The Effectiveness of Interventions to Reduce Contact Rates during a Simulated Influenza Pandemic on Attack, Hospitalization, and Mortality Rates

Michael J. Haber PhD\(^1\), David K. Shay MD, MPH\(^2\), Xiaohong M. Davis PhD\(^2\)*
Rajan Patel PhD\(^3\)  Xiaoping Jin\(^2\), Eric Weintraub MPH\(^4\)  Evan Orenstein\(^5\)
William W. Thompson PhD\(^2\)

Author affiliations:
1. Department of Biostatistics, Rollins School of Public Health, Emory University
2. Influenza Division (proposed), Centers for Disease Control and Prevention
3. Amgen, INC.
4. Immunization Safety Office, Office of the Chief Science Officer, Centers for Disease Control and Prevention
5. Yale University

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control & Prevention.

Corresponding author:
Dr. Michael J. Haber, Department of Biostatistics, Rollins School of Public Health, Emory University, Atlanta, GA 30322, U.S.A
Phone: 404-727-7698
Fax: 404-727-1370
e-mail: mhaber@sph.emory.edu

* Dr. Davis is now with the Division of Global Migration and Quarantine, Centers for Disease Control and Prevention
Keywords
influenza; models, statistical; patient isolation; quarantine; stochastic processes.

Summary
Selected measures to reduce contact rates early during an influenza pandemic might substantially reduce adverse health outcomes
Abstract

Measures to decrease contact rates between individuals during an influenza pandemic have been included in pandemic response plans. We used stochastic simulation models to explore the effects of voluntary confinements of ill persons and their household contacts, school closings, and reductions in contacts among long-term care facility residents on pandemic-related morbidity and mortality. Our findings suggest that if persons who develop influenza-like symptoms and their household contacts were encouraged to withdraw to their homes, then rates of illness and mortality might be reduced by ~50%. By preventing ill long-term care facility residents from making contacts with other residents, morbidity and mortality in this vulnerable population might be reduced by ~60%. However, short-term school closings would not have a substantial effect on pandemic-related outcomes. Restrictions in activities of infected individuals early in a pandemic could decrease its health impact.
Three influenza pandemics occurred in the twentieth century (in 1918, 1957 and 1968), and another pandemic is inevitable (1). The requirements for a pandemic virus include the existence of a new influenza A hemagglutinin for which there is little immunity, the ability to infect humans efficiently, and the occurrence of person-to-person transmission. Such viruses are likely to arise in densely populated agricultural communities where contact between humans and birds or pigs are close and persistent (2). In 1997, a highly pathogenic avian A(H5N1) influenza virus was transmitted from live poultry to humans in Hong Kong, killing six out of 18 infected individuals. From December 2003 through 6 June 2006, the World Health Organization has confirmed 225 human cases and 128 deaths associated with H5N1 infections in humans (3), and in October 2005, H5N1 infections among birds were identified for the first time in Europe. Currently circulating H5N1 viruses appear to infrequently infect humans, and person-to-person transmission, if it occurs, is certainly not efficient. However, international health officials are concerned that as human exposure to such viruses increases, so does the possibility that a pandemic virus might appear.

The next influenza pandemic in the United States could result in 89,000 to 207,000 deaths, 314,000 to 734,000 hospitalizations, 18 to 42 million outpatient visits, with a direct economic impact between US$71 and $166 billion, according to one set of estimates (4). Others have described the possible effects of vaccine and antiviral interventions. One study estimated that vaccinating 60% of the population would be necessary to achieve optimal cost-benefits, assuming that development and mass production of a vaccine would require 6-8 months after the pandemic virus was characterized (4). Longini et al (5) estimated the effectiveness of rapid targeted antiviral prophylaxis of individuals early in a pandemic by using epidemic stochastic
simulations. They found that if the next pandemic virus was similar in its impact to the 1957-58 virus, then delivering prophylaxis to 80% of exposed people for up to eight weeks could reduce attack rates by 2-33% and death rates by 0.04-0.58 per 1000 people. However, such a strategy would require a stockpile of 1.9 billion doses of antivirals, which exceeds the current production capacity for these drugs for at least 5 years.

In the absence of adequate supplies of vaccines and antiviral agents, at least during the first wave of an influenza pandemic, it is logical to consider the use of interventions designed to reduce the number of contacts between infected or exposed individuals and susceptible persons. The U.S. Department of Health and Human Services Influenza Pandemic Plan discusses a number of possible containment strategies, including those targeting individuals or entire communities (6). We used new stochastic simulation models to estimate the effects of several interventions of this kind. These models represented the spread of a pandemic in an urban U.S. community, allowing for contacts in different settings (or mixing groups), including households, day care centers, schools, workplaces and long-term care facilities. Using the age distribution of the U.S. population (7), each individual in the community was placed in a stratum, defined by age group and (if aged 65 or above) by residence in the community or in a long-term care facility (LTCF). Person-to-person transmission probabilities depended on the daily duration of contacts. Contact rates and their duration varied by each individual’s stratum and mixing groups. By using these models to simulate an influenza pandemic, we estimated the effects of school closings, home confinement of ill individuals (i.e., isolation) or their household contacts (i.e., quarantine), and reduction of contacts among residents of LTCFs on overall illness attack rates, hospitalization rates, and mortality rates.
Materials and Methods

