SYMPOSIUM

Public Health Strategies for Distribution of Influenza Vaccine During an Influenza Pandemic

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In order to consider the ethical issues around vaccine distribution during an influenza pandemic, it is critical to have an understanding of the role of influenza vaccine in a pandemic, the rate at which vaccine is likely to become available, who will likely produce and “own” the vaccine, how vaccine distribution and administration might be accomplished, and which are the groups that might be deemed highest priority to be vaccinated against influenza. The United States and Connecticut have been considering the more challenging of these issues and have learned from Canada, which previously discussed and made decisions on the challenges related to vaccine distribution. Although there is still some critical advance thinking that needs to be done, planning for the response to an influenza pandemic is now at an advanced stage. The keys to preparedness at this stage are to be aware of the vaccine distribution options, to know the benefits and limitations of each option, and to be flexible but nimble in dealing with a real pandemic.

INTRODUCTION

A discussion of the ethical aspects of pandemic influenza planning necessarily includes an overview of public health strategies for influenza vaccine distribution. There are a number of challenges with ethical overtones involved in planning for distribution of what is surely likely to be initially a very limited supply of influenza vaccine. Central to this discussion is familiarity with the role of influenza vaccine in a pandemic, the rate at which vaccine is likely to become available, who will likely produce and “own” the vaccine, how the vaccine distribution and administration might be accomplished, and what are the groups that might be deemed highest priority to be vaccinated against influenza. The United States and Connecticut have been considering the more challenging of these issues, using the Canadian plan as a model [1]. Canada has already discussed and made decisions on the challenges related to vaccine distribution.

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†Abbreviations: ACIP, Advisory Committee on Immunization Practices; CDC, Centers for Disease Control and Prevention; DHHS, Department of Health and Human Services; NVAC, National Vaccine Advisory Committee.
INFLUENZA CONTROL TOOLS

There are three main influenza control tools once a pandemic starts: Vaccination, antiviral agents, and limitation of exposure. Each of these tools has its benefits and limitations.

Vaccination is effective in preventing both infection and severe disease. The major limitations are that there may be little to no vaccine initially and that it may take two doses given no sooner than 30 days apart to achieve full protection.

Antiviral agents can be taken in anticipation of exposure or at the time of exposure to prevent infection. However, they are only effective the days they are being taken — they have no residual benefits. Their use is limited by their cost, limited supplies, side effects, resistance of some influenza virus strains to them, and the competing need to use them for treatment instead of prevention.

Limitation of exposure to the influenza virus can protect the individual and slow the spread of influenza in the population. Avoidance of exposure can be done at the individual level in several ways. Healthy individuals can judiciously use masks and handwashing and avoid close contact with symptomatic persons. Infectious ill persons can be effectively isolated from others, and opportunities for mass exposure and spread can be minimized by limiting gatherings, including school attendance. Curbing contact in congregate settings may only be able to be taken so far on a practical basis, however, as there is a major potential for societal and economic disruption.

Figure 1 shows schematically where each of these prevention tools fit into an emerging pandemic flu situation. Initially, when there is little to no vaccine, we will be dependent upon measures to limit exposure and disease transmission and on antiviral agent use. As we get more vaccine, vaccination will increasingly be the key to limiting impact.

STRATEGIC VACCINATION PLANNING ISSUES

There are three main strategic planning issues related to the use of vaccine: First, how much vaccine is available? Second, what are the goals for the use of limited amounts of vaccine? Within this second issue, what are the priority groups for vaccination, and are two doses needed or one? Finally, what is the most effective
distribution method to reach the goals? Distribution will depend in part on who is in charge of the vaccine supply and who is in a position to administer the available vaccine. In addition, there is a distributional choice to be made as to how much vaccine is administered in private medical versus public clinic settings.

Although eventually there will be enough vaccine to vaccinate everyone, the initial distribution strategy will depend in part on how much is immediately available and how quickly more will become available. The planning assumption provided by the CDC is that initially, less than 10 percent of needs will be met. It takes close to six months from the time an influenza vaccine production line starts for the first doses to be ready to be administered.

