US CDC Evaluations of Influenza Vaccine Effectiveness

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International Meeting on Influenza Vaccine Effectiveness
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Expansion to Universal Vaccination in U.S.

- Adults age 65+, chronically ill, and pregnant women
- Adults age 50-64
- Healthy adults age 18-49
- Children age 24-59 months and close contacts
- Children age 6-23 months and close contacts
- Children age 5-17 years

Before 2000

2000

2003

2006

2008

2010
CDC’s Influenza Division Program to Measure Influenza Vaccine Effectiveness (VE) in the U.S.

<table>
<thead>
<tr>
<th>New Vaccine Surveillance Network</th>
<th>6-59 mo. Outpatient and Hospitalized</th>
</tr>
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<tbody>
<tr>
<td>Emerging Infections Program (EIP)</td>
<td>6-59 mo. Hospitalized</td>
</tr>
<tr>
<td>Marshfield Clinic, WI</td>
<td>Adults &gt;18 Hospitalized</td>
</tr>
<tr>
<td>US Flu VE Network 4 sites</td>
<td>Adults &gt;50 Hospitalized</td>
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<tr>
<td>Vulnerable populations studies</td>
<td></td>
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<tr>
<td>US Flu VE Network 5 sites</td>
<td>VE for pregnant women 2010-12</td>
</tr>
<tr>
<td></td>
<td>VE estimates from 2011-12 Season</td>
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</tbody>
</table>

**VE for pregnant women 2010-12**

**VE estimates from 2011-12 Season**

- Pregnant women, HCP, and children
- MAARI and Non-MAARI
- All Ages
- Hospital & Outpatient
- Vulnerable populations studies

**Influenza season**

- 03-04
- 04-05
- 05-06
- 06-07
- 07-08
- 08-09
- 09-10
- 10-11
- 11-12
- 12-13
US Flu VE Network: Five Study Sites and Principal Investigators

Lisa Jackson
Mike Jackson

Ed Belongia

Arnold Monto
Suzanne Ohmit

Manju Gaglani

Rick Zimmerman
Patricia Nowalk
US Flu VE Network: Methods

- **Purpose:** Estimate VE for prevention of outpatient healthcare visits due to influenza
- **Design:** Prospective case-control study
  - **Cases:** MAARI and RT-PCR influenza
  - **Controls:** MAARI but negative for influenza
- **Vaccination status:** Confirmed by medical record or registry
- **Immunization:** Receipt of 1+ dose of vaccine ≥14 days before illness onset
- **Analysis:** VE = (1 – adjusted OR) x 100%, estimated with logistic regression
  - Standard covariates: site, race, age in months, days from onset to enrollment
  - Adjusts for potential confounding by self-rated health and high risk medical conditions
US Flu VE Network 2011-12 Season:
Number of cases and controls and percentage vaccinated by week

MMWR Week, 2012
US Flu VE Network 2011-12 Season:
Adjusted VE Summary

Adjusted Influenza VE

90%
80%
70%
60%
50%
40%
30%
20%
10%
0%

6 mo. – 8 yrs. 9 – 18 yrs. 19 – 49 yrs. 50+ yrs. A(H1N1) A(H3N2) Influenza B
Against All Viruses By Age

By Virus for All Ages

42% 60% 44% 50% 64% 37% 60%
US Flu VE Network

**Strengths**

- Highly sensitive and specific test
- Study and refine TND
- Common protocol
- Geographic diversity
- Diversity in age and health status of enrollees
- Vaccination status confirmed by EMR and registries

Will facilitate cross-season pooling and comparisons
US Flu VE Network: Adjusted VE against A(H3N2) by Age in 2010-11

Adjusted Influenza VE

66%  39%  52%

0%  10%  20%  30%  40%  50%  60%  70%  80%  90%

6 mo. - 8 years   9-49 years   50+ years
Season 2010-11

US Flu VE Network:
Adjusted VE against A(H3N2) by Age in 2010-11 and 2011-12 seasons

- 66% (6 mo. - 8 years, Season 2010-11)
- 39% (9-49 years, Season 2010-11)
- 52% (50+ years, Season 2010-11)
- 39% (6 mo. - 8 years, Season 2011-12)
- 45% (9-18 years, Season 2011-12)
- 33% (19-49 years, Season 2011-12)
- 36% (50+ years, Season 2011-12)
US Flu VE Network

