Testing and Treatment of 2020-2021 Seasonal Influenza During the COVID-19 Pandemic

Clinician Outreach and Communication Activity (COCA) Webinar

Thursday, September 17, 2020

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Objectives

- Review influenza activity since the onset of the COVID-19 pandemic.
- Provide background on influenza tests and antivirals for influenza.
- Describe influenza testing guidance for patients with acute respiratory illness for the 2020-2021 season, including during community co-circulation of influenza viruses and SARS-CoV-2.
- Describe antiviral treatment recommendations for patients with suspected or confirmed influenza for the 2020-2021 season, including during community co-circulation of influenza viruses and SARS-CoV-2.

To Ask a Question

- All participants joining us today are in listen-only mode.
- Using the Webinar System
  - Click the “Q&A” button.
  - Type your question in the “Q&A” box.
  - Submit your question.
- The video recording of this COCA Call will be posted at https://emergency.cdc.gov/coca/calls/2020/callinfo_091720.asp and available to view on-demand a few hours after the call ends.
- If you are a patient, please refer your questions to your healthcare provider.
- For media questions, please contact CDC Media Relations at 404-639-3286, or send an email to media@cdc.gov.

Today's Presenters

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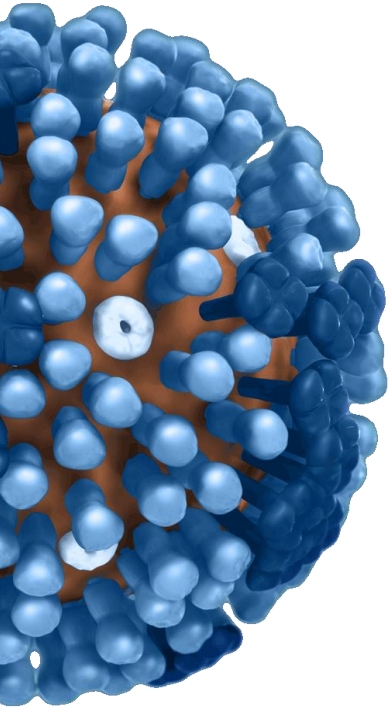
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Testing and Treatment of 2020-2021 Seasonal Influenza During the COVID-19 Pandemic



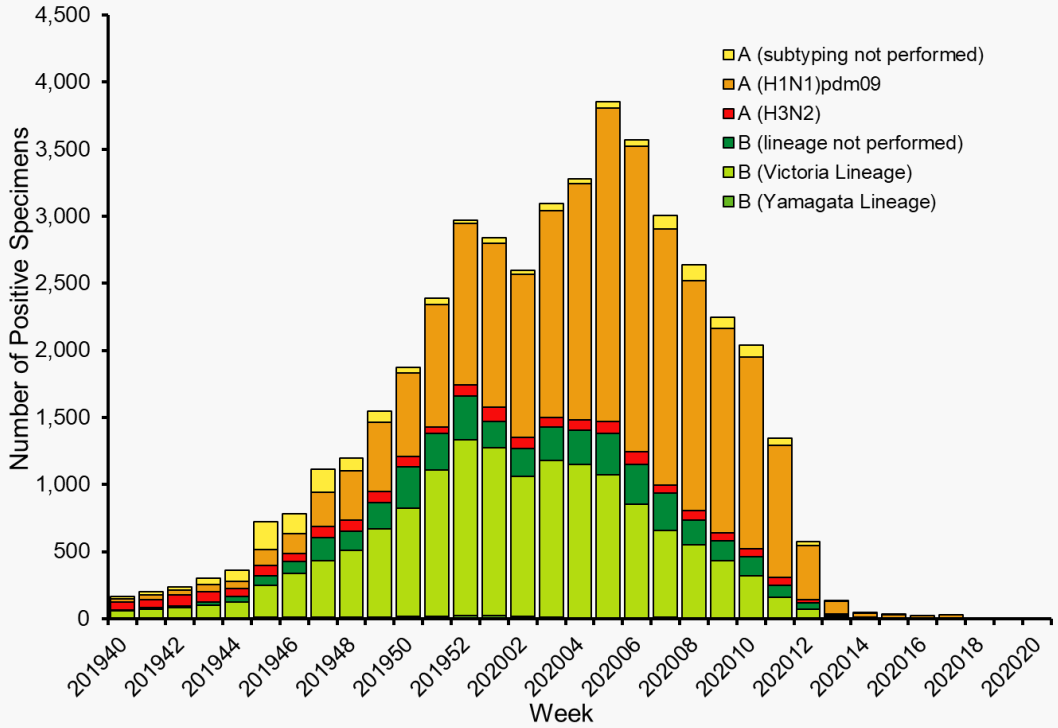
2019-2020 Influenza Season Activity

U.S. Influenza Surveillance Reports

FluView Interactive

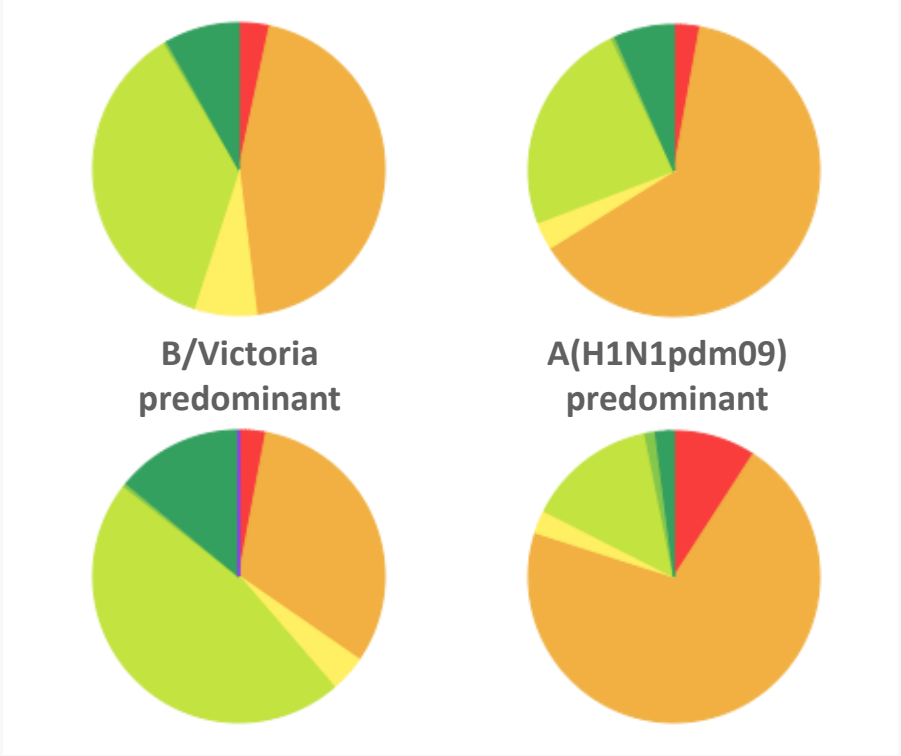
https://www.cdc.gov/flu/weekly/fluactivitysurv.htm

Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, 2019-2020 Season

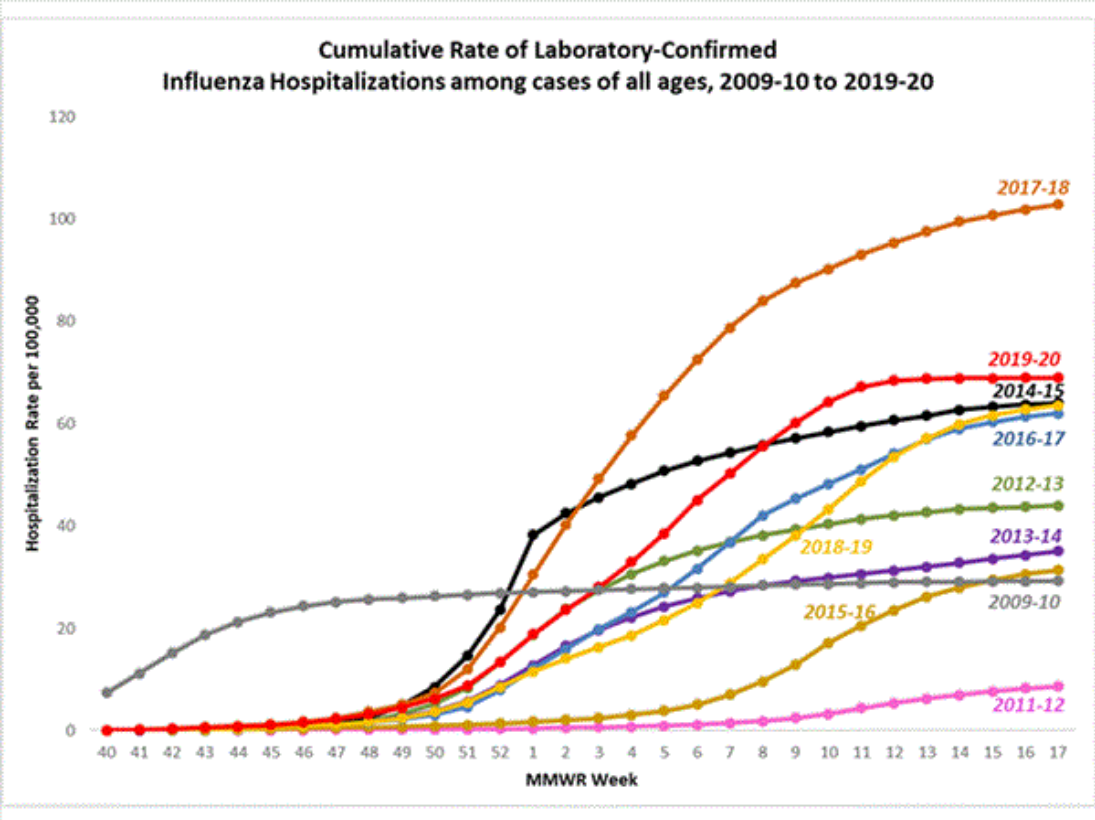


- Two waves of activity; started early in some parts of the country.
- Initial peak due to B/Victoria lineage viruses, followed by second higher peak of A(H1N1)pdm09 viruses.
- Few A(H3N2) viruses and very small numbers of B/Yamagata lineage viruses circulated.