It is estimated that the maximum vaccine production rate for the country is 5 million doses per week. Assuming each person will need two doses, that means continued production will only be enough to meet the needs of approximately 1 percent of the U.S. population (2.8 million people) each week. Thus, it could take up to two years to produce enough vaccine to fully vaccinate the entire population.

This rate could be improved substantially if only one dose were needed per person, if smaller doses of vaccine were used (e.g., the vaccine were administered intradermally [2]), or if more manufacturers were able to produce for the U.S. market. Decisions about dosage size and route of administration would have to be made by the FDA and be evidence-based. Thus, data needs to be gathered in advance to facilitate decision-making during a crisis.

**GOALS FOR USE OF LIMITED AMOUNTS OF VACCINE**

A major issue needing resolution when vaccines are in short supply is determination of the main goal for vaccine use. In this context, there are at least three competing strategic goals: One goal is prevention of death. If that is the goal, then direct protection of persons who are most vulnerable might be the best choice for the initial use of vaccine. Another goal is prevention of infection and its spread. If this were our number one vaccination goal, we should be vaccinating healthcare workers, school-aged children, and, possibly, their parents. Yet another goal is maintenance of essential public services. To be sure critical services are not compromised by absenteeism due to illness, we should emphasize protection of certain classes of workers. Unfortunately, there will not be enough vaccine initially to work on all three goals simultaneously — we will have to make a choice.

Table 1 shows the priority groups to achieve each of these goals and the percentage of the population that they make up. Notably, there is little overlap between the persons in these groups, with the exception of healthcare workers, who appear in those most likely to spread influenza and those providing essential services.

The fact that two doses may be needed to provide full immunity creates another set of challenges to vaccination strategies [3]. First, a rapid study will be needed early on to determine the relative efficacy of one versus two doses. A critical decision will be needed as soon as possible. Should some people get a second dose before giving everyone a first dose? In addition, if two doses are needed, then it will be important to let everyone know they need another dose and to keep records to enable reminders and call-backs for a second dose.

**VACCINE DISTRIBUTION**

A critical determinant of initial vaccine distribution strategy is who controls the vaccine supply and, thus, its distribution. Since vaccine is made by private manufacturers, this is not a simple answer.

There are three major options for distribution from the manufacturer: First, the vaccine manufacturer can control the
entire supply and simply take orders first come-first serve or from the highest bidders. Second, the government can purchase a percentage of the supply and control its subsequent distribution. This is the usual case for most vaccines when there is no crisis, including influenza vaccine. On average, government at federal, state and local levels purchases 20 to 30 percent of the supply for use for special public health initiatives and for vaccination of the poorer segment of the population, with the manufacturer distributing the rest according to supply and demand. The third option is for the government to purchase the whole supply, ideally at a pre-negotiated price, and then be entirely in charge of distribution.

When vaccine is in very short supply relative to demand, only the third scenario is likely to work well and be enforceable. Notably, it cost the public health system an extraordinary amount of money and time during the 2004-05 influenza season trying to redistribute the initially unevenly and largely privately purchased and distributed vaccine when there was a sudden influenza vaccine shortage [4].

Because of the importance of this issue, in 2002, stakeholders were brought together by CDC to develop recommendations regarding federal purchase of influenza vaccine in a time of shortage. They recommended federal purchase of all vaccine during the time of peak demand relative to supply [5]. However, thus far, no national decision or commitment to do so has been made public. Thus, preparedness efforts at the state level need to account for multiple possibilities.

Once vaccine ownership is established, its subsequent distribution will depend in part on who will administer it. Usually, influenza vaccine is administered in a variety of settings. Most primary care providers administer it to their own patients including those in long-term care facilities, accounting for 70 to 80 percent of vaccination. Historically, to reach those with less regular medical care, there have been public-sector clinics open to all comers. Public sector initiatives account for about 20 to 30 percent of all vaccination. More recently, special workplace employee clinics and commercial clinics open to all comers have been added to encourage increasingly large segments of the population to get vaccinated.

