COCA Call Information

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- **Webinar ID: 772 478 726**
- **All questions for the Q&A portion must be submitted through the webinar system.**
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Update on the 2017-2018 Influenza Season for Clinicians

Clinician Outreach and Communication Activity (COCA) Webinar

February 8, 2018

Continuing Education for COCA Calls

All continuing education (CME, CNE, CEU, CECH, ACPE, CPH, and AAVSB/RACE) for COCA Calls are issued online through the CDC Training & Continuing Education Online system (http://www.cdc.gov/TCEOnline/).

Those who participated in today's COCA Call and who wish to receive continuing education should complete the online evaluation by March 8, 2018 with the course code WC2922.

Those who will participate in the on demand activity and wish to receive continuing education should complete the online evaluation between March 8, 2018 and March 8, 2020 will use course code WD2922.

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Continuing Education Disclaimer

- In compliance with continuing education requirements, CDC, our planners, our presenters, and their spouses/partners wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters.
- Planners have reviewed content to ensure there is no bias. Content will not include any discussion of the unlabeled use of a product or a product under investigational use with the exception of Dr. Uyeki's discussion of oseltamivir antiviral treatment. He will be discussing that CDC recommends oseltamivir antiviral treatment for patients of all ages, and for hospitalized influenza patients.
- CDC did not accept commercial support for this continuing education activity.

To Ask a Question

- **Using the Webinar System**
  - Click the **Q&A** button in the webinar
  - Type your question in the **Q&A** box
  - Submit your question
- **For media questions, please contact CDC Media Relations at 404-639-3286 or send an email to media@cdc.gov.**
- **If you are a patient, please refer your questions to your healthcare provider.**

At the conclusion of the session, participants will be able to accomplish the following:

- **Explain the current status of influenza activity in the United States.**
- **Identify available influenza tests.**
- **List complications associated with influenza.**
- **Describe antiviral treatment recommendations for influenza patients.**

Today's First Presenter

Alicia P. Budd, MPH
Epidemiologist
Influenza Division
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

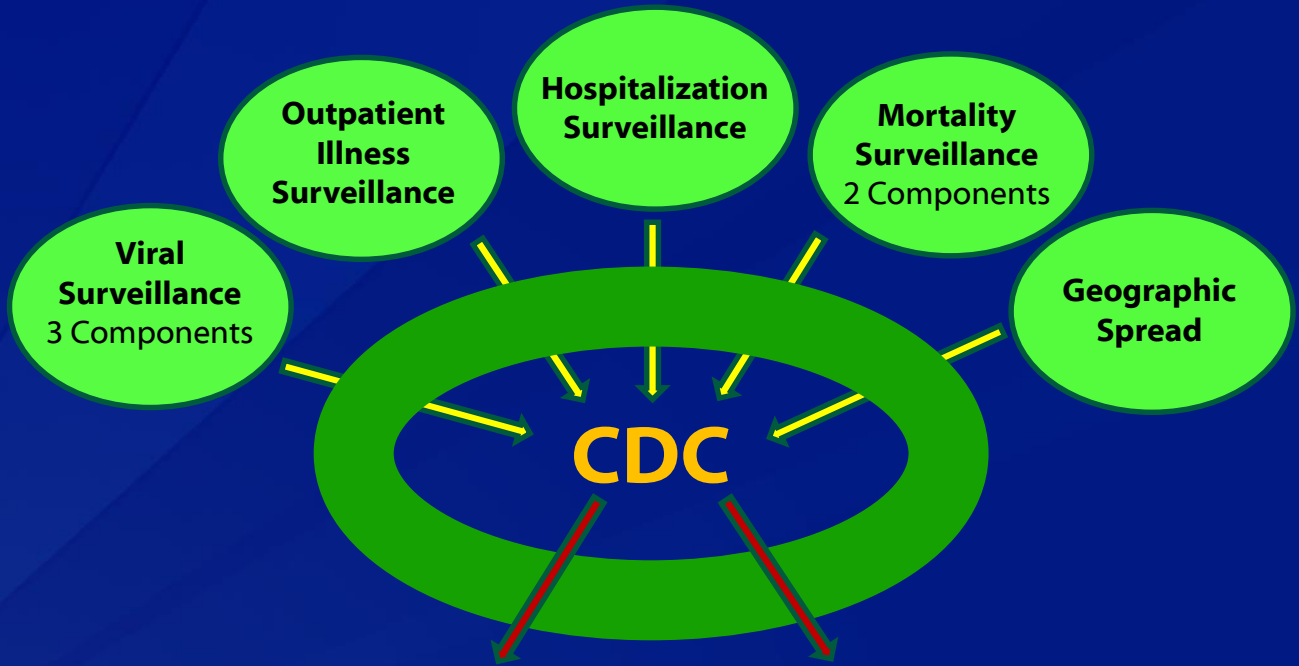
Today's Second Presenter

Tim Uyeki MD, MPH, MPP
Chief Medical Officer
Influenza Division
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

