

# Protecting residential care facilities from pandemic influenza

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It is widely believed that protecting health care facilities against outbreaks of pandemic influenza requires pharmaceutical resources such as antivirals and vaccines. However, early in a pandemic, vaccines will not likely be available and antivirals will probably be of limited supply. The containment of pandemic influenza within acute-care hospitals anywhere is problematic because of open connections with communities. However, other health care institutions, especially those providing care for the disabled, can potentially control community access. We modeled a residential care facility by using a stochastic compartmental model to address the question of whether conditions exist under which nonpharmaceutical interventions (NPIs) alone might prevent the introduction of a pandemic virus. The model projected that with currently recommended staff–visitor interactions and social distancing practices, virus introductions are inevitable in all pandemics, accompanied by rapid internal propagation. The model identified staff reentry as the critical pathway of contagion, and provided estimates of the reduction in risk required to minimize the probability of a virus introduction. By using information on latency for historical and candidate pandemic viruses, we developed NPIs that simulated notions of protective isolation for staff away from the facility that reduced the probability of bringing the pandemic infection back to the facility to levels providing protection over a large range of projected pandemic severities. The proposed form of protective isolation was evaluated for social plausibility by collaborators who operate residential facilities. It appears unavoidable that NPI combinations effective against pandemics more severe than mild imply social disruption that increases with severity.

nonpharmaceutical interventions | SEIR stochastic model | self-isolation periods | social distancing | visitor and staff restrictions

It has been nearly 40 years since the last influenza pandemic in 1968. A sporadic, but steadily larger series of human cases of H5N1 avian influenza with a case fatality rate >50% stands as a harbinger of the devastating potential a novel influenza virus might pose. To validate estimates of mortality and morbidity, and to explore options for the control of an influenza pandemic, several researchers have modeled both the process of influenza transmission and various intervention measures aimed at mitigating its consequences (1–7). Many of these studies suggest that antiviral pharmaceutical agents and vaccines would be the most effective interventions, with nonpharmaceutical interventions (NPIs) relegated to a subordinate, incremental role. However, it is also clear that the levels of antivirals and vaccines needed for effective control are not likely to be available at the start of a pandemic, even in the most affluent societies, and should resistance to current antivirals emerge, NPIs would be thrust to the fore.

Recognizing the potentially critical importance of delays of a few weeks or months after the demonstration of human-to-human transmissibility of a new influenza virus, the current global strategy is focused initially on containment of outbreaks (8). Although it is uncertain whether sufficient antiviral and

vaccine resources will be available to provide effective pandemic control in economically developed countries, it is certain that the bulk of control efforts will rely on NPIs in less economically developed settings in which most of the world's population now lives. Mathematical models (2, 3, 7) used together with historical studies of the 1918–1919 influenza pandemic in the United States (9, 10) suggest that the timely implementation of NPIs at the community level may have been somewhat effective in curtailing pandemic influenza. However, these studies conclude that most implementations began too late and were halted too soon. A comprehensive review of NPI containment strategies used by U.S. communities during the 1918–1919 pandemic concluded that the timely and continuous implementation of NPIs seemed to have curtailed the outbreak (11–13).

A recent study (7) focused on the application of NPIs for pandemic control within both the social community and acute-care hospitals. The dynamical model used in that study revealed that the tight coupling between acute-care hospitals and the community within which they are embedded limits the extent to which NPI measures can effectively control pandemic spread within the hospital itself. The essential finding was that for a pandemic of moderate severity (e.g.,  $R_0 \approx 2.1$ ) or greater, there was no practical level of within-hospital transmission control that could protect the institution from being overwhelmed.

The open nature of community access makes containment in acute-care hospital settings nearly impossible. However, other health care and social institutions have the potential to restrict community access to a greater degree. These include  $\approx 16,000$  institutions within the United States that care for individuals who require assistance with activities of daily living, such as the disabled (mostly elderly) and the mentally and developmentally challenged (14). The aim of this modeling study was to estimate the levels of NPIs that would be required to protect any residential care facility (with the capability of controlling community access) against the introduction of a pandemic virus. We chose an extension of a Susceptible–Exposed–Infected–Recovered (SEIR) stochastic compartmental model to represent a facility providing residential care to disabled persons. The objective of this work was threefold: (i) to determine whether an intrinsic ability to control access to these facilities provided a basis for protection against pandemic influenza, (ii) to identify specific NPIs and combinations thereof that could achieve community access control, and (iii) to develop practical implementations of these NPI combinations sufficient for protection over the full range of projected pandemic categories.

