Epidemiology in History

Short-Term Birth Sequelae of the 1918–1920 Influenza Pandemic in the United States: State-Level Analysis

Siddharth Chandra*, Julia Christensen, Svenn-Erik Mameland, and Nigel Paneth

* Correspondence to Dr. Siddharth Chandra, Asian Studies Center, Michigan State University, 427 N. Shaw Lane (Room 301), East Lansing, MI 48824-1035 (e-mail: chandr45@msu.edu).

Initially submitted April 15, 2018; accepted for publication July 20, 2018.

This paper examines short-term birth sequelae of the influenza pandemic of 1918–1920 in the United States using monthly data on births and all-cause deaths for 19 US states in conjunction with data on maternal deaths, stillbirths, and premature births. The data on births and all-cause deaths are adjusted for seasonal and trend effects, and the residual components of the 2 time series coinciding with the timing of peak influenza mortality are examined for these sequelae. Notable findings include: 1) a drop in births in the 3 months following peak mortality; 2) a reversion in births to normal levels occurring 5–7 months after peak mortality; and 3) a steep drop in births occurring 9–10 months after peak mortality. Interpreted in the context of parallel data showing elevated premature births, stillbirths, and maternal mortality during times of peak influenza mortality, these findings suggest that the main impacts of the 1918–1920 influenza on reproduction occurred through: 1) impaired conceptions, possibly due to effects on fertility and behavioral changes; 2) an increase in the preterm delivery rate during the peak of the pandemic; and 3) elevated maternal and fetal mortality, resulting in late-term losses in pregnancy.

1918; deaths; fertility; influenza; mortality; pandemic; preterm births; United States

Accounting for an estimated 675,000 deaths in the United States and 50 million deaths worldwide, the 1918–1920 influenza pandemic dealt a severe blow to populations across the world (1). While the mortality effects of the pandemic have received substantial attention, its effects on a second key demographic driver—births—are not well studied. Yet we know that epidemic influenza had profound impacts on those planning to get pregnant, pregnant women, and fetal outcomes. For example, a 1919 study of maternal mortality during the pandemic found that “in cases complicated by pneumonia, 50 percent of patients died.” (2, p. 980) (see also Titus and Jamison (3)). In addition, a report from the Bureau of the Census revealed a noticeable decline in the birth rate in 1919 (4), suggesting that, even after adjusting for maternal deaths, births declined.

Viewed in this context, an understanding of the associations between the pandemic and subsequent patterns of births can shed light on a variety of significant health phenomena: 1) the risks posed to the developing fetus from the influenza virus (5); 2) the implications of infection for preterm births and preparedness for such outcomes; 3) vaccination policy for pregnant women; 4) effects of infection on fertility (6); and 5) possible behavioral interruptions that may affect conceptions in a time of widespread illness (7–9). The aim of this paper is to explore the short-term birth sequelae of the influenza pandemic of 1918–1920 in the United States with a view to parsing out the various mechanisms, listed above, linking influenza to subsequent births. In order to ascertain the robustness of the findings, we examined not only the well-recognized October 1918 wave of the pandemic but also the subsequent and hitherto ignored February 1920 wave.

METHODS

Data

In order to explore associations between the 1918–1920 influenza pandemic and patterns of births, we collected state-level time-series data on monthly births and all-cause deaths for the years 1916–1921, for a total of 72 observations for each series for each state. We chose to use excess all-cause deaths rather than deaths from respiratory illnesses as an indicator of the timing of the pandemic for 2 reasons. First, the toll of the pandemic was manifested by elevated mortality from a long list of causes. A report from Massachusetts, for example, listed 85 different conditions as possible causes of pandemic-related mortality, among them influenza, 3 types of pneumonia, tuberculosis, meningitis, heart disease, and “accidents” of pregnancy and labor (10, p. 180–89). Second, the
states that reported monthly statistics on mortality from respiratory diseases did not do so in a uniform manner.

Most US states were not part of the national births and deaths registration area by 1918 (11, 12). Therefore, we used monthly data on deaths and births for the 19 states that had joined the registration area by 1917 to study these patterns (Table 1). This balanced the need for data from a geographically diverse array of states with the need for including a mix of pre- and postpandemic data with which to establish baseline patterns of births and deaths. These data were obtained from birth and mortality statistics produced by the US Bureau of the Census (4, 11–20).

We also used a geographically and temporally sparse set of monthly data on numbers of preterm births, mortality from preterm births, stillbirths, and maternal mortality to interpret the findings on births and deaths (10, 21–28; Table 2).

A common limitation of data on births and deaths is underreporting. However, the emphasis of this paper is not on the number of births and deaths but rather on the timing of peaks and troughs in births and deaths. Therefore, even if births and deaths were being systematically underreported, significant one-time fluctuations would be captured in the data, as evidenced by the October 1918 and February 1920 spikes in mortality (Figure 1A–1D).

