8.143***
	(2.845)	(2.429)		(2.177)	(1.995)
Depression/anxiety/emotional problem	-8.861***	-0.704	Digestive problem	10.96***	4.112*
	(1.036)	(0.734)		(3.580)	(2.367)
Diabetes	6.412***	6.861***	Endocrine problem	3.784	1.526
	(1.657)	(1.496)		(3.799)	(2.746)
Digestive problem	-3.502	1.759	Fatigue	-3.928*	-2.160
	(2.490)	(1.843)		(2.008)	(1.570)
Endocrine problem	-8.438***	0.883	Fracture/bone/joint injury	9.050***	-0.388
	(2.661)	(2.177)		(1.278)	(0.676)
Other mental problem	-13.00***	0.872	Genitourinary problem	2.529	3.928
	(1.973)	(1.586)		(4.460)	(3.122)
Fatigue	-9.428	1.309	Hearing problem	2.810	-1.277
	(9.472)	(6.069)		(3.877)	(3.476)

Fracture/bone/joint injury	12.37***	-0.706	Heart problem	17.02***	3.053*
	(1.540)	(0.953)		(2.607)	(1.807)
Genitourinary problem	-0.262	0.0670	Hypertension	3.540	2.444
	(2.728)	(1.932)		(2.571)	(1.991)
Hearing problem	-3.130	-2.826	Missing limb/finger	26.48***	5.864
	(2.409)	(2.160)		(6.593)	(5.025)
Heart problem	6.398***	0.416	lung/breathing problem	15.01***	2.364**
	(1.795)	(1.287)		(1.926)	(1.180)
Hypertension	0.677	-0.289	Other mental problem	2.352	1.550
	(1.810)	(1.410)		(5.635)	(2.831)
Missing limb/finger	21.17***	-1.174	Musculoskeletal problem	5.719***	0.573
	(4.459)	(3.143)		(0.903)	(0.608)
Lung/breathing problem	10.44***	-0.106	1st unclassified cause	3.259	1.437
	(1.732)	(1.141)		(2.096)	(1.450)
Musculoskeletal problem	15.74***	-0.274	2nd unclassified cause	14.56	-25.38***
	(1.375)	(0.890)		(20.24)	(9.816)
Nervous conditions	10.00***	3.050***	Nervous system problem	18.10***	2.858***
	(1.454)	(1.056)		(1.696)	(1.087)
Old age	-20.26**	17.75	Old age	-7.845**	-1.996
	(9.038)	(12.85)		(3.093)	(2.559)
Other developmental problem	16.23***	0.612	Other developmental problem	43.04***	10.61***
	(3.220)	(1.658)		(6.488)	(4.089)
Other injury	6.161***	1.460	Other injury	7.164***	0.924
	(2.097)	(1.388)		(1.815)	(1.117)
Pregnancy	-12.17*	-2.817	Pregnancy	2.609	-1.083
	(6.864)	(3.866)		(1.838)	(1.714)
Intellectual disability	-9.354***	1.737	Intellectual disability	8.320**	8.968***
	(1.863)	(1.630)		(3.774)	(3.166)
Senility	1.590	4.319	Senility	10.65	-4.239
	(5.021)	(3.320)		(10.80)	(8.313)
Skin problem	23.20**	-5.494	Skin problem	12.44	5.744
	(10.40)	(3.542)		(9.524)	(8.028)
Stroke	15.73***	8.305***	Stroke	27.38***	8.988***
	(2.447)	(2.084)		(3.844)	(3.246)
Surgical after-effects	-6.615	-3.699	Surgical after-effects	7.131*	-0.254
	(6.810)	(3.481)		(4.214)	(2.866)

Vision problem	-4.656**	53.15***	Vision problem	5.284*	47.63***
	(1.886)	(1.926)		(2.716)	(2.776)
Weight problem	11.50***	-6.815***	Weight problem	-1.980	-3.776***
	(2.321)	(1.581)		(1.288)	(0.816)
Observations	14,181	14,176	Observations	16,236	16,237

