CDC Influenza Division Key Points
January 9, 2015

In this document:

Summary Key Messages

- This week's FluView report indicates that flu activity remains high in the United States and is now widespread in 46 states and Guam (an increase from 43 states last week).
- While the proportion of outpatient visits for influenza-like illness (ILI) dipped slightly from 6.0% to 5.6%, it was above the national baseline for the seventh consecutive week.
- CDC also continues to receive reports of flu hospitalizations and deaths.
- Twenty-six pediatric deaths have been reported so far this season.
- Activity so far this season is similar to the 2012-2013 season, the last season when H3N2 viruses predominated.
- Some states have probably peaked at this point and are on the decline of their flu season, whereas other states are seeing increasing activity.
- Flu activity is likely to continue nationally for several weeks.
- 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.
- Influenza A (H3N2) viruses continue to be most common so far in the United States, accounting for more than 99% of all subtyped influenza A viruses reported to CDC from U.S. WHO and NREVSS collaborating laboratories.
- H3N2-predominant seasons have been associated with more severe illness and mortality compared to H1N1- or B-predominant seasons, especially in older people and young children.

- For example, 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.
- Hospitalization rates among people 65 and older are climbing steeply. Last week the hospitalization rate for people 65 and older was 75.1 per 100,000. This week it is 91.6 per 100,000. That is high, but typical of H3N2-seasons, which – as we've explained before – are more severe for older people and young children.
- In the last H3N2-predominant season (2012-2013), the cumulative hospitalization rate for people 65 and older at the end of the season was 183.2 per 100,000. It would not be surprising for us to see similar rates at the end of this season.
- The 122 Cities data shows that for the first time this season flu deaths are elevated (7.0%) above the epidemic threshold.
- It's likely that flu deaths will reach higher levels later this season since mortality tends to lag behind other indicators.
- So far, more than two-thirds of the influenza A (H3N2) viruses analyzed since October 1 are antigenically or genetically different from the H3N2 vaccine virus component this season. (See the FluView Activity Update below.)
- The vaccine may not work as well against these different A (H3N2) viruses.
- Two factors play an important role in determining the likelihood that flu vaccines will protect a person from flu illness: 1) the characteristics of the person being vaccinated (such as their age and health), and 2) the similarity or "match" between the flu viruses in the vaccine and those spreading in the community.
- Preliminary vaccine effectiveness (VE) estimates for the 2014-2015 season are expected to be available in mid- to late-January 2015. (See the section Influenza Vaccine Effectiveness below.)
- **CDC is urging influenza vaccination for any persons who have not been vaccinated yet this season, as vaccine may still offer benefit. This includes people who may have already gotten the flu this season; flu vaccine protects against three or four different viruses and it's possible that other viruses will circulate later in the season.**
- Antivirals drugs are a second line of defense to treat flu illness. People at high risk should take antiviral medications for the treatment of influenza illness if they have been prescribed.
- 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.)

- Antivirals are under-prescribed by health care professionals.
- On January 9, 2015, CDC held a telebriefing highlighting flu activity in the United States so far this season and reviewing the agency's antiviral treatment recommendations. A transcript of this media availability will be available following the briefing at CDC's web site: www.cdc.gov/media.
- 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.
- 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.

Vaccination

Annual flu vaccination is the first and most important step in protecting against flu and its potentially serious complications.

- As of early November 2014, fewer than half of Americans had reported getting a flu vaccine.
- The flu vaccine protects against three or four different influenza viruses, depending on which vaccine you get (trivalent or quadrivalent).
- Flu vaccination can reduce flu illnesses, doctors' visits, and missed work and school due to flu, as well as prevent flu-related hospitalizations and deaths.
- 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.)

- Even when some circulating viruses are different from the vaccine viruses, CDC continues to recommend flu vaccination.
- We cannot know which viruses will circulate over the season.
- Antibodies created through vaccination with one influenza virus can sometimes offer protection against drifted influenza viruses (this is called "cross-protection").
- While this year's vaccine may not work as well against the drifted H3N2 viruses, it can still protect many people and prevent flu-related complications.
- If we have a severe season (with H3N2 viruses predominating) getting a vaccine that provides even partial protection may be more important than ever.
- It is not too late to get vaccinated.
- Health care professionals should continue to vaccinate patients who have not yet received influenza vaccine this season.
- The HealthMap Vaccine Finder can be used to locate flu vaccine.

