U.S. Influenza Surveillance and Vaccine Effectiveness Update

Lisa A. Grohskopf, MD, MPH

U.S. Food and Drug Administration

Vaccine and Related Biologic Products Advisory Committee Meeting

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Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories, National Summary, 2015-2016 Season
Virus Characterization: Influenza A Viruses

- All 271 influenza A (H1N1)pdm09 viruses were antigenically characterized as A/California/7/2009-like.

- All 242 H3N2 viruses genetically sequenced belonged to genetic groups for which a majority of viruses antigenically characterized were similar to the cell-propagated A/Switzerland/9715293/2013.
  - Of 109 H3N2 viruses also antigenically characterized, 102 (93.5%) were A/Switzerland/9715293/2013-like by HI testing or neutralization testing.
Virus Characterization: Influenza B Viruses

- All 88 B/Yamagata-lineage viruses antigenically characterized were B/Phuket/3073/2013-like, which is included as an influenza B component of the 2015-2016 Northern Hemisphere trivalent and quadrivalent influenza vaccines.

- 58 of 59 B/Victoria-lineage viruses antigenically characterized were B/Brisbane/60/2008-like, which is included as an influenza B component of the 2015-2016 Northern Hemisphere quadrivalent influenza vaccines.
Percentage of Visits for Influenza-like Illness (ILI) Reported by the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), Weekly National Summary, 2015-2016 and Selected Previous Seasons

% of Visits for ILI

Week

2015-16 Season
2014-15 season
2013-14 season
2011-12 season
2010-11 season
2009-10 season
National Baseline
Laboratory-Confirmed Influenza Hospitalizations

Preliminary cumulative rates as of Feb 20, 2016

Age Group
- 0-4 yr
- 5-17 yr
- 18-49 yr
- 50-64 yr
- 65+ yr
Pneumonia and Influenza Mortality from the National Center for Health Statistics Mortality Surveillance System

Data through the week ending February 6, 2016, as of February 25, 2016

% of All Deaths Due to P&I

- Epidemic Threshold
- Seasonal Baseline

MMWR Week

Number of Influenza-Associated Pediatric Deaths by Week of Death: 2012-2013 season to present

- **2012-2013**: Number of Deaths Reported = 171
- **2013-2014**: Number of Deaths Reported = 111
- **2014-2015**: Number of Deaths Reported = 148
- **2015-2016**: Number of Deaths Reported = 14

Week of Death

- Deaths Reported Previous Week
- Deaths Reported Current Week
Weekly Influenza Activity Estimates Reported by State & Territorial Epidemiologists*

Week ending February 20, 2016 - Week 7

* This map indicates geographic spread & does not measure the severity of influenza activity
Summary of Influenza Activity

- Influenza activity to date is low compared to the previous 3 seasons
  - Rate of influenza associated hospitalizations low
  - Pneumonia and influenza mortality has not exceeded threshold levels
- Influenza A (H1N1) viruses have predominated but A (H3N2) and B viruses of both lineages have co-circulated
- Majority of viruses are similar to vaccine viruses
In summary, interim results from the US Flu VE Network for the 2015-16 season (based on enrollment through February 12, 2016) indicate vaccine effectiveness of 59 percent against medically attended influenza. The interim estimate for this season is similar to previous seasons when vaccine was well-matched to circulating influenza viruses. Significant protection against circulating influenza H1N1pdm09 and B viruses was observed for all ages combined while VE was not estimated against H3N2 viruses due to the small number of cases. Enrollment continues. Interim estimates are less precise due to low numbers of flu cases enrolled and end-of-season VE estimates may differ from interim estimates
Interim Estimates of 2015–16 Seasonal Influenza Vaccine Effectiveness against Medically-Attended Influenza from the U.S. Flu VE Network

Enrollment through February 12, 2016
Interim estimates of influenza vaccine effectiveness for this season are being presented to ACIP and have not been published. These interim estimates included patients enrolled from November 2015 through February 2016.
**Enrollees:** Outpatients aged ≥6 months with acute respiratory illness with cough ≤7 days duration

**Dates of enrollment:** November 2, 2015–February 12, 2016

**Design:** Test-negative design

- Comparing vaccination odds among influenza RT-PCR positive cases and RT-PCR negative controls

- **Vaccination status:** receipt of **at least one dose** of any 2015–16 seasonal flu vaccine according to medical records, immunization registries, and/or self-report

- **Analysis:** \( \text{VE} = (1 – \text{adjusted OR}) \times 100\% \)
  - Adjustment for study site, age, self-rated general health status, race/Hispanic ethnicity, interval (days) from onset to enrollment, and calendar time
Methods used by the U.S. Flu VE Network have been previously described. Methods used to produce these interim estimates were the same as those used for interim estimates in previous seasons. Briefly, outpatients 6 months of age and older with acute respiratory illness and cough of 7 or fewer days duration were enrolled at five U.S. Flu VE network sites from November 2, 2015 through February 12, 2016. We use a test-negative design to estimate vaccine effectiveness by comparing vaccination odds among influenza RT-PCR positive cases and RT-PCR negative controls. Vaccination status was defined as receipt of at least one dose of any 2015-16 seasonal flu vaccine according to medical records, immunization registries and/or self report. Vaccine effectiveness is estimated as one minus the adjusted odds ratio times 100. Variables included in the models for adjustment are those listed.
US Flu VE Network: Interim Results

