Incidence of Invasive Pneumococcal Disease (IPD) by Race, United States, 2008–2016

Almea Matanock, MD, MS
Advisory Committee on Immunization Practices
June 21, 2018
Background

- IPD rates have historically been higher in some racial minorities
- Socioeconomic status (SES) and race are often interdependent, but SES might not account for all differences in IPD incidence between races
- Increased IPD incidence among people of black race might be driven by higher prevalence of certain chronic medical conditions
Observed IPD incidence rates among persons <5 years of age, by race and serotype—Active Bacterial Core surveillance, 1998 –2009 (Wortham, 2014)

CI: confidence interval
IPD: invasive pneumococcal disease
PCV7: 7-valent pneumococcal conjugate vaccine
PCV13: 13-valent pneumococcal conjugate vaccine

<table>
<thead>
<tr>
<th>Serotypes</th>
<th>Pre-PCV7 Rate Ratio (95% CI)</th>
<th>2002 Rate Ratio (95% CI)</th>
<th>2009 Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>2.5 (2.3-2.8)</td>
<td>1.6 (1.3-2.0)</td>
<td>2.2 (1.8-2.7)</td>
</tr>
<tr>
<td>PCV7</td>
<td>2.6 (2.4-2.8)</td>
<td>1.7 (1.2-2.4)</td>
<td>1.5*</td>
</tr>
<tr>
<td>Non-PCV7</td>
<td>2.3 (1.9-2.8)</td>
<td>1.6 (1.3-2.0)</td>
<td>2.2 (1.8-2.7)</td>
</tr>
</tbody>
</table>
Objective

- Evaluate racial disparities in IPD incidence since PCV13 introduction
Methods

- Active Bacterial Core Surveillance (ABCs):
  - Active laboratory and population-based surveillance
  - Pneumococcus isolated from sterile site
  - Race defined as a single race reported in medical chart
  - Race imputed for the 13% of IPD cases it was missing

- US Census Bureau race-bridged post-census population estimates as denominators
Methods

- Isolates serotyped by Quellung or PCR at reference labs and grouped for analysis:
  - For children:
    - PCV13 serotypes\textsuperscript{1}: 13 serotypes in PCV13 plus 6C due to cross-protection\textsuperscript{2}
    - Non-PCV13 serotypes: all other non-PCV13 or 6C serotypes
  - For adults:
    - PCV13 serotypes as defined in children
    - PPV11 serotypes\textsuperscript{3}: 11 serotypes unique to PPSV23
    - Non-vaccine types (NVT): all other non-PCV13, non-PPV11, not 6C pneumococcal serotypes

- Compared overall and serotype-specific IPD incidence (cases/100,000 population) from 2008–2009 (pre-pediatric PCV13 introduction baseline) to 2015–2016

1. Serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F
2. Cooper et al. 2011
# Race and Syndrome by Age among IPD Cases, 2008–2016

<table>
<thead>
<tr>
<th></th>
<th>Age in Years:</th>
<th>&lt;5</th>
<th>≥65</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Race n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td></td>
<td>776 (32%)</td>
<td>1,234 (12%)</td>
</tr>
<tr>
<td>White</td>
<td></td>
<td>1,438 (59%)</td>
<td>8,845 (84%)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>229 (9%)</td>
<td>434 (4%)</td>
</tr>
<tr>
<td><strong>Syndrome n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td></td>
<td>224 (9%)</td>
<td>399 (4%)</td>
</tr>
<tr>
<td>Bacteremia without Focus</td>
<td></td>
<td>1,074 (44%)</td>
<td>1,618 (15%)</td>
</tr>
<tr>
<td>Pneumonia with Bacteremia</td>
<td></td>
<td>813 (33%)</td>
<td>7,998 (76%)</td>
</tr>
</tbody>
</table>
IPD Incidence by Serotype Group among Children <5 Years Old, 2008–2016

CI: 95% confidence interval
ARD: absolute rate difference
IRR: incidence rate ratio
PCV13 Serotype IPD Incidence among Children <5 Years Old, 2008–2016

<table>
<thead>
<tr>
<th>PCV13 Incidence</th>
<th>Black</th>
<th>White</th>
<th>All Other Races</th>
</tr>
</thead>
<tbody>
<tr>
<td>-ARD</td>
<td>8.5</td>
<td>REF</td>
<td>4.9</td>
</tr>
<tr>
<td>-IRR</td>
<td>1.8</td>
<td>REF</td>
<td>1.5</td>
</tr>
</tbody>
</table>
Non-PCV13 Serotype IPD Incidence among Children <5 Years Old, 2008–2016