Statistical methods

The original monthly time-series data on deaths and births were decomposed into 3 components using the SAS (SAS Institute, Inc., Cary, North Carolina) PROC X12 seasonal decomposition algorithm (29, 30) with outlier detection. These included the seasonal (wavelength of 12 months), trend (long wavelength), and irregular (residual or nonseasonal/nontrend) components. This method is appropriate for filtering out those components of births and deaths that were attributable to systematic seasonal (such as seasonal influenza) or trend (such as long-term improvements

| State          | Population in 1910 (59) | Population in 1920 (60) | Geographic Region (61) | Subregion (61) |
|----------------|-------------------------|-------------------------|------------------------|--------------|
| Connecticut    | 1,114,756               | 1,380,631               | Northeast              | New England  |
| Indiana        | 2,700,876               | 2,930,390               | Midwest                | East North Central |
| Kansas         | 1,690,949               | 1,769,257               | Midwest                | West North Central |
| Kentucky       | 2,289,905               | 2,416,630               | South                  | East South Central |
| Maine          | 742,371                 | 768,014                 | Northeast              | New England  |
| Maryland       | 1,295,346               | 1,449,661               | South                  | South Atlantic |
| Massachusetts  | 3,366,416               | 3,852,356               | Northeast              | New England  |
| Michigan       | 2,810,173               | 3,668,412               | Midwest                | East North Central |
| Minnesota      | 2,075,708               | 2,387,125               | Midwest                | West North Central |
| New Hampshire  | 430,572                 | 443,083                 | Northeast              | New England  |
| New York       | 9,113,614               | 10,385,227              | Northeast              | Middle Atlantic |
| North Carolina | 2,206,287               | 2,559,123               | South                  | South Atlantic |
| Ohio           | 4,767,121               | 5,759,394               | Midwest                | East North Central |
| Pennsylvania   | 7,665,111               | 8,720,017               | Northeast              | Middle Atlantic |
| Utah           | 373,351                 | 449,396                 | West                   | Mountain      |
| Vermont        | 355,956                 | 352,428                 | Northeast              | New England  |
| Virginia       | 2,061,612               | 2,309,187               | South                  | South Atlantic |
| Washington     | 1,141,990               | 1,356,621               | West                   | Pacific       |
| Wisconsin      | 2,333,860               | 2,632,067               | Midwest                | East North Central |

| Variable                  | Location                      |
|---------------------------|-------------------------------|
|                           | Buffalo, New York             | State of New York | State of Massachusetts |
| Premature births          | 1917, 1918, 1919               |                  |                        |
| Prematurity-associated deaths | 1917, 1920                   | 1917, 1918, 1919, 1920 |
| Stillbirths                | 1917, 1918, 1919               |                  |                        |
| Childbirth-associated deaths | 1917, 1920                   | 1917, 1918, 1919, 1920 |
in life-saving health interventions) phenomena, bringing into focus one-time events such as the influenza pandemic. The irregular component of the death series was used as the measure of excess deaths associated with the pandemic. We applied the same methods to the birth data and examined the irregular component of the birth data in the (temporal) vicinity of the pandemic for anomalies whose timing may have been associated with the pandemic. The algorithm provided satisfactory results for the birth data for all 19 states. However, for 7 of the 19 states, the decomposition algorithm allocated a large portion of the excess deaths to the trend component rather than the irregular component. This misallocation occurred for states for which the mortality peak occurred for an extended period of time (2 or 3 months, rather than the more commonly observed 1 month), resulting in the algorithm treating a portion of the deaths occurring at that time as regular. In these cases, the influenza-attributable deaths were computed as the sum of the trend and irregular components of the original series (henceforth “seasonally adjusted” mortality) rather than just the irregular (henceforth “excess” mortality) component, bringing the data into alignment with the data for the other 12 states.

RESULTS

Table 3 provides a summary of the results for the 19 US states considered. Figure 1A–1D shows patterns of excess deaths and births occurring at the time of the pandemic for the 4 states with the highest numbers of excess deaths, estimated using only the irregular component of the original series (New York, Pennsylvania, Massachusetts, and Maryland). These are states for which birth-related sequelae are most likely to be detectable given the greater impact of the pandemic in terms of lives lost and, presumably, infections. The first point to note is how similar the graphs are for the 4 states. All 4 states experienced a major excess mortality peak in October 1918, followed by a second and smaller excess mortality peak in February 1920. The immediate aftermath of the October 1918 mortality peak was marked by a dip in births, followed by a noticeable spike in births peaking at 6 months after the excess mortality peak, and then followed by a precipitous drop in births in July 1919, 9 months after the October 1918 mortality peak. This last phenomenon is also discernible for the United States as a whole in a graph published in the Birth Statistics report of 1921 (4), reproduced here.
Table 3. Summary of Results on Timing of Influenza-Attributable Excess Deaths and Deficit or Excess Births for 19 States in the United States, 1918

