POLICY REVIEW

Nonpharmaceutical Interventions for Pandemic Influenza, National and Community Measures

World Health Organization Writing Group*[1]

The World Health Organization's recommended pandemic influenza interventions, based on limited data, vary by transmission pattern, pandemic phase, and illness severity and extent. In the pandemic alert period, recommendations include isolation of patients and quarantine of contacts, accompanied by antiviral therapy. During the pandemic period, the focus shifts to delaying spread and reducing effects through population-based measures. Ill persons should remain home when they first became symptomatic, but forced isolation and quarantine are ineffective and impractical. If the pandemic is severe, social distancing measures such as school closures should be considered. Nonessential domestic travel to affected areas should be deferred. Hand and respiratory hygiene should be routine; mask use should be based on setting and risk, and contaminated household surfaces should be disinfected. Additional research and field assessments during pandemics are essential to update recommendations. Legal authority and procedures for implementing interventions should be understood in advance and should respect cultural differences and human rights.

This article is the second of a 2-part series that summarizes the scientific basis for nonpharmaceutical public health interventions recommended by the World Health Organization (WHO) to contain or reduce transmission of pandemic influenza caused by a novel human influenza subtype; it is designed to be read in conjunction with the recommendations (*1*), which are intended as guidance and not formal WHO advice (Appendix 1, available online at http://www.cdc.gov/ncidod/EID/vol12no01/05-1371_app1.htm) (*2*). The evidence base for recommendations is limited, consisting primarily of historical and contemporary observations, rather than controlled scientific studies. The first part of this series summarized the transmission characteristics of influenza viruses and the basis for interventions to reduce international spread (*3*). This second part addresses measures at the national and community levels that are intended to reduce exposure of susceptible persons to the novel virus. The observations that pandemics do not infect all susceptible persons in the first wave and that subsequent waves occur suggest that preventing disease by reducing exposure is an achievable objective (*3*). By limiting exposure, people who are not infected during the first wave may have an increased chance of receiving virus-specific vaccine as it becomes available. In addition, if the virus becomes less virulent over time, persons who fall ill in subsequent waves may have milder illnesses. This article does not address public communication or infection-control measures for patient care (*4,5*).

Measures To Reduce Spread within Populations

Isolation of Patients and Quarantine of Contacts

Community Level

Reports from many countries indicate that mandatory case reporting and isolating patients during the influenza

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pandemic of 1918 did not stop virus transmission and were impractical. In Canada, the medical officer of health for the province of Alberta concluded that forced home isolation of patients, posting signs on houses, and "quarantine" (details unspecified) captured only ≈60% of patients in the community because of diagnostic difficulties involving mild cases and failure to notify cases to authorities. As the medical officer noted, "many citizens regarded the placard [sign outside the quarantined person's house] as an injustice, either because they did not believe the diagnosis justified, or because their neighbors were alleged by them to be avoiding quarantine by concealment or evasion… Charges of discrimination were frequently made against the health department" (*6*).

In the Australian state of New South Wales, compulsory reporting was deemed helpful to identify the first introduction of cases into a community. However, once the number of cases grew, reporting cases was not useful or feasible. Also, mild cases were not reported. Compulsory home isolation (which automatically followed reporting) prevented neighbors from bringing needed assistance and was replaced by requesting patients to remain at home (*7*). The reports do not assess the potential impact that requests for ill persons to remain at home voluntarily could have on the reduction of disease within the community.

Closed Settings

In closed settings (e.g., military barracks and college dormitories), early identification and isolation of patients in 1918 usually did not completely stop virus transmission but appeared to decrease attack rates, especially when supplemented by restrictions on travel to and from the surrounding community (*8*). In 1 report, 2 sections (A and B) of the student army training corps at the University of Chicago were housed in similar dormitories and fraternity houses, but they had separate classrooms and eating places and no formal contact with each other. In section A, the men received frequent instructions to report illness; all ill persons with "simple colds" or suspected influenza were immediately isolated in hospitals or sent home. In section B, "more or less close contact between sick and well members" was maintained for several days. Lectures and classes were held as usual. From October 17 to November 8, 1918, a total of 26 of 685 men in section A had influenza (attack rate 39/1,000), which was one tenth the attack rate for section B (398/1,000, 93/234 men). New cases ceased in section B after daily inspection and patient isolation were implemented, but these measures were taken late in the epidemic. Among 82 other students living at home or in boarding houses, 7 became ill with influenza (*9*). Similarly, an Australian Quarantine Service review of ship epidemics in 1918 and 1919, including ships quarantined at ports of entry, indicates that daily temperature checks and immediate isolation of patients did not completely prevent transmission but may have reduced the number of cases (*3*).

