Estimating Pneumococcal Pneumonia Burden Among U.S. Adults and Progress on the Research Agenda for Potential Policy Change

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Advisory Committee on Immunization Practices
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Overview

- Pneumococcal conjugate vaccines have dramatically reduced invasive pneumococcal disease (IPD) in adults through indirect effects

- ACIP recommended routine use of 13-valent pneumococcal conjugate vaccine (PCV13) in series with 23-valent pneumococcal polysaccharide vaccine (PPSV23) for adults aged ≥65 years in 2014
  - PCV13 effective against IPD including pneumonia with bacteremia
  - PCV13 demonstrated efficacy against vaccine-type non-bacteremic pneumococcal pneumonia (NBPP)

- What is the burden of NBPP?
- What is the impact of PCV13 on NBPP for adults ≥65 years old?
Pneumococcal pneumonia as a cause of community acquired pneumonia (CAP)

- *S. pneumoniae* is a common cause of CAP
  - Estimated to cause 27% of CAP pre-PCV13\(^1\)
- CAP incidence attributable to *S. pneumoniae* is difficult to estimate
  - Blood culture has low sensitivity
    - Detects 25% of pneumococcal pneumonia cases
  - Pneumococcal urinary antigen test (UAT)
    - Pooled sensitivity 74–75% and specificity 95–97%\(^2,3\)
    - Not universally available or routinely used by all providers

Multiple studies have estimated the incidence of adult pneumococcal hospitalizations. Two studies, Storms and Yu, reported CAP incidence and the pneumococcal proportion was calculated using the 27% presented on the previous slide. Storms looked at years 2006 through 2010, while Yu looked at 2007 through 2008.

- U.S. Vaccine Safety Datalink sites
- ICD pneumonia discharges including sepsis and respiratory failure
- Calculated pneumococcal pneumonia incidence as 27% of pneumonia discharges to be 108/100,000

- U.S. Medicare Part A primary discharges of pneumonia or sepsis or respiratory failure with pneumonia elsewhere
- Calculated pneumococcal pneumonia incidence as 27% of pneumonia discharges to be 462/100,000

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**Chart:**

Adult Pneumococcal Pneumonia Hospitalization Incidence Estimates

- Storms calculated (≥18 yo)
- Yu calculated (≥18 yo)
- Bewick (≥16 yo)
- Jain (≥18 yo)
- Rodrigo (≥16 yo) [Bewick follow up]
- Ramirez calculated (≥18 yo)
Three studies, Bewick, Rodrigo, and Jain, measured pneumococcal pneumonia. Bewick looked at years 2008 through 2010, Rodrigo looked at 2012 through 2013, and Jain looked at 2010 through 2012.

-U.K. adults admitted to 2 academic hospitals, diagnosis using culture and serotype specific UAT
-Pneumococcal CAP incidence among adults (≥16 years old) 37/100,000

-Follow up study to Bewick presenting post-PCV13 incidence 21/100,000

-U.S. adults admitted to 5 urban hospitals with radiographically confirmed pneumonia, diagnosis using culture, PCR, and UAT
-Measured pneumococcal pneumonia incidence 12/100,000, which was 5% of CAP

- U.S. adults hospitalized with radiographically confirmed pneumonia in Louisville, KY
- Calculated pneumococcal pneumonia incidence as 27% of CAP 171/100,000
Surveillance for Non-invasive Pneumococcal Pneumonia (SNiPP): Objectives

- Describe noninvasive pneumococcal pneumonia among adults
- Estimate the disease burden of noninvasive pneumococcal pneumonia
- Examine the potential impact of the 2014 ACIP recommendation for routine PCV13 among adults 65 years and older
SNiPP: Methods

- Built into Active Bacterial Core surveillance (ABCs)
- Cases defined as adults (≥18 years) hospitalized with clinically or radiographically confirmed pneumonia and a positive pneumococcal urinary antigen test (UAT)
  - Cases excluded if invasive pneumococcal disease (IPD) or another positive UAT within 30 days
- Prospective since 2015 with retrospective data collection to 2013
  - Pre-PCV13 period (≥65 year old PCV13 recommendation) 2013–2014
  - Post-PCV13 period 2015–2016
## Characteristics of SNiPP Cases, 2013–2014