| State         | Peak Month            | Excess Deaths | Excess or Deficit Births | Lag (in Months) Between Mortality Peak and Change in Births |
|---------------|-----------------------|---------------|--------------------------|------------------------------------------------------------|
|               | Peak Deaths,          | Lowest Month  | Deficit No. at           | Excess No. at Peak of Spike, Irregular Only (Trend Excluded) | Dip      | Spike |
|               | Seasonally Adjusted   | of Dip        | Lowest Month, Irregular  | Excess as % of All Births                                  |          |       |
|               | (Trend Included), No. |               | Only (Trend Excluded)    |                                                             |          |       |
|               |                       |               |                          |                                                             |          |       |
| Connecticut   | October 1918          | 7,589         | July 1919                | −356                                                       | May 1919 | 216   |
|               |                       | 5,489         |                          | 15                                                         | May 1919 | 216   |
| Indiana       | October to December   | 16,884        | −566                     | 12                                                         | March 1919 | 154   |
|               | 1918                   | 9,916         | August 1919              | 10                                                         | March 1919 | 154   |
| Kansas        | October to December   | 9,916         | −297                     | 10                                                         | March 1919 | 154   |
|               | 1918                   | 12,399        | August 1919              | 8                                                          | March 1919 | 154   |
| Kentucky      | October to November   | 2,742         | −181                     | 16                                                         | May 1919   | 245   |
|               | 1918                   | 1,524         | August 1919              | 16                                                         | May 1919   | 245   |
| Maine         | October 1918          | 9,147         | −236                     | 10                                                         | April 1919  | 427   |
| Maryland      | October 1918          | 17,273        | −827                     | 13                                                         | April 1919  | 219   |
| Massachusetts | October to December   | 19,481        | −553                     | 13                                                         | April 1919  | 219   |
|               | 1918                   | 12,055        | August 1919              | 8                                                          | April 1919  | 261   |
| Michigan      | October to December   | 9,489         | −424                     | 11                                                         | April 1919  | 236   |
|               | 1918                   | 1,934         | August 1919              | 11                                                         | April 1919  | 236   |
| Minnesota     | October to November   | 2,555         | −71                      | 12                                                         | May 1919    | 261   |
|               | 1918                   | 1,934         | July 1919                | 12                                                         | May 1919    | 261   |
| New York      | October 1918          | 45,333        | −1,403                   | 8                                                          | April 1919  | 817   |
| North Carolina| October 1918          | 8,721         | −330                     | 6                                                          | April 1919  | 447   |
| Ohio          | October to December   | 37,370        | −673                     | 7                                                          | April 1919  | 515   |
|               | 1918                   | 13,600        | August 1919              | 7                                                          | April 1919  | 515   |
| Pennsylvania  | October 1918          | 48,938        | −2,512                   | 17                                                         | April 1919  | 1,172 |
| Utah          | October to November   | 2,097         | −188                     | 10                                                         | June 1919   | 92    |
|               | 1918                   | 1,208         | July to August 1919      | 10                                                         | June 1919   | 92    |
| Vermont       | October 1918          | 1,715         | −38                      | 7                                                          | March to April 1919 | 60  |
| Virginia      | October 1918          | 8,974         | −321                     | 7                                                          | April 1919  | 142   |
| Washington    | October to December   | 7,276         | −65                      | 2                                                          | May 1919    | 125   |
|               | 1918                   | 5,523         | July to August 1919      | 2                                                          | May 1919    | 125   |
| Wisconsin     | October to December   | 14,481        | −439                     | 10                                                         | May 1919    | 125   |
|               | 1918                   | August 1919   | −439                     | 10                                                         | May 1919    | 125   |

a Sum for multiple months.
as Figure 2. These findings extend to the other states examined, albeit with more variability as states with lower numbers of deaths are included in the sample, as follows:

1. There is a depression in births for 3 months after peak mortality (Figure 1A–1D).

2. There is an apparent spike in births occurring 5–7 months after peak mortality. This phenomenon is seen in 15 of the 19 states. The (arithmetic) mean size of the spike in births in percentage terms across the states is 6% (Table 3). This spike occurs uniformly between March and June 1919; for 10 of the 15 states, it occurs in April 1919 (Table 3). For the 6 largest states (in terms of seasonally adjusted as well as excess mortality), this peak uniformly occurs 6 months after the mortality peak, in April 1919 (Table 3).

3. There is a notable depression in births occurring 9–10 months after peak mortality in all 19 states analyzed. The (arithmetic) mean size of the dip in births in percentage terms across the states is 10% (Table 3), which is related to the decline in the birth rate seen in 1919 in Figure 2, from approximately 23 per 1,000 population to 20 per 1,000 population or 13%. This dip occurs uniformly in July or August 1919 (Table 3).

An additional notable finding is that the fall 1918 mortality wave was followed in early 1920 by another wave. This 1920 wave, although also noted in Chile, Japan, Scandinavia, and Taiwan, has not been closely examined in the context of the United States or much of Europe (1, 8, 9, 31). Although the data show that the 1920 wave was less severe than the 1918 wave in most (but not all) locations, it was widespread and reported in both the domestic and international press (32–35). In addition to the states for which we have data, a number of others also experienced the 1920 wave, including Texas and Hawaii (36–38). A *Manchester Guardian* headline referred to “the American influenza epidemic” on January 23, 1920 (35), although press reports indicate that the 1920 wave struck Europe as well (39, 40).

Our analysis found that the 1920 wave occurred in February in 17 of the 19 states for which we have data, and in February and March in the remaining 2 (Table 4). Interestingly, here again we observe 2 dips in births, the first during the 3 months immediately following the February 1920 mortality peak and then again 9 months after the peak (Table 4 and Figure 1A–1D).

