



appendix D: NVAC/ACIP recommendations for prioritization of pandemic influenza vaccine and NVAC recommendations on pandemic antiviral drug use

Advisory Committee recommendations ... provide guidance for planning purposes and form the basis for further discussion of how to equitably allocate medical countermeasures that will be in short supply early in an influenza pandemic.

Advisory Committee recommendations are presented in this report to provide guidance for planning purposes and to form the basis for further discussion of how to equitably allocate medical countermeasures that will be in short supply early in an influenza pandemic.

Two federal advisory committees, the Advisory Committee on Immunization Practices (ACIP) and the National Vaccine Advisory Committee (NVAC), provided recommendations to the Department of Health and Human Services on the use of vaccines and antiviral drugs in an influenza pandemic.

Although the advisory committees considered potential priority groups broadly, the main expertise of the members was in health and public health. The primary goal of a pandemic response considered was to decrease health impacts including severe morbidity and death; secondary pandemic response goals included minimizing societal and economic impacts. However, as other sectors are increasingly engaged in pandemic planning, additional considerations may arise. The advisory committee reports explicitly acknowledge the importance of this, for example highlighting the priority for protecting critical components of the military. Finally, HHS has recently initiated outreach to engage the public and obtain a broader perspective into decisions on priority groups for pandemic vaccine and antiviral drugs. Though findings of the outreach are preliminary, a theme that has emerged is the importance of limiting the effects of a pandemic on society by preserving essential societal functions.

Based on this guidance, state, local, and tribal implementation plans should be developed to 1) include more specific definitions of the priority groups (e.g., which functions are indeed critical to maintaining continuity) and their size; 2) define how persons in these groups will be identified; and 3) establish strategies for effectively and equitably delivering vaccines and antiviral drugs to these populations. The committees acknowledged that further work is needed, in particular, to identify the functions that must be preserved to maintain effective services and critical infrastructures and to identify the groups that should be protected to achieve this goal. The committees also acknowledge that the specific composition of some priority groups may differ between states or localities based on their needs and that priority groups should be reconsidered when a pandemic occurs and information is obtained on its epidemiology and impacts.



On July 19, 2005, ACIP and NVAC voted unanimously in favor of the vaccine priority recommendations summarized in Table D-1. These votes followed deliberations of a joint Working Group of the two committees, which included as consultants representatives of public and private sector stakeholder organizations and academic experts. There was limited staff level participation from DoD, DHS, and VA. Several ethicists also served as consultants to the Working Group.

A. Critical assumptions

The recommendations summarized in Table D-1 were based on the following critical assumptions:

- **Morbidity and mortality.** The greatest risk of hospitalization and death—as during the 1957 and 1968 pandemics and annual influenza—will be in infants, the elderly, and those with underlying health conditions. In the 1918 pandemic, most deaths occurred in young adults, highlighting the need to reconsider the recommendations at the time of the pandemic based on the epidemiology of disease.
- **Healthcare system.** The healthcare system will be severely taxed if not overwhelmed due to the large number of illnesses and complications from influenza requiring hospitalization and critical care. CDC models estimate increases in hospitalization and intensive care unit demand of more than 25% even in a moderate pandemic.
- **Workforce.** During a pandemic wave in a community, between 25% and 30% of persons will become ill during a 6 to 8 week outbreak. Among working-aged adults, illness attack rates will be lower than in the community as a whole. A CDC model suggests that at the peak of pandemic disease, about 10% of the workforce will be absent due to illness or caring for an ill family member. Impacts will likely vary between communities and work sites and may be greater if significant absenteeism occurs because persons stay home due to fear of becoming infected.
- **Critical infrastructure.** Only limited information was available from which to assess potential impacts on critical infrastructure sectors such as transportation and utility services. Because of changes in business practices and the complexity of networks, information from prior pandemics was not considered applicable.
- **Vaccine production capacity.** The U.S.-based vaccine production capacity was assumed at 3 to 5 million 15µg doses per week with 3 to 6 months needed before the first doses are produced. Two doses per person were assumed to be required for protection. Subsequent results of an NIH clinical trial of influenza A (H5N1) vaccine suggest that higher doses of antigen will be needed to elicit a good immune response; thus, the assumptions made by the committee could potentially substantially exceed the amount of vaccine that would be produced.