In a pandemic situation, there will be substantial challenges to “usual” practice. Even without a pandemic, the generally intense two-month long influenza vaccin-
tion season puts a substantial burden on primary care providers, who must balance vaccination with provision of acute medical care. Most recently, pediatricians, in response to new recommendations first made during the 2003-04 season [6] are struggling with how to get two doses into all their patients who are 6 to 23 months of age over a two-month time period. During a pandemic, there will be a huge surge in acute care needs, which will decrease the time available for preventive care.

To make matters worse, it is likely that patients will be demanding and that there will be those who demand vaccine even if they are not in an initial priority group. This puts the provider in a terribly awkward position: If they enforce the recommendations and withhold vaccine from one of their patients, they could lose clients. Beginning in January 1998, Rhode Island had a community outbreak of meningococcal meningitis and decided to recommend vaccination of all children [7]. While they started with the premise that it could be done by regular pediatric care providers purchasing vaccine on their own, the providers quickly became overwhelmed by long lines and demanding parents. In the end, the state bought all the vaccine needed and held special vaccination clinics. In such situations, special clinics take the burden off of acute care providers. However, special clinics still face the challenge of enforcing the recommendations that only certain people be vaccinated. In this context, government-run public health clinics are usually in a better position than hospital or provider-run clinics to do such enforcement, in large part because they are able to call on public safety personnel to assist.

There are three main options for who administers vaccine: 100 percent private sector, the usual private-public sharing, or 100 percent public sector vaccine administration. Most likely there will be a combination strategy, with more public sector administration initially followed by increasing involvement of the private sector as vaccine supply becomes sufficient to meet demand.

At the user level, people will need to know where they will get vaccinated, whether it will be at work, at their usual healthcare provider’s office, in a public clinic with lines and waits, or in a public clinic by appointment. If appointments are needed, they will need to know how they can get an appointment. The dissemination of this information will likely be done by state and local public health officials.

The settings where vaccine is administered will be an extension of who conducts the vaccine administration and what groups are first priority. If healthcare providers are the priority group, most likely vaccine will be given to them to vaccinate each other. If the elderly or children are the priority, vaccination may be done either by their regular care providers or in special clinics by appointment. During the 2004-05 influenza season with the influenza vaccine shortage, we found that in Connecticut we could successfully use a variety of settings to get vaccine to the priority groups [8]. The likelihood that vaccine will be in extremely short supply relative to demand will make enforcement more of a challenge than achieving high volume.

**VACCINATION STRATEGY PLANNING**

There has been long-standing advice to all states to conduct pandemic influenza planning and to have a plan. However, until 2005, guidance was limited. There was no national plan to use as a model, and it was only recommended, not required, that states do planning.

In the past several years, much has happened. The combination of concern about the evolving avian influenza situation and the emphasis in the past few years on public health preparedness created the demand and planning mechanisms neces-
sary to move forward. In August 2004, a draft national response plan was distributed [9]. In addition, states were required to have their own written response plans in place as of August 2005 as a condition of receiving federal public health preparedness and immunization program funding. The resulting individual state plans are available on the DHHS website [10].

The initial draft national plan developed in August 2005 on which state plans were based was not complete. In particular, it did not include specific guidance on vaccination strategies or priority groups. Since then, a list of priority groups to receive initially available vaccine has been developed by the CDC and DHHS workgroups and published as part of the complete national DHHS pandemic influenza response plan in November 2005 [11].

The process for developing guidance for vaccination strategies is ongoing. For the recently completed phase to develop vaccine priority groups, it consisted of convening three separate working groups, each of which made recommendations on vaccination priorities. These groups included a special CDC workgroup, the DHHS’s National Vaccine Advisory Committee (NVAC), and the CDC’s Advisory Committee on Immunization Practices (ACIP). The groups met in parallel and had some overlapping members. The key charge to each group was to discuss and make recommendations on vaccination goals and which groups should have priority for vaccination. Since Canada had already addressed these issues [1], each group was charged with beginning with the Canadian priority groups and determining whether modifications should be made.