The Simulation Model

We simulated an influenza outbreak in a small urban U.S. community. The simulation model used data from the A(H2N2) Asian flu pandemic in 1957-58 (5) and from studies on U.S. influenza-related rates of excess morbidity and mortality (8-10). The simulation process begins with the generation of a community of households, where the distributions of sizes of the households and of the ages of the household members follow the 2000 U.S. Census. Every person in the community belongs to one of five age-dependent strata: preschool children (aged 0-4 years), school children (aged 5-18 years), adults (aged 19-64 years), seniors (aged 65+ years) living at home and seniors (aged 65+ years) living in a LTCF. In addition, each person belongs to one or more mixing groups, according to her/his stratum: households, daycare centers, schools, work places, LTCF’s and the community. The mixing matrix is presented as Table 1.

On any given day, a susceptible person, A, makes contacts with other individuals that may lead to her/him becoming infected. These contacts take place in each of A’s mixing groups. The probability that A becomes infected depends on the following input parameters: (1) the number of different individuals who A contacts in each mixing group, (2) the total duration, in minutes, of all the contacts with each of these individuals, and (3) the per-minute rates of infection transmission if the contacted person is infectious. The number and duration of contacts may be different on week days and weekend days. The values of the parameters that were used in this
study are presented in the ‘Supplementary Materials’. Once person A becomes infected, s/he undergoes a latent period which is followed by a period in which s/he is infectious. The mean length of the latent and infectious periods are input parameters.

This model has three new features that are not shared by the commonly used simulation models (such as the model in Longini et al) for transmission of influenza: (1) The probability of transmission depends on the total duration of all contacts between two individuals, rather than of the number of times they make a contact, (2) the transmission parameters do not depend on the population size, and (3) different contact parameters can be specified for week days and weekend days. Technical details of the simulation model are presented in the Supplementary Materials. The basic reproductive number ($R_0$) for this model is 2.7. This value is within the range (2.0-3.0) estimated by Mills et al (11) for the 1918 influenza pandemic.

**Interventions**

The interventions we examined in this simulation study were: school closings, confinement of ill persons and their household contacts to their homes, and reduction in contact rates among residents of LTCFs.

*School closing*

When this intervention was implemented, then schools closed when the prevalence of illness among children in the school exceeded a pre-determined threshold, set to 10%, 15% or 20% in the simulations. A school remained closed for a pre-determined period (7, 14 or 21 days). On weekdays, household and community contact parameters of children whose school
was closed were at their weekend levels; their contacts with other children who continued to attend school and with working adults did not change.

*Confine ment to home*

When this intervention was implemented, a given fraction of households were assumed to comply. If a household complied, then all its members followed the confinement rules unless they were previously ill and had recovered. We considered two types of confinement: ill persons only, or ill persons and all the members of the same household. Confinement began after a given number of days of illness (1, 2 or 3 days) and did not depend on the severity of illness. If symptoms were severe, then the individual reduced her/his duration of contacts with other household members by 50%.

When a person was confined on a weekday (because of his/her illness or illness of another household member) and did not withdraw due to severe symptoms, then the duration of contacts with household members who continued to go to school or work did not change. Durations of contacts with household members who stayed at home and were not withdrawn were the same as on a weekend day.

When ill cases were confined, they returned to school or work a day after their illness ended. When ill cases and other household members were confined, then an individual returned to school or to work a day after her/his illness ended (even if there were other ill people in the household). A person who did not become ill returned to school or work on the third day.
following the last day of illness of any household member (as the length of the latent/incubation period was assumed to be two days).

Reduction of contacts in long-term care facilities.

We examined the effects of two interventions on LTCF residents: reduction in duration of contacts with other residents who were ill, and reduction in duration of contacts with visiting family members.

Effectiveness of Interventions

We first ran a set of 200 simulations with the baseline settings for all the parameters, without any interventions (see Supplementary Data). The average rates for the three outcomes of interest -- overall illness rate, hospitalization rate and death rate -- were calculated for 200 simulations and used as baseline rates. For each intervention, we ran a set of 200 simulations and used the averages of these simulations as estimates of the expected rates under this intervention. The effectiveness of each intervention was defined as:

Effectiveness = [(Baseline rate) – (Rate with intervention)] / Baseline rate.

Sensitivity Analysis

We performed a sensitivity analysis to assess the robustness of our findings regarding the effectiveness of the three modeled interventions. In common with all simulation studies, our findings depended on several parameters for which we have estimated values that we believe are reasonable starting points. These values included baseline contact rates, the probability of illness given infection, the relative infectiousness of an infected person without influenza symptoms, the
probability of withdrawal to home because of severe symptoms, and the reduction in contact rates due to severe symptoms. We varied the values of these parameters, and examined the impact of these changes on estimates of the effectiveness of school closings and confining ill individuals to home.