Notes: This table presents linear regression estimates of the association between specific causes of limitations and disability. Standard errors in parentheses. * p<0.10, ** p<0.05, *** p<0.01. All indicator outcomes are scaled from 0 to 100 for readability. Analytic sample includes aged 25 to 58. Analytic samples obtained from the pooled IPUMS NHIS 2011-2017 and represent aged 25 to 58 with an activity or functional limitation. All regressions include dummies for sex, age, and race and are corrected for variance estimation. Sample means weighted using the weight associated with disability adjusted for years of pooled data.

Appendix Table A9: Economic Outcomes - Alternative Influenza Measure

	Child Attended School Past 3 Months	High School Completion	Educational Attainment (Years)	In the Labor Force	Below 150% of Poverty Threshold	Duncan Socioeconomic Index	Wage and Salary Income ($1999)	Welfare, Social Security, and SSI ($1999)
Multiple cause mortality per 100,000	-0.00380	-0.00900**	-0.00134***	-0.00113	0.000875	-0.0126***	-10.94**	0.0331
	(0.00550)	(0.00440)	(0.000382)	(0.00588)	(0.00699)	(0.00368)	(4.968)	(0.259)
Observations	3,491,429	5,887,104	5,887,104	5,887,104	5,692,072	5,347,364	5,887,104	5,887,104
Effect of an intense flu:	-0.16	-0.38	-0.06	-0.05	0.04	-0.53	-457.5	1.39

Notes: This table presents linear regression estimates of the long term effects of prenatal exposure to influenza using the multiple cause measure as an alternative exposure variable. All indicator outcomes are scaled from 0 to 100 for readability. Standard errors in parentheses. * p<0.10, ** p<0.05, *** p<0.01. Analytic sample includes aged 25 to 58 (except child school attendance, which includes aged five to 17). Multiple cause mortality represents the sum of influenza- and pneumonia-related multiple cause mortality per 100,000 during the course of a hypothetical pregnancy (current and previous three quarters). Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976), equal to approximately 41.8 deaths per 100,000. All regressions include dummies for sex, age, and race, as well as state of birth-quarter of birth fixed effects, birth year-quarter fixed effects, current year fixed effects, and state-specific linear time trends. Standard errors clustered by state of birth-quarter of birth. All regressions weighted using the person survey weight.

Appendix Table A10: Disability - Alternative Influenza Measure

	Any Disability Type	Cognitive Difficulty	Ambulatory Difficulty	Independent Living Difficulty	Self-Care Difficulty	Vision Difficulty	Hearing Difficulty
Multiple cause mortality per 100,000	0.00108	0.000974	-0.000471	-0.00127	0.000548	-0.000398	0.00251
	(0.00448)	(0.00329)	(0.00272)	(0.00266)	(0.00178)	(0.00179)	(0.00171)
Observations	5,887,104	5,887,104	5,887,104	5,887,104	5,887,104	5,887,104	5,887,104
Effect of an intense flu:	0.05	0.04	-0.02	-0.05	0.02	-0.02	0.11

Notes: This table presents linear regression estimates of the long term effects of prenatal exposure to influenza using the multiple cause measure as an alternative exposure variable. Standard errors in parentheses. * p<0.10, ** p<0.05, *** p<0.01. All indicator outcomes are scaled from 0 to 100 for readability. Analytic sample includes aged 25 to 58. Multiple cause mortality represents the sum of influenza- and pneumonia-related multiple cause mortality per 100,000 during the course of a hypothetical pregnancy (current and previous three quarters). Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976), equal to approximately 41.8 deaths per 100,000. All regressions include dummies for sex, age, and race, as well as state of birth-quarter of birth fixed effects, birth year-quarter fixed effects, current year fixed effects, and state-specific linear time trends. Standard errors clustered by state of birth-quarter of birth. All regressions weighted using the person survey weight.