Virus Distribution by Age Group, 2019-2020 Season

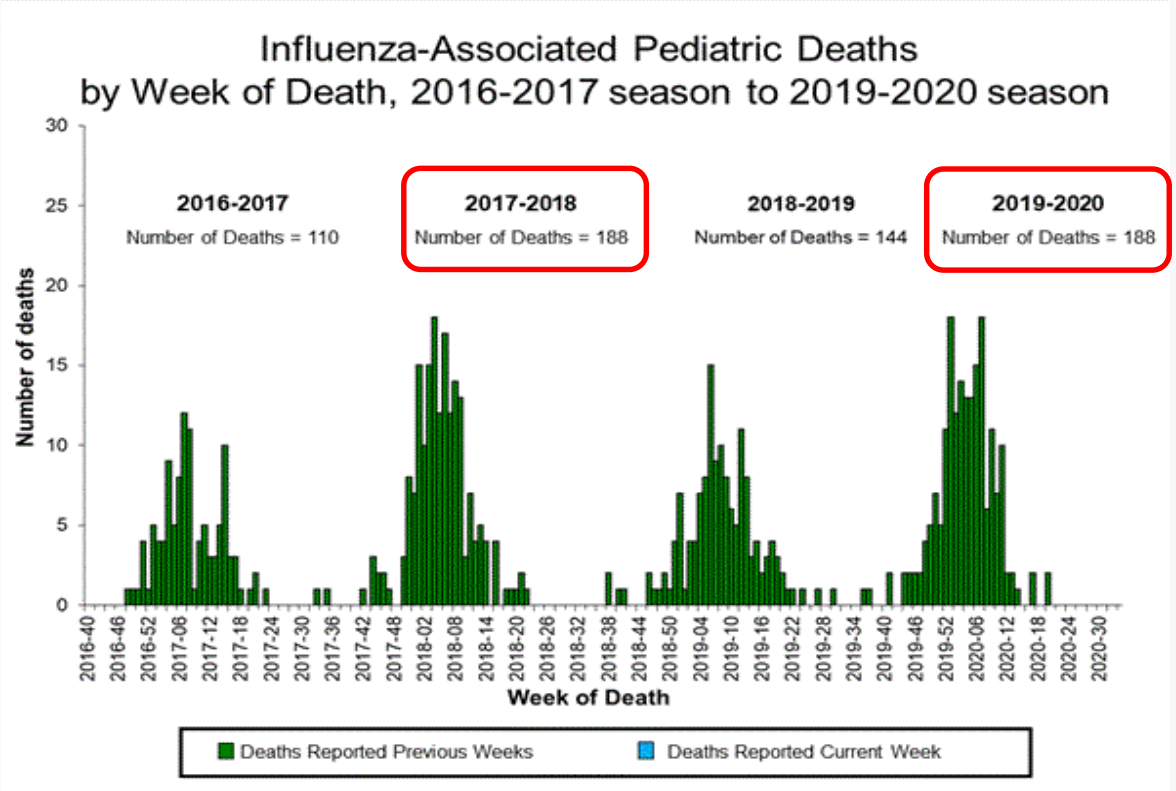


Laboratory Confirmed Influenza Associated Hospitalizations, Cumulative Rate per 100,000; 2011-2012 to 2019-2020 Seasons

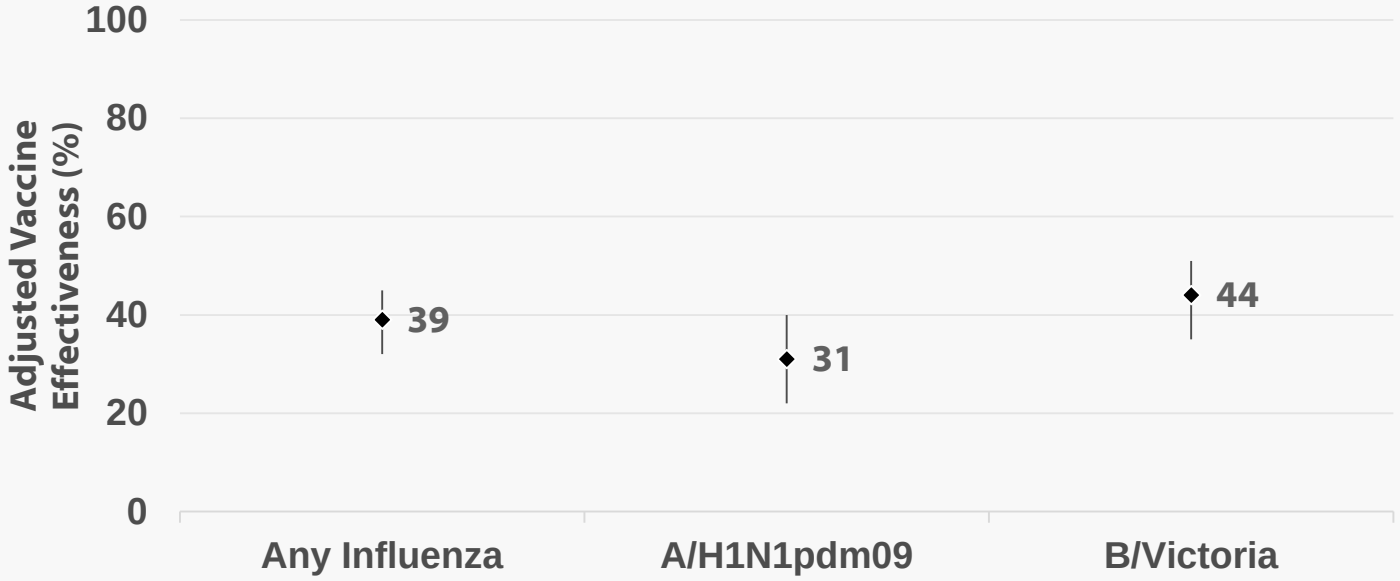


Age Group	2019-2020 Season Cumulative Rate per 100,000 Population
Overall	69.0
0-4 years	93.3
5-17 years	23.9
18-49 years	34.0
50-64 years	89.9
65+ years	173.5

Deaths in Children with Laboratory-Confirmed Influenza: 2019-2020 and Previous Seasons



PRELIMINARY Adjusted Vaccine Effectiveness Against Medically Attended Influenza, US Flu VE Network, 2019–2020 (as of June 9, 2020)

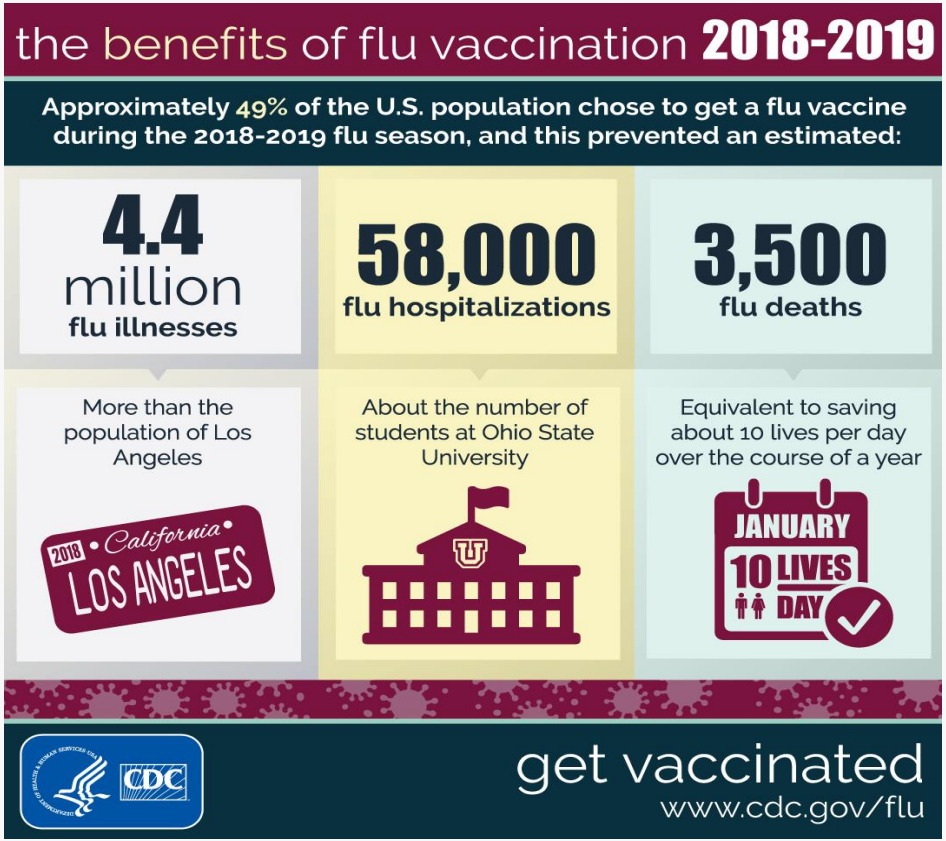


*Multivariable logistic regression models adjusted for site, age, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time.