**DISCUSSION**

The effects of influenza on reproductive outcomes can take many forms, only some of which can be directly monitored in vital data of the time. Early fetal deaths are not recorded in any vital data system, and during the period of interest, stillbirths were only occasionally recorded on a monthly basis (10, 21–28). Monthly infant deaths were frequently distinguished in vital data, as were childbirth-associated maternal deaths. Therefore, while monitoring some of the direct effects of reproductive damage from the influenza of 1918 is possible, for other effects it remains difficult.
A few authors have examined birth rates in periods surrounding the peak mortality of the epidemic in an attempt to infer the likely effect of the epidemic on the course of pregnancy (5–9). However, ambiguities necessarily attend such an exercise. For example, the US Army was at war in Europe during the height of the pandemic. In November 1918, the draft and mobilization were at full capacity. By May 1918, hundreds of thousands of troops were deploying overseas monthly (41). The extensive mobilization process feeding this system had to be reversed over the course of winter 1918–1919. Thus, troops from overseas did not return in large numbers until late spring and summer 1919, with the last division arriving in September 1919 (42). Based on this chronology, we would expect a steady decline in births starting 9 months after the first sizeable deployments. Such a drawdown would be captured and filtered out in the trend component of the time series. Notably, the draft appears to have had only a slight impact on the birth rate (43) and, as Table 5 shows, there is no evidence in US birth rate statistics of a baby boom in the aftermath of the war.

More important for the purposes of this study, a deficit of births in relation to the epidemic could arise from voluntary postponement due to fear of infection or not wishing to infect the spouse, failure to conceive because of illness or spousal death from influenza or spousal separation associated with the war, from maternal death while pregnant, from fetal death, from preterm birth, or from any combination of these adversities. The timing of the birth deficit, however, might differ among these outcomes. If we use the time of peak mortality as the time when the strongest effects of influenza were felt on men or women of reproductive age, then a deficit of births 9 months later would likely indicate impaired fertility. If the effect on births were partly because of maternal deaths in pregnancy, the deficit in births would be observed whenever, in gestation, influenza during pregnancy was most lethal. The literature of the time (2, 3, 44) suggests that the largest maternal mortality effect occurred in the third trimester of pregnancy, often shortly after delivery of a stillborn infant near term but sometimes without the mother going into labor. Such patterns would be likely to manifest as a birth deficit within the first few months after peak mortality. This phenomenon is also visible in Figure 1A–1D.

The timing of a deficit of births in relation to an effect of influenza on miscarriage or fetal death without maternal death is likely

### Table 4. Summary of Results on Timing of Influenza-Attributable Excess Deaths and Deficit Births for 19 States of the United States, 1920 Wave

| State      | Peak Month | Peak Deaths, Seasonally Adjusted (Trend Included), No. | Peak Deaths, Irregular Only (Trend Excluded), No. | Lowest Month of Dip | Deficit No. at Lowest Month, Irregular Only (Trend Excluded), No. | Deficit as % of All Births | Lag Between Mortality Peak or Dip in Births, months |
|------------|------------|------------------------------------------------------|-------------------------------------------------|---------------------|-----------------------------------------------------------------|---------------------------|-----------------------------------------------|
| Connecticut| February   | 2,680                                                | 1,188                                           | November            | −55                                                             | 2                         | 9                                             |
| Indiana    | February   | 5,348                                                | 2,056                                           | December            | −150                                                            | 3                         | 10                                            |
| Kansas     | February   | 3,172                                                | 1,647                                           | November            | −189                                                            | 6                         | 9                                             |
| Kentucky   | February   | 7,201                                                | 2,056                                           | December            | −415                                                            | 10                        | 9–10                                          |
| Maine      | February   | 1,668                                                | 739                                             | December            | −40                                                             | 3                         | 10                                            |
| Maryland   | February   | 2,949                                                | 1,268                                           | October             | −101                                                            | 4                         | 8–9                                           |
| Massachusetts| February | 7,011                                                | 2,710                                           | October             | −154                                                            | 2                         | 8                                             |
| Michigan   | February   | 8,645                                                | 4,163                                           | November            | −379                                                            | 4                         | 9                                             |
| Minnesota | February   | 3,724                                                | 1,670                                           | November            | −429                                                            | 11                        | 9                                             |
| New Hampshire| February | 808                                                  | 283                                             | September           | −15                                                             | 2                         | 7                                             |
| New York   | February   | 19,141                                               | 7,867                                           | November            | −373                                                            | 2                         | 9                                             |
| North Carolina| February | 4,689                                                | 2,259                                           | November            | −345                                                            | 6                         | 9                                             |
| Ohio       | February   | 11,084                                               | 4,936                                           | October             | −350                                                            | 4                         | 8                                             |
| Pennsylvania| February | 17,896                                               | 8,609                                           | October             | −401                                                            | 2                         | 8                                             |
| Utah       | February   | 1,009                                                | 636                                             | November            | −96                                                             | 9                         | 9                                             |
| Vermont    | February   | 1,265                                                | 636                                             | November            | −25                                                             | 5                         | 8–9                                           |
| Virginia   | February   | 4,101                                                | 1,795                                           | December            | −161                                                            | 3                         | 10                                            |
| Washington | February   | 2,336                                                | 1,134                                           | November            | −172                                                            | 9                         | 9                                             |
| Wisconsin | February   | 4,319                                                | 1,975                                           | November            | −254                                                            | 6                         | 9                                             |

* a Sum for both months.
* b Figure for October 1920: −314.
* c Figure for October 1920: −344.
* d Figure for December 1920: −228.
* e Figure for November 1920: −140.
to be highly variable, depending on when in gestation the principal effect occurred. In reports at the time, pregnancy losses without maternal death seemed for the most part evenly distributed throughout pregnancy (3, 44). This contrasts with the ordinary pattern of pregnancy losses, where first trimester losses exceed later stillbirths by an order of a magnitude. One must keep in mind, however, that the earliest losses were more likely to remain unreported. If influenza increased preterm birth, then one might see an excess of preterm deliveries during the peak mortality, followed by an equivalent deficit in subsequent months.

