Guideline Summary NGC-7080

Guideline Title

Seasonal influenza in adults and children - diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines by the Infectious Diseases Society of America.

Bibliographic Source(s)

Harper SA, Bradley JS, Englund JA, File TM, Gravenstein S, Hayden FG, McGeer AJ, Neuzil KM, Pavia AT, Tapper ML, Uyeki TM, Zimmerman RK, Expert Panel of the Infectious Diseases Society of America. Seasonal influenza in adults and children--diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines of the Infectious Diseases Society of America. Clin Infect Dis 2009 Apr 15;48(8):1003-32. PubMed

Guideline Status

This is the current release of the guideline.

Scope

Disease/Condition(s)

Seasonal (inter-pandemic) influenza virus infection

- Influenza A (H1N1) virus infection
- Influenza A (H3N2) virus infection
- Influenza B virus infection

Note: These guidelines apply to seasonal (inter-pandemic) influenza and not to avian or pandemic disease.

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Allergy and Immunology

Cardiology

Family Practice

Geriatrics

Infectious Diseases

Internal Medicine

Nephrology

Obstetrics and Gynecology

Pediatrics

Preventive Medicine

Pulmonary Medicine

Rheumatology

Intended Users

Hospitals

Physicians

Guideline Objective(s)

To provide recommendations for diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza virus infection in adults and children

Target Population

- All patients, institutional residents, and healthcare personnel suspected or considered to have influenza
- Non-infected individuals who are at high risk for complications of influenza infection and household and institutional contacts (see "Major Recommendations" section for specific patients groups targeted for chemoprophylaxis)

Interventions and Practices Considered

Diagnosis/Evaluation

1. During influenza season, persons who may have influenza and should be considered for influenza testing
   - Immunocompetent and immunocompromised persons with acute onset of fever and respiratory symptoms, especially if they have underlying conditions placing them at risk for complications
   - Persons hospitalized with fever and respiratory symptoms, including those with community-acquired pneumonia
   - Persons with fever and exacerbation of underlying chronic lung disease
   - Infants and young children with fever and no other signs or symptoms
   - Elderly persons with new or worsening respiratory symptoms, with or without fever
   - Elderly persons or infants with sepsis syndrome or fever of unknown origin
   - Severely ill persons with fever or hypothermia
   - Persons that develop fever and respiratory symptoms after hospital admission
   - Healthcare personnel, residents, or visitors during an influenza outbreak
   - Persons who are epidemiologically linked to an influenza outbreak
2. Specimen collection in persons with suspected influenza
3. Influenza tests for suspected influenza
   - Reverse-transcriptase polymerase chain reaction
   - Immunofluorescence
   - Commercial rapid influenza diagnostic tests
   - Viral isolation (in standard cell culture and shell vial culture)
4. Interpretation of influenza testing results (positive or negative screening test)

Management/Treatment

1. Antiviral treatment is recommended or considered for specific at risk populations (see "Major Recommendations" field.)
2. Antiviral drug treatment
   - Influenza A (H1N1): zanamivir or an adamantane
   - Influenza A (H3N2): oseltamivir or zanamivir
   - Influenza B: oseltamivir or zanamivir
3. Antivirals for chemoprophylaxis
   - Deciding on target groups for antiviral chemoprophylaxis
   - Initiation and duration of antiviral chemoprophylactic regimens
   - Antiviral drugs for chemoprophylaxis
     - Influenza A (H1N1): zanamivir or an adamantane
     - Influenza A (H3N2): oseltamivir or zanamivir
     - Influenza B: oseltamivir or zanamivir
4. Management of influenza outbreaks in institutional settings

Major Outcomes Considered

- Incidence of influenza
- Sensitivity and specificity of diagnostic tests

- Antiviral resistance rate
- Safety and efficacy of antiviral agents
- Emergency room and hospitalization visits
- Complications of influenza
- Mortality

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

PUBMED literature searches were performed of the English-language literature from 1966 to 2008, using the terms: influenza or influenza plus virus, infection, treatment, prophylaxis, chemoprophylaxis, or outbreak, and focused on human studies.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence	
I	Evidence from ≥1 properly randomized, controlled trial.
II	Evidence from ≥1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments.
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Adapted from Canadian Task Force on the Periodic Health Examination.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

