CDC Influenza Division: Key Points on Influenza MMWRs
February 14, 2019

Topline Key Points

- *Two influenza-related MMWRs were published today: Update: Influenza Activity — United States, September 30, 2018–February 2, 2019 and Interim Estimates of 2018–19 Seasonal Influenza Vaccine Effectiveness — United States, February 2019.*
  - *A review of seasonal influenza flu surveillance data from October 1 through February 2 indicates flu activity remained elevated as of February 2 and while the flu season had been less severe than recent seasons, CDC estimates that as many as 16,000 people may have already died from flu. This underscores the fact that every flu season brings serious consequences.*
  - *A separate report on the effectiveness of this season's flu vaccines showed that flu vaccination this season has reduced the risk of medically attended flu illness by about half overall among people who got vaccinated. This is an early, interim finding and while effectiveness estimates at the time are inconsistent across age groups, effectiveness of more than 60% in children is especially encouraging.*
- *Significant flu activity is expected to continue for weeks and so CDC continues to recommend a 3-pronged strategy to fight flu.*
  1. *Take time to get a flu vaccine.*
  2. *Take everyday preventive actions like covering coughs to help prevent the spread of germs, and;*
  3. *Take influenza antiviral drugs as recommended.*
- *Visit www.cdc.gov/flu for more information.*

In this document

Activity Summary:

- Flu activity for the week ending February 2, 2019 was the highest it had been all season:
- While it is difficult to assess severity before the season has peaked, at this time indicators suggest a "low severity" season. (Information about how CDC classifies severity is available at https://www.cdc.gov/flu/professionals/classifies-flu-severity.htm.)
- This severity classification may change as the season progresses and severity indicators rise.
- Influenza H1N1 viruses had been predominant overall and in all parts of the country except for the southeastern region, where H3N2 viruses predominated.
- In recent weeks H3N2 viruses have accounted for a growing proportion of influenza viruses detected in several other regions. Earlier in the season, 7 states were H3N2 predominant. For the week ending February 2, 10 states were H3N2 predominant.

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- As of February 2, the majority of circulating viruses were well-matched to ("antigenically like") the cell-grown recommended vaccine components according to the results of current laboratory tests using ferret antisera to measure reactivity between viruses and antibodies.
- For the first time, CDC released preliminary in-season estimates of the number of flu deaths that occurred between October 1, 2018 and February 2, 2019 in the United States. These estimates are based on modelling.
- CDC estimates that between 9,600 and 15,900 people had died from flu so far this season.
- To put these numbers into context, total, end-of-season estimates for flu deaths going back to 2010 have ranged from: 12,000 to 79,000 deaths annually.
- As there are weeks of flu activity likely to come this season, this number is expected to go up and will be updated weekly.

Vaccine Effectiveness (VE) Summary:

- **Preliminary VE estimates indicate flu vaccination is reducing the overall risk of having to seek medical care for flu illness by about half in people who were vaccinated.** (47% with a 95% confidence interval of 34% to 57%).
- This is within the range of what we've seen over recent seasons (40% to 60%) when the recommended vaccine viruses have been well-matched to most circulating viruses.
- Interim estimates do suggest that vaccine may not be working the same across all age groups.
    - Broken down by age, the interim VE against all flu are as follows:
        - 6 months-17 years: 61% (95% Confidence Interval [CI] of 44% to 73%)
        - 18-49: 37% (95% CI of 9% to 56%)
        - 50 years and older: 24 (95% CI of -15% to 51%)*
- CDC's vaccine effectiveness network was able to generate estimates for protection against medically attended illness caused by H1N1 and H3N2 viruses.
- Flu vaccine reduced the risk of medically attended illness against the vastly predominant H1N1 virus by 46%.
    - Children who got vaccinated reduced their risk of H1N1 medically attended flu illness by 62%.
    - Among people 50 and older, VE against H1N1 flu was estimated at 8% with a wide 95% confidence interval (CI) that crossed zero (-59% to 46%)*.
- VE against H3N2 illness was 44% overall. Effectiveness against H3N2 by age group could not be calculated because of small sample size.
- The 44% VE against H3N2 is higher than what was observed last season (22%), but similar to what has been observed during other well-matched H3N2 seasons. (Note the H3N2 component of the vaccine had been updated for this season.)
- ***Note: The estimates for people 50 and older have wide confidence intervals that cross zero.**
    - Confidence intervals are important because they provide context for understanding the precision or exactness of a VE point estimate.
    - The wider the confidence interval, the less exact the point value estimate of vaccine effectiveness becomes.
    - A confidence interval that crosses zero is said to be statistically insignificant.

