CDC Influenza Division Key Points
MMWR Updates
February 20, 2014

In this document:

Summary Key Messages

- On February 20, 2014, CDC published interim adjusted estimates on how well the 2013-2014 influenza vaccine protected against having to go to the doctor for flu this season. The MMWR report is available on the CDC website at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6307a1.htm?s_cid=mm6307a1_w.
- In the same MMWR, CDC published a second report with a surveillance update on flu activity in the United States so far this season. The report entitled "MMWR Update: Influenza Activity – United States, September 29, 2013–February 8, 2014" is available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6307a3.htm?s_cid=mm6307a3_w.
- A report on severe influenza illness among California residents younger than 65 years was also published in the MMWR. The report, "Influenza-Associated Intensive-Care Unit Admissions and Deaths — California, September 29, 2013-January 18, 2014," is available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6307a2.htm?s_cid=mm6307a2_w.
- The VE study results indicate that influenza vaccination offered substantial protection against the flu this season, reducing a vaccinated person's risk of having to go to the doctor for flu illness by about 61% across all ages.
- VE estimates against influenza A and B ranged from 52% for people 65 and older to 67% for children 6 months to 17 years.
- More specifically, VE estimates against this season's predominant H1N1 strain ranged from 56% in people 65 and older to 67% for children 6 months to 17 years.
- The interim VE estimates this season are comparable to results from studies during other seasons when the viruses in the vaccine have been well-matched with circulating influenza viruses.
- The estimates also are similar to interim estimates from Canada for 2013-14 published recently.
- While flu vaccine can vary in how well it works, vaccination offers the best protection currently available against influenza infection. CDC recommends that everyone 6 months and older get an annual flu vaccine.

- The VE study results show that vaccinated people were substantially better off this season than people who did not get vaccinated.
- The surveillance report highlights the predominance of the 2009 H1N1 flu virus this season and the high proportions of flu hospitalizations and deaths that have occurred in younger- and middle-aged adults this season.
- Of the hospitalizations reported to CDC this season, 61% have been in people 18 to 64 years old.
- More commonly, most flu hospitalizations occur in people 65 and older. Usually 50-60% of flu hospitalizations occur in people aged 65 years and older.
- Additionally, this season, people 25 years to 64 years of age have accounted for about 60% of flu deaths compared with 18%, 30%, and 47% for the three previous seasons respectively. During 2009-2010, people 25 years to 64 years accounted for an estimated 63% of deaths.
- These hospitalizations and deaths are a somber reminder that flu can be serious for anyone – not just the very young and people aged 65 and older and underscores the importance of vaccination for everyone.
- Unfortunately, younger adults – especially those who are otherwise healthy – are less likely to get vaccinated.
- Estimates as of early-November 2013 indicate that among people 18-64 years of age, only 34% had been vaccinated. This vaccine coverage estimate is lower than vaccine coverage estimates for people aged 6 months-17 years of age (41%) and people 65 and older (62%) in the U.S. during that same time period.
- Seasonal flu is responsible for severe illness and death every year, but who is most affected each season can vary depending on the predominant circulating virus.
- This season's pattern of higher levels of flu-related deaths and hospitalizations among younger and middle-aged adults is similar to what was seen in 2009 when the H1N1 virus emerged to cause a pandemic.
- For example, a report in today's MMWR describes the epidemiologic, laboratory, and clinical characteristics of 405 severe influenza cases (94 influenza-associated deaths and 311 intensive care unit [ICU] admissions) among California residents younger than 65 years old as reported to the California Department of Public Health (CDPH).
- The number of fatal and ICU cases reported to the CDPH as of January 18, 2014 is more than has been recorded in any season since the 2009 pandemic.
    - Of 405 ICU and fatal influenza cases, 266 (66%) occurred among patients aged 41-64 years; 39 (10%) severe influenza illnesses occurred among children aged <18 years.

    - The majority of patients with fatal illness tested positive for 2009 H1N1 virus, suffered from underlying medical conditions that predisposed them to severe influenza complications (most commonly diabetes, COPD, asthma and morbid obesity), and had not received 2013-14 seasonal influenza vaccine.

