



HEALTH

Center for Domestic and International Health Security

Non-Pharmaceutical Public Health Interventions for Pandemic Influenza

Sam A. Bozzette

Julia E. Aledort

Nicki Lurie

Goals & Overall Approach

- **Identify array of non-pharmaceutical interventions (NPIs)**
- **Assess current state of knowledge**
 - Conduct expedited search of literature on “real world” effectiveness
 - Convene expert panel to review, validate & supplement evidence
 - Survey panelists to capture recommendations
- **Perform modeling-based analysis of potential benefit of alternate NPIs**

NPIs that can Influence Human-to Human Transmission

- **Infection control**
 - to reduce transmission during contact
- **Patient management**
 - to reduce contact with the symptomatically infected
- **Contact management**
 - to reduce contact with the possibly exposed
- **Compulsory and voluntary community restrictions**
 - to limit mixing of groups containing possibly infected

NPIs That Can Slow Human-to Human Transmission

Infection Prevention & Control

- Surveillance & case reporting
- Early rapid viral diagnosis
- Disinfection
- Hand hygiene
- Respiratory etiquette
- Masks & other PPE

Patient Management

- Isolation of sick individuals
- Provision of social support services

Community Restrictions

- Cancellation of group events
- School & workplace closures
- International & domestic travel restrictions

Contact Management

- Quarantine
- Voluntary sheltering
- Contact tracing

Expedited Literature Review

Gather Evidence on “Real World” Effectiveness of NPIs

- **Consult experts to identify recent & ongoing studies**
- **Identify and review recent & ongoing studies**
- **Review recent review articles (2000-present)**
- **Focused search in top-tier medical & PH journals (1966-present)**
- **Search of scientific & historical literature on NPIs, respiratory infections & other infectious diseases (1966 – present)**
- ***2,552 titles evaluated; 156 reviewed***

Literature Review: Themes & Findings

- **Evidence for NPIs consists of:**
 - Historical experiences, e.g. plague, past pandemics
 - Contemporary observations, e.g, SARS
 - Inferences from biology & pathophysiology
- **In general, search revealed scant confirmatory evidence on effectiveness of NPIs in influenza**
 - Infection control recommendations generally made on the basis of *plausible* effectiveness of evidence from different settings, e.g., SARS
 - Patient isolation evidence is typically historical in nature and/or drawn from the experience of SARS
 - Effectiveness of contact management for pandemic influenza is derived largely from mathematical models

Literature Review: Infection Control Measures

- **Some evidence that handwashing may be effective against the spread of viral respiratory disease**
- **Effectiveness of widespread use of masks is limited by the uncertain efficacy of gauze or similar masks and the requirement that N95 masks be fitted**
- **Use of PPE (e.g., masks, gowns, eye covers, gloves/handwashing by hospital staff) in SARS was associated with a lower risk of infection, with most of the effect seemingly due to mask use and extremely rigid adherence to infection control practices**

Literature Review: Patient Management Measures

- In 1918, mandatory reporting was useful for *identifying* but not necessarily *controlling* disease spread
- Hospital isolation using appropriate infection control measures may be effective
- Compulsory home isolation will likely miss many patients and prevent needed assistance from reaching the ill
- Models indicate that effective isolation of symptomatic persons may be sufficient for control, but measures to lower the transmission rate (i.e., increasing social barriers) are *perhaps* more important in practice

Literature Review: Contact Management Measures

- **In SARS, quarantine of low-risk contacts and screening of travelers had little direct effect**
 - Few cases were related to travel
 - Asymptomatic transmission did not occur
- **Inferences from smallpox transmission models suggest that partial quarantine *may be somewhat effective***
- **Models indicate benefit from quarantine in several settings**
- **Aggressive tracing and quarantine of higher-risk SARS contacts during the incubation period seemed to have been effective**
- **Costs of quarantine may be substantial**
 - Direct and indirect costs, personal distress, threats to privacy & civil liberty

Literature on School Closure Inconclusive

- **School closure decreases rate of epidemic spread**
 - Evidence suggests that in 1959 and probably 1918, influenza epidemics accelerated after the fall opening of schools
 - A study of school children in Israel found significant decreases in respiratory infections after school closures (Heymann et al. 2004)
 - In recent years, attack rates for influenza and other respiratory infections among French children decreased during holidays
- **School closure increases rate of epidemic spread**
 - In 1918, some cities with open monitored schools had lower attack rates than those with closed schools, and that attack rates rose over the holidays in Chicago
- **Models infer that school closing may be effective assuming that children stay home**

