Considerations for PCV13 Use Among Adults ≥65 Years Old and A Summary of the Evidence to Recommendations Framework

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Advisory Committee on Immunization Practices
June 2019 Meeting
Key Questions

- What **indirect effects** from pediatric PCV13 use were observed among adults aged ≥65 years before 2014?
- What **effects** from PCV13 use have we observed among adults aged ≥65 years since 2014?
- What **additional benefits** are expected from continued PCV13 use among adults aged ≥65 years given the remaining disease burden?
Population Covered by the Policy Question

Adults ≥65 years old without an immunocompromising condition are included in the current policy discussion

**Not** included in the current policy discussion:

- Adults ≥19 years old with an immunocompromising condition including:

  - Chronic renal failure
  - Nephrotic syndrome
  - Immunodeficiency
  - Iatrogenic immunosuppression
  - HIV
  - Cochlear implants
  - CSF leaks
  - Generalized malignancy
  - Hodgkin disease
  - Leukemia or Lymphoma
  - Multiple myeloma
  - Solid organ transplants
  - Congenital or acquired asplenia
  - Sickle cell disease or other hemoglobinopathies

  - Recommended to receive PCV13 in series with PPSV23 (ACIP 2012)
What indirect effects from pediatric PCV13 use were observed among adults aged ≥65 years?
Indirect Effects on IPD in Adults ≥65 Years Old

Key Points

- Nine-fold reduction in PCV13-type IPD from 2000 through 2014
- Three-fold reduction in PCV13-type IPD after PCV13 introduction for children (2010-2014)

1 Active Bacterial Core Surveillance, unpublished data
Indirect Effects on Pneumonia in Adults ≥65 Years Old

- Reductions in all-cause pneumonia in adults ≥65 years old were demonstrated after pediatric PCV7 introduction in 2000\(^1\)
- Analysis of Healthcare Cost and Utilization Project (HCUP) data between 2010-2014 demonstrated \(^2\)
  - No reductions in all-cause pneumonia
  - Decline in pneumococcal pneumonia
    - -35% (-40% to -17%) for adults 65-74 years
    - -20% (-40% to 8%) for adults ≥75 years

\(^1\)Tsaban et al. 2017
\(^2\)Lessa ACIP October 2018
What indirect effects from pediatric PCV13 use were observed among adults ≥65 years by age, race, ethnicity, and underlying chronic medical conditions?
Indirect Effects by Age

PCV13-type IPD Incidence by Age Group, 1998–2014

Key Points

- Indirect effects observed for all age groups
- Disparities by age in PCV13-type disease reduced but not eliminated

1Active Bacterial Core Surveillance, unpublished data
Indirect Effects On PCV13-type IPD Incidence Among Older Adults by Race and Ethnicity

Key Points

- Indirect effects reduced PCV13-type IPD among adults of black race, Navajos, and Alaska Natives.
- Disparities in PCV13-type IPD for Alaska Natives and Navajos vs the general population reduced but not eliminated.

1 Active Bacterial Core Surveillance, unpublished data
2 John Hopkins Center for American Indian Health, unpublished data
3 CDC, Arctic Investigations Program, unpublished data
## Indirect Effects by Underlying Medical Conditions

<table>
<thead>
<tr>
<th>Serotype group</th>
<th>Pre-PCV13 2007-2008 (95%CI)</th>
<th>Post-PCV13 2013-2014 (95%CI)</th>
<th>Percent change (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>27.0 (25,30)</td>
<td>15.4 (14, 17)</td>
<td>-43 (-50,-35)</td>
</tr>
<tr>
<td>PCV13</td>
<td>12.8</td>
<td>3.7</td>
<td>-71 (-77,-64)</td>
</tr>
<tr>
<td>CMC*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>51.6 (48,55)</td>
<td>35.4 (33,38)</td>
<td>-31 (-37,-25)</td>
</tr>
<tr>
<td>PCV13</td>
<td>21.4</td>
<td>6.8</td>
<td>-68 (-72,-63)</td>
</tr>
</tbody>
</table>

*Chronic medical conditions (CMC) include chronic heart, liver, and lung disease, diabetes, alcohol abuse, and cigarette smoking

### Key Point
- Percent reduction from indirect effects are similar among older adults with and without CMC

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1Active Bacterial Core Surveillance, unpublished data
What effects from PCV13 use have we observed among adults aged ≥65 years since 2014?