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**Table 1. The final epidemic size is denoted by  $Episize_i$ , where  $i$  marks its maximum, mean, and median value**

$R_0$	$Episize_{max}$	$Episize_{mean}$	$Episize_{median}$
Baseline :: Plan Category 1–2			
1.4	(143 :: 20)	(71 :: 2)	(78 :: 0)
1.6	(160 :: 22)	(106 :: 3)	(122 :: 1)
1.8	(177 :: 86)	(132 :: 7)	(142 :: 1)
2.0	(176 :: 91)	(148 :: 8)	(153 :: 1)
2.2	(183 :: 104)	(161 :: 11)	(164 :: 2)
2.4	(185 :: 143)	(170 :: 26)	(171 :: 9)
2.6	(192 :: 125)	(173 :: 45)	(177 :: 45)
2.8	(194 :: 159)	(178 :: 81)	(179 :: 88)
Plan Category 3–4 :: Plan Category 5			
1.4	(13 :: 1)	(0 :: 0)	(0 :: 0)
1.6	(16 :: 1)	(1 :: 0)	(0 :: 0)
1.9	(29 :: 1)	(1 :: 0)	(0 :: 0)
2.0	(34 :: 1)	(1 :: 0)	(0 :: 0)
2.2	(39 :: 1)	(2 :: 0)	(0 :: 0)
2.4	(88 :: 1)	(3 :: 0)	(1 :: 0)
2.6	(104 :: 1)	(12 :: 0)	(2 :: 0)
2.8	(118 :: 2)	(26 :: 0)	(12 :: 0)

Results for the baseline and intervention plans simulated (punctuation mark :: separates these outcomes). These findings assumed that interventions had no effect on asymptomatic persons ( $\rho_i = 1$ ). Mortality cases corresponding to these simulations may be obtained by multiplying  $Episize_i$  by the case fatality proportion (CFP) in Table 2.

outbreaks, and that higher levels of NPIs, requiring greater social restriction and higher levels of cooperation, were needed to manage more severe outbreaks.

**Plan: Category 1–2.** The preparedness plan for category 1–2 pandemics was designed to simulate the implementation of various NPIs discussed in most U.S. state plans. We assumed that these plans would produce a 50% reduction in transmission. This level of effect reduced the epidemic size (median) from 171 to 9 cases for  $R_0 = 2.4$  (Table 1, baseline :: plan category 1–2) for the case in which the NPIs were assumed not to apply to asymptomatic persons. Results for simulations of the case in which NPIs were assumed to apply to asymptomatic persons with an effect comparable to that on infected persons are virtually indistinguishable in Fig. 1. This is because, for pandemic viruses, our information is that the asymptomatic class is likely to be both very much smaller and much less infectious than for seasonal

influenza (see *Discussion*). Although the probability of a virus introduction remained significant [ $p(\text{Intro}) \geq 0.5$ ,  $R_0 > 1.4$ ], Fig. 1 *Lower* shows that, if a 50% reduction in transmission can be achieved, the probability of an outbreak would be reduced by at least twofold for most pandemics ( $R_0 < 2.4$ ); and that varying the impact of the asymptomatic class over the full range did not demonstrably change the simulation result.

**Plan: Category 3–4.** The simulations for category 1–2 pandemics revealed that employee entry–reentry was the most important element in the control of influenza introductions into a facility. Further revealed was that approximately a 10-fold reduction in the probability of an introduction was required to provide substantive protection against more severe pandemics. This could be accomplished by increasing employee commitments to 10 or more days in continuous residence at the facility, but this was considered socially unworkable. However, any attempt to reduce the number of days on-site (from 10) necessarily required a mechanism for a corresponding reduction in the probability of reintroduction of the pandemic virus to compensate for the increased frequency of reentry. By using data on time from infection to symptomatic illness for A(H3N2) and A(H5N1) viruses (P. Glezen, R. Couch, and R. Belshe, personal communications), we simulated the effects of scenarios in which employees, together with all with whom they shared their domicile, entered isolation from the community within their own homes during the last portion of off-time away from a residential facility.