<table>
<thead>
<tr>
<th>Year</th>
<th>NVT Incidence</th>
<th>-ARD</th>
<th>-IRR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>16.9</td>
<td>9.3</td>
<td>2.2</td>
</tr>
<tr>
<td>2009</td>
<td>7.6</td>
<td>REF</td>
<td>REF</td>
</tr>
<tr>
<td>2010</td>
<td>11.2</td>
<td>3.6</td>
<td>1.5</td>
</tr>
</tbody>
</table>

CI: 95% confidence interval
ARD: absolute rate difference
IRR: incidence rate ratio
IPD Incidence by Serotype Group among Adults ≥65 Years Old, 2008–2016
PCV13 Serotype IPD Incidence among Adults ≥65 Years Old, 2008–2016

<table>
<thead>
<tr>
<th>Year</th>
<th>Black</th>
<th>White</th>
<th>All Other Races</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>20.1</td>
<td>18.0</td>
<td>16.1</td>
</tr>
<tr>
<td>2010</td>
<td>2.1</td>
<td>REF</td>
<td>-1.9</td>
</tr>
<tr>
<td>2011</td>
<td>1.1</td>
<td>REF</td>
<td>0.9</td>
</tr>
<tr>
<td>2012</td>
<td>0.5</td>
<td>REF</td>
<td>0.5</td>
</tr>
</tbody>
</table>

CI: 95% confidence interval
ARD: absolute rate difference
IRR: incidence rate ratio
PPSV23 Unique Serotype IPD Incidence among Adults ≥65 Years Old, 2008–2016

<table>
<thead>
<tr>
<th>Black</th>
<th>White</th>
<th>All Other Races</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPV11</td>
<td>9.6</td>
<td>8.4</td>
</tr>
<tr>
<td>-ARD</td>
<td>1.2</td>
<td>REF</td>
</tr>
<tr>
<td>-IRR</td>
<td>1.1</td>
<td>REF</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Black</th>
<th>White</th>
<th>All Other Races</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPV11</td>
<td>10.4</td>
<td>8.0</td>
</tr>
<tr>
<td>-ARD</td>
<td>2.4</td>
<td>REF</td>
</tr>
<tr>
<td>-IRR</td>
<td>1.3</td>
<td>REF</td>
</tr>
</tbody>
</table>
Non-Vaccine Serotype IPD Incidence among Adults ≥65 Years Old, 2008–2016

<table>
<thead>
<tr>
<th>Black</th>
<th>White</th>
<th>All Other Races</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVT</td>
<td>18.0</td>
<td>12.8</td>
</tr>
<tr>
<td>-ARD</td>
<td>5.2</td>
<td>REF</td>
</tr>
<tr>
<td>-IRR</td>
<td>1.4</td>
<td>REF</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Black</th>
<th>White</th>
<th>All Other Races</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVT</td>
<td>15.5</td>
<td>10.0</td>
</tr>
<tr>
<td>-ARD</td>
<td>5.5</td>
<td>REF</td>
</tr>
<tr>
<td>-IRR</td>
<td>1.6</td>
<td>REF</td>
</tr>
</tbody>
</table>

Indirect effects for adults ≥65 years old

Indirect and direct effects for adults ≥65 years old

CI: 95% confidence interval
ARD: absolute rate difference
IRR: incidence rate ratio
### Incidence Comparisons Before and After PCV13 Introduction

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Black*</td>
<td>All Other Races*</td>
<td>Black*</td>
<td>All Other Races*</td>
</tr>
<tr>
<td>Children &lt;5 Years Old</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCV13 IPD Absolute Rate Difference (ARD)</td>
<td>8.5</td>
<td>4.9</td>
<td>0.8</td>
<td>1.2</td>
</tr>
<tr>
<td>PCV13 IPD Incidence Rate Ratio (IRR)</td>
<td>1.8</td>
<td>1.5</td>
<td>1.7</td>
<td>2.0</td>
</tr>
<tr>
<td>Total IPD ARD</td>
<td>17.8</td>
<td>8.6</td>
<td>5.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Total IPD IRR</td>
<td>2.0</td>
<td>1.5</td>
<td>1.7</td>
<td>1.3</td>
</tr>
<tr>
<td>Adults ≥65 Years Old</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCV13 IPD ARD</td>
<td>2.1</td>
<td>-1.9</td>
<td>=</td>
<td>-2.9</td>
</tr>
<tr>
<td>PCV13 IPD IRR</td>
<td>1.1</td>
<td>0.9</td>
<td>1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Total IPD ARD</td>
<td>8.5</td>
<td>-3.8</td>
<td>7.9</td>
<td>-5.6</td>
</tr>
<tr>
<td>Total IPD IRR</td>
<td>1.2</td>
<td>0.9</td>
<td>1.3</td>
<td>0.8</td>
</tr>
</tbody>
</table>