With these considerations in mind, we now turn to the available monthly data on 4 phenomena: preterm births, deaths attributable to preterm births, stillbirths, and childbirth-associated maternal deaths. Figures 3A–3C, 4, and 5 demonstrate that all 4 numbers spiked during the October 1918 or February 1920 pandemic mortality waves. Viewed in the context of these observations, we offer the following interpretations.

Observation 1

There was a drop in births in the 3 months following each of the mortality peaks of October 1918 and February 1920.

Interpretation: This phenomenon is consistent with the observed excess of preterm births and prematurity-associated mortality during the pandemic (Figures 3A, 4, and 5). Reports of the course of pandemic influenza in pregnancy in recent epidemics have indicated increases in premature labor and preterm births in women with severe disease, in some but not all epidemics (3, 44). The severe Asian influenza of 1957 produced few reports of pregnancy complications. One exception was a series of some 700 pregnant women in Baltimore monitored monthly for influenza symptoms and seroconversion (45). Approximately 83% of the women were found to be seropositive for influenza A/Japan/305-57, with peaks of both reported symptoms and positive serology in October 1957. An overall relative risk of preterm birth of 1.6 (not significant) compared with uninfected women was found, but if infection occurred in the first trimester, the relative risk was 2.4 ($P < 0.05$).

Neonatal mortality rates are greatly influenced by prematurity rates, and further evidence for an effect of influenza on prematurity is seen in a report of elevated neonatal mortality in the United Kingdom in the first half of 1970, especially the first quarter of that year (46). This elevated mortality was linked to the severe Asian influenza (A2, Hong Kong variant) of the winter of 1969–1970. The British report found both an increase in mortality diagnostic codes linked to prematurity and increases in low birthweight prevalence in several parts of the United Kingdom that paralleled the neonatal mortality increase.

Table 5. Birth Rate According to Year, United States, 1916–1921

| Year | Birth Rate per 1,000 Population |
|------|-------------------------------|
| 1916a | 24.8                          |
| 1917b | 24.6                          |
| 1918b | 24.4                          |
| 1919b | 22.3                          |
| 1920b | 23.7                          |
| 1921b | 24.3                          |

a Source is Bureau of the Census, 1921 (14).
b Source is Bureau of the Census, 1922 (15).
The occurrence of this excess neonatal mortality only months after the epidemic peak was interpreted as further evidence for an effect on preterm birth. Interestingly, no increase in neonatal mortality was found in UK vital data in relation to 4 earlier severe influenza epidemics in the United Kingdom (1951, 1953, 1959, and 1961). A French report also linked the 1969–1970 influenza to an increase in prematurity (47), but the effect of the Hong Kong influenza on neonatal mortality in other countries was mixed (46), with increases similar to those found in the United Kingdom in New York City, Scotland, Germany, and the Netherlands. However, there were no changes in prematurity rates in Poland or Ireland.

The 2009 pandemic A/H1N1 influenza is the most studied pandemic in recent history. Numerous reports from that epidemic have reported substantial increases in preterm birth, with relative risk ranging from 2 to 5 (48–54), and several series described prematurity rates above 30%. This effect, however, was largely restricted to hospitalized or severely ill pregnant patients. Studies reflecting the general-population experience showed little or no increase in preterm birth (55, 56). The 1918–1919 experience, in which the number of severely affected women was very high, appears to be compatible with the increases in preterm birth found in severely affected women during some pandemics of recent years, especially the pandemics of 1969 and 2009, although the number of severely affected cases in 2009 was apparently too few to change the overall prematurity rate in the general population.

In addition to elevated preterm deliveries, fetal loss coinciding with the pandemic could explain a deficit in births in the first few months after peak mortality if the infection had occurred in the third trimester of pregnancy (i.e., producing stillbirths (Figures 3B and 4) and not early fetal losses). Contemporary accounts of the course of influenza in pregnancy also uniformly describe high maternal mortality, often occurring late in pregnancy, with concomitant fetal loss shortly before death (2, 3, 44, 57; Figures 3C and 5). Thus, this early drop in births may have reflected a combination of preterm births and stillbirths associated with maternal deaths. Among women who died from influenza in pregnancy, only a small fraction appear to have delivered a live infant (2, 3, 44, 57).

**Observation 2**

There was a noticeable spike in births occurring 5–7 months after peak mortality. This phenomenon was seen in 15 of the 19 states. For the 6 worst affected states (in terms of seasonally adjusted as well as excess mortality), this peak uniformly occurred 6 months after the mortality peak.

Interpretation: This spike reflects a reversion in the direction of normal levels of births for a brief period between the declines in births immediately following the pandemic (observation 1, above) and the subsequent drop 8–10 months after the pandemic (observation 3, below). The seasonal adjustment algorithm identifies this mean reversion as a spike (i.e., excess births) because it is observed against the backdrop of lower levels of births in the preceding and subsequent months. Yet evidence from both birth statistics and birth rates shows that this “spike” merely brought these numbers back into the normal range (see, for example the data for the spring of 1919 in Figure 2).

**Observation 3**

There was a notable dip in births occurring 8–10 months after peak mortality in 18 of the 19 states analyzed with Washington, the exception, showing a dip 7–10 months after the mortality peak.

