ACIP Recommendations for Pneumococcal 13-valent Conjugate and 23-valent Polysaccharide Vaccine Use among Adults
ACIP Recommendations through 2012: Pneumococcal Polysaccharide Vaccine (PPSV23)

- All adults 65 yrs and older
- Adults 19-64 years old with the following conditions

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Underlying medical condition or other indication</th>
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<tbody>
<tr>
<td>Immunocompetent persons</td>
<td>Chronic heart disease (excluding hypertension)*</td>
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<tr>
<td></td>
<td>Chronic lung disease†</td>
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<td></td>
<td>Diabetes mellitus</td>
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<td>Cerebrospinal fluid leaks</td>
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<td>Cochlear implant</td>
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<td>Alcoholism</td>
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<td>Chronic liver disease, including cirrhosis</td>
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<td>Cigarette smoking</td>
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<td>Persons with functional or anatomic asplenia§</td>
<td>Sickle cell disease and other hemoglobinopathies</td>
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<tr>
<td>Immunocompromised persons§</td>
<td>Congenital or acquired asplenia, splenic dysfunction, or splenectomy</td>
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<td></td>
<td>Congenital or acquired immunodeficiencies†</td>
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<td>HIV infection</td>
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<td>Chronic renal failure</td>
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<td>Nephrotic syndrome</td>
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<td>Leukemias</td>
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<td>Lymphomas</td>
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<td>Generalized malignancy</td>
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<td>Diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids or radiation therapy</td>
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<td>Solid organ transplantation</td>
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<td>Multiple myeloma</td>
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</tbody>
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* Including congestive heart failure and cardiomyopathies.
† Including chronic obstructive pulmonary disease, emphysema, and asthma.
§ A second dose of PPSV23 is recommended 5 years after the first dose for persons with functional or anatomic asplenia and for immunocompromised persons.
§§ Includes B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease).
13-valent Pneumococcal Conjugate Vaccine (PCV13) for Adults

- Licensed for use among adults ≥50 years old on 12/30/11
- FDA approved under the Accelerated Approval Pathway
- Based on non-inferior immunogenicity compared to PPSV23

Indications
- Prevention of pneumococcal disease (including pneumonia and invasive disease) in adults 50 years of age and older
- Prevention of disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F

Post-approval condition of licensure: Randomized controlled trial of PCV13 against pneumococcal pneumonia among adults ≥65 years old in the Netherlands (CAPiTA)
ACIP Recommendations in 2012

- Deferred recommendation for adults ≥65 years old until more data available
  - Efficacy against pneumonia (CAPiTA)
  - Indirect (herd) effects of PCV13 use in children
- Recommended a dose of PCV13 in sequence with PPSV23 for adults with immunocompromising conditions (highest risk for pneumococcal disease)
## ACIP 2014: New Evidence Supporting PCV13 use among adults, CAPiTA results

<table>
<thead>
<tr>
<th>Study/population</th>
<th>Endpoint</th>
<th>Vaccine Efficacy (95% CI)</th>
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<tbody>
<tr>
<td>CAPITA ~85,000 Adults 65+ Netherlands</td>
<td>PCV13-serotype IPD</td>
<td>75% (41%, 91%)</td>
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<tr>
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<td>PCV13-serotype non-bacteremic pneumonia</td>
<td>45% (14%, 65%)</td>
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</tbody>
</table>

CAPITA, ACIP June 2014
Summary of evidence supporting PCV13 use among adults ≥65 years of age

- Prevents IPD and non-bacteremic pneumonia\(^1\)
  - 75% reduction in vaccine type IPD
  - 45% reduction in vaccine type non-bacteremic pneumonia

- Immune response non-inferior or improved (for some serotypes) for PCV13 (or PCV7) vs. PPSV23\(^2,3\)

- Safety demonstrated in clinical trials

\(^1\)CAPITA, June 2014 ACIP
\(^2\)Phase III trials, Pfizer, ACIP 2011, 2012
\(^3\)DeRoux et al. CID 2008, Goldblatt et al 2009
Summary of evidence supporting PCV13 use among adults ≥65 years of age

- Vaccine preventable disease burden remaining among adults ≥65 years
  - Estimated 2,600 PCV13 type IPD cases in 2013\(^1\)
  - Over 50,000 PCV13-type inpatient CAP\(^2\)

- In the short-term, PCV13 likely provides adequate coverage of disease causing serotypes
  - 20-25% IPD due to PCV13 types\(^1\)
  - ~10% of all CAP due to PCV13 types\(^2\)

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\(^1\)Active Bacterial Core Surveillance, 2013

\(^2\)Estimate based on studies using serotype-specific urine antigen test, Pfizer.

