CDC Influenza Division Key Points

January 23, 2015

In this document:

Summary Key Messages

- This week's FluView report indicates that flu activity -- still caused mostly by H3N2 flu viruses -- remains high in the United States and severity indicators continue to climb.
    - This week 11 pediatric deaths were reported, bringing the total number of flu-associated pediatric deaths reported so far this season to 56. (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 increased from 8.5% to 9.3%. (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 176.1 per 100,000 people, up from 143.3 per 100,000 the prior week. (During the 2012-2013 season (the last H3N2-predominant season), the hospitalization rate for week 2 was 103.5 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.
- 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.)
- 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.
- This week CDC reported the first oseltamivir-resistant 2009 H1N1 virus. However, the majority of 2009 H1N1 viruses circulating in the United States remain susceptible to the neuraminidase inhibitor antiviral medications, oseltamivir and zanamivir.

FluView Activity Update

- According to this week's FluView report, flu activity is widespread in most of the country and key indicators used to measure severity are climbing sharply. H3N2 viruses remain the most common.
- Flu activity has been elevated for nine consecutive weeks. 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 17, 2015:
    - For the week ending January 17, the proportion of people seeing their health care provider for influenza-like illness (ILI) increased slightly to 4.5%, and remains above the national baseline (2.0%) for the ninth consecutive week. It is too soon to tell whether influenza activity has peaked yet this season. 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 23 states experienced high ILI activity; a decrease from 24 states during the previous week. New York City and ten states (Delaware, Hawaii, Indiana, Maryland, Massachusetts, New Jersey, New Mexico, Pennsylvania, Rhode Island, and Tennessee) experienced moderate ILI activity. Ten states (Arizona, Florida, Iowa, Kentucky, Maine, Michigan, Montana, Nebraska, Ohio, and South Carolina) experienced low ILI activity. Seven states (Alaska, Georgia, Illinois, New Hampshire, Oregon, Vermont, 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 44 states; a decrease from the 46 states that reported widespread activity during the previous week. Guam, Puerto Rico, 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 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 9,926 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 36.3 hospitalizations per 100,000 population. Last week, the overall cumulative rate was 29.9 hospitalizations per 100,000 population.
    - The hospitalization rate in people 65 years and older is 176.1 per 100,000. This is the highest rate of any age group. (During the 2012-13 season, the hospitalization rate for people 65 and older for the same week was 103.5 per 100,000, and for the following week was 120.1 per 100,000.* The 2012-2013 flu season was the last influenza A (H3N2)-predominant season in the United States.)
    - 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 continues to climb sharply, reaching 9.3% this week, which is above the epidemic threshold of 7.1%. Last week, P&1 was 8.5%. (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%.)

- Eleven influenza-associated pediatric deaths were reported to CDC during the week ending January 17.
  - Three deaths were associated with an influenza A (H3) virus and occurred during weeks 51, 53, and 1 (weeks ending December 20, 2014, January 3, and January 10, 2015, respectively). Eight deaths were associated with an influenza A virus for which no subtyping was performed and occurred during weeks 51, 52, 53, 1, and 2 (weeks ending December 20, December 27, 2014, and January 3, January 10, and January 17, 2015, respectively).
  - A total of 56 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 17 was 19.5%. For the most recent three weeks, the regional percentage of respiratory specimens testing positive for influenza viruses ranged from 16.6% to 29.1%.
- 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 17, 4,800 (94%) of the 5,104 influenza-positive tests reported to CDC were influenza A viruses and 304 (6.0%) were influenza B viruses. Of the 1,824 influenza A viruses that were subtyped, 99.8 % were influenza A (H3) viruses and 0.2% were influenza A (H1N1)pdm09 viruses.
- CDC has antigenically or genetically characterized 508 influenza viruses, including 10 influenza A (H1N1) pdm09, 395 influenza A (H3N2) viruses and 103 influenza B viruses, collected in the United States since October 1, 2014.
  - All 10 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.
  - 141 (35.7%) of the 395 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 254 (64.3%) influenza A (H3N2) viruses tested were different from A/Texas/50/2012. The majority of these 254 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 14 influenza A (H1N1) pdm09, 724 influenza A (H3N2), and 127 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, one influenza A (H1N1)pdm09 virus reported this week showed resistance to oseltamivir and peramivir. (Because H1N1 viruses have been so rare this season, one virus accounts for 7.1% 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.

*There was an extra week of reporting during the 2014-2015 season.

Antiviral Drug-Resistant Influenza Virus

- Influenza viruses can sometimes develop resistance to antiviral medications.

- Antiviral resistance means that a virus has changed in such a way that the antiviral drug is less effective in treating or preventing illnesses caused by the virus.
- Influenza viruses constantly change as the virus makes copies of itself. Some changes can result in the viruses being resistant to one or more of the antiviral drugs that are used to treat or prevent influenza.
- Resistance of influenza A viruses to antiviral drugs can occur spontaneously or emerge during the course of antiviral treatment.
- Antiviral resistance is detected through laboratory testing.
- CDC reports specimens collected and tested through national surveillance as well as additional specimens tested at public health laboratories who share testing results with CDC.
- The vast majority of influenza viruses circulating in the United States remain susceptible to the neuraminidase inhibitor antiviral medications, oseltamivir, zanamivir and peramivir.
- Very few 2009 H1N1 viruses have been identified this season, accounting for less than 1% of all subtyped influenza A viruses reported to CDC from U.S. WHO and NREVSS collaborating laboratories.
- Of the 14 2009 H1N1 viruses analyzed for antiviral resistance this season, one (7.1%), 2009 H1N1 virus showed resistance to oseltamivir and peramivir. This is the first antiviral drug-resistant virus reported this season.
- Antiviral resistance among 2009 H1N1 viruses is rare.
- Oseltamivir-resistant viruses often have a single known substitution in the neuraminidase protein of the virus (H275Y) that confers oseltamivir resistance. The 2009 H1N1 virus reported this week has this substitution.
- CDC and state and local partners will continue to watch influenza viruses closely for possible emerging patterns of antiviral resistance in addition to watching for antigenic changes.
- Three FDA-approved influenza antiviral medications are recommended for use in the United States during this influenza season: oseltamivir (Tamiflu®), zanamivir (Relenza®), and peramivir (Rapivab®). More information about antiviral drug resistance can be found at http://www.cdc.gov/flu/about/qa/antiviralresistance.htm and http://www.cdc.gov/flu/antivirals/index.htm.
- Information on the monitoring of antiviral resistance of influenza viruses to oseltamivir and zanamivir is updated weekly in the CDC FluView surveillance report, which is available at: http://www.cdc.gov/flu/weekly/.

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.
- 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.

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 detecting small numbers of antigenic variants is common, without ever circulating 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, 65% 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

- Eleven influenza-associated pediatric deaths were reported to CDC this week.
- A total of 56 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.

Timing of Flu Season

- The timing of flu season can vary in different parts of the country, as can the length of the flu season.
- Since the 2001-2002 season, ILI has remained elevated for between 1 and 19 weeks each season, with an average of 13 weeks.

Take 3 Platform

- CDC always recommends three actions to fight flu:
    1. Take time to get a flu vaccine.
    2. Take everyday preventive actions like covering coughs and sneezes, staying away from sick people and washing your hands often to help stop the spread of respiratory viruses like flu, respiratory syncytial virus (RSV), rhinovirus and enterovirus D68.
    3. Take antivirals drugs for flu treatment if your doctor prescribes them. (If you have a high risk factor and get flu symptoms, see your doctor or another health care professional.)