Objectives

- Review end-of-season estimates of 2015-16 influenza vaccine effectiveness (VE) from US Flu VE Network

- Compare LAIV and IIV effectiveness among children and adolescents aged 2–17 years during 2015-16
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

Week 2009-10 season 2010-11 season 2011-12 season 2013-14 season 2014-15 season 2015-16 Season
National Baseline

% of Visits for ILI

% of Visits for ILI

Week
US Flu VE Network: 5 Sites and Principal Investigators

Group Health Cooperative
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Mike Jackson

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Huong McLean

University of Michigan
Arnold Monto
Suzanne Ohmit

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Rick Zimmerman
Tricia Nowalk

CDC
Alicia Fry
Brendan Flannery

Baylor Scott and White Health
Manju Gaglani
Enrollees: Outpatients aged ≥6 months with acute respiratory illness with cough ≤7 days duration

Dates of enrollment: November 2, 2015–April 15, 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 plausible self-report

Analysis: VE = (1 – adjusted OR) x 100%
  - Adjustment for study site, age, self-rated general health status, race/Hispanic ethnicity, interval (days) from onset to enrollment, and calendar time
Number of enrolled participants with RT-PCR confirmed influenza and percent positivity by week of onset

- **Inf A-positive**
- **Inf B-positive**
- **Percent influenza positive**

### Surveillance Week
- 2015: 43, 44, 45, 46, 47, 48, 49, 50, 51, 52
- 2016: 1 to 15

### Number of influenza RT-PCR positive enrollees
- 0 to 140

### Percent of all enrollees positive for influenza by RT-PCR
- 0% to 35%
US Flu VE Network: Interim Results

- 7563 enrolled from Nov 2, 2015–Apr 15, 2016 at 5 sites
- 6213 (82%) influenza RT-PCR negative
- 1341 (18%) influenza RT-PCR positive
- 9 (<1%) influenza RT-PCR inconclusive/unrepeatable

Cases enrolled by (sub)type:

- H1N1pdm09 (772)
- H3N2 (76)
- Unsubtypable A (23)
- B/Yamagata (251)
- B/Victoria (207)
- Unk lineage B (5)
- Coinfection (7)
Laboratory characterization of influenza viruses from US Flu VE Network, 2015-16

- **A/H1N1pdm09**
  - 100% A/CALIFORNIA/07/2009-LIKE (n=67)
  - 99% clade 6B.1 (n=72), 1 clade 6B (A/CALIFORNIA/07/2009-LIKE)

- **A/H3N2**
  - 100% A/SWITZERLAND/9715293/2013-LIKE (H3N2) (n=16)
  - 62% (n=11) A/Hong Kong/14 (clade 3C.2a) and
    - 38% (n=18) A/Switzerland/13 (clade 3C.3a)

- **B/Yamagata**
  - 100% B/PHUKET/3073/2013-LIKE (n=43)
  - 97% clade Y3 (n=33) and 1 clade Y3V1A (B/PHUKET/3073/2013-LIKE)

- **B/Victoria**
  - 100% B/BRISBANE/60/2008-LIKE (n=43)
  - 100% clade V1A (n=34)
Adjusted VE against medically attended influenza, US Flu VE Network, 2015-16

<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>514/1332</td>
<td>39</td>
<td>3037/5708</td>
</tr>
<tr>
<td></td>
<td>(38 to 51)</td>
<td></td>
<td>(39 to 53)</td>
</tr>
<tr>
<td>6m – 8 y</td>
<td>108/277</td>
<td>39</td>
<td>765/1410</td>
</tr>
<tr>
<td></td>
<td>(30 to 59)</td>
<td></td>
<td>(31 to 61)</td>
</tr>
<tr>
<td>9–17 y</td>
<td>33/164</td>
<td>20</td>
<td>277/694</td>
</tr>
<tr>
<td></td>
<td>(43 to 75)</td>
<td></td>
<td>(44 to 77)</td>
</tr>
<tr>
<td>18–49 y</td>
<td>146/499</td>
<td>29</td>
<td>841/1957</td>
</tr>
<tr>
<td></td>
<td>(32 to 56)</td>
<td></td>
<td>(35 to 59)</td>
</tr>
<tr>
<td>50–64 y</td>
<td>149/283</td>
<td>53</td>
<td>562/918</td>
</tr>
<tr>
<td></td>
<td>(8 to 46)</td>
<td></td>
<td>(-3 to 43)</td>
</tr>
<tr>
<td>≥65 y</td>
<td>78/109</td>
<td>72</td>
<td>592/729</td>
</tr>
<tr>
<td></td>
<td>(8 to 63)</td>
<td></td>
<td>(10 to 66)</td>
</tr>
<tr>
<td>IIV3/4, all ages</td>
<td>472/1290</td>
<td>37</td>
<td>2893/5564</td>
</tr>
<tr>
<td></td>
<td>(40 to 53)</td>
<td></td>
<td>(41 to 56)</td>
</tr>
</tbody>
</table>