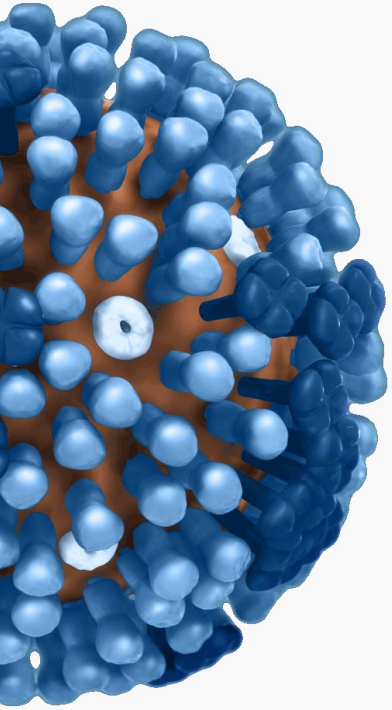
Preliminary results presented at ACIP, June 24, 2020. For more information on the US Flu VE Network: https://www.cdc.gov/flu/vaccines-work/us-flu-ve-network.htm

Estimated Benefits of Influenza Vaccination, 2018–2019

- Estimated vaccine effectiveness for 2018-2019:
  - 29% overall
- Estimated vaccination coverage:
  - 49% overall

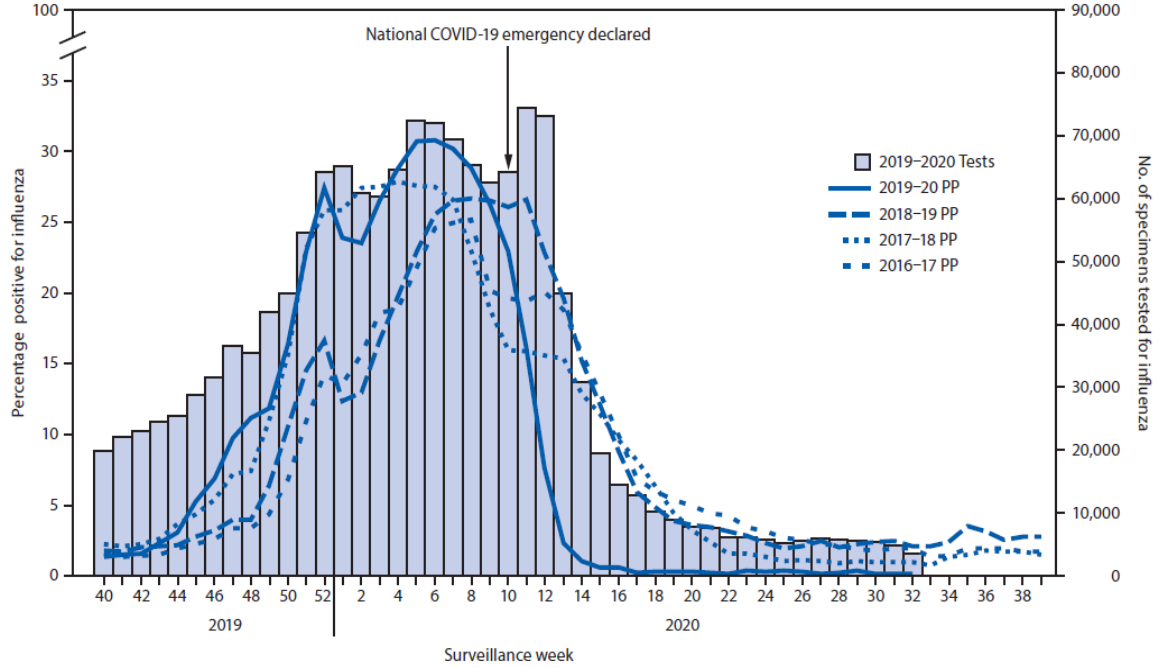


https://www.cdc.gov/flu/about/burden-averted/2018-2019.htm



What Will the 2020-2021 Influenza Season Bring?

U.S. Influenza Activity Declined Sharply From Late February to March 2020

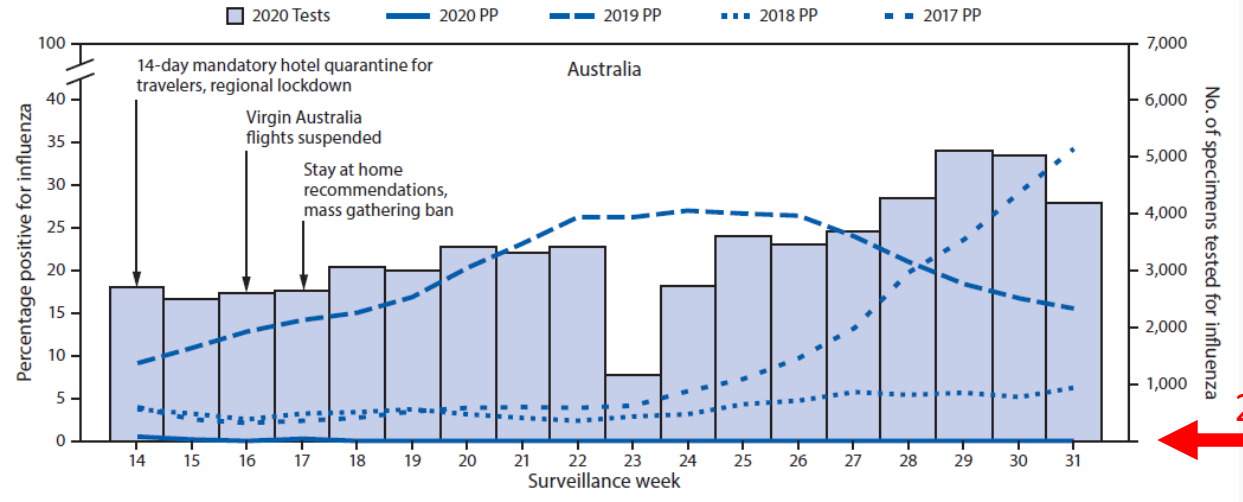


Source: FluView Interactive. https://www.cdc.gov/flu/weekly/fluviewinteractive.htm.
Abbreviation: PP = percentage positive.

- 61% decrease in number of specimens tested for influenza but a 98% decrease in the number testing positive.
- Declines attributed to:
  - Fewer people left home to seek medical care
  - COVID-19 mitigation measures
- Inter-seasonal circulation is now at historical lows.

Olsen et al. MMWR 17 Sept 2020

Southern Hemisphere: Australia, Chile, and South Africa with Decreased Influenza Virus Circulation

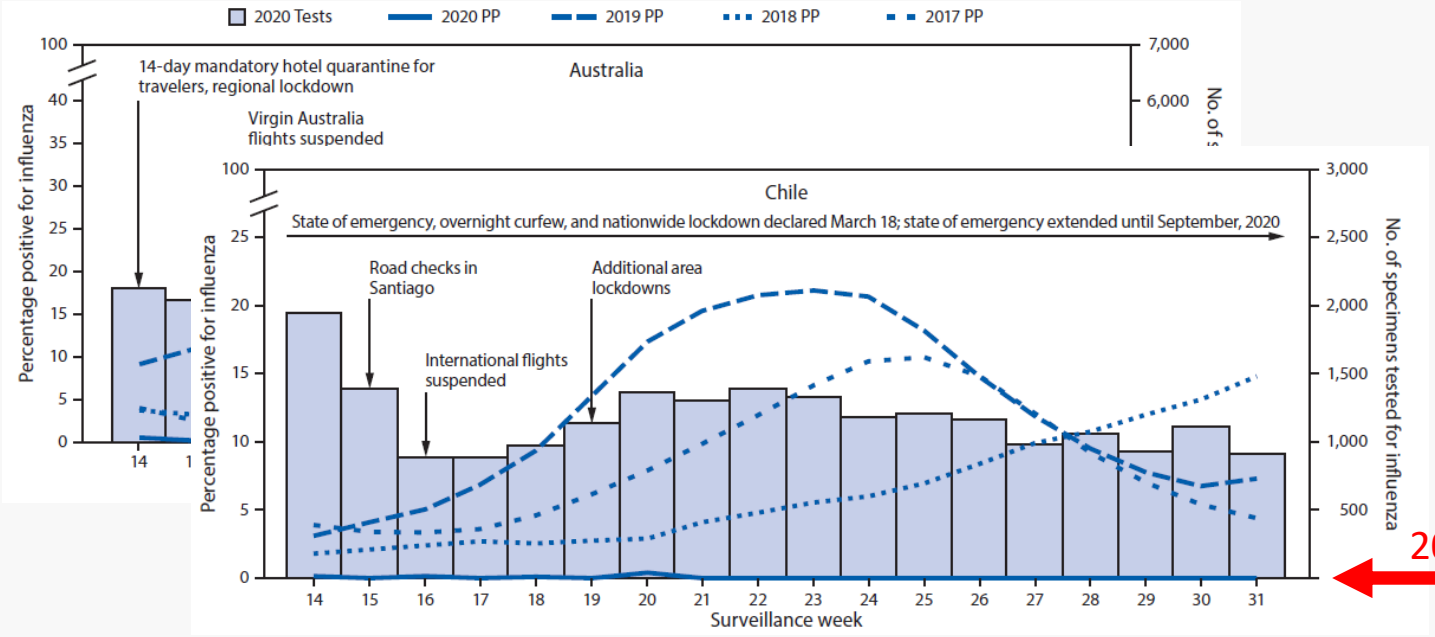


2020 % Pos

https://www.who.int/influenza/surveillance_monitoring/updates/latest_update_GIP_surveillance/en