Table D-1: Vaccine Priority Group Recommendations*

Tier	Subtier	Population	Rationale
1	A	<ul style="list-style-type: none"> ■ Vaccine and antiviral manufacturers and others essential to manufacturing and critical support (~40,000) ■ Medical workers and public health workers³ who are involved in direct patient contact, other support services essential for direct patient care, and vaccinators (8-9 million) 	<ul style="list-style-type: none"> ■ Need to assure maximum production of vaccine and antiviral drugs ■ Healthcare workers are required for quality medical care (studies show outcome is associated with staff-to-patient ratios). There is little surge capacity among healthcare sector personnel to meet increased demand.
	B	<ul style="list-style-type: none"> ■ Persons ≥ 65 years with 1 or more influenza high-risk conditions, not including essential hypertension (approximately 18.2 million) ■ Persons 6 months to 64 years with 2 or more influenza high-risk conditions, not including essential hypertension (approximately 6.9 million) ■ Persons 6 months or older with history of hospitalization for pneumonia or influenza or other influenza high-risk condition in the past year (740,000) 	<ul style="list-style-type: none"> ■ These groups are at high risk of hospitalization and death. Excludes elderly in nursing homes and those who are immunocompromised and would not likely be protected by vaccination
	C	<ul style="list-style-type: none"> ■ Pregnant women (approximately 3.0 million) ■ Household contacts of severely immunocompromised persons who would not be vaccinated due to likely poor response to vaccine (1.95 million with transplants, AIDS, and incident cancer x 1.4 household contacts per person = 2.7 million persons) ■ Household contacts of children <6 month olds (5.0 million) 	<ul style="list-style-type: none"> ■ In past pandemics and for annual influenza, pregnant women have been at high risk; vaccination will also protect the infant who cannot receive vaccine. ■ Vaccination of household contacts of immunocompromised and young infants will decrease risk of exposure and infection among those who cannot be directly protected by vaccination.
	D	<ul style="list-style-type: none"> ■ Public health emergency response workers critical to pandemic response (assumed one-third of estimated public health workforce=150,000) ■ Key government leaders 	<ul style="list-style-type: none"> ■ Critical to implement pandemic response such as providing vaccinations and managing/monitoring response activities ■ Preserving decision-making capacity also critical for managing and implementing a response

³ This is inclusive of federal healthcare providers to Indian nations and tribes.

Table D-1. Continued

Tier	Subtier	Population	Rationale
2	A	<ul style="list-style-type: none"> ■ Healthy 65 years and older (17.7 million) ■ 6 months to 64 years with 1 high-risk condition (35.8 million) ■ 6-23 months old, healthy (5.6 million) 	<ul style="list-style-type: none"> ■ Groups that are also at increased risk but not as high risk as population in Tier 1B
	B	<ul style="list-style-type: none"> ■ Other public health emergency responders (300,000 = remaining two-thirds of public health work force) ■ Public safety workers including police, fire, 911 dispatchers, and correctional facility staff (2.99 million) ■ Utility workers essential for maintenance of power, water, and sewage system functioning (364,000) ■ Transportation workers transporting fuel, water, food, and medical supplies as well as public ground public transportation (3.8 million) ■ Telecommunications/IT for essential network operations and maintenance (1.08 million) 	<ul style="list-style-type: none"> ■ Includes critical infrastructure groups that have impact on maintaining health (e.g., public safety or transportation of medical supplies and food); implementing a pandemic response; and on maintaining societal functions
3		<ul style="list-style-type: none"> ■ Other key government health decision-makers (estimated number not yet determined) ■ Funeral directors/embalmers (62,000) 	<ul style="list-style-type: none"> ■ Other important societal groups for a pandemic response but of lower priority
4		<ul style="list-style-type: none"> ■ Healthy persons 2-64 years not included in above categories (179.3 million) 	<ul style="list-style-type: none"> ■ All persons not included in other groups based on objective to vaccinate all those who want protection

*The committee focused its deliberations on the U.S. civilian population. ACIP and NVAC recognize that Department of Defense needs should be highly prioritized. DoD Health Affairs indicates that 1.5 million service members would require immunization to continue current combat operations and preserve critical components of the military medical system. Should the military be called upon to support civil authorities domestically, immunization of a greater proportion of the total force will become necessary. These factors should be considered in the designation of a proportion of the initial vaccine supply for the military.

Other groups also were not explicitly considered in these deliberations on prioritization. These include American citizens living overseas, non-citizens in the U.S., and other groups providing national security services such as the border patrol and customs service.

B. Definitions and rationales for priority groups

1. Healthcare workers and essential healthcare support staff

a) Definition

Healthcare workers (HCW) with direct patient contact (including acute-care hospitals, nursing homes, skilled nursing facilities, urgent care centers, physician's offices, clinics, home care, blood collection centers, and EMS) and a proportion of persons working in essential healthcare support services needed to maintain healthcare services (e.g. dietary, housekeeping, admissions, blood collection center staff, etc.). Also included are healthcare workers in public health with direct patient contact, including those who may administer vaccine or distribute influenza antiviral medications, and essential public health support staff for these workers.

b) Rationale

The pandemic is expected to have substantial impact on the healthcare system with large increases in demand for healthcare services placed on top of existing demand. HCW will be treating influenza-infected patients and will be at risk of repeated exposures. Further, surge capacity in this sector is low. To encourage continued work in a high-exposure setting and to help lessen the risk of healthcare workers transmitting influenza to other patients and HCW family members, this group was highly prioritized. In addition, increases in bed/nurse ratios have been associated with increases in overall patient mortality. Thus, substantial absenteeism may affect overall patient care and outcomes.

