

CDC Influenza Technical Key Points

February 15, 2018

In this document:

- [Summary Key Points](#)
- [U.S. Vaccine Effectiveness](#)
- [U.S. Flu Activity Update](#)

Summary Key Points

- On Thursday, February 15, 2018 two influenza-related reports appeared in the Morbidity and Mortality Weekly Report ([MMWR](#)): “Interim Estimates of 2017-18 Seasonal Influenza Vaccine Effectiveness – United States, February 2018” and “Update: Influenza Activity — United States, October 1, 2017– February 3, 2018”
- This flu season started early and has been intense, with record-breaking levels of influenza-like illness and hospitalization rates.
- As of February 3, flu activity was high and widespread across most of the country and significant activity is expected to continue for several weeks.
- CDC estimates that U.S. flu vaccines this season were 36% effective overall against all influenza A and B viruses.
- This means that this season’s vaccine reduced a vaccinated person's risk of getting sick and having to go to the doctor for flu by about one-third.
- Estimates showed that effectiveness varied by virus type, subtype and even by the age of the people being vaccinated in some cases.
- As expected, effectiveness against the most common H3N2 virus was lower (25%) while effectiveness against H1N1 (67%) and influenza B viruses (42%) was higher.
- A notable exception to lower VE against H3N2 viruses was that it offered good protection (51%) for children 6 months to 8 years.
- This season’s vaccine performed as we expected and offers protection for many people who received it.
- These findings also underscore the need for better flu vaccines, and the scientific data to help guide efforts to improve flu vaccines.
- CDC continues to recommend getting a flu vaccine. While flu vaccine varies in how well it works, it is the best available way to prevent influenza and can reduce illnesses, doctor's visits and hospitalizations.
- While flu vaccine effectiveness can vary, CDC recommends an annual flu vaccine as the best way to prevent seasonal flu.
- CDC also recommends rapid treatment of seriously ill and high-risk suspect flu patients with influenza antiviral drugs.

U.S. Flu Vaccine Effectiveness Estimates

Topline Messages

- On February 15, CDC published a Morbidity and Mortality Weekly Report (MMWR) entitled “Interim Estimates of 2017-18 Seasonal Influenza Vaccine Effectiveness – United States, February 2018.” This report is available online at <https://www.cdc.gov/mmwr/index.html> .
- During each flu season since 2004-2005, CDC has estimated the effectiveness of seasonal flu vaccines to prevent laboratory-confirmed flu illness resulting in a doctor’s visit.*

CDC Influenza Technical Key Points

February 15, 2018

*Clinically what is being measured is laboratory confirmed influenza associated with medically attended acute respiratory illness (ARI).

- This report uses data from 4,562 children and adults enrolled in the U.S. Influenza Vaccine Effectiveness Network (U.S. Flu VE Network) during November 2, 2017 – February 3, 2018.
- During this period, overall adjusted vaccine effectiveness (VE) against influenza A and B virus infection was **36%** (95% CI: 27% to 44%).
- This means that CDC's early 2017-2018 estimates show the flu vaccine has performed similarly to what CDC expected at the beginning of the season with A(H3N2) viruses driving the majority of flu activity. Overall, the seasonal flu vaccine has reduced the risk of getting sick and having to go to the doctor from flu by about one third.
- Influenza A(H3N2) viruses were responsible for most (69%) of the flu infections reported in this study, and as expected, VE was lower against influenza A(H3N2) viruses.
- VE was **25%** (95% CI: 13%–36%) against illness caused specifically by influenza A(H3N2) viruses.
- Of note: VE was much higher in children 6 months through 8 years of age: overall VE against influenza A and B viruses was **59%** (95% CI: 44%–69%) in this age group.
- Children in this age group also had higher VE specifically against A(H3N2). VE against A(H3N2) viruses was 51% (95% CI: 29%–66%) in children 6 months through 8 years of age. This means the risk for A(H3N2) illness that required a doctor's visit was reduced by more than half among this group of vaccinated children.
- VE against other flu viruses, including against influenza A(H1N1) and influenza B viruses, also was higher than against A(H3N2).
 - VE was **67%** (CI:54%–76%) against influenza A(H1N1)pdm09 viruses
 - VE was **42%** (CI: 25%–56%) against influenza B viruses, providing a moderate level of protection.
- These interim VE estimates reflect the ongoing challenges with creating effective flu vaccines against influenza A(H3N2) viruses. (H3N2 viruses have proven problematic since the 2011–12 season.)
- The interim estimate of 25% VE against A(H3N2) viruses this season shows that seasonal flu vaccines are providing some protection, in contrast to recently reported, non-significant interim estimates of 17% from Canada and 10% from Australia.
- These results also are similar to the final U.S. VE estimates of 32% against A(H3N2) viruses reported last season (2016-2017).
- However, there is room for improvement.
- There are many possible reasons for lower effectiveness against H3N2 viruses, and it's important to get more data to help develop better flu vaccines.