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.
- As of the week ending January 3, 2015, 68.4% of H3N2 viruses isolated in the United States since October 1, 2014 were drifted from the H3N2 vaccine virus component.

Implications on Vaccine Effectiveness

- So far this season, more than two-thirds of H3N2 viruses are different from the H3N2 vaccine virus.
- It's possible that vaccine effectiveness against these H3N2 viruses may be reduced.
- However, seasonal influenza vaccination can sometimes protect against antigenically different viruses.
- Influenza vaccination still offers the best way to prevent seasonal flu.
- In the context of reduced vaccine effectiveness, however, the use of influenza antiviral drugs as a second line of defense against the flu becomes even more important, especially for high risk people and people who are very sick (e.g., hospitalized).
- See the Influenza Vaccine Effectiveness section below for more information about measuring how well influenza vaccines work.

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.
- 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.
- The Food and Drug Administration has not received any reports of local, regional or national shortages of influenza antiviral drugs from manufacturers at this time.
- 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.
- It's still possible that spot shortages may occur in local areas. If needed, pharmacies should work with authorized distributors to obtain additional supplies of antivirals.
- It's also possible that in places with elevated influenza activity, locating influenza antiviral drugs may be more difficult.
- 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.
- CDC and FDA will continue to work with manufacturers to assess influenza antiviral supply this season.
- 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

FluView Activity Update

- According to this week's FluView report, influenza activity in the U.S. remains high overall and is likely to continue for several weeks.
- The severity of flu disease so far this season is similar to some previous seasons during which influenza A (H3N2) viruses have circulated predominantly. H3N2-predominant seasons often cause more severe disease among children younger than 5 years and adults 65 years and older compared to H1N1 seasons.
- Below is a summary of the key flu indicators for the week ending January 3, 2015:
  - For the week ending January 3, the proportion of people seeing their health care provider for influenza-like illness (ILI) decreased slightly to 5.6%, but is above the national baseline (2.0%) for the seventh consecutive week. Activity is beginning to decline in parts of the country and is increasing in others. 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 26 states experienced high ILI activity; a decrease from 29 states during the previous week. New York City and eight states (California, Florida, Illinois, Michigan, Nebraska, New Jersey, South Dakota, and Wyoming) experienced moderate ILI activity. Seven states experienced low ILI activity. Eight states experienced minimal ILI activity, and the District of Columbia and one state 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 Guam and 46 states, an increase from 43 states during the previous week. Puerto Rico, the U.S. Virgin Islands, and three states (Alaska, Arizona, and California) reported regional geographic influenza activity. Local flu activity was reported by the District of Columbia and one state (Hawaii). Geographic spread data show how many areas within a state or territory are seeing flu activity.
  - A total of 5,492 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 20.1 hospitalizations per 100,000 population. Last week, the overall cumulative rate was 12.6 hospitalizations per 100,000 population.

        - The hospitalization rate in people 65 years and older is 91.6 per 100,000. This is the highest rate of any age group. (The hospitalization rate for people 65 and older for the same week during 2012-2013 was 79.1 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 is now slightly above the epidemic threshold of 6.9%.
    - Five influenza-associated pediatric deaths were reported to CDC during the week ending January 3. All five deaths were associated with an influenza A virus for which no subtyping was performed and occurred during weeks 50, 51, 52, and 53 (weeks ending December 13, December 20, December 27, 2014, and January 3, 2015, respectively). A total of 26 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 3 was 24.7%. For the most recent three weeks, the regional percentage of respiratory specimens testing positive for influenza viruses ranged from 18.9% to 37.2%.
    - 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 3, 7,218 (96.0%) of the 7,515 influenza-positive tests reported to CDC were influenza A viruses and 297 (4.0%) were influenza B viruses. Of the 2,494 influenza A viruses that were subtyped, 99.7 % were influenza A (H3) viruses and 0.3% were influenza A (H1N1) pdm09 viruses.
    - CDC has antigenically or genetically characterized 355 influenza viruses, including 10 influenza A (H1N1) pdm09, 288 influenza A (H3N2) viruses and 57 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.
        - Ninety-one (31.6%) of the 288 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 197 (68.4%) influenza A (H3N2) viruses tested were different from A/Texas/50/2012. The majority of these 197 influenza A (H3N2) viruses were antigenically similar to A/Switzerland/9715293/2013, the influenza A (H3N2) component of the 2015 Southern Hemisphere influenza vaccine.
- Forty (70.2%) of the 57 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.
- Fifteen (88.2%) of the 17 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. Two (11.8%) of the B/Victoria-lineage viruses tested showed reduced titers to B/Brisbane/60/2008.