2. Groups at high risk of influenza complications

a) Definition

Persons 2–64 years with a medical condition for which influenza vaccine is recommended and all persons 6–23 months and 65 years and older. Excludes nursing home residents and severely immunocompromised persons who would not be expected to respond well to vaccination.

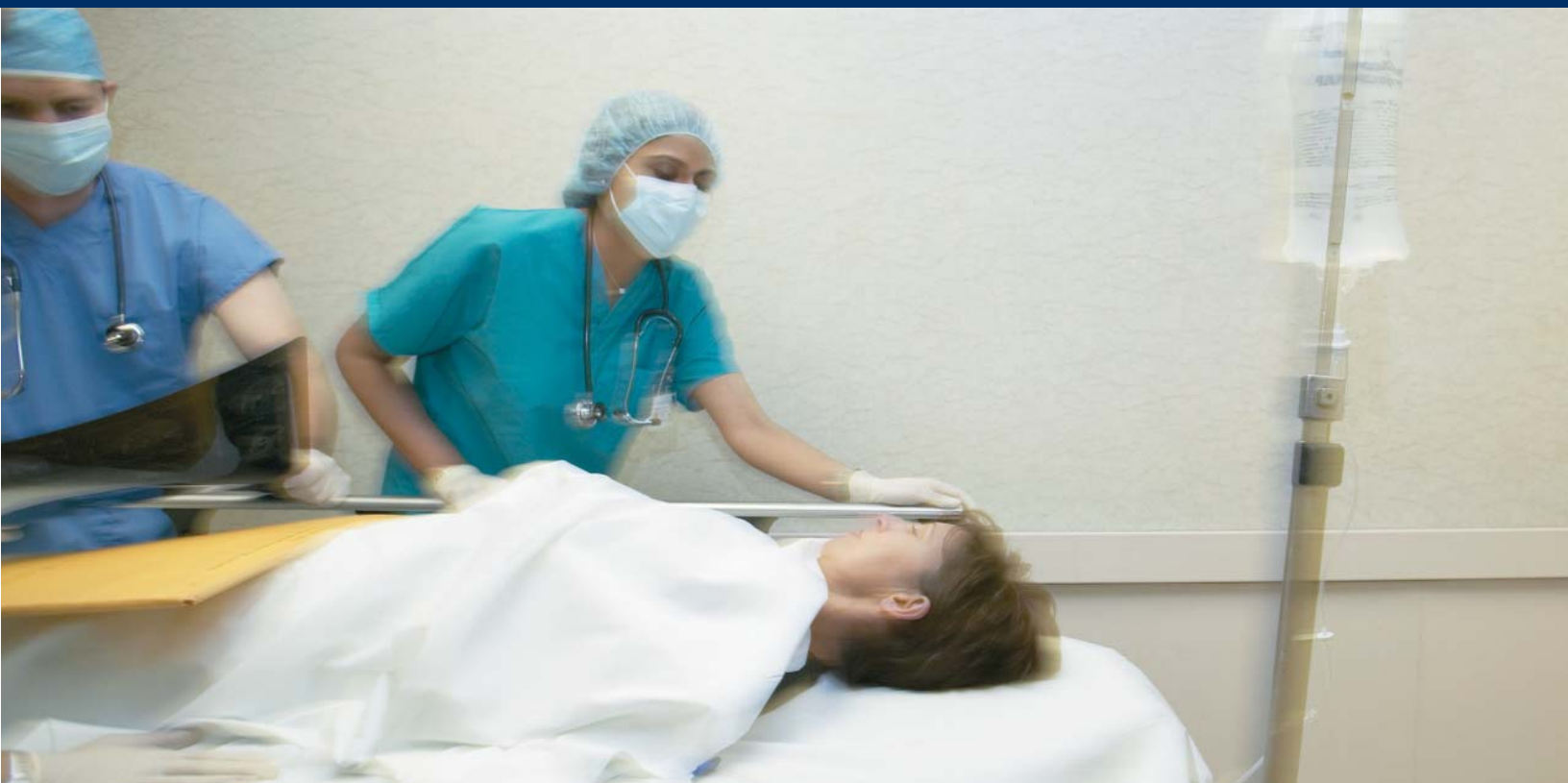
b) Rationale

These groups were prioritized based on their risk of influenza-related hospitalization and death and also their likelihood of vaccine response. Information from prior pandemics was used whenever possible, but information from interpandemic years was also considered. Nursing home residents and severely immunocompromised persons would be prioritized for antiviral treatment and/or prophylaxis and vaccination of healthcare workers and household contacts who are most likely to transmit influenza to these high risk groups.

