Public Health Strategies for Pandemic Influenza: Ethics and the Law

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Ethics and the Law

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HIGHLY PATHOGENIC INFLUENZA A(H5N1) IS ENdemic in avian populations in Southeast Asia, with serious outbreaks now in Africa, Europe, and the Middle East.[1] Human cases, although rare, continue to increase, with high reported case-fatality rates. Industrialized countries place great emphasis on scientific solutions. The White House strategic plan and congressional appropriation both devote more than 90% of pandemic influenza spending to vaccines and antiviral medications.[2] Yet, medical countermeasures, discussed in a previous *JAMA* Commentary, will not impede pandemic spread: experimental H5N1 vaccines may not be effective against a novel human subtype, neuraminidase inhibitors may become resistant, and medical countermeasures will be extremely scarce.[3] This Commentary focuses on traditional public health interventions, drawing lessons from past influenza pandemics and the outbreaks of severe acute respiratory syndrome (SARS)[4] (TABLE).

Public health strategies are difficult to evaluate. First, evidence of effectiveness is often historical or anecdotal, with few randomized trials or systematic studies.[5] Adequate resources for population-based research are urgently needed. Second, an intervention's effectiveness depends on the transmission pattern, which cannot be fully understood in advance. Key issues include viral shedding (infectivity during presymptomatic and postsymptomatic stages); mode and efficiency of transmission (large droplet, aerosol, contaminated hands and surfaces); incubation period; and serial interval between cases.[6] Third, the usefulness of an intervention depends on the pandemic phase. In the pandemic alert period, surveillance, medical prophylaxis, and isolation are important tools. Yet, during a pandemic, the focus shifts to delaying spread through population-based measures.[7] Thus, the key question is which measure, or combination of measures, works best at each stage of the pandemic? Multiple, targeted approaches are likely to be most effective but can have deep adverse consequences for the economy and civil liberties.

The Public Health System: Surveillance

Surveillance is the backbone of public health, providing essential data to understand the epidemic and inform the public. Surveillance strategies include rapid diagnosis, screening, reporting, case contact investigations, and monitoring trends. Currently, influenza A(H5N1) is not reportable in the United States, which requires reform of state law. The US public health infrastructure is deficient in laboratories, workforce, and data systems. Congress recently appropriated only $350 million to upgrade state and local capacity—approximately 9% of a total of $3.8 billion for pandemic influenza.[2] Furthermore, this limited funding will be significantly eroded by a $105 million cut in federal support for state public health and an unfunded mandate for states to purchase antiviral drugs.[8]

The new international health regulations (IHR) require countries to develop core public health capacities to detect, assess, and notify the World Health Organization (WHO) of health emergencies with international significance.[9] The mandate, however, is vacant without adequate resources for poor countries, which lack the capacity for human or animal surveillance and containment of outbreaks. Recently, donor countries pledged $1.9 billion to meet the costs estimated by the World Bank to contain avian influenza.[10]

Surveillance poses privacy risks as government collects sensitive health information from patients, travelers, and other vulnerable populations. The IHR require states to keep data "confidential and processed anonymously as required by national law." The United States and the European Union have data protection statutes, but both make exceptions for surveillance. The United States and other countries should enact public health information privacy laws to prohibit wrongful disclosures—for example, to employers, insurers, and immigration or criminal justice authorities.[11]

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Animal-Human Pathogen Interchange

Close proximity between animals and humans poses serious risks as novel pathogens mutate and jump species. Live bird markets, migrant poultry workers, fighting cocks, and migratory birds are vectors for spreading avian influenza.[12] Consequently, a critical early preventive strategy is to limit contact that results in animal-human pathogen interchange. Risk reduction strategies include separation of animal and human populations, health and safety in animal farming, and quarantines or culls of diseased or exposed animals. However, these strategies are difficult to carry out in poor countries in which laboratory capabilities are limited or nonexistent and in which farmers are reluctant to kill birds or other animals necessary for their sustenance and livelihood.

International law does not effectively control animal-human pathogen interchange. The World Organization for Animal Health serves as an information clearinghouse but does not have regulatory power; its mandate proscribes interference with state sovereignty. The Codex Alimentarius Commission and the Food and Agricultural Organization of the United Nations regulate food hygiene and labeling, but these agencies are principally concerned with food safety and fair trade. National laws do regulate occupational health and safety in animal husbandry. The US Department of Agriculture has the power to inspect, quarantine, and cull diseased or exposed animals and has recently exercised its power to control outbreaks of low-pathogenicity avian influenza.[13]

Avian influenza has severe impact on finance and trade. Hundreds of millions of domesticated fowl have been culled or have died of infection.[10] The United States bans the import of all birds from affected areas, while European authorities ban poultry and feathers from the Black Sea region. Safe farming practices and separation of animals and humans, therefore, are critically important from a public health and economic perspective.

