Pandemic flu may be well mitigated until vaccine is available

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An outbreak of pandemic influenza in the U.S. could be mitigated with prompt implementation of social-distancing measures combined with antiviral treatment and prophylaxis until a vaccine is available, according to new findings published in the online Early Edition of *PNAS*.

Working closely with federal officials, three teams of researchers in the United States and England collaboratively studied various intervention combinations to guide national pandemic planning. The three research teams and an informatics group that participated are part of the Models of Infectious Disease Agent Study (MIDAS) Network, an effort funded by the National Institute of General Medical Sciences, or NIGMS.

The lead author, M. Elizabeth Halloran, M.D., D.Sc., and co-author Ira M. Longini Jr., Ph.D., both researchers at Fred Hutchinson Cancer Research Center and professors of biostatistics at the University of Washington, use mathematical and statistical methods to study the natural course of infectious diseases.

Prior to publication, Longini presented the findings at the White House and at the Institute of Medicine.

“The federal government wanted three separate infectious-disease-modeling groups working on the same problem just to make sure the results were robust, since this data would be used to inform national pandemic planning,” Longini said. “We got the highest level of input.”

A vaccine was unavailable at the time the study began, so the researchers were asked to focus on analyzing the effectiveness of a combination of antiviral and social-distancing interventions, such as closing schools, in thwarting a flu pandemic. Previous similar modeling studies had shown that even a low-efficacy vaccine would be quite helpful in slowing a pandemic if it were available.

“The good news was that all three of the disease-modeling groups involved in the study found that an outbreak of pandemic flu similar to the pandemic of 1918 could be mitigated if these measures were implemented quickly,” Halloran said.

Halloran, Longini, Shufu Xu, a computer scientist in their group, and collaborators at the Los Alamos National Laboratories constituted one of the research teams. A second group included researchers at Imperial College in London and the University of Pittsburgh. A third group included investigators at the Virginia Bioinformatics Institute at Virginia Tech in Blacksburg, Va.

To conduct the study, the researchers used three separate but similar computer models to calculate the spread of influenza within a population similar to that of Chicago, with approximately 8.6 million people. Members of this virtual community interacted the way people normally do: within households, schools and workplaces, and the community at large. All three models were set up to have attack-rate patterns similar to those of past U.S. flu pandemics.

Predicting the spread of an infectious disease such pandemic influenza requires much more than simply connecting dots on a map. Instead, Halloran and colleagues rely on a tool called stochastic modeling to take into account real-world unpredictability, as well as many factors about the disease and the affected population. In constructing these models, the researchers begin with assumptions about how people interact and how the virus spreads. They also introduce and evaluate the effectiveness of various intervention strategies.

The study assessed the effectiveness of two broad categories of intervention: medical (the use of surveillance to identify cases and to use antiviral agents to treat flu patients and prevent the disease among their close contacts) and non-pharmaceutical (social distancing, such as school closures, voluntary quarantine, and travel restrictions.)

The researchers tested combinations of targeted antiviral treatment and prophylaxis (prevention) and general social-distancing strategies with five intervention scenarios of different levels of stringency and disease transmissibility. The researchers calculated the transmissibility of the virus by the average number of secondary cases infected by each primary case at the beginning of the epidemic, and by the speed at which such cases arose. Such parameters help predict whether an epidemic will turn into a full-fledged pandemic.

In the absence of any intervention, all three computer models produced similar illness-attack rates, ranging from nearly 47 percent to nearly 60 percent of the population having symptomatic influenza.

The least-stringent scenario had the following characteristics: interventions were not implemented until 1 percent of the population had developed symptomatic influenza, schools were closed, only 60 percent of clinical cases were treated with antivirals and their contacts prophylaxed, compliance with quarantine was only 30 percent and compliance with social distancing was only 60 percent.

Even with these limitations, at the lower transmissibility of the flu virus, the combined intervention strategies tested by the three computer-modeling groups achieved a reduction in influenza cases of between 83 percent and 94 percent.

"We ran this simulation with the assumption that the pandemic was as virulent and lethal as the 1918 pandemic," Longini said. "Even when modeling the situation of pandemic flu, with a modest compliance range in social-distancing measures, and modest ability to identify and treat and prophylax with antivirals, the interventions were similarly – though not identically – effective in all three models," he said.

These findings have significant policy implications, the authors wrote. "If one could achieve these levels of compliance, ascertainment and social distancing, then there is a possibility of considerably mitigating a pandemic until a vaccine was available."

However, the authors caution, it is not known whether the levels of disease ascertainment and compliance modeled in these studies are realistic.

"These models, which are built from the best available data and with the best tools, contribute greatly to our understanding of how a pandemic could spread and what measures might protect the public's health," said Jeremy M. Berg, Ph.D., director of the NIGMS, which supports the MIDAS program. "But they are not our only resource; field work and experimental studies remain critical and will enhance the quality and reliability of these and other models."

Source: Fred Hutchinson Cancer Research Center