CDC Influenza Division Key Points
January 30, 2015

In this document:

Summary Key Messages

- This week's FluView report indicates that flu activity remains widespread across most of the United States and severity indicators are high.
    - This week five pediatric deaths were reported, bringing the total number of flu-associated pediatric deaths reported so far this season to 61. (Since 2004 when flu-associated pediatric deaths became a nationally notifiable condition, the number of deaths reported to CDC each season has ranged from 37 to 171.)
    - The proportion of deaths attributed to pneumonia and influenza (P&I) based on the 122 Cities Mortality Reporting System is still high, but reduced slightly from 9.2% to 9.1%. (During recent previous seasons characterized as "moderately severe" with H3N2 viruses predominating, P&I has reached 10.4% (2003-2004) and 9.9% (2012-2013).
    - The hospitalization rate for people 65 years and older is now 198.4 per 100,000 people, up from 176.1 per 100,000 the prior week. This is the highest hospitalization rate among this age group since CDC began tracking this information in 2005. (During the 2012-2013 season (the last H3N2-predominant season), the hospitalization rate for week 3 was 120.1 per 100,000. The final hospitalization rate for that season was 183.2 per 100,000 people.)
- More hospitalizations and deaths are typical of H3N2 seasons, which hit young children and older people harder. (CDC estimates that an average of 28,909 people died from

flu during H3N2-predominant seasons, compared to 10,648 people during non-H3N2 predominant seasons.)

- Activity so far this season is most similar to the 2012-2013 season, the last season when H3N2 viruses predominated.
- Flu activity is likely to continue nationally for several weeks, though some states are showing declines.
- About two-thirds of the H3N2 viruses circulating this season are different or "drifted" from the vaccine virus.
- The predominance of drifted viruses is likely to be responsible for the reduced protection being offered by this season's vaccine. (Early estimates indicate that getting a flu vaccine this season reduced a person's risk of having to go to the doctor because of flu by 23 percent among people of all ages.)
- The reduced protection offered by flu vaccine this season makes the appropriate use of influenza antiviral (or "anti-flu") medications more important than usual.
- Antivirals drugs are a second line of defense against influenza, to treat flu illness. (See section "Antiviral Drugs" for more information.)
- A meta-analysis released today in *The Lancet* demonstrates that treatment of laboratory-confirmed influenza in adults with oseltamivir (Tamiflu®) shortened the amount of time it took for symptoms to resolve by about 21%, reduced the risk of lower respiratory tract complications (44%), and reduced the risk of hospitalization (63%). (See section *The Lancet* Study below for more information.)
- CDC recommends that all hospitalized and high risk patients (either hospitalized or outpatient) with suspected influenza should be treated as soon as possible with one of three available influenza antiviral medications, without waiting for confirmatory influenza testing.
- While antiviral drugs work best when given early, therapeutic benefit has been observed even when treatment is initiated later.
- On January 29, 2015, CDC and partners jointly called on health care professionals to promptly treat young children and people age 65 and older with flu antiviral drugs. The letter is available on the CDC website at http://www.cdc.gov/flu/pdf/professionals/antiviral-letter-providers-2014-2015.pdf.

FluView Activity Update

- According to this week's FluView report, flu activity is widespread in most of the United States and severity indicators are high.
- The hospitalization rate for people 65 years and older is the highest recorded since CDC began tracking that information.