2017-2018 INFLUENZA SEASON
UNITED STATES

ACTIVITY THROUGH JANUARY 27, 2018

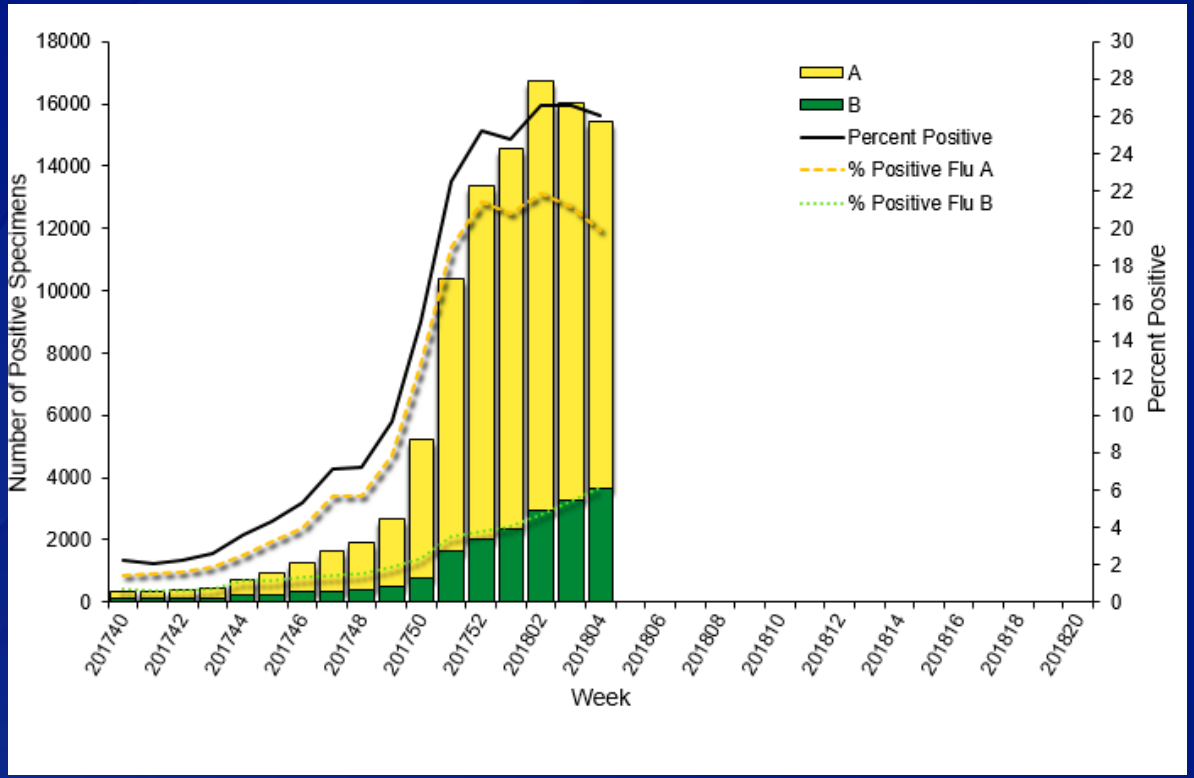
U.S. Influenza Surveillance System



U.S. Influenza Surveillance Reports

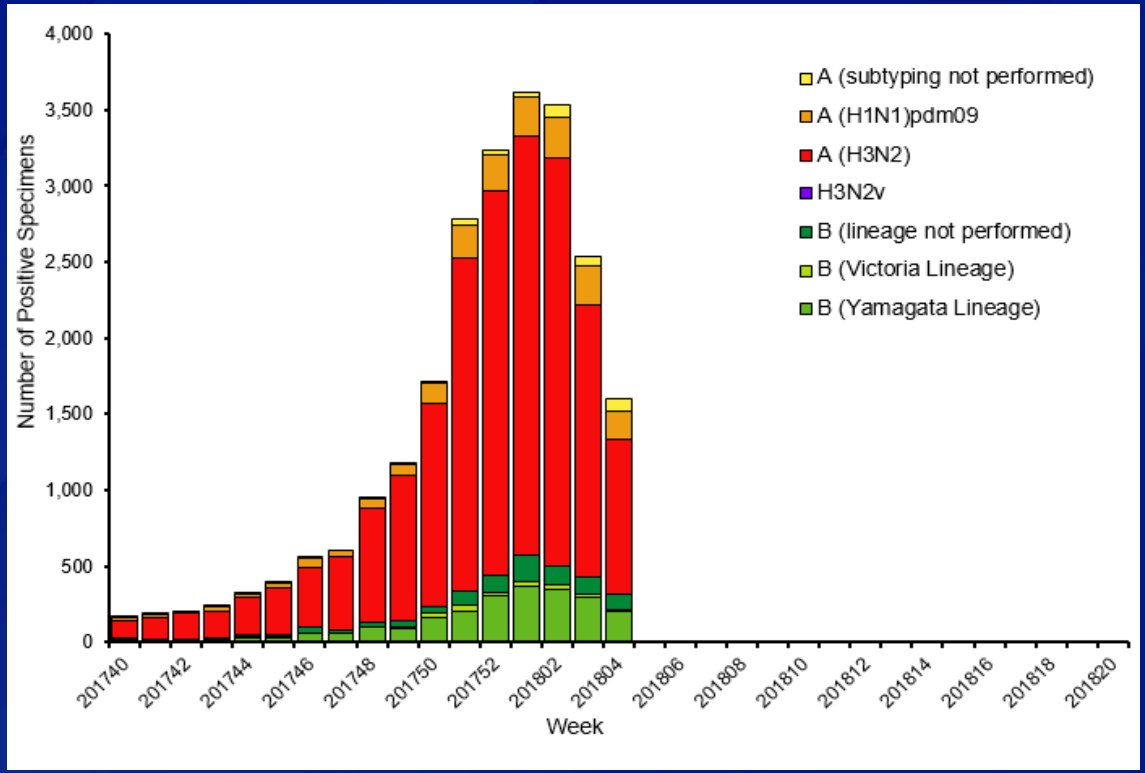
https://www.cdc.gov/flu/weekly/fluactivitysurv.htm

Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories, 2017-2018 Season*



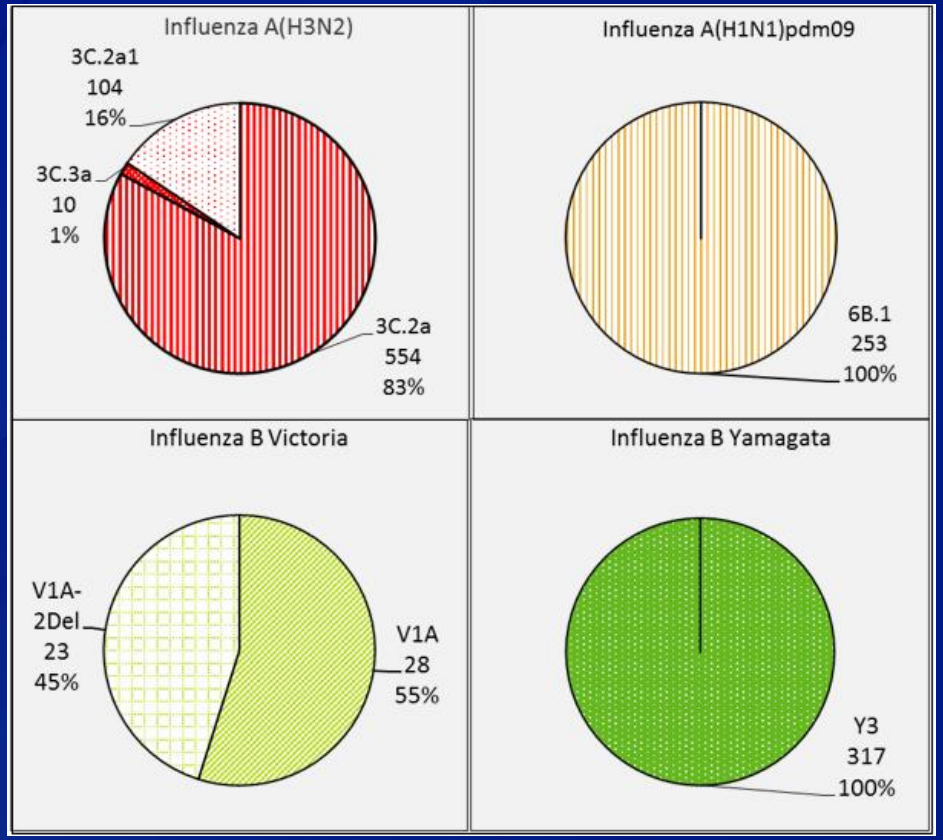
* As of February 2, 2018

Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, 2017-2018 Season*

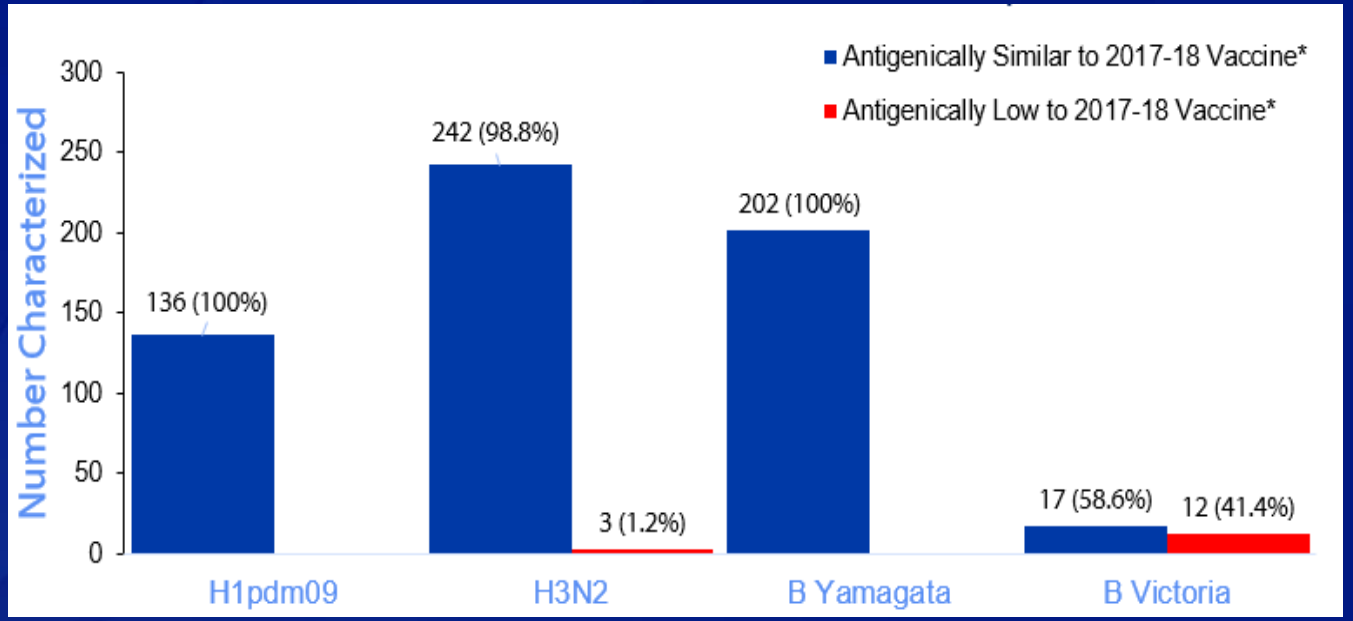


* As of February 2, 2018

Genetic Characterization of U.S. Viruses Collected October 1, 2017 to present



Antigenic Characterization of U.S. Viruses Collected October 1, 2017 to present



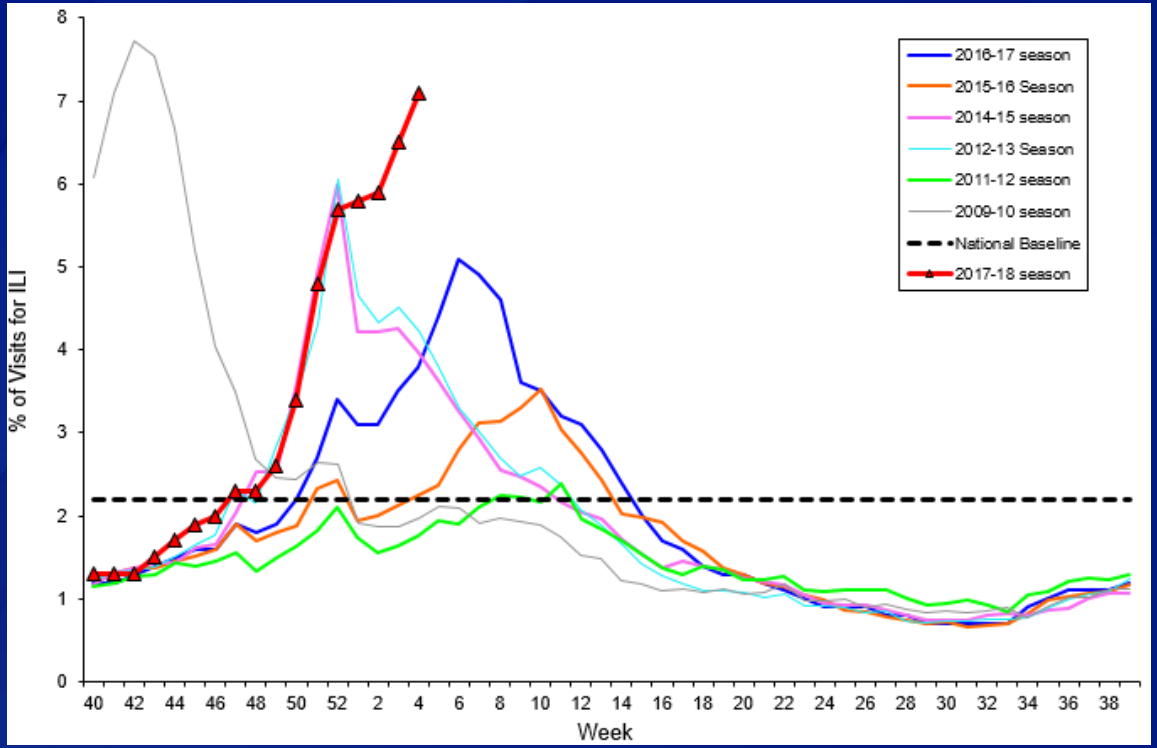
*Against reference viruses representing NH 2017-2018 vaccine component
A(H1N1)pdm09 - A/Michigan/45/2015
A(H3N2) – A/Hong Kong/4801/2014
B/Yam - B/Phuket/3073/2013
B/Vic – B/Brisbane/60/2008

