U.S. Influenza Surveillance and Vaccine Effectiveness Update

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FDA Vaccines and Related Biologic Products Advisory Committee Meeting
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U.S. INFLUENZA SURVEILLANCE
Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories, 2016-2017 Season
Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, 2016-2017 Season

![Bar chart showing the number of positive specimens for different subtypes of influenza over the 2016-2017 season. The y-axis represents the number of positive specimens, and the x-axis represents the weeks of the season. The chart includes bars for A (subtyping not performed), A (H1N1)pdm09, A (H3N2), and H3N2v. The total number of positive specimens increases throughout the season.](image-url)
Influenza Positive Specimens Reported by U.S. Public Health Laboratories, Cumulative, 2016-2017 season

- **Influenza A (H3)**: 21303
- **Influenza A (H1pdm09)**: 3C.2a (740, 96%) and 6B.1 (154, 100%)
- **Influenza B Yamagata**: Y3 (172, 100%)
- **Influenza B Victoria**: V1A (21303, 534, 330, 707, 1067, 576)
- **Influenza A (subtype unknown)**
- **Influenza B (lineage not determined)**
Antigenic Characterization of U.S. Influenza Viruses Collected October 1, 2016 to Present

- A (H1N1)pdm09: all 112 viruses antigenically characterized using ferret post-infection antisera are A/California/07/2009-like, the H1N1 component of the 2016-17 vaccine
- A(H3N2): 387 of 399 (97%) were antigenically characterized as A/Hong Kong/4801/2014-like, the H3N2 component of the 2016-17 vaccine
- B/Victoria lineage: 123 of 134 (92%) were antigenically characterized as B/Brisbane/60/2008-like, which is included in both quadrivalent and trivalent influenza vaccines for the 2016-17 season
- B/Yamagata lineage: All 121 were antigenically characterized as B/Phuket/3073/2013-like, an influenza B virus included in the quadrivalent influenza vaccines for the 2016-17 season
Percentage of Visits for Influenza-like Illness (ILI) Reported by the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), Weekly National Summary, 2016-2017 and Selected Previous Seasons
Laboratory-Confirmed Influenza Hospitalizations
Preliminary cumulative rates as of Feb 25, 2017
Pneumonia and Influenza Mortality from the National Center for Health Statistics Mortality Surveillance System
Data through the week ending February 11, 2017, as of March 2, 2017
Deaths Reported Current Week
Deaths Reported Previous Week

Number of Influenza-Associated Pediatric Deaths by Week of Death: 2013-2014 season to present

- **2013-2014**
  - Number of Deaths Reported = 111

- **2014-2015**
  - Number of Deaths Reported = 148

- **2015-2016**
  - Number of Deaths Reported = 89

- **2016-2017**
  - Number of Deaths Reported = 40

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Week of Death

- **Green**: Deaths Reported Previous Week
- **Blue**: Deaths Reported Current Week
Summary of the U.S. Season

- Influenza A(H3N2) viruses have predominated during the 2016-17 season
  - Influenza B activity has increased in recent weeks
- So far, influenza activity has been moderate, and may have peaked nationally
- The circulating stains are similar to those contained in the 2016-17 vaccine
U.S. VACCINE EFFECTIVENESS--INTERIM ESTIMATES
US Flu VE Network sites and principal investigators

Group Health Cooperative
- Mike Jackson
- Lisa Jackson

Marshfield Clinic Research Foundation
- Ed Belongia
- Huong McLean

University of Michigan
- Arnold Monto
- Emily Martin

University of Pittsburgh
- Rick Zimmerman
- Tricia Nowalk

Baylor Scott and White Health
- Manju Gaglani
US Flu VE Network Methods

**Enrollees:** Outpatients aged ≥6 months with acute respiratory illness with cough ≤7 days duration

**Dates of enrollment:** November 28, 2016–February 4, 2017

**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 2016–17 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
Interim Results

- 3,144 enrolled from Nov 28, 2016–Feb 4, 2017 at 5 sites
- 744 (24%) influenza RT-PCR positive
- 2,400 (76%) influenza RT-PCR negative
Number of enrolled participants by influenza RT-PCR result and percent positivity by week of onset

Note: Week 5 only includes patients with completed laboratory tests and thus does not reflect all enrolled patients during that week across study sites.
Interim adjusted vaccine effectiveness against medically attended influenza, 2016–17