- Some states where flu activity started earlier are seeing signs of declines in activity, while other states are showing increases. Flu activity has been elevated for 10 consecutive weeks nationally.
- An average season lasts about 13 weeks. However, because this season started relatively early, it could last longer than average.
- Below is a summary of the key flu indicators for the week ending January 24, 2015:
    - For the week ending January 24, the proportion of people seeing their health care provider for influenza-like illness (ILI) increased slightly to 4.4%, and remains above the national baseline (2.0%) for the tenth consecutive week. All 10 U.S. regions reported ILI activity at or above region-specific baseline levels. The length of a flu season can vary. For the past 13 seasons ILI has remained at or above the national baseline for between one and 19 weeks each season, with an average of 13 weeks.
    - Puerto Rico and 29 states experienced high ILI activity; an increase from 23 states during the previous week. New York City and seven states (Arizona, Delaware, Hawaii, Maine, North Dakota, South Carolina, and South Dakota) experienced moderate ILI activity. Six states (Alaska, Georgia, Maryland, Michigan, Montana, and New Hampshire) experienced low ILI activity. Eight states (Florida, Illinois, Indiana, Iowa, Kentucky, Ohio, Oregon, and Wisconsin) experienced minimal ILI activity and the District of Columbia did not have sufficient data to calculate an activity level. ILI activity data indicate the amount of flu-like illness that is occurring in each state.
    - Widespread influenza activity was reported by Puerto Rico and 44 states. The same number of states reported widespread activity during the previous week. The U.S. Virgin Islands and five states (Alabama, Georgia, Hawaii, Minnesota, and Tennessee) reported regional geographic influenza activity. Local flu activity was reported by Guam, the District of Columbia and one state (Alaska). Geographic spread data show how many areas within a state or territory are seeing flu activity.
    - A total of 11,077 laboratory-confirmed influenza-associated hospitalizations have been reported through the Influenza Hospitalization Surveillance Network (FluSurv-NET) since October 1, 2014. This translates to a cumulative overall rate of 40.5 hospitalizations per 100,000 population. Last week, the overall cumulative rate was 36.3 hospitalizations per 100,000 population. This is slightly higher than seen for the same week during 2012-2013 when the overall hospitalization rate was 27.4 per 100,000 people.
        - The hospitalization rate in people 65 years and older is 198.4 per 100,000. This is the highest rate of any age group and the highest hospitalization rate recorded since data collection on laboratory-confirmed influenza-associated hospitalization in adults began in the 2005-2006

season. Previously, the highest recorded hospitalization rate was 183.2 per 100,000, which was the cumulative hospitalization rate for people 65 years and older for the 2012-13 season. (The 2012-2013 season was the last H3N2-predominant season.)

- The hospitalization rate for children 0-4 years is 38.2 per 100,000 population. During 2012-2013, the hospitalization rate for that age group for the same week was 37.4 hospitalizations per 100,000 population.
- Hospitalization data are collected from 13 states and represent approximately 9% of the total U.S. population. The number of hospitalizations reported does not reflect the actual total number of influenza-associated hospitalizations in the United States.

- The proportion of deaths attributed to pneumonia and influenza (P&I) based on the 122 Cities Mortality Reporting System decreased slightly to 9.1% this week, but remains high and above the epidemic threshold of 7.1%. Last week, P&I was 9.2%. (During 2012-2013, P&I peaked at 9.9%. This was the highest recorded P & I in nearly a decade, but was comparable to recorded percentages for past severe seasons, including the 2003-2004 season when P&I reached 10.4%.)
- Five influenza-associated pediatric deaths were reported to CDC during the week ending January 24.
    - Four deaths were associated with an influenza A (H3) virus and occurred during weeks 53, 1, 2, and 3 (weeks ending January 3, January 10, January 17, and January 24, 2015, respectively). One death was associated with an influenza A virus for which no subtyping was performed and occurred during week 1.
    - A total of 61 influenza-associated pediatric deaths have been reported for the 2014-2015 season at this time.
- Nationally, the percentage of respiratory specimens testing positive for influenza viruses in the United States during the week ending January 24 was 19.9%. For the most recent three weeks, the regional percentage of respiratory specimens testing positive for influenza viruses ranged from 14.3% to 27.4%.
- Influenza A (H3N2) viruses have been most common in the United States this season. Few influenza B viruses have been detected and even fewer influenza A (H1N1)pdm09 viruses have been detected. During the week ending January 24, 4,343 (93.4%) of the 4,651 influenza-positive tests reported to CDC were influenza A viruses and 308 (6.6%) were influenza B viruses. Of the 1,700 influenza A viruses that were subtyped, 99.9 % were influenza A (H3) viruses and 0.1% were influenza A (H1N1)pdm09 viruses.

