Effectiveness of PCV13 in Adults Hospitalized with Pneumonia Using Centers for Medicare & Medicaid Services Data, 2014-2017

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Project Question

What is the direct effect of new adult PCV13 recommendation on pneumonia hospitalizations among adults ≥ 65 years of age?
METHODS

- CMS Medicare Part A/B Data
- Study Cohort
  - U.S. Medicare beneficiaries ≥ 65 years old enrolled in part A/B on September 1, 2014
  - After September 1, 2014, only beneficiaries who got part A/B coverage within 6 months of their 65th birthday were included
  - Cohort observed until December 31, 2017
  - Beneficiaries dropped from the cohort before the end of study if they:
    - died
    - moved out of the United States
    - dis-enrolled from part A/B
    - developed the outcome of interest

- Pneumococcal vaccination categories
  - PCV13 only, PPSV23 only, both vaccines (PCV13+PPSV23), no pneumococcal vaccine
**High Risk Groups**

- Four mutually exclusive groups based on underlying conditions

<table>
<thead>
<tr>
<th>High Risk Group*</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk 1 (HR1) only</td>
<td>Asplenia, CKD, generalized malignancy, HIV, hematologic malignancies, iatrogenic immunosuppression, immunodeficiencies, nephrotic syndrome, sickle cell anemia, solid organ transplant</td>
</tr>
<tr>
<td>High risk 2 (HR2) only</td>
<td>Alcoholism, chronic heart disease, chronic liver disease, chronic lung disease**, cigarette smoking, diabetes**</td>
</tr>
<tr>
<td>High risk 1 + 2 (Both)</td>
<td>At least one HR1 and one HR2 condition</td>
</tr>
<tr>
<td>Low risk</td>
<td>None of the conditions in HR1 or HR2</td>
</tr>
</tbody>
</table>

* Based on [https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6140a4.htm](https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6140a4.htm)

** Prevalence of 42% among beneficiaries

Underlying conditions captured using inpatient (IP) and outpatient (OP) hospital facility claims for malignancies and IP+OP+ Physician/supplier part B (PB) for non-cancer conditions
Outcomes of Interest

- Based on inpatient claims
- CAP: Community-Acquired Pneumonia (Griffin et al algorithm*)
  - Primary diagnosis of pneumonia
  - Primary diagnosis of meningitis, sepsis, empyema, or acute respiratory failure with a pneumonia diagnosis in any secondary position

- Non-HA CAP: Non-healthcare associated CAP
  - CAP in a patient without admission to hospital or skilled nursing facility in the prior 30 days and without a prior healthcare-associated pneumonia hospitalization (SUBSET OF CAP)

- Lobar Pneumonia
  - Inpatient hospital claim with a diagnosis of lobar/pneumococcal pneumonia (ICD9:481/ICD10: J13/J181) in any discharge diagnosis position

* Griffin et al. NEJM. 2013 369:155-63
Statistical Approach

- Discrete time survival model
  - Instantaneous hazard ratio ≡ Incidence rate ratio
- Outcome: hospitalization with outcome of interest occurred in given month (yes/no)
- Generalized estimating equations (GEE) to adjust for correlations
- Incidence rate ratios and 95% confidence intervals
  - Vaccine effectiveness (VE) = (1-IRR)*100
Four Separate Models

- Stratified by influenza season and influenza vaccination status
  - Influenza season (October-April)
  - Non-influenza season (May-September)

Rationale:
  a) Biological interaction between flu vaccine and outcome of interest
  b) Pneumococcal and influenza vaccines are not independent observations
  c) Flu vaccinated individuals ≠ flu unvaccinated individuals*

* Jackson ML Lancet. 2008
Model Adjustment Variables

- Age group (5-year bands)
- High risk condition category
- State
- Race
- Gender
- Hospital visits in prior year
- Outpatient non-ER visits in prior year
- Charlson comorbidity index
- Reason to enter CMS (Age, ESRD, Disabled, other)
- Month of year (e.g., January, February)
- Year
- Interactions: vaccine and age group, vaccine and risk group, age and risk group
Number of Hospitalizations Averted by PCV13

- Estimated the number of hospitalizations for each outcome in the absence of PCV13 based on model results
  - Observed/IRR

- Number of hospitalizations averted
  - Expected – Observed
RESULTS
### Patients Characteristics at Start and End of Cohort

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Sept 2014</th>
<th>Dec 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=26,598,266</td>
<td>N=24,121,625</td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>65-74</td>
<td>14,428,556 (54.2)</td>
<td>13,312,649 (55.2)</td>
</tr>
<tr>
<td>75-84</td>
<td>8,230,539 (30.9)</td>
<td>7,481,999 (31.0)</td>
</tr>
<tr>
<td>85+</td>
<td>3,939,171 (14.8)</td>
<td>3,326,997 (13.8)</td>
</tr>
<tr>
<td>Male</td>
<td>11,546,396 (43.4)</td>
<td>10,527,650 (43.6)</td>
</tr>
<tr>
<td>PCV13 use</td>
<td>210,567 (0.8)</td>
<td>10,018,855 (41.5)</td>
</tr>
<tr>
<td>High Risk 1</td>
<td>1,473,002 (5.5)</td>
<td>1,451,503 (6.0)</td>
</tr>
<tr>
<td>High Risk 2</td>
<td>9,967,701 (37.5)</td>
<td>8,521,792 (35.3)</td>
</tr>
<tr>
<td>Both HR1 and HR2</td>
<td>8,111,269 (30.5)</td>
<td>7,980,206 (33.1)</td>
</tr>
<tr>
<td>Low risk</td>
<td>7,046,294 (26.5)</td>
<td>6,168,124 (25.6)</td>
</tr>
<tr>
<td>Charlson score≥3</td>
<td>7,692,162 (28.9)</td>
<td>6,521,748 (27.0)</td>
</tr>
<tr>
<td>Outpatient visit ≥5</td>
<td>7,224,776 (27.2)</td>
<td>6,961,482 (28.9)</td>
</tr>
</tbody>
</table>

57.6% of 65+ US population
Are there differences in characteristics among PCV13 vaccinated seniors compared to unvaccinated*?