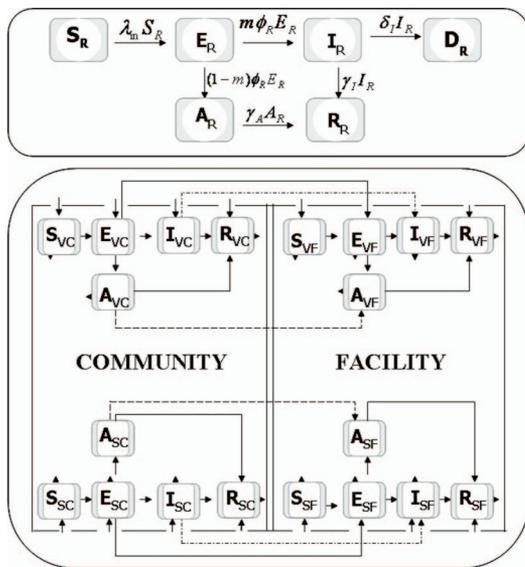
The consequences of a 4-days-on/4-days-off/2.3-days isolation period lowered the probability of reintroduction of the virus by approximately a 16-fold (at  $R_0 = 2$ ) compared with daily 12-h shifts; and was considered socially acceptable by collaborators working closely with residential care facilities. Except for the introduction of employee off-shift isolation periods and increased restrictions on visitors, both of which are accounted for explicitly in the dynamical model, the NPIs for this plan were similar to those of plan category 1–2. Therefore, we again assumed an overall reduction in transmission of 50%. With this assumption, the estimated probability of virus introduction was reduced to <50% for  $R_0 < 2$ ; and the probability of an outbreak was reduced by >50% from baseline for all but the most severe simulated pandemic ( $R_0 = 2.8$ ) (see Fig. 1 *Lower*). Again, the impact of excluding the small and relatively noninfectious asymptomatic class from the reduction of transmission ( $\rho_i = 1$ ; solid curves in Fig. 1) produced no discernible difference in the simulations.

**Table 2. Variables, parameter definitions, and values assumed in the numerical simulation of a resident facility**

Variables	Parameters	Values	References
$R_0$	Basic reproduction number	1.4–2.8	4, 6, 15
$m$	Fraction of exposed that progress to infection	0.667	16
$1/\phi_{i^*}$	Average latency period, days	1.9	5, 6
$1/\gamma_A$	Average recovery period for asymptomatic, days	5	4, 17
$1/\gamma_i$	Average recovery period for infected, days	5	4, 17
CFP	Case fatality proportion	0.03–0.15	18
$\delta_i$	Resident mortality rate, $\delta_i = (\text{CFP}/1 - \text{CFP}) \gamma_i$ (day <sup>-1</sup> )	0.0062–0.035	16
$\pi_i^*$	Transmission reduction parameter when applied to infected	0.05–1	4
$\rho_i^*$	Transmission reduction parameter when applied to asymptomatic	0.05–1	4
$\eta_i^*$	Infectiousness of asymptomatics relative to symptomatics	0.02	16
$1/\xi_{VF_i}$ , $1/\xi_{VC}$	Average time spent between locations by visitors, hours; days	0–2; 7	14
$1/\xi_{SF_i}$ , $1/\xi_{SC}$	Average time spent between locations by staff, hours; hours	8–12; 12–16	14
$p_A$	Probability of having asymptomatics escape monitoring efforts	1	Estimated
$p_E$	Probability of having exposed escape monitoring efforts	0.14–1	Estimated
$p_I$	Probability of having infecteds escape monitoring efforts	0.1–1	Estimated

\* $i = R, SF, VF, SC, VC$ .





**Fig. 2.** Compartmental epidemic model for residents in a facility (Upper) and visitors and staff in the community and in a resident facility (Lower).

propagating pandemics. The most important limitation of this study, however, is the absence of a modeling approach that captures the level of detail in the various control measures proposed, and validates the level of transmission reduction assumed. Our model simulated the estimated consequences of these interventions rather than simulating the actions themselves at the individual level.