- CDC has antigenically or genetically characterized 602 influenza viruses, including 21 influenza A (H1N1)pdm09, 478 influenza A (H3N2) viruses and 103 influenza B viruses, collected in the United States since October 1, 2014.
    - All 21 influenza A (H1N1)pdm09 viruses tested were characterized as A/California/7/2009-like. This is the influenza A (H1N1) component of the 2014-2015 Northern Hemisphere quadrivalent and trivalent influenza vaccines.
    - 159 (33.3%) of the 478 influenza A (H3N2) viruses tested have been characterized as A/Texas/50/2012-like. This is the influenza A (H3N2) component of the 2014-2015 Northern Hemisphere quadrivalent and trivalent influenza vaccine.
    - The remaining 319 (66.7%) influenza A (H3N2) viruses tested were different from A/Texas/50/2012. The majority of these 319 influenza A (H3N2) viruses were antigenically similar to A/Switzerland/9715293/2013, the influenza A (H3N2) component of the 2015 Southern Hemisphere influenza vaccine.
    - Sixty-nine (67.0%) of the 103 influenza B viruses tested belonged to the B/Yamagata/16/88 lineage and were characterized as B/Massachusetts/2/2012-like. This is an influenza B component of the 2014-2015 Northern Hemisphere trivalent and quadrivalent influenza vaccine.
    - Thirty (88.2%) of the 34 other influenza B viruses belonged to the B/Victoria lineage of viruses, and were characterized as B/Brisbane/60/2008-like. This is the recommended influenza B component of the 2014-2015 Northern Hemisphere quadrivalent influenza vaccine. Four (11.8%) of the B/Victoria-lineage viruses tested showed reduced titers to B/Brisbane/60/2008.
- Since October 1, 2014, CDC has tested 16 influenza A (H1N1)pdm09, 948 influenza A (H3N2), and 139 influenza B viruses for resistance to neuraminidase inhibitors (oseltamivir, zanamivir, and peramivir). While the vast majority of the viruses that have been tested are sensitive to oseltamivir, zanamivir, and peramivir, so far this season, one influenza A (H1N1)pdm09 virus showed resistance to oseltamivir and peramivir. (Because H1N1 viruses have been so rare this season, one virus accounts for 6.3% of the H1N1 viruses analyzed for antiviral resistance this season.)
    - Previously, the neuraminidase inhibitors oseltamivir and zanamivir were the only recommended influenza antiviral drugs. On December 19, 2014, the U.S. Food and Drug Administration approved Rapivab (peramivir) to treat influenza infection in adults.

        - As in recent past seasons, high levels of resistance to the adamantanes (amantadine and rimantadine) continue to persist among influenza A (H1N1)pdm09 and influenza A (H3N2) viruses. Adamantanes are not effective against influenza B viruses.
    - FluView is available – and past issues are archived – on the CDC website.

Note: Delays in reporting may mean that data changes over time. The most up to date data for all weeks during the 2014-2015 season can be found on the current FluView.

***The Lancet* Study: Oseltamivir Treatment for Influenza in Adults**

- "Oseltamivir treatment for influenza in adults: a meta-analysis of randomized controlled trials" by non-CDC authors J Dobson, RJ Whitley, S Pocock, and AS Monto was published online in The Lancet on January 30, 2015. (A corresponding Comment "Influenza: the rational use of oseltamivir" by H Kelly and BJ Cowling was also published.)
- This study did an individual patient data meta-analysis using published and unpublished randomized controlled clinical trial data that compared oseltamivir with placebo for treatment of seasonal influenza in adults, with regard to symptom alleviation, complications and safety. The meta-analysis included data from nine clinical trials including 4,328 outpatients.
- This meta-analysis was funded by the Multiparty Group for Advice on Science (MUGAS) Foundation which received an unrestricted grant from Roche.
- Similar to other studies, the authors demonstrate that treatment of laboratory-confirmed influenza in adults with oseltamivir shortened the amount of time it took for symptoms to resolve by about 21 percent.
- Findings also show that treatment of influenza in adults with oseltamivir reduced the risk of lower respiratory tract complications by 44 percent. Among those treated with oseltamivir, 4.9 percent had respiratory tract complications, compared with 8.7 percent among those treated with a placebo.
- Findings also show that treatment of influenza in adults with oseltamivir reduced the risk of hospitalization by 63 percent. Among those treated with influenza, 0.6 percent were admitted to hospital, compared with 1.7 percent among those treated with a placebo.
- The value of influenza antiviral drugs to reduce severe outcomes has been the subject of debate.