Olsen et al. MMWR 17 Sept 2020

Southern Hemisphere: Australia, Chile, and South Africa with Decreased Influenza Virus Circulation



2020 % Pos

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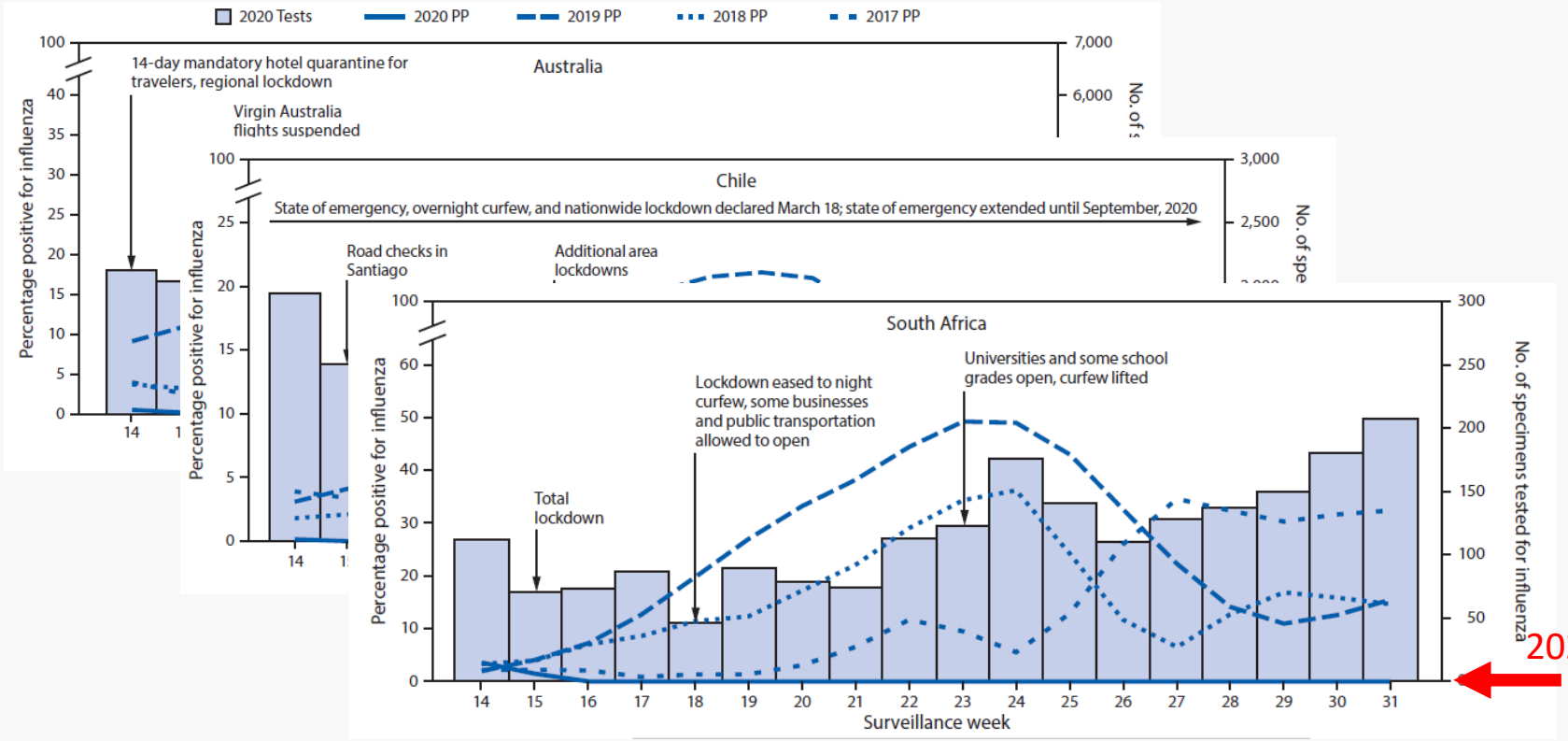
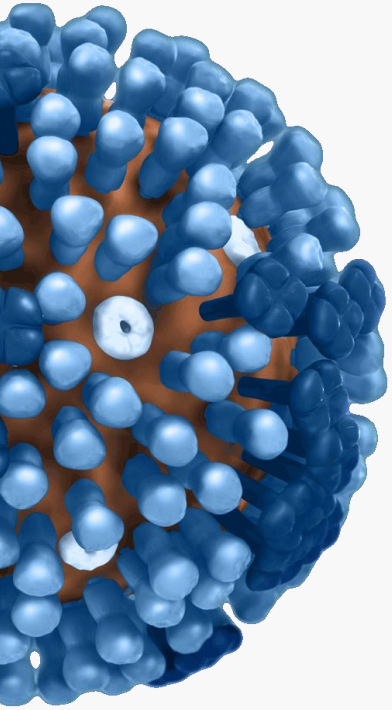


https://www.who.int/influenza/surveillance_monitoring/updates/latest_update_GIP_surveillance/en

Olsen et al. MMWR 17 Sept 2020

Summary

- The 2019-2020 U.S. influenza season was predominated by early onset influenza B/Victoria viruses followed by influenza A(H1N1)pdm09 virus circulation.
  - Cumulative hospitalization rates among pediatric and young adult populations were the highest in the last 10 seasons.
  - Pediatric influenza deaths tied with 2017-2018 for highest recorded.
- If there is continued widespread use of COVID-19 prevention strategies, along with seasonal influenza vaccination, the impact of influenza in the Northern hemisphere during the upcoming influenza season may be reduced.
  - However, influenza viruses are currently circulating among people in locations where less mitigation is exercised.
- Because it is not possible to predict exactly what will happen this fall and winter, it is imperative to prepare for circulation of both influenza and SARS-CoV-2 viruses.
  - Influenza vaccination remains the best method for influenza prevention.

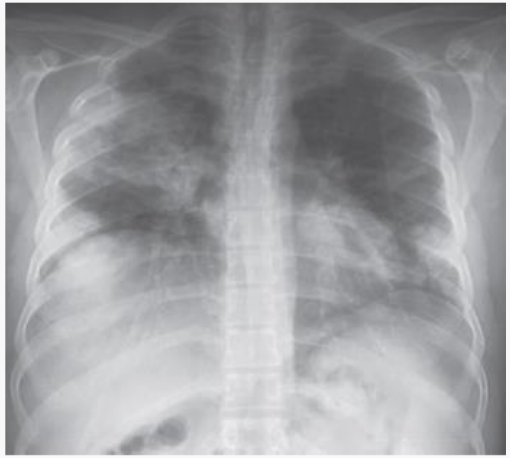


Clinical Manifestations of Influenza Virus Infection

Spectrum of Influenza Virus Infection

- Disease severity and clinical manifestations vary by age, host factors, immunity, virus type/subtype
  - Asymptomatic infection
  - Upper respiratory tract illness
    - Typical: abrupt onset of fever, cough, chills, muscle aches, fatigue, headache, sore throat, runny nose
    - GI symptoms (more common in children)
    - Infants can have fever alone, irritability, may not have respiratory symptoms
    - Fever may not always be present (such as in elderly, immunosuppressed, others with uncomplicated influenza)
  - Complicated illness

Influenza Complications



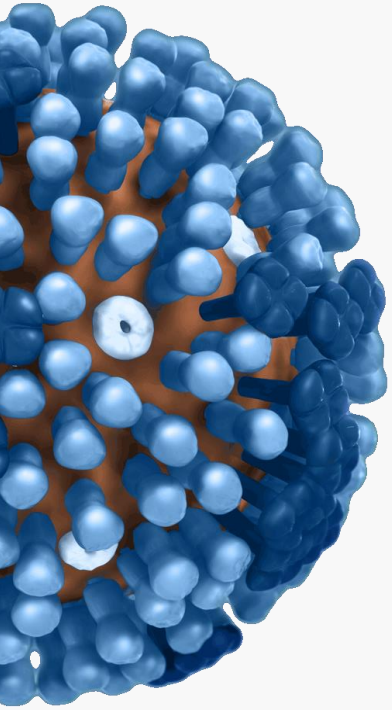
- Otitis media common in children, sinusitis
- Worsening of underlying chronic disease
- Dehydration
- Pneumonia (primary viral or secondary bacterial) or other respiratory (croup, bronchiolitis, respiratory failure, acute respiratory distress syndrome)
- Extra-pulmonary: renal failure, myocarditis, pericarditis, myositis/ rhabdomyolysis, encephalopathy and encephalitis, Guillain-Barre syndrome, acute disseminated encephalomyelitis, sepsis, multi-organ failure
  - Sepsis is listed as a complication in up to 30% of pediatric death reports
- Invasive bacterial co-infection can cause severe and fulminant disease
  - *S. pneumoniae*, *S. aureus* (MSSA and MRSA), and *S. pyogenes*

Uyeki NEJM 2009

People at High Risk for Influenza Complications for Whom Antiviral Treatment is Recommended

- Children <2 years old (although all children <5 years old are considered at high risk for complications, highest risk is for children <2 years old)
- Adults aged 65 years and over
- Pregnant/postpartum women
- American Indians/Alaska Natives
- Children ≤18 years old receiving long-term aspirin therapy
- People with underlying medical conditions (e.g., pulmonary, cardiac, immunosuppression, neurologic and neurodevelopment conditions, BMI ≥40)
- Residents of nursing homes/chronic care facilities

https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm



Influenza Diagnostic Testing

Why Test for Influenza?