Novel Influenza A Virus Infection: United States, 2017-18 Season*

- **Human infection with an influenza A virus that is different from currently circulating human seasonal viruses**
- **Five occurring this season**
  - States reporting - CO, IA (2), MI, NE
  - Viruses - H3N2v (3), H1N1v, H1N2v
  - Level of care sought
    - Two hospitalized, 3 outpatient/emergency department
    - All fully recovered
  - Exposure
    - Swine (3)
    - Swine and household member with confirmed H3N2v
    - Household member had exposure to swine
  - No ongoing human-to-human transmission

* As of February 2, 2018

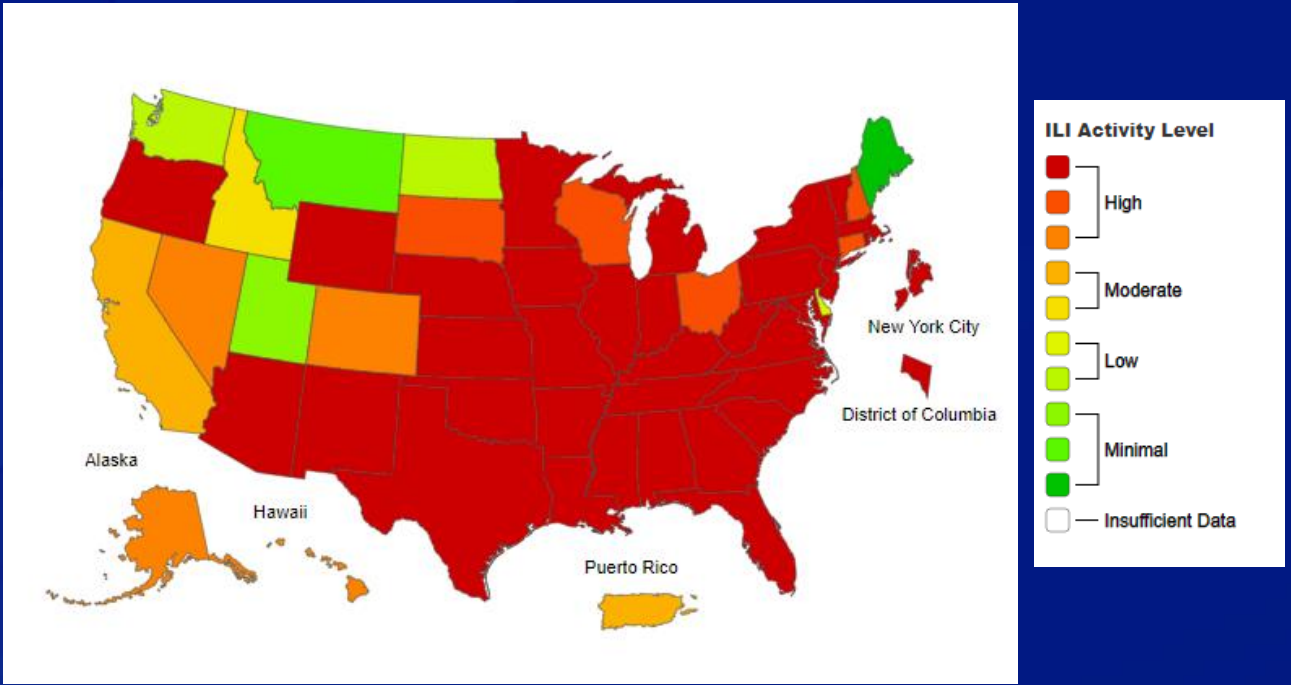
Percentage of Visits for Influenza-like Illness (ILI) Reported by the U.S. Outpatient ILI Surveillance Network (ILINET), 2017-2018* and Selected Previous Seasons



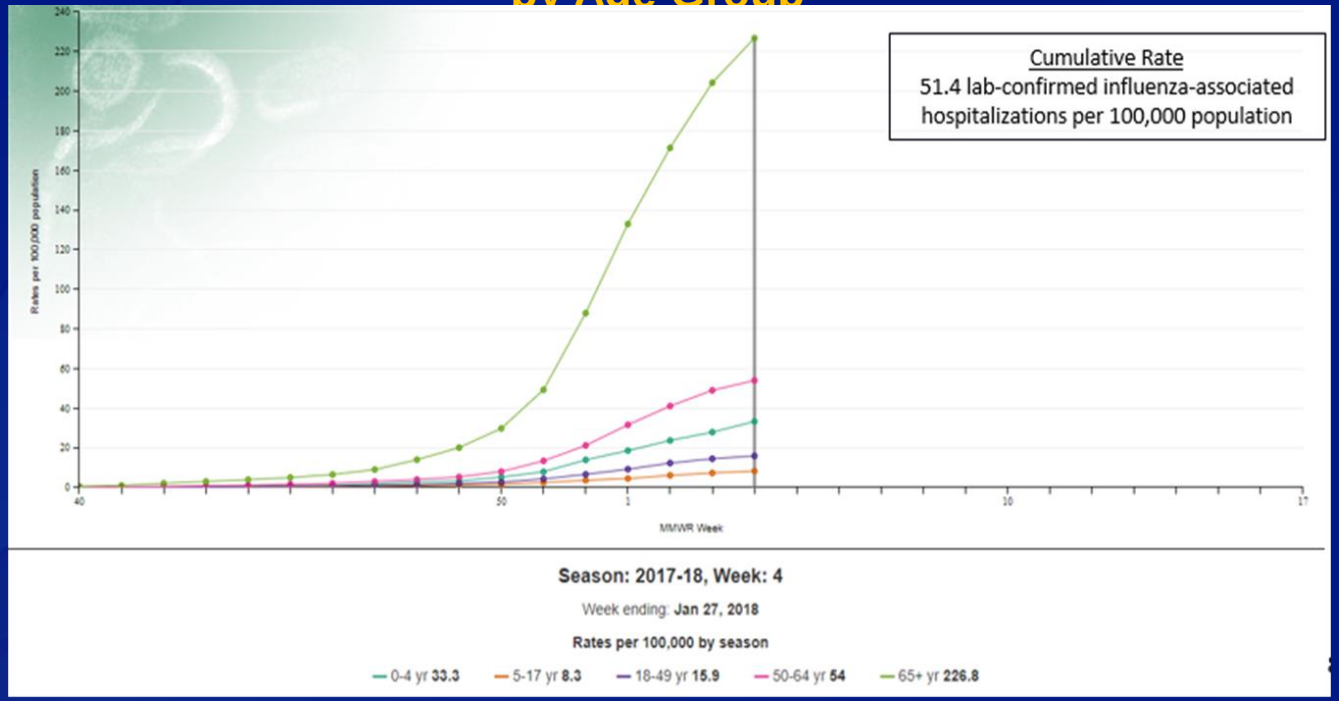
* As of February 2, 2018

Influenza-Like Illness (ILI) Activity Level Indicator Determined by Data Reported to ILINET,