**Results**

**Baseline rates**

Based on the 200 simulations conducted with the baseline values of the pandemic parameters, the baseline rate of illness was 32.1%, (95% confidence interval (CI) 31.2%-32.9%), the baseline rate of hospitalization was 196.9 per 100,000 (95% CI 183.2-210.6) and the baseline rate of death was 63.4 per 100,000 (95% CI 56.2-70.6). These results were based on the assumption that the illness rates would be similar to their values in the 1957 influenza pandemic.

**School Closings**

Two parameters affected the effectiveness of school closings: the percent of ill school children required to close a school and the number of days the school remained closed. The effectiveness of the intervention varied as a function of the percent ill required for closing a school, and the duration of the closure (Figure 1). For example, if each school was closed for 7 days when the proportion of ill children exceeded 10%, then the overall illness rate was 0.288 (95% CI 0.278-0.297). The baseline illness rate was 0.321; therefore, the effectiveness of this intervention was (0.321-0.288)/0.321 = 0.103 (95% CI 0.075-0.131). As expected, effectiveness usually decreased as the percent ill required to close a school increased. The effect of the length of closure was less clear (Figure 2). When schools were closed, transmission in households and
in the community increased; thus, school closings could increase rates of morbidity and mortality in some groups. For example, when the illness rate required for school closing was 10%, then closing schools for 14 days had the largest effect on hospitalization rates, compared to closings of 7 or 21 days. However, when the rate for closing was 20%, then closing schools for 14 days had a smaller effect on hospitalization rates than closing for 7 or 21 days.

Confinement to Home

In our models, confinement to home took place after a person developed symptoms of influenza. There was a delay of 1, 2 or 3 days between onset of symptoms (which coincided with the onset of infection) and the beginning of the confinement period. This delay and the proportion of households that complied with the confinement rules affected the effectiveness of the intervention. Figure 2 presents the effectiveness of these interventions as function of the percent of households that comply (between 0 and 80 percent) for a delay of 2 days. As expected, effectiveness usually increased with the compliance percentage. Confining the ill and their household members was more effective than confining the ill only. For example, given a delay of two days and 60% compliance, the effectiveness of these interventions on illness rates was 0.33 for confining the ill only and 0.80 for confining ill persons and their household members. Effectiveness decreased when the length of the delay was increased.

Reducing Contacts in Long-term Care Facilities

Reduction of contacts with ill residents of LTCFs decreased the rates of illness, hospitalization and death among long-term care facility residents by more than 50% (Table 2). It
also reduced the rates of hospitalization and death in the general population by up to 14% and 24%, respectively.

**The Effect of Intervention on the Dynamics of the Pandemic**

Figure 3 presents the dynamics of the pandemic (a) without any intervention, (b) when schools are closed for 14 days as the proportion of ill children exceed 10%, and (c) when ill persons and all their household contacts are confined after the second day of illness of the index case, and compliance is 40%. We see that these interventions do not affect the time to the peak of the pandemic (around week 5). The rate of decline following the peak does not change under confinement to home, while it slightly decreases under school closing.

**Sensitivity Analysis**

The value of the basic reproductive number ($R_0$) for the baseline setting of our parameters is 2.7. Since this value is higher than values used in recent simulation studies (12,13) we evaluated the effectiveness of the interventions under smaller values of $R_0$. We found that reducing $R_0$ results in an increase in the effectiveness of confinement to home and a decrease in the effectiveness of school closings. Hence, our findings regarding the effectiveness of confinement and the lack of effectiveness of school closings remain valid for smaller values of $R_0$. 
The results of additional sensitivity analyses were as follows:

School Closings

The most important parameters related to the effectiveness of school closings are those that underlie the contacts between children while they are in school. In our simulations we assumed that on a school day each child makes contacts with ten other school children, each lasting 120 minutes (see Section D.1.a in the Supplementary Materials). Some of these contacts may be concurrent. In order to examine the impact of changing each child’s exposure to other school children on effectiveness of school closures, we increased and decreased the baseline duration of 120 minutes by 50%. Table 3 presents the effectiveness of closing schools for 14 days for the three baseline values of school contact durations. As we see, higher or lower contact durations while schools are open do not result in substantial changes in the effectiveness of school closings.

Confinement to Home

We varied the values of several parameters in the baseline model, and examined the effect of these changes on estimates of the effectiveness of confinement of ill individuals to their homes (Table 4). We assumed that 40% of ill persons without severe symptoms were confined to their home within 2 days of symptom onset. When the fraction of infected persons who developed symptoms was increased from 0.67 to 0.93, then the illness rate without an intervention (i.e., at the baseline level) changed only from 0.333 to 0.319, while implementation of the intervention changed this rate from 0.272 to 0.242. Thus, the effectiveness of this intervention increased from 0.183 to 0.241. The alternative values we used in Table 2 modeled a more severe pandemic than the pandemic modeled with the baseline initial values.
Discussion

The continuing epizootic of influenza A(H5N1) among birds in Asia and Europe has raised concerns that the likelihood of an influenza pandemic may be increasing. Shortages in the supply of neuraminidase inhibitors, the antiviral agents most likely to be effective against a pandemic influenza strain, and the months needed from the isolation of a pandemic strain until the availability of vaccine, suggest that reducing contact rates between infected and uninfected individuals will represent one of the few sets of interventions that can be rapidly implemented. We used a stochastic simulation model to estimate the effectiveness of several interventions that could reduce contact rates on pandemic-related outcomes.