DHHS/RAND Expert Panel on NPIs

- **Convened 17-18 January 2006 (Arlington, VA)**
- **Composition**
 - 18 distinguished international members
 - 3 RAND researchers
 - Disciplines of biomedical research, clinical practice, epidemiology, ethics, law, history & policy
- **Objectives**
 - Define a set of NPIs and criteria for evaluation
 - Assess efficacy, effectiveness, feasibility, acceptability
 - Synthesize information to produce policy and research recommendations

Expert Panel Participants

- **John Barry**
- **Georges Benjamin**
- **Wändi Bruine de Bruin**
- **Jim Curran**
- **Walter Dowdle**
- **David Fidler**
- **Harvey Fineberg**
- **Baruch Fischhoff**
- **Barbara Goldrick**
- **Lawrence Gostin**
- **David Heyman**
- **James Hughes**
- **Howard Markel**
- **Allison McGeer**
- **Thomas Murray**
- **Michael Osterholm**
- **Wing Hong Seto**
- **Isaac Weisfuse**

Evaluation Criteria

- **Efficacy**: Will NPIs work under ideal conditions?
- **Effectiveness**: Will NPIs work in the "real-world"?
 - *Feasibility*: Can the NPI be implemented?
 - Is operational capability & infrastructure in place?
 - What will it cost?
 - *Acceptability*: Should the NPI be implemented?
 - Are there legal, ethical and/or equity concerns?
 - Potential unintended negative consequences?
- **Setting**: Where will NPI be applied?
- **Pandemic phase**: When will NPIs be most useful?

Expert Panel: Themes & Findings (1)

- **Information needs are pervasive as research-based evidence is nearly non-existent for most NPIs**
- **Supply and supply chain limitations will limit implementation of most NPIs**
- **Measures to decrease interpersonal contact become increasingly suspect as epidemics progress**
- **Effective risk communication and educational campaigns are essential for success of any NPI**

Expert Panel: Themes & Findings (2)

Broad agreement on some NPIs:

- **Panelists endorsed importance of**
 - **Hand hygiene and respiratory etiquette**
 - **Rapid viral diagnosis and triage**
 - **Isolation- only in hospital during early stages**
 - **Enhanced provision of social services to the ill and sheltering**
 - **Guidance on voluntary sheltering and cloistering**
- **Panelists rejected**
 - **Broader use of disinfection**
 - **Quarantine in established epidemic**
 - **Isolation in public facilities outside of health care institutions**
 - **Mandatory travel restrictions**

Follow-up questionnaire

- **200 items queried (NPI-setting-phase triads)**
- **Experts rated items from 'not recommended' (1) to 'strongly recommended' (5)**
- **Thirteen of seventeen experts responded (76%)**
- **Scored for agreement then recommendation**

Experts Favored Voluntary & Lower Cost NPIs

Non-Pharmacologic Intervention	Pandemic Phase			
	None	Elsewhere	Early Localized	Advanced
Hand Hygiene - Hospital	●	●	●	●
Hand Hygiene - Ambulatory	●	●	●	●
Hand Hygiene - Community and/or Home	●	●	●	●
Respiratory Etiquette - Hospital	●	●	●	●
Respiratory Etiquette - Ambulatory	●	●	●	●
Human surveillance	●	●	●	○
Case Reporting	●	●	●	○
Rapid Viral Diagnosis and Triage§	●	●	●	○
Advisories (voluntary restrictions) on departures from affected international regions	●	○	○	○
Voluntary Self-Isolation of the Sick in the Home§	–	●	●	●
Provision of Social Support Services (to isolated or quarantined persons) - Hospital§	–	○	●	●
Provision of Social Support Services (to isolated or quarantined persons) - Ambulatory§	–	○	●	●
Other PPE - Hospital§	○	○	●	●
N95 Respirators - Hospital§	○	○	●	●
Respiratory Etiquette - Community and/or Home	○	○	●	○
Surgical masks - Hospital§	○	○	○	●
Surgical masks - Ambulatory§	○	○	○	●
Provision of Social Support Services (to isolated or quarantined persons) - Home§	–	○	○	●

§ Results based on 9, 10, 11 or 12 responses (of out of a possible 13). All remaining results are based on all 13 responses.