CDC Influenza Technical Key Points

February 15, 2018

- Several hypotheses for why flu vaccines provide less benefit against H3N2 viruses could include the following:
 - Host factors, such as how a person’s unique immune system responds to vaccination or previous flu infections.
 - Note: some existing science suggests that the flu viruses people are exposed to early in life will affect the way their immune systems respond to flu infection or vaccination later in life – a process called “imprinting” or “original antigenic sin.”
 - Another factor could be the unique characteristics of circulating H3N2 viruses and changes that occur in H3N2 viruses over time.
 - And lastly, the egg-adapted changes that occur with greater frequency in H3N2 viruses when they are grown in eggs as part of the flu vaccine manufacturing process. Note: A(H3N2) viruses are particularly difficult to grow in eggs.
- While these points represent factors that public health scientists and officials must study and better understand in the future, these early VE estimates also underscore the need for ongoing influenza prevention and treatment measures now.
- CDC continues to recommend flu vaccination because the flu vaccine can still prevent some infections with flu viruses that are expected to continue circulating for several weeks.
 - Vaccine effectiveness point estimates for influenza B and A (H1N1) indicate that 2017-2018 flu vaccines will reduce people’s risk of flu illness associated with influenza B or A(H1N1) viruses that results in a doctor’s visit by 42% to 67%.
 - Also, even with vaccine effectiveness of 25% against H3N2 viruses, flu vaccination will still prevent a substantial amount of illness due to this virus.
 - Flu vaccination has prevented thousands of hospitalizations during previous seasons when A(H3N2) viruses were predominant, including during the 2014–15 season when interim VE estimates were similar to those reported here.
- In the United States, annual vaccination against seasonal flu is recommended for all people 6 months of age and older.
- In addition, appropriate use of flu antiviral medications for treatment of severely ill people or people at high risk for complications from the flu who develop flu symptoms is important, especially among older adults, who currently have the highest hospitalization rates.
- The VE estimates being reported today are interim estimates for the 2017-2018 season, and the final VE estimates will be published after the season is over. The final season VE estimates may differ from these interim estimates, and based on previous end of season estimates, they may be a little lower than the interim estimates.
- CDC will continue to monitor vaccine effectiveness through the rest of the season. Yearly monitoring of vaccine effectiveness is critical to identifying vaccine issues that need to be understood and corrected.

CDC Influenza Technical Key Points

February 15, 2018

Methods

- At five study sites, patients 6 months of age and older seeking outpatient medical care for ARI with cough within 7 days of illness onset were enrolled. The five study sites of the U.S. Flu VE Network are located in the following states:
 - Wisconsin,
 - Michigan,
 - Washington
 - Pennsylvania, and
 - Texas.
- Participants were interviewed to collect demographic data, information on general and current health status, and symptoms, and 2017-2018 vaccination status.
 - (Note: a limitation of this current data is that vaccination status included self-report at four of five sites. Self-reporting can bias results towards higher vaccination rates.)
- Nasal and oropharyngeal swabs (or nasal swabs) were collected to obtain respiratory specimens.
- Specimens were tested at U.S. Flu VE Network laboratories using CDC's rRT-PCR protocol.
- VE against all influenza virus types combined and against viruses by type/subtype were estimated as $100\% \times (1 - \text{odds ratio})$.
- Estimates were adjusted for study site, age group, sex, race/ethnicity, self-rated general health, number of days from illness onset to enrollment, and week of illness.
- Interim VE estimates for the 2017-18 season were based on patients enrolled through February 3, 2018.