The Pandemic Influenza Strategic Plan and Public Health Guidance for State and Local Partners prepared by the U.S. Department of Health and Human Services was released on November 2, 2005 (6). This plan discusses the use of individual-level containment measures (e.g., isolation and quarantine) and community-level measures (e.g., school closings). Our study considered possible interventions of both kinds, including early identification and confinement of cases and their household contacts, limiting visits to LTCFs and closing of schools.

Our findings suggest that closing schools would result in relatively small reductions in morbidity and mortality rates during a pandemic. For example, when schools were closed when at least 10% of children had influenza symptoms and remained closed for 14 days, then the rates of illness, hospitalizations and death decreased from the baseline rates of 32.1%, 197 per 100,000, and 63 per 100,000 to 26.5%, 170 per 100,000 and 54 per 100,000, respectively. Thus,
the effectiveness of school closings was about 14-18 percent. When we increased the threshold of illness incidence required for school closing to 20%, then these rates were 31.9%, 203 per 100,000 and 69 per 100,000 respectively. These mild decreases in the rates of morbidity and mortality following school closures are explained by the fact that in our models, children whose school was closed were more likely to increase their contacts with other groups. The attack rate of 62% that we used for school-age children may be considered high. However, if the attack rate was reduced, then school closings would have an even smaller effect. Our results do not contradict recent findings that vaccination of school children could be effective in controlling the transmission during a seasonal influenza epidemic (14). Vaccination of children reduces their chances of infection and of transmitting infection to household and community contacts, while closing schools may not decrease the likelihood of infection substantially, and could increase the probability that an infected child will infect household and community contacts (13).

The effect of school closings on overall illness rates in an influenza pandemic has been estimated in other recent simulation studies. Germann et al. (15) modeled the impact of a pandemic on the entire U.S. population. They found that for $R_0 \geq 1.9$, closing of schools without any additional interventions was not very effective. On the other hand, for $R_0 \leq 1.6$ school closings reduced the illness burden. Carrat et al. (16), using a simulation model for the spread of influenza in a community, found school closings very effective. We believe that these inconsistencies in the reported effects of school closings depend on the details of the various simulation models, especially on the way the community is affected by school closing in terms of increased contact rates of school children when their school is closed.
Our simulations predict that it might be possible to decrease rates of morbidity and mortality by as much as 50% by reducing the contact rates of all ill individuals. However, achieving this level of effectiveness would require persuading 60% of those with symptoms to withdraw to their homes and confine themselves. Simulation studies by Longini et al (12) and Ferguson et al (13) found that quarantine, when used in conjunction with vaccines and antiviral agents, is effective in containing an influenza pandemic in South East Asia. One should remember that the effectiveness of any behavioral/social intervention may vary across cultures.

Residents of LCTFs are likely to be at high risk for serious pandemic-related morbidity and mortality. We found that by limiting contacts of ill residents it is possible to reduce morbidity and mortality among other residents. These are important findings, as this vulnerable population responds poorly to seasonal influenza vaccination, and they are unlikely to receive the limited quantities of pandemic vaccine when it first becomes available.

The effectiveness of any particular intervention designed to reduce contact rates depends upon the initial values selected for the parameters affecting influenza transmission (e.g., contact durations, probability of withdrawal due to severe symptoms, etc.), and a limitation of our study is that few data exist on which to base these values. Studies designed to obtain reliable estimates of these parameters during seasonal, inter-pandemic influenza outbreaks should be a high priority. However, the major findings of this study seem to be robust, given a range of realistic values for the parameters we used. The target attack rates we used to calibrate the contact parameters (provided in the Supplementary Materials) are high, but lowering these attack rates
should not have a major impact on our findings, because both the pre- and post-intervention incidence rates would decrease concomitantly.

We did not make formal estimates of the economic costs and benefits of the interventions we examined. However, it is possible to consider some likely consequences of school closings, given current childcare practices. Obviously, the longer the duration of school closure, the more costly the consequences as working parents either have to take time off work to supervise children, or pay for somebody else to care for them. If a large number of school days are lost, school districts might consider extending the school year, which would incur additional costs, although the conditions would be expected to vary greatly between school districts. These increased costs would have to be weighed against the limited predicted effectiveness of this intervention. Encouraging the voluntary withdrawal of ill individuals appears to be a more effective strategy than school closings in reducing the impact of a pandemic, and it may represent a relatively inexpensive intervention. However, researchers have found that U.S. workers routinely miss less than 1 day from work after reporting onset of influenza-like illness (17). Encouraging longer durations of work loss could decrease compliance with self-isolation and increase the economic cost per case avoided. Home quarantine of the immediate family members of an ill individual would likely increase the costs per case averted. For example, during the SARS-related quarantine efforts in Toronto (18), many families found it too expensive to rigidly comply with a household-level quarantine of 7 or more days.