In evaluating the evidence regarding the Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of seasonal influenza, the Panel followed a process used in the development of other Infectious Diseases Society of American (IDSA) guidelines. The process included a systematic weighting of the quality of the evidence and the grade of recommendation.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The Infectious Diseases Society of America (IDSA) Standards and Practice Guidelines Committee (SPGC) convened experts in the diagnosis, treatment, chemoprophylaxis, and management of institutional outbreaks of seasonal influenza and included representatives from the following collaborating organizations: American Academy of Family Physicians (AAFP), American Academy of Pediatrics (AAP), American College of Physicians (ACP), Centers for Disease Control and Prevention (CDC), Pediatric Infectious Diseases Society (PIDS) and the Society for Healthcare Epidemiology of America (SHEA). The Panel members are listed in Appendix 1 of the original guideline document.

The Panel met on eleven occasions via teleconference and in person to complete the work of the guideline. The purpose of the meetings was to discuss the questions to be addressed, make writing assignments, and discuss recommendations. All members of the panel participated in the preparation and review of the draft guideline.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

Category/Grade	Definition
Strength of Recommendation	
A	Good evidence to support a recommendation for use.
B	Moderate evidence to support a recommendation for use.
C	Poor evidence to support a recommendation.

Adapted from Canadian Task Force on the Periodic Health Examination.

Cost Analysis

Published cost analyses were reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Feedback from external peer reviews was obtained. All collaborating organizations were also asked to provide feedback and endorse the guidelines. The guideline was reviewed and approved by the Infectious Diseases Society of American (IDSA) Standards and Practice Guidelines Committee and the Board of Directors prior to dissemination.

Recommendations

Major Recommendations

Ratings of quality of evidence (**I-III**) and strength of recommendation (**A-C**) are defined at the end of the "Major Recommendations" field.

Diagnostic Issues

Who Should Be Considered to Have Influenza?

1. During influenza season (defined as periods when influenza viruses are circulating in the community), the diagnosis of influenza should be considered in the following patients, regardless of vaccination status:

- Immunocompetent and immunocompromised persons (both adults and children), including healthcare personnel, with fever and the acute onset of respiratory signs and symptoms **(A-II)**.
- Persons with fever and acute exacerbation of underlying chronic lung disease **(A-II)**.
- Infants and young children with fever and no other signs or symptoms **(A-II)**.
- Elderly persons with new or worsening respiratory symptoms, including exacerbation of congestive heart failure, or altered mental status with or without fever **(A-II)**.
- Severely ill persons with fever or hypothermia **(A-II)**.
- Hospitalized children admitted without fever and acute respiratory symptoms that subsequently develop fever or febrile respiratory illness after admission **(A-II)**.
- Hospitalized adults admitted without fever and acute respiratory symptoms that subsequently develop febrile respiratory illness after admission **(A-II)**.

2. During any time of the year, influenza should be considered in immunocompetent and immunocompromised persons with febrile acute respiratory signs and symptoms who are epidemiologically linked to an influenza outbreak (e.g., healthcare personnel, residents, or visitors in an institution experiencing an influenza outbreak; household and close contacts of persons with suspected influenza; returned travelers from countries where influenza viruses may be circulating; participants in international mass gatherings; cruise ship passengers) **(A-II)**.

Who Should Be Tested for Suspected Influenza?

3. If the result will influence clinical management (decisions on initiation of antiviral treatment, impact upon other diagnostic testing, antibiotic treatment decisions, and infection control practices), considering the sensitivity and specificity of the test used and information about local influenza virus circulation, the following persons should be considered for influenza testing (see Table 2 in the original guideline document):

During Influenza Season

- Outpatient immunocompetent persons of any age at high-risk for complications of influenza (e.g., hospitalization, death) (see Table 5 in the original guideline document) presenting with acute febrile respiratory symptoms, within 5 days of illness onset, when virus is usually being shed **(A-II)**.
- Outpatient immunocompromised persons of any age presenting with febrile respiratory symptoms, irrespective of time from illness onset, since immunocompromised persons can shed influenza viruses for weeks to months **(A-II)**.
- Hospitalized persons of any age (immunocompetent or immunocompromised) with fever and respiratory symptoms, including those with a diagnosis of community acquired pneumonia, irrespective of time from illness onset **(A-II)**.
- Elderly persons and infants presenting with suspected sepsis or fever of unknown origin irrespective of time from illness onset **(A-III)**.
- Children with fever and respiratory symptoms presenting for medical evaluation irrespective of time from illness onset **(A-II)**.
- Persons of any age that develop fever and respiratory symptoms after hospital admission, irrespective of time from illness onset **(A-II)**.
- Immunocompetent persons with acute febrile respiratory symptoms but not at high risk of complications secondary to influenza infection may be tested for purposes of obtaining local surveillance data (**A-III**).