Appendix Table A11: Economic Outcomes - Robustness Checks

	Child Attended School Past 3 Months	High School Completion	Educational Attainment (Years)	In the Labor Force	Below 150% of Poverty Threshold	Duncan Socioeconomic Index	Wage and Salary Income ($1999)	Welfare, Social Security, and SSI ($1999)
Age-adjusted								
Influenza-related mortality per 100,000	-0.131**	-0.0187**	0.000680	-0.0449***	0.0143	0.00986	9.971	1.032
	(0.0508)	(0.00895)	(0.000872)	(0.0139)	(0.0126)	(0.00840)	(13.06)	(0.719)
Observations	3,491,429	9,188,753	9,188,753	9,188,753	8,931,557	8,226,222	9,188,753	9,188,753
Effect of an intense flu:	-0.86	-0.12	0.00	-0.30	0.09	0.06	65.4	6.77
Pandemic cohort excluded								
Influenza-related mortality per 100,000	-0.101**	-0.0327**	0.000577	-0.0855***	0.0311	0.00996	21.45	2.531**
	(0.0453)	(0.0139)	(0.00132)	(0.0225)	(0.0206)	(0.0133)	(21.25)	(1.155)
Observations	3,491,429	8,715,017	8,715,017	8,715,017	8,468,688	7,804,600	8,715,017	8,715,017
Effect of an intense flu:	-0.46	-0.15	0.00	-0.39	0.14	0.05	97.5	11.51
State-specific linear time trends excluded								
Influenza-related mortality per 100,000	-0.0747*	-0.145***	-0.00240	-0.164***	-0.147***	-0.00439	-246.3***	10.11***
	(0.0438)	(0.0188)	(0.00162)	(0.0248)	(0.0229)	(0.0125)	(26.99)	(1.421)
Observations	3,491,429	9,188,753	9,188,753	9,188,753	8,931,557	8,226,222	9,188,753	9,188,753
Effect of an intense flu:	-0.34	-0.66	-0.01	-0.74	-0.67	-0.02	-1119.9	45.96

Notes: This table presents linear regression estimates of the long term effects of prenatal exposure to influenza with changes to the primary specification. Standard errors in parentheses. * p<0.10, ** p<0.05, *** p<0.01. All indicator outcomes are scaled from 0 to 100 for readability. Analytic sample includes aged 25 to 58 (except child school attendance, which includes aged five to 17). Influenza-related mortality represents the sum of mortality per 100,000 during the course of a hypothetical pregnancy (current and previous three quarters). Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976), equal to approximately 4.55 deaths per 100,000 (6.56 age-adjusted deaths per 100,000). Unless noted otherwise, all regressions include dummies for sex, age, and race, as well as state of birth-quarter of birth fixed effects, birth year-quarter fixed effects, current year fixed effects, and state-specific linear time trends. Standard errors clustered by state of birth-quarter of birth. All regressions weighted using the person survey weight.

