Updates on Diagnostic Testing and Outpatient Treatment for COVID-19 and Influenza

Clinician Outreach and Communication Activity (COCA) Call

Thursday, October 10, 2024

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Objectives

At the conclusion of today's session, the participant will be able to accomplish the following:

1. Describe recommended antivirals for treating COVID-19 and influenza and clinical benefits.
2. Cite factors for deciding who receives treatment for COVID-19 and influenza.
3. Outline indications for testing before starting treatment for COVID-19 and influenza.
4. Review available treatment options for COVID-19 and influenza among different populations.

To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

Today's Presenters

- **Pragna Patel, MD, MPH**
  Chief Medical Officer
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  National Center for Immunization and Respiratory Diseases
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- **Tim Uyeki, MD, MPH, MPP**
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COVID-19 and Influenza Testing and Treatment

October 10, 2024

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Overview

- Respiratory Virus Vaccine Recommendations
- COVID-19 Epidemiology
- SARS CoV-2 Testing and Antiviral Treatment of COVID-19
- Influenza Activity and Burden of Disease
- Influenza Testing and Antiviral Treatment

Who should get 2024–2025 COVID-19, 2024–2025 influenza, and RSV immunizations?

	2024–2025 COVID-19[1]	2024–2025 Influenza[2]	RSV[3]
Infants & Children	**6 months – 17 years** Some children 6 months through 4 years may need multiple doses	**6 months – 17 years** Some children 6 months through 8 years may need multiple doses	**All infants <8 months* and children 8 through 19 months with risk factors should get nirsevimab** Typically, October through March, *if birthing parent not vaccinated with maternal RSV vaccine OR **32–36 weeks gestation should get RSV vaccine (Pfizer, Abrysvo only)** Typically, September–January
Pregnant People	**All**	**All**	
Adults 18–59	**All**	**All**	See pregnant people
Adults 60+	**All**	**All** High-dose, recombinant, or adjuvanted flu vaccine preferred for 65+, if available	**All adults 75+ and adults 60 through 74 years with risk factors should get a single dose of RSV vaccine at this time.**

[1] Immunocompromised may get additional dose(s) of COVID-19 vaccine regardless of age.

[2] Solid organ recipients ages 18 through 64 years on immunosuppressives may get high-dose or adjuvanted flu vaccine, if available, but not preferred.

[3] All infants should be protected by either maternal RSV vaccine or nirsevimab. Both are not needed for most infants. For infants born during October through March, nirsevimab should be administered in the first week of life — ideally during the birth hospitalization.

Adults aged 60–74 years at higher risk for RSV should get the RSV vaccine

Chronic cardiovascular disease

Severe obesity
(body mass index ≥40 kg/m^2)

Diabetes mellitus
complicated by chronic kidney disease, neuropathy, retinopathy or other end-organ damage

Chronic lung or respiratory disease

End stage renal disease/dialysis dependence

Chronic hematologic conditions

Chronic liver disease

Neurological or neuromuscular conditions causing impaired airway clearance or respiratory muscle weakness

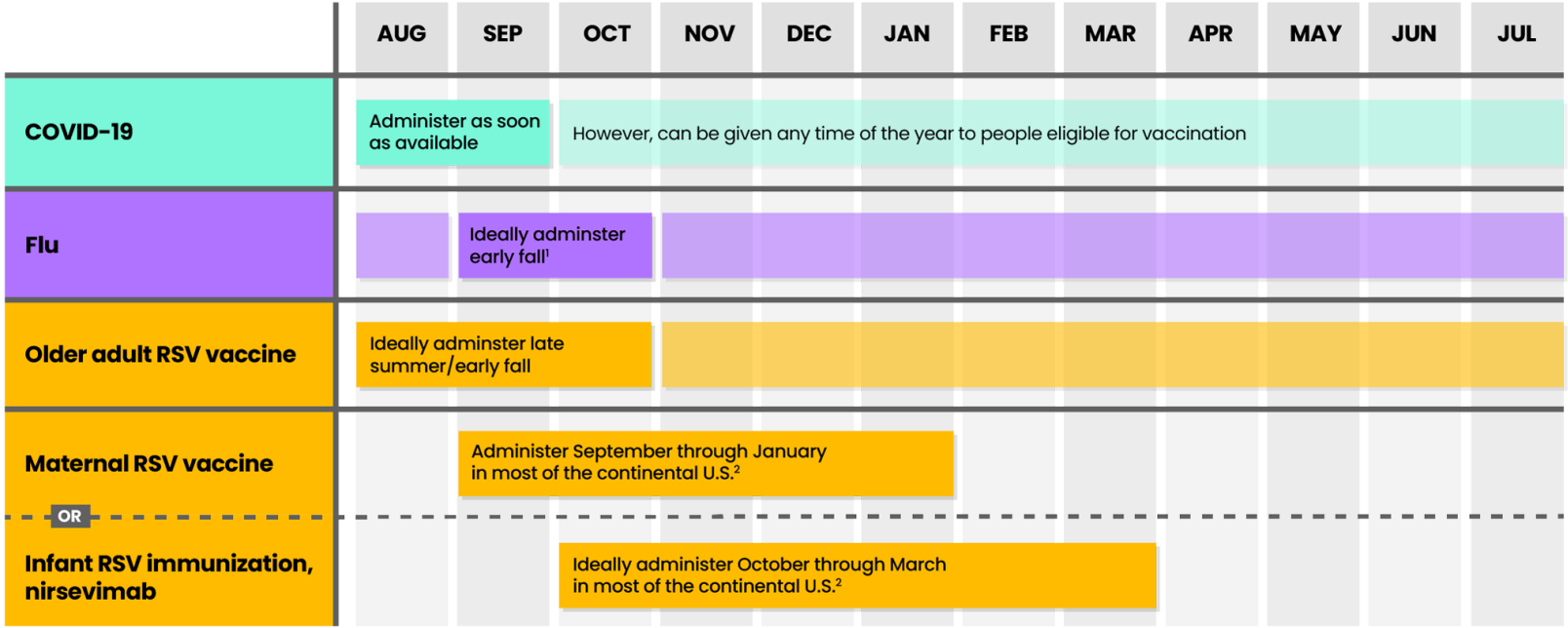
Residence in a nursing home

Moderate or severe immunocompromise

Other factors that a provider determines would increase risk of severe disease due to viral respiratory infection (e.g., frailty)

Data source: https://www.cdc.gov/mmwr/volumes/73/wr/mm7332e1.htm

Timing and administration of COVID-19, influenza, and RSV immunizations



[1] Children who need 2 doses should receive their first dose as soon as possible (including during July and August). One dose of flu vaccine can be considered for pregnant people in their third trimester during July and August.

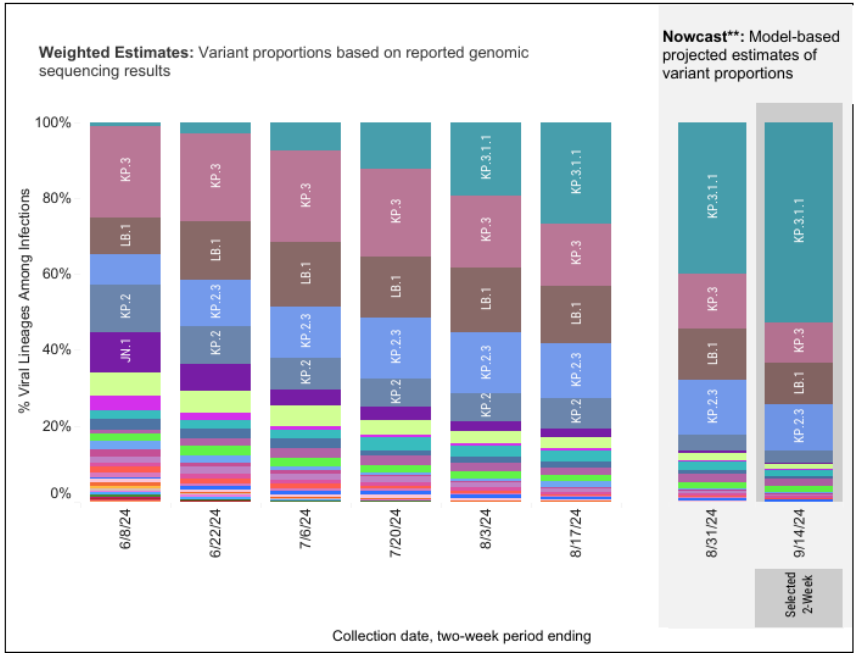
[2] In jurisdictions with RSV seasonality that differs from most of the continental United States, including Alaska, southern Florida, Guam, Hawaii, Puerto Rico, U.S.-affiliated Pacific Islands, and U.S. Virgin Islands, providers should follow state, local, or territorial guidance. However, nirsevimab may be administered outside of routine seasonal administration (ie., October through March) based on local RSV activity and other special circumstances. For infants born during October through March, nirsevimab should be administered in the first week of life—ideally during the birth hospitalization.

COVID-19 Epidemiology

SARS CoV-2 Variants – KP.3.1.1 Predominant

Weighted and Nowcast Estimates in United States for 2-Week Periods in 5/26/2024 – 9/14/2024

Hover over (or tap in mobile) any lineage of interest to see the amount of uncertainty in that lineage's estimate.