- **Accurate and prompt influenza diagnosis is important for clinical decision-making** (ambulatory & inpatient settings)
  - **Guide antiviral treatment** *(if testing will change clinical management, versus prescribing empiric antiviral treatment)*
  - **Facilitate implementation of Infection prevention & control measures**
    - Prevention and control of nosocomial transmission in hospitals
    - Control of other institutional outbreaks
  - **Guide other clinical decisions**
    - Reduce inappropriate antibiotic use, reduce use of other diagnostic tests, reduce time in clinical care (e.g. Emergency Department)

Egilmezer Rev Med Virol 2018; Brendish Lancet Resp Med 2017

Influenza Tests in Clinical Settings

- **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**
    - Point-of-care assays (CLIA-waived)
    - Moderately complex (requires clinical laboratory)
    - Highly complex (large clinical laboratories, public health labs)

Influenza Tests Available for Clinicians - Antigen Detection

- **Antigen detection**
  - Detect influenza A and influenza B viral antigens in respiratory specimens (FDA-cleared for upper respiratory tract specimens)
  - **Rapid immunoassays** (rapid tests) (10-15 minutes)
    - With or without analyzer device
  - Direct florescent antibody staining (2-4 hours)
    - Requires florescent microscope
  - ➢ ***Low to moderately high sensitivities, high specificity to detect influenza viral antigens compared to nucleic acid detection assays***

Influenza Tests Available for Clinicians - Nucleic Acid Detection

- **Nucleic acid detection (molecular assays)**
  - Detect influenza A and B virus nucleic acids in respiratory specimens
    - Most are FDA-approved for upper respiratory tract specimens, some approved for lower respiratory tract specimens
  - **Rapid molecular assays** (15-30 minutes to results)
  - **Other molecular assays** (60-80 minutes to 4-8 hours to results)
    - Single-plex PCR: Detect influenza A and B viruses
    - Multiplex PCR: Detect influenza viruses and other respiratory pathogens
    - ➢ FDA Emergency Use Authorization (EUA) issued for assays that detect influenza viruses and SARS-CoV-2
  - ➢ ***High sensitivity and high specificity***

https://www.cdc.gov/flu/professionals/diagnosis/table-nucleic-acid-detection.html; https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas#individual-molecular; https://www.cdc.gov/flu/professionals/diagnosis/table-flu-covid19-detection.html

Rapid Influenza Molecular Assays Have High Sensitivity

Pooled Sensitivity to detect influenza A and B viruses versus RT-PCR (N=162 studies) (Pooled Specificity >98%)

- **Rapid antigen tests: 53-54%**
- **Rapid antigen tests with analyzer device: 77-80% (digital immunoassays)**
- **Molecular assays: 92-95%**


Annals of Internal Medicine REVIEW

Diagnostic Accuracy of Novel and Traditional Rapid Tests for Influenza Infection Compared With Reverse Transcriptase Polymerase Chain Reaction

A Systematic Review and Meta-analysis

Joanna Merckx, MD, MSc; Rehab Wali, BSc, MBBS; Ian Schiller, MSc; Chelsea Caya, MScPH; Genevieve C. Gore, MLIS; Caroline Chartrand, MD, MSc; Nandini Dendukuri, PhD; and Jesse Papenburg, MD, MSc


Clinical Infectious Diseases

REVIEW ARTICLE

IDSA hivma

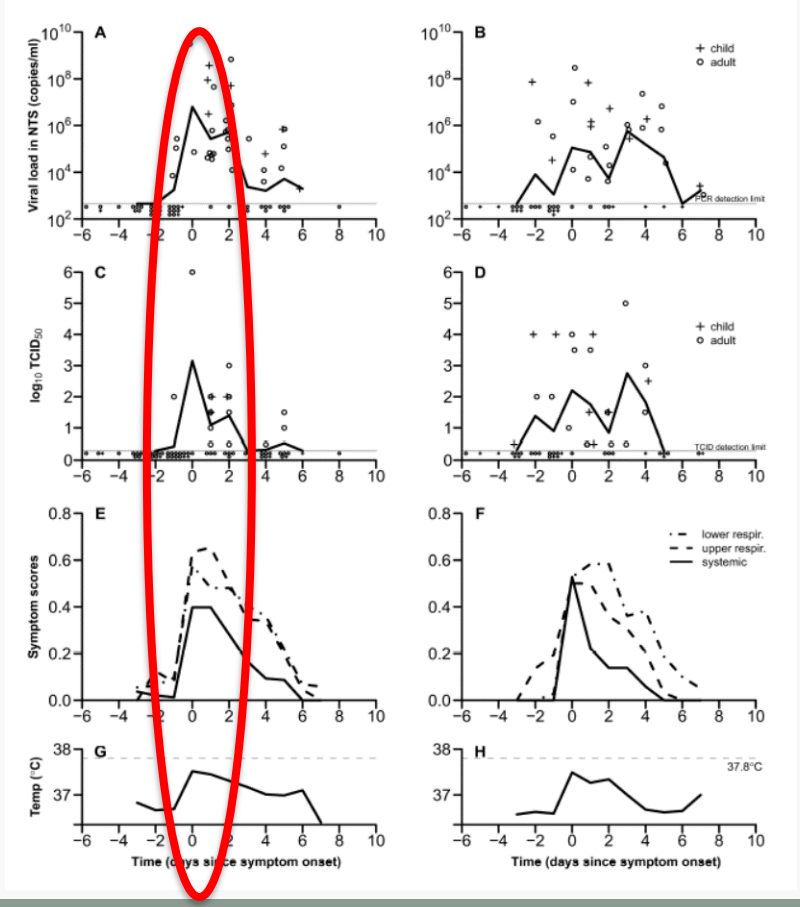
Rapid Molecular Tests for Influenza, Respiratory Syncytial Virus, and Other Respiratory Viruses: A Systematic Review of Diagnostic Accuracy and Clinical Impact Studies

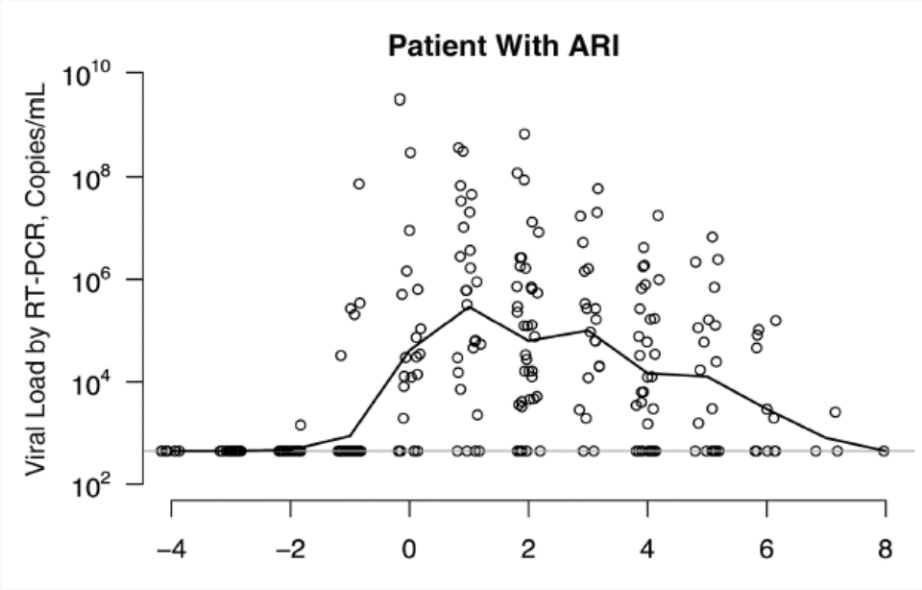
Laura M. Vos,[1] Andrea H. L. Bruning,[2] Johannes B. Reitsma,[3] Rob Schuurman,[4] Annelies Riezebos-Brilman,[4] Andy I. M. Hoepelman,[1] and Jan Jelrik Oosterheert[1]

- **Meta-analysis of Rapid Influenza Molecular Assays (N=29 studies)**
  - **Pooled Sensitivity: 87.9%**
  - **Pooled Specificity: 97.4%**