3. Critical infrastructure

a) Definitions and rationale

Those critical infrastructure sectors that fulfill one or more of the following criteria: have increased demand placed on them during a pandemic, directly support reduction in deaths and hospitalization; function is critical to support the healthcare sector and other emergency services, and/or supply basic



necessities and services critical to support of life and healthcare or emergency services. Groups included in critical infrastructure are needed to respond to a pandemic and to minimize morbidity and mortality, and include the following sectors:

- Persons directly involved with influenza vaccine and antiviral medication manufacturing and distribution and essential support services and suppliers (e.g., growers of pathogen-free eggs for growth of vaccine virus) production activities
- Key government leaders and health decision-makers who will be needed to quickly move policy forward on pandemic prevention and control efforts
- Public safety workers (firefighters, police, and correctional facility staff, including dispatchers) are critical to maintaining social functioning and order and will contribute to a pandemic response, for example by ensuring order at vaccination clinics and responding to medical emergencies
- Utility service workers (water, power, and sewage management) are prioritized as the services they provide are also essential to the healthcare system as well as to preventing additional illnesses from lack of these services unrelated to a pandemic.
- Transportation workers who maintain critical supplies of food, water, fuel, and medical equipment and who provide public transportation, which is essential for provision of medical care and transportation of healthcare workers to work and transportation of ill persons for care
- Telecommunication and information technology services critical for maintenance and repairs of these systems are also essential as these systems are now critical for accessing and delivering medical care and in support of all other critical infrastructure.
- Mortuary services will be substantially impacted due to the increased numbers of deaths from a pandemic and the fact that impact will be high in the elderly, a growing segment of the population

4. Public health emergency response workers

a) Definition

This group includes persons who do not have direct patient care duties, but who are essential for surveillance for influenza, assessment of the pandemic impact, allocation of public health resources for the pandemic response, development and implementation of public health policy as part of the response, and development of guidance as the pandemic progresses.

b) Rationale

Persons in this sector have been critical for past influenza vaccine pandemics and influenza vaccine shortages and little surge capacity may be available during a public health emergency such as a pandemic.

5. Persons in skilled nursing facilities

a) Definition

Patients residing in skilled nursing facilities. Not included in this group are persons in other residential settings (e.g., assisted living) who are more likely to be mobile, in a setting that is less closed, and have decentralized healthcare.

b) Rationale

This group was not prioritized for vaccine because of the medical literature finding poor response to vaccination and occurrence of outbreaks even in the setting of high vaccination rates. Other studies have suggested that vaccination of healthcare workers may be a more effective strategy to prevent influenza in this group. Further, surveillance for influenza can be conducted in this group and antiviral medications used widely for prophylaxis and treatment. Ill visitors and staff should also be restricted from visiting nursing home facilities during outbreaks of pandemic influenza.

This strategy for pandemic influenza vaccine differs from the interpandemic vaccination strategy of aggressively vaccinating nursing home residents. The rationale considers several factors: 1) these populations are less likely to benefit from vaccine than other groups who are also at high risk; 2) other prevention strategies feasible for this group are not possible among other high-risk groups; 3) the overall morbidity and mortality from pandemic is likely to severely impact other groups of persons who would be expected to have a better response to the vaccine; and 4) a more severe shortage of vaccine is anticipated.

6. Severely immunocompromised persons

a) Definition

Persons who are undergoing or who have recently undergone bone marrow transplantation and others with severe immunodeficiency (e.g., AIDS patients with CD4 counts <50, children with SCID syndrome, recent bone marrow transplant patients). The numbers of persons in these categories is likely much smaller than the anticipated number assumed in tiering above, but sources for more specific estimates have not been identified.

b) Rationale

These groups have a lower likelihood of responding to influenza vaccination. Thus, strategies to prevent severe influenza illness in this group should include vaccination of healthcare workers and household contacts of severely immunocompromised persons and use of antiviral medications. Consideration should be given to prophylaxis of severely immunocompromised persons with influenza antivirals and early antiviral treatment should they become infected.

7. Children <6 months of age

a) Rationale

Influenza vaccine is poorly immunogenic in children <6 months and the vaccine is currently not recommended for this group. In addition, influenza antiviral medications are not FDA-approved for use in children <1 year old. Thus, vaccination of household contacts and out-of-home caregivers of children <6 months is recommended to protect this high-risk group.

C. Other discussion

There was substantial discussion on priority for children. Four potential reasons were raised for making vaccination of children a priority:

- At the public engagement session, many participants felt that children should have high priority for vaccination.
- Children play a major role in transmitting infection, and vaccinating this group could slow the spread of disease and indirectly protect others.
- Children have strong immune systems and will respond well to vaccine whereas vaccination of the elderly and those with illnesses may be less effective.
- Some ethical frameworks would support a pediatric priority.