Week Ending January 27, 2018

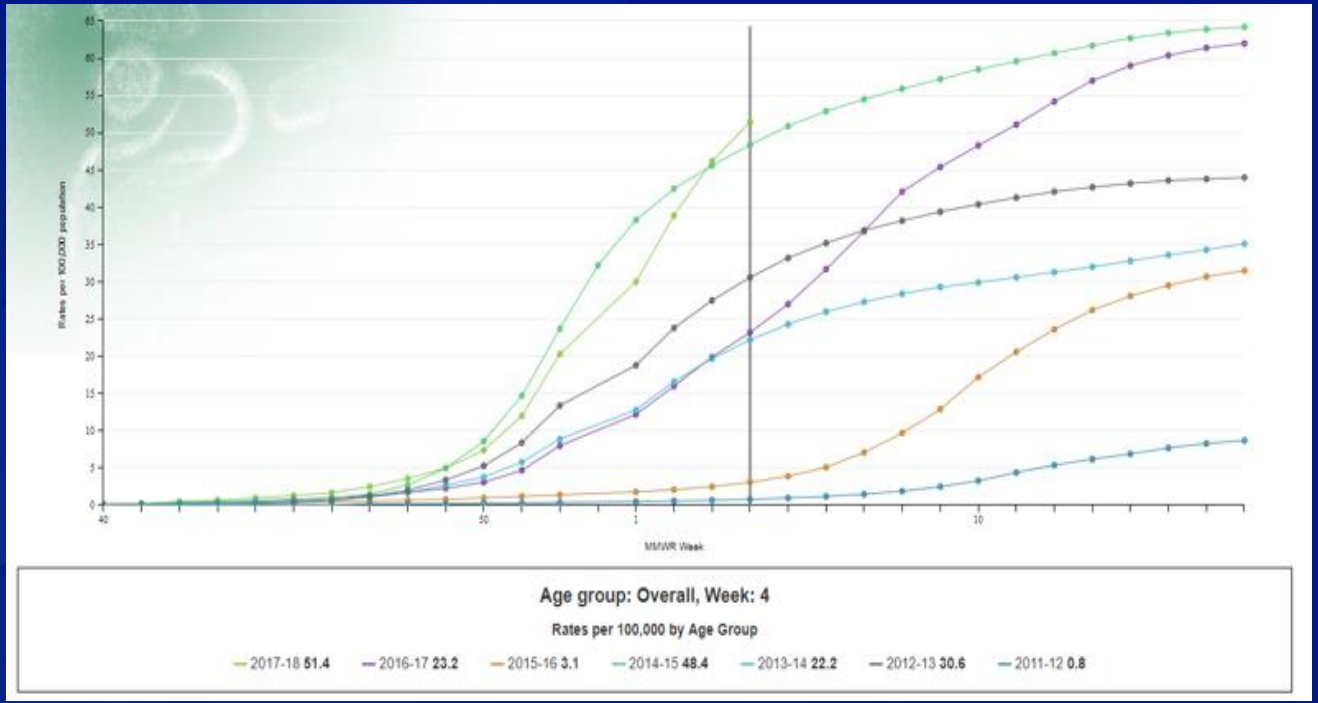


Laboratory-Confirmed Influenza-Associated Hospitalizations
Preliminary* Cumulative Rates for 2017-2018 Season, by Age Group



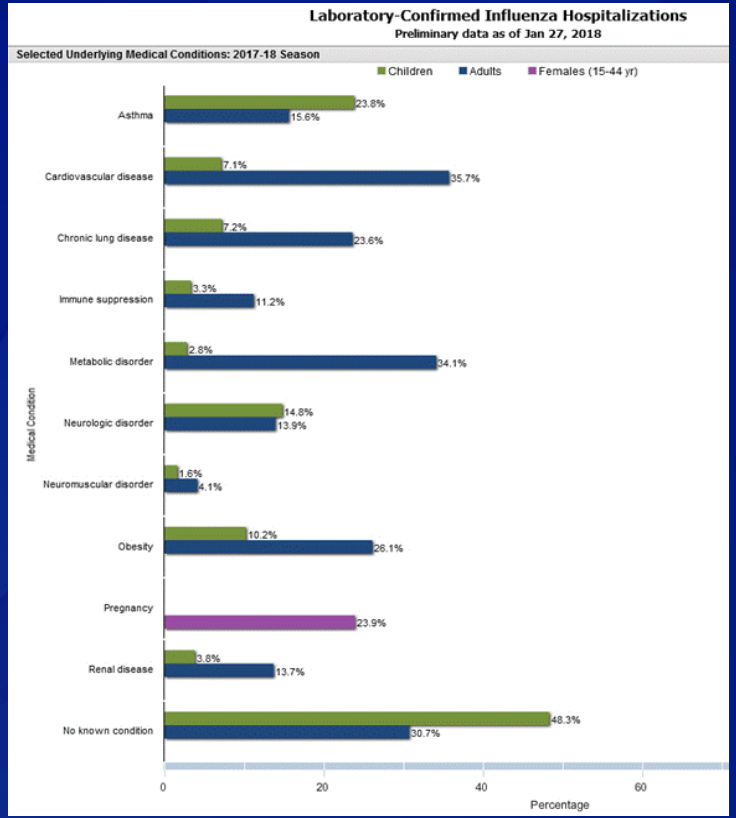
* As of February 2, 2018

Laboratory-Confirmed Influenza-Associated Hospitalizations, 2017-2018* and Selected Previous Seasons



* As of February 2, 2018

Laboratory-Confirmed Influenza-Associated Hospitalizations, Selected Underlying Medical Conditions, 2017-2018 Season*



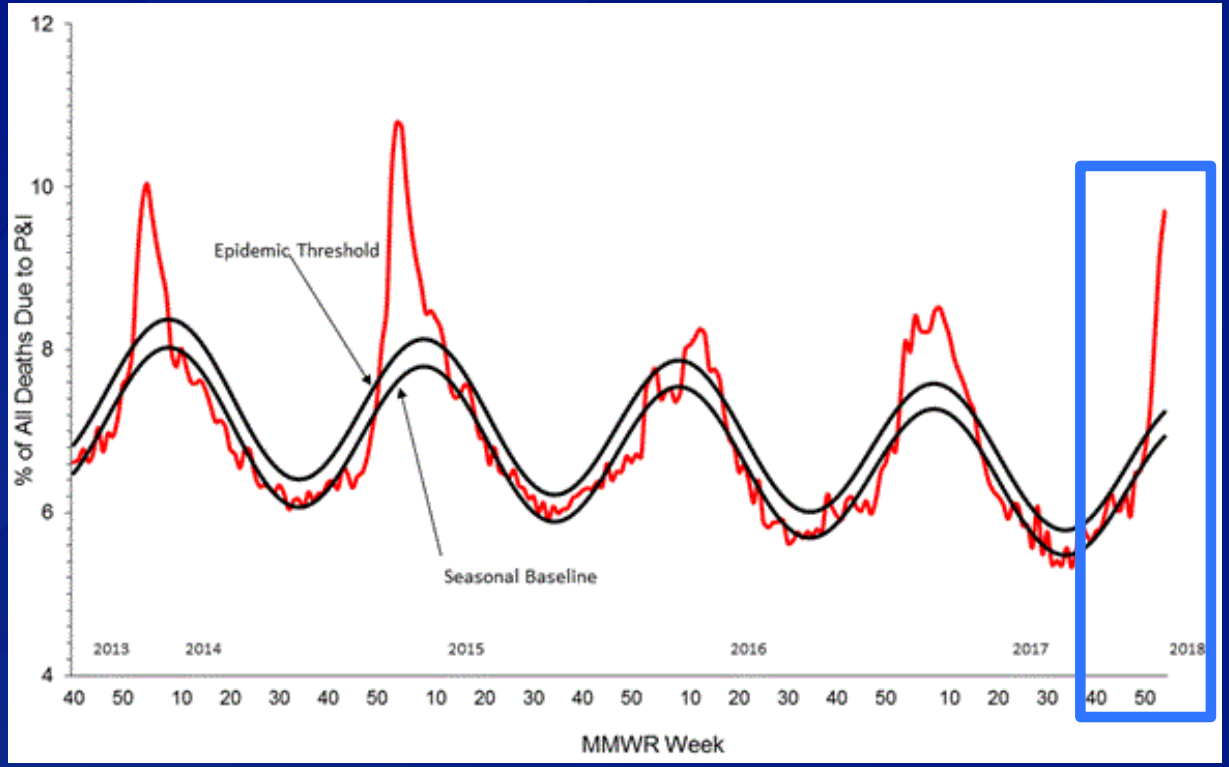
Any Reported Underlying Condition

- **69% of adults**
- **52% of children**

* As of February 2, 2018

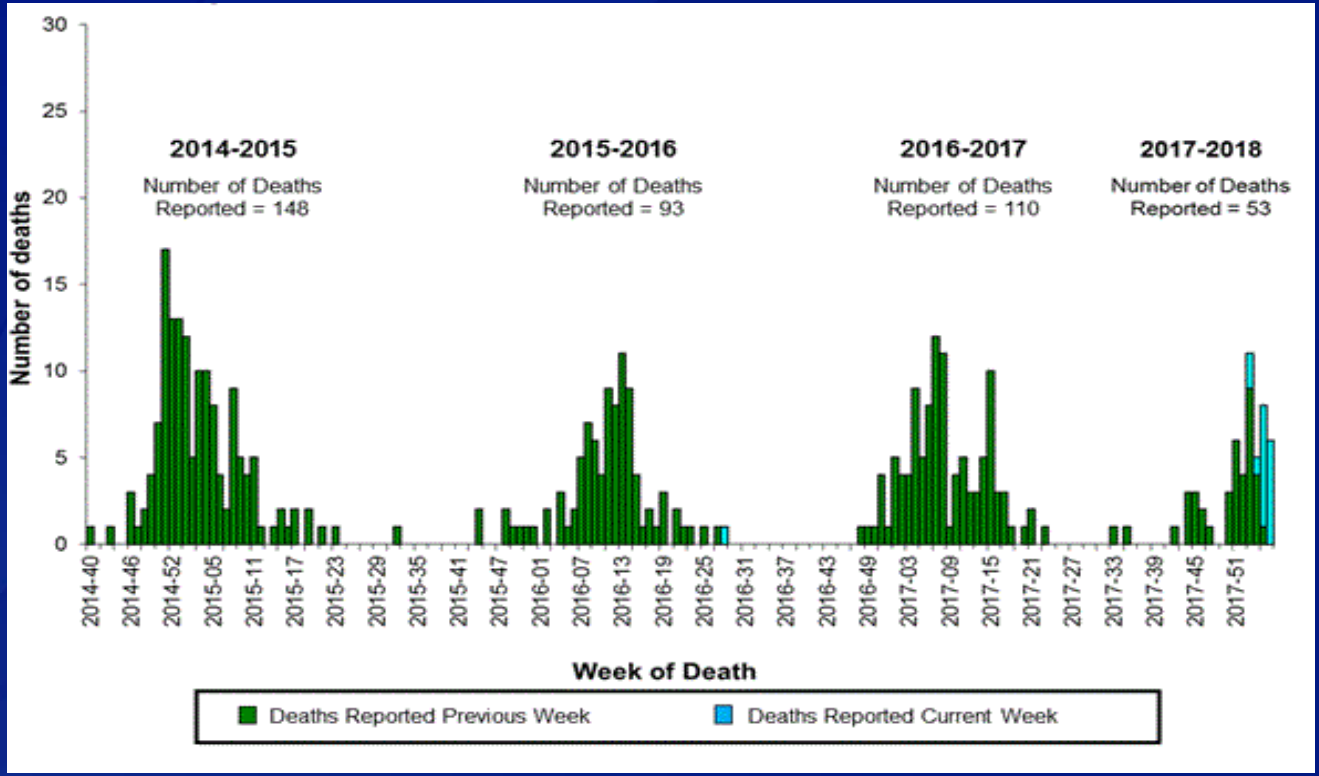
Pneumonia and Influenza Mortality from the National Center for Health Statistics Mortality Surveillance System