Reports from several countries (e.g., Australia, Canada, British-occupied Togo) refer to "isolation of contacts" (the preferred modern terminology is isolation of patients and quarantine of contacts) in 1918 and 1919. Details are unclear, but these reports imply that contacts were confined at home. Such measures were consistently described as ineffective and impractical (*6,7,10*)

Some of the lessons learned from the 2003 severe acute respiratory syndrome (SARS) epidemic can be applied to influenza, including the success of public campaigns to encourage self-recognition of illness, telephone hotlines providing medical advice, and early isolation when potential patients seek health care. Thermally scanning intercity travelers was inefficient in detecting cases. Early isolation of patients and quarantine of contacts successfully interrupted SARS transmission, but influenza's shorter serial interval and earlier peak infectivity, plus the presence of mild cases and possibility of transmission without symptoms, suggest that these measures would be considerably less successful than they were for SARS (*3,11,12*).

Social Distancing Measures

Avoiding Crowding

A WHO consultation in 1959 concluded that the 1957 influenza pandemic tended to appear first in army units, schools, and other groups where contact was close. Also noting the reduced incidence in rural areas, the consultation suggested that avoiding crowding could reduce the peak incidence of an epidemic and spread it over many, rather than a few, weeks (*13*).

Closing Schools and Childcare Centers

A 1959 WHO consultation concluded, "In the Northern hemisphere at least, the opening of schools after the summer holidays seems to have played an important role in initiating the main epidemic phase" (*13*). Despite the propensity of influenza epidemics to be amplified in primary schools (*14*), data on the effectiveness of school closures are limited. Apparently no data or analyses exist for recommending illness thresholds or rates of change that should lead to considering closing or reopening schools.

During a 2-week teachers' strike during an influenza epidemic in Israel in 2000, significant decreases were seen in the rates of diagnoses of respiratory infections, medication purchases, and other parameters for children 6–12 years of age; when school reopened, rates for these parameters rose again. The study did not report on illness in family members (*15*). In 21 regions of France from 1984 to 2000, a temporal relationship was reported between school holidays and a decrease in the incidence of influenza diagnoses by general practitioners 10–20 days later and the daily death rate 30–40 days later, although the time delay raises the question of whether outbreaks may have been subsiding on their own (*16*).

On a small island in the United States in 1920, the single public school was a focal point for the spread of influenza, and a report from that period concluded that "prompt closure of the school would probably not have prevented the epidemic, but might have delayed it" (*17*). School closure might be less effective in some urban areas than in rural areas because urban children can more easily meet elsewhere: in 1918, more influenza cases developed among pupils in a Chicago school after a holiday than when schools were in session (*9*). In Connecticut, the 3 largest cities (Bridgeport, Hartford, and New Haven) kept schools open under "close medical supervision," and their death rates were reportedly lower than those in some Connecticut cities (New London and Waterbury) that closed their schools (*8*).

Universal influenza vaccination of children is controversial, but its use has provided data that help assess the potential effect of reducing transmission by schoolchildren. For example, in 1968–1969, when 86% of its schoolchildren were vaccinated against influenza, the small town of Tecumseh, Michigan, had one third the illness rate of nearby towns where children were not vaccinated (*18*). In Japan, when most schoolchildren were vaccinated against influenza (1962–1987), excess death in the entire population decreased 3- to 4-fold and rose again when the program was discontinued (*19*).

Simultaneous Use of Multiple Measures

Influenza and other respiratory viral infections apparently declined in Hong Kong during the 2003 SARS epidemic, as determined on the basis of a review of viral diagnostic laboratory records (*20*). Public health interventions included closing schools, swimming pools, and other public gathering places; cancelling sports events; and disinfecting taxis, buses, and public places. A high percentage of people wore masks in public and washed hands frequently, and in general, much less social mixing occurred.