*Based on Dec 2017 data
Incidence per 100,000 Beneficiary-Months by Outcome of Interest, Sept 2014-Dec 2017

- CAP: 148
- Non-HA CAP: 115
- Lobar: 6
CAP Incidence per 100,000 Beneficiary-Months by Age Group, 2014-2017

Age Groups

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Incidence per 100,000 person-month</th>
</tr>
</thead>
<tbody>
<tr>
<td>65-74</td>
<td>86</td>
</tr>
<tr>
<td>75-84</td>
<td>170</td>
</tr>
<tr>
<td>85+</td>
<td>334</td>
</tr>
</tbody>
</table>
CAP Incidence per 100,000 Beneficiary-Months by Risk Group, 2014-2017

- Low Risk: 21
- High Risk 1 Only: 62
- High Risk 2 Only: 115
- Both HR1 + HR2: 303

Incidence per 100,000 person-month
Model Results – PCV13 VE Estimates
### Characteristics of Beneficiaries in Each Model Across Entire Study Period (40 months)

<table>
<thead>
<tr>
<th></th>
<th>Flu season/ Flu Vac</th>
<th>Flu Season/ Flu Unvac</th>
<th>Non-flu season/ Flu Vac</th>
<th>Non-flu season/ Flu Unvac</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total person months</td>
<td>234,757,324</td>
<td>366,014,989</td>
<td>189,023,134</td>
<td>182,313,686</td>
</tr>
<tr>
<td>% 65-74 years</td>
<td>48.3%</td>
<td>58.9%</td>
<td>47.8%</td>
<td>62.3%</td>
</tr>
<tr>
<td>% 75-84 years</td>
<td>34.9%</td>
<td>28.3%</td>
<td>35.2%</td>
<td>26.2%</td>
</tr>
<tr>
<td>% HR1+HR2</td>
<td>37.1%</td>
<td>28.3%</td>
<td>37.7%</td>
<td>26.0%</td>
</tr>
<tr>
<td>% Low Risk</td>
<td>19.2%</td>
<td>30.1%</td>
<td>18.6%</td>
<td>33.1%</td>
</tr>
</tbody>
</table>

**Healthier elderly**
VE and 95% Confidence Interval for PCV13 only vs. Unvaccinated Against CAP Across the FOUR Models

- **Flu season/Flu Vac:** CAP 6.0%
- **Flu Season/Flu Unvac:** CAP 11.4%
- **Non-flu season/Flu Vac:** CAP 9.3%
- **Non-flu season/Flu Unvac:** CAP 10.2%

**VE CAP: 6.0%–11.4%**

Adjusted for age, risk condition, healthcare utilization, state, race, gender and month
VE and 95% Confidence Interval for PCV13 only vs. Unvaccinated Against Non-HA CAP

Adjusted for age, risk condition, healthcare utilization, state, race, gender and month
VE and 95% Confidence Interval for PCV13 only vs. Unvaccinated Against LOBAR Pneumonia Across the FOUR Models

VE Lobar Pneumonia: 1.3%–11.0%

Adjusted for age, risk condition, healthcare utilization, state, race, gender and month
### Hospitalizations Averted Due to PCV13 From September 2014 – December 2017 in the Study Cohort

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Episodes Averted during 40 Months of Study n (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAP</td>
<td>28,600 (21,000–36,600)</td>
</tr>
<tr>
<td>Non-HA CAP</td>
<td>18,700 (12,000–25,800)</td>
</tr>
<tr>
<td>Lobar</td>
<td>1,100 (190 – 1900)</td>
</tr>
</tbody>
</table>

18,700 (13,000-25,000) from Jan-Dec 2017
Changes in risk group distribution among PCV13 vaccinated individuals

PCV13 only

PCV13 + PPSV23

Limitations

- Residual confounding
  - ICD codes fail to remove all confounding in pharmacoepidemiologic studies among seniors\(^1\)-\(^3\)
    - Lack of reliable ICD codes to measure functional status
    - Adjustment for chronic diseases and healthcare utilization can reduce biases but do not completely eliminate them

- Misclassification of vaccination status
  - Influenza vaccine: ~30% of individuals with documentation of flu vaccine based on HAIVEN\(^*\) misclassified as unvaccinated in CMS
  - Pneumococcal vaccine: adequate capture of PCV13 status but ~30% of misclassification of PPSV23 status based on ABCs data


\(^*\)US hospitalized Influenza Vaccine Effectiveness Network
Summary

- CAP incidence is highest among individuals $\geq 85$ years of age and those with HR1+HR2 conditions

- Individuals who got PCV13 were older, sicker and had more healthcare exposures

- Effectiveness of PCV13 observed against first episode of CAP, non-HA CAP and lobar pneumonia
Conclusion

- PCV13 VE for all-cause CAP: 6.0%–11.4%
  - Similar to Gessner et al (clinical trial)*: PCV13 VE of 8.1% (1.0%–14.6%) against all-cause CAP

- ~28,600 CAP hospitalizations averted within 40 months after implementation of new adult PCV13 recommendation
  - 18,700 (65%) prevented in 2017
    - Likely related to the characteristics of the individuals who are receiving the vaccine in more recent years
    - Represents 5.1% of all CAP hospitalizations in 2017 being prevented

*Gessner et al (Pfizer funded). Vaccine 2018
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