Our stochastic simulation model has several strengths. The model considers the length of time two persons are in contact, in addition to the total number of contacts. The model
parameters we used are not related to the size of the simulated population, unlike previous models (5). We repeated the simulations conducted for this study with a population twice as large as the original population and the same input parameters. The resulting rates were almost unchanged, so the differences can be attributed to the random effects associated with these simulations. The weaknesses of our present model are (i) it requires many input parameters, and (ii) it does not include the effects of antiviral medications. Our model allows for estimating vaccine effects for susceptibility and infectiousness, however this option was not used in the present study.

On February 1st 2007 the Centers for Disease Control and Prevention (CDC) issued an Interim Pre-Pandemic Planning Guidance: Community Strategy for Pandemic Influenza Mitigation in the United States (20). This document recommends several non-pharmaceutical interventions during a severe pandemic, including isolation of persons with confirmed or probable influenza, voluntary home quarantine of members of households with confirmed cases, dismissal of students from schools and school-based activities, and closure of child care programs. During a pandemic with a severity index of 4 or 5 (defined as a case fatality rate of 1% or greater), this new guidance recommends not only school dismissals of ≤ 12 weeks but also measures to protect children from being exposed or exposing others to the pandemic virus via reduction of their out-of-school social contacts and community mixing. In this paper, we assessed the effectiveness of school closures of 1-3 weeks duration after school absenteeism rates reached high levels. We assumed that children dismissed from schools would increase their out-of-school contacts. These assumptions reduced the effectiveness of school closures in our model. In future work, we will
explore the effectiveness of early dismissal of students from schools, together with changes in out-of-school contacts, and other interventions using our model.

In summary, if individuals who suspect they are infected with pandemic influenza were to withdraw to their homes quickly, it may be possible to substantially reduce the morbidity and mortality associated with a pandemic. Withdrawal of all household contacts may further reduce rates of morbidity and mortality, but this additional intervention is likely to be relatively costly and difficult to implement. Restriction of the movement of ill long-term care facility residents will be beneficial in reducing their adverse health outcomes. Before early and rapid implementation of such interventions during a pandemic is feasible, it will be necessary to educate the public about the early symptoms of influenza and to develop measures to increase the social acceptability of self-isolation when ill

Acknowledgements

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Biographical sketch

Dr. Haber is a Professor of Biostatistics at the Rollins School of Public Health in Atlanta. His research focuses on statistical models and methods for infectious disease epidemiology.
References


20. Centers for Disease Control and Prevention. Interim Pre-Pandemic Planning Guidance:
Table 1. Mixing matrix for the simulation model

<table>
<thead>
<tr>
<th>Age Stratum</th>
<th>Household</th>
<th>Daycare Center</th>
<th>School</th>
<th>Workplace</th>
<th>Community</th>
<th>LTCF</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 4 years</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>5-18 years</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>19-64 years</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>65+ years at home</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>65+ years in LTCF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>
Table 2. Estimated effects of pandemic interventions in long-term care facilities on illness, hospitalization, and death rates.

A. Decreases in outcome rates by reductions in contacts with ill residents

<table>
<thead>
<tr>
<th>% Reduction</th>
<th>Population rates</th>
<th>Long-term care facility rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Illness</td>
<td>Hospitalization</td>
</tr>
<tr>
<td>25</td>
<td>0.02*</td>
<td>0.10</td>
</tr>
<tr>
<td>50</td>
<td>0.04</td>
<td>0.13</td>
</tr>
<tr>
<td>75</td>
<td>0.04</td>
<td>0.14</td>
</tr>
<tr>
<td>100</td>
<td>0.03</td>
<td>0.14</td>
</tr>
</tbody>
</table>

* Thus, a 25% reduction in contacts with ill residents of long-term care facilities was estimated to reduce the population illness rate by 2 percent, and the illness rate in long-term care facilities by 22%.

B. Decreases in outcome rates by reductions in contacts with visitors

<table>
<thead>
<tr>
<th>% Reduction</th>
<th>Population rates</th>
<th>Long-term care facility rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Illness</td>
<td>Hospitalization</td>
</tr>
<tr>
<td>25</td>
<td>0.01</td>
<td>0.11</td>
</tr>
<tr>
<td>50</td>
<td>0.02</td>
<td>0.06</td>
</tr>
<tr>
<td>75</td>
<td>0.04</td>
<td>0.15</td>
</tr>
<tr>
<td>100</td>
<td>0.04</td>
<td>0.07</td>
</tr>
</tbody>
</table>

* Thus, a 25% reduction in contacts with ill residents of long-term care facilities was estimated to reduce the population illness rate by 2 percent, and the illness rate in long-term care facilities by 22%.
Table 3: The impact of baseline contact durations in school on effectiveness of closing schools for 14 days.