Reports from the 1918 influenza pandemic indicate that social-distancing measures did not stop or appear to dramatically reduce transmission, but research studies that might assess partial effectiveness are apparently unavailable. For example, in Lomé, British-occupied Togo, case-patients, suspected case-patients, and contacts were isolated; traffic was halted; schools and churches were closed; public meetings were banned. Despite these and other measures, influenza was well established in Lomé by October (*10*). In Edmonton, Canada, isolation and quarantine were instituted; public meetings were banned; schools, churches, colleges, theaters, and other public gathering places were closed; and business hours were restricted without obvious impact on the epidemic (*21*,*22*). In the United States, a comprehensive report on the 1918 pandemic concluded that closing schools, churches, and theaters was not demonstrably effective in urban areas but might be effective in smaller towns and rural districts, where group contacts are less numerous (*8*).

Measures for Persons Entering or Exiting an Infected Area

In Australia in 1919, political tensions arose among state governments and between states and the national government as individual states sought to protect themselves. Issues included delayed disease reporting by the initially affected state, controls at interstate borders, resistance to quarantine measures, impoundment of the transcontinental train in the state of Western Australia, and conflict between national and state authorities in the Australian federal system (*23*).

Specific details were recorded by the State of New South Wales (NSW) (*24*): "After the first case was diagnosed in Sydney (capital of NSW State) …and determined to have come from (the) adjacent (state of) Victoria, measures were taken by New South Wales at the interstate border to prevent importation of additional cases. These included at first, prohibition of all inbound land traffic, later replaced by quarantine detention camps at which inbound travelers were required to remain at first 7, later 4 days. Also ships from Victoria State were required to anchor in Sydney harbor for 4 days, after which disembarking persons were medically inspected. After Sydney had nevertheless become severely affected, (unspecified) restrictions on traveling out of Sydney were also imposed." The report states that any benefits of land quarantine or interstate or intrastate travel restrictions were "very meager."

In Canada in 1918, one report noted, "Many small towns attempted to isolate themselves with complete quarantines, reminiscent of medieval attempts to stave off plague, in which no one was allowed to enter or leave town. No one was allowed to buy railway tickets to these towns and passengers were barred from disembarking at them. The Canadian Pacific Railway reported 40–45 towns closed in the province of Manitoba during the height of the epidemic; the Canadian Northern line bypassed 15 more. The Alberta Provincial Police guarded roadblocks on major highways in the Province of Alberta in an effort to keep influenza from reaching three prairie municipalities. These measures were nonetheless 'lamentably inefficient in checking the spread of the disease.' Quite simply, isolating individuals and families or quarantining entire communities did not work" (*6*,*21*,*22*).

In the United States, some towns in Colorado and Alaska implemented measures, such as a 5-day quarantine on entering travelers, to exclude infected people. Some towns apparently succeeded in escaping the disease, but others did not (*8*,*25*). In July 1921, an explosive outbreak of influenza occurred on the Pacific island of New Caledonia, a French territory. Authorities implicated a ship that had recently arrived at the capital city of Nouméa from Australia, where normal seasonal (winter) influenza cases were occurring. Illness spread rapidly in Nouméa and the southern portion of the colony, in part because of numerous gatherings in celebration of Bastille Day on July 14. However, authorities successfully prevented spread to the isolated northern third of the island. Travel by land to the north was prohibited, a measure that was facilitated by the lack of major roads to the area. Ships leaving Nouméa for the north were required to remain in quarantine for at least 48 hours before departure, and during that time, temperatures of passengers and crew were monitored (*26*).

Recent modeling studies have supported the use of quarantine measures in the unique circumstances of containing an emerging influenza subtype originating in rural Thailand as a supplement to geographically targeting antiviral drugs to the surrounding population. In 1 model, administering antiviral drugs to 90% of people in a 5-km radius within 2 days after detecting illness in 20 persons was estimated to contain a novel subtype with a basic reproduction number (R_0) of 1.5 (R_0 is the mean number of secondary cases generated by 1 infected person in a fully susceptible population). If prophylaxis were supplemented by closing 90% of schools and 50% of workplaces and reducing movement in and out of the affected area by 80%, the model predicted a 90% probability of containment if $R_0 = 1.9$ (*27*). These additional measures would help overcome shortcomings in case identification and treatment rates; the epidemic could be contained after <200 cases had been detected. Unsuccessful containment nevertheless delayed widescale spread by $\geq$1 month in the model. A second modeling study predicted that if every case-patient stayed at home and 70% of susceptible persons remained in their neighborhoods (but no antivirals were given), disease containment would be 98% if $R_0 = 1.4$ and 57% if $R_0 = 1.7$ (*28*). These estimates were based on the population structure and interaction dynamics in Thailand and apply to early detection of cases emerging in a rural area.