ACIP and NVAC did not make children a priority (other than those included in tiers, because of their underlying diseases [Tiers 1B and 2A] or as contacts of high-risk persons [Tier 1C]) for several reasons:

- Healthy children have been at low risk for hospitalization and death in prior pandemics and during annual influenza seasons.
- It is uncertain whether vaccination of children will decrease transmission and indirectly protect others. Studies that show this impact or mathematical models that predict it rely on high vaccination coverage that may not be possible to achieve given limited supplies in a pandemic.
- The committees recognize that this is an area for further scientific work; that children may be a good target population for live-attenuated influenza vaccine (FluMist®) if it is available; and that education of the public will be needed to provide the rationale for the recommendations.



NVAC recognizes that recommendations [for antiviral drug use] will need to be reconsidered at the time of a pandemic when information on the available drug supply, epidemiology of disease, and impacts on society are known.

The committee considered the primary goal of a pandemic response to decrease health impacts including severe morbidity and death. Minimizing societal and economic impacts were considered secondary and tertiary goals.

NVAC RECOMMENDATIONS ON PANDEMIC ANTIVIRAL DRUG USE

On July 19, 2005, NVAC voted unanimously in favor of the antiviral drug use priority recommendations described here and summarized in Table D-2. These votes followed deliberations of a Working Group, which included as consultants representatives of public and private sector stakeholder organizations and academic experts. There was limited staff level participation from DoD, DHS, and VA. Several ethicists also served as consultants to the Working Group.

The recommendations were made considering pandemic response goals, assumptions on the impacts of a pandemic, and after thorough review of past pandemics, annual influenza disease, data on antiviral drug impacts, and recommendations for pandemic vaccine use.

Recommendations were made to guide planning needed for effective implementation at state and local levels. The committee recognizes that recommendations will need to be reconsidered at the time of a pandemic when information on the available drug supply, epidemiology of disease, and impacts on society are known.

The committee considered the primary goal of a pandemic response to decrease health impacts including severe morbidity and death. Minimizing societal and economic impacts were considered secondary and tertiary goals.

A. Critical assumptions

Assumptions regarding groups at highest risk during a pandemic and impacts on the healthcare system and other critical infrastructures are the same as those underlying the vaccine priority recommendations. Additional assumptions specific for antiviral drugs included:

- Treatment with a neuraminidase inhibitor (oseltamivir [Tamiflu®] or zanamivir [Relenza®]) will be effective in decreasing risk of pneumonia, will decrease hospitalization by about half (as shown for inter-pandemic influenza), and will also decrease mortality.
- Antiviral resistance to the adamantanes (amantadine and rimantadine) may limit their use during a pandemic.
- The primary source of antiviral drugs for a pandemic response will be the supply of antiviral drugs that have been stockpiled. Before annual influenza seasons about 2 million treatment courses of oseltamivir are available in the U.S. U.S.-based production of oseltamivir is being established; expected capacity is projected at about 1.25 million courses per month.
- Treating earlier after the onset of disease is most effective in decreasing the risk of complications and shortening illness duration. Generally, treatment should be given within the first 48 hours.
- Assumptions for the amount of antiviral drug needed for defined priority groups is based on the population in those groups and assumptions that 35% of persons in the priority groups will have influenza-like illness and 75% will present within the first 48 hours and be eligible for treatment. For persons admitted to the hospital, the committee assumed that 80% would be treated, as the 48-hour limit may sometimes be relaxed in more ill patients.
- Unlike vaccines, where each tier would be protected in turn as more vaccine is produced, for antiviral drugs, the number of priority groups that can be covered would be known at the start of the pandemic based on the amount of drug that is stockpiled. Additional supply that would become available during the pandemic could provide some flexibility.