- The 2009 H1N1 virus has continued to circulate since the pandemic as a seasonal flu virus, but this is the first flu season since the pandemic that this virus has circulated so widely.
- All flu vaccines this season are designed to protect against H1N1 and VE against H1N1 this season was estimated to be 62% for all age groups.
- At this time, even with a recent decrease in several key indicators, influenza activity remains elevated overall nationally and is expected to continue for a number of weeks in certain parts of the country.
- Annual influenza vaccination efforts should continue for as long as influenza viruses are circulating.
- Influenza vaccination is especially important for people at high risk for serious flu complications including: 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.
- While vaccination is the first and best way to prevent flu, CDC recommends antiviral medications as a second line of defense to treat influenza in certain patients, regardless of vaccination status.
- Antiviral treatment can avert serious outcomes and should begin as quickly as possible in high risk persons, including people 65 and older, young children, pregnant women, and people with certain underlying conditions like asthma, heart disease, diabetes and neurological disorders.
- A health care provider can determine if the patient needs influenza antiviral drugs. These drugs work best when started soon after influenza symptoms begin (within 2 days), but observational studies have shown that giving antivirals 48 or more hours after symptom onset can still prevent serious flu-related outcomes.
- In addition to vaccination and antiviral drugs, everyday preventive actions can help mitigate the risk of infection. Flu spreads mainly in droplets expelled when people with flu cough, sneeze or talk.
- As always, stay away from people who are sick. If you are sick, stay home to avoid spreading your illness to others.

- At this point in the season, people may have to check with more than one vaccine provider in order to locate vaccine, but supplies of vaccine should still be available.
- CDC routinely recommends that vaccination efforts continue as long as influenza viruses are circulating. People seeking vaccination may need to call more than one provider to locate vaccine at this time. The flu vaccine finder at http://flushot.healthmap.org/ may be helpful.

MMWR: Interim Estimates of 2013-14 Seasonal Influenza Vaccine Effectiveness—United States, February 2014

- CDC recommends influenza vaccination as the first step to prevent illness caused by flu viruses. As of February 8, 2014, influenza activity was still elevated across most of the United States.
- On February 21, 2014, CDC published a report of interim adjusted estimates of 2013-2014 influenza vaccine effectiveness (VE) in the Morbidity and Mortality Weekly Report (MMWR) entitled: "Interim Estimates of 2013-14 Seasonal Influenza Vaccine Effectiveness—United States, February 2014."
- The MMWR report is available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6307a1.htm?s_cid=mm6307a1_w.
- Data collected from 2,319 children and adults were used to estimate the overall effectiveness of seasonal influenza vaccine for preventing outpatient medically-attended acute respiratory infection (ARI). The outpatients were enrolled at five study sites across the United States through the U.S. Influenza Vaccine Effectiveness (Flu VE) Network.
- CDC reported an overall vaccine effectiveness of 61% (95% confidence interval [CI]:52% to 68%) against any influenza infection. This estimate was adjusted for study site, age, sex, race/ethnicity, self-rated health and days from illness onset to enrollment.
- **These findings indicate that vaccination with the 2013-2014 influenza season vaccine reduced the risk of outpatient medical visits due to influenza by approximately 60% for children and adults.**
- An adjusted VE estimate of 62% (CI=53% to 69%) against 2009 H1N1 influenza viruses was reported.
    - While other studies have found that the flu vaccine generally appeared to work best among healthy adults and older children, similar vaccine effectiveness against 2009 H1N1 was observed among *all* age groups in this study.

  - During the study period, 2009 H1N1 influenza viruses accounted for 98% of the influenza viruses detected.
  - This is the H1N1 virus that emerged in 2009 to cause a pandemic. This virus has continued to circulate since the pandemic as a seasonal flu virus, but this is the first flu season since the pandemic that 2009 H1N1 has circulated so widely.
  - These interim adjusted VE estimates against 2009 H1N1 medically-associated outpatient visits are comparable to VE estimates measured for monovalent 2009 H1N1 vaccine during the H1N1 pandemic and for seasonal vaccines in years when the vaccine is well-matched to circulating strains.