Nowcast Estimates in United States for 9/1/2024 – 9/14/2024

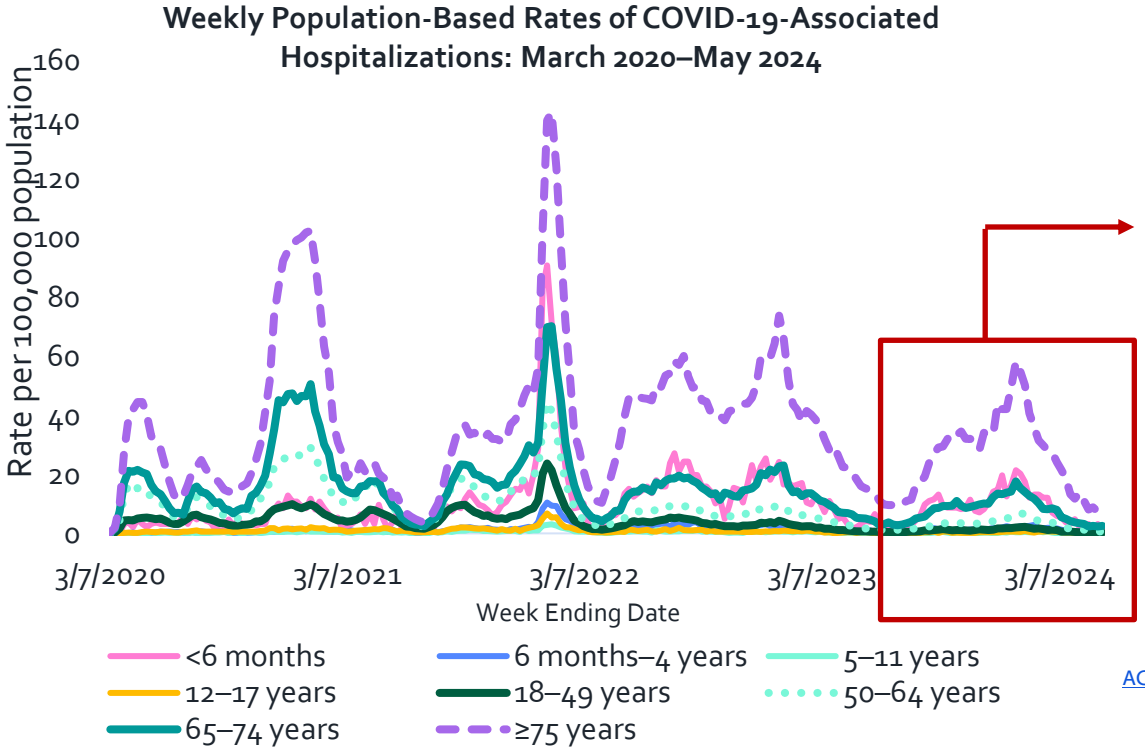
USA

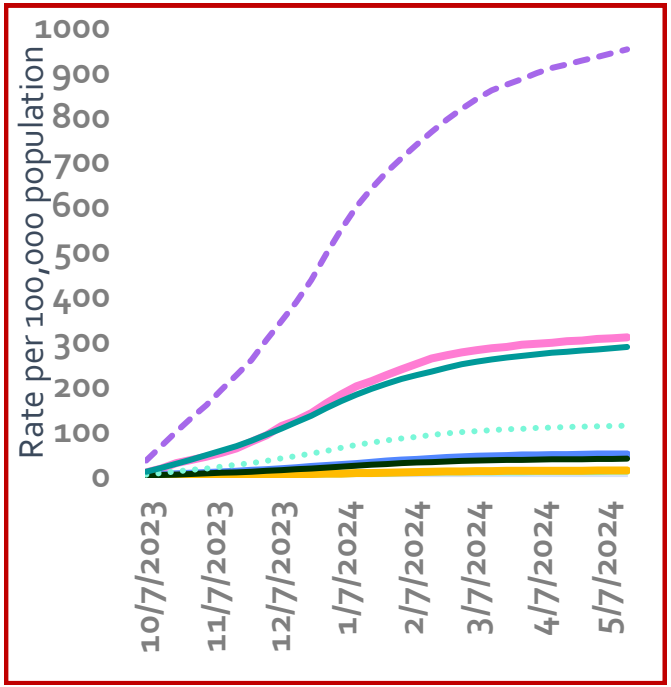
WHO label	Lineage #	%Total	95%PI
Omicron	KP.3.1.1	52.7%	48.6-56.8%
	KP.2.3	12.2%	10.8-13.8%
	LB.1	10.9%	9.4-12.6%
	KP.3	10.6%	9.3-12.1%
	KP.2	3.1%	2.2-4.2%
	LP.1	2.1%	1.4-3.0%
	KP.1.1.3	1.9%	1.4-2.8%
	JN.1.18	1.7%	0.6-4.0%
	KP.1.1	1.5%	1.2-1.9%
	KS.1	0.7%	0.4-1.0%
	KP.2.15	0.7%	0.4-1.0%
	LF.3.1	0.6%	0.4-0.9%
	JN.1.16.1	0.6%	0.4-0.8%
	KP.4.1	0.2%	0.1-0.4%
	JN.1.11.1	0.2%	0.1-0.3%
	JN.1	0.2%	0.1-0.3%
	KW.1.1	0.0%	0.0-0.1%
	XDV.1	0.0%	0.0-0.1%
	JN.1.16	0.0%	0.0-0.0%
	JN.1.7	0.0%	0.0-0.0%
	KP.1.2	0.0%	0.0-0.0%
	KQ.1	0.0%	0.0-0.0%
	JN.1.8.1	0.0%	0.0-0.0%
	JN.1.32	0.0%	0.0-0.0%

[CDC COVID Data Tracker: Variant Proportions]

COVID-19 Hospitalizations by Age

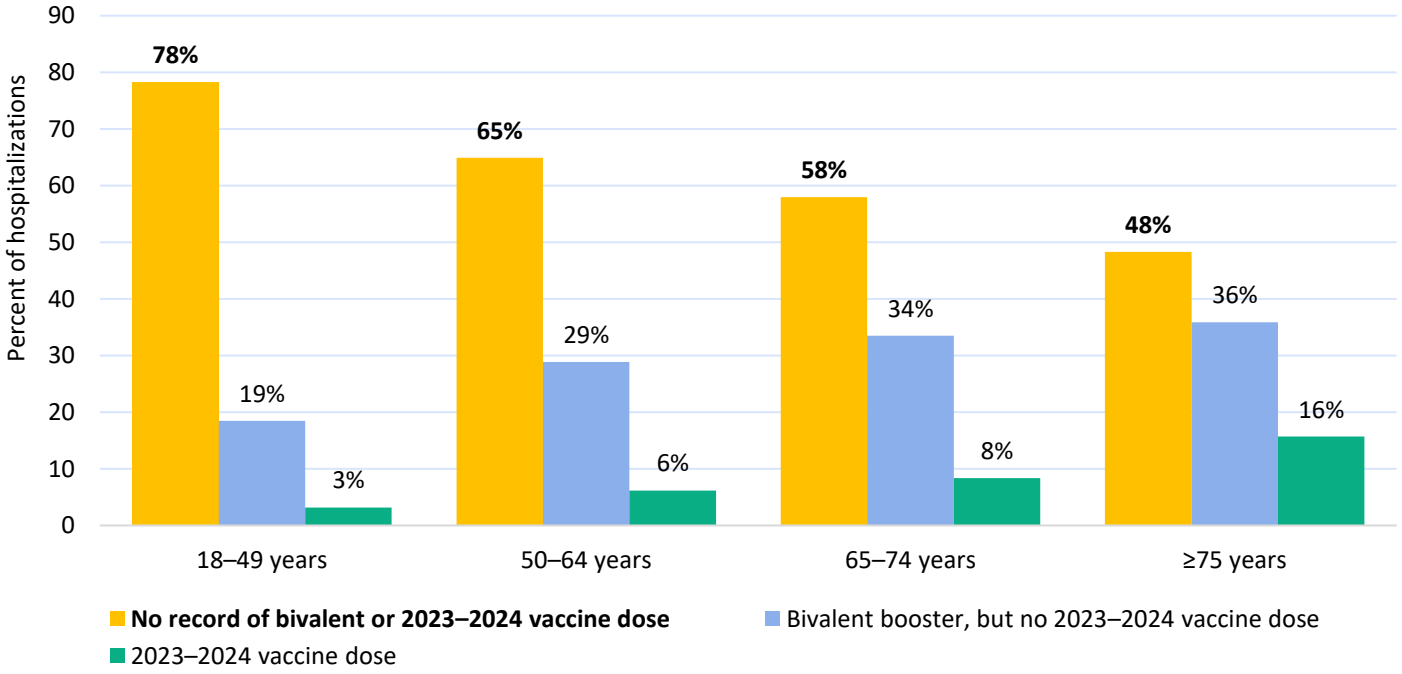
Adults 75+ at highest risk of being hospitalized for COVID-19 compared with any other age group