Results

- Among the 4,562 children and adults with ARI enrolled at the five study sites from November 2, 2017 through February 3, 2018, a total of 1,712 (38%) tested positive for influenza by rRT-PCR, including 1,392 (81%) influenza A viruses and 323 (19%) influenza B viruses.
- Among 1,340 subtyped influenza A viruses, 1,143 (85%) were A/(H3N2) viruses and 208 (16%) were A(H1N1)pdm09 viruses.
- Most (98%) of influenza B viruses belonged to the B/Yamagata lineage.
- The proportion of patients with influenza differed by study site, sex, age group, race/ethnicity, self-rated health status, and interval from illness onset to enrollment.
- The percentage of patients who were vaccinated ranged from 45% to 59% among study sites and differed by sex, age group, race/ethnicity, and self-rated health status.

CDC Influenza Technical Key Points

February 15, 2018

- Among ARI patient participants, 43% of those with influenza had received the 2017-2018 seasonal influenza vaccine, compared with 53% of influenza –negative participants.
- VE During this period, overall adjusted vaccine effectiveness (VE) against influenza A and B virus infection associated with medically attended ARI was **36%** (95% CI: 27% to 44%).
 - Most (69%) of influenza infections were caused by influenza A(H3N2) viruses.
 - VE was estimated to be **25%** (95% CI: 13%–36%) against illness caused by influenza A(H3N2) viruses
 - Of note: statistically significant protection against medically attended influenza was found among children 6 months through 8 years of age: VE was 59% (95% CI: 44%–69%).
 - VE was estimated to be **67%** (CI:54%–76%) against A(H1N1)pdm09 viruses
 - VE was estimated to be **42%** (CI: 25%–56%) against influenza B viruses.
- As of February 3, 2018, a total of 257 influenza A(H3N2) viruses from U.S. Flu VE Network participants had been characterized by CDC.
 - 240 (93%) belonged to either genetic group 3C.2a (226 viruses) or to the related subgroup 3C.2a1 (14), whereas 17 (7%) belonged to group 3C.3a.
 - Genetic group 3C.2a includes the A/Hong Kong/4801/2014 reference virus representing the A(H3N2) component of the 2017-2018 Northern Hemisphere influenza vaccines.

Background

- Each season, CDC studies how well flu vaccines work by collecting data through the U.S. VE network of five sites across the United States.
- Flu vaccine effectiveness can vary each year based on a number of factors, including the match between vaccine viruses and circulating viruses, what viruses are circulating, and the age and immune factors of the person being vaccinated.
- CDC will continue to publish influenza laboratory and disease surveillance data weekly in FluView.
- Updated VE estimates will be provided as warranted and final VE estimates will be published after the season ends. Final season VE estimates may differ from the interim estimates, and may be a little lower than the interim estimates.

U.S. Flu Activity Update

MMWR: Influenza Activity — Influenza Activity — United States, October 1, 2017–February 3, 2018 Seasonal Flu Update:

The MMWR report is available on CDC’s website at: <https://www.cdc.gov/mmwr/index.html>.

Influenza illness during the 2017-2018 season has been substantial thus far, with some of the highest levels of ILI and hospitalization rates in recent years and elevated activity occurring in most of the country simultaneously.

CDC Influenza Technical Key Points

February 15, 2018

- Clinical laboratories tested 666,493 specimens for influenza virus, and 124,316 (18.7%) tested positive.
 - The percentage of specimens testing positive for influenza A viruses peaked at 21.8% during the week ending January 13; the percentage testing positive for influenza B viruses has continued to increase and was 8.1% during the week ending February 3.
- Public health laboratories tested 51,014 specimens for influenza virus, and 27,669 tested positive.
 - This includes 23,257 (84.1%) for influenza A and 4,412 (15.9%) for influenza B viruses.
- Nearly all the influenza viruses characterized during this period were genetically or antigenically similar to the cell grown reference viruses representing vaccine components recommended for production in the 2017–18 Northern Hemisphere influenza vaccines.
- For the A(H3N2) viruses, 98.1% were antigenically similar to the cell-propagated reference virus representing the vaccine component but only 64.4% were antigenically similar to the egg-propagated reference virus representing the vaccine component.
- Four viruses (all A(H1N1pdm09 viruses) collected in the U.S. this season were found to be resistant to oseltamivir and peramivir. No antiviral resistance to oseltamivir, zanamivir, or peramivir has been identified among influenza A(H3N2) or influenza B viruses collected since October 1, 2017.

