End-of-Season Estimates of 2019–20 Seasonal Influenza Vaccine Effectiveness against Medically Attended Influenza from three U.S. Networks

Data from the US Flu VE Network, New Vaccine Surveillance Network (NVSN), and Hospitalized Adult Influenza Vaccine Effectiveness Network (HAIVEN)

Advisory Committee on Immunization Practices
October 28, 2020
Preliminary results

Three networks to evaluate vaccine effectiveness against laboratory-confirmed influenza in ambulatory and inpatient settings
Ambulatory patients—ages ≥6 months: US Flu VE* Network sites and principal investigators

<table>
<thead>
<tr>
<th>US Flu VE</th>
<th>Setting</th>
<th>Ages</th>
<th>Symptoms</th>
<th>Symptom duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ambulatory</td>
<td>≥6 months</td>
<td>ARI</td>
<td>≤7</td>
</tr>
</tbody>
</table>

*US Flu VE* US Influenza Vaccine Effectiveness Network
Inpatients—adults aged ≥18 years: HAIVEN* sites and principal investigators

<table>
<thead>
<tr>
<th>Setting</th>
<th>Inpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ages</td>
<td>≥18 years</td>
</tr>
<tr>
<td>Symptoms</td>
<td>ARI</td>
</tr>
<tr>
<td>Symptom duration</td>
<td>≤10</td>
</tr>
</tbody>
</table>

*HAIVEN-Hospitalized Adult Influenza Vaccine Effectiveness Network
Inpatients—children aged 6 months–17 years: NVSN* sites and principal investigators

<table>
<thead>
<tr>
<th>NVSN</th>
<th>Setting</th>
<th>Ages</th>
<th>Symptoms</th>
<th>Symptom duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Inpatient/ED</td>
<td>6 months-17 years</td>
<td>ARI</td>
<td>≤10</td>
</tr>
</tbody>
</table>

*NVSN—New Vaccine Surveillance Network
Methods

Design: Test-negative design

- Comparing odds of influenza vaccination among patients with laboratory-confirmed influenza vs. patients testing influenza negative by RT-PCR
- Vaccination status: receipt of one dose (≥1 dose for children 6m-8 years) of any 2019–20 seasonal flu vaccine at least 14 days prior to illness onset (if known)
- Sources: Medical records, immunization registries, and/or self-report

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

- Adjustment for potential confounding variables (i.e. study site, age, calendar time)
# Influenza virus type/subtype distribution by VE network

<table>
<thead>
<tr>
<th></th>
<th>US Flu VE</th>
<th>HAIVEN</th>
<th>NVSN-Hosp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrollment period</td>
<td>Nov-Mar</td>
<td>Oct-Mar</td>
<td>Sep-May</td>
</tr>
<tr>
<td>Enrolled</td>
<td>8,845</td>
<td>3,116</td>
<td>2,029</td>
</tr>
<tr>
<td>Influenza pos (%)</td>
<td>2,722 (31%)</td>
<td>553 (18%)</td>
<td>335 (17%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th>NVSN-ED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrollment period</td>
<td></td>
<td></td>
<td>Sep-May</td>
</tr>
<tr>
<td>Enrolled</td>
<td></td>
<td></td>
<td>2,102</td>
</tr>
<tr>
<td>Influenza pos (%)</td>
<td></td>
<td></td>
<td>671 (32%)</td>
</tr>
</tbody>
</table>
Influenza Virus Infections in NVSN Hospitalized and ED Subjects, 2019–2020

Number of patients

- A(H1N1)pdm09
- A(H3N2)
- A, unsubtyped
- B/Victoria
- B/Yamagata
- B, lineage unknown
- Influenza negative

2019

2020
Influenza virus infections in the HAIVEN Network inpatients aged ≥18 years, 2019-2020

![Graph showing influenza virus infections in the HAIVEN Network inpatients aged ≥18 years, 2019-2020. The graph displays the number of patients infected with different influenza subtypes, including A(H1N1)pdm09, A(H3N2), A, unsubtyped, B/Victoria, B/Yamagata, B, lineage unknown, coinfection, and influenza negative. The graph is divided into two periods, 2019 and 2020, with epidemiologic weeks indicated on the x-axis. The y-axis represents the number of patients.]
Influenza virus infections in US Flu VE Network outpatients aged ≥6 months, 2019-2020