Merckx Annals of Int Med 2017; Vos Clin Infect Diseases

Influenza Viral Shedding Peaks Within 24 Hours of Illness Onset





Day of illness onset

Lau J Infect Dis 2010; Ip Clin Infect Dis 2017

Influenza A(H1N1)pdm09 Viral Shedding Varies by Disease Severity

Viral Shedding is Longer with Severe Disease

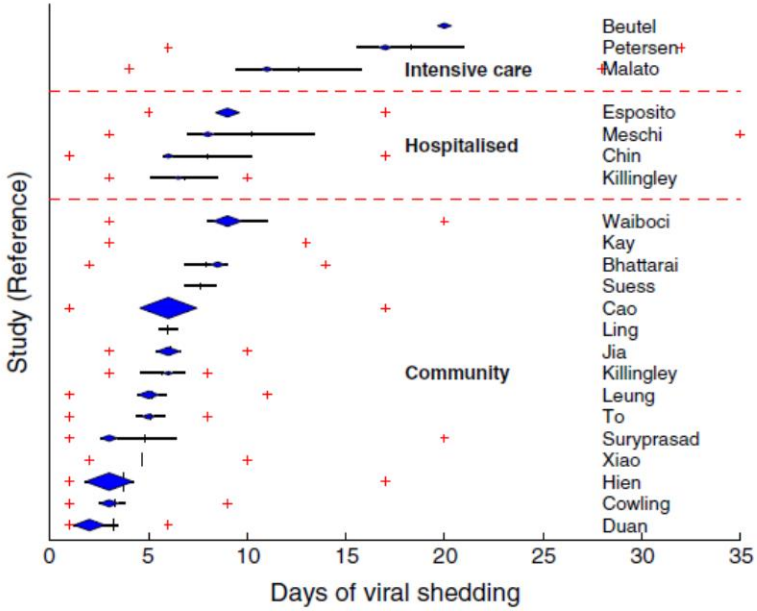


Figure 1. Shedding duration of influenza A(H1N1)pdm09 by study and patient setting. (Legend: cross = minimum and maximum; middle of diamond = median; area of diamond = study size; vertical line = mean; horizontal line = 95% confidence interval)

Viral Shedding Duration is Similar in Children and Adults

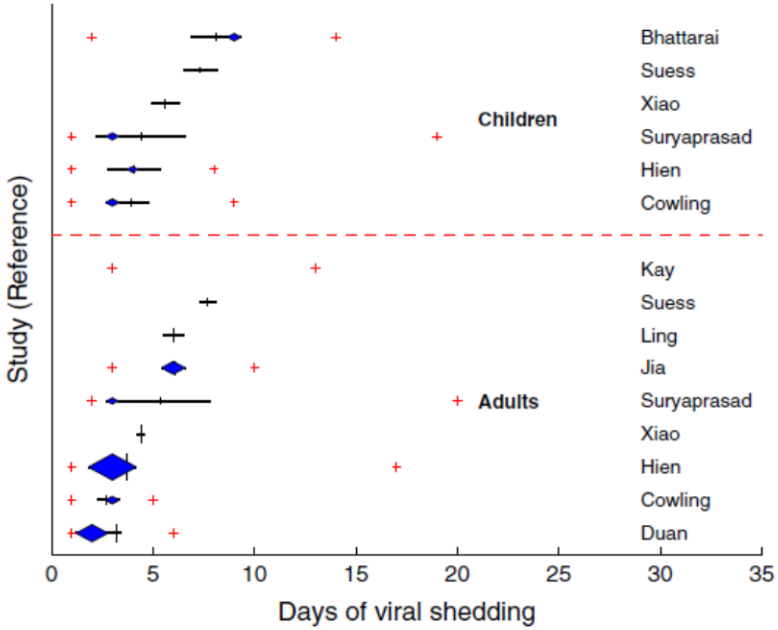


Figure 2. Shedding duration of influenza A(H1N1)pdm09 in studies of community-based cases, by study and age group.

Fielding Influenza and Other Respiratory Viruses 2014

Influenza Testing and Specimen Source

- **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 RNA detection may be prolonged with corticosteroids, immunosuppression**
- **Lower respiratory tract**
  - **Higher, prolonged viral replication in severe lower respiratory tract disease**
    - **Influenza viruses may be detectable 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**

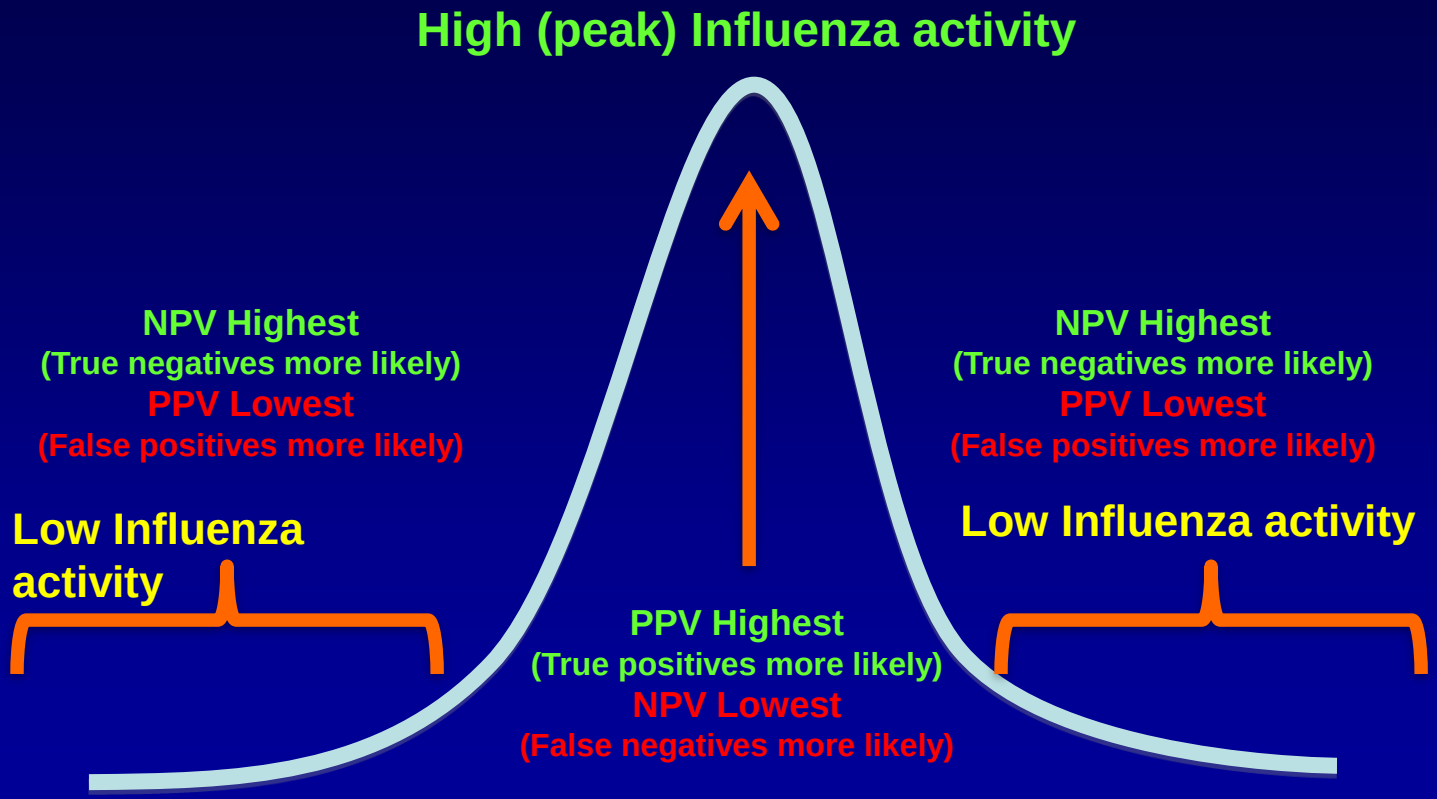
Rello Crit Care 2009; Fleury Eurosurveillance 2009; Blyth NEJM 2009

Importance of Influenza Prevalence

- **Influenza activity (prevalence) impacts:**
  - Influenza testing decisions (when to test?)
  - **How to interpret results** (e.g. negative results)?
  - Treatment decisions (when to prescribe empiric antiviral treatment?)

- **Clinicians should be aware of local influenza activity**
  - National influenza surveillance data (e.g. U.S. CDC)
  - State and local influenza surveillance data, local hospital laboratory data

Prevalence (Influenza Activity) and Predictive Values of Influenza Tests



Uyeki Chapter 177; Feigin and Cherry's Pediatric Infect Dis 2013

Influenza Testing Recommendations: Outpatients*

- **Which outpatients should be tested for influenza during influenza season?**
  (Test if the results will influence clinical management)
  - **High-risk persons with influenza-like illness, pneumonia, non-specific acute respiratory illness**
  - **Patients with acute onset of respiratory symptoms and exacerbation of chronic medical conditions** (e.g. asthma, COPD, heart failure) or known influenza complications
  - **Consider testing for:**
    - **Persons not at high-risk for complications of influenza who present with acute respiratory illness** *(ILI, pneumonia, ARI without fever) if the results might change clinical management (support antiviral treatment, reduce unnecessary antibiotic use, reduce more diagnostic testing or time in the emergency department)*

*History of influenza vaccination does not exclude influenza

IDSA 2018 Influenza Clinical Practice Guidelines Clinical Infect Dis 2019

Influenza Testing Recommendations: Hospitalized Patients*

- **Which patients being hospitalized should be tested for influenza during influenza season?**
  - **All patients requiring admission with acute respiratory illness**, including pneumonia, with or without fever
  - **All patients with acute worsening of chronic cardiopulmonary disease** (e.g. COPD, asthma, coronary artery disease, heart failure)
  - **All immunocompromised and high-risk patients with acute onset of respiratory symptoms with or without fever**
  - **All patients during hospitalization who develop acute onset of respiratory symptoms with or without fever, or respiratory distress, without a clear diagnosis**

*History of influenza vaccination does not exclude influenza

IDSA 2018 Influenza Clinical Practice Guidelines Clinical Infect Dis 2019

What Respiratory Specimens Should Be Collected?

