

## EMERGING INFECTIOUS DISEASES:

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### Conference Summary

#### Findings, Gaps, and Future Direction for Research in Nonpharmaceutical Interventions for Pandemic Influenza

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In June 2006, the Centers for Disease Control and Prevention (CDC) released a request for applications to identify, improve, and evaluate the effectiveness of nonpharmaceutical interventions (NPIs) to mitigate the spread of pandemic influenza within communities and across international borders (RFA-CI06-010) ([1](#)). Eleven studies ([Table 1](#)) were funded to identify optimal, discrete, or combined NPIs for implementation during an influenza pandemic. During March 4–6, 2009, the principal investigators met to share results, identify research gaps, and define future research needs in 9 areas as described here. A total of 16 research gaps were identified ([Table 2](#)).

NPI behaviors can be successfully taught to and adopted by a variety of persons through community health education, interactive classroom teaching, or Internet-based instruction ([3](#)).

Urban Hispanics had misunderstandings about influenza (e.g., 88% thought that influenza was caused by bacteria). Their knowledge, attitudes, and practices improved through a community education program (4). Acceptability of NPIs also depends on early planning, consistent and targeted communication during implementation, and clear delineation of responsibilities and authority. Acceptability further requires communication from traditional (i.e., emergency response organizations) and nontraditional (i.e., churches) sources.

Behaviors perceived as typical daily behavior were more readily accepted than nontypical daily behaviors. Hand sanitizing with alcohol-based preparations, washing with soap, covering sneezes and coughs, and being aware of one's hands (e.g., touching face) showed relatively high compliance. Only 1 of 5 projects had good adherence to face mask use, which is not a typical behavior (2).

In addition, efficacy of face masks for preventing transmission of influenza viruses has yet to be fully determined. Influenza virus nucleic acid was present in fine-particle aerosols from influenza patients in tidal breathing (14%–33%) and coughing (64%) (5). Preliminary results demonstrate that surgical ear-loop face masks limit the generation of droplets ( $\geq 5.0 \mu\text{m}$  in diameter) containing influenza virus RNA.

NPIs can be efficacious for reducing rates of influenza and influenza-like illness (ILI) in community settings. Household secondary attack ratios were substantially reduced (adjusted odds ratio 0.33, 95% CI 0.13–0.87) if all household members practiced frequent hand washing and wore face masks within 36 hours after symptom onset in the index patient (6). University students had a 50%–65% reduced rate of ILI over a 6-week intervention period, using hand hygiene and masks (7). Mask use was substantial (4–5 hours per day average), which was attributed to adoption of masks as a daily behavior, rather than as a response to illness. Elementary school students using a 5-layered NPI approach, including hand hygiene and cough etiquette, had 53% fewer laboratory-confirmed influenza A infections and 26% fewer total absences compared with a control group.

Household crowding (measured as a deficit of  $\geq 2$  bedrooms) can be a factor in community influenza transmission, significantly increasing the relative risk (RR) for hospitalization for pneumonia or influenza (RR = 1.20, 95% CI 1.05–1.37; age standardized). The mean serial interval (i.e., the time between successive cases of infectious diseases in the chain of transmission) was 3.6 days, based on pairs of persons in 14 households (8).

School dismissal is part of CDC's pandemic planning, but dismissed students may congregate elsewhere. The number of social contacts by children dropped 67% ( $p < 0.05$ ) during school holidays, suggesting that recongregation may not be a factor in school closure and that school dismissal might increase social distancing during pandemic influenza.

Three studies assessed the use of Quidel QuickVue Influenza A+B Rapid Test in the community and found a median sensitivity of 27%, despite manufacturer reports of 73%. No cause for this sensitivity has been shown (9).

Rapid, large-scale risk-based entry screening of air travelers for ILI that used questionnaires and health assessments was conducted successfully at 2 airports for 177 flights. Seventy-five percent of passengers who provided contact details were followed up, but few of those with symptoms were prepared to go to a laboratory for collection of a respiratory specimen. On the basis of preliminary analysis, investigators concluded that voluntary travel restrictions would sufficiently protect only isolated populations with low numbers of visitors ([10](#)).

Investigators have collected newspapers, official health reports at all levels, scholarly literature, and archived material from governments and agencies. This material is being compiled into The American Influenza Epidemic of 1918–1919: A Digital Encyclopedia, an archive of historical material ([11,12](#)).

Meeting participants concluded that evidence exists of the effectiveness of NPIs, including face masks, hand hygiene, cough etiquette, reduced crowding, and school closures, in reducing the spread of influenza. Insufficient sample sizes, exacerbated by a mild influenza season during the first funding year, underreporting of disease, and challenges faced by influenza surveillance limited the statistical power of most studies. Further studies with larger sample sizes, common methods to allow pooling of data, and study durations that cover multiple influenza seasons are needed to address these limitations. In addition, studies using engineering controls, such as upper-room ultraviolet C lighting, in populations with naturally acquired infection are needed to address the relative contribution of transmission modalities, e.g., small vs. large respiratory droplets and contact transmission.