ACIP Presentation Slides: June 26-28, 2024 Meeting | ACIP | CDC

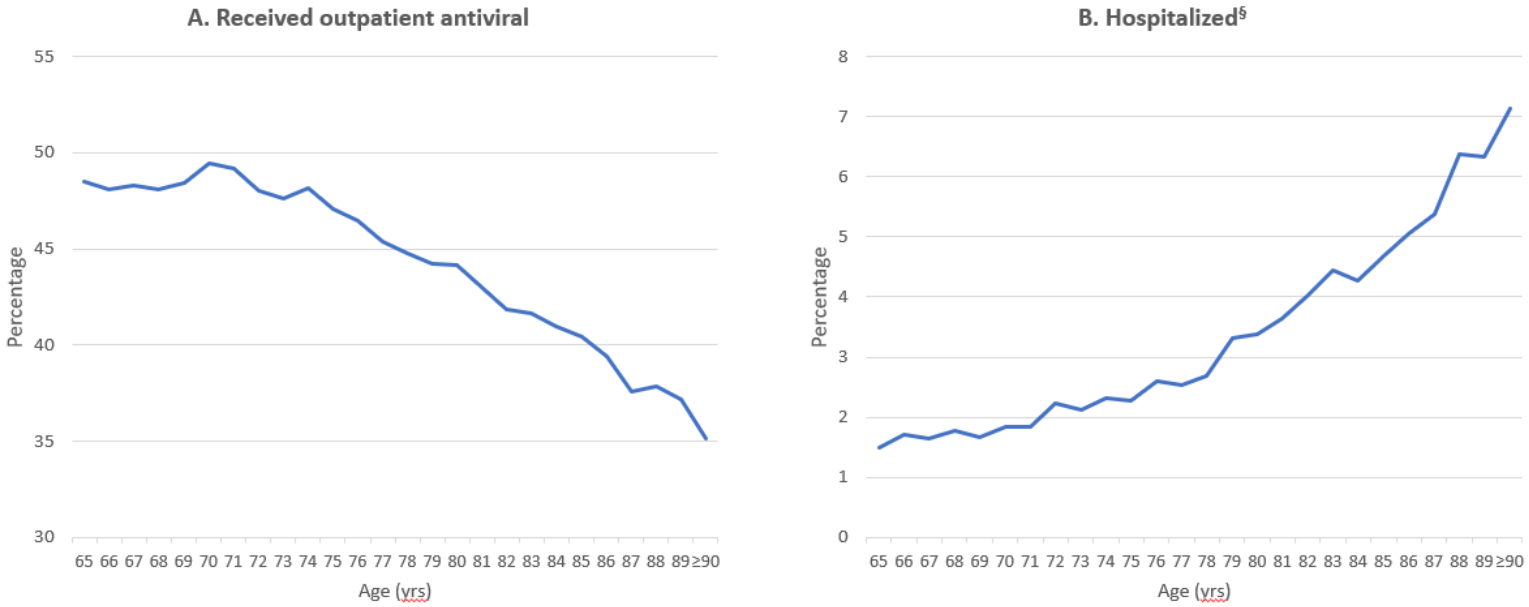
Vaccination Status among Adults Ages ≥18 Years with COVID-19-associated Hospitalization, by Age Group — COVID-NET, October 2023–March 2024



- **11%** of adults ages ≥18 years with COVID-19-associated hospitalizations **received a 2023–2024 vaccine dose.**
- **57%** of COVID-19-associated hospitalizations among adults ages ≥18 years had not received a COVID-19 vaccine after August 2022.

ACIP Presentation Slides: June 26-28, 2024 Meeting | ACIP | CDC

Percentage* of adults aged ≥65 years with COVID-19† who received an outpatient antiviral medication (A) and who were hospitalized (B), by age — National Patient-Centered Clinical Research Network, United States, April 2022–September 2023



*Y-axis scales are different in panels A and B.

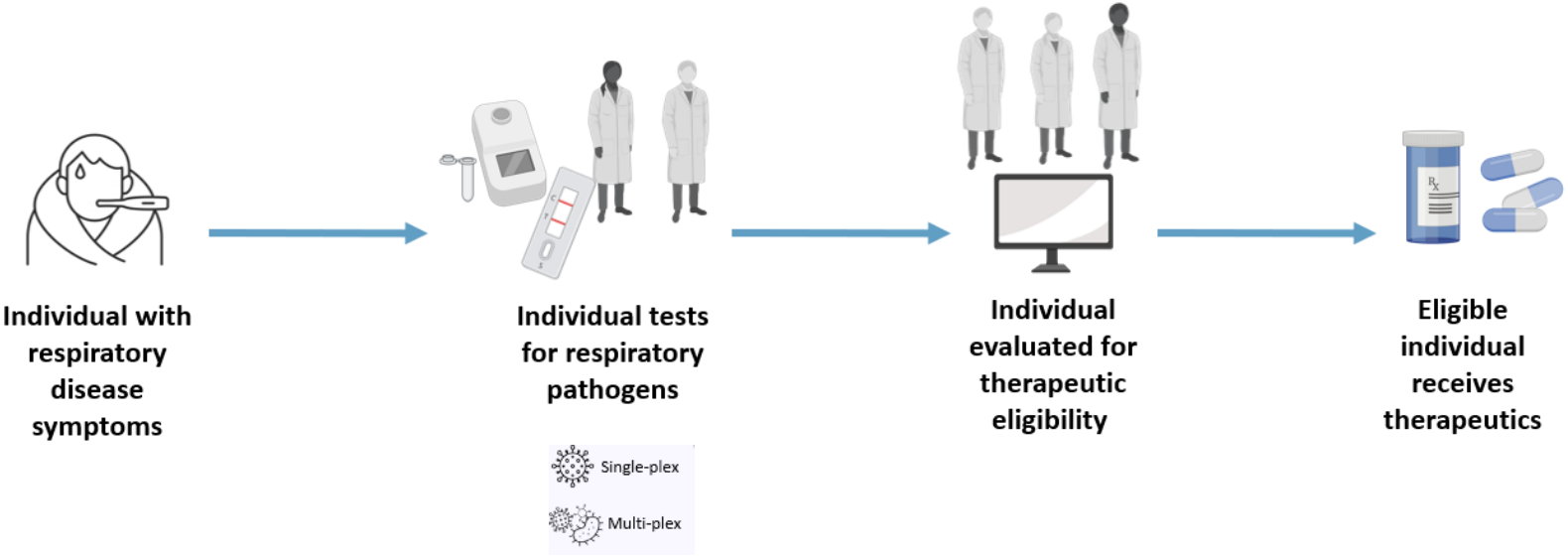
†Patients with SARS-CoV-2 infection were identified using at least one of the following inclusion criteria: 1) laboratory-confirmed SARS-CoV-2 test identified with Logical Observation Identifiers Names and Codes; 2) an *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) diagnostic code for COVID-19 (U07.1 or U07.2); or 3) prescription or administration of an outpatient COVID-19 treatment (nirmatrelvir-ritonavir, molnupiravir, monoclonal antibody, or remdesivir). The earliest COVID-19 infection diagnosis date by one of these three criteria was defined as the index date.

§Hospitalizations were inpatient encounters within 16 days of the index date.

Differences in COVID-19 Outpatient Antiviral Treatment Among Adults Aged ≥65 Years by Age Group — National Patient-Centered Clinical Research Network, United States, April 2022–September 2023 | MMWR (cdc.gov)

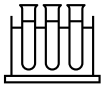
SARS CoV-2 Testing

Testing can facilitate early treatment



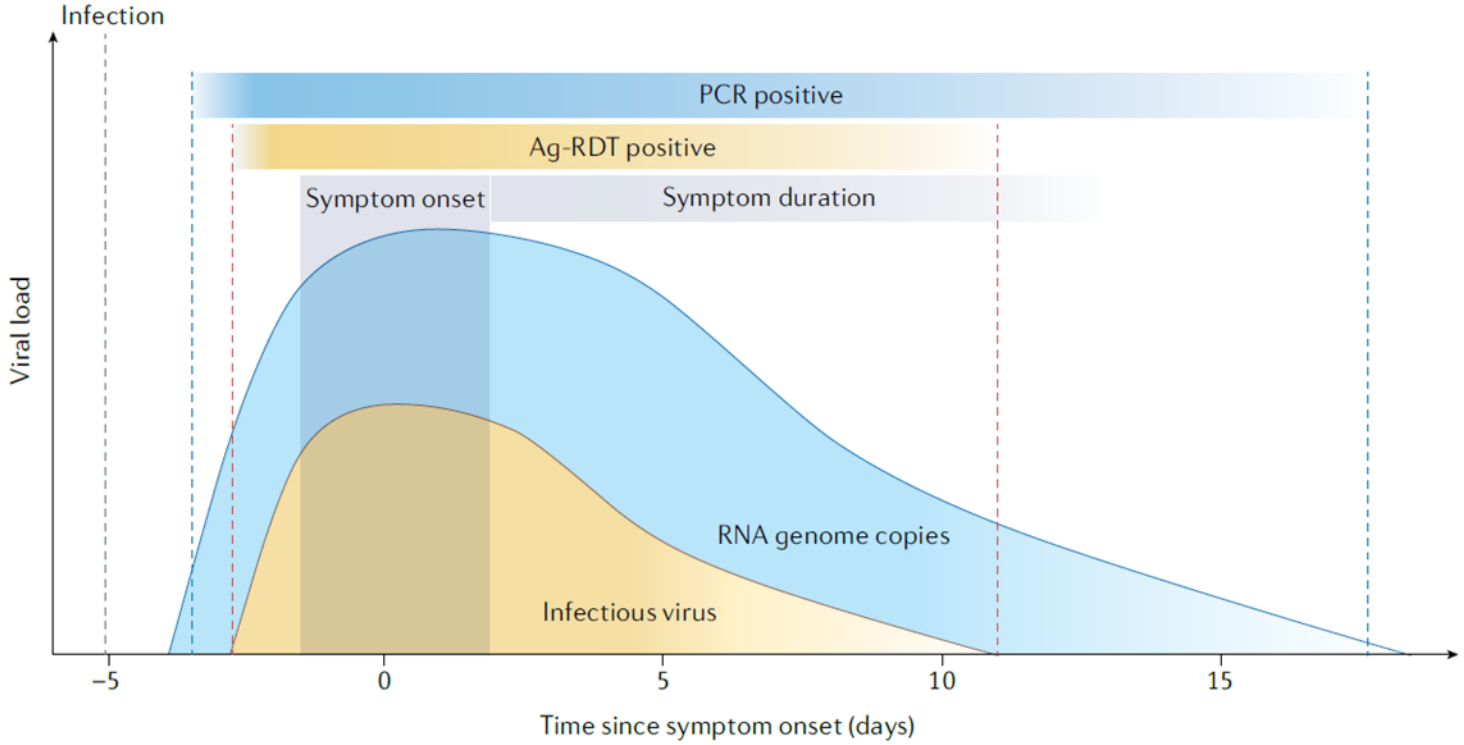
- Most important for people at higher risk of severe illness such as older adults and residents of nursing homes
- A documented positive test for SARS CoV-2 or influenza is not required to initiate treatment
- U.S. households eligible to order 4 free COVID-19 tests as of late September
- People who are under-insured or uninsured, can get free COVID-19 testing through ICATT