During Any Time of the Year

- Healthcare personnel, residents, or visitors in an institution experiencing an influenza outbreak, who present with febrile respiratory symptoms, within 5 days of illness onset **(A-II)**.

- Persons who are epidemiologically linked to an influenza outbreak (e.g., household and close contacts of persons with suspected influenza; returned travelers from countries where influenza viruses may be circulating; participants in international mass gatherings; cruise ship passengers), within 5 days of illness onset **(A-II)**.

What Specimens Should Be Collected for Influenza Testing from Persons with Suspected Influenza?

4. In immunocompetent persons, respiratory tract specimens should be obtained as close to illness onset as possible, preferably within 5 days of illness onset. Collection of specimens after 5 days from illness onset might result in falsely negative results due to substantially decreased viral shedding, especially in older children and adults. Infants and young children commonly shed influenza viruses for one week or longer. In infants and young children, optimal specimens are nasal aspirates and swabs. In older children and adults, nasopharyngeal aspirates and swabs are preferred specimens. Oropharyngeal specimens (e.g., throat swabs) and sputum may have lower yield for detection of human influenza viruses but may still produce positive results **(A-II)**.

5. Immunocompromised persons of any age with influenza virus infection may shed influenza viruses for weeks to months, even without fever or respiratory symptoms. Therefore, collection of upper and lower respiratory specimens (e.g., with bronchoalveolar lavage) after 5 days from illness onset may still be useful for influenza testing in these persons **(A-II)**.

6. Upper and lower respiratory tract samples should be obtained from mechanically ventilated patients within 5 days of illness onset, though testing may be positive even after this period. Lower respiratory tract samples include endotracheal aspirates and washes, and bronchoalveolar lavage fluid **(A-II)**.

7. Respiratory specimens should be tested for influenza as soon as possible after collection and should be refrigerated pending testing but should not be frozen **(A-II)**.

8. Clinicians should consult test instructions for the recommended clinical specimens for each specific influenza test **(A-II)**.

9. Acute serum specimens should not be obtained for diagnostic purposes. Paired acute and convalescent sera are needed for determination of antibody titers (by hemagglutinin inhibition, enzyme-linked immunosorbent assay (ELISA), or complement fixation, available only through reference laboratories), but results cannot be attained in a timely fashion and will not influence clinical management **(A-II)**.

What Influenza Tests Should Be Used for Persons with Suspected Influenza?

10. Tests that yield results in a timely manner that can influence clinical management (decisions on initiation of antiviral treatment, impact upon other diagnostic testing, antibiotic treatment decisions, and infection control practices) are recommended to guide patient care. Results of testing should take into account the a priori likelihood of influenza infection based on the patient's signs and symptoms, the sensitivity and specificity of the test used, and information on circulation of influenza in the community. An in-depth description of influenza testing methods is also available at http://www.cdc.gov/flu/professionals/diagnosis/labprocedures.htm.

In order of priority, the following influenza tests are recommended, if available:

- **Reverse-transcriptase polymerase chain reaction (RT-PCR)**. This is currently the most sensitive and specific of testing modalities for influenza, with results available within 4-6 hours of specimen submission. RT-PCR shows greater sensitivity than viral culture, may be used as a confirmatory test, and is useful for quickly differentiating between influenza types and subtypes. RT-PCR is also the preferred test for specimens from persons with a history of exposure to animals with possible influenza illness (e.g., influenza A (H5N1) in poultry in Eurasia or swine influenza in any part of the world, including North America) **(A-II)**.

- **Immunofluorescence**. Direct Fluorescent Antibody staining (DFA) or Indirect Fluorescent Antibody staining (IFA) for influenza antigen detection are used as screening tests. Immunofluorescence exhibits slightly lower sensitivity and specificity than viral isolation in cell culture, but results are available within hours of specimen submission. Performance of these assays depends heavily on laboratory expertise and the quality of the specimen collected (i.e., must include respiratory epithelium cells) **(A-II)**.

