# Influenza

## About the Guideline

- This guideline is an update of the 2009 Infectious Diseases Society of America publication.
- The Guideline Panel consisted of 16 experts in infectious diseases, pediatrics, emergency medicine, healthcare epidemiology, and obstetrics and gynecology.
- The guideline presents 58 recommendations and 79 statements on the diagnosis, treatment, use of antiviral chemoprophylaxis in community settings, and institutional outbreak control of seasonal influenza. The recommendations include 53 strong recommendations, 6 weak recommendations, and 20 best-practice statements.
- In the United States and globally, seasonal influenza A and B viruses are associated with significant morbidity and mortality annually.
- The guideline addresses new information on diagnostic testing, the use of antiviral medications, considerations for the use of antibiotics, testing for antiviral resistance, and evidence against the routine use of corticosteroids.
- The guideline does not address infection prevention and control for seasonal influenza in all healthcare settings, outbreaks outside healthcare settings, diagnosis, or treatment of novel influenza A of animal origin, recommendations for supportive care of complications of influenza virus infections, or recommendations for influenza vaccination.

## Key Clinical Considerations

Become familiar with the recommendations and best-practice statement provided in this guideline, especially if you work in an acute care setting or an outpatient setting.

- Timely diagnosis of influenza
    - Decreases unnecessary lab testing for other etiologic agents.
    - Decreases the use of unnecessary antibiotics.
    - Improves the efficacy of infection prevention and control measures.
    - Increases the appropriate use of antiviral medication.
- Early treatment with antiviral medications
    - Reduces the duration of symptoms and the risk of complications and hospitalization, and it may reduce mortality in high-risk patients.
    - Can prevent or control outbreaks in selected situations with the use of chemoprophylaxis (pre- or postexposure).

**Testing and Diagnosis**

Testing for influenza should be done to guide clinical management of individuals with acute onset of respiratory symptoms.

<u>Outpatient settings (physician offices, clinics, ambulatory care centers, or urgent care centers, as well as emergency departments)</u>

- During influenza season, when cases of seasonal influenza A and B viruses are present in the local community, test the following patients for influenza:
    - High-risk patients (those at greatest risk for developing complications associated with influenza, such as immunocompromised patients) exhibiting influenza-like illness, pneumonia, or nonspecific respiratory illness such as a cough without fever
    - Patients who are at high risk for developing complications from influenza:
        - Children younger than 5 years of age, specifically those less than 2 years of age
        - Adults older than 65 years of age
        - People with chronic pulmonary disease (including asthma), cardiovascular disease (excluding those with only hypertension), renal, hepatic, hematologic diseases (including sickle cell disease), metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy, stroke, intellectual disability, moderate to severe developmental delay, muscular dystrophy, or spinal cord injury)
        - Immunosuppressed individuals, including those with immunosuppression caused by medications or human immunodeficiency virus (HIV) infection
        - Women who are pregnant or postpartum (within 2 weeks of delivery)
        - Children and adolescents through 18 years of age who are receiving aspirin- or salicylate-containing medications and who may be at risk for Reye syndrome after influenza virus infection
        - American Indian/Alaska Native people
        - Persons with a body mass index (BMI) ≥ 40 kg/m$^2$
        - Residents of nursing homes and other chronic care facilities
    - Patients exhibiting an acute onset of respiratory symptoms with or without fever and either an exacerbation of chronic medical conditions or known complications of influenza
- Consider testing symptomatic patients who are not at high risk for influenza complications and who will be discharged home if the testing results might:
    - influence antiviral treatment.
    - reduce the use of unnecessary antibiotics.
    - decrease time in the emergency department.
    - influence antiviral treatment or chemoprophylaxis decisions for high-risk household contacts.
- During low influenza activity in the community, consider influenza testing for immunocompromised and high-risk patients with an acute onset of respiratory symptoms with or without fever.

<u>Hospitalized patients</u>

- During influenza activity in the community, test for influenza at admission for all patients with the following:
    - Acute respiratory illness including pneumonia, with or without fever
    - Acute worsening of chronic cardiopulmonary disease

    - Acute onset of respiratory illness with or without fever who are immunocompromised or at high risk of complications
- During influenza activity in community, test any hospitalized patient with acute onset of respiratory symptoms, with or without fever or respiratory distress and no obvious alternative diagnosis.
- During periods of low influenza activity in the community:
    - Test for influenza on admission to the hospital any patient with an acute onset of respiratory illness, with or without fever, and who has had contact with persons diagnosed with influenza, or who is part of a respiratory illness outbreak, or who has recently travelled from an area with influenza activity.
    - Consider testing for influenza any patient with an acute, febrile respiratory tract illness, especially any children or adults who are immunocompromised or are at high risk of complications, or if the results would guide antiviral treatment or chemoprophylaxis for high-risk household contacts.