Relative advantages and disadvantages of different tests

	Advantages	Disadvantages
Nucleic acid amplification tests (NAAT) 	Most sensitive test method available Short turnaround time for NAAT POC tests, but few available Usually does not need to be repeated to confirm results	Longer turnaround time for lab-based tests (1–3 days) Higher cost per test After SARS CoV-2 infection has ended, and the risk of transmission has passed, people may have detectable RNA and test positive for up to 90 days
Antigen tests 	Short turnaround time (approximately 15 minutes) Cost-effective Some can be performed at home, or anywhere else	Less sensitive (more false negative results) compared to NAATs, especially among asymptomatic people and with some variants For SARS CoV-2 negative tests should be confirmed by NAAT or repeated as recommended by FDA

Overview of Testing for SARS-CoV-2 | COVID-19 | CDC

Viral Kinetics of SARS-CoV-2 Infection Relative to Symptom Onset



Puhach et al. SARS CoV 2 viral load and shedding kinetics. Nature Reviews.2023

Antiviral Treatment

Antiviral Therapy for Mild and Moderate COVID-19

- Prevents the virus from replicating inside of the body
- Should be given as early as possible
- Prevents hospitalization and death among persons with mild to moderate COVID-19
- Most severe symptoms do not develop until 7-10 days
- Clinical judgment is needed to accurately assess a person's risk on a case-by-case basis and determine whether treatment is indicated
- Decision to start treatment is based on risk for severe disease and not symptom severity
- Benefit of treatment outweighs risk of rebound among persons with higher risk of severe disease

COVID-19 Treatment Clinical Care for Outpatients | COVID-19 | CDC
SARS-CoV-2 Rebound With and Without Use of COVID-19 Oral Antivirals. *MMWR*.2023

Risk Factors for Severe Disease

- Risk factors for severe COVID-19 include:
  - Age over 50 years, with risk increasing substantially at age ≥ 65 years
  - Being unvaccinated or not being up to date on COVID-19 vaccinations
  - Specific medical conditions, including, chronic lung disease, cardiovascular disease, diabetes, obesity and risk increasing with multiple medical conditions
  - Immunocompromising conditions or use of immunosuppressive medications, such as chemotherapy
- Some groups are disproportionately affected by COVID-19 because of many factors, including limited access to vaccines and healthcare

COVID-19 Treatment Clinical Care for Outpatients | COVID-19 | CDC

Recommended COVID-19 Treatment for Outpatient Therapy

Drug	Efficacy*	Age	Route	Duration	Time from Illness Onset	Specific Issues
Nirmatrelvir/ Ritonavir (Paxlovid)	88%	≥12 years	Oral	5 days	≤5 days	• Adjust dosing in some cases • Not recommended with severe kidney or liver disease • Drug-drug interactions
Remdesivir (Veklury)	87%	≥28 days	Intravenous (IV)	3 days	≤7 days	• Infusion over 30-120 min • Infusions over 3 consecutive days
Alternate Therapy						
Molnupiravir (Lagevrio)	30%	≥18 years	Oral	5 days	≤5 days	• Persons of reproductive age should use birth control

**Eligible population for these clinical trails were non-hospitalized, unvaccinated persons with at least one risk factor for severe disease*

COVID-19 Treatment Clinical Care for Outpatients | COVID-19 | CDC

Real World Effectiveness of COVID-19 Antivirals

Nirmatrelvir-ritonavir (Paxlovid)

- Systematic review of 23 studies of 314 353 patients included in meta-analysis

Outcome	Odds Ratio (OR)	95% Confidence Interval (CI)
Mortality Rate	0.25	0.14–0.45
Hospitalization Rate	0.40	0.24-0.69
Mortality or Hospitalization Rate	0.17	0.06-0.46

- Not effective at reducing hospitalizations and death among persons with standard risk for severe disease

Amani B, Amani B. Efficacy and safety of nirmatrelvir/ritonavir (Paxlovid) for COVID-19: a rapid review and meta-analysis. J Med Virol. 2023;95:e28441.

Real World Effectiveness of COVID-19 Antivirals (cont.)

Remdesivir (Veklury)

- Few real-world effectiveness studies among outpatients
- Benefit shown among patients who are hospitalized on low-flow oxygen pre-Omicron
- Most benefit in hospitalized patients if started early

Molnupiravir (Lagevrio)

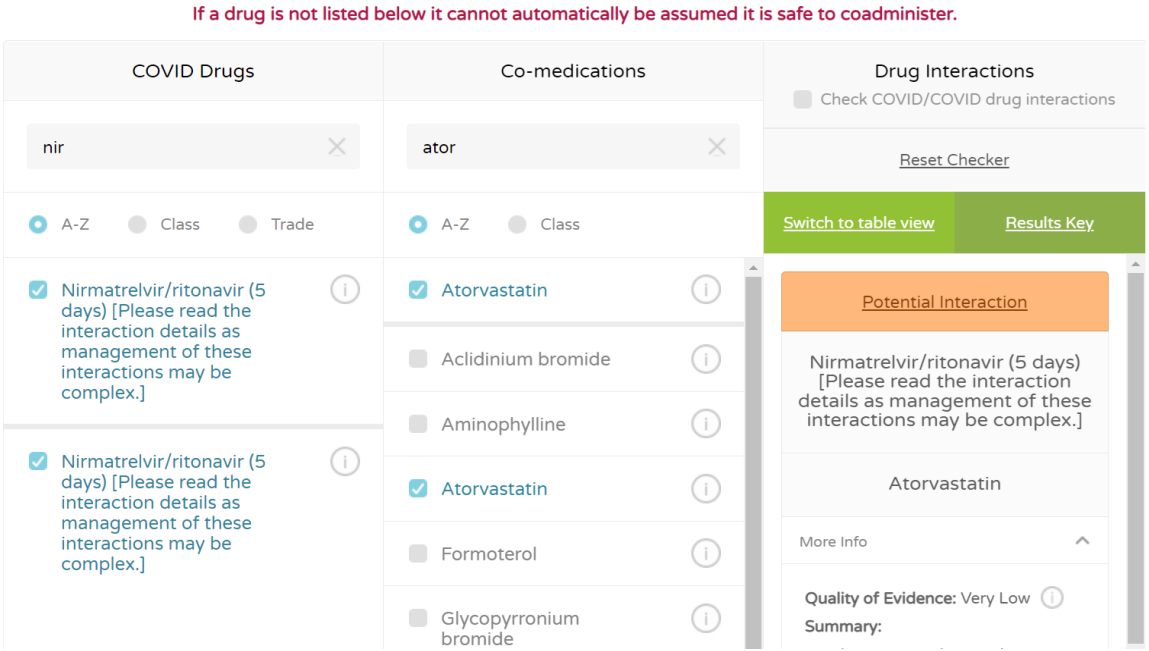
- Not effective at reducing hospitalizations or death
- Associated with earlier recovery
- Mutations might develop in patients with persistent virus

Butler et al. Molnupiravir plus usual care versus usual care alone as early treatment for adults with COVID-19 at increased risk of adverse outcomes (PANORAMIC): an open-label, platform-adaptive randomised controlled trial *Lancet* 2023; 401: 281–93

Garibaldi. Real world effectiveness of remdesivir in adults hospitalized with COVID-19.CID. 2022;75(1):e516–24

Liverpool COVID-19 Drug Interactions Database

https://www.covid19-druginteractions.org/checker



FDA Website Resources

- Fact Sheet for Health Care Providers: https://www.fda.gov/media/155050/download
- PAXLOVID Patient Eligibility Screening Checklist Tool for Prescribers: https://www.fda.gov/media/158165/download

Access to COVID-19 Antivirals

Drug	Antiviral Program	Patient Eligibility	Description
Paxlovid (Nirmatrelvir-ritonavir)	Pfizer Co-Pay Savings Program	Privately insured	Paxlovid reimbursement program Out-of-pocket costs determined by insurer and pharmacy benefit manager. Payment as little as $0 with Co-Pay Savings Program. Enrollment form only requires brief personal information.
Paxlovid (Nirmatrelvir-ritonavir)	U.S. Government Patient Assistance (USG PAP)	Uninsured: Medicare (with or without Part D, Part B, or Part C and inclusive of Medicare Advantage); Medicaid/CHIP; TRICARE, VA Community Care Network	Paxlovid at no charge; operated by Pfizer. Prescription required to apply. Enrollment through patient portal. Prescription required for enrollment.
Veklury (Remdesivir)	Gilead's Advancing Access	Veklury eligible; insured and uninsured	Financial support options to access Veklury may be available. Requires a form to be filled out by the patient and prescriber who will need to enter prescription information.
Lagevrio (Molnupiravir)	Merck Patient Assistance Program	Eligible patients with financial hardship; must be enrolled as an urgent request	Free of charge for patients who can't afford without assistance. Each enrollment is valid for up to 12 months. Requires a form to be filled out by the patient and prescriber who will need to enter prescription information.

Self-knowledge Check: **A 70-year-old woman presents with fever, cough, and sore throat. She has no medical conditions and maintains an active lifestyle, playing tennis three times per week. She received the current COVID-19 vaccine but had not yet received influenza vaccine this season, as it was not available the day she went to the clinic. She is a former smoker who quit over 20 years ago. Her lab results indicate she is positive for SARS-CoV-2. Would you start her on treatment? Why or why not?**

A. No, she has no underlying medical conditions associated with higher risk for severe disease and is healthy, so she does not need to be treated.
B. No, COVID-19 antivirals are not effective among vaccinated persons.
C. Yes, her age alone increases her risk for severe disease, so she should be treated to prevent disease progression.
D. A & B
E. None of the above

Answer: Yes, her age alone increases her risk for severe disease, so she should be treated to prevent disease progression.