- **Commercial rapid influenza diagnostic tests**. These currently available antigen detection tests provide results in 10-30 minutes but exhibit decreased sensitivity (70-90% for children, <40-60% in adults) compared with RT-PCR and with viral culture (see Table 3 in the original guideline document). Performance of these assays depends heavily on patient age, duration of illness, sample type, and perhaps viral type. Given the lower sensitivity of immunofluorescence and commercial rapid tests, follow-up testing with RT-PCR and/or viral culture should be considered to confirm negative test results **(A-II)**.

11. **Viral Isolation (in Standard Cell Culture and Shell Vial Culture)** is not a screening test, but during periods of low influenza activity (late spring, summer, early fall) should be performed on respiratory specimens collected from persons with suspected influenza that present for medical care within 5 days of illness onset, especially if such persons are known to be epidemiologically linked to an influenza outbreak. During influenza season, viral culture should be done on respiratory specimens from a subset of persons for routine virologic surveillance purposes and to confirm some negative test results from rapid antigen and immunofluorescence testing, particularly in the setting of institutional outbreaks **(A-II)**.

12. Serologic testing is usually not recommended to detect evidence of human influenza virus infection for management of acute illness. Influenza serology on a single serum specimen cannot reliably be interpreted. Paired acute and convalescent sera are needed for determination of antibody titers (by hemagglutinin inhibition, ELISA, or complement fixation, available only through reference laboratories), but results cannot be attained in a timely fashion and will not influence clinical management. Paired serum specimens are useful only for retrospective diagnosis and for research purposes **(A-II)**.

How are Influenza Testing Results Interpreted?

13. To properly interpret testing results, clinicians should consider and understand the limitations of influenza tests, especially for screening tests such as immunofluorescence and commercially available rapid influenza tests, and the level of influenza activity among the population being tested (see Table 4 in the original guideline document). Clinicians should also consider that a positive influenza test does not rule out bacterial co-infection and evaluation

for the potential need for antibiotics **(A-II)**.

- A positive screening test result is most likely to be truly positive during periods of peak influenza activity in the population tested.
- A positive screening test result is most likely to be falsely positive during periods of low influenza activity in the population tested, including early and late in the influenza season. A confirmatory test such as PCR or viral culture should be considered.
- A negative screening test result is most likely to be truly negative during periods of low influenza activity in the population tested.
- A negative screening test result is most likely to be falsely negative during periods of peak influenza activity in the population tested. A confirmatory test such as PCR or viral culture should be considered.

Antivirals for Treatment

Who Should Be Treated with Antivirals?

14. Treatment is **recommended** for **both adults and children** with influenza virus infection meeting the following criteria:

- Persons with laboratory-confirmed or highly suspected influenza virus infection at high risk of complications (see Table 5 in the original guideline document) within 48 hours of symptom onset. Benefits have been best evaluated mostly among otherwise healthy adults with uncomplicated influenza with treatment initiated within 48 hours of symptom onset, although smaller numbers of persons with conditions increasing the risk of influenza complications have also been included in trials. Fewer data are available by which to make recommendations on treating persons 48 hours after symptom onset. Treatment is recommended regardless of influenza vaccination status, and regardless of severity of illness **(A-II)**.
- Persons requiring hospitalization for laboratory confirmed or highly suspected influenza illness, regardless of underlying illness or influenza vaccination status, if treatment can be initiated within 48 hours of onset of symptoms **(A-II)**. However, persons requiring hospitalization for laboratory-confirmed influenza whose positive laboratory test for influenza is from a specimen taken more than 48 hours after the onset of illness may also benefit from treatment **(B-II)**.

15. Treatment should be **considered** for **both adults and children** with influenza virus infection meeting the following criteria:

- Outpatients at high risk of complications (see Table 5 in the original guideline document) with illness that is not improving, and who have a positive influenza test result from a specimen obtained more than 48 hours from onset of symptoms **(C-III)**.
- Outpatients with laboratory-confirmed or highly suspected influenza virus infection not at increased risk of complications whose onset of symptoms is within 48 hours of presentation, and who wish to shorten the duration of illness and further reduce their relatively low risk of complications **(A-I)**, or who are in close contact with persons at high risk of complications secondary to influenza infection (see Table 5 in the original guideline document). Those with onset of symptoms greater than 48 hours prior to presentation, with persisting moderate to severe illness may also benefit from treatment, but safety and efficacy in this population have not been evaluated prospectively **(B-III)**.