## Methods

**Mathematical Model.** The dynamics of residents in a facility and staff and visitors circulating between the community and a facility were simulated stochastically by using a compartmental model depicted in Fig. 2. These dynamics were simulated for a facility housing 200 residents and 75 on-site staff. The model assumed that each resident received an average of 3 h of care daily and that staff members worked an average of 8 h/day shifts (5 day/week schedules). The model assumed an initial population size of 40 visitors who had contact with residents (only 1 resident in 5 receives any visitors at all), visitations averaging 2 h, and homogenous mixing of the effect of visitation on all residents. Table 3 provides the population sizes assumed in these simulations. Residents were classified according to the epidemiological classes: susceptible ( $S_R$ ), exposed ( $E_R$ ), asymptomatic ( $A_R$ ), infectious ( $I_R$ ), recovered ( $R_R$ ), and deceased ( $D_R$ ). Susceptible individuals became exposed at rate  $\lambda_{in}$ . A fraction  $m$  of exposed persons became symptomatic and progressed to infection ( $I_R$ ) at rate  $\phi_R$ , whereas the remaining  $1 - m$  remained asymptomatic and infectious at a reduced level ( $A_R$ ). Infected individuals recovered at rate  $\gamma_I$  or succumbed to disease at rate  $\delta_I$ . Asymptomatic individuals recovered at rate  $\gamma_A$ . Mortality rates ( $\delta_I$ ) for infected residents were estimated from the case-fatality proportion of residents (CFP), as  $\delta_I = ((CFP)/(1 - CFP))\gamma_I$ . Case fatality rates attributable to infection by pandemic influenza will likely vary from pandemic wave to wave in a manner that cannot be known *a priori*. Our results assume a constant relationship between attack rates and mortality rates both within and between pandemic waves. Mortality projected by our

**Table 3. Initial conditions assumed in the numerical simulation of a resident facility**

Epidemiological classes	Initial population size	Reference
$S_C, S_R, S_{VC}, S_{VF}, S_{SC}, S_{SF}$	50,000, 200, 27, 13, 8, 75	14
$E_C, E_R, E_{VC}, E_{VF}, E_{SC}, E_{SF}$	1, 0, 1, 0, 1, 0	14
$I_C, I_R, I_{VC}, I_{VF}, I_{SC}, I_{SF}$	1, 0, 1, 0, 1, 0	14
$A_i, R_i, D_i$	0, 0, 0	14

models can be obtained by multiplying the total estimated number of cases for all scenarios by the CFP that appears in Table 2.

The circulation dynamics of visitors and staff between a facility and the community are depicted in Fig. 2. These populations were defined according to their immediately current location (e.g., community or facility) and the epidemiological states: susceptible ( $S$ ), exposed ( $E$ ), asymptomatic ( $A$ ), infected ( $I$ ), and recovered ( $R$ ). Visitors located in the community or in the facility were indexed by  $VC$  and  $VF$ , respectively. Similarly, staff located in the community or a facility were indexed by  $SC$  and  $SF$ , respectively. We indexed individuals in the general community by  $C$ . We let  $1/\xi_i$  denote the average time that visitors ( $i = VF, VC$ ) and staff ( $i = SF, SC$ ) spent in the facility and the community (Table 2) (see also Table S4). For simplicity, we have assumed that the time spent by staff and visitors in the community/facility was exponentially distributed.

The total population was given by  $N_{tot} = N_{in} + N_{out}$ , where  $N_{in}$  and  $N_{out}$  describe the total population size inside and outside a facility, respectively. The per capita rates at which susceptible individuals acquired infection inside and outside the facility were denoted by  $\lambda_{in}$  and  $\lambda_{out}$ , respectively. The rate  $\lambda_{in}$  is also called the force of infection for individuals inside the facility. It included the contribution of all individuals that circulate within a facility (residents, staff, and visitors).  $\lambda_{in} = [\sum_{i=R,SF,VF} \beta_i(\pi_i I_i + \rho_i \eta_i A_i)]/N_{in}$ , where  $\beta_i$  represents the disease transmission of both populations and  $\eta_i$  represents the relative lack of infectiousness of the  $A_i$  population. Efforts to reduce disease transmission were accounted via the parameters  $\pi_i$  and  $\rho_i$ . We considered two cases,  $\rho_i = 1$  (NPIs not applicable to asymptomatic persons) and  $\rho_i = \pi_i$  (NPIs equally applicable to infected and asymptomatic persons). Similarly,  $\lambda_{out}$  is the force of infection for individuals outside a facility. It included contributions from contacts among staff off-duty (indexed by  $SC$ ), visitors in the community (indexed by  $VC$ ), and general community members (indexed by  $C$ ).  $\lambda_{out} = \sum_{i=SC,VC,C} \beta_i(\pi_i I_i + \rho_i \eta_i A_i)/N_{out}$ . Further details on the model formulation, the force of infection, simulation approach, and the calculation of the basic reproduction number are provided in the *SI Text*.