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All cases (N=1,213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (range)</td>
<td>64 years (18–102)</td>
</tr>
<tr>
<td>≥65 years old (%)</td>
<td>605 (50%)</td>
</tr>
<tr>
<td>Median from admission to diagnosis</td>
<td>1 day (-2–30)</td>
</tr>
<tr>
<td>Median hospitalization length in days (range)</td>
<td>5 days (1–152)</td>
</tr>
<tr>
<td>Radiographically confirmed pneumonia (%)</td>
<td>1,208 (99%)</td>
</tr>
<tr>
<td>ICU admissions (%)</td>
<td>402 (33%)</td>
</tr>
<tr>
<td>Died (%)</td>
<td>75 (6%)</td>
</tr>
</tbody>
</table>
Case Count Adjustments for Incidence Estimates

- Not all suspected pneumococcal pneumonia cases are tested by UAT
  - Adjust the UAT case count by the proportion of pneumonia tested by UAT at that hospital (Adjustment A)
    - Obtained from hospital discharge records and clinical labs

- Not all hospitals use UAT
  - Adjust the UAT case count by the proportion of pneumonia in the catchment area that was seen at hospitals offering UAT (Adjustment B)
    - Obtained from hospital discharge records and county level discharge data
Adjustment Methods

- Pneumonia discharges* tested by pneumococcal UAT (Adjustment A)
  - Sample of hospital within the catchment area (n 22)
    - Randomly select sample 20 pneumonia discharges/age group/month
    - Match randomly selected sample with laboratory pneumococcal UAT (positive and negative)

- Pneumonia discharges* in the catchment area seen at hospitals offering pneumococcal UAT (Adjustment B)
  - 37 hospitals in 7 urban areas (CO, CT, GA, MD, NY, and 2 TN)
    - 70% have 200–500 beds/hospital

*Pneumonia defined as 1st ICD pneumonia or empyema or 1st ICD sepsis with pneumonia or empyema elsewhere
### Hospital Characteristics Across Catchment Areas Included in Adjustments

<table>
<thead>
<tr>
<th>Location</th>
<th>Reported UAT Positive Cases</th>
<th>Hospitals with UAT Positive Cases</th>
<th>Average 2013–2014 Population (Total 10,000,148)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>% Pneumonia Tested by UAT (n 22 hospitals)</td>
<td>% Catchment Area Pneumonia (n 37 hospitals)</td>
</tr>
<tr>
<td>CO</td>
<td>121</td>
<td>32%</td>
<td>11%</td>
</tr>
<tr>
<td>CT</td>
<td>282</td>
<td>47%</td>
<td>63%</td>
</tr>
<tr>
<td>GA</td>
<td>42</td>
<td>13%</td>
<td>17%</td>
</tr>
<tr>
<td>MD</td>
<td>551</td>
<td>72%</td>
<td>83%</td>
</tr>
<tr>
<td>NY</td>
<td>131</td>
<td>60%</td>
<td>42%</td>
</tr>
<tr>
<td>TN₁</td>
<td>9</td>
<td>2%</td>
<td>34%</td>
</tr>
<tr>
<td>TN₂</td>
<td>29</td>
<td>14%</td>
<td>36%</td>
</tr>
<tr>
<td>Average</td>
<td>166</td>
<td>32%</td>
<td>41%</td>
</tr>
</tbody>
</table>

- Crude incidence based on reported UAT positive NBPP cases only
  - 6 cases/100,000
- Adjusted annual incidence area hospitals (n 22)
  - 99 cases/100,000
  - Examined incidence by percent of pneumonia tested by UAT

<table>
<thead>
<tr>
<th>% pneumonia tested by UAT</th>
<th>Number of hospitals</th>
<th>Incidence per 100,000</th>
<th>(Range by hospital)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>16</td>
<td>82</td>
<td>(13–173)</td>
</tr>
<tr>
<td>30%</td>
<td>11</td>
<td>79</td>
<td>(13–173)</td>
</tr>
<tr>
<td>50%</td>
<td>6</td>
<td>97</td>
<td>(49–173)</td>
</tr>
</tbody>
</table>
Limitations