PCV13 effectiveness and safety
Summary of Evidence Supporting PCV13 Use Among Adults ≥65 Years Old in 2014

- Prevents IPD and non-bacteremic pneumonia
  - 75% reduction in vaccine type IPD
  - 45% reduction in vaccine type non-bacteremic pneumonia
- Safety demonstrated in clinical trials
- In 2014, GRADE evaluation demonstrated strong quality evidence supporting PCV13 use in series with PPSV23 for all adults ≥65 years
### PCV13 Effectiveness and Safety: GRADE Summary in 2019

<table>
<thead>
<tr>
<th>Type</th>
<th>Outcomes</th>
<th>Individual-Level Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefits</td>
<td>PCV13-type IPD</td>
<td>VE: 47–75%</td>
</tr>
<tr>
<td></td>
<td>PCV13-type non-bacteremic pneumococcal pneumonia (NIPP)</td>
<td>VE: 38–71%</td>
</tr>
<tr>
<td></td>
<td>All-cause pneumonia</td>
<td>VE: 6–11%</td>
</tr>
<tr>
<td></td>
<td>PCV13-type disease mortality</td>
<td>Limited data, but no VE demonstrated</td>
</tr>
<tr>
<td>Harms</td>
<td>Serious adverse events associated with PCV13</td>
<td>No new safety signals or unexpected patterns observed</td>
</tr>
</tbody>
</table>

**Key Points**

- Post licensure observational studies demonstrate that PCV13 is safe and effective
- GRADE analysis consistent with 2014 findings
PCV13 uptake among adults ≥65 years
What effects from PCV13 use have we observed among adults aged ≥65 years since 2014?

Population-level impact: combined direct and indirect effects
Population-Level Impact on IPD

IPD Incidence Among Adults ≥65 Years Old, 2013–2017

Key Point

- No changes in IPD incidence since 2014
  - No direct or indirect effects observed at the population level since 2014
- Non-PCV13 serotypes now make up the majority of the disease burden

1Active Bacterial Core Surveillance, unpublished data
Population-Level Impact on PCV13-type IPD Associated Deaths

PCV13-type Mortality Among Adults ≥65 Years Old, 2013-2017

Key Points

- No population-level impact on mortality associated with PCV13-type IPD since 2014
- No changes in case fatality ratio

1Active Bacterial Core Surveillance, unpublished data
### Population-Level Impact on Non-Invasive and Invasive Pneumonia

#### Non-invasive pneumococcal pneumonia

- **PCV13 introduction for adults ≥65 years old**

#### Invasive pneumococcal pneumonia incidence

- **PCV13 introduction for adults ≥65 years old**

### Key Points:

- Decline in non-invasive pneumonia observed between 2013 and 2014 (indirect effects)
- No further population-level impact on non-invasive or invasive pneumonia since 2014

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2. Active Bacterial Core Surveillance (ABCs), unpublished data
### Population-Level Impact on PCV13-type Pneumonia

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td></td>
<td>Incidence per 100,000 (95%CI)</td>
<td>Incidence per 100,000 (95%CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥65y All</td>
<td>Indirect Effects</td>
<td>Indirect and Direct Effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PCV13 coverage 11%, May 2015†</td>
<td>PCV13 coverage 36%, May 2016†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause CAP</td>
<td>2412 (2317, 2511)</td>
<td>2080 (1992, 2172)</td>
<td>332</td>
<td>13.8 (8.5, 18.7)</td>
</tr>
<tr>
<td>PCV13-type CAP</td>
<td>112 (93, 135)</td>
<td>76 (61, 96)</td>
<td>36</td>
<td>31.5 (8.3, 48.9)</td>
</tr>
<tr>
<td>% of CAP Caused by</td>
<td>4.6%</td>
<td>3.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCV13 Serotypes</td>
<td></td>
<td></td>
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</tbody>
</table>

*95% confidence interval is based on Poisson distribution.
†Uptake estimates are specific to Louisville (Jefferson County) Kentucky and were based on IQVIA administrative claims (numerator) and US Census data (denominator). CAP=community-acquired pneumonia; PCV13=13-valent pneumococcal conjugate vaccine; SSUAD=PCV13 serotype-specific urinary antigen detection assay.

**Key Points:**
- Population-level impact on PCV13-type pneumonia and all-cause pneumonia
- PCV13-type pneumonia ~4% of all-cause pneumonia

1 Swerdlow. ACIP June 2018. Pfizer, Louisville Cohort Study, unpublished data.
What additional benefits are expected from continued PCV13 use among adults ≥65 years given the remaining disease burden?
Current PCV13 Burden Among Adults ≥65 Years Old

- PCV13-type IPD incidence 5/100,000 (20% of all IPD)\(^a\)
  - Common PCV13 serotypes (% of PCV13-types): 3 (66%), 19A (13%), 7F (13%), 19F (12%)\(^a\)

- PCV13-type pneumonia incidence ~17\(^b\)–76\(^c\)/100,000 (~4% of all pneumonia)
  - Common PCV13 serotypes (% of PCV13-types): 3 (37%), 19A (28%), 6A (12%), 5 (9%), 7F (7%)\(^c\)