- Since October 1, 2014, CDC has tested 11 influenza A (H1N1) pdm09, 450 influenza A (H3N2), and 85 influenza B viruses for resistance to neuraminidase inhibitors (oseltamivir, zanamivir, and peramivir). All viruses showed susceptibility to oseltamivir, zanamivir and peramivir.
  - Previously, the neuraminidase inhibitors oseltamivir and zanamivir were the only recommended influenza antiviral drugs. On December 19, 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.

Influenza-Associated Pediatric Deaths

- Five influenza-associated pediatric deaths were reported to CDC this week.

- A total of 26 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.

Vaccine Supply

- Seven influenza vaccine manufacturers have projected that as many as 151 million to 156 million doses of influenza vaccine will be available for use in the United States during the 2014-2015 influenza season.
- Of the overall flu vaccine supply projected for the 2014-2015 season, manufacturers estimate that 76 million doses will be available as quadrivalent flu vaccines.
    - Of the total quadrivalent flu vaccine supply, as many as 18 million doses of the nasal spray influenza vaccine (LAIV) have been projected by the manufacturer to be available.
- As of December 5, 2014, manufacturers reported having shipped 145.4 million doses of flu vaccine.
- For the latest information on flu vaccine supply, including projections and doses distributed, visit http://www.cdc.gov/flu/professionals/vaccination/vaccinesupply.htm.

Influenza Vaccine Effectiveness

- Preliminary vaccine effectiveness (VE) estimates for the 2014-2015 flu season are expected to be available in mid- to late-January 2015.
- These estimates will be based on data from the U.S. Flu Vaccine Effectiveness (VE) Network.

- The U.S. Flu VE Network is designed to provide estimates of clinical effectiveness of licensed vaccines by age group and by influenza type and subtype.
- The network currently consists of five study sites spread across the United States.
- The five study sites include Marshfield, WI; Southeast Michigan; Seattle, WA; Pittsburgh, PA; and Temple, TX.
- Enrollees are patients evaluated in outpatient settings for acute respiratory symptoms with cough.
- Enrollment begins after laboratory-confirmed influenza cases are reported in local surveillance for two consecutive weeks, and continues for the rest of flu season.
- Patients are eligible to be enrolled in the study if they are older than six months of age (thus being eligible to receive influenza vaccination), they have reported acute respiratory illness with cough within seven days, and they have not been treated with influenza antiviral medications.
- Eligible patients complete an enrollment interview and answer basic questions regarding their influenza vaccination status, age, underlying health conditions, and other characteristics. When possible, influenza vaccination status is later confirmed by reviewing records. Following enrollment, a respiratory specimen is collected and tested for influenza by the CDC real-time reverse transcription polymerase chain reaction (RT-PCR). Influenza-positive samples are then typed and subtyped.

Background on Vaccine Effectiveness

How well the flu vaccine works can vary from year to year and from one person to another.

- Vaccine effectiveness (VE) can vary depending on 1) vaccine match and 2) the health and age of the person getting vaccinated.
- If the influenza viruses spreading are very different from the vaccine viruses, the vaccine won’t work as well.
- In general, the flu vaccine works best among young healthy adults and older children.
- Some older people and people with certain chronic illnesses might develop less immunity than healthy young adults after vaccination.
- This means that VE can vary by season; it can vary by virus type and strain and it can vary from person to person, depending on how well they respond to vaccination.
- While the vaccine match can vary, when the match is good, vaccination offers substantial benefit--reducing illnesses, antibiotic use, doctors' visits and lost work, and preventing hospitalizations and deaths.