**Baseline.** This scenario assumed that staff spent 8 h (per day) caring for residents, and visitors spent, on average, 2 h (per week) in the facility without restrictions. Our information was that only one resident in five receives visitors, and these were assumed not to modify their visiting behavior on the basis of their own infectious state. Because of our assumption of homogeneous mixing within each model compartment, we treated this situation as equivalent to a reduction in overall visitation effect by a factor of 1/5. Staff and visitors did not apply social distancing measures during the time spent outside the facility, and in-facility monitoring was not implemented. Intervention plans scenarios considered included the baseline above and plans that simulated the consequences of implementing the following nonpharmaceutical interventions: (i) Restrictions on visitors and staff entering the facility, (ii) social distancing measures for staff and visitors, (iii) monitoring of staff returning to the facility, and (iv) isolation of symptomatic residents and immediate removal from the premises of symptomatic staff. The range of visitor restrictions considered included reducing average visiting periods to a single hour and complete restriction of all visitor-resident contact. Social distancing practices implemented by visitors and staff involved both those directed to the community (e.g., abstaining from social gatherings and public places such as schools, churches, and theaters) and those directed to intra-facility interactions (e.g., maintaining 3-foot distances for other than required direct contact and eliminating meetings and resident gatherings). In-facility monitoring of staff returning to work was conceptualized to involve assessment of oral temperature and evaluation of stated history.

**Plan: Category 1–2.** Control measures in this plan increased staff shifts from five 8-h shifts per week to four 12-h shifts per week, assumed social distancing practices for staff and visitors that directly reduced a resident's risk of infection by 50%, and reduced the average duration of visits in the facility from 2 to 1 h. We considered both the case in which  $\rho_i = \pi_i$  (NPIs fully applicable to persons without symptoms) and  $\rho_i = 1$  (NPIs inapplicable to asymptomatic persons).

**Plan: Category 3–4.** In addition to the array of NPIs delineated in plan category 1–2, the category 3–4 plan further assumed the following: complete visitor restrictions, temperature monitoring and history assessment of returning staff. Visitor restrictions involved communication via electronic devices and/or from behind transparent impermeable barriers with airflow control. Most importantly, plan category 3–4 introduced an employee work schedule that comprised four full days on-site and four full days off-site with a period of isolation from the community at home for the last portion of the time off-site. A 2.3-day self-isolation period was defined as the employee entering isolation with her/his living group within her/his home on the evening of the second day

off-work. The employee entered sequestration only if she/he and all members of her/his living group were asymptomatic and afebrile at the time scheduled for entry. Subsequently, the employee reported to the facility at the end of the isolation period (the morning of the fifth day) only if all members of the household remained asymptomatic and afebrile. As for plan category 1–2, we separately considered the case in which the NPIs for category 3–4 were applicable ( $p_i = \pi_i$ ) and not applicable ( $p_i = 1$ ) to asymptomatic persons. Because the combination of NPIs assembled for this plan was otherwise similar to the NPIs for plan category 1–2, we again assumed a reduction in the residents' risk of infection of 50%.

**Plan: Category 5.** For ultimately severe pandemics, we evaluated a plan that included all interventions used in the plan category 3–4 pandemics, increased isolation periods to 3.3 days (while maintaining a 4-day-on/4-day-off staff shift scheduling), and assumed increased social distancing measures to the level at which a resident's risk of infection was reduced by 95%. This might be achieved by completely banishing visitation and imposing strict viral mitigation monitoring on all material and high-priority services entering the facility.

**Numerical Simulations.** We solved the model (illustrated in Fig. 2) numerically via stochastic simulations (Matlab, Mathworks) with 100 realizations for each

of the intervention plans for an array of pandemic severity levels, separately considering the interventions to be applicable/inapplicable to asymptomatic persons. The simulation approach assumed that the number of individuals transitioning between the various epidemiological states (e.g., susceptible, infected, recovered) were Poisson distributed.

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