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## Comments to the Authors

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**Table 1.** List of projects funded during 2007–2009 under Centers for Disease Control and Prevention Nonpharmaceutical Intervention Studies for Pandemic Influenza RFA-CI06-010\*

Study title	Institution	Principal investigator(s)	Description
Evaluation of Masks as a Source Control NPI, School of Health and Environment	University of Massachusetts Lowell, Massachusetts, USA	Donald K. Milton	Built an exhaled breath sampling device for influenza virus; measured number and aerosol size distribution of exhaled influenza virus; and measured the effect of wearing a surgical mask on generation of large- and fine-particle aerosols containing influenza virus.
Stopping Upper Respiratory Infections (URIs) and Flu in the Family: The Stuffy Trial	School of Nursing, Columbia University, New York, New York, USA	Elaine L. Larson	Tested the effectiveness of 1) alcohol based hand sanitizer and 2) sanitizer coupled with face masks on the rates of laboratory-confirmed influenza, symptoms of influenza, and viral upper respiratory infections.
Community-based Nonpharmaceutical Intervention for Pandemic Influenza	RTI International, Research Triangle Park, North Carolina, USA	Scott F. Wetterhall	Assessed, implemented, and evaluated community-level NPI strategies to prevent influenza in rural North Carolina communities.
A Controlled Trial of Masks and Hand Hygiene for Reducing Influenza Transmission	School of Public Health, The University of Hong Kong, Hong Kong, People's Republic of China	Gabriel M. Leung and Benjamin J. Cowling	Tested the effectiveness of 1) hand hygiene (hand washing and the use of alcohol-based hand sanitizer) and 2) hand hygiene combined with surgical face masks to prevent influenza transmission within household from persons at an outpatient clinic

Pittsburgh Influenza Prevention Project (PIPP)	Center for Public Health Practice, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania, USA	Donald S. Burke and Sam Stebbins	Tested hand hygiene and etiquette, hand sanitizer, and home isolation on the transmission of influenza and other diseases, and absenteeism in kindergarten through 5th-grade schools.
Reducing Transmission of Influenza by Face Masks (M-FLU)	Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, Michigan, USA	Arnold S. Monto and Allison E. Aiello	Evaluated face masks and hand hygiene to estimate the reduction in the rate of influenza infection and ILI among students living in university residence halls.
REDucing Influenza-like illness among University Students: The REDI-US Study	Center for Infectious Diseases & Emergency Readiness, School of Public Health, University of California, Berkeley, California, USA	Tomas J. Aragon	Tested the effectiveness of online education of respiratory and cough etiquette, hand hygiene, hand awareness, and face mask use in reducing the occurrence of ILI among university students.
Pandemic Influenza Control at the Borders of Island Countries and in Households	Pandemic Influenza Research Group, University of Otago, New Zealand	Michael G. Baker, Patricia Priest, Lance Jennings, Nick Wilson, and Heath Kelly	Assessed the effectiveness of maritime quarantine for preventing entry of the 1918 pandemic into Pacific Island countries. Estimated the reduction in travel volumes and the quarantine duration needed to exclude pandemic influenza from island nations. Analyzed the relationship between influenza hospitalization and levels of household crowding and other potentially modifiable factors among public housing residents. Screened travelers on international flights for seasonal influenza.

Surveillance of Influenza-like Illness among International Air Travelers	Hawai`i Department of Health, Honolulu, Hawaii, USA	Sarah Y. Park	Assessed regional capacity and feasibility to implement voluntary risk-based entry screening of air travelers for ILI.
History Informing Public Health Preparedness Policy in the 21st Century: A Qualitative Study of Nonpharmaceutical Interventions and Community Experiences during the 1918–1919 Influenza Pandemic	Center for the History of Medicine, University of Michigan, Ann Arbor, Michigan, USA	Howard Markel, Alexandra M. Stern, and J. Alexander Navarro	Examined the role of NPI for epidemic mitigation in 43 cities in the continental United States from 1918–19 influenza pandemic. Began creating the first historical atlas on the 1918–19 influenza pandemic in the United States.
A Randomized Controlled Trial of Nonpharmaceutical Interventions to Reduce Household Influenza Transmission: Bangkok "HITS" Study (Household Influenza Transmission Study)	The Influenza Division, International Emerging Infections Program, Thailand Ministry of Public Healty–US CDC Collaboration, Bangkok, Thailand	Mark Simmerman	Evaluated 1) hand washing and 2) hand washing plus face mask use to reduce the spread of influenza in households of pediatric hospital–based clinic patients, testing positive for influenza.

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\*NPI, nonpharmaceutical intervention; ILI, influenza-like illness.

**Table 2.** Research gaps in identifying, improving, and evaluating the effectiveness of NPIs in mitigating the spread of pandemic influenza\*

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Behavioral and social sciences

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Knowledge, attitudes, and practices related to use of NPIs across diverse populations

Role of social, demographic, and cultural factors on NPI practice

Decision-making dynamics with respect to NPI recommendations

Effective risk communication strategies for enhancing NPI compliance

Extent of barriers to implementation of NPIs

How behavioral and social determinants influence NPI efficacy

Biological and technological sciences

Adequate clinical influenza definitions

Prevalence and impact of asymptomatically influenza-infected persons

Sensitive and specific influenza rapid tests for community-based studies

Relative contributions of influenza virus transmission modalities (i.e., large droplet, small-particle droplet nuclei, and contact) to disease spread

The clinical implications of influenza viral load

The prevalence, risk factors, and impact of influenza superspreaders on disease transmission

The impact of environmental, crowding, and density on influenza transmission

The influence of international travel on transmission of influenza

Sensitive and specific screening tools for identifying influenza-infected travelers at international borders

Efficacy of different types of masks, hand hygiene, and combinations of personal protective measures for reducing transmission of influenza

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\*NPI, nonpharmaceutical intervention.

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