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eInfluenza Review



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June 2007: VOLUME 1, NUMBER 8

We are proud to announce that **Jonathan M. Zenilman, MD, Chief, Infectious Diseases Division at The Johns Hopkins Bayview Medical Center** has joined as **Co-Program Director**.

In this issue...

Community Strategy for Epidemic Influenza Mitigation in the United States

As long as the possibility of an influenza pandemic exists, the need for a comprehensive and coordinated mitigation plan remains a priority. In February 2007, the CDC issued a planning guidance document addressing the issues surrounding community mitigation. Designed as a first iteration, to be revised as knowledge gained from continuing research becomes available, a primary focus of the document is on non-pharmaceutical interventions (NPIs).

In this issue, in a departure from our usual format, we highlight the CDC's key recommendations for supplementing what can be achieved with medications in the event of pandemic influenza.

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1.0 hours Physicians
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LEARNING OBJECTIVES

At the conclusion of this activity, participants should be able to:

- Describe the CDC recommendations for mitigating person-to-person transmission of pandemic influenza
- Explain the criteria proposed to implement the proposed strategies
- Discuss the additional research required to develop these initial recommendations

STRATEGIC OVERVIEW

The primary strategies for combating influenza are: 1) vaccination, 2) treatment of infected and exposed individuals with antiviral medications, and 3) implementation of infection control and social distancing measures. Although the single most effective intervention will be vaccination, it is highly unlikely that a well-matched vaccine will be available when a pandemic begins – and current vaccine technology would require a probable 4 to 6 months after the start of a pandemic to make such a vaccine available. In addition, it is likely that the amounts of vaccine produced will not be adequate to cover the entire population. Further, it is unknown whether sufficient quantities of antiviral medications will be available, as well as whether a vaccine will be effective in-vivo even if it is active in-vitro.

Therefore, in preparation for a pandemic situation without sufficient quantities of vaccine and antivirals, the CDC issued *Interim Pre-pandemic Planning Guidance: Community Strategy for Pandemic Influenza Mitigation in the United States* in February 2007 (www.pandemicflu.gov/plan/community/mitigation.html). Most of the guidelines presented are based on the concept of "social distancing." Among the assumptions the authors make are that person-person contact is the major method of transmission of influenza; viral shedding begins about one day before the onset of symptoms and reaches a zenith during the first few days of the infection; and that children have the highest titers of virus, the most prolonged periods of shedding, and are the major vectors of disease. The recommendations provided are based in part on "Models of Infectious Disease Agent Studies," which are computer simulations of influenza outbreaks funded by the NIH¹⁻³, as well as historical data drawn from experiences recorded during the 1918 pandemic⁴. It should be noted that in the latter, when comparing cities that did extensive influenza planning (such as St. Louis) versus those that did not (such as Philadelphia), strategies based on social distancing showed a significant public health benefit. The conclusion by the CDC is that the experience in 1918 and the computer modeling studies show "strands of evidence" that indicate the currently proposed methods would benefit public health by limiting or slowing community influenza transmission, with the ultimate effect of reduced mortality and a broadened epidemic curve – thus lessening the intensity of a pandemic's impact on both the healthcare system and society in general.

It should be emphasized at the onset that while many of the interventions proposed may provide these potential benefits, their implementation is complicated by substantial concerns about societal impact, which is categorized as the "second and third order consequences." For example, closing schools requires home care for children, which may prevent parents from working (and subsequent loss of

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income), which may lead to reduced community-based services including healthcare services, the supply chain, food delivery, etc⁵. This is simply one example of the cascading effects of the interventions proposed.