Data through the week ending January 13, 2018*

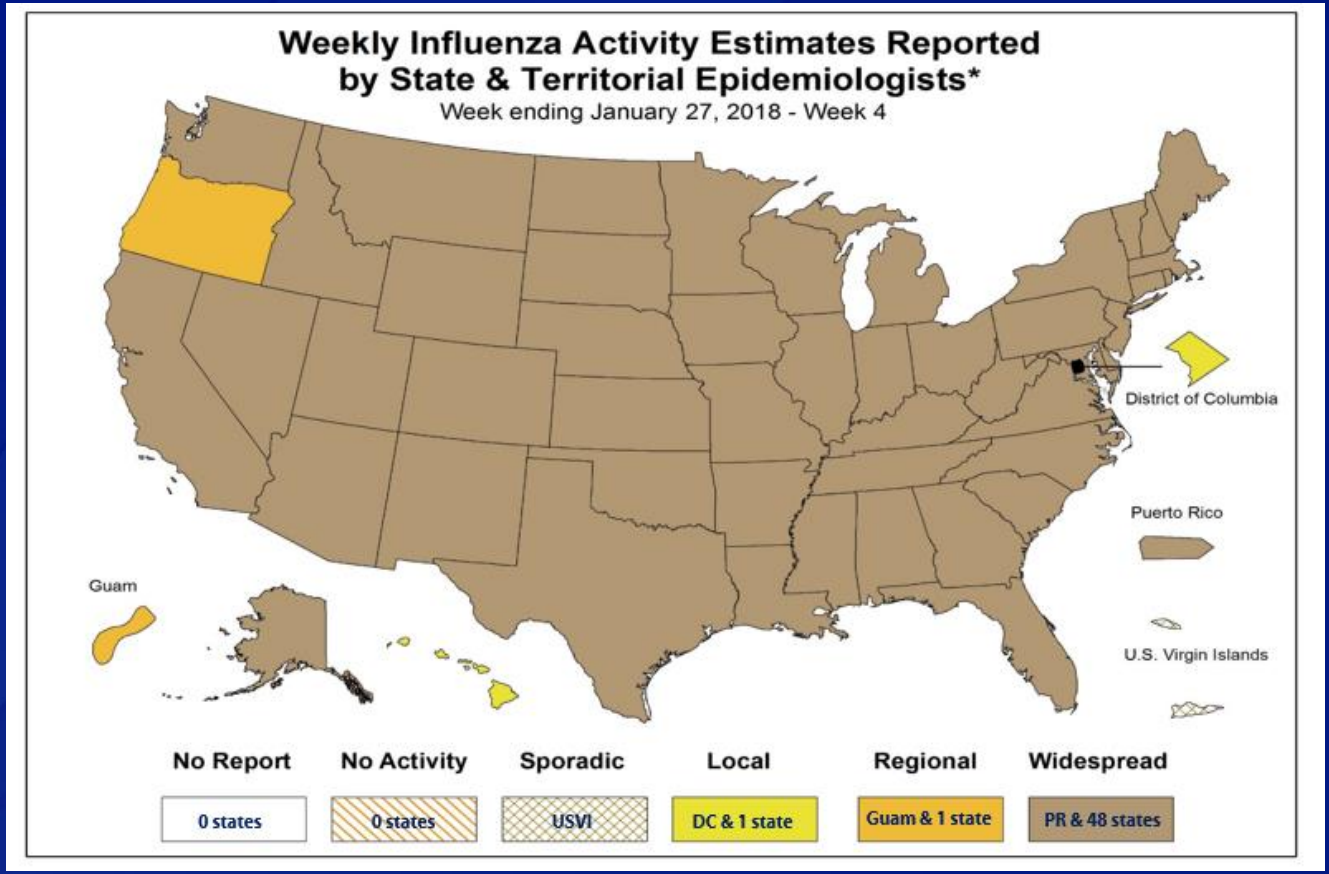


* As of February 2, 2018

Influenza-Associated Pediatric Deaths, by Week of Death: 2014-2015 season to present*



* As of February 2, 2018


Weekly Influenza Activity Estimates Reported by State & Territorial Epidemiologists*
Week ending January 27, 2018 - Week 4
District of Columbia
Puerto Rico
U.S. Virgin Islands
Guam
No Report
No Activity
Sporadic
Local
Regional
Widespread
0 states
0 states
USVI
DC & 1 state
Guam & 1 state
PR & 48 states

Summary: 2017-2018 Influenza Season*

- **Activity began to increase at the beginning of November and remains elevated through late January.**
- **Influenza A(H3N2) viruses are the most frequently identified viruses so far this season; A(H1N1)pdm09 and B viruses are also circulating.**
- **It's not possible to know yet how severe this season will be but several indicators are as high or higher than what was seen in the 2014-15 season, a high severity A(H3N2) predominant season.**
  - H3N2 predominant seasons are often associated with higher mortality and hospitalization rates among older adults and young children.
  - Flu activity indicators are notable for the high levels of activity occurring nearly simultaneously across the country for several weeks.
  - Outpatient ILI levels are the highest seen since the pandemic.
  - Hospitalization rates have surpassed what was reported during the same week of the 2014-15 season.

* As of February 2, 2018

UPDATE ON INFLUENZA FOR CLINICIANS

FEBRUARY 8, 2018

Viral Shedding (Upper Respiratory Tract)

- **Influenza viruses infect epithelial cells of the upper respiratory tract**
- Incubation period: typically 2-3 days (1-4 days)
- Viral shedding can begin 1 day before illness onset
- Peak viral shedding occurs on Day 1 of illness
- Duration/contagious period
  - Most contagious within 3 days of illness onset
  - Adults may shed viruses for 4-6 days
  - Young children may shed for longer periods
  - Immunocompromised can shed for prolonged periods
    - May be asymptomatic with prolonged viral replication
    - Antiviral resistant virus strains can evolve during/after antiviral treatment

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Pathogenesis

- Depends upon viral and host factors (age, immune function, underlying conditions)
- Influenza virus infection of the respiratory tract stimulates the host immune response
  - Innate and adaptive immune response triggered
    - Some people can experience an exaggerated inflammatory response
      - Pro-inflammatory & antiviral effects; apoptosis
      - Cytokine dysregulation can result in tissue inflammation and damage
      - Pulmonary & extra-pulmonary injury, necrosis
- Influenza viremia very rarely detected
- Invasive bacterial co-infection can cause severe disease

Spectrum of influenza virus infection

- **Wide spectrum of illness**
  - Disease severity and clinical manifestations can vary by age, host factors, immunity, virus strain
    - Asymptomatic infection, Uncomplicated illness, Complications
- **Most symptomatic persons experience mild illness**
  - Uncomplicated influenza (with or without fever), self-limited
    - Estimated 8% of U.S. population symptomatic each season (2010-2016)
- **Wide range of complications**
  - Moderate to critical illness can occur
    - ➢ Certain persons are at higher risk of complications from influenza
    - ➢ Can occur in otherwise healthy persons of any age

Tokars Clin Infect Disease 2018

High-Risk Groups for Influenza Complications (U.S.)

