Comparison of Influenza Vaccine Effectiveness against outpatient and inpatient illness in the 2021–22 season

Data from the US Flu VE Network, New Vaccine Surveillance Network (NVSN), and Flu and Other Viruses in the Acutely Ill Network (IVY)

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Advisory Committee on Immunization Practices
October 20, 2022
Preliminary results

3 networks to evaluate vaccine effectiveness against laboratory-confirmed influenza-associated outpatient visits, emergency department visits, and hospitalization
VE against influenza-associated outpatient visits among patients aged ≥6 months

US Flu VE Network
US Flu VE Network Sites, 2021–2022 Influenza Season

- Kaiser Permanente Washington
- Kaiser Permanente Southern California
- Baylor Scott & White Health
- Marshfield Clinic Research Institute
- University of Michigan
- University of Pittsburgh
- Vanderbilt University
- Kaiser Permanente Southern California
US Flu VE Network Methods

**Enrollees:** Ambulatory patients aged ≥6 months with acute respiratory illness with fever or cough ≤7 days duration

**Dates of enrollment:** October 4, 2021–April 30, 2022

**Design:** Test-negative design

- Comparing vaccination odds among influenza RT-PCR positive cases and influenza RT-PCR negative controls, excluding persons testing positive for SARS-CoV-2
- Vaccination status: receipt of at least one dose of any 2021–22 seasonal flu vaccine according to medical records, immunization registries, and/or self-report

**Analysis:** VE = (1 – adjusted OR) x 100%

- Adjustment for study site, age, self-rated general health status, race/ethnicity, and month of onset
### Preliminary vaccine effectiveness against outpatient medically attended A/H3N2, 2021–22

<table>
<thead>
<tr>
<th>Influenza A/H3N2</th>
<th>Influenza positive</th>
<th>Influenza negative(^1)</th>
<th>Vaccine Effectiveness</th>
<th>Vaccine Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N vaccinated /Total (%)</td>
<td>N vaccinated /Total (%)</td>
<td>Unadjusted VE % 95% CI</td>
<td>Adjusted (^2) VE % 95% CI</td>
</tr>
<tr>
<td>All ages ≥6 mos</td>
<td>182/440 41</td>
<td>2265/3844 59</td>
<td>51 (40 to 60)</td>
<td>36 (20 to 49)</td>
</tr>
<tr>
<td>6 mos –17 years</td>
<td>72/212 34</td>
<td>570/1121 51</td>
<td>50 (32 to 63)</td>
<td>45 (22 to 61)</td>
</tr>
<tr>
<td>18–64 years</td>
<td>93/205 45</td>
<td>1363/2311 59</td>
<td>42 (23 to 57)</td>
<td>28 (2 to 47)</td>
</tr>
<tr>
<td>≥65 years</td>
<td>17/23 74</td>
<td>332/412 81</td>
<td>32 (-79 to 74)</td>
<td>NR(^3) NR(^3)</td>
</tr>
</tbody>
</table>

\(^1\) Persons testing negative for both influenza and SARS-CoV-2 using molecular assays.

\(^2\) Multivariable logistic regression models adjusted for site, age, month of onset, self-rated general health status, and race/ethnicity.

\(^3\) Not Reported
VE against influenza-associated emergency department visits and hospitalization among patients aged 6 months – 17 years

NVSN

Preliminary Results
NVSN* Pediatric Inpatient Network sites, 2021-2022

*NVSN--New Vaccine Surveillance Network
NVSN Methods

**Enrollees:** Inpatient and ED patients aged \( \geq 6 \) months to 17 years with acute respiratory illness within 10 days of illness onset

**Dates of enrollment:** November 27, 2021–June 7, 2022

**Design:** Test-negative design

- Comparing vaccination odds among influenza RT-PCR positive cases and influenza RT-PCR negative controls, excluding persons testing positive for SARS-CoV-2
- Vaccination status: Receipt of at least one dose of any 2021–22 seasonal flu vaccine according to medical records, immunization registries, and/or self-report

**Analysis:** \( VE = (1 - \text{adjusted OR}) \times 100\% \)

- Adjustment for site, age, and calendar time
Preliminary vaccine effectiveness against laboratory confirmed influenza A/H3N2 in **hospital** and **ED**, NVSN, 2021–2022

<table>
<thead>
<tr>
<th></th>
<th>Influenza positive</th>
<th>Influenza negative(^1)</th>
<th>Vaccine Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N vaccinated /Total (%)</td>
<td>N vaccinated /Total (%)</td>
<td>Unadjusted</td>
</tr>
<tr>
<td>Influenza A/H3N2</td>
<td></td>
<td></td>
<td>VE %</td>
</tr>
<tr>
<td>All 6 mos –17 years</td>
<td>107/297 36</td>
<td>1428/2849 50</td>
<td>44 (28 to 56)</td>
</tr>
<tr>
<td>ED</td>
<td>74/227 33</td>
<td>644/1471 44</td>
<td>38 (17 to 54)</td>
</tr>
<tr>
<td>Inpatient</td>
<td>33/70 47</td>
<td>784/1378 57</td>
<td>32 (-9 to 58)</td>
</tr>
</tbody>
</table>

\(^1\) Persons testing negative for both influenza and SARS-CoV-2 using molecular assays.