- The findings of this study shed light on this issue, further supporting CDC's existing recommendation to use neuraminidase inhibitor antiviral drugs (oral oseltamivir, inhaled zanamivir) to treat and prevent serious flu outcomes.
- When initially approved for the U.S. market in 1999, these drugs were recommended for the treatment of uncomplicated influenza in otherwise healthy persons.
- Over time, more data became available about the value of these drugs in preventing serious outcomes.
- CDC's antiviral recommendations are available at http://www.cdc.gov/flu/professionals/antivirals/index.htm.

Antiviral Drugs

Antiviral drugs can be used to treat flu illness and prevent serious flu complications.

- There are prescription drugs, called "influenza antiviral drugs" that can be used to treat the flu or to prevent infection with flu viruses.
- Treatment with antivirals works best when begun within 48 hours of getting sick, but can still be beneficial when given later in the course of illness.
- Treatment with flu antiviral drugs can make flu illness milder and shorter. Treatment with antivirals also can lessen serious flu complications that can result in hospitalization or death.
- Antiviral drugs become even more important when circulating flu viruses are different from the vaccine viruses, which can mean that the vaccine doesn't work as well in protecting against infection with those viruses.
- Antiviral drugs are effective across all age and risk groups.
- Studies show that antiviral drugs are under-prescribed for high risk people who get flu.
    - One study showed that less than one-fifth (19%) of patients who were at high risk for flu complications and presented for care within two days of symptom onset (i.e., the period of time when antiviral treatment is most beneficial) received a prescription for antivirals, regardless of laboratory testing for influenza infection (Havers, 2014).
    - The study demonstrates that clinicians are still more likely to prescribe antibiotics rather than antiviral medications to outpatients with flu, including to high-risk patients who would benefit from early empiric antiviral treatment.
- CDC has done some limited qualitative research into clinician knowledge, attitudes and practices (KAPs) related to antiviral drugs.

- The findings suggest that there are probably a number of factors involved that may act as barriers to prescribing, including low clinician awareness of CDC's antiviral guidance, a perception that these drugs may not work, that some physicians may require a positive flu test before they prescribe and that some physicians may not prescribe antivirals after the 2-day window during which benefit is optimal.
- These are all areas where CDC is working to improve clinician awareness.
- Treating high risk people or people who are very sick with flu with antiviral drugs is very important. It can mean the difference between having a milder illness instead of very serious illness that could result in a hospital stay.
- Health professionals should empirically give prompt treatment with antiviral medications to persons with suspected or confirmed flu who are hospitalized; have severe or progressive illness; or are at increased risk for influenza complications
- Three FDA-approved influenza antiviral agents are recommended for use in the United States during the 2014-2015 influenza season: oseltamivir, zanamivir and peramivir.
    - On December 19, 2014, the FDA approved peramivir (trade name Rapivab®), an intravenous antiviral drug, to treat uncomplicated influenza infection in adults age 18 and older. Read more at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm427755.htm.
- A summary of antiviral recommendations for clinicians is available on the CDC website at http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm.
- A CDC Health Update reminding clinicians about the importance of flu antiviral medications was distributed via the CDC Health Alert Network on January 9, 2015, and is available at http://emergency.cdc.gov/HAN/han00375.asp.
- Visit http://www.cdc.gov/flu/professionals/antivirals/index.htm for information about how antiviral medications can be used to prevent or treat influenza when influenza activity is present in your community.
- CDC has provided an algorithm for medical offices to use to evaluate patients for possible influenza over the telephone: http://www.cdc.gov/flu/professionals/antivirals/office-evaluation.htm.
- A CDC Expert commentary on antiviral recommendations for the 2014-2015 flu season is available through Medscape at http://www.medscape.com/viewarticle/837284.
- As always, people who are at high risk for influenza complications should see a health care professional promptly if they get flu symptoms, even if they have been vaccinated this season.
    - People at high risk for serious flu complications include: people with underlying chronic medical conditions such as asthma, diabetes, heart disease, or

neurological conditions; pregnant women; those younger than 5 years or older than 65 years of age; or anyone with a weakened immune system. A full list of high risk factors is available at http://www.cdc.gov/flu/about/disease/high_risk.htm.