Table D-2: Antiviral Drug Priority Group Recommendations*

	Group	Estimated population (millions)	Strategy**	# Courses (millions)		Rationale
				For target group	Cumulative	
1	Patients admitted to hospital***	10.0	T	7.5	7.5	Consistent with medical practice and ethics to treat those with serious illness and who are most likely to die
2	Health care workers (HCW) with direct patient contact and emergency medical service (EMS) providers ⁴	9.2	T	2.4	9.9	Healthcare workers are required for quality medical care. There is little surge capacity among healthcare sector personnel to meet increased demand.
3	Highest risk outpatients—immunocompromised persons and pregnant women	2.5	T	0.7	10.6	Groups at greatest risk of hospitalization and death; immunocompromised cannot be protected by vaccination.
4	Pandemic health responders (public health, vaccinators, vaccine and antiviral manufacturers), public safety (police, fire, corrections), and government decision-makers	3.3	T	0.9	11.5	Groups are critical for an effective public health response to a pandemic.
5	Increased risk outpatients—young children 12-23 months old, persons ≥ 65 yrs old, and persons with underlying medical conditions	85.5	T	22.4	33.9	Groups are at high risk for hospitalization and death.
6	Outbreak response in nursing homes and other residential settings	NA	PEP	2.0	35.9	Treatment of patients and prophylaxis of contacts is effective in stopping outbreaks; vaccination priorities do not include nursing home residents
7	HCWs in emergency departments, intensive care units, dialysis centers, and EMS providers	1.2	P	4.8	40.7	These groups are most critical to an effective healthcare response and have limited surge capacity. Prophylaxis will best prevent absenteeism.
8	Pandemic societal responders (e.g., critical infrastructure groups as defined in the vaccine priorities) and HCW without direct patient contact	10.2	T	2.7	43.4	Infrastructure groups that have impact on maintaining health, implementing a pandemic response, and maintaining societal functions
9	Other outpatients	180	T	47.3	90.7	Includes others who develop influenza and do not fall within the above groups
10	Highest risk outpatients	2.5	P	10.0	100.7	Prevents illness in the highest risk groups for hospitalization and death.
11	Other HCWs with direct patient contact	8.0	P	32.0	132.7	Prevention would best reduce absenteeism and preserve optimal function.

* This is inclusive of Federal healthcare providers to Indian Nations and Tribes.

B. Definitions and rationale for draft priority groups

1. Persons admitted to hospital with influenza infection

a) Definition

Persons admitted to acute care facilities (traditional or non-traditional with a clinical diagnosis of influenza; laboratory confirmation not required). Excludes persons admitted for a condition consistent with a bacterial superinfection (e.g., lobar pneumonia developing late after illness onset) or after viral replication and shedding has ceased (e.g., as documented by a negative sensitive antigen detection test)

b) Strategy

Treatment within 48 hours of system onset.

c) Rationale

This group is at greatest risk for severe morbidity and mortality. Although there are no data to document the impacts of antiviral drug treatment among persons who already suffer more severe influenza illness, benefit is biologically plausible in persons with evidence of ongoing virally-mediated pathology (e.g., diffuse pneumonia, ARDS). Providing treatment to those who are most ill is also consistent with standard medical practices, would be feasible to implement, and would be acceptable to the public.

d) Population size

The number of persons admitted to hospital in an influenza pandemic would vary substantially depending on the severity of the pandemic and on the ability to expand inpatient capacity, if needed.

e) Unresolved issues

More specific guidance should be provided to healthcare workers on implementing antiviral treatment, including when and when not to treat. In some persons with severe illness, the ability to take oral medication or its absorption may be important issues. For infants <1 year old admitted to hospital,

*The committee focused its deliberations on the domestic U.S. civilian population. NVAC recognizes that Department of Defense (DoD) needs should be highly prioritized. A separate DoD antiviral stockpile has been established to meet those needs. Other groups also were not explicitly considered in deliberations on prioritization. These include American citizens living overseas, non-citizens in the U.S., and other groups providing national security services such as the border patrol and customs service.

**Strategy: Treatment (T) requires a total of 10 capsules and is defined as 1 course. Post-exposure prophylaxis (PEP) also requires a single course. Prophylaxis (P) is assumed to require 40 capsules (4 courses) though more may be needed if community outbreaks last for a longer period.

***There are no data on the effectiveness of treatment at hospitalization. If stockpiled antiviral drug supplies are very limited, the priority of this group could be reconsidered based on the epidemiology of the pandemic and any additional data on effectiveness in this population.



decisions about whether to treat with antiviral drugs may depend on the child's age and potential risk versus benefit as the neuraminidase inhibitors are not licensed for use in infants. If possible, data on time from symptom onset to hospital admission, current use of antiviral drug treatment among inpatients, and its impacts should be collected during interpandemic influenza seasons.

2. Healthcare workers and emergency medical service providers who have direct patient contact

a) Definition

Persons providing direct medical services in inpatient and outpatient care settings. Includes doctors, nurses, technicians, therapists, EMS providers, laboratory workers, other care providers who come within 3 feet of patients with influenza, and persons performing technical support functions essential to quality medical care.

b) Strategy

Treatment within 48 hours of symptom onset.

c) Rationale

Maintaining high quality patient care is critical to reduce health impacts of pandemic disease and to prevent adverse outcomes from other health conditions that will present for care during the pandemic period. Treatment of healthcare providers will decrease absenteeism due to influenza illness and may decrease absenteeism from fear of becoming ill, given the knowledge that treatment can prevent serious complications of influenza. Good data exist documenting the impacts of early treatment on duration of illness and time off work, and on the occurrence of complications such as lower respiratory infections. Treating healthcare providers is feasible to implement, especially for inpatient care providers who can be provided drugs through the occupational health clinic. It also would be acceptable to the public, who would recognize the importance of maintaining quality healthcare and would understand that persons with direct patient contact are putting themselves at increased risk.

d) Population size

There are about 12.6 million persons designated as healthcare workers by the Bureau of Labor Statistics and about 820,000 EMS providers. Among HCWs, two-thirds are estimated to provide direct patient care services.

e) Unresolved issues

Further work is needed to hone definitions and estimate population sizes. Implementation issues include the approach to identifying healthcare providers who would be eligible for treatment and where the treatment would be provided, particularly for outpatient care providers.