What Antiviral Drug Should Be Used for Treatment?

16. Influenza viruses and their susceptibilities to available antiviral medications evolve rapidly. Clinicians should maintain familiarity with local patterns of influenza circulation in their communities throughout influenza season. Current and frequently updated information on antiviral resistance and recommendations on antiviral use may be found at http://www.cdc.gov/flu. Based on antiviral susceptibility patterns current as of February 2009, infection with an influenza A (H1N1) virus should be treated with either zanamivir or an adamantane (preferably rimantadine due to its more favorable side effect profile); oseltamivir should not be used for influenza A (H1N1). Infection with an influenza A (H3N2) virus should be treated with oseltamivir or zanamivir; the adamantanes should not be used for influenza A (H3N2). If subtype information is unavailable, influenza A should be treated either with zanamivir, or with a combination of oseltamivir and rimantadine. Infection with an influenza B virus should be treated only with oseltamivir or zanamivir. See Table 6 in the original guideline document for detailed information on antiviral regimens in appropriate age groups **(A-II)**.

Antivirals for Chemoprophylaxis

Who Should Be Considered for Antiviral Chemoprophylaxis to Prevent Influenza?

17. Influenza vaccination is the primary tool to prevent influenza, and antiviral chemoprophylaxis is not a substitute for influenza vaccination. When influenza viruses are circulating in the community, chemoprophylaxis can be considered for high-risk persons during the 2 weeks post-vaccination before an adequate immune response to inactivated vaccine develops (6 weeks for children who were not previously vaccinated and who require 2 doses of vaccine) **(A-I)**.

18. Antiviral chemoprophylaxis should be considered for adults and children ≥ 1 year of age at high risk of complications from influenza for whom influenza vaccination is contraindicated, unavailable, or is expected to have low effectiveness (e.g., persons who are significantly immunocompromised) **(B-II)**. Contraindications to vaccination include anaphylactic hypersensitivity to eggs or other vaccine components; moderate to severe febrile illness; and as a precaution, a history of Guillain-Barré Syndrome within 6 weeks of a previous influenza vaccination (Fiore et al., 2008).

19. Antiviral chemoprophylaxis (in conjunction with prompt immunization with the inactivated vaccine) should be considered for adults and children who are aged ≥1 year that are at high risk of complications from influenza virus infection (see Table 5 in the original guideline document) and have not yet received influenza vaccine when influenza activity has already been detected in the community. Whenever possible, influenza vaccine should be administered, and vaccination should continue in recommended persons until influenza is no longer in community circulation **(B-II)**.

20. Antiviral chemoprophylaxis may be considered for unvaccinated adults, including healthcare workers, and

children aged ≥1 year who are in close contact with persons at high risk for influenza complications during periods of influenza activity. Whenever possible, influenza vaccine should be administered, 2 weeks after which chemoprophylaxis may be discontinued (6 weeks for children who were not previously vaccinated and who require 2 doses of vaccine) **(B-III)**.

21. Antiviral chemoprophylaxis is recommended for all residents (vaccinated and unvaccinated) in institutions such as nursing homes and chronic care facilities that are experiencing influenza outbreaks **(A-I)**.

22. The strongest consideration for use of antiviral chemoprophylaxis should be given to those at the highest risk of influenza-associated complications. The risk of influenza-associated complications is not identical among all high risk persons, and antiviral chemoprophylaxis is likely to have the greatest benefit among those at highest risk of influenza complications and death, such as recipients of hematopoietic stem cell transplantation **(B-III)**.

23. Antiviral chemoprophylaxis should be considered for persons at high-risk of complications from influenza if influenza vaccine is not available due to shortage. When vaccine is available, it should be administered to these persons **(A-I)**.

24. Antiviral chemoprophylaxis can be considered in high-risk persons (Table 5 in the original guideline document) in situations where there is documented low influenza vaccine clinical effectiveness due to the circulation of influenza virus strains which are antigenically distant from the vaccine strains such that a substantial increase in vaccine failures is anticipated, as determined by federal, state, and local public health authorities **(C-II)**.

When Should Antiviral Chemoprophylactic Regimens Be Started?