<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>333/744 (45)</td>
<td>1317/2400 (55)</td>
<td>33 (21 to 44)</td>
</tr>
<tr>
<td>Age group (yrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 mos–8</td>
<td>32/97 (33)</td>
<td>330/614 (54)</td>
<td>58 (33 to 73)</td>
</tr>
<tr>
<td>9–17</td>
<td>36/122 (30)</td>
<td>92/247 (37)</td>
<td>29 (-12 to 56)</td>
</tr>
<tr>
<td>18–49</td>
<td>89/208 (43)</td>
<td>363/783 (46)</td>
<td>13 (-18 to 36)</td>
</tr>
<tr>
<td>50–64</td>
<td>76/189 (40)</td>
<td>261/425 (61)</td>
<td>58 (40 to 70)</td>
</tr>
<tr>
<td>≥65</td>
<td>100/128 (78)</td>
<td>271/331 (82)</td>
<td>21% (-31 to 52)</td>
</tr>
</tbody>
</table>

* Multivariate logistic regression models adjusted for site, age, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time.
Interim adjusted vaccine effectiveness against medically attended influenza by virus type, 2016–17

<table>
<thead>
<tr>
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<th>Influenza positive</th>
<th>Influenza negative</th>
<th>Vaccine Effectiveness</th>
</tr>
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<tr>
<td></td>
<td>N vaccinated</td>
<td>(%)</td>
<td>N vaccinated</td>
</tr>
<tr>
<td></td>
<td>/Total</td>
<td></td>
<td>/Total</td>
</tr>
<tr>
<td>Influenza A/H3N2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>282/595</td>
<td>(47)</td>
<td>1317/2400</td>
</tr>
<tr>
<td>Age group (yrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 mos–8</td>
<td>24/68</td>
<td>(35)</td>
<td>330/614</td>
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<tr>
<td>9–17</td>
<td>28/94</td>
<td>(30)</td>
<td>92/247</td>
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<td>18–49</td>
<td>73/168</td>
<td>(43)</td>
<td>363/783</td>
</tr>
<tr>
<td>50–64</td>
<td>70/154</td>
<td>(45)</td>
<td>261/425</td>
</tr>
<tr>
<td>≥65</td>
<td>87/111</td>
<td>(78)</td>
<td>271/331</td>
</tr>
<tr>
<td>Influenza B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>23/90</td>
<td>(26)</td>
<td>1317/2400</td>
</tr>
</tbody>
</table>

* Multivariate logistic regression models adjusted for site, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time.
Summary

- Interim results for 2016–17 season (through February 4, 2017) indicate vaccine effectiveness of 48% against medically attended influenza
  - Interim estimate similar to previous seasons when vaccine was well matched to circulating influenza viruses

- Significant protection against circulating influenza A(H3N2) and B viruses (predominantly B/Yamagata)
  - VE not estimated against H1N1pdm09 or B/Victoria due to small number of cases

- Enrollment continues – end-of-season VE estimates may differ from interim estimates
VE against influenza A (H3N2) viruses

- VE of 43% against A (H3N2) similar to antigenically matched H3N2 viruses
  - 2011-12 (39%) and 2012-13 (39%)
  - Meta-analysis\(^1\) of test-negative VE studies: 33% (26% - 39%)
- VE against A (H1N1)pdm09 (61%) and B viruses (54%) tend to be higher\(^1\)
- A (H3N2) viruses have required more frequent vaccine updates
- Candidate A (H3N2) vaccine viruses more often have antigenic changes after adaptation to growth in eggs
- Efforts ongoing to improve VE against A (H3N2) viruses

\(^1\) Belongia et al. Lancet Infect Dis, 2016
Repeat Vaccination

- Prior season vaccination is a significant effect modifier for most seasons.
- The point estimate for current season only vaccination is consistently higher than current plus prior season vaccination, overlapping CIs.
- There is evidence for residual protection from the prior season vaccination, consistently for B and H1N1pdm and sometimes for H3N2.
- Complex issue that is an actively evolving area of research.
US Flu VE Network


- **University of Pittsburgh Schools of the Health Sciences and UPMC:** Richard K. Zimmerman, Mary Patricia Nowalk, Todd M. Bear, Heather Eng, Samantha Ford, Krissy K. Moebling, Jonathan M. Raviotta, Sean Saul, Terrie Sax, Michael Susick, G.K. Balasubramani, Rina Chabra, Edward Garofolo, Philip Iozzi, Barbara Kevish, Donald B. Middleton, Christopher Olbrich, Evelyn C. Reis, Leonard Urbanski, John V. Williams, Monika Johnson

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