**Specimens and Tests for Diagnosing Influenza**

- Collect a nasopharyngeal specimen as soon as possible, preferably within 4 days of symptom onset, using a flocked swab.
- If a nasopharyngeal specimen is not available, collect and combine a mid-turbinate nasal swab or nasal and throat swab specimens.
- Collect an endotracheal aspirate or bronchoalveolar lavage fluid specimen from hospitalized patients with respiratory failure receiving mechanical ventilation, even if there are negative influenza test results on upper respiratory tract specimens.
- Do not collect or test nonrespiratory specimens for diagnosis of seasonal influenza as they take too long for effective clinical management.
- Use rapid molecular assays or reverse-transcription polymerase chain reaction (RT-PCR) over other rapid influenza diagnostic tests (RIDTs), unless the more sensitive molecular assays are not available.
    - Use multiplex RT-PCR assays that test for a panel of respiratory pathogens, including influenza viruses, in hospitalized immunocompromised patients.
    - Consider using multiplex RT-PCR assays for testing nonimmunocompromised patients if results will guide clinical decisions.
- Do not use viral culture or serologic testing for the initial or primary diagnosis of influenza as the results will not be available in time to guide clinical management.

**Treatment**

- Antiviral treatment should be started as soon as possible for adults and children with documented or suspected influenza, regardless of their influenza vaccination history, in the following situations:
    - Patients hospitalized with influenza regardless of duration of illness before hospitalization.
    - Outpatients of any age with severe or progressive illness, regardless of duration of illness.

    - Outpatients at a high risk of complications from influenza, such as patients with chronic medical conditions and those who are immunocompromised.
    - Children less than two years of age and adults ≥ 65.
    - Pregnant women and those within 2 weeks postpartum.
- In the following situations, consider antiviral treatment for adults and children with documented or suspected influenza who are not at high risk for influenza complications, regardless of vaccination history:
    - Outpatients whose illness onset is ≤ 2 days before presentation.
    - Symptomatic outpatients who are household contacts of high-risk individuals, especially those who are severely immunocompromised.
    - Symptomatic healthcare providers who care for patients at high risk of developing complications from influenza.
- Antiviral agents for treatment
    - Start a single neuraminidase inhibitor (NAI) for treatment; do not use a combination of NAIs.
    - In otherwise healthy adults with uncomplicated influenza use one of the following:
        - Oral oseltamivir: treat for 5 days.
        - Inhaled zanamivir: treat for 5 days.
        - Intravenous peramivir: single dose.
    - Do not routinely use higher doses of NAI drugs.
    - A longer duration of treatment may be considered in cases of immunocompromised patients or for those with severe lower respiratory tract disease, because of the extended duration of influenza viral replication.
- Consider, investigate, and treat for bacterial coinfections of the upper or lower respiratory tract in the following patient populations:
    - Patients with suspected or confirmed influenza and who present with severe disease such as pneumonia, respiratory failure, hypotension, and fever.
    - Patients whose conditions worsen after initial antiviral treatment.
    - Patients who do not improve or whose condition worsens even on antiviral treatment should be evaluated for causes other than influenza.
- If clinical improvement does not occur with antiviral treatment or the patient's clinical condition deteriorates or worsens, consider the following:
    - Investigate causes other than influenza virus infection.
    - Test for influenza NAI resistance in the following patient populations:
        - Patients who develop laboratory-confirmed influenza while on or immediately following NAI chemoprophylaxis.
        - Patients with an immunocompromising condition, evidence of persistent influenza viral replication (e.g., persistently positive RT-PCR or viral culture results after 7 to 10 days), and who remain ill during or after NAI treatment.
        - Patients with laboratory-confirmed influenza who inadvertently received subtherapeutic NAI dosing.

- Corticosteroid adjunct therapy should not be used for treatment of suspected or confirmed seasonal influenza or associated complications unless clinically indicated for other reasons.
- Intravenous immunoglobulin should not be used routinely for treatment of uncomplicated influenza.

**Antiviral Chemoprophylaxis to Prevent Influenza**

Antiviral medications should not be used routinely or for chemoprophylaxis in large populations other than for the management of institutional outbreaks.