SPECIFIC STRATEGIES PROPOSED

The pandemic mitigation interventions described in the document include:

- **Isolation of cases:** Infected patients who do not require hospitalization should be isolated and treated at home.
- **Voluntary home quarantine of household members:** Household members with confirmed or probable influenza should stay at home, where they would receive treatment that would include antiviral agents (if there is a sufficient supply and the drug is active against the pandemic strain). Other household contacts would also be included, in part because these are the persons at highest risk of both infection and of transmitting the disease. Requirements for success include prompt recognition of illness, appropriate use of hygiene and infection control practices in the home setting; measures to promote voluntary compliance; commitment of employers to support the recommendation that ill employees stay home; and support for the financial, social, physical, and mental health needs of patients and caregivers. In addition, special consideration should be made for persons who live alone, as many of these individuals may be unable to care for themselves if ill.
- **Closure of schools:** Childcare facilities and schools represent an important point of epidemic amplification, while children themselves are thought to be efficient transmitters of disease in any setting. Therefore, both to protect children and to decrease introduction of the virus into households and the community at large, the CDC plan calls for closing public and private schools, day care centers, and colleges and universities. The closure recommendation is based on the assumption that for social distancing to be effective, it needs to be further implemented in concert with closure of areas of "community mixing": thus, malls, theaters, and other gathering sites where students might congregate would need to be included in the plans for control. In the event of a full-scale pandemic, schools may be closed for up to 12 weeks.
- **Closure of businesses and cancellation of public gatherings:** The goals of workplace social distancing measures are not only to reduce transmission within the workplace and thus into the community at large and ensure a safe working environment, but also to maintain business continuity, especially for critical infrastructure. Workplace measures such as encouragement of alternatives to in-person meetings ("telework"), as well as modifications to work schedules (such as staggered shifts) may be important in reducing social contacts and the accompanying increased risk of transmission. The success of these measures are dependent on the commitment of employers to provide options and make changes in work environments to reduce contacts while maintaining operations.

Within the community, cancellation or postponement of large gatherings, such as concerts or theatre showings may reduce transmission risk. Modifications to mass transit policies to decrease passenger density may reduce transmission risk, but such changes will likely create challenging second and third order consequences. It is noted, for example, that 4.5 million people use the NYC subway system daily. Closure might make it impossible to provide vital services including healthcare.

- **Infection control measures:** Included in the plan is public education regarding methods to prevent transmission, such as cough etiquette, hand hygiene and the use of surgical masks or N95 respirators.

While the CDC document contains in-depth guidance on how these recommendations can be



implemented, providing the step-by-step details for each NPI is beyond the scope of this eLiterature Review. Further, as the ultimate responsibility for public health intervention in the US is state-based, these proposed recommendations need to be reviewed and endorsed or rejected by state and local health departments.

WHEN WOULD THESE STRATEGIES BE IMPLEMENTED?

Implementing these measures *prior* to the pandemic may result in economic and social hardship without public health benefit, as well as, over time, "intervention fatigue" and an erosion of public adherence. Conversely, implementing these interventions *after* extensive spread of pandemic influenza in a community may limit the public health benefits. This guidance suggests that the primary activation trigger for initiating interventions be a laboratory-confirmed cluster of infection, with a novel influenza virus, and evidence of community transmission (ie, epidemiologically-linked cases from more than one hospital).

There are 3 important variables that dictate the intervention and the specific strategy:

1. The first is the severity of the influenza strain based on case-fatality rates. This CDC guidance document introduces a Pandemic Severity Index (PSI), which uses case fatality ratio as the critical driver for categorizing the severity of a pandemic. The index is designed to enable estimation of the severity of a pandemic on a population level, allowing public health officials to better forecast the impact of a pandemic and match mitigation interventions to the predicted severity. Future pandemics will be assigned to 1 of 5 discrete categories of increasing severity (Category 1 to Category 5), as summarized below:

Pandemic Severity Index (PSI)		
PSI Category	Case Fatality Ratio	Projected US Deaths
1	<0.1%	<90,000
2	0.1% – <0.5%	90,000 – <450,000
3	0.5% – <1.0%	450,000 – <900,000
4	1.0% – <2.0%	900,000 – <1,800,000
5	≥2.0%	≥1,800,000

For reference it should be noted that the mortality associated with seasonal influenza in the US is less than 0.1%, and that the highest mortality experienced in an influenza epidemic was the 1918 pandemic, with a case-fatality rate of 2.4%. It is therefore sobering to realize that the case-fatality rate for Avian influenza (which is now sporadic) is about 60%.