The three national planning groups each included representatives from medical organizations, such as the American Medical Association and the American Hospital Association; from public health organizations, including state and local health departments; and an ethicist. NVAC also had consumer representation.

Of importance, the ACIP is the only group that can put out recommendations that are truly independent; meaning, they do not have to be reviewed by federal officials for policy considerations. Their independence in being able to make recommendations regarding who should be vaccinated in advance against smallpox was valued by many in the medical and public health communities.

National level planning has been taking place with the following scenario in mind. First, it has been assumed, until proven otherwise, that all persons will need two doses of vaccine. Second, it is assumed that all will be fully susceptible to the pandemic strain. Third, the rate of vaccine production will not exceed enough to vaccinate 1 percent of the U.S. population with two doses each week. These are all “worst-case” scenario assumptions — it may be that only one dose of vaccine would be needed, only certain age groups in the population would be fully susceptible, and that vaccine production could be faster or stretched by using smaller doses for vaccination, as previously mentioned.

At this time, it is unclear who at the federal level will decide on other aspects of vaccination strategies, particularly the key question of whether all vaccine will be purchased by the federal government at the beginning.

**STATE AND LOCAL PUBLIC HEALTH PLANNING PROCESS**

State and local health departments have the responsibility to determine how to carry out the national guidance in their jurisdictions. In particular, states have the responsibility of distributing limited supplies purchased with federal funding to providers, including local health departments, and local health departments have responsibility for determining how publicly purchased vaccine will be administered in their towns.
Given that the national plan establishes vaccine priority groups but provides no clear guidance on vaccine distribution strategies, states have had to make their own planning assumptions in order to move ahead.

In Connecticut, the national planning scenario and priority groups have been the basis for planning. In addition, we assume that all vaccine initially will be purchased by the state and federal government. The current Connecticut vaccine distribution plan is that vaccine would be given directly to hospitals to vaccinate their staff. Most vaccine, though, would be given to local health departments on a population basis to hold special clinics to vaccinate the priority groups in their areas and to enable enforcement of the recommendations. To deal with the issue of having some very small, part-time local health departments that are inadequately staffed, the state has been divided into 41 mass vaccination regions with a population of at least 50,000 each. Each of these is headed by a full-time health director and receives substantial public health preparedness funding. These regions are prepared to do mass vaccination or antibiotic dispensing in case of an emergency, and are also charged with vaccination activities related to pandemic influenza.

VACCINATION PRIORITY GROUPS

The Canadians determined three main objectives of vaccination in hierarchical order: 1) limit societal disruption and maintain essential services; 2) limit severe morbidity and mortality; and 3) prevent influenza (Table 2). Notably, the number one priority within this group is vaccination of healthcare providers. This includes all hospital and medical office staff — including support staff. This group is the one with the highest risk of contact with influenza and the one that will likely have the largest workload with an explosion of ill persons seeking care.

The second priority group is essential service providers, a fairly broadly constituted group that includes government leaders. Some in these groups would like their family members included, feeling that there is a risk they could bring influenza home to family members and claiming that many will refuse to work unless all in their families are also protected. This poses interesting ethical issues. The Canadian plan is clear that family members of these groups are not included.