- More information about everyday preventive actions that help fight flu is available at http://www.cdc.gov/flu/protect/habits.htm.

Antiviral Drug Supply

- Influenza antiviral drugs are commercially manufactured and supplies of these drugs are dependent upon those commercial manufacturers.
- Manufacturers have stated they have sufficient product on hand to meet the projected high demand for the 2014-2015 flu season.
- CDC and influenza antiviral drug manufacturers are aware of some spot shortages being experienced, specifically for Tamiflu (oseltamivir).
- A statement on Tamiflu® supply from the manufacturer Genentech is available at: http://www.gene.com/media/statements/ps_121814.
- Rapivab® (peramivir)—an intravenous antiviral medication that was FDA-approved for use on December 19, 2014—is in ample supply and available for ordering during the 2014-2015 flu season.
- If needed, pharmacies should work with authorized distributors to obtain additional supplies of antivirals.
- Patients should consider calling a pharmacy in advance to see if they have drug on their shelf. If the pharmacy does not have product, they may be able to identify another pharmacy in the area that has antiviral drugs in stock.
- Patients who have been prescribed an influenza antiviral drug by their health care provider may need to call more than one pharmacy to fill their prescription.
- If the exact prescribed formulation cannot be located, patients should consult with their physician or pharmacist for additional options.
- It's also possible that in places with elevated influenza activity, locating influenza antiviral drugs may be more difficult.
- FDA and the American Society of Health-System Pharmacists (ASHP) provide updated information about specific drug shortages to guide patients and pharmacies:
    - FDA website: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm
    - ASHP website: http://www.ashp.org/menu/DrugShortages

- **CDC Antiviral Call Center**: For long-term care facilities experiencing difficulty accessing antiviral supplies, CDC will coordinate with commercial partners to facilitate the rapid resolution of large orders of antiviral drugs for these *institutional outbreak settings*.
    - Beginning on Monday, January 12, the Division of Strategic National Stockpile (DSNS) is available from 7:00 a.m. to 7:00 p.m., EST Monday through Friday, to assist public health officials and health care facilities by coordinating with supply chain partners to rapidly redirect supply to the identified location.
    - Contact DSNS at dsns-Request@cdc.gov for assistance with facility specific unmet antiviral drug supply needs. For emergency needs overnight and on weekends, public health officials can contact the CDC Emergency Operations Center through established protocols.
- CDC and FDA will continue to work with manufacturers to assess influenza antiviral supply this season.

Flu & Parotitis This Season

- Symptoms of influenza infection include fever, chills, cough, sore throat, runny or stuffy nose, muscle or body aches, headache, fatigue (tiredness), and sometimes vomiting and diarrhea (more common in children than adults).
- Influenza infection can sometimes lead to complications including bacterial pneumonia, ear infection, sinus infection, dehydration and worsening of chronic medical conditions such as congestive heart failure, asthma, and diabetes.
- Parotitis is not a common symptom of influenza infection, although cases of parotitis with influenza infection have been reported in the past. Parotitis is much more commonly seen following infection with other pathogens such as the mumps virus.
- Since December 2014, multiple states have notified CDC of laboratory-confirmed influenza infections in persons who have swelling of their salivary glands (a condition called 'parotitis').
- Of the cases of influenza infection with parotitis that have been reported to CDC, the majority have occurred in young adults with influenza A (H3) infection, and have resulted in mild illness. No deaths have been reported.
- CDC is currently investigating the situation in order to understand the characteristics of patients and the occurrence of parotitis during the 2014-2015 influenza season.
- On January 10, 2015, CDC issued a request to state health departments to report laboratory-confirmed cases of influenza with parotitis.
- CDC will provide updates at www.cdc.gov/flu as more information becomes available.