Community Hygiene

Hygienic measures to prevent the spread of respiratory infections are broadly accepted and have been widely used in previous influenza pandemics[14] and the SARS outbreaks.[15,16] Infection control includes handwashing, disinfection, respiratory hygiene (etiquette for coughs, sneezes, spitting), and personal protective equipment (masks, gloves, gowns, eye protection). Strong evidence supports hand hygiene, but the effectiveness of disinfection, respiratory hygiene, and personal protective equipment is unclear.[16] Research is needed to understand the appropriate role of community hygiene in a future pandemic. For example, mask use was common, even legally required, in the 1918 influenza pandemic and the SARS outbreaks, but no controlled studies have evaluated its effectiveness.[7]

Table. Public Health Strategies—Public Benefits and Private Rights

Intervention (Measures)	Public Benefits	Private Interests/Rights	Recommendations
Surveillance (screening, reporting, contact tracing, monitoring)	Essential data: early warning, transmission, incidence, response	Privacy Fair information practices	Improve public health infrastructure: laboratories, workforce, data systems
Animal-human interchange (occupational health, quarantines, culls)	Protect animal health Prevent "species jump" to humans	Farmer livelihood National economy International trade	Improve hygiene and infection control in animal farming Improve international law and cooperation
Community hygiene (handwashing, disinfection, respiratory hygiene, PPE)	Reduce transmission in families and the community	Minimal but requires behavioral change	Public education grounded in risk communication science
Hospital infection control (handwashing, disinfection, PPE, health care worker vaccination)	Reduce transmission among patients, health care workers, and their families/communities	Collective bargaining agreements Health care worker autonomy Freedom of religion and conscience	Training/monitoring in infection control Encourage greater acceptance of vaccination
Decreased social mixing (close public places, cancel public events, restrict mass transit)	Slow spread of infection in public settings	Free association Free commerce	Target closures to high-risk settings based on evidence
Border controls (screening [entry/exit], reporting, health alerts, passenger data, travel advisories, hygiene [inspection, disinfection, pest extermination])	Prevent cross-border spread of infectious disease	Free travel International trade	Adequate resources for surveillance, treatment, and response in affected areas and US borders
Isolation and quarantine (home, hospital, school, workplace, institutional settings, "shelter in place")	Separate the infected or exposed from the healthy	Free movement Personal health and livelihood Nondiscrimination	Safe/humane settings Ensure necessities of life Logistics Modern laws with due process
Medical countermeasures (vaccines, antiviral agents)	Prophylaxis Reduced infectiousness Treatment	Bodily integrity Fairness to disadvantaged Intellectual property Business and trade	Stable, economically viable supplies: incentives, public/private partnerships, tort reform, compensation

Abbreviation: PPE, personal protection equipment.

Even if hygienic measures are effective, the public must use them properly and sustainably. Infection control is challenging (eg, masks must be appropriately fitted) and must be used reliably until the risk subsides. The general public has not uniformly adopted even basic hygiene practices such as handwashing. Consequently, public education campaigns grounded in the science of risk communication are important, as the acceptability of health measures is vital to community adherence.

Hospital Infection Control

The SARS-associated coronavirus spread efficiently in hospitals that did not adopt strict infection control.[15] Disinfection, hand hygiene, personal protective equipment, and aerosol-generating procedures should be standard hospital practices. Since hospital infection control is inconsistent, it is vital to train and monitor health care workers. Policy makers will also have to address the problem of critical shortages in infection control and patient care equipment (N95 respirators, ventilators, intensive care beds).

Influenza vaccination can be critically important in preventing transmission, but only 40% of health care workers are vaccinated annually.[17] Voluntary measures (education, incentives, peer advocacy, and easy access) could increase the vaccination rate. Hospitals could consider stronger measures such as requiring vaccination as a condition of employment.[18] However, a federal court recently upheld an arbitrator's decision that a hospital could not implement a mandatory influenza vaccination policy under its collective bargaining agreement with nurses.[19] The law can also require vaccination: 15 states (Alabama, Arkansas, Florida, Kentucky, Maine, Maryland, New Hampshire, New York, North Carolina, Oklahoma, Oregon, Pennsylvania, Rhode Island, Texas, and Utah) have mandatory influenza vaccination laws for long-term care facilities, and 3 of these apply to hospital workers. However, these statutes are limited by weak enforcement and numerous exceptions (religious belief, medical contraindication, or failure to provide consent).