2. The second variable is determining which of the interventions described above should be instituted. These are based on the PSI level, and are summarized below:

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Summary of the Community Mitigation Strategy by Pandemic Severity			
Intervention by Setting	Pandemic Severity		
	1	2 and 3	4 and 5
HOME Voluntary isolation of ill at home (adult and children); combine with use of antiviral treatment as available and indicated	Recommend	Recommend	Recommend
Voluntary quarantine of household members in homes with ill persons (adult and children); consider combining with antiviral prophylaxis if effective, feasible, and quantities sufficient	Generally not recommended	Consider	Recommend
SCHOOL Children social distancing – Dismissal of students from schools and school based activities, and closure of child care programs	Generally not recommended	Consider: 4 weeks	Recommend: 12 weeks
– Reduce out-of-school contacts and community mixing	Generally not recommended	Consider: 4 weeks	Recommend: 12 weeks
WORKPLACE/COMMUNITY Adult social distancing – Decrease number of social contacts (e.g., encourage teleconferences, alternatives to face-to-face meetings)	Generally not recommended	Consider	Recommend
– Increase distance between persons (e.g., reduce density in public transit, workplace)	Generally not recommended	Consider	Recommend
– Modify, postpone, or cancel selected public gatherings to promote social distance (e.g., postpone indoor stadium events, theatre performances)	Generally not recommended	Consider	Recommend
– Modify workplace schedules and practices (e.g., telework, staggered shifts)	Generally not recommended	Consider	Recommend

SOURCE: www2a.cdc.gov/phlp/docs/community_mitigation.pdf

3. The third variable is the WHO (World Health Organization) phase for pandemic flu. WHO has defined 6 phases, occurring before and during a pandemic, which are linked to the characteristics of a new influenza virus and its spread through the population. Summarizing the WHO phases:

WHO Phases	
Inter-Pandemic Period	
1	No new influenza virus subtypes have been detected in humans. An influenza virus subtype that has caused human infection may be present in animals. If present in animals, the risk of human disease is considered to be low.
2	No new influenza virus subtypes have been detected in humans. However, a circulating animal influenza subtype poses a substantial risk to humans.
Pandemic Alert Period	
3	Human infection(s) with a new subtype, but no human-to-human spread, or at most rare instances of spread to a close contact.
4	Small cluster(s) with limited human-to-human transmission but spread is highly localized, suggest that the virus is not well adapted to humans.
5	Larger cluster(s) but human-to-human spread still localized, suggesting that the virus is becoming increasingly better adapted to humans, but may not yet be fully transmissible (substantial pandemic risk).
Pandemic Period	
6	Pandemic phase: increased and sustained transmission in general population.

Source: www2a.cdc.gov/php/docs/community_mitigation.pdf

Note that the mitigation strategies suggested in this CDC document are designed to provide specific pre-pandemic planning guidance for the use of non-pharmacological interventions only in the advent of WHO Phase 6. We are currently (June 2007) experiencing Phase 3. While the WHO phases provide succinct statements about the global risk for a pandemic and provide benchmarks against which to measure global response capabilities, the US Government's approach to pandemic response characterizes the stages of an outbreak in terms of the immediate and specific threat a pandemic virus poses to the US population. The following stages provide a framework for Federal Government actions:

Federal Government Response Stages	
Stage 0	New domestic animal outbreak in at-risk country
Stage 1	Suspected human outbreak overseas
Stage 2	Confirmed human outbreak overseas
Stage 3	Widespread human outbreaks in multiple locations overseas
Stage 4	First human case in North America
Stage 5	Spread throughout United States
Stage 6	Recovery and preparation for subsequent waves

SOURCE: www2a.cdc.gov/php/docs/community_mitigation.pdf

Using the Federal Government's approach, this CDC document provides pre-pandemic planning guidance from Stages 3 through 5 for step-by-step escalation of activity, from pre-implementation preparedness, through active preparation for initiation of the recommendations, to actual use.