- **Adults aged ≥65 years**
- **Young children aged <2 years**
- **Persons with certain chronic medical conditions**
  - **Heart or lung disease, including asthma**
  - **Metabolic disease, including diabetes**
  - **HIV/AIDs, other immunosuppression**
  - **Conditions that can compromise respiratory function or the handling of respiratory secretions**
  - **Neurological and neurodevelopmental conditions** [including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy (seizure disorders), stroke, intellectual disability (mental retardation), moderate to severe developmental delay, muscular dystrophy, or spinal cord injury].
  - **Morbid obesity**
- **Pregnant women**
- **Nursing home residents**
- **American Indian or Alaskan Native**

https://www.cdc.gov/flu/about/disease/high_risk.htm

Uncomplicated influenza

- **Upper respiratory tract illness: usually sudden onset**
  - **With or without fever**, headache, sore throat, nasal congestion, non-productive cough, muscle aches (@4-7 days)
  - Signs and symptoms vary with age and host factors
    - Infants may have high fever, irritability, with or without respiratory symptoms
    - Diarrhea can occur in young children
    - Elderly and immunosuppressed persons may not have fever
    - Elderly may have malaise, fatigue, prolonged cough for several weeks

Influenza Complications

- **Moderate:** otitis media in young children, sinusitis; exacerbation of chronic disease (all ages)
- **Severe:**
  - **Exacerbation of chronic disease** (e.g. pulmonary, cardiac)
  - **Respiratory**: pneumonia, croup, bronchiolitis, status asthmaticus, tracheitis, viral pneumonitis, respiratory failure, ARDS
  - **Cardiac:** myocarditis, pericarditis, heart failure, myocardial infarction
  - **Neurologic:** encephalopathy & encephalitis, cerebrovascular accident, GBS, Acute Disseminated Encephalomyelitis (ADEM), Reye's syndrome
  - **Bacterial co-infection:** invasive bacterial infection (pneumonia)
  - **Musculoskeletal:** myositis, rhabdomyolysis
  - **Sepsis, multi-organ failure** (respiratory failure, renal failure, septic shock)

Sellers Influenza Other Resp Viruses 2017, Kwong NEJM 2018

Bacterial Complications of Influenza

- ***Secondary invasive bacterial co-infection***
  - May occur after 1-2 days of influenza onset or later
  - Can progress rapidly to critical illness, death
    - *Staphylococcus aureus (MSSA, MRSA)*
    - *Streptococcus pneumoniae*
    - *Group A Strept* (*Streptococcus pyogenes*)
  - ➢ Bacterial pneumonia in otherwise healthy persons, chronically ill
  - ➢ Bacteremia and septic shock
  - ➢ Bacterial meningitis can occur
    - ➢ *Streptococcus pneumoniae*
    - ➢ *Neisseria meningitidis*

Complications of Influenza: Pneumonia

- ***Primary influenza viral pneumonia (all ages)***
  - Influenza virus infection of lower respiratory tract tissues
    - Can trigger cytokine dysregulation ("cytokine storm") and result in acute lung injury, diffuse alveolar damage
    - May progress rapidly to respiratory failure, acute respiratory distress syndrome (ARDS), and refractory hypoxemia
  - More common in elderly, immunosuppressed patients
  - Young and middle-aged adults: influenza A(H1N1)pdm09 virus infection

Influenza A(H1N1)pdm09 Radiographic Findings

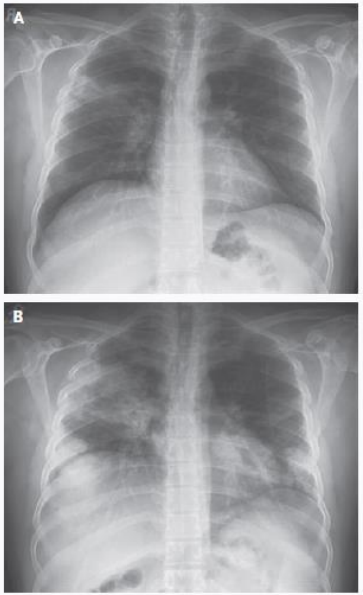


Figure 1. Chest Radiographs.

A chest radiograph obtained at the other hospital 3 days before admission to this hospital (Panel A) shows consolidation in the right upper lobe. A radiograph obtained 2 days later (Panel B) shows progression of the consolidation in the right upper lobe and new air-space opacities in multiple lobes.

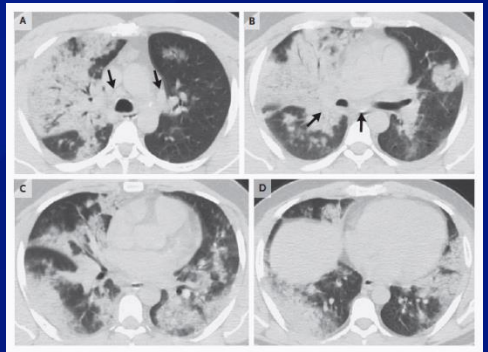


Figure 2. CT Scans Obtained on Admission to this Hospital.

Lung windows from axial CT of the chest performed without contrast material show bilateral multifocal consolidation (Panels A through D) and paratracheal, prevascular, hilar, and subcarinal lymphadenopathy (arrows).

29-yo previously well non obese male with fever and progressive respiratory distress, developed respiratory failure, multi-organ failure, ARDS, died

23-yo obese female with respiratory failure at Day 10 of illness, survived

Uyeki NEJM 2009; Hui CHEST 2009

Influenza and Sepsis

- **Influenza virus infection can trigger life-threatening sepsis**
  - Respiratory tract infection triggers abnormal host inflammatory response
    - Cytokine dysregulation
  - ➢ Onset and progression can be rapid (including in previously healthy persons)
    - Can result in tissue damage, organ dysfunction and failure, death
    - Viral pneumonia, respiratory failure, ARDS, septic shock, multi-organ failure
- **Secondary invasive bacterial co-infection can trigger sepsis**
  - Can occur shortly after influenza onset, or after initial improvement
  - ➢ Can cause fulminant progression to critical illness and death in previously healthy children and adults
    - Bacterial pneumonia progressing to respiratory failure, septic shock, multi-organ failure, death

https://www.cdc.gov/sepsis

Neurologic Complications

- **Wide spectrum of neurologic manifestations associated with influenza** *(simple febrile seizures to transient encephalopathy to fulminant brain death)*
- **Severe complications**
  - Encephalopathy >24 hours (with or without cerebral edema)
    - High fever, seizures, altered mental status, confusion, hallucinations, abnormal behavior
    - Acute necrotizing encephalopathy/encephalitis (inflammatory, cytokine dysregulation)
      - Rapid progression to coma, survivors with neurologic sequelae, high mortality
  - Cerebral vascular accident
  - Sub-arachnoid hemorrhage
  - Reye's syndrome (elevated NH_3 & transaminases, hypoglycemia, altered mental status)
  - Acute Disseminated Encephalomyelitis (ADEM)
  - Transverse myelitis
  - Guillian Barre Syndrome

Mitzuguchi Inf Other Resp Vivurs 2013; Morishima Clin Infect Dis 2002; Sellers Inf Other Resp Viruses 2017

Acute Influenza Encephalopathy

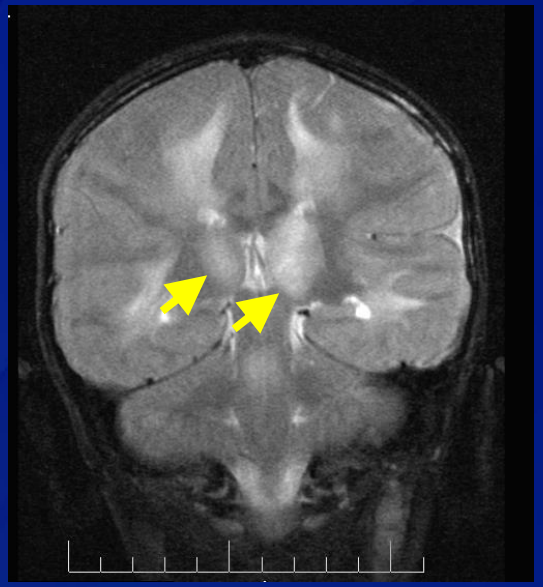


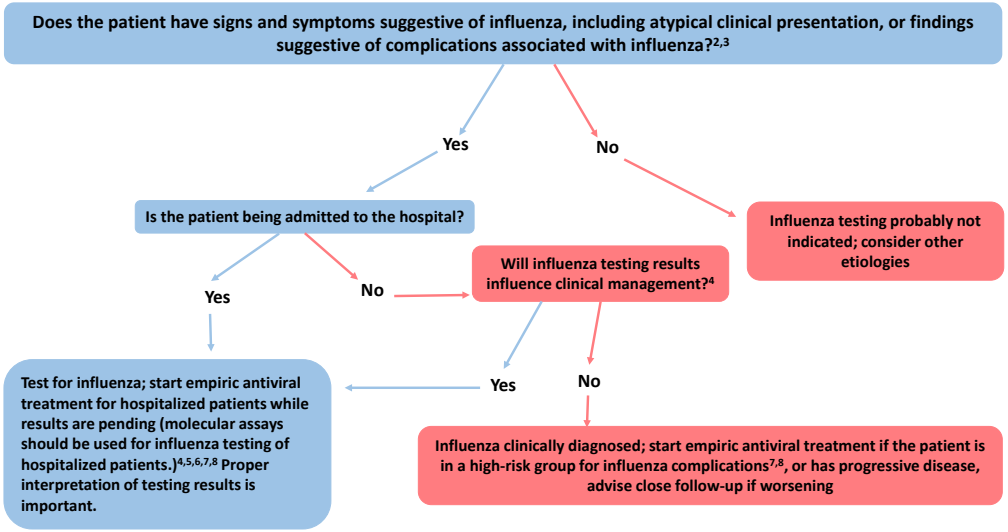
Figure 3: Coronal T2-weighted magnetic resonance image of a previously healthy 5-year-old patient with fulminant progression of acute necrotizing encephalopathy associated with influenza, displaying bilateral confluent signal hyperintensity in the thalami (arrows) and white matter.