Appendix Table A12: Disability - Robustness Checks

	Any Disability Type	Cognitive Difficulty	Ambulatory Difficulty	Independent Living Difficulty	Self-Care Difficulty	Vision Difficulty	Hearing Difficulty
Age-adjusted							
Influenza-related mortality per 100,000	0.0281***	0.0116	0.0143*	0.00524	0.00500	0.0119***	0.00342
	(0.00997)	(0.00728)	(0.00745)	(0.00697)	(0.00442)	(0.00430)	(0.00439)
Observations	9,188,753	9,188,753	9,188,753	9,188,753	9,188,753	9,188,753	9,188,753
Effect of an intense flu:	0.18	0.08	0.09	0.03	0.03	0.08	0.02
Pandemic cohort excluded							
Influenza-related mortality per 100,000	0.0527***	0.0230*	0.0317***	0.00954	0.0112	0.0214***	0.00572
	(0.0153)	(0.0120)	(0.0110)	(0.0111)	(0.00683)	(0.00670)	(0.00687)
Observations	8,715,017	8,715,017	8,715,017	8,715,017	8,715,017	8,715,017	8,715,017
Effect of an intense flu:	0.24	0.11	0.14	0.04	0.05	0.10	0.03
State-specific linear time trends excluded							
Influenza-related mortality per 100,000	0.241***	0.0647***	0.216***	0.0833***	0.0567***	0.0747***	0.0468***
	(0.0235)	(0.0128)	(0.0184)	(0.0117)	(0.00667)	(0.00833)	(0.00753)
Observations	9,188,753	9,188,753	9,188,753	9,188,753	9,188,753	9,188,753	9,188,753
Effect of an intense flu:	1.10	0.29	0.98	0.38	0.26	0.34	0.21

Notes: This table presents linear regression estimates of the long term effects of prenatal exposure to influenza with changes to the primary specification. Standard errors in parentheses. * p<0.10, ** p<0.05, *** p<0.01. All indicator outcomes are scaled from 0 to 100 for readability. Analytic sample includes aged 25 to 58. Influenza-related mortality represents the sum of mortality per 100,000 during the course of a hypothetical pregnancy (current and previous three quarters). Effect of an intense flu represents the impact of exposure to the peak 1975-76 flu season (sum of the state average between Jan. and Apr., 1976), equal to approximately 4.55 deaths per 100,000 (6.56 age-adjusted deaths per 100,000). Unless noted otherwise, all regressions include dummies for sex, age, and race, as well as state of birth-quarter of birth fixed effects, birth year-quarter fixed effects, current year fixed effects, and state-specific linear time trends. Standard errors clustered by state of birth-quarter of birth. All regressions weighted using the person survey weight.

Appendix Table A13: Estimating Effect of Vaccination Changes on Influenza-Related Mortality

	Historical vaccination rates (percent)					*Future vaccination policy*		Change in vaccination rate (percentage points)	Impact on influenza- and pneumonia-multiple cause deaths per 100,000	Impact on influenza-related deaths per 100,000
	1959	1971	1991	1992	2004	Baseline: 2016-17	Future			
Birth outcomes		3.7			30.89			27.19	-6.69	**-0.728**
Child outcome			14.68		30.89			16.21	-3.99	**-0.434**
Adult outcomes	0			17.78				17.78	-4.37	**-0.476**
All outcomes						45.2	70	24.80	-6.10	**-0.664**
Source:	Burney (1960b), vaccination rate estimated as zero (1)	Interpolation between vaccination rate in 1959 (Burney, 1960b) and weighted average of vaccination rates across adult age groups in 1989 (NHIS) (2)	NHIS, weighted average of vaccination rates across adult age groups (3)	NHIS: weighted average of vaccination rates across adult age groups; average of 1991 and 1993 vaccination rates (4)	NHIS: weighted average of vaccination rates across adult age groups (5)	Healthy People 2020 data (from NHIS, CDC/NCHS) (6)	Healthy People 2020 Target (6)		White (2019) (7)	Scaled using the ratio of the means of influenza-related mortality to influenza- and pneumonia-related mortality during a severe flu season (8)