25. In persons at high-risk of complications who are not adequately protected due to poor immune responses (e.g., in persons who are significantly immunocompromised), lack of influenza immunization, or ineffective vaccine (e.g., when drift variants are circulating), antiviral chemoprophylaxis should be initiated at the onset of sustained influenza community activity as determined by local public health authorities **(B-II)**.

26. Antiviral chemoprophylaxis use for appropriate persons within households should be initiated when one family member develops suspected or confirmed influenza and any other family member is at high risk for complications secondary to infection, including infants less than 6 months of age (Table 5 in the original guideline document). In this setting, all non-infected family members should receive antiviral chemoprophylaxis. Ideally, all eligible family members in such settings should be vaccinated, making chemoprophylaxis unnecessary **(A-I)**.

27. Antiviral chemoprophylaxis and other control measures should be initiated in institutions such as hospitals and long-term care facilities, such as nursing homes, when an influenza outbreak is detected, or when influenza is strongly suspected but the etiology of the outbreak has yet to be determined **(A-II)**.

How Long Should Chemoprophylaxis Continue?

28. If inactivated influenza vaccine is administered, antiviral chemoprophylaxis can generally be stopped two weeks post-vaccination for persons in non-institutional settings. Children aged <9 years who receive inactivated influenza vaccine for the first time require 2 doses of vaccine, with the second dose administered at least 4 weeks after the first dose. The immune response peaks 2 weeks after the second dose. Thus, a minimum of 6 weeks of chemoprophylaxis (i.e., chemoprophylaxis for at least 4 weeks after the first dose of vaccine and an additional 2 weeks of chemoprophylaxis after the second dose) would be needed depending on the amount of delay between the two vaccine doses **(B-II)**.

29. When antiviral chemoprophylaxis is used within a household following diagnosis of influenza in one family member, chemoprophylaxis should be continued for 10 days **(A-I)**.

30. In persons at high risk of complications from influenza for whom influenza vaccination is contraindicated, unavailable, or is expected to have low effectiveness (e.g., persons who are significantly immunocompromised), chemoprophylaxis should continue for the duration of time that influenza viruses are circulating within the community during influenza season **(B-III)**.

What Antiviral Drugs Should Be Used for Chemoprophylaxis?

31. Influenza viruses and their susceptibilities to available antiviral medications evolve rapidly. Clinicians should maintain familiarity with local patterns of influenza circulation in their communities throughout influenza season. Current and frequently updated information on antiviral resistance and recommendations on antiviral use may be found at http://www.cdc.gov/flu. Based on antiviral susceptibility patterns current as of February 2009, chemoprophylaxis for influenza A (H1N1) viruses should occur with either zanamivir or an adamantane (preferably rimantadine due to its more favorable side effect profile); oseltamivir should not be used for influenza A (H1N1) chemoprophylaxis. Chemoprophylaxis for influenza A (H3N2) virus should occur with oseltamivir or zanamivir; the adamantanes should not be used for influenza A (H3N2) chemoprophylaxis. If subtype information is unavailable, chemoprophylaxis for influenza A should occur either with zanamivir, or with a combination of oseltamivir and rimantadine. Chemoprophylaxis for influenza B virus should occur only with oseltamivir or zanamivir. See Table 6 in the original guideline document for detailed information on antiviral regimens in appropriate age groups **(A-I)**.

Outbreak Management in Institutional Settings

When Should An Influenza Outbreak Be Suspected in an Institution?

32. During influenza season, when 2 or more institutional residents manifest signs and symptoms of influenza-like illness (ILI) within 72 hours, testing for influenza should occur. When influenza viruses are circulating in the community, even one laboratory-positive laboratory result in conjunction with other compatible illnesses on the unit indicates an outbreak of influenza is occurring **(A-II)**.

What Is the Role for Testing Institutional Residents with Influenza-Like Illness after a Diagnosis of Influenza Has Already Been Established in One or More Residents?

33. After a single laboratory-confirmed case of influenza among residents has been identified in an institution, it is likely that subsequent cases of temporally-associated ILI are also caused by influenza virus infection, though mixed outbreaks due to other respiratory pathogens may occur. While it might not be possible to obtain specimens from all ill residents for influenza testing in the context of an outbreak, persons developing compatible symptoms more than 72 hours after implementation of antiviral chemoprophylaxis or among persons residing on previously unaffected units should be tested for influenza and other respiratory pathogens. If influenza testing is positive,

consider the possibility of a drug-resistant virus; spread of influenza to previously unaffected areas of the facility where antiviral use has not been implemented; or multiple introductions of influenza from the community to facility residents **(B-III)**.