- **Outpatients: Collect upper respiratory tract specimens as soon after illness onset as possible, preferably with 4 days of symptom onset**
  - **Nasopharyngeal (NP) specimens**
  - If NP specimens are not available, collect combined nasal and throat specimens
  - Mid-turbinate nasal swab specimens should be collected over throat swabs
  - Flocked swabs should be used over non-flocked swabs
- **Hospitalized patients:**
  - **Patients without severe lower respiratory tract disease:**
    - ***Collect NP specimens, mid-turbinate nasal, or combined nasal-throat swab specimens***
  - **Patients with respiratory failure receiving invasive mechanical ventilation:**
    - ***Collect endotracheal aspirate (or bronchoalveolar lavage (BAL) fluid specimens - if performed for other diagnostic purposes)***

IDSA 2018 Influenza Clinical Practice Guidelines Clinical Infect Dis 2019

What Influenza Tests Are Recommended?

- **Outpatients:**
  - **Rapid influenza molecular assays are recommended over rapid influenza antigen detection tests**
- **Hospitalized patients:**
  - **RT-PCR or other molecular assays are recommended**
    - Rapid antigen detection tests and immunofluorescence assays are not recommended 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**

IDSA 2018 Influenza Clinical Practice Guidelines Clinical Infect Dis 2019

Co-circulation of Influenza Viruses and SARS-CoV-2

- **Co-infection with influenza A or B viruses and SARS-CoV-2 can occur**
  - Documented in case reports, case series
  - Overlapping signs, symptoms with either infection alone
  - Frequency, severity, and risk factors are unknown
    - N=93 COVID-19 hospitalized adult patients in Wuhan; 49.5% with influenza (serologically-diagnosed)
  - Implications
    - Testing is needed to distinguish influenza from COVID-19
      - **Consider influenza virus infection, SARS-CoV-2 infection, co-infection**
    - Treatment issues
      - Consider potential for co-infection
      - Dexamethasone treatment of severe COVID-19 may prolong influenza viral replication

Cuadrado-Payan Lancet 2020; Azekawa ID Cases 2020; Ma Int J Infect Dis 2020; Ding J Med Virology 2020; Wu Emerg Inf Dis 2020

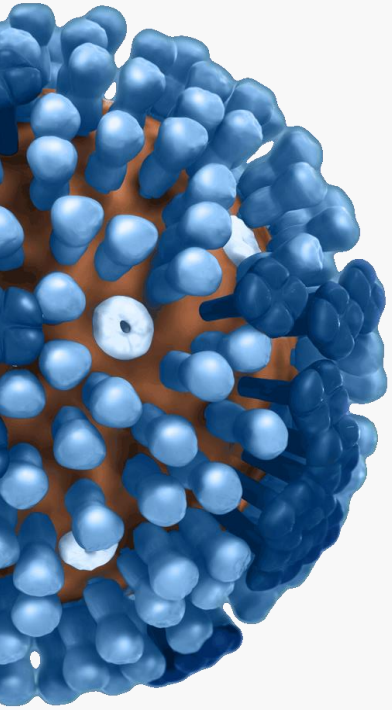
Multiplex Assays for Influenza Viruses and SARS-CoV-2

- **Multiplex Nucleic Acid Detection Assays**
  - **Several assays that can detect Influenza A and B viruses and SARS-CoV-2 simultaneously in respiratory specimens have received FDA Emergency Use Authorization (EUA)**
    - **Variable turnaround time to results (20 minutes to 8 hours)**
    - **High complexity, moderate complexity, CLIA-waived**

https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas#individual-molecular; https://www.cdc.gov/flu/professionals/diagnosis/table-flu-covid19-detection.html

Use of Telemedicine

- Clinicians can utilize telemedicine in place of office visits for patients with acute respiratory illness.
  - Providers can consider implementing phone triage lines for high-risk patients
- **Patients at higher risk for influenza complications should be advised to call their provider as soon as possible if they have acute respiratory illness symptoms (with or without fever) for consideration of infection with influenza A or B viruses (and early antiviral treatment), SARS-CoV-2, and other respiratory pathogens.**



Antiviral Treatment of Influenza

Recommended Antivirals 2020-2021

- Four FDA-approved antivirals are recommended for use in the United States
  - Neuraminidase inhibitors:
    - **oseltamivir** (oral)
    - **zanamivir** (inhaled)
    - **peramivir** (intravenous)
  - Cap-dependent endonuclease inhibitor: **baloxavir** marboxil (oral)

Drug	Route	Treatment
Oseltamivir	Oral	Any age
Zanamivir	Inhaled	≥ 7 years
Peramivir	Intravenous	≥ 2 years
Baloxavir	Oral	≥ 12 years

https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

Clinical Benefit of Early Oseltamivir Treatment - Outpatients

- Meta-analysis of RCTs of early oseltamivir treatment (starting treatment <2 days of onset) versus placebo in outpatients with uncomplicated influenza
  - **Adults: →Early oseltamivir treatment significantly reduced illness duration, lower respiratory tract complications requiring antibiotics, and hospitalizations for any cause**
    - **25.2-hour reduction of illness duration; increased risk of nausea and vomiting**
    - **44% reduction of respiratory tract complications requiring antibiotics** (RR: 0.56, 95% CI: 0.42-0.75, p=0.0001)
    - **63% reduction in hospitalizations for any cause** (RR: 0.37, 95% CI: 0.17-0.81, p=0.013)
  - **Children: →Early oseltamivir treatment significantly reduced illness duration in non-asthmatic children, and risk of otitis media**
    - **17.6-hour reduction in illness duration; increased risk of vomiting**
    - **35-hour reduction in illness duration in children without asthma in pooled analysis**
    - **34% reduction in risk of otitis media** (RR: 0.66, 95% CI: 0.47-0.95)
    - No reduction in illness duration in children with asthma in 2 RCTs

Dobson Lancet 2015; Malosh 2018

Baloxavir for Early Treatment of Uncomplicated Influenza

- **RCTs of baloxavir, oseltamivir, and placebo treatment of otherwise healthy patients 12-64 years with uncomplicated RT-PCR+ influenza (N=1066) or high-risk patients ≥12 years (N=1163)**

Clinical benefit

- **Otherwise healthy 12-64 years: Baloxavir reduced median time to alleviation of symptoms by 26.5 hours vs. placebo (p<0.001)**
- **High-risk ≥12 years: Baloxavir reduced median time to improvement of symptoms by 29.1 hours vs. placebo (p<0.001)**
- **Baloxavir (single-dose) and oseltamivir (5 days, twice daily) had similar overall benefit in these RCTs**
  - **In high-risk patients with influenza B, baloxavir reduced median time to improvement of symptoms by 26 hours vs. placebo (p<0.0138) and 27 hours vs. oseltamivir (p<0.0251)**

Virology:

- **Median duration of infectious virus detection in upper resp tract specimens was shorter for baloxavir (24 hours) vs. oseltamivir (72 hours) (p<0.001); 10% of baloxavir recipients had emergence of reduced baloxavir susceptibility**
- **Median time to cessation of infectious viral shedding was significantly shorter for baloxavir (48 hours) vs. placebo (96 hours) or oseltamivir (96 hours) (p<0.0001); 5% of baloxavir recipients had emergence of reduced baloxavir susceptibility**

Hayden NEJM 2018; Ison Lancet Infect Dis 2020

Neuraminidase Inhibitor Effectiveness Data in Outpatients

- **Individual patient data meta-analysis of >3000 outpatients with high-risk conditions (children and adults) with laboratory-confirmed influenza**
- **Neuraminidase inhibitor treatment (mostly oseltamivir) significantly reduced risk of hospital admission versus no treatment in children and adults**
  - Adults aged ≥16 years (adjusted OR: 0.26, 95% CI: 0.19-0.35; p<0.001)
  - Children aged <16 years (adjusted OR: 0.25, 95% CI: 0.18-0.34; p<0.001)

Venkatesan Clin Infect Dis 2017

Observational Studies in Hospitalized Influenza Patients

- No fully enrolled RCTs of oseltamivir versus placebo in hospitalized influenza patients have been completed or published - thus observational data are considered
- Many observational studies of effectiveness of oseltamivir or other neuraminidase inhibitor treatment of hospitalized patients with laboratory-confirmed influenza have been published of variable quality, some controlled for biases
  - **Most, <u>but not all</u>, reported clinical benefit of early oseltamivir treatment (started within 2 days of onset) versus later initiation of treatment (>2 days after onset)**
  - **Most, <u>but not all</u>, reported clinical benefit of oseltamivir treatment versus no treatment**

➢ **Observational studies have reported that starting neuraminidase inhibitor treatment within 6 hours of admission or at the time of admission was associated with shorter duration of hospitalization**

Katzen Clin Infect Dis 2018; Venkatesan J Infect Dis 2020

Effectiveness of Neuraminidase Inhibitor (NAI) Treatment of Influenza in Hospitalized Patients