  - There was low enrollment of H1N1 cases in the VE network among people 50 and older as of February 2, 2019, which resulted in the wide confidence intervals.
  - CDC will continue to monitor VE estimates as the season progresses.
- It's important to note that CDC monitors vaccine protection against hospitalized illness and other serious outcomes but estimates from this system are not available at this time. **The interim overall estimate for the U.S. is lower than the recently reported interim estimates of 72% effectiveness against H1N1 in Canada during the 2018–2019 season and 78% against H1N1 in Australia during the 2018 Southern Hemisphere influenza season.**
  - This could be due to enrollment, geographic differences in circulating viruses, and genetic variation within virus subtypes.
  - Again, it's important to note that the U.S. estimates (and the Canadian as well) are interim and may change as the season progresses.
  - CDC will continue to monitor VE estimates as the season progresses.
- The reasons for some of the lower VE point estimates against H1N1 compared to other reported estimates against H1N1 are not clear at this time.
- CDC has been estimating total numbers of illnesses, hospitalizations and deaths **prevented** by vaccination in order to give a better picture of the benefits of flu vaccine.
- These estimates are not available until after the season is over, but during other H1N1 seasons (2015-2016) with VE in a similar range (48%), CDC estimates that vaccination prevented more than 5 million flu illnesses, 71,000 hospitalizations, and 3,000 deaths.
- Last season, which was an H3N2 predominant season with 38% overall vaccine effectiveness, CDC estimates that influenza vaccination prevented 7.1 million illnesses 7 million illnesses, 4 million medical visits, 109,000 hospitalizations, and 8,000 deaths in the United States.

Technical Key Points

"*Update: Influenza Activity – United States, September 30, 2018 – February 2, 2019*"

- Between Sept. 30, 2018, and Feb. 2, 2019, influenza activity in the United States was low during October and November, increased in late December, and remained elevated through early February.
- Flu activity was at its highest for the current season as of the week ending February 2 with ILI at 4.3% and 48 states reporting widespread activity.
- Hospitalization rates through February 2 had been relatively low, with the highest rate observed among people 65 and older, which is typical. Most hospitalizations (93.8%) had been associated with influenza A viruses, and among those for which subtype information was known, 76.8% were A(H1N1)pdm09 virus.
- Pneumonia &Influenza (P & I) had been at or above the epidemic threshold for 3 weeks, which is relatively low compared to other seasons.
- Twenty-eight flu pediatric deaths had been reported to CDC as of February 2. Among the 22 children who were eligible for influenza vaccination and for whom vaccination status was known, only 3 were fully vaccinated.
- As of Feb. 2, 2019, the indicators that CDC uses to classify severity suggested to date that 2018-2019 had been of "low severity."
- This classification may change as the season progresses.

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- The classification methodology CDC uses compares the severity of flu seasons relative to each other, using the peak level of flu activity in three indicators to determine severity.
- While influenza A(H1N1)pdm09 viruses have been predominate overall, influenza A(H3N2) viruses predominated in the southeastern United States and in recent weeks accounted for a growing proportion of influenza viruses detected in several other regions. Small levels of B viruses have been detected.
- Among positive tests at public health laboratories, the highest percent occurred in people aged 5-24 (32.4%) and 25-64 years (37.1%). Children 0-4 years and adults 65 and older each comprised around 15% of positive tests.
- Most positive tests reported from public health laboratories showed A(H1N1)pdm09 viruses. The percentage of influenza A(H3N2) viruses ranged from 30.1% among persons aged ≥65 years to 13.5% in persons aged 25–64 years.
- The majority of the influenza viruses characterized antigenically and genetically are similar to the cell-grown reference viruses representing the 2018–19 Northern Hemisphere influenza vaccine viruses.
- In recent weeks, however, there has been an increasing proportion of influenza A(H3N2) viruses from a sub-clade called "3C.3a" that are different from the recommended H3N2 vaccine component.
- CDC is watching this carefully. (It's important to note that H3N2 viruses only account for 20% of circulating viruses this season and that 3C.3a H3N2 viruses make up only about 30% of cumulative H3N2 viruses.)
- Antiviral resistance has been very rarely detected this season.
- The season is ongoing and current influenza forecasts predict that elevated influenza activity in the United States will continue for several more weeks.