![Bar chart showing the number of patients infected with different types of influenza viruses from 2019 to 2020. The chart includes data for A(H1N1)pdm09, A(H3N2), A, unsubtyped, B/Victoria, B/Yamagata, B, lineage unknown, Coinfection, and Influenza negative.](image-url)
Ambulatory settings – ages ≥6 months

US Flu VE Network
Adjusted vaccine effectiveness against medically attended influenza ages ≥6 months, US Flu VE Network, 2019–20

* Multivariable logistic regression models adjusted for site, age, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time.
Adjusted vaccine effectiveness against influenza B/Victoria by age group, US Flu VE Network, 2019–20

* Multivariable logistic regression models adjusted for site, age, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time.
Adjusted vaccine effectiveness against influenza A/H1N1pdm09 by age group, US Flu VE Network, 2019–20

* Multivariable logistic regression models adjusted for site, age, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time.
VE against influenza associated hospitalization and ED visits among patients aged 6 months to 17 years

NVSN preliminary results
2019–2020 VE* against influenza hospitalizations, ED visits, by virus type, aged 6m–17 yrs, NVSN

- Final models adjusted for study site, age as a continuous variable and calendar time (monthly intervals)
- n values show the total number of influenza positive subjects in each group
2019–2020 VE* against influenza hospitalizations, ED and outpatient visits by virus type, aged 6m–17 yrs, NVSN/Flu VE

- Final models adjusted for study site, age as a continuous variable and calendar time (monthly intervals)
- n values show the total number of influenza positive subjects in each group
2019–2020 VE* against influenza hospitalizations, ED and outpatient visits aged 6m–17 yrs, by age group, NVSN/Flu VE

- Final models adjusted for study site, age as a continuous variable and calendar time (monthly intervals)
- n values show the total number of influenza positive subjects in each group
Hospitalized Adult Influenza Vaccine Effectiveness Network (HAIVEN) preliminary results
2019–2020 VE* against influenza hospitalizations and outpatient visits among adults, by virus type, HAIVEN/Flu VE

* Final models adjusted for study site, age, sex, race/ethnicity, days from illness onset to specimen collection, timing of illness onset, ≥1 hospitalizations (versus none) in prior year (HAIVEN)
2019–2020 VE* against influenza hospitalizations and outpatient visits among adults, by age group, HAIVEN/Flu VE

* Final models adjusted for study site, age, sex, race/ethnicity, days from illness onset to specimen collection, timing of illness onset, ≥1 hospitalizations (versus none) in prior year (HAIVEN)
Limitations

- VE by vaccine type not included
  - Limited use of LAIV4 among children in NVSN and Flu VE to estimate VE for LAIV4 against A(H1N1)pdm09
  - Challenges estimating VE of egg-based vs non-egg based vaccines (recombinant/cell-culture) due to site-specific differences in vaccines offered
  - Among inpatients and outpatients aged ≥65 years, patient characteristics differed by vaccine type (majority received IIV4-HD)
- VE estimates include reported vaccination and partially vaccinated children; results are preliminary pending final vaccination data
Summary—Importance of three VE networks

- 2019–20 influenza vaccination significantly reduced laboratory confirmed medically attended influenza in all VE networks:
  - 39% (95%CI: 32, 44) against outpatient illness aged ≥6 months (Flu VE)
  - 62% (95%CI: 52, 71) against pediatric hospitalizations (NVSN)
  - 56% (95%CI: 46, 65) against pediatric ED visits (NVSN)
  - 41% (95%CI: 27, 52) against adult hospitalizations (HAIVEN)

- Important protection against influenza B virus given severity of 2019-20 season for children and vaccine mismatch

- Outpatient VE trended lower among pediatric outpatient than inpatients/ED visits; outpatient and inpatient VE similar among adults
Acknowledgments
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Advisory Committee on Immunization Practices
October 28, 2020
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FluView, Week 42 (ending October 17, 2020): Virologic Surveillance
FluView, Week 42 (ending October 17, 2020):

Influenza-Like Illness Surveillance
Work Group Discussion and Considerations

- Influenza WG heard and discussed presentation of trial of Flucelvax Quadrivalent for children aged ≥2 through <18 years.

- Some clarifying questions concerning study design and study population.

- No specific concerns raised.
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.