Personal Protection and Hygiene Measures

Wearing Masks in Public

Apparently no controlled studies assess the efficacy of mask use in preventing transmission of influenza viruses. During the 1918 influenza pandemic, mask use was common and even required by law in many jurisdictions. Skepticism arose, however; the medical officer of health for Alberta, Canada, noted that cases of disease continued to increase after mask use was mandated, and public confidence in the measure's efficacy gave way to ridicule (*6*).

In Australia, mask-wearing by healthcare workers was thought to be protective, and given evidence of transmission in a closed railway carriage, it was concluded that mask wearing "in closed tramcars, railway carriages, lifts, shops, and other in enclosed places frequented by the public had much to recommend it." However, mask-wearing in the open air, as initially required in Sydney, was later thought to be unnecessary (*24*).

In the United States, persons also wore masks as a protective measure. A report from Tucson, Arizona, noted that early measures included "…isolation of ill people, closure of schools, churches, theatres, etc. The epidemic worsened however. As weeks passed, criticism of the measures was expressed, most vocally by businesses losing money but also by religious and educational institutions. To allow some businesses to reopen, city officials ordered 'masks to be worn in any place where people meet for the transaction of necessary business' … (and later by) all persons appearing in public places. Within a few days, there was virtually universal compliance with mask wearing, but the epidemic was subsiding" (29).

During the SARS epidemic in 2003, 76% of Hong Kong residents reported wearing masks in public. As noted above, influenza virus isolation rates decreased, but since multiple measures were implemented, the contribution of mask use, if any, is uncertain (*20*). In case-control studies conducted in Beijing and Hong Kong, wearing masks in public was independently associated with protection from SARS in a multivariate analysis. One study found a dose-response effect (*30*). Methodologic limitations of the studies (e.g., retrospective questionnaire design) limit drawing conclusions (*30*,*31*).

Hygiene and Disinfection

Recommendations for "respiratory hygiene/cough etiquette," such as covering one's mouth when coughing and avoiding spitting, have been made more on the basis of plausible effectiveness than controlled studies (*32*). As summarized in part 1 of this article, influenza virus can remain viable on environmental surfaces and is believed transmissible by hands or fomites (*3*). Most, but not all, controlled studies show a protective effect of handwashing in reducing upper respiratory infections (Appendix 2, available online at http://www.cdc.gov/ncidod/EID/vol12no01/05-1371_app2.htm). Most of the infections studied were likely viral, but only a small percentage were due to influenza (*33*). No studies appear to address influenza specifically. In addition, only 1 study (in Pakistan) has been conducted on the effect of handwashing on severe disease (*34*). Most studies have been in care or institutional settings and involve children; the few involving adults were of college students and military recruits. Antibacterial handwashing products do not offer an advantage over soap and water. In the SARS outbreak in Hong Kong in 2003, a case-control study found that washing hands >10 times per day and "disinfecting living quarters thoroughly" (not otherwise defined and reported retrospectively by telephone) appeared to be protective in a multivariate analysis (*31*).

Discussion

The knowledge base for use in developing guidance for nonpharmaceutical interventions for influenza is limited and consists primarily of historical and contemporary observations, supplemented by mathematical models, rather than controlled studies evaluating interventions. Accordingly, WHO guidance is subject to revision based on additional information. Aside from transmission characteristics of the pandemic strain, which can be estimated but not completely known before a pandemic is under way, guidance for interventions at the national and community level depends on the phase of the pandemic, the severity of disease (a more virulent strain will justify more socially demanding measures), and the extent of transmission in the particular country and community. Animal sources of virus that has been linked to human infection should be controlled and human exposure to infected animals minimized (*35*). In phases 4 and 5 of the pandemic-alert period, which is characterized by limited and highly localized human-to-human transmission, aggressive measures to detect and isolate case-patients and to quarantine their contacts are recommended and should be accompanied by restrictions on movement in and out of affected communities and consideration of geographically targeted antiviral therapy. These measures, however, are considered much less likely to be feasible in an urban population (*1*,*3*,*27*).