Preliminary Estimates of 2018-2019 Flu Illnesses, Medical Visits, Hospitalizations and Deaths

- Through February 2, 2019, CDC estimates that flu had caused:
    - 13.2 to 15.2 million flu illnesses,
    - 6.2 to 7.2 million flu medical visits,
    - 155,000 to 186,000 flu hospitalizations, and
    - 9,600 to 15,900 flu deaths. (The in-season estimate of deaths is being released for the first time in this report.)
- To put these numbers into context, total, end-of-season estimates for flu illnesses, medical visits and hospitalizations going back to 2010 have ranged from:
    - 9.3 million to 49 million illnesses annually,
    - 4.3 million to 23 million medical visits annually,
    - 140,000 to 960,000 hospitalizations annually, and
    - 12,000 to 79,000 deaths.

CDC Recommendations

- Health care providers should continue to offer and encourage vaccination to all unvaccinated persons aged ≥6 months as long as influenza viruses are circulating.

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- Regardless of vaccination status, it is important that persons with confirmed or suspected influenza who have severe, complicated, or progressive illness; who require hospitalization; or who are at high risk for influenza complications be treated with antiviral medications.

"Interim Estimates of 2018-19 Seasonal Influenza Vaccine Effectiveness — United States, February 2019"

- 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 medical visit.
    - Clinically what is being measured is laboratory-confirmed influenza associated with medically attended acute respiratory illness (ARI).
- This report uses data from 3,254 children and adults enrolled in the U.S. Vaccine Effectiveness Network (U.S. Flu VE Network) during November 23, 2018 – February 2, 2019.
- Among the 3,254 children and adults with ARI enrolled in the five study sites from November 23, 2018 through February 2, 2019, a total of 465 (14%) tested positive for influenza virus by real time RT-PCR, including 456 (98%) influenza A viruses and 9 (2%) influenza B viruses.
- Among 394 subtyped influenza A viruses, 293 (74%) were A(H1N1)pdm09 viruses and 101 (26%) were A(H3N2) viruses.
- Of the influenza B viruses with lineage information available, four belonged to the B/Victoria lineage and four belonged to the B/Yamagata lineage.
- Overall adjusted vaccine effectiveness (VE) against medically attended ARI caused by all influenza virus types combined was **47%** (95% CI = 34% - 57%).
    - Among enrollees, most of influenza infections were caused by influenza A(H1N1), though some enrollees were infected with influenza A(H3N2); few influenza B virus infections were detected.
    - VE for all ages was estimated to be **46%** (95% CI = 30%-58%) against illnesses caused by influenza A(H1N1)pdm09 viruses
    - VE for all ages was estimated to be **44%** (95% CI = 13%-64%) against illnesses caused by influenza A(H3N2) viruses
    - Among children aged 6 months through 17 years, VE against medically attended ARI caused by all influenza virus types was 61% (95% CI = 44%-73%), and VE against medically attended ARI caused by A(H1N1)pdm09 was 62% (95% CI = 40%–75%).
- The effectiveness of flu vaccines in reducing the risk for medically attended influenza illness has ranged from approximately 40% to 60% across all ages during flu seasons when vaccine viruses and circulating viruses have been well-matched.
- The proportion of patients with influenza differed by study site, age group, self-rated health status, and interval from illness onset to enrollment.
- The percentage of patients who were vaccinated ranged from 46% to 61% among study sites and differed by study site, sex, age group, race/ethnicity, and interval from illness onset to enrollment.
- The overall interim estimate of 47% VE in all age groups this season shows that seasonal flu vaccines are reducing the risk of medically attended flu illness in vaccinated persons overall by about half.

- However, better protection and improved vaccination coverage are needed to realize the full potential of influenza vaccines.

CDC Recommendation

- CDC continues to recommend flu vaccination because the flu vaccine can still prevent some infections, hospitalizations, and deaths due to currently circulating influenza viruses, or other influenza viruses that may circulate later in the season.

Methods

- At five study sites, patients 6 months of age and older seeking 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:
    - Texas,
    - Pennsylvania,
    - Washington,
    - Michigan, and
    - Wisconsin.
- Participants were interviewed to collect demographic data, information general and current health status and symptoms, and 2018-19 influenza 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 real-time reverse transcription polymerase-chain reaction (rRT-PCR) protocol.
- VE against all influenza virus types combined and against viruses by type/subtype was estimated as 100% x (1 – 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.

Background

- Each season, CDC studies how well flu vaccines work by collecting data through the U.S. VE network of five sites across the U.S.
- 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.
- Updated VE estimates will be provided as warranted and final VE estimates will be published after the season ends.