

# Influenza and COVID-19

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Summary Recommendations
<p><b>Influenza Vaccination</b></p> <ul style="list-style-type: none"><li>• People with acute COVID-19 who have not received an influenza vaccine during influenza season should be vaccinated after they recover from acute illness and are no longer in isolation (<b>BIII</b>).</li><li>• Patients may be vaccinated while they are still in isolation if they are in a health care setting.</li><li>• An influenza vaccine and a COVID-19 vaccine may be administered concurrently at different injection sites. The <a href="#">Advisory Committee on Immunization Practices</a> and the <a href="#">Centers for Disease Control and Prevention</a> (CDC) provide more information on COVID-19 and influenza vaccines.</li></ul> <p><b>Diagnosis of Influenza and COVID-19 When Influenza Viruses and SARS-CoV-2 Are Cocirculating</b></p> <ul style="list-style-type: none"><li>• Only testing can distinguish between SARS-CoV-2 and influenza virus infections and identify SARS-CoV-2 and influenza virus coinfection.</li><li>• The COVID-19 Treatment Guidelines Panel (the Panel) recommends performing influenza testing in addition to SARS-CoV-2 testing in outpatients with acute respiratory illness if the results will change the clinical management strategy for the patient (e.g., administering antiviral treatment for influenza) (<b>BIII</b>).</li><li>• The Panel recommends testing for both viruses in all hospitalized patients with acute respiratory illness (<b>AIII</b>).</li><li>• Clinicians should consider performing additional testing in specific clinical circumstances. Secondary bacterial infection is more common with influenza than with COVID-19, so additional testing for bacterial pathogens is important in patients with influenza who have clinical signs that suggest bacterial superinfection, especially for those who are immunocompromised or intubated.</li><li>• See the CDC webpage <a href="#">Information for Clinicians on Influenza Virus Testing</a> and the Infectious Diseases Society of America (IDSA) <a href="#">clinical practice guidelines</a> for more information.</li></ul> <p><b>Antiviral Treatment of Influenza When Influenza Viruses and SARS-CoV-2 Are Cocirculating</b></p> <ul style="list-style-type: none"><li>• Antiviral treatment for influenza is the same for all patients regardless of SARS-CoV-2 coinfection (<b>AIII</b>).</li><li>• For information on using antiviral drugs to treat influenza in hospitalized and nonhospitalized patients, see the <a href="#">CDC</a> and <a href="#">IDSA</a> recommendations.</li><li>• There are no clinically significant drug-drug interactions between the antiviral agents used to treat influenza and the antiviral agents or immunomodulators used to treat COVID-19.</li><li>• The Panel recommends starting hospitalized patients who are suspected of having influenza on empiric treatment for influenza with <b>oseltamivir</b> as soon as possible regardless of their COVID-19 status and without waiting for influenza test results (<b>AIIb</b>).</li><li>• Oseltamivir treatment should be continued until nucleic acid detection assay results rule out influenza. For patients who are not intubated, assays should be performed on upper respiratory tract specimens. For patients who are intubated, assays should be performed on both upper and lower respiratory tract specimens.</li></ul> <p>Each recommendation in the Guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III). See <a href="#">Guidelines Development</a> for more information.</p>

## Introduction

Clinicians should monitor local influenza and SARS-CoV-2 activities during influenza season to inform the evaluation and management of patients with acute respiratory illness. This can be done by tracking local and state public health surveillance data, assessing the results of testing performed at health care facilities, and reviewing the Centers for Disease Control and Prevention (CDC) [Weekly U.S. Influenza Surveillance Report](#).

## Influenza Vaccination

### *For Patients With Acute COVID-19 or Those Recovering From COVID-19*

The Advisory Committee on Immunization Practices (ACIP) recommends offering an influenza vaccine by the end of October to all people aged  $\geq 6$  months in the United States.<sup>1</sup> Unvaccinated persons can still benefit from influenza vaccination after October as long as influenza viruses are still circulating in the community. People with acute COVID-19 who have not received an influenza vaccine should be vaccinated after they recover from acute illness and are no longer in isolation (**BIII**). Patients may be vaccinated while they are still in isolation if they are in a health care setting.

There are currently no data on the safety, immunogenicity, or efficacy of administering influenza vaccines to patients with acute COVID-19 or those who are recovering from COVID-19. Vaccination in people who have mild illness is safe and effective.<sup>2</sup> Clinicians should consider deferring influenza vaccination for symptomatic patients with moderate or severe COVID-19 until they have recovered and completed their COVID-19 isolation period. It is not known whether administering dexamethasone or other immunomodulatory therapies to patients with severe COVID-19 will affect the immune response to the influenza vaccine. People with asymptomatic SARS-CoV-2 infection or mild COVID-19 should seek influenza vaccination when they no longer require isolation. They may be vaccinated sooner if they are in a health care setting for other reasons. See the influenza vaccine recommendations from the [CDC](#) and the [American Academy of Pediatrics](#).

### *Coadministration of COVID-19 Vaccines and Influenza Vaccines*

Coadministration of a COVID-19 vaccine and an influenza vaccine at different injection sites has been shown to be safe.<sup>3-6</sup> Providers and patients should be aware of a potential increase in reactogenicity when both vaccines are administered concurrently. The [CDC](#) and [ACIP](#) provide more information on coadministering influenza and COVID-19 vaccines.

## Clinical Presentation of Influenza Versus COVID-19

The signs and symptoms of uncomplicated, clinically mild influenza overlap with those of mild COVID-19. Loss of taste and smell can occur with both diseases, but these symptoms are more common with COVID-19 than with influenza. Fever is not always present in patients with either disease, particularly in young infants, adults of advanced age, and patients who are immunosuppressed. Complications of influenza and COVID-19 can be similar, but the onset of influenza complications and severe disease typically occurs within a week of illness, whereas the onset of severe COVID-19 usually occurs in the second week of illness.