Interpretation: This suggests that primary infertility was produced by the epidemic, with fewer conceptions for either behavioral or biological reasons. This dip in births 9 months after the peak mortality month parallels findings on Japan, Taiwan, and Norway (6–9). The behavioral reasons for a drop in conceptions during the peak of the epidemic in October 1918 include voluntary postponement of conceptions due to fear from the pandemic and a wish not to infect the spouse and, among couples not pregnant, spousal sickness or death (6, 7). A biological reason for a decline in conception was the temporary sterility reported among men (but not women) infected by influenza (58).
Conclusion

From our analysis of nationally disaggregated data on pandemic activity, stillbirths, birth rates, preterm births, deaths from preterm births, and childbirth-associated mortality from both the October 1918 and the February 1920 waves of the influenza pandemic, we can conclude, first, that the major impact of the pandemic on reproduction was felt through impaired conceptions. The degree to which this phenomenon can be attributed to effects on fertility and behavioral changes is a topic for future research. Second, a combined phenomenon of elevated preterm delivery and mortality, maternal mortality, and fetal mortality was observed coinciding with peak influenza mortality, followed by a natality depression in the 3 months immediately following the pandemic peaks. This shows that significant fetal losses occurred late in pregnancy. Third, we do not see evidence in these data for early pregnancy loss as hypothesized in earlier research (5), which used nationally aggregated data on pandemic activity, stillbirths, and birth rates to find a natality depression that reached its nadir 6.1–6.8 months after peak influenza activity and concluded that first-trimester miscarriages were responsible for this phenomenon. In other words, the risks posed to the developing fetus from the influenza virus in 1918 and 1920 appear to have stemmed primarily from the mechanisms of maternal mortality, preterm delivery, and fetal infection. These risks could have important implications for vaccination policies relating to pregnant women, indicating the need for a second line of research emerging from our findings.

ACKNOWLEDGMENTS

Author affiliations: Asian Studies Center, Michigan State University, East Lansing, Michigan (Siddharth Chandra, Julia Christensen); James Madison College, Michigan State University, East Lansing, Michigan (Siddharth Chandra, Julia Christensen); Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, Michigan (Siddharth Chandra, Nigel Paneth); and Work Research Institute, Oslo Metropolitan University, Oslo, Norway (Svenn-Erik Mamelund).

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. S. C. and J. C. gratefully acknowledge financial support from Michigan State University’s James Madison College and International Studies and Programs.

Conflict of interest: none declared.

REFERENCES

1. Johnson NP, Mueller J. Updating the accounts: global mortality of the 1918–1920 “Spanish” influenza pandemic. Bull Hist Med. 2002;76(1):105–115.
2. Harris J. Influenza occurring in pregnant women: a statistical study of thirteen hundred and fifty cases. JAMA. 1919; 72(14): 978–980.
3. Titus P, Jamison J. Pregnancy complicated by epidemic influenza. JAMA. 1919;72(23):1665–1668.
4. Bureau of the Census. Birth Statistics for the Registration Area of the United States 1921. Washington, DC: Government Printing Office; 1923. https://babel.hathitrust.org/cgi/pt?id=hvd.li4xns;view=1up;seq=3. Accessed December 9, 2018.
5. Bloom-Feshbach K, Simonsen L, Viboud C, et al. Natality decline and miscarriages associated with the 1918 influenza pandemic: the Scandinavian and United States experiences. J Infect Dis. 2011;204(8):1157–1164.
6. Mamelund SE. Can the Spanish influenza pandemic of 1918 explain the baby boom of 1920 in neutral Norway? Population (Engl Ed). 2004;59(2):229–260.
7. Mamelund SE. Fertility fluctuations in times of war and pandemic influenza. J Infect Dis. 2012;206(1):140–141.
8. Chandra S, Yu YL. Fertility decline and the 1918 influenza pandemic in Taiwan. Biodemography Soc Biol. 2015;61(3):266–272.
9. Chandra S, Yu YL. The 1918 influenza pandemic and subsequent birth deficit in Japan. Demogr Res. 2015;33(11):313–326.
10. Office of the Secretary of the Division of Vital Statistics, The Commonwealth of Massachusetts. Seventy-Seventh Annual Report of the Vital Statistics of Massachusetts: Births, Marriages, Divorces, and Deaths for the Year 1918. Boston, MA: Wright & Potter Printing Co., State Printers; 1920. https://babel.hathitrust.org/cgi/pt?id=uc1.b5327610;view=1up;seq=5. Accessed June 16, 2018.
11. Bureau of the Census. Birth Statistics for the Registration Area of the United States 1917. Third Annual Report. Washington, DC: Government Printing Office; 1919. https://babel.hathitrust.org/cgi/pt?id=uiu1.b312051430939;view=1up;seq=3. Accessed November 30, 2018.
12. Bureau of the Census. Mortality Statistics 1917: Eighteenth Annual Report. Washington, DC: Government Printing Office; 1919. https://babel.hathitrust.org/cgi/pt?id=msu.31293008112728. Accessed December 2, 2017.
13. Bureau of the Census. Birth Statistics for the Registration Area of the United States 1918. Fourth Annual Report. Washington, DC: Government Printing Office; 1920. https://babel.hathitrust.org/cgi/pt?id=uiu1.b312051430939;view=1up;seq=3. Accessed November 30, 2018.
14. Bureau of the Census. Birth Statistics for the Registration Area of the United States 1919. Washington, DC: Government Printing Office; 1921. https://babel.hathitrust.org/cgi/pt?id=hvd.li4xnr;view=1up;seq=3. Accessed December 1, 2017.
15. Bureau of the Census. Birth Statistics for the Registration Area of the United States 1920. Washington, DC: Government Printing Office; 1922. https://babel.hathitrust.org/cgi/pt?id=hvd.li4xnr;view=thumb;seq=1. Accessed December 1, 2017.
16. Bureau of the Census. Mortality Statistics 1918: Nineteenth Annual Report. Washington, DC: Government Printing Office; 1920. https://babel.hathitrust.org/cgi/pt?id=msu.31293008112736;view=thumb;seq=1. Accessed December 2, 2017.
17. Bureau of the Census. Mortality Statistics 1919: Twentieth Annual Report. Washington, DC: Government Printing Office; 1921. https://babel.hathitrust.org/cgi/pt?id=msu.31293008112744;view=thumb;seq=1. Accessed December 2, 2017.
18. Bureau of the Census. Mortality Statistics 1920: Twenty-First Annual Report. Washington, DC: Government Printing Office; 1922. https://babel.hathitrust.org/cgi/pt?id=msu.31293008112751. Accessed December 2, 2017.
19. Bureau of the Census. Mortality Statistics 1921: Twenty-First Annual Report. Washington, DC: Government Printing Office; 1923. https://babel.hathitrust.org/cgi/pt?id=uiu1.c3036838;view=thumb;seq=9. Accessed December 2, 2017.
20. Bureau of the Census. Special Tables of Mortality from Influenza and Pneumonia in Indiana, Kansas, and Philadelphia, Pa. September 1 to December 31, 1918. Washington DC: Government Printing Office; 1920. https://babel.hathitrust.org/cgi/pt?id=coo1.ark:/13960/t1fc5s4q;view=thumb;seq=1. Accessed December 14, 2017.