Influenza-like Illness

- The weekly percentage of outpatient visits to health care providers participating in ILINet for ILI ranged from 1.3% to 7.7%.
- The percentage first exceeded the national baseline level of 2.2% during the week ending November 25, 2017 (week 47) and has remained at or above the baseline for 11 consecutive weeks.
- From the week ending December 23, 2017, (week 51), through the week ending February 3, 2018, (week 5), all 10 HHS regions reported a percentage of outpatient visits for ILI at or above their region-specific baseline levels.
- Since the week ending December 30, 2017, more than half of the 53 jurisdictions (50 states, District of Columbia, New York City, and Puerto Rico) experienced high ILI activity each week, with the largest number of jurisdictions (46, 87%) experiencing high ILI activity during the week ending February 3, 2018.
- During the past five seasons, the largest number of jurisdictions experiencing high ILI activity in a single week ranged from 16 (30%) during the 2015–16 season to 31 (58%) during the 2012–13 and 2014–15 seasons.

Geographic Spread:

- During the 2017–18 season, the peak number of jurisdictions reporting widespread activity in a single week was 50 (93%); this occurred for the 3 consecutive weeks (weeks ending January 6, January 13, and January 20, 2018).

CDC Influenza Technical Key Points

February 15, 2018

- During the previous five influenza seasons, the peak number of jurisdictions reporting widespread activity in a single week during each season has ranged from 41 (76%) in the 2015–16 season to 48 (89%) during the 2012–13 season.

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Hospitalizations:

- From October 1, 2017–February 3, 2018, 17,101 laboratory-confirmed influenza-related hospitalizations were reported, representing a cumulative incidence among all age groups of 59.9 per 100,000 population.
 - The cumulative influenza hospitalization rates per 100,000 population during October 1, 2017–February 3, 2018, for persons aged 0–4 years, 5–17 years, 18–49 years, 50–64 years, and ≥65 years were 40.0, 10.3, 18.3, 63.1, and 263.6, respectively.
- Persons aged ≥65 years had the highest rate and accounted for 59% of reported influenza-associated hospitalizations.
- Among all hospitalizations, 14,770 (86.4%) were associated with influenza A virus infection.
 - The remaining hospitalizations included 2,251 (13.2%) with influenza B virus infection, 43 (0.3%) with influenza A virus and influenza B virus coinfection, and 37 (0.2%) with influenza virus infection for which the type was not determined.
- Among the 3,841 patients for whom influenza A subtype information was available, 3,308 (86.1%) were infected with influenza A(H3N2) viruses and 533 (13.9%) with influenza A(H1N1)pdm09 viruses.
- Among hospitalized persons aged 0–64 years for whom influenza A subtype information was available, 23.6% were infected with influenza A(H1N1)pdm09 viruses, compared with only 7.0% of those aged ≥65 years.
- Information on underlying medical conditions was available for 2,147 (12.6%) hospitalized patients with laboratory-confirmed influenza as of February 3, 2018.
 - Among 1,955 hospitalized adults with information on underlying medical condition available, 1,325 (67.8%) had at least one underlying medical condition that placed them at high risk for influenza-associated complications.
 - The most commonly reported medical conditions were cardiovascular disease (35.5%), metabolic disorders (33.0%), obesity (25.2%), and chronic lung disease (23.6%).
- Among 192 hospitalized children with information on underlying medical conditions available, 97 (50.5%) had at least one underlying medical condition.
 - The most commonly reported conditions were asthma (22.8%), neurologic disorders (14.4%), and obesity (10.1%).
- Among 151 hospitalized women aged 15–44 years with information on pregnancy status, 36 (23.8%) were pregnant.

CDC Influenza Technical Key Points

February 15, 2018

Pneumonia and Influenza-Attributed Deaths:

CDC tracks pneumonia and influenza (P&I)–attributed deaths through the National Center for Health Statistics (NCHS) Mortality Reporting System. According to this CDC surveillance system:

- From October 1, 2017, to January 20, 2018, the weekly percentage of deaths attributed to P&I has ranged from 5.8% to 10.1% and has exceeded the epidemic threshold for 5 consecutive weeks.
- P&I percentages for recent weeks are likely to be artificially low because of a delay in manual coding for deaths occurring in 2018.
 - The percentage of deaths caused by P&I is higher among manually coded death certificates than among machine-coded death certificates.
 - The percentage of deaths caused by P&I will likely increase as more data become available.