A. No, she has no underlying medical conditions associated with higher risk for severe disease and is healthy, so she does not need to be treated.
B. No, COVID-19 antivirals are not effective among vaccinated persons.
C. Yes, her age alone increases her risk for severe disease, so she should be treated to prevent disease progression.
D. A & B
E. None of the above

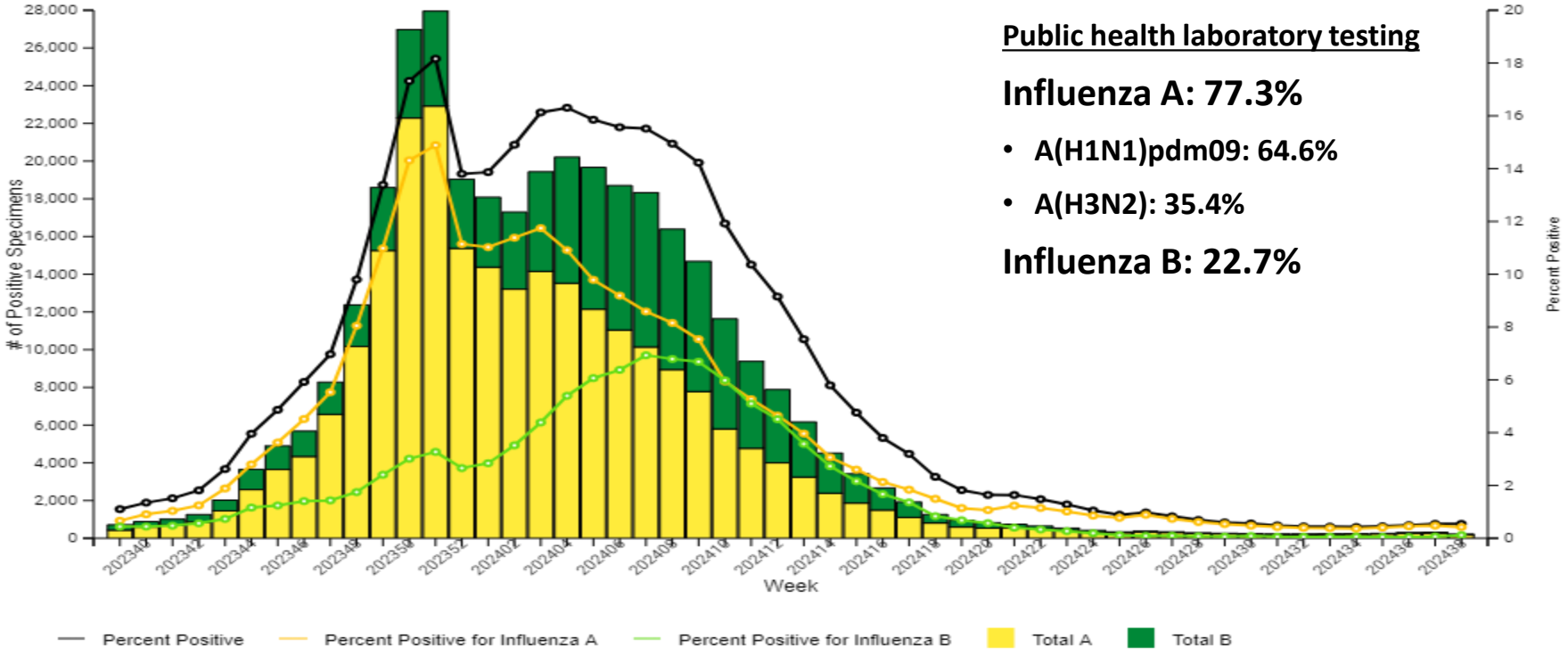
Rationale: Age is the most important risk factor for severe COVID-19. Although she has no underlying medical conditions, given her age, she is at increased risk of progression to severe disease, regardless of her COVID-19 vaccination status. Therefore, she should be treated with a COVID-19 antiviral. For outpatient treatment, two options can be considered: nirmatrelvir/ritonavir and remdesivir.

Influenza Activity and Disease Burden

FLUVIEW interactive

CDC U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION

Influenza Positive Tests Reported to CDC by Clinical Laboratories, National Summary, 2023-24 Season, week ending Sep 28, 2024



Public health laboratory testing

Influenza A: 77.3%

- **A(H1N1)pdm09: 64.6%**
- **A(H3N2): 35.4%**

Influenza B: 22.7%

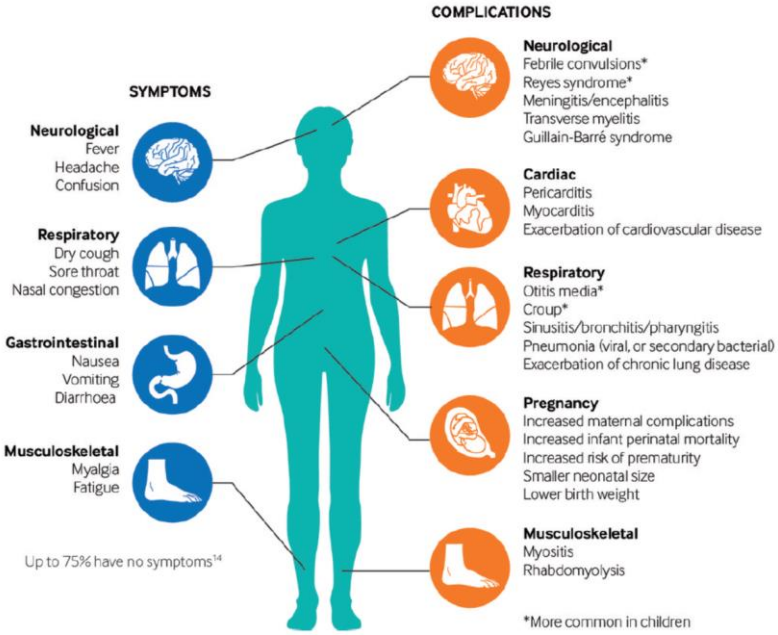
Spectrum of Influenza Virus Infection

- Disease severity and clinical manifestations vary by age, host factors, immunity, influenza virus type/subtype
  - **Asymptomatic infection**
  - **Uncomplicated illness** [incubation period: 1-2 days (range 1-3)]
    - Upper respiratory tract illness (with or without fever)
    - Fever may not be present (e.g., elderly, immunosuppressed)
    - Typical: abrupt onset of fever, cough, chills, myalgia, fatigue, headache, sore throat, runny nose
    - Gastrointestinal symptoms (more common in young children)
    - Infants can have fever alone, irritability, may not have respiratory symptoms
  - **Complicated illness**

Uyeki Clin Infect Dis 2019; Uyeki Lancet 2022

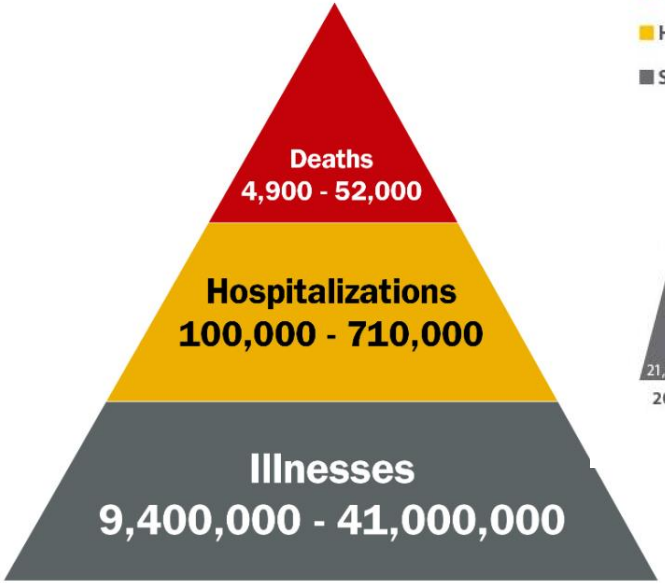
Influenza Complications

- **Moderate Illness**:
  - Otitis media in young children, sinusitis
  - Exacerbation of chronic disease
- **Severe to Critical Illness:**
  - **Exacerbation of chronic disease**
  - **Respiratory:** viral pneumonia, croup, status asthmaticus, bronchiolitis, tracheitis, ARDS
  - **Cardiac:** myocarditis, pericarditis, myocardial infarction
  - **Neurologic:** encephalopathy & encephalitis, cerebrovascular accident, Guillain-Barre syndrome (GBS), Acute Disseminated Encephalomyelitis (ADEM), Reye syndrome
  - **Bacterial co-infection:** invasive bacterial infection (e.g. community-acquired pneumonia)
    - *Staphylococcus aureus* (MSSA, MRSA), *Streptococcus pneumoniae*, group A *Streptococcus*
  - **Musculoskeletal:** myositis, rhabdomyolysis
  - **Multi-organ failure** (respiratory, renal failure, septic shock)
  - **Healthcare-associated infections** (e.g. bacterial or fungal ventilator-associated pneumonia)