Vaccination

- Protection from flu vaccination is reduced this season. Early estimates from CDC indicate that getting a flu vaccine this season decreased your risk of having to go to the doctor for flu by 23%. (See section "Influenza Vaccine Effectiveness" for more information.)
- CDC continues to recommend vaccination, even during seasons when the vaccine offers reduced protection.
    1. Flu vaccination can still reduce some flu illnesses, as well as prevent flu-related hospitalizations and deaths.
        - About one-third of circulating H3N2 viruses are well-matched with the vaccine virus.
        - Antibodies created through vaccination with one influenza virus can sometimes offer protection against drifted influenza viruses (this is called "cross-protection").
    2. There is some evidence to suggest that even if you do get sick, your symptoms will be milder if you got vaccinated.
    3. We cannot know which viruses will circulate over the season. The flu vaccine protects against three or four different influenza viruses, depending on which vaccine you get (trivalent or quadrivalent). It's common for there to be a second wave of flu activity toward the end of the season and the flu vaccine should offer better protection against those viruses.
- Vaccination is particularly important for people at high risk of serious flu-related complications and their close contacts. (People at high risk include infants, pregnant women, kids and adults with chronic medical conditions like asthma, diabetes, or heart disease, and adults aged 65 and older.)
- Health care professionals should continue to vaccinate patients who have not yet received influenza vaccine this season.
- As of January 16, 2015, manufacturers reported having shipped 147.4 million doses of flu vaccine.
- The HealthMap Vaccine Finder can be used to locate flu vaccine.
- See the Influenza Vaccine Effectiveness section below for more information about measuring how well influenza vaccines work.

Vaccine Match

- Influenza viruses are constantly changing – they can change from one season to the next or they can even change within the course of the same season. This kind of gradual change is called "antigenic drift."
- In order for any vaccine to be delivered in the fall, the viruses in the vaccine must be chosen in February.
- When the vaccine viruses for the Northern Hemisphere 2014-2015 influenza season were selected, A/Texas/50/2012 was the most common circulating influenza H3N2 virus.
- Drifted H3N2 viruses were first detected during routine surveillance testing during late March 2014, after WHO recommendations for the vaccine composition for the Northern Hemisphere for the 2014-2015 season had been made in mid-February.
- At that time, just a very small number of these viruses had been found among the thousands of specimens that had been collected and tested.
- Influenza viruses are constantly changing and it is common to detect small numbers of antigenic variants that never circulate widely.
- Many antigenic variants emerge and spread in a limited way and then die out.
- Early on, there is no way to predict if a given antigenic variant will circulate widely.
- Over the summer, these viruses were detected in greater proportions and by the fall had become common among H3N2 viruses in the United States and abroad.
- By September 20, 2014, about half of H3N2 viruses isolated worldwide since May were drifted from the H3N2 vaccine virus component of the 2014-2015 Northern Hemisphere influenza vaccine.
- Since October 1, 2014, about two-thirds of H3N2 viruses collected in the United States that were characterized at CDC were drifted from the H3N2 vaccine virus component.

Influenza Vaccine Effectiveness: Early Estimates

- Since 2004-2005, CDC has been conducting vaccine effectiveness (VE) studies each season to measure how well the vaccine is protecting vaccinated people from having to go to the doctor because of flu.
- Study results from the U.S. Influenza Vaccine Effectiveness (Flu VE) Network have varied from 10% to 60% between 2004-2005 and 2013-2014. (See http://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm for adjusted vaccine effectiveness estimates for influenza seasons from 2005-2014.)

- Early estimates for the current season were published in the January 16, 2015 edition of the Morbidity and Mortality Weekly Report. The MMWR report is available on the CDC web site at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6401a4.htm?s_cid=mm6401a4_w.
- Data so far this season indicate that influenza vaccination reduced a vaccinated person's risk of having to go to the doctor for flu illness by about 23% across all ages.
- These early VE estimates are lower compared to some other seasons, likely reflecting the fact that about two-thirds of circulating H3N2 viruses this season have been antigenically or genetically different from the H3N2 vaccine virus.
- A meta-analysis of influenza vaccine effectiveness studies, published in 2012, found that VE against medically attended illness is around 60% during seasons when circulating viruses and vaccine viruses are well-matched.[1]
- While offering reduced protection, this season's vaccine can still prevent some infections with currently circulating H3N2 viruses and also lessen related complications.
- The reduced protection offered by flu vaccine this season underscores the need for additional prevention and treatment efforts, including the appropriate use of influenza antiviral medications for treatment.