3. Outpatients at highest risk for severe morbidity or mortality from influenza infection

a) Definition

The Advisory Committee on Immunization Practices defines groups at high risk (or increased risk) of complications from influenza infection during annual outbreaks based on age (6-23 months and >65 years) and underlying illnesses. Among this population of about 88 million persons, some can be identified who are at highest risk of severe disease and death. These include persons with hematopoietic stem cell transplants (HSCT) and solid organ transplants; those with severe immunosuppression due to cancer therapy or hematological malignancy; persons receiving immunosuppressive therapy for other illnesses (e.g., rheumatoid arthritis); persons with HIV infection and a CD4 count <200; persons on dialysis; and women who are in the second or third trimester of pregnancy.

b) Strategy

Treatment within 48 hours of symptom onset.

c) Rationale

Of the large group of persons who are at increased risk of severe disease or death from influenza, these groups represent the population at highest risk and who are least likely to be protected by vaccination. Studies show that neuraminidase inhibitor therapy decreases complications and hospitalizations from influenza in high-risk persons and one unpublished study shows a significant decrease in mortality among patients who have undergone a hematopoietic stem cell transplant.

d) Population size

About 150,000 persons have had an HSCT or solid organ transplant. Assuming that the period of severe immunosuppression after a cancer diagnosis lasts for 1 year, the population targeted with non-skin, non-prostate cancers would equal the incidence of about 1.35 million persons. Based on a birth cohort of 4.1 million, a 28-week risk period during the second and third trimesters, and an 8-week pandemic outbreak in a community, there would be about 400,000 pregnant women included in this risk group. Further work is needed to estimate the size of other immunosuppressed groups.

e) Unresolved issues

Specific definition of included groups and population sizes.

4. Pandemic health responders, public safety workers, and key government decision-makers

a) Definition

Public health responders include those who manufacture vaccine and antiviral drugs; persons working at health departments who are not included as healthcare workers; and those who would be involved in implementing pandemic vaccination or other response components. Public safety workers include police, fire, and corrections personnel. Key government decision-makers include chief executives at federal, state, and local levels.

b) Strategy

Treatment within 48 hours of symptom onset.

c) Rationale

Preventing adverse health outcomes and social and economic impacts in a pandemic depend on the ability to implement an effective pandemic response. Early treatment of pandemic responders will minimize absenteeism and ensure that vaccination and other critical response activities can be maintained. Implementing early treatment for public health workers and vaccine manufacturers is feasible at workplace settings. Public safety workers prevent intentional and unintentional injuries and death, are critical to maintaining social functioning, and will contribute to a pandemic response, for example by ensuring order at vaccination clinics. A small number of decision-makers at federal, state, and local levels are needed to for an effective pandemic response.

d) Population size

An estimated 40,000 workers who produce pandemic vaccine and antiviral drugs in the U.S.; ~300,000 public health workers who would not be included in the HCW category; 3 million public safety workers; and a small number of government decision-makers.

e) Unresolved issues

Need to define the exact composition and size of this group.

5. Outpatients at increased risk of severe morbidity or mortality from influenza

a) Definition

For planning purposes, this group would include those currently designated as high-risk groups, except for those who have been categorized as being at highest-risk and included in a separate category. This increased-risk group includes persons 6–23 months and >65 years old, or who have underlying illnesses defined by the ACIP as associated with increased risk. Definition of this group may change based on the epidemiology of the pandemic.

b) Strategy

Treatment within 48 hours of symptom onset.

c) Rationale

Early treatment has been shown to significantly decrease lower respiratory infections and to reduce the rate of hospitalization in elderly and high-risk populations. By extrapolation and based on the results of one small uncontrolled study, significant reductions of mortality can be expected as well. As these risk groups are familiar to the public given recommendations for annual vaccination, communication would be easy and acceptability high.

d) Population size

About 85.5 million persons are included in this group. Although all are at increased risk of annual influenza compared with the healthy under-65 year old population, there are different levels of increased risk for severe complications and death within this category. Further stratification may be possible based on several parameters including number of underlying conditions; recent hospitalization for a high-risk condition, pneumonia, or influenza; and age.

e) Unresolved issues

Stratifying this group into those at greater and lesser risk may be important if antiviral supplies are limited. Implementing treatment will be challenging given that it should be provided at the initial point of care to accrue the greatest benefit from early therapy.