\(^a\)Active Bacterial Core Surveillance (ABCs), unpublished data
\(^b\)Gierke. ACIP October 2018. Surveillance for Non-Invasive Pneumococcal Pneumonia (SNiPP), unpublished data
\(^c\)Swerdlow. ACIP June 2018. Pfizer, unpublished data
## Estimated Public Health Impact: Cases Averted
Over the Lifetime of the Cohort (2.7 Million Adults 65 Years Old)

<table>
<thead>
<tr>
<th>Health Outcomes</th>
<th>CDC 2018 (PCV13 VE for ST3 IPD and ST3 pneumonia 0%)</th>
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<th>Pfizer 2018 (PCV13 VE for ST3 IPD 26% and ST3 pneumonia 45%)</th>
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<td>IPD Cases</td>
<td>-76</td>
<td>-84</td>
<td>-175</td>
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<tr>
<td>Hospitalized Pneumonia Cases</td>
<td>-2,047</td>
<td>-5,262</td>
<td>-2,826</td>
</tr>
<tr>
<td>Non-hospitalized Pneumonia Cases</td>
<td>-2,205</td>
<td>-5,611</td>
<td>-2,965</td>
</tr>
<tr>
<td>Deaths due to IPD</td>
<td>-10</td>
<td>-11</td>
<td>-25</td>
</tr>
<tr>
<td>Deaths due to Pneumonia</td>
<td>-79</td>
<td>-207</td>
<td>-199</td>
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## Estimated Public Health Impact: Cases Averted and Cost Over the Lifetime of the Cohort (2.7 Million Adults 65 Years Old)

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<td>-207</td>
<td>-199</td>
</tr>
<tr>
<td>QALYs</td>
<td>709</td>
<td>1,624</td>
<td>1,542</td>
</tr>
<tr>
<td>Life-years</td>
<td>1,101</td>
<td>2,611</td>
<td>1,865</td>
</tr>
<tr>
<td>Medical Costs</td>
<td>-$25</td>
<td>-$63</td>
<td>-$51</td>
</tr>
<tr>
<td>Vaccine Costs</td>
<td>$423</td>
<td>$423</td>
<td>$357</td>
</tr>
<tr>
<td>Total Cost</td>
<td>$398</td>
<td>$361</td>
<td>$306</td>
</tr>
<tr>
<td>Cost/QALY</td>
<td>$561,417</td>
<td>$222,132</td>
<td>$199,000</td>
</tr>
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### Annual Number Needed to Vaccinate (NNV) Among Adults ≥65 Years Old*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Incidence per 100,000</th>
<th>Vaccine Effectiveness (VE) (95%CI)</th>
<th>NNV (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCV13-type:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPD</td>
<td>5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>76&lt;sup&gt;b&lt;/sup&gt;%</td>
<td>(48, 89) 26,300 (22,500, 41,700)</td>
</tr>
<tr>
<td>Inpatient Pneumonia</td>
<td>17&lt;sup&gt;c&lt;/sup&gt;–76&lt;sup&gt;d&lt;/sup&gt;</td>
<td>43&lt;sup&gt;e&lt;/sup&gt;%</td>
<td>(12, 63) 3,000–14,000 (2,100, 50,200)</td>
</tr>
<tr>
<td>Outpatient Pneumonia</td>
<td>88&lt;sup&gt;f&lt;/sup&gt;</td>
<td>43&lt;sup&gt;e&lt;/sup&gt;%</td>
<td>(12, 63) 2,600 (1,800, 9,500)</td>
</tr>
</tbody>
</table>

*Calculation: NNV= 1/(incidence rate x VE)*

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<sup>a</sup> Active Bacterial Core Surveillance, unpublished data

<sup>b</sup> Bonten et al. CAPiTA. 2015.

<sup>c</sup> Gierke. ACIP October 2018. Surveillance for Non-Invasive Pneumococcal Pneumonia (SNiPP), unpublished data—estimated by applying the %PCV13-type IPD to the NIPP incidence estimate

<sup>d</sup> Swerdlow. ACIP June 2018. Pfizer, unpublished data

<sup>e</sup> Webber et al. CAPiTA. 2017.