Which Residents Should Be Treated with Antiviral Medications during an Outbreak?

34. All residents with laboratory-confirmed influenza virus infection should be treated with an appropriate influenza antiviral medication. After one case of laboratory-confirmed influenza is detected in a facility resident, all persons in the facility subsequently developing influenza-like illness or other signs or symptoms consistent with influenza (e.g., isolated altered mental status in an elderly resident) should be considered for treatment with an influenza antiviral medication **(A-III)**.

Which Residents Should Receive Antiviral Chemoprophylaxis during an Outbreak?

35. During documented long-term care facility influenza outbreaks, all residents should receive influenza antiviral chemoprophylaxis, regardless of influenza vaccination status. Ideally, chemoprophylaxis should be implemented on all floors and wards of the facility since breakthrough cases frequently occur when antiviral medications are administered only to those persons on the affected unit or ward and not to all residents in the facility **(A-I)**.

Which Healthcare Personnel Should Receive Antiviral Chemoprophylaxis during an Outbreak?

36. For all institutional employees who are unable to receive influenza vaccine or in whom vaccine is contraindicated, or when the vaccine is expected to be ineffective (e.g., due to the circulation of influenza virus strains which are antigenically distant from the vaccine strains such that a substantial increase in vaccine failures is anticipated), antiviral medications should be used for chemoprophylaxis **(B-III)**. Contraindications to vaccination include anaphylactic hypersensitivity to eggs or other vaccine components; moderate to severe febrile illness; and as a precaution, a history of Guillain-Barré Syndrome within 6 weeks of a previous influenza vaccination (Fiore et al., 2008).

How Long Should Antiviral Chemoprophylaxis Continue in Residents and Staff during an Outbreak?

37. In the setting of an institutional outbreak, antiviral chemoprophylaxis should be continued for 14 days or for 7 days after the onset of symptoms in the last person infected, whichever is longer **(A-II)**.

Definitions:

Strength of Recommendation and Quality of Evidence

Category/Grade	Definition
Strength of Recommendation	
A	Good evidence to support a recommendation for use.
B	Moderate evidence to support a recommendation for use.
C	Poor evidence to support a recommendation.
Quality of Evidence	
I	Evidence from ≥1 properly randomized, controlled trial.
II	Evidence from ≥1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments.
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Adapted from Canadian Task Force on the Periodic Health Examination.

Clinical Algorithm(s)

None provided

Evidence Supporting the Recommendations

References Supporting the Recommendations

Fiore AE, Shay DK, Broder K, Iskander JK, Uyeki TM, Mootrey G, Bresee JS, Cox NS, Centers for Disease Control and Prevention (CDC), Advisory Committee on Immunization Practices (ACIP). Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008. MMWR Recomm Rep 2008 Aug 8;57(RR-7):1-60. [502 references] PubMed

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and treatment of seasonal influenza and appropriate management of institutional influenza outbreak

Potential Harms

Adverse Effects of Antiviral Agents

- Nausea and vomiting are the most common adverse event associated with oseltamivir therapy, and were reported

in 9%-10% of adults receiving treatment. In children, adverse effects after oseltamivir administration are also principally gastrointestinal, with 14% of oseltamivir-treated children reporting vomiting, compared with 8% of influenza-infected placebo treated children. In Japan, neuropsychiatric adverse events were reported at a frequency of about 1 in 100,000 oseltamivir prescriptions, especially in adolescents. It is not clear whether these events were due to oseltamivir, influenza, or some combination that may include genetic susceptibility to these adverse events.

- Neuropsychiatric events have occasionally been reported in adults taking oseltamivir. The package inserts for both oseltamivir and zanamivir in the U.S. contain warnings about potential adverse neuropsychiatric events.
- There are no adverse events that have been reported to occur in more than 1% of zanamivir recipients. However, zanamivir is an orally inhaled powder, and there are case reports of bronchospasm related to zanamivir treatment. Concerns regarding bronchospasm and decreased pulmonary function after inhalation of zanamivir in pediatric and adult patients with underlying airways disease, including asthma and chronic obstructive pulmonary disease (COPD), prompted a warning not to use zanamivir in these persons.