* Multivariate logistic regression models adjusted for site, age categories (6m-8y, 9-17y, 18-49y, 50-64y, ≥65y), sex, race/Hispanic ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time (biweekly intervals)
## Adjusted VE against A/H1N1pdm09

<table>
<thead>
<tr>
<th>Influenza A (H1N1)pdm09</th>
<th>N vaccinated / Total</th>
<th>(%)</th>
<th>N vaccinated / Total</th>
<th>(%)</th>
<th>Influenza positive</th>
<th>Influenza negative</th>
<th>Vaccine Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Unadjusted</td>
<td>Adjusted*</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>320/781</td>
<td>41</td>
<td>3037/5708</td>
<td>53</td>
<td>39</td>
<td>(29 to 47)</td>
<td>41</td>
</tr>
<tr>
<td>6m–8 y</td>
<td>70/173</td>
<td>40</td>
<td>765/1410</td>
<td>54</td>
<td>43</td>
<td>(21 to 58)</td>
<td>47</td>
</tr>
<tr>
<td>9–17 y</td>
<td>11/51</td>
<td>22</td>
<td>277/694</td>
<td>40</td>
<td>59</td>
<td>(18 to 79)</td>
<td>62</td>
</tr>
<tr>
<td>18–49 y</td>
<td>98/311</td>
<td>32</td>
<td>841/1957</td>
<td>43</td>
<td>39</td>
<td>(21 to 53)</td>
<td>42</td>
</tr>
<tr>
<td>50–64 y</td>
<td>110/194</td>
<td>57</td>
<td>562/918</td>
<td>61</td>
<td>17</td>
<td>(-14 to 39)</td>
<td>9</td>
</tr>
<tr>
<td>≥65 y</td>
<td>31/52</td>
<td>60</td>
<td>592/729</td>
<td>81</td>
<td>66</td>
<td>(39 to 81)</td>
<td>68</td>
</tr>
<tr>
<td>IIV3/4, all ages</td>
<td>295/756</td>
<td>39</td>
<td>2893/5564</td>
<td>52</td>
<td>41</td>
<td>(31 to 49)</td>
<td>44</td>
</tr>
</tbody>
</table>

* Multivariate logistic models adjusted for site, age categories (6m-8y, 9-17y 18-49y, 50-64y, ≥65y), sex, race/Hispanic ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time (biweekly intervals).
### Adjusted VE against A/H3N2 and B lineage


<table>
<thead>
<tr>
<th>Influenza A(H3N2)</th>
<th>Influenza positive</th>
<th>Influenza negative</th>
<th>Unadjusted</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N vaccinated/Total</td>
<td>(%)</td>
<td>N vaccinated/Total</td>
<td>(%)</td>
</tr>
<tr>
<td>All ages</td>
<td>32/75</td>
<td>43</td>
<td>3037/5708</td>
<td>53</td>
</tr>
<tr>
<td>IIV, all ages</td>
<td>32/75</td>
<td>43</td>
<td>2893/5564</td>
<td>52</td>
</tr>
</tbody>
</table>

#### Influenza B/Yamagata

| All ages          | 92/256             | 36                 | 3037/5708    | 53 | 51   | (36 to 62) | 55 | (41 to 66) |
| IIV, all ages     | 82/246             | 33                 | 2893/5564    | 52 | 54   | (39 to 65) | 59 | (45 to 69) |

#### Influenza B/Victoria

| All ages          | 64/207             | 31                 | 3037/5708    | 53 | 61   | (47 to 71) | 55 | (38 to 68) |
| IIV, all ages     | 57/200             | 29                 | 2893/5564    | 52 | 63   | (50 to 73) | 58 | (40 to 70) |