**Strengths**
- Highly sensitive and specific test
- Study and refine TND
- Common protocol
- Geographic diversity
- Diversity in age and health status of enrollees
- Vaccination status confirmed by EMR and registries

**Limitations**
- Lack post-vaccination serology
- Lack tests of antigenic match for all positives
- No control over vaccines offered locally
- Difficult to enroll sufficient numbers of important vulnerable groups:
  - Pregnant women
  - Elderly
PREGNANCY & INFLUENZA PROJECT (PIP): PRELIMINARY VE FINDINGS
Pregnancy & Influenza Project (PIP): Methods 1

- **Purpose:** Estimate VE in preventing RT-PCR influenza during pregnancy
- **Setting:** Kaiser Permanente (KP) in Northern California and Oregon during 2010-11 season and 2011-12 season
- **Design:** Prospective nested case-cohort study
  - **Cases:** ARI positive and RT-PCR influenza
  - **Matched Controls:** ARI negative before index case illness onset and matched by site and trimester
  - **Test-Negative Controls:** ARI positive but influenza negative

Pregnancy & Influenza Project (PIP): Methods 1

- **Surveillance:**
  - Daily surveillance of MAARI visits for all eligible pregnant women during both seasons
  - Weekly internet- and telephone-based surveillance during season one
  - NP swabbed women with fever and cough ≤8 days of illness onset
  - RT-PCR confirmed influenza by Marshfield Clinic
### PIP: Number of cases and controls

<table>
<thead>
<tr>
<th></th>
<th>Season One (2010-11)</th>
<th>Season Two (2011-12)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Influenza-Positive Cases</strong></td>
<td></td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Medically attended ARI</td>
<td>36</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Not medically attended ARI</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ARI-Negative Matched Controls</strong></td>
<td></td>
<td></td>
<td>200</td>
</tr>
<tr>
<td>From prospective cohort</td>
<td>106</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From all eligible pregnant women</td>
<td></td>
<td>94</td>
<td></td>
</tr>
<tr>
<td><strong>ARI-Positive but Influenza-Negative Controls</strong></td>
<td></td>
<td></td>
<td>192</td>
</tr>
<tr>
<td>Medically attended ARI</td>
<td>74</td>
<td>77</td>
<td></td>
</tr>
<tr>
<td>Not medically attended ARI</td>
<td>41</td>
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</tbody>
</table>
Pregnancy & Influenza Project (PIP): Methods 2

- **Immunization:** Vaccination documented by medical record at KP or self-report if received outside the health plan ≥14 days before illness onset of index case

- **Analysis:** VE = (1 – adjusted OR) x 100%, estimated with logistic regression, with 95% CI for 0-100% VE
  - Standard covariates: Age, race, ethnicity, season, site, trimester, high risk status, MAARI, and days between illness onset and swabbing
  - Adjusted for potential confounding by BMI
  - Assessed potential effect modification by prior seasonal influenza vaccination

PIP Adjusted VE and 95% CI Compared with MAARI VE among Adults from US Flu VE Network

Adjusted Influenza VE

0% 10% 20% 30% 40% 50% 60% 70% 80%

Matched ARI Negative Controls Test-Negative Controls Season 2010-11 Test-Neg Controls Season 2011-12 Test-Neg Controls

PIP Seasons 2010-11 and 2011-12 US Flu VE Network Adults MAARI

- 44%
- 43%
- 51%
- 44%
Conclusion

- US Flu VE Network can contribute to pooled and cross-season comparisons
- New insights may come from looking at multi-year vaccine program vs. seasons
- Multiple questions require multiple methods
- PIP observed significant but modest VE among pregnant women, in line with other adult studies
- Effect of repeated vaccination on VE deserves renewed attention
Acknowledgements

**US Flu VE Network**
- **CDC**: David Shay, Swathi Thaker, Sarah Spencer, Jill Ferdinands, Po-Yung Cheng, Alicia Fry
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- **Scott & White**: Manju Gaglani
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- **U Pittsburgh**: Rick Zimmerman, Tricia Nowalk

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- **Vanderbilt**: Marie Griffin

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