

Rapid response was crucial to containing the 1918 flu pandemic

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One of the persistent riddles of the deadly 1918 Spanish influenza pandemic is why it struck different cities with varying severity. Why were some municipalities such as St. Louis spared the fate of the hard-hit cities like Philadelphia when both implemented similar public health measures? What made the difference, according to two independent studies funded by the National Institutes of Health (NIH), was not only how but also how rapidly different cities responded.

Cities where public health officials imposed multiple social containment measures within a few days after the first local cases were recorded cut peak weekly death rates by up to half compared with cities that waited just a few weeks to respond. Overall mortality was also lower in cities that implemented early interventions, but the effect was smaller. These conclusions--the results of systematic analyses of historical data to determine the effectiveness of public health measures in 1918--are described in two articles published online this week in the journal *Proceedings of the National Academy of Sciences*.

“These important papers suggest that a primary lesson of the 1918 influenza pandemic is that it is critical to intervene early,” says Anthony S. Fauci, M.D., director of NIH’s National Institute of Allergy and Infectious Diseases (NIAID), which funded one of the studies. “While researchers are working very hard to develop pandemic influenza vaccines and increase the speed with which they can be made, nonpharmaceutical interventions may buy valuable time at the beginning of a pandemic while a targeted vaccine is being produced.”

The historical analyses are part of an ongoing effort called the Models of Infectious Disease Agent Study (MIDAS), which is supported by NIH's National Institute of General Medical Sciences (NIGMS). Through MIDAS, researchers have developed computer models to examine how a future pandemic influenza virus might spread and what interventions could minimize the impact.

“Although the MIDAS models can't predict the exact spread of a potential influenza pandemic, they have all suggested that introducing public health measures soon after the first cases appear could greatly reduce the number of people who get sick,” says NIGMS Director Jeremy M. Berg, Ph.D. “The historical analyses help validate the models' conclusion and their potential usefulness in preparing for a pandemic.”

The ideal way to contain a potential influenza pandemic would be to vaccinate large numbers of people before they were exposed to an influenza virus strain that is easily transmitted from person to person. Developing such a vaccine in advance, however, is difficult because an influenza virus mutates as it replicates, and over time these mutations can alter the virus enough that older vaccines are no longer effective. With current technologies, it would take months to develop a new vaccine after the first cases of pandemic influenza appear.

Nonpharmaceutical interventions may limit the spread of the virus by imposing restrictions on social gatherings where person-to-person transmission can occur. The first of the two historical studies, conducted by a team of researchers from NIAID, the Department of Veterans Affairs, and the Harvard School of Public Health, looked at 19 different public health measures that were implemented in 17 U.S. cities in the autumn of 1918. The second study, undertaken at Imperial College London, looked at 16 U.S. cities for which both the start and stop dates of interventions were available.

Schools, theaters, churches and dance halls in cities across the country were closed. Kansas City banned weddings and funerals if more than 20 people were to be in attendance. New York mandated staggered shifts at factories to reduce rush hour commuter traffic. Seattle's mayor ordered his constituents to wear face masks. The first study found a clear correlation between the number of interventions applied and the resulting peak death rate seen. Perhaps more importantly, both studies showed that while interventions effectively mitigated the transmission of influenza virus in 1918, a critical factor in how much death rates were reduced was how soon the measures were put in place.

Officials in St. Louis introduced a broad series of public health measures to contain the flu within two days of the first reported cases.

Philadelphia, New Orleans and Boston all used similar interventions, but they took longer to implement them, and as a result, peak mortality rates were higher. In the most extreme disparity, the peak mortality rate in St. Louis was only one-eighth that of Philadelphia, the worst-hit city in the survey. In contrast to St. Louis, Philadelphia imposed bans on public gatherings more than two weeks after the first infections were reported. City officials even allowed a city-wide parade to take place prior to imposing their bans.

If St. Louis had waited another week or two, they might have fared the same as Philadelphia, says the lead author on the first study, Richard Hatchett, M.D., an associate director for emergency preparedness at NIAID. Despite the fact that these cities had dramatically different outcomes early on, all the cities in the survey ultimately experienced significant epidemics because, in the absence of an effective vaccine, the virus continued to spread or recurred as cities relaxed their restrictions.

The second study also shows that the timing of when control measures were lifted played a major part. Cities that relaxed their restrictions after the peak of the pandemic passed often saw the re-emergence of

infection and had to reintroduce restrictions, says Neil Ferguson, D.Phil., of Imperial College, London, the senior author on the second study. In their paper, Dr. Ferguson and his coauthor used mathematical models to reproduce the pattern of the 1918 pandemic in different cities. This allowed them to predict what would have happened if cities had changed the timing of interventions. In San Francisco, which they found to have the most effective measures, they estimate that deaths would have been 25 percent higher had city officials not implemented their interventions when they did. But had San Francisco left its controls in place continuously from September 1918 through May 1919, the analysis suggests, the city might have reduced deaths by more than 90 percent.

The fact that the early, nonpharmaceutical interventions were effective at the height of the pandemic can inform pandemic planners today, the authors of both studies say. In particular, the two studies lend weight to guidance that the Centers for Disease Control and Prevention recently released on the use of nonpharmaceutical interventions during a pandemic

(<http://www.pandemicflu.gov/plan/community/mitigation.html>), which recommends precisely such a rapid early response.

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