*Incidence among persons of white race used as reference group*
Preliminary Conclusions

- IPD incidence has dramatically decreased for all racial groups driven by reduction in PCV13-type IPD
- PCVs have nearly eliminated the absolute difference in PCV13-type IPD incidence between people of black and white races
- Disparities in IPD remain due to non-vaccine type IPD
- Further analysis is planned to look at the contribution of SES and underlying medical conditions by race
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- Kari Burzlaff
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Thank you!
Overview of the Evidence to Recommendations Framework for the ongoing review of the PCV13 recommendation for adults ≥65 years old
ACIP Evidence to Recommendation (EtR) Framework

- Statement of problem
  - Public health priority
  - Burden of disease
- Benefits and harms
  - Balance of desirable and undesirable effects
  - Certainty in evidence
- Values and preferences of target population
- Acceptability to stakeholders
- Resource use
  - Health economic analyses
- Feasibility
  - Implementation considerations
Current Adult PCV13 Recommendations

- In 2012 ACIP recommended PCV13 in series with PPSV23 for adults ≥19 years old with immunocompromising conditions, asplenia, cochlear implants, or cerebrospinal fluid leaks.
- In 2014 ACIP added an age based recommendation for PCV13 in series with the previously recommended PPSV23 for all PCV13-naïve adults ≥65 years old.
Formulating a Question to Re-Evaluate the Adult Age Based PCV13 Recommendation

- Should PCV13 be administered routinely to all immunocompetent adults aged ≥65 years given sustained indirect effects?
  - Population: Immunocompetent adults 65 years and older
  - Intervention: PCV13 at ≥65 years old in series with PPSV23 in the context of indirect effects
  - Comparison(s): PPSV23 alone at ≥65 years old
  - Outcomes: pneumococcal disease, mortality, and vaccine safety
Grading of Recommendations Assessment, Development and Evaluation (GRADE) Process

- Choosing Outcomes
  - PCV13-type IPD
  - Non-bacteremic pneumococcal pneumonia (NBPP) as measured by all-cause pneumonia, NBPP, and PCV13-type pneumonia
  - Mortality due to IPD and NBPP
  - Serious or systemic events associated with PCV13
Evidence Added Today--Safety

- No new safety signals or unexpected patterns observed in VAERS surveillance
- No increase in adverse events observed VSD cohort study
- Will continue to monitor and provide updates as needed
Evidence Added Today--Pneumonia

- Pneumococcal pneumonia causing a high burden of disease
  - From Jun 2014 to May 2016, PCV13-type pneumonia among ≥65 years olds decreased (31% relative reduction [95% CI: 8.3, 43.9])
    - Limited ability to observe trends in 2 years
    - Combined direct and indirect effects
  - 4–6% pneumonia in adults ≥65 years olds caused by PCV13 serotypes
  - 66% of pneumonia incidence in adults ≥65 years olds was in patients with immunocompromising conditions or HCAP

- Population characteristics and case definitions contribute to variation in pneumonia incidence

- Studies estimating all-cause and pneumococcal pneumonia incidence and vaccine impact are anticipated in October
Evidence Added Today—Evaluation of Racial Disparities in Pneumococcal Disease

- Pediatric PCV introduction has reduced racial disparities in IPD
  - IPD incidence has dramatically decreased for all racial groups driven by reduction in PCV13-type IPD, nearly eliminating the absolute difference in PCV13-type IPD incidence between people of different races
- Carriage of PCV13 serotypes in American Indian children and adults similar overall carriage in the U.S.
- Among American Indians in the southwestern US, 26% of chest x-ray confirmed pneumonia was caused by pneumococcus, but PCV13-types did not predominate
Tentative Timeline

- Data to be shared with ACIP at the upcoming meeting (October 2018)
  - PCV13 impact on all-cause pneumonia and NBPP from studies examining administrative and clinical surveillance data
  - Potential public health impact and cost-effectiveness of changing the PCV13 policy for adults ≥65 years old
- EtR with GRADE finalized by the following meeting (February 2019)
- Potential vote (February or if additional time needed June 2019)
Upcoming ACIP Meetings

- Policy question under consideration:
  - Should PCV13 be administered routinely to all immunocompetent adults aged ≥65 years in a setting of sustained PCV13 indirect effects?
- What additional evidence should be included in future presentations to ACIP and GRADE review to help the committee with decision making?
Thank you!

For more information, contact CDC
1-800-CDC-INFO (232-4636)

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.