- Missing data from hospitals and laboratories
- Reliant on administrative codes (ICD) for adjustments
- Sampling methods used to estimate percent of pneumonia tested by UAT
  - Not all hospitals offering UAT sampled
  - Variability in the percent of pneumonia tested by UAT
Because of these limitations, we wanted to check our incidence estimates using all pneumonia discharge codes, similar to the calculations I made with the background literature. Taking all pneumonia discharges from the SNiPP catchment areas, we have 440 pneumonia cases/100,000. Assuming 27% of CAP is *S. pneumoniae* we get 120 pneumococcal pneumonia cases. From the Said metanalysis, we can also estimate that NBPP is ¾ of all pneumococcal pneumonia which brings us to 90 NBPP cases/100,000 as compared to 99 NBPP using our adjustment methods.
Putting this in perspective with the other studies, the two SNiPP estimates fall just below the Storms calculated estimate, but above the measured incidences reported in Bewick, Jain, and Rodrigo.
SNiPP: Next Steps

- Complete data collection and cleaning
- Model the proportion of patients with pneumonia discharge diagnoses tested by UAT (Adjustment A) for hospitals not sampled
- Examine age adjusted annual incidence
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Progress on the Research Agenda for Potential Policy Change
Key Questions

- In light of indirect effects observed, what is the impact of direct effects of PCV13 on pneumococcal disease among adults ≥65 years old?

- What benefits would we expect from continued PCV13 use among adults ≥65 years old?
Evidence Presented to Date

- Pneumococcal carriage among adults ≥65 years old
  - Very low pneumococcal carriage (1.8%)
  - PCV13-type carriage 0.2% in 2015-2016

- PCV13 coverage among adults ≥65 years old around 40%
  - Lower among 19–64 year olds, but varies by indication
Evidence Presented to Date

- Invasive pneumococcal disease (IPD)
  - PCV13-type IPD declined among all age groups
  - IPD incidence in adults ≥65 years old plateaued in 2014-2016
  - Modeled direct and indirect PCV13 effects on IPD in adults ≥65 years old project relatively few cases prevented
  - Serotype 3 IPD does not follow the same pattern as other PCV13-types
## Evidence Presented to Date

### Vaccine effectiveness (VE) against PCV13-type* IPD

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>VE</th>
<th>(95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPiTA</td>
<td>Randomized control trial Dutch adults ≥65 years old</td>
<td>75%</td>
<td>(41–91)</td>
</tr>
<tr>
<td>CDC Traditional Methods</td>
<td>IPD cases identified through ABCs matched with population-based controls</td>
<td>65%</td>
<td>(19–85)</td>
</tr>
<tr>
<td>CDC CMS</td>
<td>Medicare part B IPD cases matched with controls</td>
<td>47%</td>
<td>(4–71)</td>
</tr>
</tbody>
</table>

* CDC Traditional Methods and CDC CMS VE includes serotype 6C

### VE against PCV13-type pneumococcal pneumonia

<table>
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<tr>
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<th>Population</th>
<th>VE</th>
<th>(95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPiTA</td>
<td>Randomized control trial Dutch adults ≥65 years old</td>
<td>45%</td>
<td>(14–65)</td>
</tr>
<tr>
<td>Louisville Pneumonia Study</td>
<td>Test negative design in a cohort U.S. adults ≥65 years old</td>
<td>73%</td>
<td>(13–92)</td>
</tr>
</tbody>
</table>
Upcoming ACIP Meetings

- Continued updates about PCV13 impact on pneumonia
- Model estimating public health impact and cost-effectiveness of different policy options including:
  - No PCV13 for adults $\geq$ 65 years old
  - Expanding indications for adults < 65 years old
Discussion

- What additional information will the committee need to help determine whether continued PCV13 use in adults ≥65 years old is warranted?