\(^2\) Multivariable logistic regression models adjusted for age (categorical), NVSN site, calendar time (screening month).
VE against influenza-associated hospitalization among patients aged ≥18 years

IVY

Preliminary Results
IVY* Adult Inpatient Network sites, 2021-2022

*IVY—Influenza and Other Viruses in the Acutely Ill
**IVY Methods**

**Enrollees:** Hospitalized patients aged ≥18 years with acute respiratory illness and molecular testing for influenza and SARS-CoV-2 within 10 days of illness onset

**Dates of enrollment:** January 31, 2022–June 15, 2022

**Design:** Test-negative design

- Comparing vaccination odds among influenza positive cases and influenza negative controls, excluding persons testing positive for SARS-CoV-2
- Vaccination status: receipt of at least one dose of any 2021–22 seasonal flu vaccine according to medical records, immunization registries, and/or self-report

**Analysis:** $VE = (1 – \text{adjusted OR}) \times 100\%$

- Adjustment for study site, age, sex, race/ethnicity, and calendar time (biweekly intervals)
Vaccine effectiveness against laboratory confirmed influenza A/H3N2 in **inpatient** setting, 2022

<table>
<thead>
<tr>
<th>Influenza A/H3N2</th>
<th>Influenza positive</th>
<th>Influenza negative¹</th>
<th>Vaccine Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N vaccinated /Total (%)</td>
<td>N vaccinated /Total (%)</td>
<td>Unadjusted</td>
</tr>
<tr>
<td>≥18 years</td>
<td>139/295 (47)</td>
<td>622/1175 (53)</td>
<td>21 (-2 to 39)</td>
</tr>
<tr>
<td>18–64 years</td>
<td>49/139 (35)</td>
<td>279/624 (45)</td>
<td>33 (1 to 54)</td>
</tr>
<tr>
<td>≥65 years</td>
<td>90/156 (58)</td>
<td>343/551 (62)</td>
<td>17 (-19 to 42)</td>
</tr>
</tbody>
</table>

¹ Persons testing negative for both influenza and SARS-CoV-2 using molecular assays.
² Multivariable logistic regression models adjusted for study site, age, sex, race/ethnicity, and calendar time (biweekly intervals).
Comparison of VE by setting and age group

Preliminary Results
Comparing Outpatient, ED, and Inpatient VE against influenza A/H3N2 by age group, 2021-2022

Vaccine Effectiveness (%)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Flu VE</th>
<th>NVSN ED</th>
<th>NVSN IPT</th>
<th>Flu VE</th>
<th>IVY</th>
<th>Flu VE*</th>
<th>IVY</th>
</tr>
</thead>
<tbody>
<tr>
<td>6m–17 yr</td>
<td>45</td>
<td>19</td>
<td>31</td>
<td>28</td>
<td>26</td>
<td>32</td>
<td>-3</td>
</tr>
<tr>
<td>18–64 yr</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥65 yr</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Unadjusted
Discussion
Summary—Importance of three Flu VE networks

- 2021–2022 influenza vaccination provided low to non-significant protection against predominant influenza A/H3N2 illness of varying severity
  - 36% (95%CI: 20, 49) against outpatient illness aged ≥6 months (Flu VE)
  - 19% (95%CI: -12, 41) against pediatric ED visits (NVSN)
  - 31% (95%CI: -14, 58) against pediatric hospitalizations (NVSN)
  - 11% (95%CI: -19, 33) against adult hospitalizations (IVY)
- Protection was similar to pre-pandemic A/H3N2-dominant seasons
- Trend suggested higher VE in outpatient setting compared to pediatric hospitalization/ED visits but not adult inpatient influenza
Acknowledgments
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- Johns Hopkins University: David Hager
- Montefiore Medical Center: Michelle Gong
- The Ohio State University: Matthew Exline
- University of Colorado: Adit Ginde
- University of Iowa: Nicholas Mohr
- University of Miami: Christopher Mallow
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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
VE against laboratory confirmed influenza A/H3N2 in inpatients stratified by immunocompromising condition (IC), 2022

<table>
<thead>
<tr>
<th>IC status</th>
<th>Influenza positive</th>
<th>Influenza negative¹</th>
<th>Vaccine Effectiveness</th>
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<tbody>
<tr>
<td></td>
<td>N vaccinated /Total (%)</td>
<td>N vaccinated /Total (%)</td>
<td>Unadjusted</td>
</tr>
<tr>
<td>No</td>
<td>101/233 43</td>
<td>453/900 50</td>
<td>24 (-1 to 44)</td>
</tr>
<tr>
<td>Yes</td>
<td>38/62 61</td>
<td>169/275 61</td>
<td>1 (-75 to 44)</td>
</tr>
<tr>
<td>No IC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–64 years</td>
<td>28/100 28</td>
<td>199/471 42</td>
<td>47 (15 to 67)</td>
</tr>
<tr>
<td>≥65 years</td>
<td>73/133 55</td>
<td>254/429 59</td>
<td>16 (-24 to 43)</td>
</tr>
</tbody>
</table>

¹ Persons testing negative for both influenza and SARS-CoV-2 using molecular assays.
² Multivariable logistic regression models adjusted for study site, age, sex, race/ethnicity, and calendar time (biweekly intervals).