Pediatric Deaths:

As of February 3, 2018, (week 5), 63 laboratory-confirmed influenza-associated pediatric deaths occurring during the 2017–18 season were reported to CDC.

Of the 63 deaths:

- Fifteen deaths were associated with an influenza A(H1N1)pdm09 virus infection
- Sixteen were associated with an influenza A(H3N2) virus infection
- Fourteen were associated with infection with an influenza A virus for which no subtyping was performed, and 18 were associated with an influenza B virus infection.
- Among the children for whom medical history is known, 54% were otherwise healthy.
- Of the children who were eligible for vaccination (≥ 6 months of age) and for whom vaccination status was known, 26% received at least 1 dose of influenza vaccine before onset of illness.

Since influenza-associated pediatric mortality became a nationally notifiable condition in 2004, the number of influenza-associated pediatric deaths per season has ranged from 37 to 171, excluding the 2009 pandemic, when there were 358 pediatric deaths during April 15, 2009–October 2, 2010 were reported to CDC.

Flu Severity:

- With several more weeks of elevated influenza activity anticipated this season, it is too early to assess overall severity of the season.
- However, estimates of the burden of influenza disease from the 2012–13 and 2014–15 seasons provide an indication of what might be anticipated for the 2017–18 season.
- CDC estimated that during each of those seasons influenza accounted for as many as 35.6 million illnesses, 16.6 million medically attended visits, 710,000 hospitalizations and 56,000 deaths.

CDC Discussion/Recommendations:

CDC Influenza Technical Key Points

February 15, 2018

- Influenza A(H3N2) is the predominant influenza virus circulating this season.
- Past A(H3N2) virus–predominant seasons such as the 2012–13 and 2014–15 seasons had increased numbers of influenza related infections, hospitalizations, and deaths compared with A(H1N1)pdm09 virus-predominant seasons.
- With several more weeks of elevated influenza activity expected, an increasing proportion of influenza A(H1N1)pdm09 and influenza B viruses, and the potential to prevent significant illness through influenza vaccination, CDC continues to recommend influenza vaccination at this time.
- In the United States, annual vaccination against seasonal flu is recommended for all people 6 months of age and older.
- During influenza seasons with increased severity, influenza antiviral medications for treatment of influenza are an even more important adjunct to vaccination. Three neuraminidase inhibitor antiviral medications are approved and recommended for use in the United States during the 2017–18 influenza season:
 - Oral oseltamivir (available as a generic or under the trade name Tamiflu),
 - Inhaled zanamivir
 - Intravenous peramivir
- Treatment with influenza antiviral medications initiated as close to the onset of illness as possible is recommended for patients with confirmed or suspected influenza who have severe, complicated, or progressive illness.
- Clinical benefit of antiviral treatment is greatest when treatment begins within 48 hours after symptom onset; however, antiviral treatment initiated later than 48 hours after illness onset can still be beneficial for some patients.
- A CDC health advisory released on December 27, 2017, regarding treatment with antiviral medications is available at <https://emergency.cdc.gov/han/han00409.asp>.
- For complete CDC antiviral guidelines, please see <https://www.cdc.gov/flu/professionals/antivirals/index.htm>.

Novel Influenza A Viruses:

- Six human infections with novel influenza A viruses were reported to CDC during October 1, 2017–February 3, 2018. All of these were variant virus infections (human infections with influenza viruses that normally circulate in swine). Five of these infections were previously described. The sixth human infection with a novel influenza A virus was caused by an influenza A(H3N2) variant (A[H3N2]v) virus in Iowa in an adult patient with onset of respiratory symptoms in November 2017. This patient reported exposure to swine during the week preceding illness onset, was not hospitalized, and has fully recovered. No sustained human-to-human transmission was identified.

For more information:

CDC Influenza Technical Key Points

February 15, 2018

- Influenza surveillance reports for the United States are posted online weekly (<https://www.cdc.gov/flu/weekly>).
- Additional information regarding influenza viruses, influenza surveillance, influenza vaccine, influenza antiviral medications, and novel influenza A infections in humans is available online (<https://www.cdc.gov/flu>).