(Fatal pediatric case from Michigan, 2003)

CDC, unpublished data

Influenza Testing (all hospitalized patients, consider outpts)

Figure: Guide for considering influenza testing when influenza viruses are circulating in the community (regardless of influenza vaccination history)[1]



Respiratory Specimen Collection

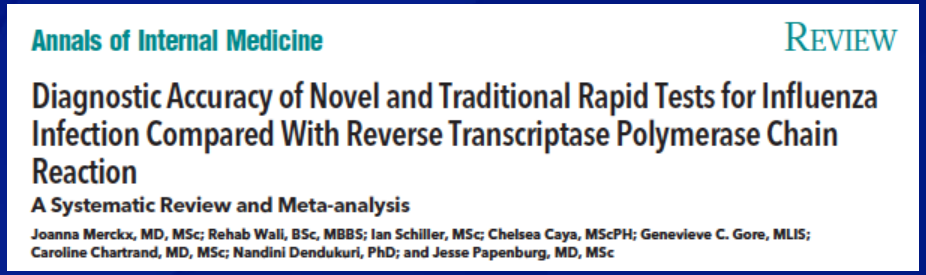
- **Collect timely respiratory specimens from immunocompetent patients (<3-4 days from illness onset)**
  - Influenza viruses primarily infect epithelial cells of the upper respiratory tract
    - Viral shedding declines substantially after about 3-4 days
    - Prolonged viral replication in young infants, immunosuppressed, critically ill
- **Collect optimal respiratory specimens (refer to manufacture's package insert)**
  - Upper respiratory tract (nasopharyngeal > nasal > throat)
  - Lower respiratory tract (hospitalized patients)
    - Critically ill patients (may detect when viral shedding is not detectable in the upper respiratory tract)
- **Proper interpretation of testing results**
  - **Consider false negative results**
    - Importance of predictive values in the context of influenza activity in the patient population tested (sensitivity and specificity are fixed test parameters; prevalence varies)

Influenza Tests Available for Clinicians

- **Molecular assays** **(high sensitivity, high specificity)**
  - Rapid molecular assays (15-30 minutes to results; some are CLIA-waived)
  - RT-PCR, nucleic acid detection assays (45-80 minutes to 4-8 hours to results)
- **Antigen detection** **(low to moderate sensitivity)**
  - Rapid influenza diagnostic tests (RIDTs) (10-15 minutes)
    - With or without analyzer device
  - Direct florescent antibody staining (2-4 hours)
    - Requires florescent microscope; one assay uses analyzer device
- **Viral culture**
  - Shell-vial (1-3 days)
  - Tissue culture, Embryonated egg culture (3-10 days)

➢ **Proper interpretation of results is important, especially negative results**

High sensitivity of rapid molecular assays



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

Pooled sensitivities to detect influenza A and B viruses versus RT-PCR (specificities >98%):

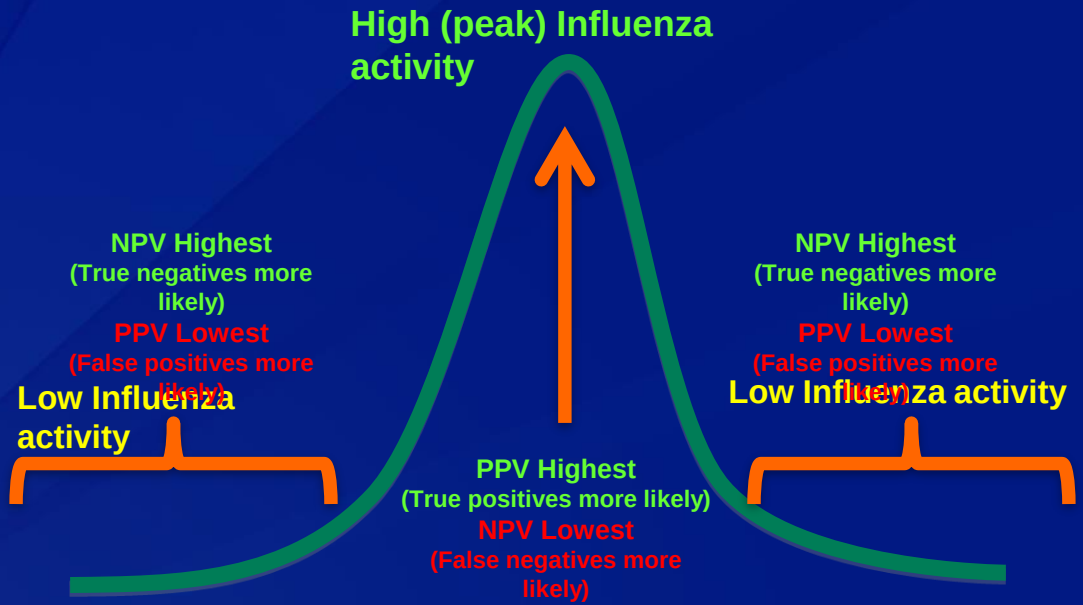
- RIDTS: sensitivity: 53-54%
- RIDTs with analyzer devices: sensitivity: 77-80%
- ➢ Rapid molecular assays: sensitivity: 92-95%

Merckx Annals of Int Med 2017

FDA re-classification of RIDTs

- FDA has re-classified RIDTs from class I to class II devices
  - Requires higher performance standards (higher sensitivity)
  - Will improve accuracy (sensitivity) of approved RIDTs
  - Some RIDTs are no longer available
    - Possible local shortages of RIDTs (increased demand)

Prevalence (Influenza Activity) and Predictive Values of RIDTs



Uyeki Textbook Ped Infect Dis 2014

Guidance on Interpretation of Influenza Testing Results

Figure: Algorithm to assist in the interpretation of influenza testing results and clinical decision-making during periods *when influenza viruses are circulating* in the community[1]

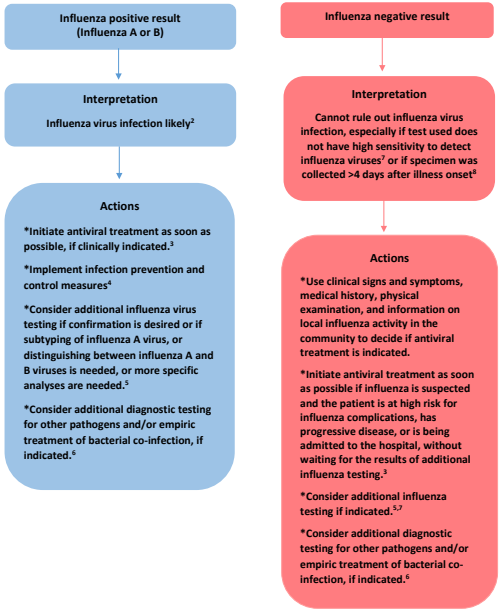


Figure: Algorithm to assist in the interpretation of influenza testing results and clinical decision-making during periods *when influenza viruses are NOT known to be circulating* in the community[1]

Influenza Tests

- **Serology**
  - **Not recommended, cannot inform clinical management**
    - Serology on a single serum specimen is uninterpretable
  - Requires paired appropriately timed acute and convalescent sera performed at specialized laboratories *(not recommended routinely)*
    - Hemagglutinin inhibition antibody (HI testing)
    - Microneutralization (MN assay)
    - No validated IgG or IgM assays
    - Investigational assays (ELISA)

Antiviral Treatment

- **One class of antivirals recommended** (very low NAI resistance in circulating viruses)
  - **Neuraminidase inhibitors** (NAIs) (block release of virus particles from infected cells):
    - Differ by approved ages, route of administration, contraindications, dosage
    - Approved for early treatment of uncomplicated influenza
  - **Oseltamivir** (oral capsules or suspension)
    - Recommended for treatment in all ages
    - Dosage based on weight and age (twice daily x 5 days)
      - Oseltamivir generic (3 manufacturers) or Tamiflu
  - **Zanamivir** (inhaled powder)
    - Recommended for treatment in ages ≥7 years (twice daily x 5 days)
      - Relenza (1 manufacturer)
  - **Peramivir** (intravenous)
    - Recommended for treatment in ages ≥2 years (single dose)
      - Rapivab (1 manufacturer)

CDC Antiviral Treatment Recommendations

- **Focused on prompt treatment of hospitalized patients and outpatients at increased risk of influenza complications**
  - **Greatest clinical benefit when treatment is started soon after onset.**

- ***Oseltamivir treatment of hospitalized patients with suspected influenza recommended as soon as possible*** (without waiting for influenza testing results)

- ***NAI treatment of suspected or confirmed influenza is recommended as soon as possible for*** (without waiting for influenza testing results):
  - Outpatients in a high-risk group for influenza complications
  - Outpatients with complications, progressive or severe illness

- *NAI treatment can be considered for non high-risk outpatients with suspected or confirmed uncomplicated influenza if treatment can be started <48 hours of illness onset, based upon clinical judgement*

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

NAI Treatment Issues

- Do not give combination NAI treatment: NAI antagonism
- Critically ill patients with severe lower respiratory tract disease and immunosuppressed patients can have prolonged influenza viral shedding in the lower respiratory tract
  - Enteric oseltamivir is absorbed in critically ill patients
  - Optimal dosing and duration of oseltamivir in critically ill patients is unknown
    - Longer duration of NAI treatment may be indicated
    - One RCT reported that double-dose oseltamivir provided no benefit to standard dose oseltamivir in hospitalized patients
- For patients who cannot tolerate or absorb oral oseltamivir because of suspected or known gastric stasis, malabsorption, or gastrointestinal bleeding, IV peramivir should be considered

Duval PLoS Med 2010; Ariano CMAJ 2010; SEAIDCRN BMJ 2013

Oseltamivir Efficacy data (RCTs in Pediatric Outpatients)

- **Meta-analysis of RCTs of early oseltamivir treatment *(starting treatment <2 days of onset)* versus placebo in outpatients with uncomplicated influenza**

- **<u>Children with laboratory-confirmed influenza</u>**

➢ ***Early oseltamivir treatment significantly reduced illness duration in non-asthmatic children, and risk of otitis media***