Notes: Vaccination rates are estimates for population aged 18+. (1) *"In the past, influenza vaccination has been sparse and sporadic and has been administered primarily in response to an epidemic or the threat of an epidemic."* (2) Vaccination rate in 1989: (3.4*54,664+10.6*15,655+30.4*14,244)/(54,664 + 15,655 + 14,244)= 9.28 percent; increase of 9.28 percent over 30 years (1959 to 1989) translates to approximate 3.7 percent increase (40% of full increase) by 1971. (3) Vaccination rate in 1991: (6.1*26,900 + 15.0*7,618 + 41.7*8,453) / (26,900+7,618+8,453). (4) Vaccination rate in 1993: (10.2*12,954+23.0*3,620+52.0*4,198)/(12,954 + 3,620 + 4,198) = 20.88 percent. (5) Vaccination rate in 2004: (17.9*18,039 + 35.9*6,933 + 64.6*5,922) / (18,039 + 6,933+ 5,922). (6) Source available: https://www.healthypeople.gov/2020/data-search/Search-the-Data#objid=6360 (7) One percentage point increase in vaccination rate causes a decrease of 0.246 influenza- and pneumonia- multiple cause deaths per 100,000. These estimates represent vaccination for the marginal person and are based on vaccination data from the years 1994 to 2016 using the average vaccination match rate over this period, which reflects the degree that the strains in the influenza vaccine correspond to the circulating strains. (8) Uses estimates from the 1975-76 flu season. Specifically, the ratio is 4.55 influenza-related deaths per 100,000 / 41.83 influenza- and pneumonia -related multiple cause deaths per 100,000.

Appendix Table A14: Estimated Effects of Population Vaccination on Outcomes with Calculations

	Birth weight (grams)	Low birth weight (<2500g) (Percent)	Child Attended School Past 3 Months (Percent)	High School Completion (Percent)	In the Labor Force (Percent)	Any Disability Type (Percent)
Historical changes across birth years	*1971 to 2004*		*1991 to 2004*		*1959 to 1992*	
Average outcome at start of period	3258.41	7.96	93.85	92.71	77.02	16.50
Average outcome at end of period	3319.87	6.04	96.96	94.80	83.22	7.46
Difference in outcome over period	61.45	-1.91	3.11	2.09	6.20	-9.04
Effect of vaccination over period	11.82	-0.31	0.04	0.01	0.03	-0.02
Share of change due to historical vaccination (percent)	**19.23**	**15.95**	**1.41**	**0.64**	**0.54**	**0.23**
Future interventions			*Baseline: 2016-2017*			
Average outcome in 2016-2017	3289.99	6.72	96.92	93.87	81.05	11.21
Effect of vaccinating 70 percent of population	10.78	-0.28	0.07	0.02	0.05	-0.03
Percent change due to 70 percent vaccination	**0.33**	**-4.13**	**0.07**	**0.02**	**0.06**	**-0.26**
Effect of eliminating all flu mortality	22.74	-0.59	0.14	0.04	0.10	-0.06
Percent change due to eliminating flu mortality	**0.69**	**-8.73**	**0.15**	**0.04**	**0.12**	**-0.55**

Notes: Uses analytic samples for births from NCHS Vital Statistics Natality data, and later life analytic sample from pooled IPUMS ACS data (aged 25 to 58, except child school attendance, which represents aged five to 17). Effects of vaccination represent the simulated effect in the outcome from my models associated with changes in vaccination levels (see ***Appendix Table A13***) or a decline in influenza-related mortality from current levels (1.4 influenza-related deaths per 100,000, calculated as the average of national influenza-related mortality per 100,000 for years 2013-2017) (CDC Wonder Multiple Cause of Death Files). Birth outcomes simulated using coefficients on months zero to nine of gestation (***Figure 3***) and later life outcomes simulated using coefficient on the full pregnancy period (***Tables 5 and 6***). Historical averages at the start and end of period are obtained from analytic samples (NCHS Vital Statistics Natality for birth outcomes and IPUMS ACS data for later life outcomes). Average outcomes in 2016-2017 are obtained birth outcomes (calculated as the national average of 2016 and 2017 for singleton births with 41 weeks of gestational age or less, United States Department of Health and Human Services CDC Wonder Natality) and IPUMS ACS data (calculated as the national average in years 2016 and 2017 for native-born individuals aged five to 17 for childhood outcomes and aged 25 to 58 for other later life outcomes). All data weighted where relevant to adjust for sample designs.