Methodology

- From November 10 to January 2, 2015, patients aged 6 months and older who sought outpatient medical care for an ARI with cough, within days of illness onset, were enrolled at five study sites within the U.S. Flu VE Network.
- Study enrollment began once laboratory-confirmed cases of influenza were identified through local surveillance.
- Patients were eligible for enrollment if they:
    1) were aged ≥6 months on September 1, 2014, and thus were eligible for vaccination;
    2) reported an ARI with onset ≤7 days prior to their visit; and
    3) had not yet been treated with influenza antiviral medication (e.g. oseltamivir) during this illness.
- Respiratory specimens were collected from each patient using nasal and/or oropharyngeal swabs (only nasal swabs were collected from children 2 years old and younger).

[1] Osterholm MT, Kelley NS, Sommer A, Belongia EA. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. Lancet Infect Dis. 2012 Jan;12(1)36-44.

- Specimens were tested at U.S. flu VE Network laboratories using CDC's real-time reverse transcription polymerase chain reaction (rRT-PCR) protocol for detection and identification of influenza viruses.
- Participants were considered vaccinated if they received at least one dose of any seasonal influenza vaccine ≥14 days prior to illness onset, according to medical records and registries (at two sites) or self-report and medical records (at three sites).
- VE was estimated by comparing the odds of vaccination among influenza-positive (cases) versus influenza-negative (controls) participants.
- Estimates were adjusted for study site, age, sex, race/ethnicity, self-rated health and days from illness onset to enrollment using logistic regression.

Background on Vaccine Effectiveness

- CDC conducts studies to measure the benefits of seasonal flu vaccination each flu season to help determine how well flu vaccines are working. These studies are called "vaccine effectiveness" studies or "VE" studies, for short.
- How well the flu vaccine works can vary by season, virus type/subtype, the vaccine, and age and other host factors of the people being vaccinated.
- Although antigenic match influences vaccine effectiveness, randomized studies of influenza vaccines have reported variable vaccine efficacy during seasons when antigenically drifted viruses predominated.
- VE is difficult to measure and study results can vary widely based on the study design, the outcome being measured and the population being studied.
- CDC has worked with researchers at universities and health systems since 2003-2004 to estimate VE in non-randomized, observational studies.
- The U.S. Flu VE Network consists of five study sites across the United States that measure the flu vaccine's effectiveness at preventing outpatient medical visits due to laboratory-confirmed influenza.
- CDC's observational studies at U.S. Flu VE Network sites measure outpatient visits for laboratory-confirmed influenza infection using a highly accurate lab test called rRT-PCR to verify the outcome.
- This is an observational study that compares the odds of vaccination among outpatients with acute respiratory illness and laboratory-confirmed influenza infection to the odds of vaccination among outpatients with ARI who test negative for influenza infection.
- The study uses a test-negative control design, which minimizes potential bias introduced by access to medical care and health care-seeking behavior.

Influenza-Associated Pediatric Deaths

- Five influenza-associated pediatric deaths were reported to CDC this week.
- A total of 61 influenza-associated deaths have been reported during the 2014-2015 season.
- Because of confidentiality issues, CDC does not discuss or give details on individual pediatric death cases.
- Additional information regarding pediatric deaths is available through FluView Interactive.
- A pediatric death is a death in a person who is a U.S. resident and younger than 18 years old resulting from a clinically compatible illness with influenza that is confirmed by an appropriate laboratory test.
- During the 2013-2014 influenza season, a total of 109 influenza-associated pediatric deaths were reported to CDC.
- A review of the available pediatric death reports from the 2013-2014 season indicates that:
    - Of the 106 deaths in which the child's medical history was known, 54% occurred in children who had underlying medical conditions that placed them at high risk of developing serious flu-associated complications. However, 46% had no recognized underlying health problems.
    - About 80% of pediatric deaths occurred in unvaccinated children.
    - These proportions are largely consistent with what has been seen in the past.
- Since 2004, when flu-associated pediatric deaths became a nationally notifiable condition, the number of deaths reported to CDC each season has ranged from 37 (2011-2012 season) to 171 (2012-2013 season).
- During the 2009 H1N1 pandemic — April 15, 2009 to October 2, 2010 — 358 pediatric deaths were reported to CDC.
- These deaths are a somber reminder of the danger flu poses to children.
- Typically, most flu-related pediatric deaths occur in children who have not been vaccinated against flu.
- Among children 6 months and older, 80 to 85 percent of flu-related pediatric deaths occur in children who have not been vaccinated.
- The single best way to protect children against seasonal flu and its potential severe consequences is to have them receive a seasonal flu vaccine each year.
- Among children, vaccination is especially important for those younger than 5 years of age and those of any age with an underlying medical condition like asthma; a

neurologic, neuromuscular or neurodevelopmental disorder; or immune suppression. These children are at higher risk of serious complications if they get the flu.