● Recommendation for use (46/200 items (23%))

○ Disagreement (117/200 items (59%))

– Not Applicable (respondents were instructed to leave blank)

Experts Rejected Higher Cost NPIs

Non-Pharmacologic Intervention	Pandemic Phase			
	None	Elsewhere	Early Localized	Advanced
Limited Case-by-Case Home-Based Mandatory Quarantine (of exposed) - Home§	—	○	○	●
Contact Tracing§	○	○	○	●
Mandatory restrictions on arrivals from affected international regions	○	○	○	●
Exit screening of travelers from affected international region to unaffected U.S. region§	○	○	○	●
Entry screening of travelers from affected international region to unaffected U.S. region§	○	○	○	●
Exit screening of travelers from affected U.S. region to unaffected U.S. region§	—	○	○	●
School Closures§	—	●	○	○
Work Closures§	—	●	○	○
Case-by-Case Cancellation of Public Events§	—	●	○	○
Mandatory restrictions on arrivals from affected U.S. regions	—	●	○	●
Entry screening of travelers from affected U.S. region to unaffected U.S. region§	—	○	●	●
Mandatory restrictions on departures from affected international regions	○	○	●	●
Surgical Masks - Community§	●	●	○	○
Surgical Masks - Home	●	●	○	○
N95 Respirators - Community§	●	●	●	○
N95 Respirators - Home§	●	●	●	○
Mandatory restrictions on departures from affected U.S. regions	—	●	●	●
Other PPE - Community§	●	●	●	●
Other PPE - Home§	●	●	●	●

§ Results based on 9, 10, 11 or 12 responses (of out of a possible 13). All remaining results are based on all 13 responses.

● Recommendation against use (37/200 items (18.5%))

○ Disagreement (117/200 items (59%))

— Not Applicable (respondents were instructed to leave blank)

Many Areas for Further Investigation

Non-Pharmacologic Intervention	Pandemic Phase			
	None	Elsewhere	Early Localized	Advanced
N95 Respirators - Ambulatory§	●	○	○	●
Surface Disinfection Beyond Usual Practice - Home	○	○	○	○
Surface Disinfection Beyond Usual Practice - Hospital§	○	○	○	○
Surface Disinfection Beyond Usual Practice - Ambulatory§	○	○	○	○
Surface Disinfection Beyond Usual Practice - Community	○	○	○	○
Limited Case-by-Case Home-Based Mandatory Quarantine (of exposed) - Hospital§	—	○	○	○
Limited Case-by-Case Home-Based Mandatory Quarantine (of exposed) - Ambulatory§	—	○	○	○
Limited Case-by-Case Home-Based Mandatory Quarantine (of exposed) - Community§	—	○	○	○
Provision of Social Support Services (to isolated or quarantined persons) - Community§	—	○	○	○
Advisories (voluntary restrictions) on arrivals from affected U.S. regions	—	○	○	○
Advisories (voluntary restrictions) on departures from affected U.S. regions	—	○	○	○
Advisories (voluntary restrictions) on arrivals from affected international regions	○	○	○	○
Voluntary quarantine of exposed§	—	○	○	○
Voluntary sheltering§	—	○	○	○
Mandatory self-isolation of the sick - Hospital§	—	○	○	○
Mandatory self-isolation of the sick - Ambulatory§	—	○	○	○
Mandatory self-isolation of the sick - Community§	—	○	○	○
Mandatory self-isolation of the sick - Home§	—	○	○	○
Other PPE - Ambulatory§	○	○	○	○

§ Results based on 9, 10, 11 or 12 responses (of out of a possible 13). All remaining results are based on all 13 responses.

○ Disagreement (117/200 items (59%))

— Not Applicable (respondents were instructed to leave blank)

Research Needs (1)

- **Surveillance**
 - How do we generate real-time international, national, state & local data at each pandemic phase?
- **Experiments & quasi-experiments to directly evaluate the effect of NPIs on real world outcomes**
 - Excess respiratory deaths in non-pandemic years
 - Evaluations of NPIs in home-based settings
 - Ventilation & air exchange studies

Research Needs (2)

- **Mathematical modeling**
 - What is the potential effectiveness of specific NPIs, alone & in combination, at different compliance thresholds?
 - What threshold compliance level is required for NPI effectiveness, with & without pharmacologic interventions?
 - Is slowing down a pandemic really preferable?
- **Public attitudes, beliefs & perceived self-efficacy**
 - What are individuals prepared to do in a pandemic?
 - How can authorities help them be successful?
 - What are the attributes of successful risk communications and public education regarding NPIs?

Research Needs (3)

- **Issues of Legal Authority**
 - When, and under what circumstances do public health officials have legal authority to act?
 - What are ethical and legal implications of NPIs as they relate to differential impact for various populations?
- **Social services & behavior**
 - What services are required to help people remain isolated?
 - How can such services be sustained?
 - What are barriers to changing cultural practices (e.g., handshaking)?



HEALTH

RAND