Contraindications

Contraindications

- Contraindications to antivirals include previous hypersensitivity reactions and, in patients considered for zanamivir, a history of underlying airways disease since its use has occasionally been reported to result in bronchospasm.
- Contraindications to vaccination include anaphylactic hypersensitivity to eggs or other vaccine components; moderate to severe febrile illness; and as a precaution, a history of Guillain-Barré Syndrome within 6 weeks of a previous influenza vaccination.

Qualifying Statements

Qualifying Statements

It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. Infectious Diseases Society of America (IDSA) considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Audit Criteria/Indicators

Personal Digital Assistant (PDA) Downloads

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

Harper SA, Bradley JS, Englund JA, File TM, Gravenstein S, Hayden FG, McGeer AJ, Neuzil KM, Pavia AT, Tapper ML, Uyeki TM, Zimmerman RK, Expert Panel of the Infectious Diseases Society of America. Seasonal influenza in adults and children--diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines of the Infectious Diseases Society of America. Clin Infect Dis 2009 Apr 15;48(8):1003-32. PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2009 Mar

Guideline Developer(s)

Infectious Diseases Society of America - Medical Specialty Society

Source(s) of Funding

Infectious Diseases Society of America (IDSA)

Guideline Committee

Infectious Diseases Society of America (IDSA) Practice Guidelines Committee

Composition of Group That Authored the Guideline

Authors: Scott A. Harper, Centers for Disease Control & Prevention, New York, New York & Atlanta, Georgia; John S. Bradley, University of California San Diego School of Medicine, San Diego, California; Janet A. Englund, University of Washington School of Medicine, Seattle, Washington; Thomas M. File, Summa Health System, Akron, Ohio; Stefan Gravenstein, Alpert Medical School, Brown University, Providence, Rhode Island; Frederick G. Hayden, University of Virginia School of Medicine, Charlottesville, Virginia; Allison J. McGeer, University of Toronto, Toronto, Ontario, Canada; Kathleen M. Neuzil, PATH, Seattle, Washington; Andrew T. Pavia, University of Utah School of Medicine, Salt Lake City, Utah; Michael L. Tapper, Lenox Hill Hospital, New York, New York; Timothy M. Uyeki, Centers for Disease Control & Prevention, New York, New York & Atlanta, Georgia; Richard K. Zimmerman, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

Financial Disclosures/Conflicts of Interest

All members of the Expert Panel complied with the Infectious Diseases Society of America (IDSA) policy on conflicts of interest, which requires disclosure of any financial or other interest that might be construed as constituting an actual, potential, or apparent conflict. Members of the Expert Panel were provided IDSA's conflict of interest disclosure statement and were asked to identify ties to companies developing products that might be affected by promulgation of the guideline. Information was requested regarding employment, consultancies, stock ownership, honoraria, research funding, expert testimony, and membership on company advisory committees. The Panel made decisions on a case-by-case basis as to whether an individual's role should be limited as a result of a conflict. Potential conflicts are listed below.

Potential Conflicts of Interest: Disclosure: J.E. has received grant/study support from Sanofi Pasteur and MedImmune; serves as a speaker for Sanofi Pasteur and serves as a consultant for Sanofi Pasteur, Roche, Novartis and GlaxoSmithKline. K.N. is a member of Adult Immunization Advisory Board of the American College of Physicians. M.T. has served as a speaker at a CME Meeting sponsored by Roche and Gilead. S.G. has consulting agreements with Juvaris, Glaxo-Smith Kline, Sanofi Aventis, Merck and is a speaker for Glaxo-Smith Kline. A.P. has served as a consultant for NexBio and Glaxo SmithKline. A.M. has received grant/study support from Roche and Glaxo-SmithKline, has served as a speaker and consultant for Sanofi Pasteur, Gilead Biosciences and Biocryst Pharmaceuticals. R.Z. serves as a consultant for MedImmune. No Conflicts: F.H., J.B., T.F., S.H. and T.U.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Infectious Diseases Society of America (IDSA) Web site.

Print copies: Available from Infectious Diseases Society of America, 1300 Wilson Boulevard, Suite 300, Arlington, VA 22209.

Availability of Companion Documents

A Personal Digital Assistant (PDA) version of the guideline is available from the Infectious Diseases Society Web site.

Additionally, suggested performance measures are provided in the original guideline document.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on March 25, 2009. The information was verified by the guideline developer on May 4, 2009.

Copyright Statement

Disclaimer

NGC Disclaimer