Decreased Social Mixing/ Increased Social Distance

Past experience shows that social separation and community restrictions form a significant response to pandemics. It is assumed, but not proven, that decreased social mixing slows the spread of respiratory disease. Thus, in the face of pandemics, societies have closed public places (schools, childcare, workplaces, mass transit) and canceled public events (sports, arts, conferences). As fear increases, individuals may shun public gatherings. Predicting the effect of policies to increase social distance is difficult, as infected persons and their contacts may be displaced into other settings, and individuals may voluntarily separate in response to perceived risk.[5]

Social separation, particularly for long durations, can cause loneliness and emotional detachment, disrupt social and economic life (education, trade, business), and infringe individual rights. Community restrictions raise profound questions of faith (religious worship), family (funeral attendance), and protection of the vulnerable (food, water, clothing, medical care). Coming together with fellow human beings in civic or spiritual settings affords comfort in a time of crisis.

The constitutional questions are equally complex, as the Supreme Court has held travel and free association to be fundamental rights.[20] Undoubtedly, the courts would uphold reasonable community restrictions, but legal and logistical questions loom: who has the power and under what criteria to order closure and for what period of time? Enforcement and assurance of population safety remain critically important but unanswered questions.

International Travel and Border Controls

Transnational public health law is increasingly important in global health, as evidenced by the WHO's IHR and the communicable disease regulations proposed by the Centers for Disease Control and Prevention.[21] These legal initiatives reflect recommendations for border controls by the WHO[22] and the Institute of Medicine.[23] Transnational measures can be far-reaching and include entry or exit screening, reporting, health alert notices, collection and dissemination of passenger information, travel advisories or restrictions, and physical examination or management of ill or exposed individuals. These kinds of powers were exercised in Asia and North America during the SARS outbreaks, although their effectiveness is unestablished.[24,25] The WHO's IHR and the CDC proposed regulations also authorize sanitary measures at frontiers or on conveyances: inspection, fumigation, disinfection, pest extermination, and destruction of infected or contaminated animals or goods.

Sovereign nations seek to safeguard their citizens' health from external threats, even in a global world in which people, animals, and goods rapidly diffuse across state boundaries. Although border protection is legitimate, it can severely disrupt travel, trade, and tourism, as well as infringe civil liberties. The freedom of movement is a basic right protected by the US Constitution and international treaties but is subject to limits when necessary for the public's health.[20,26] The World Trade Organization similarly defends free commerce but permits science-based trade restrictions to protect the public's health.[27]

In addition, the CDC proposed rules[21] require the travel industry to collect and disclose passenger data at significant cost ($118-$425 million per year in the United States) and risk to privacy.[28] Economic and privacy burdens are justified only if necessary to obtain high-quality surveillance data and in accordance with fair information practices. Consequently, transnational law requires a careful

balance between public health benefits and free trade, travel, and respect for the rights to privacy, association, and liberty.

Isolation and Quarantine

Isolation of infected persons, quarantine of exposed persons, and quarantine of a geographic area (cordon sanitaire) are the most complex and legally/ethically controversial public health powers. Isolation and quarantine were widely used in Asia and Canada during the SARS outbreaks.[4] These approaches are likely to play a limited role in the early stages of pandemic influenza but are not considered effective or practical during later stages. Unlike SARS, the transmission characteristics of influenza allow little time for isolation and quarantine: influenza has a short serial interval (the mean interval between onset of illness in 2 successive patients is 2-4 days), and infectivity is maximal early in the illness.[6]

Legal authority for isolation and quarantine must be clear and constitutionally acceptable, with criteria based on risk and fair procedures. Containment powers principally are exercised at the state level. While many existing state isolation and quarantine statutes are antiquated, 27 states have modernized their laws based on the Model State Emergency Health Powers Act.[29] Federal containment powers are reserved for interventions at US borders and to mitigate interstate spread of infection. The US government, in 2005, added novel influenza viruses with pandemic potential as a quarantinable disease.

However, the CDC proposed quarantine rule[21] inadequately safeguards the constitutional rights of individuals who are quarantined. The rule permits provisional quarantine for 3 business days and full quarantine not to exceed the period of incubation and communicability of the disease. The provisional quarantine can be ordered without a hearing. While full quarantine requires due process, individuals who are subjected to quarantine must affirmatively request a hearing, which can occur without the individual's presence, and the CDC director makes the final determination.