The prediction from mathematical models that an emerging novel human influenza virus subtype might be containable at a point of origin in rural Southeast Asia in phases 4 and 5 through the targeted use of antivirals and application of public health measures was not intended to apply once a pandemic has begun or to address other situations (for example, when a pandemic strain enters into a new country at multiple loci) (*27*,*28*). After increasing and sustained transmission occurs in the general population of even 1 country (phase 6, pandemic period), eventual worldwide spread is considered virtually inevitable, and the public health response focus would shift to reducing impact and delaying spread to allow time for vaccine development and institution of other response measures. Part 1 of this article dealt with measures at the international level, but community-level measures outlined in this part of the article will likely have a greater effect, as was true for SARS in 2003. Over time, the changing conditions during a pandemic will require a change in the public health response and recommended interventions, and the need for such changes will present a difficult but critical communications challenge.

Field studies coordinated by WHO will be needed to assess virus transmission characteristics, amplifying groups (e.g., children vs. adults), and attack and death rates. Information on these factors will be needed urgently at the onset of a pandemic because the pandemic subtype may behave differently than previous pandemic or seasonal strains. Such studies will also be needed throughout the pandemic period to determine if these factors are changing and, if so, to make informed decisions regarding public health response measures, especially those that are more costly or disruptive.

Evidence and experience suggest that in pandemic phase 6 (increased and sustained transmission in the general population), aggressive interventions to isolate patients and quarantine contacts, even if they are the first patients detected in a community, would probably be ineffective, not a good use of limited health resources, and socially disruptive. During phase 6, ill persons should be advised to remain at home, if possible, as soon as symptoms develop (and their caregivers should be advised to take appropriate precautions [*5*]), but doing so would likely require financial and other support for those off work with illness. Measures to increase social distance should be considered in affected communities, depending on the epidemiology of transmission, severity of disease (case-fatality ratio), and risk groups affected. Nonessential domestic travel to affected areas should be deferred if large areas of a country remain unaffected, but enforcing domestic travel restrictions is considered impractical in most cases.

Handwashing and respiratory hygiene/cough etiquette (*32*) should be routine for all and strongly encouraged in public health messages; such practices should be facilitated by making hand-hygiene facilities available in schools, workplaces, and other settings where amplification of transmission would be expected. WHO has recommended that mask use by the public should be based on risk, including frequency of exposure and closeness of contact with potentially infectious persons; routine mask use in public places should be permitted but not required. This recommendation might be interpreted, for example, as supporting mask use in crowded settings such as public transport. The use of masks or respirators, as well as other precautions, for occupationally exposed workers also depends on risk and is beyond the scope of this review (*4*,*5*). Disinfection of household surfaces likely to be contaminated by infectious secretions appears worthwhile, but no evidence supports the efficacy of widespread disinfection of the environment or air. The legal authority and procedures for implementing interventions should be understood by key personnel before a pandemic begins, and all such measures should respect cultural differences and human rights (*1,36*).

The need is urgent for additional research on transmission characteristics of influenza viruses and the effectiveness of nonpharmaceutical public health interventions. Such research should include epidemiologic and virologic studies and field assessments of effectiveness and cost, supplemented by modeling studies and historical inquiry. Such research could be undertaken during epidemics of seasonal influenza, and some research investment now being devoted to influenza should be dedicated to this end. Research needs include evaluating the effectiveness of mask use and cough etiquette and evaluating interventions in terms of cases detected and prevented, cost, and effectiveness in alleviating public concerns. Research is also needed to identify ways to make quarantine and other restrictions more focused and less burdensome for individual persons and societies and to assess how "leaky" restrictions can be and still be effective. Improved methods are also needed to communicate with essential partners and the public. Finally, improved informatics capabilities would allow outbreaks to be monitored and interventions to be assessed in real time to meet the needs of all who will help control future pandemics.

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