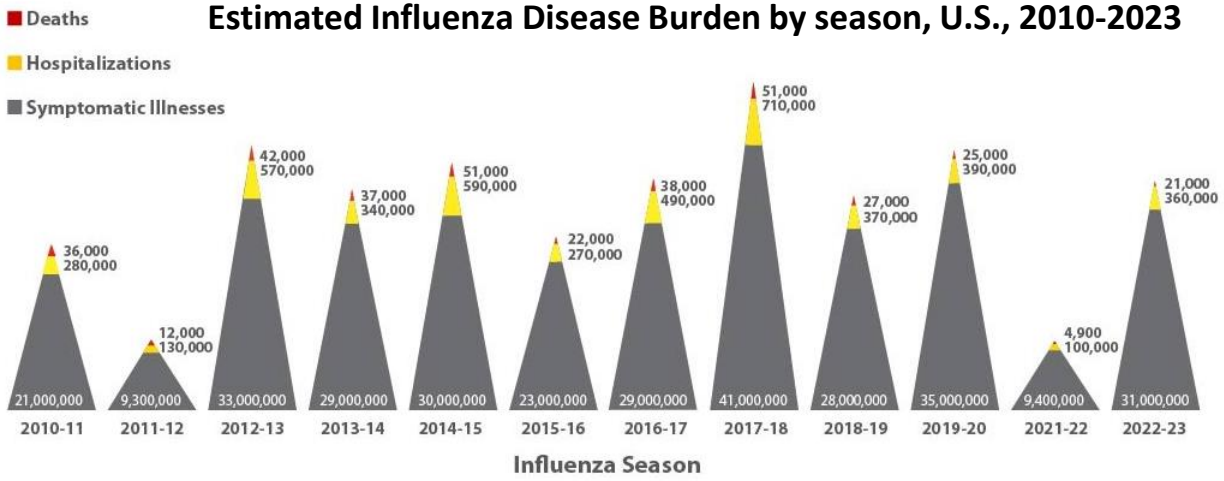


Ghebrehewet BMJ 2016

Estimated Influenza Disease Burden



Estimated Influenza Disease Burden 2010 - 2023



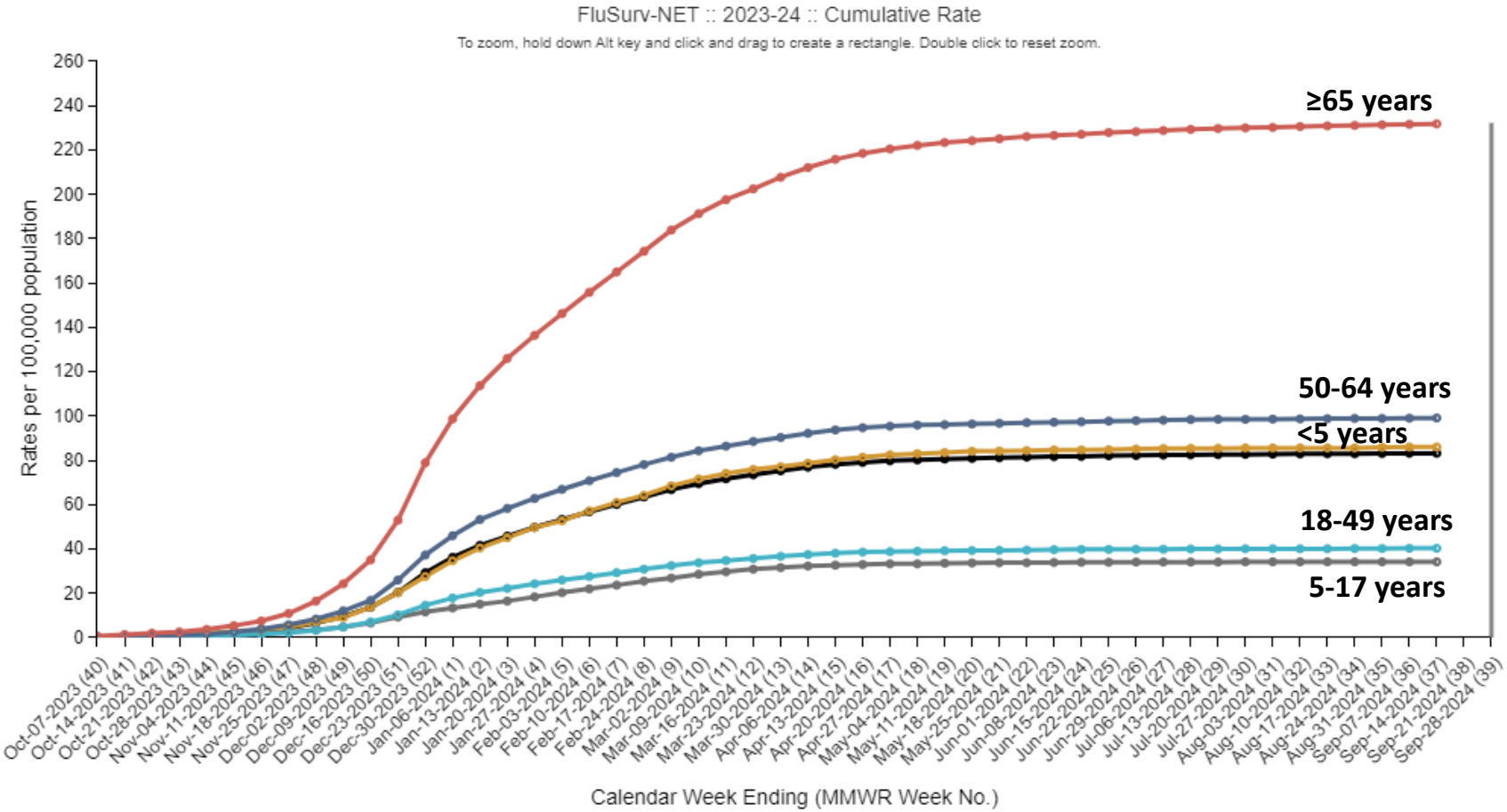
- **Seasonal influenza epidemics vary in severity**

2023-2024 (preliminary estimates as of January 20, 2024):

* 34-75 million illnesses
* 15-33 million medical visits
* 380,000 to 900,000 hospitalizations
* 17,000 to 100,000 deaths

https://www.cdc.gov/flu-burden/php/about/index.html; https://www.cdc.gov/flu-burden/php/data-vis/index.html

Lab-confirmed Influenza Hospitalization Rates by Age Group, 2023-2024



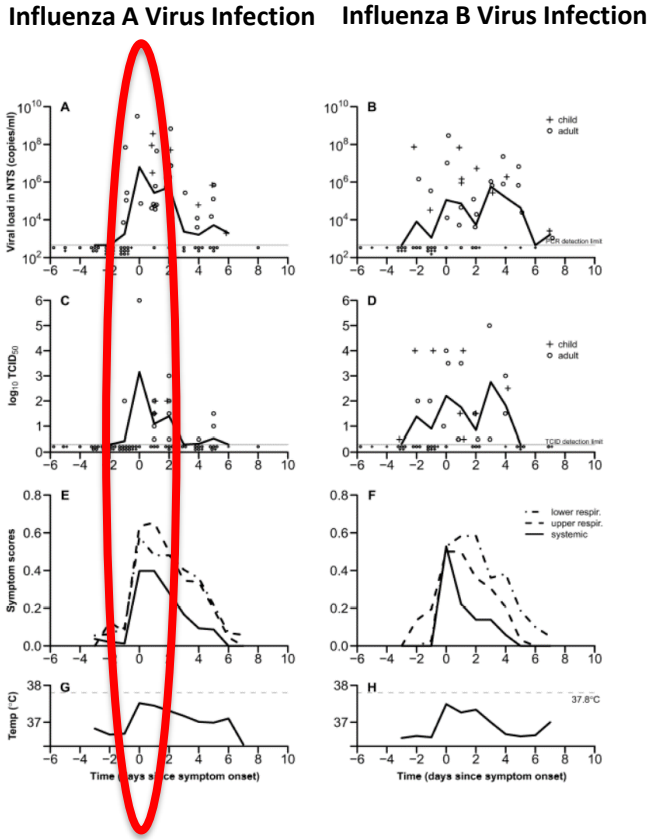
Groups at Increased Risk for Influenza Complications and Severe Illness

- **Children <2 years and adults ≥65 years**
- **Persons with chronic medical conditions**, including pulmonary (including asthma) or cardiovascular (excluding isolated hypertension), renal, hepatic, neurologic (including persons who have had a stroke) and neurodevelopmental, hematologic, metabolic or endocrine disorders (including diabetes mellitus)
- **Persons who are immunocompromised**
- **Persons with extreme obesity (BMI ≥40)**
- **Children and adolescents who are receiving aspirin-or salicylate-containing medications** (who might be at risk for Reye's syndrome after influenza virus infection)
- **Residents of nursing homes and other long-term care facilities**
- **Pregnant persons and people up to 2 weeks postpartum**
- **People from certain racial and ethnic minority groups, including non-Hispanic Black, Hispanic or Latino, and American Indian or Alaska Native persons**

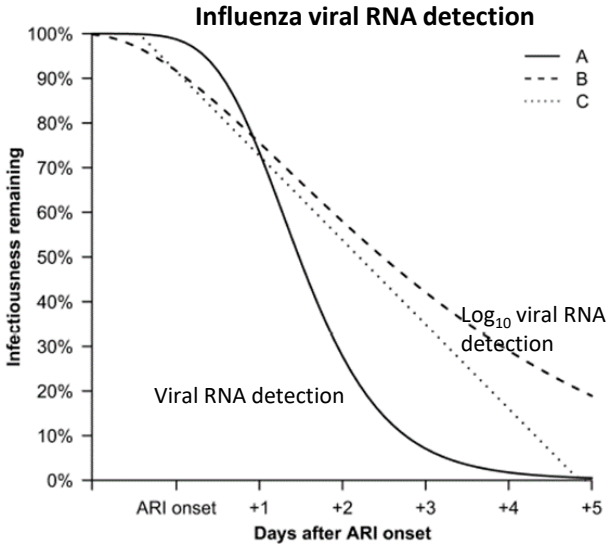
https://www.cdc.gov/flu/highrisk/index.htm

Influenza Testing

Influenza Viral Shedding Typically Peaks Within 24 Hours of Illness Onset



- **Influenza viruses can be detected in the upper respiratory tract one day before illness onset; virus levels peak within 24 hours after onset**
- **Highest infectious period is within 3 days after onset**
  - **Young children can be infectious for longer periods**
  - **Critically ill patients might have longer influenza viral replication in the lower respiratory tract**