The U.S. vaccine priority groups identified through the previously described process (Table 3) are similar to those identified by Canada. However, there are several notable differences. While the highest priority Canadian groups include a wide range of essential service providers followed by those at decreasingly high risk for severe morbidity, the U.S. priority groups interdigitate narrower definitions of essential service providers with those at increasingly high risk for severe morbidity and mortality. In other words, the U.S. recommendations

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Table 2. Vaccination goals and priority groups: Canadian Pandemic Influenza Plan, February 2004.

| Priority | Description |
|----------|-------------|
| 1.       | Limit societal disruption — maintain essential services |
|          | a. Health care providers |
|          | b. Essential service providers |
| 2.       | Limit severe morbidity and mortality: |
|          | a. Persons at high risk from fatal outcomes |
| 3.       | Prevent influenza: |
|          | a. Healthy children and adults 2 to 64 years |
emphasize prevention of morbidity and mortality more than maintenance of all but the most essential influenza-related healthcare services. In addition, the U.S. recommendations do not explicitly address whether family members of essential service providers are included when essential service providers are listed as priority.

**CRITICAL PLANNING DECISION-MAKING IN CONNECTICUT**

Advance planning decisions on how best to distribute and administer vaccine within the state are and will be made using the infrastructure that has been developed for public health preparedness planning. This includes three separate but overlapping groups that meet at least monthly with flexible agendas to enable discussion of emerging issues such as SARS and response to avian influenza. The first is the public health preparedness advisory workgroup, which is broadly constituted and includes local health and hospital representation as its core, but also representation from most health professional organizations in the state. This group is one that could readily incorporate an ethics perspective, something that is currently missing. The second planning group is hospital-specific. Each of the two public health preparedness center of excellence hospitals has monthly meetings with all other hospitals in their half of the state to coordinate and standardize hospital-specific preparedness response protocols. Finally, the public health preparedness management group consists of 10 DPH and seven local health department staff members, a group that does final decision-making on how federal public health preparedness funding coming through the CDC is spent and discusses preparedness issues most relevant to them.

No single public health strategy for influenza vaccine distribution in a pandemic has yet been determined. Rather, there are a number of key decision points where there are strategic options for how vaccines in short supply can be distributed (Figure 2). These include deciding whether the government purchases all available vaccine, who will be highest priority to be vaccinated initially, whether regular or public health providers will do the bulk of vaccine administration, and whether the available supply can be stretched to go further by using alternative administration methods.

The strategic options for vaccine distribution are likely to be affected by the

| Priority | Vaccination Goal | Group |
|----------|------------------|-------|
| 1        | Maintain essential services | • Vaccine & antiviral manufacturers  
• Medical & public health workers with direct patient contact & support staff, vaccinators |
| 2        | Limit severe morbidity | • Persons at high risk of severe disease |
| 3        | Maintain essential services | • Public health emergency workers  
• Key government leaders |
| 4        | Limit severe morbidity | • Persons at moderately high risk of severe disease |
| 5        | Maintain essential services | • Public safety, utility, transportation, communication workers, funeral directors, other public health & government workers |
| 6        | Prevent influenza | • Healthy adults and children, 2 to 64 years old |

*Adapted from DHHS Pandemic Influenza Plan Part 1, Appendix D, Table D-1.
Decision-making Points | Influencing Factors
---|---
Percentage of vaccine that federal or state governments purchase from manufacturer (federal or state decision) | Virulence of virus
Who are priority groups to get initially available vaccine (federal decision for overall groups; state decision within groups) | Rapidity of spread globally, to and within the U.S.
Who will administer vaccine to persons in priority groups (state decision) | Groups most severely affected
Whether supply can be stretched: 1 dose instead of 2; use lower than standard dose; adminster intradermally rather than sub-cutaneously (federal decisions) | Size of initial vaccine supply
| Rate at which vaccine can be produced
| Politics?

Figure 2. Vaccine distribution decision-making points and influencing factors.

Rapidity of spread and the severity of a pandemic. How quickly the pandemic strain gets to the United States, whether there is initially any vaccine, how easily it is spread, how virulent it is and which groups are most affected are all variables that could influence choice of strategic options.

Although there is still some critical advance thinking that needs to be done, planning for the response to an influenza pandemic is now at an advanced stage. The keys to preparedness at this stage are to be aware of the vaccine distribution options, to know the benefits and limitations of each option, and to be flexible but nimble in dealing with a real pandemic.

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