- These interim VE estimates for the 2013-2014 seasonal influenza vaccine suggest continued effectiveness in preventing outpatient medical visits associated with 2009 H1N1 virus infection.
- The protective benefits of the 2013-2014 influenza vaccine among children and adults shown in this report offer support to the public health benefit of the universal recommendation for annual vaccination with the seasonal influenza vaccine.
- To date, despite a decrease in several key indicators, influenza activity remains elevated overall nationally and is expected to continue for several weeks in certain parts of the country. Annual influenza vaccination efforts should continue for as long as influenza viruses are circulating.
- These interim estimates, however, indicate that some vaccinated persons will become infected with influenza despite having been vaccinated.
- Therefore, clinicians and the public are reminded of CDC's influenza antiviral treatment recommendations. Antiviral medications should be used as recommended for treatment in patients, regardless of vaccination status.
- See the CDC website for more information at Influenza Antiviral Medications: Summary for Clinicians (for health care providers) and What You Should Know about Flu Antiviral Drugs (for the public).
- CDC will continue to monitor VE throughout the season and will publish final VE estimates following the conclusion of the season.
- The final, adjusted vaccine effectiveness estimates for the 2013-2014 influenza vaccine are likely to be somewhat different from the current interim estimates for a number of reasons, including adjustments for additional potential confounders, such as chronic medical conditions in patients, which are not available for interim estimates.
- VE estimates could also change as more patient data become available, or if changes occur in the circulating influenza viruses during the remainder of this season.

Other Results

- Across study sites, the proportion of enrollees vaccinated with 2013-2014 influenza seasonal vaccine was 29% among influenza cases compared with 50% among influenza-negative controls.
- Of the 2,319 children and adults with ARI enrolled at the study sites, 784 (34%) tested positive for influenza by rRT-PCR. Of these, 778 (99%) were influenza A viruses and 6 (1%) were influenza B viruses.
    - Among 755 subtyped influenza A viruses, 742 (98%) were 2009 H1N1 viruses.
    - The 2009 H1N1 viruses tested by CDC this season, including viruses from the U.S. VE Flu Network study sites, have been antigenically similar to A/California/7/2009, the H1N1 component of the 2013-2014 influenza vaccines. Sequencing analyses of H1N1 virus specimens have also shown similarity to the recommended vaccine virus.

Methodology

- From December 2, 2013 to January 23, 2014, patients aged 6 months and older who sought outpatient medical care for an ARI with cough, within 7 days of illness onset, were enrolled at five study sites within the U.S. Flu VE Network.
- Study enrollment began at each site after at least two consecutive weeks of laboratory-confirmed cases of influenza had been identified through local surveillance.
- Patients were eligible for enrollment if they:
    1) were aged ≥6 months on September 1, 2013, and thus were eligible for vaccination;
    2) reported an ARI with onset ≤7 days prior to their visit; and
    3) had not 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).
- 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

- 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.
- 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.

MMWR Update: Influenza Activity – United States, September 29, 2013–February 8, 2014

- The February 21, 2014 Morbidity and Mortality Weekly Report (MMWR) contains a summary of influenza activity in the United States for September 29, 2013 – February 8, 2014.
- The MMWR report is available on the CDC website at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6307a3.htm?s_cid=mm6307a3_w.

- Key observations include the following:
    - Influenza activity in the United States began increasing in November and remained elevated and widespread as of February 8.
    - This season, influenza activity began to increase in the southern states and, by the end of December, high influenza activity was seen throughout the country.
    - Since the start of the season, influenza A (H1N1)pdm09 (pH1N1) viruses have predominated in the United States. Influenza A (H3N2) viruses and influenza B viruses have been identified less frequently.
    - This influenza A (H1N1) virus is the same virus that was first identified in 2009 and which caused the 2009 influenza pandemic.
    - The vast majority of influenza viruses characterized so far this flu season have been like the viruses in the 2013-2014 Northern Hemisphere influenza vaccine.
    - Influenza viruses have been a significant cause of respiratory illness this flu season. Between September 29 and February 8, of the 189,123 respiratory specimens that were tested for influenza, 19% were influenza-positive.
    - This season, the percentage of outpatient visits to doctors for influenza-like illness (ILI) equaled or exceeded the national baseline of 2.0% from the week ending November 30, 2013 to February 8, 2014 and has ranged from 1.2% to 4.6% since September 29, 2013. During the 1997–98 through 2012–13 seasons (excluding the 2009 pandemic), peak weekly percentages of outpatient visits for ILI ranged from 2.4% to 7.6%.
    - For the week ending February 8, 2014 (week 6), all 10 regions reported ILI activity above their region-specific baseline levels. This is the fourteenth week this season during which one or more regions exceeded their region-specific baselines.
    - Resistance to the antiviral drugs oseltamivir and zanamivir among currently circulating influenza viruses is low. Since Oct 1, 2013, the vast majority of influenza viruses tested have shown susceptibility to antiviral drugs oseltamivir and zanamivir.
        - Of the 3,109 pH1N1 viruses tested for antiviral resistance, 25 were found to be resistant to oseltamivir. No viruses have shown resistance to zanamivir.
        - All influenza A (H3N2) and influenza B viruses tested for antiviral resistance were sensitive to both oseltamivir and zanamivir.
    - Between September 29 and February 8, the weekly percentage of deaths attributed to pneumonia and influenza (P&I) ranged from a low of 5.3% to a high of 8.7% (week 4). As of the week ending February 8, the weekly