  - 34% reduction in risk of otitis media (RR: 0.66, 95% CI: 0.47-0.95)
  - 17.6 hour overall reduction in illness duration
  - 30-hour reduction in illness duration for 3 RCTs not specifically in asthmatic children
  - 35-hour reduction in illness duration in children without asthma in pooled analysis
  - No reduction in illness duration in children with asthma in 2 RCTs
  - Underpowered to assess other complications or hospitalizations

Malosh Clin Infect Dis 2017

Oseltamivir Efficacy data (RCTs in Adult Outpatients)

- **Meta-analysis of RCTs of early oseltamivir treatment *(starting treatment <2 days of onset)* versus placebo in outpatients with uncomplicated influenza**

- **<u>Adults with laboratory-confirmed influenza</u>**

➢ ***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 (21% reduction in time to alleviation of all symptoms)
  - Fewer lower respiratory tract complications requiring antibiotics more than 48 hours after randomization (RR: 0.56, 95% CI: 0.42-0.75, p=0.0001)
  - Fewer hospitalizations for any cause (RR: 0.37, 95% CI: 0.17-0.81, p=0.013)

Dobson Lancet 2015

Effectiveness data (Observational studies 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 high-risk children and adults***

  - In children <16 years (adjusted OR: 0.25, 95% CI: 0.18-0.34; p<0.001)
  - In adults ≥16 years (adjusted OR: 0.26, 95% CI: 0.19-0.35; p<0.001)

Venkatesan Clin Infect Dis 2017

Oseltamivir Safety data (RCTs in outpatients)

- **2 recent meta-analyses of RCTs of early oseltamivir treatment** (starting treatment <2 days of onset) versus placebo in outpatients with uncomplicated influenza

Adults with laboratory-confirmed influenza

➢ ***Early oseltamivir treatment associated with increased risk of nausea & vomiting***

- Nausea (RR 1·60, 95% CI 1·29–1·99; p<0·0001; 9·9% oseltamivir vs 6·2% placebo, risk difference 3·7%, 95% CI 1·8–6·1)
- Vomiting (RR 2·43, 95% CI 1·83–3·23; p<0·0001; 8·0% oseltamivir vs 3·3% placebo, risk difference 4·7%, 95% CI 2·7–7·3)

Children with laboratory-confirmed influenza

➢ ***Early oseltamivir treatment was associated with increased risk of vomiting***

- Vomiting (RR: 1.63, 95% CI:1.30, 2.04)

Dobson Lancet 2015; Malosh Clin Infect Dis 2017

Abnormal behavior and influenza

- Post-marketing reports of abnormal behavior with oseltamivir treatment of influenza, particularly in Japanese adolescents
- Tamiflu package insert warning:

  Neuropsychiatric events: Patients with influenza, including those receiving TAMIFLU, particularly pediatric patients, may be at an increased risk of confusion or abnormal behavior early in their illness. Monitor for signs of abnormal behavior.

- No studies in Japan have implicated oseltamivir with abnormal behavior
  - Abnormal behavior reported in untreated influenza patients, and patients who received different NAIs

➢ Wide spectrum of neurologic complications associated with untreated influenza, including encephalopathy and encephalitis

Fukushima Vaccine 2017; Nakamura J Infect Chemotherapy 2017; Nakamura PLoS ONE 2015

Hospitalized Influenza Patients and Antiviral Treatment

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

Hospitalized Influenza Patients

- Meta-analysis of >29,000 hospitalized patients (86% lab-confirmed H1N1pdm09, 14% clinically diagnosed):

➢ ***NAI treatment (mostly oseltamivir) significantly reduced mortality versus no treatment in adults; early treatment within 2 days significantly reduced mortality versus no treatment in adults***

- ***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 mortality in pregnant women*** (adjusted OR: 0.46, 95% CI: 0.23-0.89; p=0.0215) ***and in critically ill patients aged >16 years*** (adjusted OR: 0.72, 95% CI: 0.56-0.94; p=0.0155)
- ***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

Hospitalized Influenza Patients

- Meta-analysis of >29,000 hospitalized patients (86% lab-confirmed H1N1pdm09, 14% clinically diagnosed):
- ***Early NAI treatment significantly reduced mortality versus later treatment (>2 days after onset) in adults***
  - ***Early initiation of NAI treatment versus later treatment significantly reduced mortality in adults*** (adjusted OR: 0.45, 95% CI: 0.38-0.54; p<0.0001); ***in pregnant women*** (adjusted OR: 0.27, 95% CI: 0.11-0.63; p=0.0026); **and in critically ill adults** (adjusted OR: 0.62, 95% CI: 0.49-0.77; p<0.0001)
  - ***Later treatment (>2 days after illness onset) significantly reduced mortality in critically ill adults*** (adjusted OR: 0.65, 95% CI: 0.46-0.93; p=0.0183), ***but not in children, pregnant women, or critically ill children***.

Muthuri Lancet Resp Med 2014

Oseltamivir Spot Shortages

- No national shortage of oseltamivir
- Local spot shortages of oseltamivir have been reported
- Factors:
  - High demand, delays in generic oseltamivir supply
- Recommendations
  - ➢ Prioritize oseltamivir for treatment of hospitalized patients, high-risk outpatients, and those with severe or progressive illness not requiring hospitalization.
  - If suspension is not available, pharmacies can compound an oral suspension using oseltamivir 75mg capsules per FDA-approved package inserts
  - Pharmacies may need to contact multiple distributors or manufacturers for oseltamivir availability

Clinical Management

- **Implementation of recommended infection prevention and control (IPC) measures**
  - Isolation; implementation of standard, droplet precautions
  - Airborne precautions for aerosol-generating procedures
- **Prompt NAI antiviral treatment**
- **Supportive care of complications**
  - Supplemental oxygen
  - Antibiotics for suspected/documented bacterial co-infection
  - Avoid corticosteroids unless indicated (e.g. asthma or COPD exacerbation or low-dose hydrocortisone for refractory shock/septic shock/documented adrenal insufficiency)
  - Advanced organ support

Summary

- Most patients with influenza experience relatively mild uncomplicated illness
- Wide range of complications associated with influenza
  - Persons at high-risk of complications can experience severe influenza
  - Some otherwise healthy persons may experience severe influenza complications
- Influenza testing is not need for all outpatients
  - Proper interpretation of results, particularly negative results, is important
- Influenza testing with a molecular assay is recommended for hospitalized patients
- Early neuraminidase inhibitor (NAI) antiviral treatment is recommended as soon as possible for hospitalized patients, high-risk outpatients, and those with progressive disease

To Ask a Question

- **Using the Webinar System**
  - Click the Q&A button in the webinar
  - Type your question in the Q&A box
  - Submit your question
  - CDC Media: media@cdc.gov or 404-639-3286
  - Patients, please refer your questions to your healthcare provider

Today's webinar will be archived

When: A few days after the live call

What: All call recordings (audio, webinar, and transcript)

Where: On the COCA Call webpage

https://emergency.cdc.gov/coca/calls/2018/callinfo_020818.asp

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Those who participated in today's COCA Call and who wish to receive continuing education should complete the online evaluation by March 8, 2018 with the course code WC2992.

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Tuesday, February 13, 2018

2:00-3:00 ET

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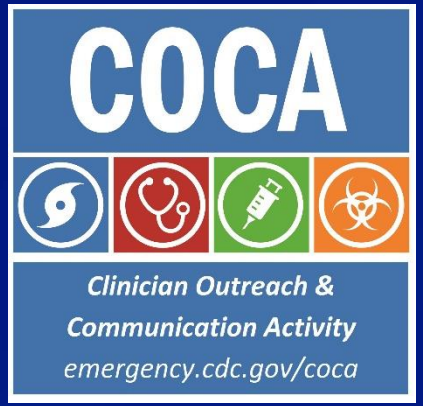

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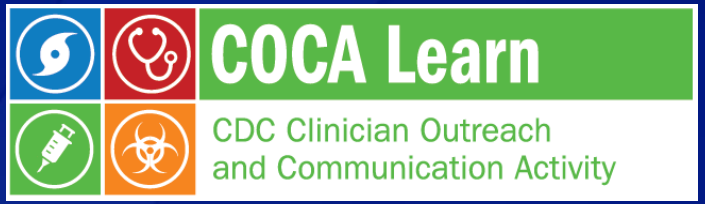

Monthly email that provides information on CDC training opportunities, conference and training resources located on the COCA website, the COCA Partner Spotlight, and the Clinician Corner.

Provides comprehensive CDC guidance so clinicians can easily follow recommendations.

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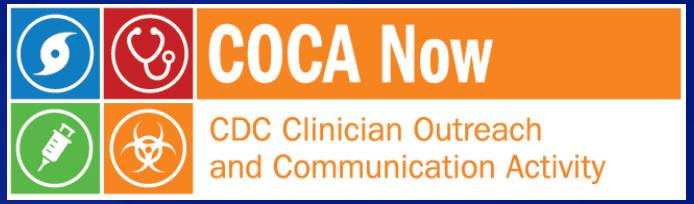

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CDC Clinician Outreach and Communication Activity - COCA

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CDC Clinician Outreach and Communication Activity - COCA shared their event.

October 31 at 1:18pm

Clinicians, you can earn FREE CE with this COCA Calll Join us for this COCA Call November 7, 2017 at 2:00PM.

Thank you for joining!

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