* Multivariate logistic models adjusted for site, age categories (6m-8y, 9-17y, 18-49y, 50-64y, ≥65y), sex, race/Hispanic ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time (biweekly intervals).
LAIV and IIV vaccine effectiveness among patients aged 2–17 years by influenza type/subtype
US Flu VE Network: Children 2–17 years

- 2286 enrolled from Nov 2, 2015–Apr 15, 2016 at 5 sites
- 1871 (82%) influenza RT-PCR negative
- 411 (18%) influenza RT-PCR positive
- 4 (<1%) influenza RT-PCR inconclusive/unrepeatable

Cases enrolled by (sub)type:

- H1N1pdm09 (193) - 47%
- H3N2 (13) - 3%
- Unsubtypable A (3) - 1%
- B/Yamagata (67) - 16%
- B/Victoria (127) - 31%
- Unk lineage B (1) - 1%
- Coinfection (7) - 31%
US Flu VE Network Methods

- **Vaccination status:** receipt of at least one dose of any 2015-16 seasonal flu vaccine
  - Documented vaccination only for those aged 2–8 years
  - Documented + plausible report for those aged 9–17 years

- **Vaccine type:** From medical record/immunization system or parent report if electronic record has no information

- **Analysis:** VE = (1 – adjusted OR) x 100%
  - Adjustment for study site, age (2–4, 5–8, 9–17 years), self-rated general health status (excellent/very good, good/fair/poor), race/Hispanic ethnicity, interval from onset to enrollment, and calendar time (biweekly intervals)
  - Independent analysis by Jessica Pruszynski, Baylor Scott&White Health
Exclusions from vaccine type analyses for children and adolescents ages 2–17 years

154/2286 (7%) of enrollees aged 2–17 years excluded from analysis

- 127 illness onset prior to confirmed influenza circulation
- 18 vaccinated 0–14 days prior to onset
- 4 inconclusive/unrepeatable lab results
- 3 illness onset after last confirmed influenza case
- 2 mixed vaccine types
LAIV and IIV vaccine effectiveness ages 2–17 years, by influenza type/subtype, 2015-16

Adjusted Vaccine Effectiveness (%)

- Any influenza
- H1N1pdm09
- B/Yamagata
- B/Victoria

Total, Flu +: 324 367 156 174 59 63 100 121
Vaccinated, Flu +: 38 81 23 41 8 12 7 28
LAIV and IIV vaccine effectiveness ages 2–8 years, by influenza type/subtype, 2015-16

<table>
<thead>
<tr>
<th>Category</th>
<th>Total, Flu +</th>
<th>Vaccinated, Flu +</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any influenza</td>
<td>183</td>
<td>28</td>
</tr>
<tr>
<td>H1N1pdm09</td>
<td>213</td>
<td>58</td>
</tr>
<tr>
<td>B</td>
<td>113</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>126</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>66</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>83</td>
<td>25</td>
</tr>
</tbody>
</table>
LAIV and IIV vaccine effectiveness ages 9–17 years, by influenza type/subtype, 2015-16

Any influenza
- LAIV4: 20%
- IIV3/4: 71%

H1N1pdm09
- LAIV4: 33%
- IIV3/4: 66%

B
- LAIV4: 17%
- IIV3/4: 69%

Total, Flu +
- LAIV4: 141
- IIV3/4: 154

Vaccinated, Flu +
- LAIV4: 10
- IIV3/4: 23

## Adjusted odds of influenza for LAIV vs IIV (relative effectiveness) ages 2–17 years

<table>
<thead>
<tr>
<th>Any influenza A or B virus</th>
<th>Vaccine type</th>
<th>N vaccinated</th>
<th>N vaccinated</th>
<th>Adjusted* Influenza Odds Ratio LAIV vs IIV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Influenza positive</td>
<td>Influenza negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>N vaccinated</td>
<td>N vaccinated</td>
<td>OR</td>
</tr>
<tr>
<td>2–17 y</td>
<td>IIV</td>
<td>81</td>
<td>672</td>
<td>REF</td>
</tr>
<tr>
<td></td>
<td>LAIV</td>
<td>38</td>
<td>110</td>
<td>2.63</td>
</tr>
<tr>
<td>H1N1pdm09</td>
<td>IIV</td>
<td>41</td>
<td>672</td>
<td>REF</td>
</tr>
<tr>
<td></td>
<td>LAIV</td>
<td>23</td>
<td>110</td>
<td>3.67</td>
</tr>
<tr>
<td>Influenza B</td>
<td>IIV</td>
<td>40</td>
<td>672</td>
<td>REF</td>
</tr>
<tr>
<td></td>
<td>LAIV</td>
<td>15</td>
<td>110</td>
<td>1.62</td>
</tr>
</tbody>
</table>