<table>
<thead>
<tr>
<th>School baseline contact duration</th>
<th>% Ill for School Closing</th>
<th>% Effectiveness Illness Rate</th>
<th>% Effectiveness Hospitalizations Rates</th>
<th>% Effectiveness Death Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>120 minutes</td>
<td>10%</td>
<td>17</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>180 minutes</td>
<td>10%</td>
<td>17</td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>60 minutes</td>
<td>10%</td>
<td>12</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>120 minutes</td>
<td>15%</td>
<td>6</td>
<td>12</td>
<td>17</td>
</tr>
<tr>
<td>180 minutes</td>
<td>15%</td>
<td>8</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>60 minutes</td>
<td>15%</td>
<td>3</td>
<td>1</td>
<td>-13</td>
</tr>
<tr>
<td>120 minutes</td>
<td>20%</td>
<td>1</td>
<td>-3</td>
<td>-8</td>
</tr>
<tr>
<td>180 minutes</td>
<td>20%</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>60 minutes</td>
<td>20%</td>
<td>-1</td>
<td>0</td>
<td>-8</td>
</tr>
</tbody>
</table>
Table 4: Effectiveness of confinement of ill individuals to their homes, with a 2-day delay and 40% compliance, for differing values of the initial parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>% effectiveness illness rates</th>
<th>% effectiveness hospitalization rates</th>
<th>% effectiveness death rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of withdrawal due to severe symptoms (children/adults)</td>
<td>0.75*/0.50*</td>
<td>0.18</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>0.55/0.30</td>
<td>0.34</td>
<td>0.40</td>
</tr>
<tr>
<td>Relative contact duration when withdrawn due to severe symptoms</td>
<td>0.50*</td>
<td>0.18</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>0.70</td>
<td>0.14</td>
<td>0.21</td>
</tr>
<tr>
<td>Fraction of infected persons having symptoms</td>
<td>0.67*</td>
<td>0.18</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>0.93</td>
<td>0.24</td>
<td>0.24</td>
</tr>
<tr>
<td>Relative infectiousness of non-ill persons</td>
<td>0.50*</td>
<td>0.18</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>0.70</td>
<td>0.19</td>
<td>0.24</td>
</tr>
</tbody>
</table>

*Values used in the baseline simulation models
Figure 1. Estimated effectiveness of closing schools on (a) illness, (b) hospitalization, and (c) death rates during a simulated pandemic.

Figure 2. Estimated effectiveness of confinement to home 2 days after onset of respiratory symptoms on (a) illness, (b) hospitalization, and (c) death rates during a simulated pandemic.

Figure 3. Dynamics of the influenza pandemic. Case 1: no interventions. Case 2: Schools are closed for 14 days when prevalence reaches 10%. Case 3: Ill persons and all their household contacts are confined to their homes after the 2nd day of illness of the index case and the compliance rate is 40%.
Supplementary Material: Details of the Simulation Model

The Model

The following parameters described how individuals made contacts with others. For individual $A$ from stratum $i_A$ and mixing group of type $k$ and stratum $j$, we denoted by $\Psi_{ijkl}$ the group of all individuals with whom $A$ made contacts on a day of type $l$, where $l = 1$ for weekdays and $l = 2$ for weekend days. These groups were referred to as ‘contact groups’. The size, $c_{ijkl}$, of $\Psi_{ijkl}$ and the average total duration in minutes, $d_{ijkl}$, of all the contacts made by $A$ with each member of $\Psi_{ijkl}$ on one day were specified as input parameters. At the beginning of each simulation, the initial contact groups $\Psi_{ijkl}$ were determined for $A$ by selecting at random $c_{ijkl}$ individuals of stratum $j$ from each mixing group other than the household to which $A$ belonged. For households ($k = 1$) the contact groups consisted of all household members (other than $A$) in the corresponding stratum. If a mixing group had fewer than $c_{ijkl}$ members of stratum $j$, then the contact group consisted of the entire mixing group.

Influenza transmission was determined by contact parameters and transmission rates. The rate of viral transmission per minute of contact from an infected individual in stratum $j$ to a susceptible individual in stratum $i$ (where $i, j = 1, 2, 3, 4, 5$) was denoted by $\lambda_{ij}$. The probability that transmission occurred during a contact of $d$ minutes was $1 - \exp\{-\lambda_{ij}d\}$. On each day of the simulated outbreak, the model calculated for each susceptible individual the probability of becoming infected that day, based on the contacts made with all individuals in each contact group. Consider a susceptible person $A$ from stratum $i_A$ and a person $B$ in one of $A$’s contact groups, $\Psi_{ijkl}$. Define $y_B = 0$ if $B$ was not infectious and $y_B = 1$ if $B$ was infectious. The probability that $A$ escaped infection from $B$ that day was $\exp\{-\lambda_{ij}d_{ijkl}y_B\}$. To remain uninfected, $A$ must have escaped infection from all the members of all her/his contacts groups.
Hence the probability that \( A \) became infected on this day was:

\[
P(\text{inf}) = 1 - \prod_k \prod_j \prod_{\Phi \in \mathbb{B}_k} \exp\{-\lambda_j d_{i,k,l} y_{B}\}.
\]

This probability was compared with a random number, \( r \), drawn from the interval \([0,1]\). The person \( A \) became infected if \( r < P(\text{inf}) \).

To illustrate the computation of the daily infection probabilities, we assume that person \( A \) is a susceptible school-aged child (stratum 2) who lives in a household with two parents (aged 19-64, stratum 3) and a younger pre-school child (stratum 1). We now calculate the probability that \( A \) will become infected on a given week day. For this illustration we make the simplifying assumption that every person with whom \( A \) makes contacts is infectious on this day. Person \( A \) makes contacts in the household, in her/his school and in the community.