<sup>f</sup> Nelson et al. 2008, estimated as 5.1% of all-cause outpatient pneumonia is PCV13-type
Additional Considerations and A Summary of the Evidence to Recommendations Framework
Values and Preferences of Older Adults Regarding PCV13 Use

- Evidence: Few studies focus on older adult perceptions of PCV13 specifically
  - Pneumonia perceived as severe (more so than influenza), sometimes fatal illness\(^1-\)\(^3\)
  - Low perceived personal susceptibility to pneumonia\(^1\)-\(^2\)
- Workgroup perspective: Potential protection against pneumonia likely outweighs the side effects of PCV13 for older adults

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\(^1\) Doshi et al. 2016
\(^2\) Brown et al. 2017 (PPSV23 only)
\(^3\) Kaljee et al. 2017
Acceptability of Continued PCV13 Use

- Limited studies assessing acceptability among stakeholders:
  - Current recommendations are confusing for providers
  - Providers recommended continuing with current recommendation
  - Keeping the current recommendations may be best programmatically if new conjugate vaccines available soon
  - Reimbursement for vaccine is still a programmatic issue

- Frequent changes in recommendations may negatively impact the perceived importance of future adult vaccine recommendations

- PCV13 provides individual-level protection for the remaining PCV13 disease burden

- PCV13 provides minimal public health benefit due to the low remaining disease burden

1 Hurley et al. 2018
2 Pfizer sponsored provider survey, unpublished, 2018
3 Association of Immunization Managers (AIM) survey, unpublished, 2018
Feasibility Considerations

- Recommendations are complex, but integrated into many health care and public health systems
- Frequent changes to recommendations could present implementation challenges
- Universal age-based recommendations are easier to effectively implement than risk-based ones
- Effective communication strategies will be needed if a policy change occurs
# Key Issues from the EtR

<table>
<thead>
<tr>
<th>Element</th>
<th>Favoring Continued PCV13 Use</th>
<th>Favoring No Longer using PCV13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burden of Disease</td>
<td>• PCV13-type disease reduced, but not eliminated through indirect effects from pediatric PCV use</td>
<td>• Indirect effects from pediatric PCV use have reduced the burden of PCV13-type disease to historic lows</td>
</tr>
<tr>
<td>Benefits</td>
<td>• PCV13 effective in preventing PCV13-type pneumococcal disease</td>
<td>• Impact from PCV13 use in older adults observed to date is minimal; no impact on IPD and inconsistent findings across studies for impact on pneumonia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Benefits from continued PCV13 use are expected to be minimal</td>
</tr>
<tr>
<td>Acceptability</td>
<td>• Frequent changes in recommendations may negatively impact the perceived importance of future adult vaccine recommendations</td>
<td>• Credibility comes from evidence-based recommendations</td>
</tr>
<tr>
<td>Resources Used</td>
<td>• A recommendation change would incur a cost to update electronic medical records, decision support tools, etc.</td>
<td>• Economic analyses results do not favor continued PCV13 use</td>
</tr>
<tr>
<td>Feasibility</td>
<td>• Universal prevention strategies are easier to implement effectively than risk-based ones</td>
<td>• Simplifies the recommendations—current recommendations have been confusing and difficult to implement</td>
</tr>
<tr>
<td></td>
<td>• Frequent changes in recommendations present implementation challenges</td>
<td></td>
</tr>
</tbody>
</table>
Proposed Policy Options

A. **Recommend PCV13**: “ACIP recommends **PCV13** for all adults 65 years or older who have not previously received PCV13. PCV13 should be given first, followed by a dose of PPSV23.”

B. **Shared clinical decision making**: “ACIP recommends **PCV13** based on shared clinical decision making for adults 65 years or older who do not have an immunocompromising condition* and who have not previously received PCV13. All adults 65 years or older should receive a dose of PPSV23.”

C. **No longer recommend PCV13**: “ACIP no longer recommends **PCV13** for adults 65 years or older who do not have an immunocompromising condition.* All adults 65 years or older should receive a dose of PPSV23.”

*Immunocompromising conditions defined as chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, HIV, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, cochlear implants, CSF leaks, congenital or acquired asplenia, sickle cell disease, or other hemoglobinopathies.
Guidance for PCV13 and PPSV23 Use Based on the Proposed Policy Options

- **A. Recommend PCV13**
  - Current guidance for PCV13 in series with PPSV23 would be unchanged

- **B. PCV13 recommended based on shared clinical decision making**
  - Guidance will be updated to reflect options for PCV13 and PPSV23 in series and PPSV23 alone

- **C. No longer recommend PCV13**
  - Pre-2014 policy guidance would apply, i.e. PPSV23 alone
Discussion

Proposed Policy Options

A. **Recommend PCV13**: “ACIP recommends PCV13 for all adults 65 years or older who have not previously received PCV13. PCV13 should be given first, followed by a dose of PPSV23.”

B. **Shared clinical decision making**: “ACIP recommends PCV13 based on shared clinical decision making for adults 65 years or older who do not have an immunocompromising condition and who have not previously received PCV13. All adults 65 years or older should receive a dose of PPSV23.”

C. **No longer recommend PCV13**: “ACIP no longer recommends PCV13 for adults 65 years or older who do not have an immunocompromising condition. All adults 65 years or older should receive a dose of PPSV23.”
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.