- Yearly vaccination also is especially important for people who come in contact with high risk children in order to protect the child (or children) from the flu.
- Even previously healthy children can become seriously ill if they get the flu. Data on laboratory-confirmed influenza hospitalizations collected through FluSurv-Net during the 2013-2014 flu season indicated that 50.3% of children hospitalized with the flu had no identified underlying medical conditions.
- Flu-associated deaths in children younger than 18 years old should be reported through the Influenza-Associated Pediatric Mortality Surveillance System. The number of flu-associated deaths among children reported during the 2014-2015 flu season is updated each week and can be found at http://www.cdc.gov/flu/weekly/.
- Additional information about the pediatric deaths, including basic demographics, underlying conditions and week and place of death, for the 2014-2015 season as well as past influenza seasons, is available through the Influenza Associated Pediatric Mortality application of FluView Interactive at http://gis.cdc.gov/GRASP/Fluview/PedFluDeath.html.

Human Infection with influenza A H1N1 variant virus ("H1N1v")

- This week's FluView includes a report of a human infection with influenza A (H1N1) variant ("H1N1v") virus.
- This case of H1N1v occurred in October 2014 and is the first reported case of human infection with H1N1v since 2013. (See Case Count: Detected U.S. Infections with Variant Influenza Viruses by State since December 2005 for details.)
- Routine surveillance performed at CDC confirmed the virus as a H1N1v virus using genetic sequencing.
- The reported case was an adult in Minnesota who had indirect exposure to swine (pigs) seven days prior to illness onset. The patient has since fully recovered.
- No evidence of human-to-human transmission of H1N1v or any increases in flu-like illness among the patient's contacts were reported.
- Genetic sequencing showed that this H1N1v virus has the matrix (M) gene from the influenza A (H1N1)pdm09 lineage (the contemporary H1N1 subtype that has circulated in humans since the 2009 H1N1 pandemic). The other genes of this virus are typical of classical swine H1N1 viruses.

Background

- Swine flu viruses do not normally infect humans. However, sporadic human infections with influenza viruses that normally circulate in swine have occurred.

- When this happens, these viruses are called "variant viruses." They also may be denoted by adding the letter "v" to the end of the virus subtype designation.
- Human infections with H1N1v, H1N2v, and H3N2v viruses have been detected in the United States.
- Most commonly, human infections with variant viruses occur in people with exposure to infected pigs (e.g., children near pigs at agricultural fairs or workers in the swine industry).
- There have been documented cases of multiple persons becoming sick after exposure to one or more sick pigs and also cases of limited spread of variant influenza viruses from person to person.
- The vast majority of human infections with variant influenza viruses do not result in person-to-person spread.
- However, each case of human infection with a variant influenza virus should be fully investigated to a) be sure that such viruses are not spreading in an efficient and ongoing way in humans, and b) to limit further exposure of humans to infected animals if infected animals are identified.
- CDC recommends that people with health or age factors that put them at high risk for serious flu complications avoid pigs and swine barns.
- CDC has issued guidance for people attending fairs where swine might be present during fair season, including additional precautions for people who are at high risk for serious flu complications.
- High-risk people include children younger than 5 years, people 65 years and older, people with underlying health conditions like asthma, diabetes and heart disease, and pregnant women. A full list of conditions that increase the risk of influenza-related complications is available at http://www.cdc.gov/flu/about/disease/high_risk.htm.
- In addition, people at high risk of flu complications who develop flu symptoms after exposure to pigs at a fair or had other possible contact with pigs should contact a health care professional.
- People who go to a doctor for flu symptoms following direct or close contact with swine should tell their doctor about this exposure. CDC recommends that people at high risk of flu complications get influenza antiviral treatment as quickly as possible if they experience flu-like symptoms.