RESEARCH NEEDS

The CDC report acknowledges that a comprehensive research agenda for pandemic influenza is needed to improve the evidence base of the proposed interventions described in the current interim guidance. The agency calls for conducting studies to gain more knowledge about: the epidemiology of influenza, the effectiveness of community-based interventions, the use of medical countermeasures that complement community interventions, the modification of existing mathematical modeling to include adverse societal consequences, and the development of new modeling frameworks to assess the effectiveness of interventions. Additional key areas where research is needed include:

- **Enhancing epidemiologic and laboratory surveillance systems for influenza:** Existing influenza surveillance systems have gaps in timeliness and completeness that will hamper adequate functioning during a pandemic; therefore, a high priority must be given to the development of more timely surveillance for laboratory-confirmed cases of human infections, methods to rapidly estimate the excess mortality rate during a pandemic, and the development of platforms that can be used to assess the effectiveness of pandemic interventions.
- **Development of rapid diagnostics:** Laboratory diagnosis of influenza is critical for the treatment, prophylaxis, surveillance, vaccine development, and timing of the initiation of pandemic mitigation strategies. The development of sensitive and specific point-of-care rapid tests for influenza A subtypes with pandemic potential will play a critical role in pandemic preparedness.

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- **Measurement of effectiveness of personal protective equipment (PPE, eg, surgical masks and respirators) in community settings:** Quantification of the effectiveness of PPE for infection prevention, training community members to correctly use PPE, the utility of PPE for children and the elderly for whom PPE is not currently designed, and the relative contribution of PPE to safety in the context of other interventions should be undertaken. The main issue here is to develop a thorough understanding of the relative merits of the surgical mask and the N95 respirator.
- **Determination of the trigger points for implementation of interventions:** While the historic data from 1918 on the use of non-pharmacological interventions indicate an ecological relationship between timing and effectiveness, additional prospective data on timing of each of these measures will usefully complement the value of historic evidence.

SUMMARY

Planning and preparedness for implementing pandemic mitigation strategies is complex and requires participation and specific actions by all levels of government and all segments of society, including individuals, families, schools, businesses, and community organizations. It should be emphasized that the responsibility for public health in the US is state-based, requiring all states to develop individual plans; however, many have acknowledged that they do not have the expertise to make decisions about closing schools and businesses, and have looked to the federal government for guidance. This CDC document is the initial step in providing that guidance.

The Pandemic Severity Index, in which case fatality ratio serves as the critical driver for categorizing the severity of a pandemic, is designed to enable better forecasting of the impact of a pandemic, providing a basis for selecting the most appropriate interventions and balancing the potential benefits against the expected costs and risks.

While the "social distancing" interventions advocated (school and business closure, etc) may seem severe, there is evidence from mathematical models and retrospective analyses from the 1918 pandemic that cities which implemented community mitigation were successful in reducing mortality and were more adequately prepared for the surge in demand for hospital beds and medical personnel. The greatest challenge is the trade-off: keeping people home sounds relatively simple, but it can be terribly disruptive, especially if the duration is the anticipated 8-12 weeks. Note, however, that the recommended plan is meant to be implemented only if we are in Phase 6 of the WHO classification, which means there is increased and sustained transmission in the general population at some place in the world.

As stated above, it is not within the scope of this eLiterature Review to fully detail the thinking behind, and the complete recommendations of, the CDC's Interim Pre-pandemic Planning Guidance: Community Strategy for Pandemic Influenza Mitigation in the United States. Clinicians may view the entire document from the CDC website or by [downloading this PDF](#).

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- **Jonathan M. Zenilman, MD** has disclosed no relationship with commercial supporters.
- **Jason E. Farley, PhD(c), MPH, NP** has disclosed no relationship with commercial supporters.

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