percentage of deaths had exceeded the epidemic threshold for five consecutive weeks (beginning with the week ending January 11, 2014).

- Peak weekly percentages of deaths attributed to P&I in the previous five seasons range 7.9% during the 2008-2009 and 2011-2012 seasons to 9.9% in the 2012-13 season.

- As of February 8, 2014 (week 6), 50 influenza-related pediatric deaths were reported to CDC for the 2013-14 season. One pediatric death was associated with an influenza B virus, two deaths were associated with an influenza virus for which the type was not determine, one death was associated with an influenza A and influenza B virus co-infection,17 deaths were associated with influenza A virus infection that was not subtyped, and 29 deaths were associated with pH1N1 viruses.
- Between October 1 and February 8, 24.6 hospitalizations per 100,000 were associated with laboratory-confirmed influenza. People 65 years and older had the highest influenza-associated hospitalization rate (50.9 per 100,000), followed by adults 50-64 years (38.7 per 100,000).
    - As of February 8, 61.2% of the reported hospitalizations have been in people 18 to 64 years old, while 24.8% of hospitalizations have occurred in adults 65 years and older.
    - More commonly, most flu hospitalizations occur in people 65 years and older.
- The most commonly reported underlying medical conditions among children (those aged <18 years) hospitalized with influenza were asthma (24%), neurologic disorders (13%), obesity (10%), and chronic lung disease (excluding asthma) (8%). Forty-three percent of hospitalized children had no underlying medical conditions that place them at higher risk for flu-related complications.
- The most commonly reported chronic underlying medical conditions in adults were obesity (43%), metabolic disorders (33%), cardiovascular disease (29%), and chronic lung disease (excluding asthma) (27%); fifteen percent of hospitalized adults had no underlying medical conditions that place them at higher risk for flu-related complications.
- Among 301 hospitalized women of childbearing age (15–44 years), 65 (22%) were pregnant.

Additional Information

- This is the first season since the 2009 pandemic that pH1N1 has been the predominant influenza virus circulating in the United States.

- During the pandemic, when pH1N1 viruses were predominant, younger adults and children, and particularly people with chronic medical conditions, were harder hit by flu compared with adults aged 65 years and older.
- People aged 25-64 years have accounted for approximately 62% of all influenza-associated deaths so far this season, compared with 18% in 2012-13, 30% in 2011-12, 47% in 2010-11.
- The more severe impact of pH1N1 on adults aged 18–64 years is thought to result from at least two factors:
    - Persons in these age groups likely lack the cross-reactive immunity to pH1N1 that adults aged ≥65 years have acquired from past infection with antigenically related viruses.
    - In general, CDC estimates younger adults – especially those who are otherwise healthy – are less likely to get vaccinated.
- Surveillance data available from this season are a reminder that influenza can cause severe illness, even in adults aged 18-64 years.
- Vaccination is the best way to prevent influenza and its complications and is recommended annually for all persons aged 6 months and older.
- Antiviral treatment can avert serious outcomes and should begin as quickly as possible in persons with severe disease or in other persons at high risk of complications, including people 65 and older, young children, pregnant women, and people with certain underlying conditions like asthma, heart disease, diabetes and neurological disorders.
- While antiviral drugs work best when given within 48 hours of symptom onset, observational studies have shown that giving antivirals 48 or more hours after symptom onset can still prevent serious flu-related outcomes.