Because of the overlap in signs and symptoms, when SARS-CoV-2 and influenza viruses are cocirculating, diagnostic testing for both viruses is needed to distinguish between SARS-CoV-2 and influenza virus infection and to identify coinfection in people with an acute respiratory illness. Coinfection with influenza virus and SARS-CoV-2 has been described in case reports and case series,<sup>7-11</sup> but it is uncommon.<sup>12</sup> Observational studies have reported greater disease severity in adult patients with influenza virus and SARS-CoV-2 coinfection than in those with SARS-CoV-2 infection alone.<sup>13,14</sup> In pediatric patients, coinfection with the 2 viruses was associated with greater disease severity than infection with influenza virus alone.<sup>15</sup>

## Testing for SARS-CoV-2 and Influenza

The COVID-19 Treatment Guidelines Panel (the Panel) recommends performing influenza testing in addition to SARS-CoV-2 testing in outpatients with acute respiratory illness if the results will change the clinical management strategy for the patient (e.g., administering antiviral treatment for influenza) (**BIII**).

The Panel recommends testing for both viruses in all hospitalized patients with acute respiratory illness (AIII).

Several multiplex molecular assays and multiplex antigen assays that detect SARS-CoV-2 and influenza A and B viruses have received Food and Drug Administration Emergency Use Authorizations or De Novo classifications and can provide results in 15 minutes to 8 hours using a single respiratory specimen.<sup>16-18</sup> For more information, see the CDC webpage [Information for Clinicians on Influenza Virus Testing](#) and the recommendations from the [Infectious Diseases Society of America](#) (IDSA) on the use of influenza tests and the interpretation of test results.

## Treating Influenza With Antiviral Agents

Antiviral treatment for influenza is the same for all patients regardless of SARS-CoV-2 coinfection (AIII). There are no clinically significant drug-drug interactions between the antiviral agents used to treat influenza and the antiviral agents or immunomodulators used to treat COVID-19. The IDSA recommends administering antiviral treatment for influenza to all hospitalized patients with influenza.<sup>19</sup>

The Panel recommends starting hospitalized patients who are suspected of having influenza on empiric treatment for influenza with **oseltamivir** as soon as possible regardless of their COVID-19 status and without waiting for influenza test results (AIIb). Oseltamivir has no activity against SARS-CoV-2.<sup>20</sup> The standard dose of oseltamivir is absorbed well, even in critically ill patients. For patients who cannot tolerate oral or enterically administered oseltamivir (e.g., because of gastric stasis, malabsorption, or gastrointestinal bleeding), intravenous peramivir is an option.<sup>19</sup> There are no data on the activity of peramivir against SARS-CoV-2.

See the CDC webpage [Influenza Antiviral Medications: Summary for Clinicians](#) for clinical algorithms for using antiviral agents in patients with suspected or laboratory-confirmed influenza, including pregnant people and other people who are at high risk for influenza complications. The IDSA clinical practice guidelines also provide recommendations on using antiviral agents to treat influenza,<sup>19</sup> and the American Academy of Pediatrics provides recommendations on the antiviral treatment of influenza in children.<sup>21</sup>

When the result of an influenza nucleic acid detection assay from an upper respiratory tract specimen is negative in a patient who is receiving antiviral treatment for influenza:

- *In a patient who is not intubated:* Antiviral treatment for influenza can be stopped.
- *In a patient who is intubated:* Antiviral treatment for influenza should be continued, and a lower respiratory tract specimen (e.g., endotracheal aspirate) should be collected and tested using an influenza nucleic acid detection assay. If the lower respiratory tract specimen is also negative, antiviral treatment for influenza can be stopped.

## COVID-19 Treatment Considerations for Hospitalized Patients With Suspected or Confirmed Influenza Virus Coinfection

Corticosteroids, which are used to treat patients with severe COVID-19, may prolong influenza viral replication and may be associated with poor outcomes for influenza.<sup>19,22</sup> Currently, no data are available on the use of corticosteroids in patients with SARS-CoV-2 and influenza virus coinfection. However, because dexamethasone has demonstrated substantial benefits in patients with COVID-19 who require supplemental oxygen, the benefits of using corticosteroids in patients with severe SARS-CoV-2 and influenza virus coinfection likely outweigh any potential harm.

Although severe influenza may be associated with a dysregulated innate immune response, there are

no data on the use of immunomodulatory therapies, such as interleukin-6 inhibitors (e.g., tocilizumab, sarilumab) or Janus kinase inhibitors (e.g., baricitinib, tofacitinib), for the treatment of severe influenza. There are also no data on the effects these therapies may have on influenza virus infection, such as potentially prolonging viral replication. These immunomodulators have demonstrated a clinical benefit in certain patients with COVID-19. When considering using these drugs in patients with COVID-19 who have suspected or laboratory-confirmed influenza, clinicians should carefully weigh the known benefits for treatment of severe COVID-19 against the unknown theoretical risks for patients with influenza.

Observational studies have reported that co-occurrence of community-acquired secondary bacterial pneumonia appears to be infrequent in people with COVID-19; it is more common in people who have influenza.<sup>23-28</sup> Typical bacterial causes of community-acquired pneumonia with severe influenza are *Staphylococcus aureus* (both methicillin-resistant *S. aureus* [MRSA] and methicillin-susceptible *S. aureus* [MSSA]), *Streptococcus pneumoniae*, and group A *Streptococcus*.<sup>19</sup>

Patients with COVID-19 who develop new respiratory symptoms with or without fever or respiratory distress and who do not have a clear diagnosis should be evaluated for the possibility of nosocomial influenza.

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