In the household, \( A \) makes contacts lasting a total of \( d_{21} = 60 \) minutes (see Table A.3) with the pre-school child. The per-minute transmission rate from infectious younger child to person \( A \) is \( \lambda_{21} = 0.00062 \) (Table A.1). Therefore the probability that \( A \) escapes infection from that child is \( \exp(-0.00062 \times 60) = \exp(-0.0372) = 0.9635 \). Person \( A \) also makes contacts with her/his parents. The total duration of the contacts with each parent is \( d_{23} = 120 \) minutes (Table A.3), and the transmission rate from the infected parent is \( \lambda_{23} = 0.00053 \) (Table A.1). Therefore, the escape probability from each parent is \( \exp(-0.00053 \times 120) = 0.9384 \). The probability that \( A \) escapes infection from all the household members is \( 0.9635 \times 0.9384^2 = 0.8485 \).

In the school, \( A \) makes contacts with 10 other school children \( c_{22} \) (school) = 10, where the total duration of the contacts which each child is 120 minutes \( d_{22} \) (school) = 120. The per-
minute transmission rate is $\lambda_{22} = 0.00061$. Therefore the escape probability from all school contacts is $[\exp(-0.00061 \times 120)]^{10} = 0.4809$.

In the community, Person A makes contacts with one pre-school child $(c_{21}(\text{community}) = 1$, Table A.4) lasting a total of 30 minutes $(d_{21}(\text{community}) = 30)$, Table A.4), and with two school-aged children $(c_{22}(\text{community}) = 2)$, for a total of 60 minutes each $(d_{22}(\text{community}) = 60)$. The per-minute transmission rates from the pre-school child and from each school-aged child are $\lambda_{21} = 0.00062$ and $\lambda_{22} = 0.00061$, respectively. Hence the escape probability from all the community contacts is $[\exp(-0.00062 \times 30)] \times [\exp(-0.00061 \times 60)]^2 = 0.9123$.

Thus, the overall probability that person A becomes infected on this day is $1 - 0.8485 \times 0.4809 \times 0.9123 = 0.6277$. (This very high daily probability of infection is the result of the assumption that all the individuals with whom A makes contacts on this day are infectious.) To determine if A actually becomes infected, a random number between 0 and 1 is generated and if this number does not exceed 0.6277 then the simulation program determines that A becomes infected on this day.

Each newly infected individual entered a latent period, at the conclusion of which the individual became infectious to others, based on values estimated by Elveback et al (19). We assumed that the probability of developing symptoms given influenza infection was 0.67, and that an infected individual who did not become ill was 50% less infectious than one who did. An ill individual with severe symptoms withdrew to home, made contacts only with household
members, and the duration of these contacts were decreased by 50%. We assumed that 50% of adults and 75% of children develop severe symptoms and withdrew. An ill person could require hospitalization or die from influenza complications. The probabilities of hospitalization and death were determined based on the distribution of age-specific hospitalizations and deaths in an average seasonal (non-pandemic) influenza season (8-10) and on the total hospitalization and death rates expected in a pandemic that is similar to the Asian influenza pandemic of 1957-1958, for which the overall illness attack rate was estimated at 0.33, with an influenza death rate of 0.58 per 1,000 persons (5). A list of the initial settings of all the parameters used in these models is provided below.

The simulated epidemic started with a small number of infective individuals. The transmission process continued until there were no further infected persons in the community. At the end of each simulated epidemic, the program determined the proportions of individuals who became ill as well as the proportions of hospitalizations and deaths in the community. We ran 200 simulations and calculated the means of the above three proportions over these simulated epidemics.

**Baseline Values of Parameters**

*A. Influenza-related parameters (based on Longini et al. (5))*

Pandemic illness rates by age group (used for calibration of transmission rates and contact parameters):

- 0-4 years: 36%
- 5-18 years: 62%
- 19-64 years: 25%
- 65+ years: 21%
Overall rate 33%.

Probability of illness given infection = 0.67.

Relative infectiousness of infected persons who do not become ill = 0.50.

Rate of withdrawal due to ‘severe’ symptoms: in children 0.75, in adults 0.50.

Relative contact rate when withdrawn due to ‘severe’ symptoms = 0.50.

**B. Transmission rates**

We assumed that the transmission rate (transmission probability per one minute of contact) might vary by the ages of the infected and susceptible persons, but not by the mixing group or by weekday versus weekend day. The values of the transmission rates, which are presented in Table A.1, were determined in a calibration process so that the above illness attack rates were obtained.

Table A.1. Transmission rates (\(\lambda_{ij}\)) from an infectious individual in age group \(j\) to a susceptible in age group \(i\).