21. New York State Department of Health. Thirty-eighth Annual Report of the State Department of Health of New York, Volume 1. Albany, NY: J.B. Lyon Company, Printers; 1918. https://babel.hathitrust.org/cgi/pt?id=uc1.3063665;view=1up;seq=262. Accessed June 13, 2018.

22. New York State Department of Health. Forty-first Annual Report of the State Department of Health of New York, Volume 1. Albany, NY: J.B. Lyon Company, Printers; 1922. https://babel.hathitrust.org/cgi/pt?id=uc1.3063665;view=1up;seq=262. Accessed June 13, 2018.

23. Buffalo Department of Health. Buffalo Sanitary Bulletin, 1917. Buffalo, NY: Buffalo Department of Health; 1917. https://babel.hathitrust.org/cgi/pt?id=uiug.30112111808173;view=1up;seq=18. Accessed June 14, 2018.

24. Buffalo Department of Health. Buffalo Sanitary Bulletin, 1918. Buffalo, NY: Buffalo Department of Health; 1919. https://babel.hathitrust.org/cgi/pt?id=uiug.30112111808173;view=1up;seq=18. Accessed June 14, 2018.

25. Buffalo Department of Health. Buffalo Sanitary Bulletin, 1919. Buffalo, NY: Buffalo Department of Health; 1920. https://babel.hathitrust.org/cgi/pt?id=uiug.30112111808173;view=1up;seq=18. Accessed June 14, 2018.

26. Office of the Secretary of the Division of Vital Statistics, The Commonwealth of Massachusetts. Seventy-Sixth Annual Report of the Vital Statistics of Massachusetts: Births, Marriages, Divorces, and Deaths for the Year 1917. Boston, MA: Wright & Potter Printing Co., State Printers; 1920. https://babel.hathitrust.org/cgi/pt?id=mdp.39015067927635;view=1up;seq=5. Accessed June 16, 2018.

27. Office of the Secretary of the Division of Vital Statistics, The Commonwealth of Massachusetts. Annual Report on the Vital Statistics of Massachusetts: Births, Marriages, Divorces, and Deaths for the Year Ending December 31, 1919. Boston, MA: Wright & Potter Printing Co., State Printers; 1921. https://babel.hathitrust.org/cgi/pt?id=mdp.39015067927650;view=1up;seq=167. Accessed June 16, 2018.

28. Office of the Secretary of the Division of Vital Statistics, The Commonwealth of Massachusetts. Annual Report of the Vital Statistics of Massachusetts: Births, Marriages, Divorces, and Deaths for the Year Ending December 31, 1920. Boston, MA: Wright & Potter Printing Co., State Printers; 1922. https://babel.hathitrust.org/cgi/pt?id=mdp.39015067927676;view=thumb;seq=5. Accessed June 16, 2018.

29. Dagum E. The X-11-ARIMA Seasonal Adjustment Method. Ottawa, Canada: Statistics Canada; 1982. https://www.census.gov/sip/papers/1980X11ARIMAManual.pdf. Accessed June 13, 2018.

30. SAS Institute, Inc. SAS/ETS 14.1 User’s Guide. Cary, NC: SAS Institute, Inc.; 2015. https://support.sas.com/documentation/onlinedoc/ets/141/x12.pdf. Accessed April 18, 2018.

31. Chowell G, Simonsen L, Flores J et al. Death patterns during the 1918 influenza pandemic in Chile. Emerg Infect Dis. 2014; 20(11):1803–1811.