*Odds Ratios > 1.0 favor IIV. Adjusted for site, age (2–4 y, 5–8 y, 9–17 y), race/Hispanic ethnicity, sex, interval from onset to enrollment, general self/parent-rated health status, and calendar time (biweekly intervals)
DoD Laboratory-based Influenza Surveillance

- Military dependents aged 2-17 years presenting to participating facilities with influenza-like illness
- Laboratory testing by RT-PCR or culture
- Test-negative design: influenza RT-PCR negative controls
- Vaccination status from electronic medical records
- Estimates adjusted for age group (2-8; 9-17 years) and 3 time periods
DoD Laboratory-based Influenza Surveillance: LAIV and IIV effectiveness by influenza type/subtype, children 2-17 yrs, 2015-16

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* Data provided by Lt Col Susan Federinko, US Air Force
Limitations

- **Final end-of-season analyses pending**
  - Prior season vaccination status pending for one site
  - Chronic conditions not included in adjusted estimates

- **Limited precision for some VE estimates due to small numbers**
Summary

- Late influenza season (peak enrollment in March) with mixed A/H1N1pdm09 and B circulation
- Overall 47% VE against influenza A and B
  - 41% VE against H1N1pdm09, 55% VE against influenza B
- VE for LAIV significantly lower than IIV among 2–17 y
  - No significant LAIV effectiveness against A/H1N1pdm09 or B
  - Relative effectiveness favoring IIV against A/H1N1pdm09
Acknowledgments

- DoD Influenza Surveillance Program, Armed Forces Health Surveillance Branch
  - Susan Federinko
  - Laurie Demarcus
  - Michael Cooper
  - Angie Cost
  - Jeffrey Thervil

- US Flu VE Network [next page]
US Flu VE Network

- **Group Health Research Institute**: Michael L. Jackson, Lisa A. Jackson, Joyce Benoit, Erika Kiniry, Lawrence Madziwa, Matt Nguyen, and C. Hallie Phillips


- **University of Michigan and Henry Ford Health System**: Arnold S. Monto, Suzanne E. Ohmit, Joshua Petrie, Caroline Cheng, Casey Martens, EJ McSpadden, Anne Kaniclides, Lois Lamerato, Heather Lipkovich, Ryan Malosh, Emily Martin, Samantha Harrison, Kajal Magal, Brian Nixon, Jessica Obidike, Mallory Theisen, Emily Valice, Kevin Zhang

- **Baylor Scott and White Health, Texas A&M University Health Science Center College of Medicine and Baylor College of Medicine**: Manjusha Gaglani, Pedro Piedra, Donald Wesson, Michael Reis, Madhava Beeram, Jessica Pruszynski, Lydia Clipper, Archana Nangrani, Kempapura Murthy, Anne Robertson, Patricia Sleeth, Virginia Gandy, Teresa Ponder, Mary Kylberg, Hope Gonzales, Martha Zayed, Deborah Furze, Vasanthi Avadhanula, Alan Jewell, Kirtida Patel and Sneha Thaker

- **Marshfield Clinic Research Foundation**: Edward A. Belongia, Huong Q. McLean, Jennifer Meece, Jennifer King, Deanna Cole, Sandy Strey, Jackie Salzwedel, Carla Rottscheit, Sarah Koptizke, Laurel Verhagen, Gregg Greenwald, Phillip Bertz, Lynn Ivacic, Braiden Andersen, Yvonne Cerne, Terry Foss, Marla Hawks, Krista Herkert, Katie Immerfall, Marie Janz, Tami Johnson, Karen McGreevey, Vicki Moon, Jillette Petersen, Rebecca Pilsner, Samyuktha Rallapalli, Megan Sauer, Chelsey Thompson, Kailani Trainor-Bird, Suellyn Murray, Abby Winkler, and Bobbi Bradley

- **CDC**: Alicia M. Fry, Swathi N. Thaker, LaShondra Berman, Angie Foust, Wendy Sessions, Sarah Spencer, Joseph Bresee, Erin Burns, Jeremy Tokars, Daniel Jernigan