<table>
<thead>
<tr>
<th>Age group of susceptible (i)</th>
<th>0-4</th>
<th>5-18</th>
<th>19-64</th>
<th>65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group of infectious(j)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-4</td>
<td>0.00059</td>
<td>0.00062</td>
<td>0.00033</td>
<td>0.00080</td>
</tr>
<tr>
<td>5-18</td>
<td>0.00058</td>
<td>0.00061</td>
<td>0.00033</td>
<td>0.00080</td>
</tr>
<tr>
<td>19-64</td>
<td>0.00057</td>
<td>0.00053</td>
<td>0.00032</td>
<td>0.00080</td>
</tr>
<tr>
<td>65+</td>
<td>0.00057</td>
<td>0.00054</td>
<td>0.00029</td>
<td>0.00102</td>
</tr>
</tbody>
</table>

**C. Probabilities of hospitalization and death given illness, by age group**

For the purpose of estimating the hospitalization and death probabilities, we used 9 age groups. We started with data on influenza-related hospitalization and death rates for an average
seasonal influenza epidemic (8-10). We then adjusted these rates so that we obtained the predicted overall rates for a pandemic (247 and 70 per 100,000, respectively, based on Meltzer et al. (4)). To determine the conditional probabilities for ill persons we divided these rates by the expected pandemic illness rates listed in Section A. The conditional probabilities are presented in Table A.2.

Table A.2. Age-specific conditional probabilities of hospitalization and death given flu infection

<table>
<thead>
<tr>
<th>Age group</th>
<th>Hospitalization</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>0.00810</td>
<td>0.00005</td>
</tr>
<tr>
<td>5-18</td>
<td>0.00091</td>
<td>0.00003</td>
</tr>
<tr>
<td>19-49</td>
<td>0.00227</td>
<td>0.00007</td>
</tr>
<tr>
<td>50-64</td>
<td>0.00907</td>
<td>0.00148</td>
</tr>
<tr>
<td>65-69</td>
<td>0.02442</td>
<td>0.00530</td>
</tr>
<tr>
<td>70-74</td>
<td>0.04125</td>
<td>0.00928</td>
</tr>
<tr>
<td>75-79</td>
<td>0.05539</td>
<td>0.01805</td>
</tr>
<tr>
<td>80-84</td>
<td>0.08816</td>
<td>0.03529</td>
</tr>
<tr>
<td>85+</td>
<td>0.15357</td>
<td>0.09583</td>
</tr>
</tbody>
</table>

D. Contact frequencies and durations

D.1. Persons who reside at home

Four age strata are included in the simulation models: 0-4 years; 5-18; 19-64; 65+. There are 5 types of mixing groups: households, daycare centers, schools, work places and the community (for contacts of long-term facility residents, see Section D.2). For a given mixing group and type of day, and for each combination of two strata \((i,j)\) we need to determine: (i) the number of persons from stratum \(j\) contacted in one day by a person from stratum \(i\), \(c_{ij}\), and (ii)
the average total duration per day (in minutes) of all the contacts with one person, $d_{ij}$. These numbers are symmetric: $c_{ji} = c_{ij}$ and $d_{ji} = d_{ij}$.

**D.1.a. Weekdays**

**Contacts in the household:** We assumed that each member of the household contacted every other member, so we did not specify the $c_{ij}$’s. Table A.3 presents values for the $d_{ij}$’s

Table A.3. Duration of contacts with household members

<table>
<thead>
<tr>
<th>Stratum</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>120</td>
<td>60</td>
<td>120</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>120</td>
<td>120</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>60</td>
<td>120</td>
<td>120</td>
</tr>
</tbody>
</table>

**Contacts in daycare centers:** We set $c_{11} = 6$, $d_{11} = 60$. All other contact parameters are zero.

**Contacts in schools:** We set $c_{22} = 10$, $d_{22} = 120$. All other contact parameters are zero.

**Contacts in workplaces:** We set $c_{33} = 10$, $d_{33} = 120$. All other contact parameters are zero.

**Contacts in the community:** Table A.4 presents the values of $(c_{ij}, d_{ij})$. For simplicity, we assume that there are no contacts between children and adults in the community.

Table A.4. Number of contacted persons and total duration of all contacts with one person in the community

<table>
<thead>
<tr>
<th>Stratum</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2, 60</td>
<td>1, 30</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>1, 30</td>
<td>2, 60</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
<td>2, 60</td>
<td>2, 60</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>0</td>
<td>2, 60</td>
<td>2, 60</td>
</tr>
</tbody>
</table>
D.1.b Weekend days

On a weekend day, contacts are made only in households and in the community. The weekend values of the $d_{ij}$’s in households and in the community are twice the corresponding weekday values. The community weekend values of the $c_{ij}$’s are twice the corresponding weekday values.

D.2. Long-term care facility residents.

Each long-term care facility resident made contacts with 4 other residents for an average of 120 minutes (both on weekdays and on weekend days) and with 2 members of the long-term care facility staff for 120 minutes (weekdays and weekend days). In addition, this person contacts one family member for 60 minutes on weekdays and 2 family members for 120 minutes each on weekend days.
(a) illness

Effectiveness

% Illness Required to Close Schools
Fig. 1: The figure illustrates the relationship between % Compliance and Effectiveness for two different scenarios:

- **Confinement of Ill Persons Only**
- **Confinement of Ill Persons and Their Household Contacts**

The graph shows a clear upward trend, indicating that as compliance increases, effectiveness also increases. The data points for each scenario are clearly marked, allowing for a straightforward comparison.
(3) death

Weeks

x 100,000

dead case 1
dead case 2
dead case 3