Federal and state statutes rarely specify where quarantine should take place, and there are myriad options, as evidenced by the SARS outbreaks: homes, hospitals, schools, workplaces, or other institutional settings (military bases, prisons, nursing homes, stadiums). Perimeter quarantines may restrict movement to and from designated geographic areas, sometimes coupled with medical prophylaxis. Modern ideas often do not envisage formal confinement but rather "sheltering in place" ("snow days"), protective cloistering, or voluntary sequestering. The public expresses serious concerns with quarantine, such as overcrowding, exposure to infection, and inability to work, shop, or contact family.[30] Public concerns may be valid, as the logistical problems of large-scale quarantines would be formidable: ensuring safe and hygienic locations, medical and nursing care, necessities of life (food, water, clothing), and communications.[31] Monitoring and enforcement are equally problematic. Authorities often enforced SARS quarantines by intrusive surveillance such as thermal scanners, electronic bracelets, Web cameras, or placards.[4] President Bush proposed military enforcement, although the Posse Comitatus Act prohibits the military acting as a domestic police force unless authorized by statute or the Constitution.[32]

Isolation and quarantine are extreme measures that require rigorous safeguards, including scientific assessment of risk and effectiveness, a safe and habitable environment, procedural due process, and the least restrictive alternative. Above all, state power must be exercised fairly and never as a subterfuge for discrimination. As with all public health interventions, containment requires public trust and acceptance in accordance with the principles of justice. Pandemics can be deeply socially divisive, and the political response reflects profoundly on the kind of society the United States aspires to be.

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Recent Trials in Hypertension
Compelling Science or Commercial Speech?

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With rare exceptions, hypertension is an asymptomatic risk factor for cardiovascular events such as myocardial infarction, stroke, and heart failure. In contrast to small, short-term trials that evaluate drug effects on level of blood pressure as a surrogate outcome, large, long-term trials provide information about the full range of health risks and benefits associated with antihypertensive treatment. In this Commentary, we review some of the design choices made in the long-term trials of antihypertensive agents, including placebo-controlled trials and the more recent active-comparison trials.

Early trials in hypertension recruited patients with diastolic blood pressure up to 129 mm Hg and compared active treatments, primarily high-dose diuretics, with placebo.[1] The results of these trials suggested that antihypertensive treatment reduced the risk of cardiovascular events in patients with high diastolic blood pressure. Subsequent placebo-controlled trials focused on middle-aged patients with mild to moderate elevations of blood pressure[2] or older adults with isolated systolic hypertension.[3] In these and other early large trials, the first-line treatments also included β-blockers and low-dose diuretics.

Despite the publication of thousands of small, short-term, randomized clinical trials evaluating angiotensin-converting enzyme (ACE) inhibitors and calcium channel blockers, a meta-analysis published in 1997 was able to locate no large, long-term, placebo-controlled clinical trials that used either a calcium channel blocker or an ACE inhibitor as antihypertensive therapy.[4] Compared with placebo, low-dose diuretics were associated with reduced risks of all the major outcomes, including stroke (relative risk [RR], 0.66; 95% confidence interval [CI], 0.55-0.78), coronary heart disease (RR, 0.72; 95% CI, 0.61-0.85), heart failure (RR, 0.58; 95% CI, 0.44-0.76), and total mortality (RR, 0.90; 95% CI, 0.81-0.99). Compared with placebo, β-blockers—primarily atenolol, which had been used in many of the trials—were associated with reduced risks of stroke (RR, 0.71; 95% CI, 0.59-0.86) and heart failure (RR, 0.58; 95% CI, 0.40-0.84) but not of coronary heart disease (RR, 0.93; 95% CI, 0.80-1.09) or total mortality (RR, 0.95; 95% CI, 0.84-1.07).[4] The results of recent meta-analyses by Carlberg et al[5] and Lindholm et al[6] have confirmed these β-blocker findings, although heart failure was omitted as an outcome of interest.[6] The importance of β-blocker therapy in patients with heart failure was also clearly defined in the 1990s.[7]

For β-blocker therapy, an unanticipated finding was the disparity between its clear mortality benefit in the treatment of patients with coronary heart disease regardless of hypertension status[8] and its apparent inability to prevent coronary heart disease in the treatment of patients with high blood pressure. In the meta-analyses of placebo-controlled trials in hypertension,[4-6] the reductions in coronary heart disease risk associated with β-blockers have been modest, with 95% CIs that include 1.0.

Several explanations are possible. In low-risk asymptomatic populations receiving β-blockers for hypertension, a withdrawal syndrome precipitating coronary syndromes in

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