Viral RNA >900 copies/ml under fitted curve

Lau J Infect Dis 2010; Ip Clin Infect Dis 2017

Respiratory Specimens for Detecting Influenza Viruses

- **Upper respiratory tract**
  - **Influenza viruses are generally detectable for 3-4 days by antigen detection; and 5-6 days by nucleic acid detection in uncomplicated disease, longer in infants and immunosuppressed**
    - ***Highest yield: Nasopharyngeal (NP) swabs (ideally collected within 3-4 days of illness onset)***
      - Other acceptable specimens: nasal swabs, NP aspirates, nasal aspirates, combined nasal and throat swabs
  - **Slower clearance of influenza viruses in severe disease**
  - ***Influenza viral replication and viral RNA detection may be prolonged with corticosteroids, immunosuppression***
- **Lower respiratory tract**
  - **Higher, prolonged viral replication in severe lower respiratory tract (LRT) disease**
    - ***Influenza viruses may be detectable in LRT specimens when cleared from the upper respiratory tract***
      - **RT-PCR was negative in 10-19% of patients in upper respiratory tract specimens versus lower respiratory tract (BAL specimens) for influenza A(H1N1)pdm09 viral RNA**

Rello Crit Care 2009; Fleury Eurosurveillance 2009; Blyth NEJM 2009

Influenza Tests Available

- **Variety of diagnostic tests available to clinicians to detect influenza viruses in respiratory specimens**
  - Differ by time to produce results, information provided, approved respiratory specimens, approved clinical settings, and **accuracy**
    - **Antigen detection** (FDA-cleared/EUA/authorized)
      - Single-plex and Multiplex assays (e.g., also detects SARS-CoV-2)
        - One FDA-authorized multi-plex OTC/home test (e.g., also detects SARS-CoV-2)
    - **Nucleic acid detection** (FDA-cleared/EUA/authorized)
      - Single-plex and Multiplex assays (e.g., also detects SARS-CoV-2, some detect RSV)
        - One FDA-EUA OTC/Home test (self-collected anterior nasal swabs (≥14 years) or adult-collected (≥2 years)
    - **Point-of-care assays** (CLIA-waived)
    - **Moderately complex** (requires clinical laboratory)
    - **Highly complex** (large clinical laboratories, public health labs)

https://www.fda.gov/medical-devices/in-vitro-diagnostics/influenza-diagnostic-tests

Influenza Tests Available in Clinical Settings*

Test	Method	Time to Results	Performance	Notes†
Rapid diagnostic test	Antigen detection	10 min	Low to moderate sensitivity; high specificity	Negative results may not rule out influenza; most assays are approved for point-of-care use; multiplex assays can identify and distinguish among influenza A, influenza B, and SARS-CoV-2
Rapid molecular assay	Viral RNA detection	15–30 min	Moderately high to high sensitivity; high specificity	Negative results may not rule out influenza; some assays are approved for point-of-care use; multiplex assays can identify and distinguish among influenza A, influenza B, and SARS-CoV-2
Immunofluorescence assay	Antigen detection	2–4 h	Moderate sensitivity; high specificity	Negative results may not rule out influenza; requires trained laboratory personnel with fluorescent microscope in a clinical laboratory
Molecular assay	Viral RNA detection	60–80 min for some assays; up to 4–6 h for others	High sensitivity; high specificity	Negative results may not rule out influenza; multiplex assays can identify and distinguish among influenza A, influenza B, and SARS-CoV-2

Multiplex Antigen detection 15 min
(Influenza A/B, SARS-CoV-2)

Multiplex Viral RNA detection 36-45 min
(Influenza A/B, SARS-CoV-2, RSV)

Multiplex Viral RNA detection ≥60 min
(e.g., Influenza A/B, SARS-CoV-2, RSV, other viral targets)

***Proper interpretation of test results is very important, especially interpreting negative results**

Uyeki Annals of Int Med 2021

Recommended Influenza Tests

- **Outpatients:**
  - **Rapid influenza molecular assays are recommended over rapid influenza antigen tests**
- **Hospitalized patients:**
  - **RT-PCR or other influenza molecular assays are recommended**
    - Rapid antigen detection tests and immunofluorescence assays are not recommended and should not be used unless molecular assays are not available
  - **Immunocompromised patients: Multiplex RT-PCR assays targeting a panel of respiratory pathogens, including influenza viruses are recommended**

- ***Do not order viral culture for initial or primary diagnosis of influenza***

- ***Do not order serology for influenza***
  - **Results from a single serum specimen cannot be reliably interpreted, and collection of paired acute and convalescent sera 2-3 weeks apart are needed; testing at specialized laboratories**

Uyeki IDSA 2018 Influenza Clinical Practice Guidelines Clin Infect Dis 2019

Influenza Antiviral Treatment

Recommended Antivirals for Treatment of Influenza, U.S. 2024-2025

Four FDA-approved antivirals are recommended (no evidence of resistance among circulating seasonal influenza A and B viruses)

- All demonstrated efficacy in RCTs, FDA-approved for early treatment (<2 days of illness onset) in outpatients with uncomplicated influenza
- Neuraminidase inhibitors (NAIs): block release of influenza viruses from infected cells
  - Oseltamivir, Zanamivir, Peramivir
- Cap-dependent endonuclease inhibitor: inhibit influenza viral replication
  - Baloxavir marboxil

Antiviral Drug	Route of Administration	Recommended Ages for Treatment
Oseltamivir	Oral (twice daily x 5d)	All ages
Zanamivir	Inhaled (twice daily x 5d)	≥7 years
Peramivir	Intravenous (single infusion)	≥6 months
Baloxavir	Oral (single dose)	≥5 years (otherwise healthy) ≥12 years (high-risk)

https://www.cdc.gov/flu/hcp/antivirals/summary-clinicians.html

Antiviral Treatment

Focused on prompt treatment of persons with severe disease and those at increased risk of influenza complications:

- **Antiviral treatment is recommended and has the greatest clinical benefit when started *as soon as possible* for patients with confirmed or suspected influenza who are:**
  - **Hospitalized*** (without waiting for testing results) **(oral/enteric oseltamivir)**
  - **Outpatients with complicated or progressive illness of any duration (oral oseltamivir)**
  - **Outpatients at high risk for influenza complications (oral oseltamivir or oral baloxavir)**

- Antiviral treatment can be considered for any previously healthy, non-high-risk outpatient with confirmed or suspected influenza (e.g. with influenza-like illness) on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset; including empiric treatment (e.g. in-person visit or via telemedicine) **(e.g. oral oseltamivir or oral baloxavir)**

**Based on Observational studies*

https://www.cdc.gov/flu/hcp/antivirals/summary-clinicians.html

Meta-analyses of Oseltamivir Treatment RCTs

Oseltamivir treatment has significant clinical benefit when started within 36-48 hours after symptom onset versus placebo in outpatients

- Pooled meta-analysis of 5 RCTs in children (oseltamivir n=770 vs. placebo n=838)
  - **Powered for Mild Disease Outcomes: Treatment started ≤48 hours of onset:**
    - **Reduced illness duration by 18 hours overall and by 30 hours in children without asthma** (-29.9 hours; 95% CI: -53.9 to -5.8 hours; **Increased risk of vomiting** RR 1.63; 95% CI 1.3-2.04)
    - **Reduced risk of otitis media by 34%** (RR 0.66; 95% CI: 0.47-0.95)
- Pooled meta-analysis of 9 RCTs in adults (oseltamivir n=1565 vs. placebo n=1295)
  - **Powered for Mild Disease Outcomes: Treatment started ≤36 hours of onset:**
    - **Reduced illness duration by 25.2 hours** (-25.2 hours; 95% CI: -36.2 to -16.0 hours)
    - **44% Reduced risk of lower respiratory tract complications occurring >48 hours after treatment requiring antibiotics** (RR: 0.56; 95% CI: 0.42 to 0.75; p=0.0001)
    - **Increased risk of nausea** (RR 1.60; 95% CI 1.29-1.99) and **vomiting** (RR 2.43; 95% CI: 1.83-3.23)

Malosh Clinical Infect Dis 2018; Dobson Lancet 2015

Baloxavir Treatment RCTs

RCTs: Baloxavir treatment has similar clinical benefit to oseltamivir and significant clinical benefit versus placebo when started within 48 hours after symptom onset

- Non-high-risk children (aged 1 to <12 yrs)
  - **Treatment started ≤48 hours of onset (oseltamivir vs. baloxavir):**
    - **Single-dose baloxavir** (n=115) **had similar median time to alleviation of influenza signs and symptoms** (138 hours) **versus 5 days of oseltamivir** (150 hours) (n=58)

- RCTs in adolescents and adults (aged ≥12 yrs)
  - **Treatment started ≤48 hours of onset (baloxavir vs. placebo vs. oseltamivir):**
    - **Single-dose baloxavir** (n=456) **significantly reduced illness duration by a median of 26.5 hours vs. placebo** (n=231) **in *non-high-risk persons*** (95% CI, 72.6 to 87.1 hours; p<0.001)
      - **Median time to alleviation of symptoms was similar for baloxavir and oseltamivir** (n=377)
      - **Baloxavir significantly reduced influenza viral RNA levels at 24 hours, and reduced infectious virus detection versus oseltamivir (24 hours vs. 72 hours, p<0.001)**
    - **Single-dose baloxavir** (n=388) **significantly reduced illness duration by a median of 29 hours vs. placebo** (n=386) **in *persons with ≥1 high-risk condition*** (95% CI 14·6 to 42·8; p<0.0001)
      - **Median time to improvement of symptoms was similar for baloxavir and oseltamivir**
      - **Baloxavir significantly reduced median time to improvement of influenza B symptoms by 27 hours versus oseltamivir** (95% CI: 6.9 to 42.3 hours; p=0.025)

Baker Ped Infect Dis J 2020; Hayden NEJM 2018; Ison Lancet Infect Dis 2020

Special Populations

CDC Recommendations

- **Pregnant People**
  - **Oseltamivir is recommended for treatment of pregnant people and up to 2 weeks postpartum**
    - **Baloxavir is *not recommended*** for treatment of pregnant people or breastfeeding mothers
      - No efficacy or safety data for baloxavir in pregnant or lactating people
      - Substantial evidence of oseltamivir safety for pregnancy and birth outcomes
- **Immunocompromised Persons**
  - **Prolonged influenza viral replication is a possibility, with emergence of antiviral resistant viruses during/after treatment**
    - Monitoring for antiviral resistance is advised
    - Infection prevention and control precautions recommended to reduce nosocomial transmission risk
  - **Neuraminidase inhibitor treatment is recommended (e.g., oseltamivir)**
  - **Baloxavir is *not recommended* (greater risk of resistance emergence than oseltamivir)**

https://www.cdc.gov/flu/hcp/antivirals/summary-clinicians.html

Self-knowledge Check: The following statements regarding influenza testing are true EXCEPT:

A. A nasopharyngeal swab is the preferred respiratory specimen to detect influenza viruses.
B. Molecular assays have high sensitivity to detect influenza viruses in respiratory specimens.
C. Rapid antigen tests and molecular assays can detect influenza viruses in saliva specimens up to 7 days after symptom onset.
D. Some molecular assays can yield results within 30 minutes.
E. False positive results are uncommon with rapid antigen tests and molecular assays because of their high specificities.