- Even when the vaccine match is not good, vaccination can offer some benefit and is estimated to prevent thousands of flu-related hospitalizations.

VE is difficult to measure and study results can vary widely based on a) the study design, b) the outcome being measured, and c) the population being studied.

- "Randomized studies," in which people either get vaccine or placebo and then are followed to see who gets flu and who doesn't, are the "gold standard" for determining the effectiveness of a vaccine, but withholding a potentially life-saving vaccine, especially among high-risk people, has ethical implications, so CDC does not conduct randomized influenza vaccine effectiveness studies in the United States.
- Studies to determine how effective a vaccine is often use a study method where "case" patients with influenza are compared to "control" patients who do not have influenza infections. Investigators have shown that study results can vary considerably on the basis of how control patients are selected and not because of the vaccines.
- Vaccine effectiveness can be measured by looking at different outcomes, for example, measuring influenza-like illness (which can include non-influenza illness), or measuring laboratory-confirmed influenza infection which means that a laboratory test has been done to determine if a patient with respiratory illness has influenza or an infection caused by another respiratory pathogen. A broader outcome such as protection against influenza-like illness will be less precise than a more specific outcome such as laboratory-confirmed influenza infection; a more specific outcome is likely to give a better measure of VE.

In recent years, CDC has developed new and improved methodology to measure VE.

- CDC has been working with researchers at universities and hospitals since 2003-2004 to estimate VE in non-randomized studies using culture- or RT-PCR-confirmed influenza infection as the outcome.
- CDC's study methodology currently uses RT-PCR-confirmed medically attended influenza virus infections as an outcome and is therefore likely to be more accurate and more specific.
- The CDC study methodology looks at outcomes in several different sites across the United States to gather more representative data.
- The methodology also looks at people of all age groups, so it should give a more accurate assessment of VE across different age groups.
- This study methodology should capture VE associated with each season.

Recent studies show vaccine can protect about 6 out of 10 people from getting the flu during a well-matched season.

- CDC-supported recent studies looked at outcomes in four different sites across the United States.
- Overall estimates of vaccine effectiveness during the U.S. 2010-2011 through 2013-2014 influenza seasons ranged between 47%-60%.
- Similar outcomes have been reported in other publications. Examples:
    - A randomized study (Monto et al.) looking at the 2007-2008 influenza season found trivalent inactivated vaccine (flu shot) protected 7 out of 10 people from influenza illness.
    - The main study that led to the licensure of LAIV was one conducted in children that showed that LAIV protected up to 9 out of 10 children vaccinated against the flu.
    - A meta-analysis of randomized clinical trials of LAIV in children found that 2 doses of LAIV in vaccine-naïve children prevented infection with 77% of antigenically similar viruses and 72% of all viruses regardless of antigenic similarity.
    - A meta-analysis of efficacy and effectiveness studies published in the Lancet Infectious Diseases in October 2011 found:
        - Overall, the flu shot (the trivalent influenza vaccine in this study) had 59% efficacy against flu in healthy adults, according to the journal article.
        - The nasal spray flu vaccine prevented flu in 83% of children 7 years of age or younger.
        - The 2009 H1N1 monovalent vaccine used during the 2009 H1N1 pandemic had a median effectiveness of 69% against medically attended 2009 H1N1 illness in people younger than 65 years of age.
- This is considered a moderate rate of vaccine effectiveness compared with effectiveness of many childhood vaccines and it is relatively stable across many age groups.
- Improvements in vaccine technology to increase vaccine effectiveness are needed.
- However, while not perfect, the flu vaccine offers the best protection we have against influenza right now.

LAIV Effectiveness Last Season and Vaccination of Children This Season

- Since 2008, ACIP and CDC have recommended that all children 6 months and older (with rare exceptions) receive influenza vaccine annually, using any licensed age-appropriate vaccine.

