Reply to Wilson et al

TO THE EDITOR—We thank Wilson et al [1] for their comments on our study of the 1918–1919 influenza pandemic in Kentucky [2]. Our key findings were to provide evidence of break points in the mortality profile of the fall 1918 pandemic wave among individuals aged 9–10 years (ie, cohorts born during 1908–1909) and those aged 24–26 years (ie, cohorts born during 1892–1894) [2]. These age break points do not strictly align with known dates of past pandemic events, and, hence, it is not intuitive that they support or refute the hypothesis proposed by Wilson et al, in which aberrant immune responses mediated by CD8⁺ T cells were more frequent among young adults whose first influenza virus exposures were to the 1889 pandemic virus [1].

In their letter, Wilson et al contribute interesting data on influenza mortality patterns in New Zealand [1]. They report a mortality peak at ages 29–30 years in males and females (ie, cohorts born during 1888–1889), which is more in line with hypotheses invoking the 1889 pandemic than our Kentucky data. These findings could reflect true differences in the pandemic experience of geographically distant populations. Alternatively, the mortality profile in New Zealand could be influenced by a preponderance of influenza risk factors in aboriginal Maori populations or by high variance in mortality estimates due to small population size (approximately 0.85 million). Methodological factors may also contribute to the observed differences between the 2 studies, as our Kentucky analysis relied on “above baseline” excess mortality in the lethal months of October–December 1918 [2]. Future studies could compare the risks profiles of different populations via the excess mortality approach to help tease out influenza-specific effects from unrelated background mortality [3].

Wilson et al note that US population size estimates from this period may be inaccurate, potentially resulting in imprecise death rate estimates—an issue emphasized by an earlier historical study from Canada and the United States [4]. We agree that estimates of male population sizes during wartime are prone to bias because of troop movements. Hence, like Wilson et al, we combined female mortality counts with population information collated from carefully conducted decennial censuses to present a relatively unbiased picture of mortality risk at the time. We have now repeated our analysis with death count data, which we show in parallel with our analysis of excess death rates in Figure 1. Both curves indicate mortality peaks at ages 25–26 years (ie, cohorts born during 1892–1893), consistent across various diagnostic outcomes and in female-specific data. These sensitivity analyses confirm that the Kentucky cohorts at highest risk of influenza-related death were those born a few years after the 1889 pandemic, irrespective of whether we use population denominators.

Overall, our historical analysis provides unprecedented detail on the age
and sex patterns of the pandemic in Kentucky [2]. Similar to Wilson et al [1], we found a substantially increased risk of death among military populations, perhaps due to crowding and/or increased circulation of coinfecting pathogenic bacteria. However, these factors alone cannot account for the mortality risk of the 1918 pandemic among young adult civilian females. While the reasons for the unusual age patterns of the 1918 pandemic are difficult to elucidate from epidemiological data alone, the steep rise in the risk of mortality among individuals aged 10–20 years during the influenza pandemic is worth noting, especially as it consistent in data from New Zealand, Canada, and the United States [1, 2, 4]. Historical morbidity surveys indicate that clinical attack rates were similar in these age cohorts [5], suggesting that the severity of influenza-related infection increased sharply between ages 10 and 20 years, likely because of a heightened risk of pneumonia caused by common bacterial respiratory pathogens (especially pneumococci, streptococci, and staphylococci) [5–7]. People aged 10–20 years had not lived through the 1889 pandemic, although they could have been infected by descendants of the 1889 influenza virus that persisted during 1892–1918.

Although the reasons for the atypical mortality risk profile of the 1918–1919 pandemic may remain elusive, it is important to pursue efforts to analyze archival mortality records from a variety of locations, building upon the work by Wilson et al and others [1, 2, 4, 5, 8, 9]. A systematic epidemiological description of the pandemic in a variety of globally sampled populations may provide unique insights into the host and geographic factors responsible for the unusual severity of disease associated with the 1918 pandemic virus.

Notes

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