32. Evans W. How to keep well: flu wave receding. Chicago Daily Tribune. March 11, 1920.6

33. 2,551 more Chicago cases: influenza also spreads in New Jersey and Delaware. New York Times. January 24, 1920.4

34. Grip is showing steady spread: increase in disease reported in all states; death toll is increasing. Courier-Journal. January 30, 1920.8

35. The American influenza epidemic. The Manchester Guardian. January 23, 1920:11

36. Spreading of malady is seen as health officials issue report on influenza: supply of nurses said to be “adequate.” Cincinnati Enquirer. January 31, 1920:2.

37. Mamelund SE. Geography may explain adult mortality from the 1918–20 influenza pandemic. Epidemics. 2011;3(1):46–60.

38. Schmitt RC, Nordyke EC. Influenza deaths in Hawai’i, 1918–1920. Hawaiian J Hist. 1999;33:101–117.

39. Virulent influenza sweeping Poland. The Atlanta Constitution. January 19, 1920:2

40. Renwick G. Influenza affects Berlin: of a more virulent type than in 1918. New York Times. February 15, 1920:14.

41. Centers for Disease Control and Prevention. 1918 Pandemic Influenza Historic Timeline. https://www.cdc.gov/flu/pandemic-resources/1918-commemoration/pandemic-timeline-1918.htm. Reviewed March 30, 2018. Updated May 3, 2018. Accessed June 4, 2018.

42. Crowell B, Wilson R. Demobilization: Our Industrial and Military Demobilization After the Armistice, 1918–1920. Vol. 6. New Haven, CT: Yale University Press; 1921.

43. Dublin LI. War and the birth rate—a brief historical summary. Am J Public Health Nations Health. 1945;35(4):315–320.

44. Woolstone W, Conley D. Epidemic pneumonia (Spanish influenza) in pregnancy: effect in one hundred and one cases. JAMA. 1918;71(23):1898–1899.

45. Hardy JM, Azarowicz EN, Manmini A, et al. The effect of Asian influenza on the outcome of pregnancy, Baltimore, 1957–1958. Am J Public Health Nations Health. 1961;51(8):1182–1188.

46. Griffith GW, Adelstein AM, Lambert PM, et al. Influenza and infant mortality. Br Med J. 1972;3(5826):553–556.

47. Charvet F, Broussard P. Premature labor and influenza: a recent epidemic. Bull Fed Soc Gynecol Obstet Lang Fr. 1971; 23(3):320–321.

48. Bogers H, Boer K, Duvekot JJ. Complications of the 2009 influenza A/H1N1 pandemic in pregnant women in the Netherlands: a national cohort study. Influenza Other Respir Viruses. 2012;6(5):309–312.

49. Doyle TJ, Goodin K, Hamilton JJ. Maternal and neonatal outcomes among pregnant women with 2009 pandemic influenza A(H1N1) illness in Florida, 2009–2010: a population-based cohort study. PLoS One. 2013;8(10):e79040.

50. Michaan N, Amzallag S, Laskov I, et al. Maternal and neonatal outcome of pregnant women infected with H1N1 influenza virus (swine flu). J Matern Fetal Neonatal Med. 2012;25(2):130–132.

51. Mosby LG, Rasmussen SA, Jamieson DJ. 2009 pandemic influenza A (H1N1) in pregnancy: a systemic review of the literature. Am J Obstet Gynecol. 2011;205(1):10–18.

52. Pierce M, Kurinczuk JJ, Spark P, et al. Perinatal outcomes after maternal 2009/H1N1 infection: national cohort study. BMJ. 2011; 342:d3214.

53. Siston AM, Rasmussen SA, Honein MA, et al. Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. JAMA. 2010;303(15):1517–1525.

54. Yates L, Pierce M, Stephens S, et al. Influenza A/H1N1v in pregnancy: an investigation of the characteristics and management of affected women and the relationship to pregnancy outcomes for mother and infant. Health Technol Assess. 2010;14(34):109–182.
55. Acs N, Bánhidy F, Puhó E, et al. Pregnancy complications and delivery outcomes of pregnant women with influenza. J Matern Fetal Neonatal Med. 2006;19(3):135–140.
56. Fell DB, Platt RW, Basso O, et al. The relationship between 2009 pandemic H1N1 influenza during pregnancy and preterm birth: a population-based cohort study. Epidemiology. 2018;29(1):107–116.
57. Ball M. Abortion as a sequela of influenza. JAMA. 1918;71(16):1336.
58. Biraben J-N. Aspects médicaux et biologiques de la démographie historique. International Population Conference, Liège, IUSSP, 1973;3:9–22.
59. Bureau of the Census. Thirteenth Census of the United States, Taken in the Year 1910: Number and Distribution of Inhabitants. Washington, DC: Government Printing Office; 1913. 26. https://www2.census.gov/library/publications/decennial/1910/volume-1/volume-1-p3.pdf. Accessed June 9, 2018.
60. Bureau of the Census. Fourteenth Census of the United States, Taken in the Year 1920: Number and Distribution of Inhabitants. Washington, DC: Government Printing Office; 1923. 16. https://www2.census.gov/library/publications/decennial/1920/volume-1/41084484v1ch1.pdf. Accessed June 9, 2018.
61. Bureau of the Census, US Department of Commerce. Geographic Terms and Concepts - Census Divisions and Census Regions. https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf. Accessed June 9, 2018.