- During the summer of 2014, ACIP and CDC recommended that beginning during the 2014-2015 influenza season, live attenuated influenza vaccine (LAIV, or the "nasal spray vaccine") should be used for healthy children 2 through 8 years of age when immediately available and when there are no contraindications or precautions against getting that vaccine.
- This decision was based on previous data showing that LAIV offered superior protection against influenza virus infection compared to IIV in young children.
- However, recently available CDC analyses showed that there was no measurable effectiveness for LAIV against influenza A (H1N1) among children enrolled in a CDC-sponsored study last season.
- There were not enough cases of infection in the CDC study with H3N2 or B viruses to calculate vaccine effectiveness against those viruses in children last season.
- The reasons behind the lack of effectiveness against H1N1 infections for LAIV during the 2013-2014 season are not fully understood.
    - It is possible that results may be specific to the H1N1 component of LAIV. Influenza H1N1 viruses predominated during the 2013-2014 season for the first time since their emergence in 2009 when they caused a pandemic.
    - It also is possible – though less likely – that there is an unidentified issue with the study methods or analysis plan for measuring LAIV vaccine effectiveness.
- The 2013-2014 season LAIV VE estimates against H1N1 for children suggest that LAIV may not protect against H1N1 viruses during the 2014-2015 season because the same H1N1 vaccine virus from the 2013-2014 vaccine is included in the 2014-2015 vaccine.
- However, the nasal spray vaccine continues to be a recommended option for vaccination because:
    - All LAIV is designed to protect against four different influenza viruses: influenza A (H1N1), A (H3N2) and two influenza B viruses;
    - Surveillance shows that there is substantially more circulation of influenza A (H3N2) and B viruses and very little circulating H1N1 so far;
    - LAIV has been shown to offer good protection against influenza A (H3N2) and influenza B viruses in the past;
    - LAIV may offer better protection than IIV against antigenically drifted viruses that may circulate this season; and
    - Vaccine providers have received their vaccine for the 2014-2015 season and have likely administered a good proportion of it.
- People who have not been vaccinated yet this season should get vaccinated now.

- Parents should seek to get their children immunized with whatever vaccine is immediately available and indicated.
- Influenza vaccination should not be delayed to procure a specific vaccine preparation.
- The HealthMap Vaccine Finder can be used to locate vaccine.
- Children needing one dose of vaccine this season who got the nasal spray vaccine are considered fully vaccinated and do not need to be revaccinated.
- Children needing two doses of vaccine this season who have only gotten one dose can get either the nasal spray vaccine or the flu shot as their second dose, whatever is immediately available.
- See the CDC statement, "CDC Statement on LAIV Effectiveness and Vaccination of Children," at: http://www.cdc.gov/flu/news/nasal-spray-effectiveness.htm.

Influenza & Pneumococcal Vaccine

- Each year in the United States, about 18,000 adults 65 years or older die and thousands more end up in the hospital because of pneumococcal disease.
- The best way to prevent pneumococcal disease is by getting vaccinated.
- CDC recommends all adults 65 years or older receive two doses of pneumococcal vaccines:
    - One dose of pneumococcal conjugate vaccine (PCV13) first, followed 6 to 12 months later by a dose of pneumococcal polysaccharide vaccine (PPSV23).
    - Learn more about when pneumococcal vaccines are needed for adults: http://www.cdc.gov/features/adult-pneumococcal.
- The two pneumococcal vaccines should never be given together at the same visit, but it is safe to give either pneumococcal vaccine with influenza vaccine at the same visit.
- While you don't need a pneumococcal vaccine every year, it is important to get a flu vaccine each flu season because having the flu increases your chances of getting pneumococcal disease.
- Pneumococcal vaccines may be available at private doctor offices, public or community health clinics, or pharmacies.
- Most private health insurance covers pneumococcal vaccines and, beginning on February 2, 2015, Medicare part B will cover 100% of the cost of the initial dose of the pneumococcal vaccine, as well as the second pneumococcal vaccine administered one year after the first vaccine was administered.

- Talk to your health care professional to make sure you are up-to-date on pneumococcal vaccination, as well as other vaccines that may be recommended for you based on your age, health condition, job, lifestyle, or other factors.