- Preexposure chemoprophylaxis
    - Preexposure chemoprophylaxis may be considered for the duration of the influenza season for adults and children aged ≥ 3 months at very high risk of developing influenza complications **and** for whom the influenza vaccination is contraindicated, is unavailable, or is expected to have low effectiveness (i.e., hematopoietic stem cell transplant recipients in first 6 to 12 months posttransplant, and lung transplant recipients).
    - Consider short-term prophylaxis for unvaccinated adults, including healthcare personnel, and for children aged ≥ 3 months who have close contact with patients at high risk for influenza complications and who cannot take antiviral chemoprophylaxis.
    - Consider educating patients and parents of patients that early initiation of empiric antiviral medication is an alternative to chemoprophylaxis.
    - Chemoprophylaxis for influenza should be with an NAI (oral oseltamivir or inhaled zanamivir), not an adamantine antiviral.
    - Antiviral chemoprophylaxis for high-risk persons should begin as soon as influenza activity is noted in the community and continue as long as influenza is in the community.
    - Persons receiving antiviral chemoprophylaxis who then become symptomatic should be tested for influenza and begin antiviral treatment dosing with an antiviral drug that has a different resistance profile, unless contraindicated.
- Postexposure antiviral chemoprophylaxis
    - Postexposure antiviral chemoprophylaxis may be considered for patients at very high risk of developing complications from influenza and for whom vaccination is unavailable, expected to be ineffective, or contraindicated may be started on postexposure antiviral chemoprophylaxis after a household exposure to influenza.
    - Postexposure antiviral chemoprophylaxis should be started as soon as possible after exposure, preferably no later than 48 hours after exposure.
    - If more than 48 hours have passed since exposure, postexposure chemoprophylaxis should not be initiated. As soon as symptoms occur, full-dose empiric antiviral treatment should be started if treatment is indicated.
    - In a nonoutbreak setting, continue postexposure antiviral chemoprophylaxis for 7 days after the most recent exposure to a close contact with influenza.
    - Patients receiving antiviral chemoprophylaxis who then become symptomatic should be tested for influenza and begin antiviral treatment with an antiviral drug that has a different resistance profile.

  - Chemoprophylaxis for influenza should be with an NAI (oral oseltamivir or inhaled zanamivir), not an adamantine antiviral.

**Institutional Outbreak Management and Control**

- Begin active surveillance for additional cases of influenza as soon as one healthcare-associated laboratory-confirmed influenza case is identified in a hospital, or one case of laboratory-confirmed influenza is identified in a long-term care facility.
- Initiate outbreak control measures as soon as possible in the following scenarios:
  - When 2 cases of healthcare-associated laboratory-confirmed influenza are identified within 72 hours of each other in residents or patients of same ward or unit.
  - Control measures include active surveillance for new cases and antiviral chemoprophylaxis for residents or patients.
  - If the results of influenza molecular testing are not available on the day of specimen collection and one or more residents or patients has suspected healthcare-associated influenza, consider implementing outbreak control measures as soon as possible.
- During an influenza outbreak in a long-term care facility or hospital, test any resident or patient for influenza who exhibits the following:
  - one or more acute respiratory symptoms, with or without fever; or
  - any of following without respiratory symptoms: temperature elevation or reduction, or behavioral change.
- Begin empiric antiviral treatment as soon as possible for any resident or patient with suspected influenza during an influenza outbreak without waiting for results of influenza diagnostic testing.
- Administer antiviral chemoprophylaxis as soon as possible to all exposed residents or patients who do not have suspected or laboratory-confirmed influenza regardless of influenza vaccination history, in addition to implementing all other recommended outbreak control measures.
- Antiviral chemoprophylaxis should be given to residents on outbreak-affected units, and active daily surveillance for new influenza cases throughout the facility should be continued.
- During an institutional outbreak, antiviral chemoprophylaxis for residents should be given for 14 days and continued for at least 7 days after the onset of symptoms in the last identified case.
- Antiviral prophylaxis can be considered for the following healthcare personnel:
  - Unvaccinated staff, including those who have underlying conditions that put them high risk for developing complications of influenza illness, or those who have household members at high risk for developing complications of influenza illness.
  - Staff who receive inactivated influenza vaccine during an institutional outbreak for 14 days postvaccination.
  - Any staff member, regardless of influenza vaccination status, to reduce the risk of short staffing in situations where clinical staff are limited, and to reduce staff reluctance to care for patients with suspected influenza.

**Reference:**
Uyeki, T. M., Bernstein, H. H., Bradley, J. S., Englund, J. A., File, T. M., Fry, A. M., Gravenstein, S., Hayden, F. G., Harper, S. A., Hirshon, J. M., Ison, M. G., Johnston, B. L., Knight, S. L., McGeer, A., Riley, L. E., Wolfe, C. R., Alexander, P. E., & Pavia, A. T. (2019). Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, *68*(6), e1–e47. https://doi.org/10.1093/cid/ciy866

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