- Meta-analysis of >29,000 hospitalized patients (86% lab-confirmed H1N1pdm09)
  - **NAI treatment (mostly oseltamivir) significantly reduced mortality versus no treatment; early treatment within 2 days significantly reduced mortality versus no treatment**
  - ***Increase in mortality hazard rate with each day delay in starting NAI treatment up to day 5 versus starting NAI treatment within 2 days of onset*** (HR 1.23, 95% CI: 1.18-1.28; p<0.0001)
    - **NAI treatment vs. no treatment significantly reduced risk of mortality by 54% in pregnant women** (adjusted OR: 0.46, 95% CI: 0.23-0.89; p=0.0215) **and by 28% in critically ill patients aged >16 years** (adjusted OR: 0.72, 95% CI: 0.56-0.94; p=0.0155), **but not in critically ill children**
    - **NAI treatment vs no treatment was not associated with mortality reduction in children aged <16 years** (adjusted OR: 0.82, 95% CI: 0.58-1.17; p=0.28)
      [note that death is a rare outcome in children hospitalized with influenza]

Muthuri Lancet Resp Med 2014

CDC Antiviral Treatment Recommendations

- **Focused on prompt treatment of persons with severe disease and those at increased risk of influenza complications**
- **Antiviral treatment is *recommended as soon as possible*** for **any patient with confirmed or suspected influenza who is:**
  - **Hospitalized** (without waiting for testing results)
  - **Outpatients with complicated or progressive illness of any duration**
  - **Outpatients who are at high risk for influenza complications**
- 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)

https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

Oseltamivir Recommended for Hospitalized Patients

- **Oseltamivir treatment (oral or enterically-administered) is recommended as soon as possible for hospitalized patients with confirmed or suspected influenza** (without waiting for testing results)
  - Inhaled zanamivir and oral baloxavir are ***not recommended*** because of the lack of data in hospitalized influenza patients
  - Insufficient data for peramivir treatment of hospitalized influenza patients
    - For patients who cannot tolerate or absorb oral or enterically-administered oseltamivir (e.g. gastric stasis, malabsorption, or gastrointestinal bleeding), intravenous peramivir is an option
  - Optimal duration of oseltamivir treatment for critically ill patients is unclear

Recommended Antiviral Treatment for Outpatients

- **For outpatients with complications or progressive disease and suspected or confirmed influenza (e.g., pneumonia, or exacerbation of underlying chronic medical conditions), antiviral treatment with oral oseltamivir is recommended as soon as possible.**
- **For outpatients with suspected or confirmed uncomplicated influenza, oral oseltamivir, inhaled zanamivir, intravenous peramivir, or oral baloxavir may be used for early treatment, depending upon approved age groups and contraindications.**
  - In one randomized controlled trial, baloxavir had greater efficacy than oseltamivir in high-risk adolescents and adults with influenza B virus infection
- **Clinicians can consider starting early (≤48 hours after illness onset) empiric antiviral treatment of non-high-risk outpatients with suspected influenza [e.g., influenza-like illness (fever with either cough or sore throat)], based upon clinical judgement, including without an office visit. SARS-CoV-2 and other etiologies of influenza-like illness should also be considered.**

Ison Lancet Infect Dis 2020

Special Groups

- **Pregnant women**
  - **For treatment of pregnant women or women who are up to 2 weeks postpartum, oral oseltamivir is preferred**
    - **Baloxavir is *not* recommended** for treatment of pregnant women or breastfeeding mothers
      - No efficacy or safety data for baloxavir in pregnant women or lactating women
- **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 are recommended to reduce nosocomial transmission risk
  - **Neuraminidase inhibitor treatment is recommended**
  - **Baloxavir treatment is *not* recommended**

https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

Antiviral Chemoprophylaxis

- **Antiviral chemoprophylaxis of influenza is generally not recommended for widespread or routine use except for control of institutional influenza outbreaks or in special populations**
- Can be considered:
  - Longer-term: Persons at very high risk for developing complications and for whom influenza vaccination is contraindicated, unavailable, or expected to have low effectiveness (e.g. severely immunocompromised persons)
  - Short-term (2 weeks): High-risk persons receiving influenza vaccination in whom vaccination is expected to be effective
  - ➢ Persons receiving antiviral chemoprophylaxis should seek medical evaluation promptly if they develop illness consistent with influenza

IDSA 2018 Influenza Clinical Practice Guidelines Clinical Infect Dis 2019; https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

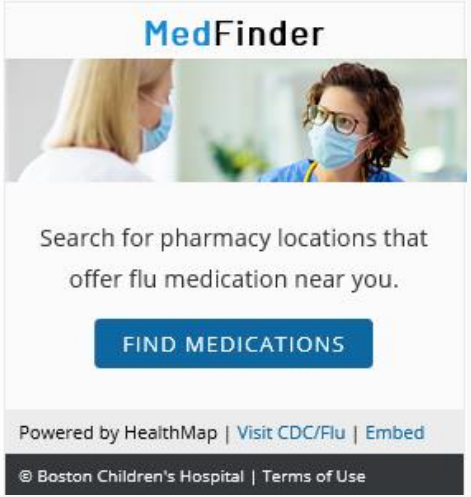
Summary

- CDC influenza testing and treatment recommendations when influenza viruses are circulating in the community are similar to those before emergence of SARS-CoV-2
- Influenza nucleic acid detection testing (molecular assay) is recommended for patients being hospitalized and can help guide treatment decisions in outpatients during influenza season
- Antiviral treatment is recommended as soon as possible for hospitalized patients with suspected influenza without waiting for influenza testing results
- Antiviral treatment is recommended as soon as possible for outpatients with progressive disease regardless of illness duration and in persons at high-risk for influenza complications
  - Can be clinically-diagnosed with influenza (empiric treatment) or patients with a positive influenza test result if timely results are available on-site
- During community co-circulation of influenza viruses and SARS-CoV-2, clinicians should consider the possibility of either influenza virus infection, SARS-CoV-2 infection, and influenza and SARS-CoV-2 viral co-infection in persons presenting with acute respiratory illness

➢ Reminder: the best way to prevent influenza is through annual influenza vaccination!

Antiviral Resources

- Treatment and Clinical Guidance
  - https://www.cdc.gov/flu/professionals/antivirals/index.htm
  - Updated recommendations for treating influenza during SARS-CoV-2 co-circulation
  - Outbreak management guidance for state/local health department response
    - Cohorting and infection control
    - Antiviral treatment and chemoprophylaxis
    - Vaccination as appropriate
- Antiviral Medicine Tool MedFinder: free, online service to search for pharmacy locations that offer anti-influenza drugs
- Antiviral Monitoring: Trends in drug availability and use are monitored using manufacturer and pharmacy supply and dispensing data
  - Expected 10 M doses available by season start



Additional CDC Influenza Resources

- CDC Influenza homepage: https://www.cdc.gov/flu/
- Influenza surveillance (FluView and FluView Interactive):
  - https://www.cdc.gov/flu/weekly/fluactivitysurv.htm
  - https://www.cdc.gov/flu/weekly/fluviewinteractive.htm
- For Professionals:
  - https://www.cdc.gov/flu/professionals/index.htm
  - 2020-2021 ACIP Influenza Recommendations: https://www.cdc.gov/mmwr/volumes/69/rr/rr6908a1.htm
  - Vaccination homepage: https://www.cdc.gov/flu/professionals/vaccination/index.htm
  - Influenza testing homepage: https://www.cdc.gov/flu/professionals/diagnosis/index.htm
  - Diagnosis homepage: https://www.cdc.gov/flu/professionals/diagnosis/index.htm
  - Antiviral homepage: https://www.cdc.gov/flu/professionals/antivirals/index.htm

To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button.
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All continuing education for COCA Calls is issued online through the CDC Training & Continuing Education Online system at https://tceols.cdc.gov/

Those who participate in today's COCA Call and wish to receive continuing education please complete the online evaluation by **October 19, 2020,** with the course code **WC2922-091720**. The access code is **COCA091720.** Those who will participate in the on-demand activity and wish to receive continuing education should complete the online evaluation between **October 20, 2020,** and **October 20, 2022,** and use course code **WD2922-091720**. The access code is **COCA091720.**

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Today's COCA Call Will Be Available On-Demand

- **When:** A few hours after the live call
- **What:** Video recording
- **Where:** On the COCA Call webpage at https://emergency.cdc.gov/coca/calls/2020/callinfo_091720.asp

Upcoming COCA Calls

- **When:** Thursday, October 8 at 2 PM EDT
  Topic: Recommendations for Influenza Prevention and Treatment in Children: An Update for Pediatric Providers

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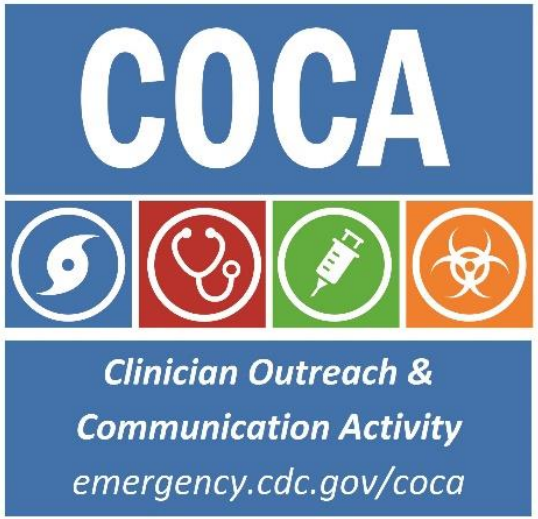

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