Answer: The following statements regarding influenza testing are true EXCEPT:

A. A nasopharyngeal swab is the preferred respiratory specimen to detect influenza viruses.
B. Molecular assays have high sensitivity to detect influenza viruses in respiratory specimens.
C. Rapid antigen tests and molecular assays can detect influenza viruses in saliva specimens up to 7 days after symptom onset.
D. Some molecular assays can yield results within 30 minutes.
E. False positive results are uncommon with rapid antigen tests and molecular assays because of their high specificities.

Rationale: saliva specimens are not recommended for detection of influenza viruses

COVID-19 and Influenza Resources

Resources

COVID-19 Testing

1. Overview of Testing for SARS-CoV-2 | COVID-19 | CDC
2. Guidance for SARS-CoV-2 Rapid Testing in Point-of-Care Settings | COVID-19 | CDC
3. COVID-19 Testing (hhs.gov)
4. Test to Treat

COVID-19 Antiviral Treatment

1. COVID-19 Treatment Clinical Care for Outpatients | COVID-19 | CDC
2. Treatment Options for COVID19 | HHS/ASPR
3. FDA COVID-19 therapeutics
4. Treatment Locator (hhs.gov)Resources to Prepare for Flu, COVID-19, and RSV | CDC
5. IDSA Guidelines on the Treatment and Management of Patients with COVID-19 (idsociety.org)
6. Outpatient Treatment of Confirmed COVID-19: Living, Rapid Practice Points From the American College of Physicians (Version 1) | Annals of Internal Medicine (acpjournals.org)
7. Outpatient Treatment of Confirmed COVID-19: Living, Rapid Practice Points From the American College of Physicians (Version 2) | Annals of Internal Medicine (acpjournals.org)
8. Underlying Conditions and the Higher Risk for Severe COVID-19 | COVID-19 | CDC

COVID-19 Vaccination/Other

1. Interim Clinical Considerations for Use of COVID-19 Vaccines | CDC
2. COVID-19 Vaccination Provider Requirements and Support | CDC
3. COVID-19 Data & Surveillance
4. Information for Pediatric Healthcare Providers | COVID-19 | CDC
5. Clinical Considerations for Special Populations | COVID-19 | CDC

Resources (cont.)

Influenza Testing

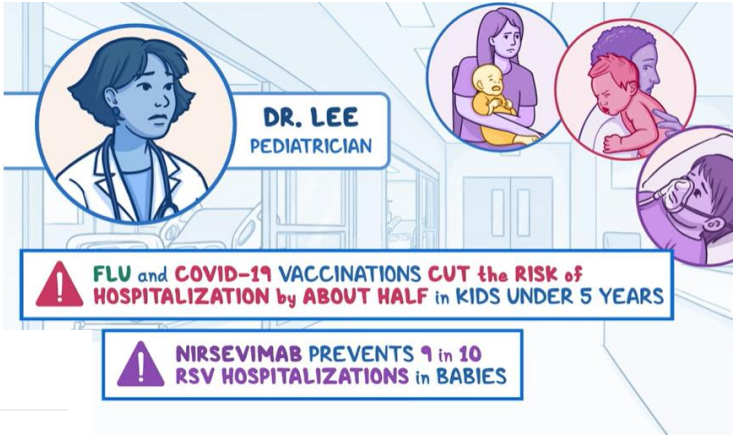
- **Information for Clinicians on Influenza Virus Testing:** Overview of Influenza Testing Methods
- **Testing and Treatment of Influenza When SARS-CoV-2 and Influenza Viruses are Co-circulating**
  - **Clinical guidance for hospitalized and non-hospitalized patients:** Clinical Guidance for Hospitalized and Non-Hospitalized Patients When SARS-CoV-2 and Influenza Viruses are Co-Circulating
  - **Clinical Guidance for Patients with Acute Respiratory Illness Being Hospitalized:** Clinical Guidance for Patients with Acute Respiratory Illness Being Hospitalized When SARS-CoV-2 and Influenza Viruses are Co-Circulating
  - **Clinical Guidance for Patients with Acute Respiratory Illness Not Being Hospitalized:** Clinical Guidance for Patients with Acute Respiratory Illness Not Being Hospitalized When SARS-CoV-2 and Influenza Viruses are Co-Circulating
  - **Testing and Management Considerations for Nursing Home Residents with Acute Respiratory Illness:** Testing and Management Considerations for Nursing Home Residents

Antiviral Treatment of Influenza

- **Antiviral treatment recommendations:** Influenza Antiviral Medications: Summary for Clinicians
- **IDSA Influenza Clinical Practice Guidelines:** https://academic.oup.com/cid/article/68/6/e1/5251935

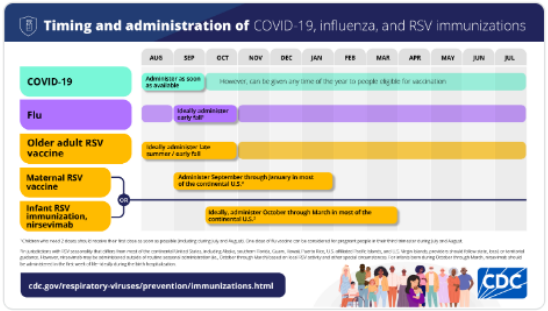
Healthcare Provider Resources

- Health care providers are the most trusted source of health information for their patients.
- Use the updated information and resources below to help your patients stay safe this fall and winter respiratory virus season.

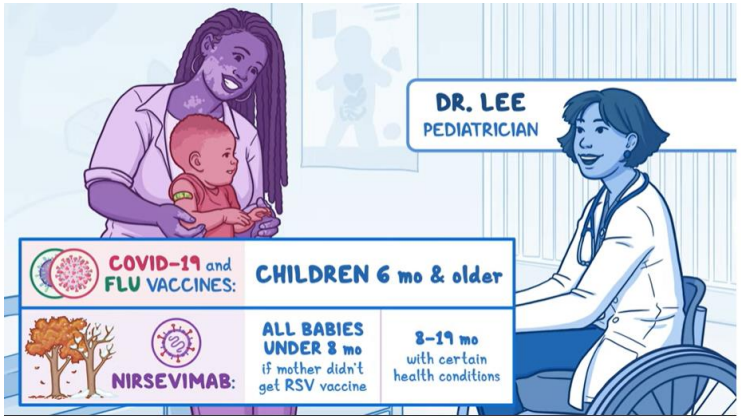


Clinical vaccination guidance

View Larger Download



Use this infographic to help determine when to administer fall and winter virus season immunizations.



[Health Care Provider Resources for Respiratory Virus Season | Respiratory Illnesses | CDC]

Thank You

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 cdc.gov
Follow us on X (Twitter) @CDCgov & @CDCEnvironment

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the U. S. Centers for Disease Control and Prevention.

To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

TRAIN

- **January 1, 2024**: Move from Training and Continuing Education Online (TCEO) to CDC TRAIN (https://www.train.org/cdctrain).
- **Existing Activities**: Continue to use TCEO for existing activities that have CE set to expire in 2024, since these courses will not move to CDC TRAIN. You may also use TCEO for existing activities with CE set to expire in 2025, before the courses transition to CDC TRAIN sometime next year. If you begin one of these courses in TCEO, we will let you know when the course will move to CDC TRAIN.
- **Transcripts & Certificates**: You can access and download CE transcripts and certificates in TCEO through the end of 2025.
- Instructions will be available on both platforms and a learner support team will be available to answer questions.

Continuing Education

- All continuing education for COCA Calls is issued online through CDC TRAIN at CDC TRAIN (https://www.train.org/cdctrain).

- Those who participate in today's COCA Call and wish to receive continuing education please complete the online evaluation by **November 11, 2024,** with the **course code WC4520R-101024.** The **registration code** is **COCA101024**

- Those who will participate in the on-demand activity and wish to receive continuing education should complete the online evaluation between **November 12, 2024,** and **November 12, 2026** and use **course code WD4520R-101024.** The **registration code** is **COCA101024.**

Today's COCA Call will be Available to View On-Demand

- **When:** A few hours after the live call ends*
- **What:** Video recording
- **Where:** On the COCA Call webpage
  - https://emergency.cdc.gov/coca/calls/2024/callinfo_101024.asp

A transcript and closed-captioned video will be available about one week after the live session.

Upcoming COCA Call

- **Title:** Resurgence of New World Screwworm in the Americas: What Healthcare Providers Need to Know
- **Date:** Thursday, October 17, 2024
- **Time:** 2:00-3:00 P.M. ET

Additional Resources

- Continue to visit https://emergency.cdc.gov/coca/ to get more details about upcoming COCA Calls.

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