6. Outbreak control

a) Definition

Use of antiviral drugs to support public health interventions in closed settings where an outbreak of pandemic influenza is occurring.

b) Strategy

Treatment of cases and post-exposure prophylaxis of contacts (once daily antiviral medication for 10 days).

c) Rationale

Influenza outbreaks in nursing homes are associated with substantial mortality and morbidity. Nursing home residents also are less likely to respond to vaccination. Post-exposure prophylaxis has been shown to be effective in stopping influenza outbreaks in closed settings.

d) Population size

The number of outbreaks that may occur during a pandemic is unclear. Measures should be implemented to prevent outbreaks including limiting visitors, vaccination of staff, furloughing non-critical staff, and screening and exclusion for illnesses consistent with influenza.

e) Unresolved issues

Should this policy also be implemented in prisons or other settings where explosive spread of illness may occur but the risk for severe complications is not high?

7. Healthcare workers in ER, ICU, EMS, and dialysis settings

a) Definition

Includes all staff in these settings who are required for effective functioning of these health care units.

b) Strategy

Prophylaxis

c) Rationale

Optimally effective functioning of these units is particularly critical to reducing the health impacts of a pandemic. Prophylaxis will minimize absenteeism in these critical settings.

d) Population size

Need to obtain population estimates.

e) Unresolved issues

Population sizes

8. Pandemic societal responders and healthcare workers who have no direct patient contact

a) Definition

This group includes persons who provide services that must be sustained at a sufficient level during a pandemic to maintain public well-being, health, and safety. Included are workers at healthcare facilities who have no direct patient contact but are important for the operation of those facilities; utility (electricity, gas, water), waste management, mortuary, and some transport workers.

b) Strategy

Treatment within 48 hours of symptom onset.

c) Rationale

Maintaining certain key functions is important to preserve life and decrease societal disruption. Heat, clean water, waste disposal, and corpse management all contribute to public health. Ensuring functional transportation systems also protects health by making it possible for people to access medical care and by transporting food and other essential goods to where they are needed.

d) Population size

Within these broad categories, there are about 2 million workers at healthcare facilities who have no direct patient contact; 730,000 utility workers; 320,000 waste management workers; 62,000 in mortuary services; and 2.3 million in transportation. Not all occupations within these categories would be classified as pandemic societal responders. Estimates are that 35% of this population will develop illness and present within 48 hours of onset regardless of pandemic severity.



e) Unresolved issues

Need to stratify within these groups to identify who fills specific pandemic societal response functions and to assess whether those functions could still operate if a substantial proportion of the workforce became ill during a 6-8 week pandemic outbreak within a community. Implementation issues need to be addressed, especially with respect to how persons would be identified as falling within this priority group when presenting for treatment and where that treatment would be provided.

9. Other outpatients

a) Definition

Includes persons not in one of the earlier priority groups.

b) Strategy

Treatment within 48 hours of illness onset.

c) Rationale

Treatment reduces the risk of complications and mortality, reduces duration of illness and shortens time off work, and decreases viral shedding and transmission. If sufficient antiviral supplies are available, providing treatment to all who are ill achieves equity and will be most acceptable to the public.

d) Population size

There are an estimated 180 million persons who are not included in previously targeted groups.

e) Unresolved issues

Consider whether there are any strata that can be defined within this population.

C. Additional NVAC recommendations on antiviral drugs for pandemic influenza

In addition to recommendations for priority groups, NVAC unanimously adopted the following recommendations:

- Sufficient drugs should be stockpiled to address top priorities. NVAC recommends that the minimum stockpile size be about 40 million courses, allowing coverage of the top 7 priority groups.
- Oseltamivir should be the primary drug stockpiled, but some zanamivir also should be obtained as it is effective against some oseltamivir-resistant strains, may be preferred for treatment of pregnant women, and supporting two manufacturers enhances security against supply disruptions. Approximately 10% of the stockpile should be zanamivir if feasible and cost effective. No additional adamantanes should be stockpiled.
- Antiviral drugs can also be used as part of an international effort to contain an initial outbreak and prevent a pandemic. Use to slow disease spread early in a pandemic may be useful but requires large amounts of drug.
- Critical research should be conducted to support development and implementation of recommendations for pandemic influenza antiviral drug use, including:
 - Impact of treatment at hospital admission on outcome
 - Optimal treatment dose for H5N1 and other potential pandemic strains
 - Sensitivity and use of rapid diagnostic tests for H5N1 and other influenza strains with pandemic potential
 - Safety and pharmacokinetics of oseltamivir among infants <1 year old
 - Investigation of the impact of other drugs (new antiviral agents and other classes such as statins) on influenza
- Additional work with public and private sector groups should be done to further hone definitions of target groups and their estimated population sizes, and to provide further guidance on antiviral drug distribution and dispensing.