- 3,333 enrolled from Nov 2, 2015–Feb 12, 2016 at 5 sites
- 3,081 (92%) influenza RT-PCR negative
- 252 (8%) influenza RT-PCR positive

Cases enrolled by (sub)type, N=234 (18 pending)

- H1N1pdm09 (113) 48%
- H3N2 (25) 11%
- B/Yamagata (56) 24%
- B/Victoria (40) 17%
From November 2, 2015 through February 12, 2016, a total of 3,333 outpatients were enrolled at the five network sites. 3,081 or 92 percent were RT-PCR negative for influenza. 252 or 8 percent of enrolled patients were influenza positive. Distribution of influenza cases by type and subtype is shown—both influenza A and B viruses circulated with a majority of influenza A viruses being H1N1pdm09 and a majority of B viruses belonging to the Yamagata lineage.
Number of enrolled participants with RT-PCR confirmed influenza and percent positivity by week of onset

Note: Week 6 only includes patients with completed laboratory tests and thus does not reflect all enrolled patients during that week across study sites.
Speaker Notes for Slide 19

- This epi curve shows the number of enrolled participants with RT-PCR-confirmed influenza A or B by epidemiologic week of enrollment and percent positivity for any influenza type by week. Note that laboratory testing is incomplete for patients enrolled during epidemiologic week 6. Few cases were enrolled before the first week of January, with low percentage of those enrolled testing positive for influenza A or B during most weeks.
### Interim adjusted vaccine effectiveness against medically attended influenza, 2015–2016

<table>
<thead>
<tr>
<th>Any influenza A or B virus</th>
<th>Influenza positive</th>
<th>Influenza negative</th>
<th>Vaccine Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N vaccinated /Total</td>
<td>(%)</td>
<td>N vaccinated /Total</td>
</tr>
<tr>
<td>Overall</td>
<td>81/227</td>
<td>36</td>
<td>1382/2537</td>
</tr>
</tbody>
</table>

* Multivariate logistic regression models adjusted for site, age categories (6m-17y, 18-49y, ≥50y), sex, race/Hispanic ethnicity, self-rated general health status, interval from onset to enrollment, and month of onset.
Speaker Notes for Slide 21

- Interim adjusted estimates of vaccine effectiveness against medically attended influenza for all patients aged 6 months and older was 59 percent with a 95 percent confidence interval from 44 percent to 70 percent.
## Interim adjusted VE against A/H1N1pdm09, B and B/Yamagata viruses, 2015–2016

<table>
<thead>
<tr>
<th>Influenza A (H1N1)pdm09</th>
<th>Influenza positive</th>
<th>Influenza negative</th>
<th>Vaccine Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N vaccinated /Total</td>
<td>(%)</td>
<td>N vaccinated /Total</td>
</tr>
<tr>
<td>All ages</td>
<td></td>
<td></td>
<td></td>
</tr>
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| Influenza B             |                    |                    |                       |                    |            |          |            |            |
| All ages                | 26/87              | 30                 | 1382/2537             | 54                 | 64         | (43 to 78) | 76         | (59 to 86) |

| Influenza B/Yamagata   |                    |                    |                       |                    |            |          |            |            |
| All ages                | 17/51              | 33                 | 1382/2537             | 54                 | 58         | (25 to 77) | 79         | (59 to 89) |

* Multivariate logistic models adjusted for site, age categories (6m-17y, 18-49y, ≥50y), sex, race/Hispanic ethnicity, self-rated general health status, interval from onset to enrollment, and month of onset.
Interim adjusted vaccine effectiveness against H1N1pdm09 for all ages combined was 51 percent, with confidence interval from 25 to 69 percent. Adjusted estimates of vaccine effectiveness against influenza B for all ages combined was 76 percent with confidence interval from 59 to 86 percent and was similar (79%) against B/Yamagata lineage viruses.
Summary

- Interim results for 2015-16 season (through February 12, 2016) indicate vaccine effectiveness of 59% against medically attended influenza
  - Interim estimate similar to previous seasons when vaccine was well-matched to circulating influenza viruses
- Significant protection against circulating influenza H1N1pdm09 and B viruses
  - VE not estimated against A(H3N2) viruses due to small numbers of cases
- Enrollment continues—end of season VE estimates may differ from interim estimates
In summary, interim results from the US Flu VE Network for the 2015-16 season (based on enrollment through February 12, 2016) indicate vaccine effectiveness of 59 percent against medically attended influenza. The interim estimate for this season is similar to previous seasons when vaccine was well-matched to circulating influenza viruses. Significant protection against circulating influenza H1N1pdm09 and B viruses was observed for all ages combined while VE was not estimated against H3N2 viruses due to the small number of cases. Enrollment continues. Interim estimates are less precise due to low numbers of flu cases enrolled and end-of-season VE estimates may differ from interim estimates.
Questions?