CAP – Community acquired pneumonia
PCV13 NOW RECOMMENDED FOR ALL ADULTS ≥65 YEARS IN SERIES WITH PPSV23
Adults ≥65 years of age with no previous pneumococcal vaccine (PCV13 or PPSV23) or unknown vaccination history

Adults 65 years of age or older who have not previously received pneumococcal vaccine or whose previous vaccination history is unknown should receive a dose of PCV13 first, followed by a dose of PPSV23
Adults $\geq 65$ years of age with no previous pneumococcal vaccine (PCV13 or PPSV23) or unknown vaccination history

Guidance on intervals for sequential use

- A dose of PPSV23 should be given 6 to 12 months following a dose of PCV13
- If PPSV23 cannot be given during this time window, a dose of PPSV23 should be given during the next visit
- Minimum interval = 8 weeks
Adults ≥65 years of age with no previous pneumococcal vaccine (PCV13 or PPSV23) or unknown vaccination history

PCV13 (@ ≥ 65 years) + PPSV23

6-12 months*

*Minimum interval between sequential administration of PCV13 and PPSV23 is 8 weeks
**PCV13-naïve adults ≥65 years of age previously vaccinated with PPSV23**

Adults 65 years of age or older who have not previously received PCV13 and who have previously received one or more doses of PPSV23 should receive a dose of PCV13.

**Guidance on intervals for sequential use:**
A dose of PCV13 should be given at least 1 year after the receipt of the most recent PPSV23 dose. For those for whom an additional dose of PPSV23 is indicated, such dose should be given 6 to 12 months after PCV13 and at least 5 years since the most recent dose of PPSV23.
PCV13-naïve adults ≥65 years of age previously vaccinated with PPSV23

PPSV23* (+ @ ≥ 65 years) + PCV13

≥1 years

≥5 years

PPSV23* (+ @ < 65 years) + PCV13 (+ @ ≥ 65 years) + PPSV23 (+ @ ≥ 65 years)

≥1 years

6-12 months

* Doses already received
Categories of adults $\geq 65$ years old

Received PCV13 previously?

Yes

No additional PCV13 doses needed

No or Unknown

Received one or more doses of PPSV23 previously?

Yes

Received at age $\geq 65$ years?

Yes

PCV13 at least one year later

No

PCV13 (at age $\geq 65$ years and $\geq 1$ year post PPSV23) followed by PPSV23 6-12 months later and $\geq 5$ years after previous PPSV23

No or Unknown

PCV13 (at age $\geq 65$ years) followed by PPSV23 6-12 months later
Potential time-limited utility of routine PCV13 use among adults $\geq 65$ years

The recommendations for routine PCV13 use among adults $\geq 65$ years old should be re-evaluated in 2018 and revised as needed.
Potential time-limited utility of routine PCV13 use among adults ≥65 years

- Monitoring of the implementation and impact of the new recommendation in the target population of adults ≥65 years old
- Continued monitoring of disease trends among PCV13-naïve adults is needed to evaluate the impact of herd effects and the long-term utility of routine PCV13 use among adults
- ACIP should be routinely updated on the changes in vaccine-preventable disease burden among adults due to PCV13 direct and indirect effects during the next 3 years
- These data should inform revisions as needed to the proposed adult PCV13 recommendations in 2018
Medicare Coverage

- Medicare covers pneumococcal vaccination under Part B:
  - generally once in a lifetime for all Medicare beneficiaries
  - additional vaccinations in certain instances based on risk or uncertainty of beneficiary pneumococcal vaccination status
  - a second dose for the highest risk (specifically defined) persons when given at least 5 years after the first dose

- ACIP now recommends a two dose regimen (PCV13-PPSV23):
  - CMS will review the new recommendation and the supporting evidence
  - if a change in Medicare coverage is supported, CMS will determine the best mechanism to change the current policy
  - timeframe will depend on the process required to implement a change in coverage if appropriate.
Medicare Coverage

- **Given current Medicare coverage of pneumococcal vaccines:**
  - Beneficiary presenting for the first dose would be covered for a dose of PCV13 (the first in a 2-dose series recommended for vaccine naïve adults)
  - Beneficiary with unknown vaccination status would have coverage for a dose of PCV13
  - Beneficiaries with a known status of previous pneumococcal vaccination would NOT be covered for a second pneumococcal dose until new CMS regulations could be put into effect
Advisory Committee on Immunization Practices

Recommendations for PCV13 and PPSV23 use among adults ≥19 years with immunocompromising conditions

ACIP 2012
Recommendation for PCV13 and PPSV23 among adults with immunocompromising conditions

- **Vaccine naïve adults:**
  - PCV13 dose is recommended to be given before PPSV23, whenever possible
  - PPSV23 should be given at least 8 weeks after a dose of PCV13
  - Recommendations for 2nd dose of PPSV and a dose at age 65 years or older remain unchanged

- **PPSV23-immunized adults**
  - A dose of PCV13 is recommended to be given to adults with immunocompromising conditions who received 1 or more doses of PPSV23 1 or more years after the last PPSV23 dose
  - Total number and interval between PPSV23 doses unchanged from current PPSV23 recommendations
### Indications for PCV13 and PPSV23 for adults ≥19 years

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Underlying medical condition</th>
<th>PCV13 Recommended</th>
<th>PPSV23 Recommended</th>
<th>Revaccination 5 yrs after first dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunocompetent persons</td>
<td>Chronic heart disease†</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td></td>
<td>Chronic lung disease§</td>
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<td>Diabetes mellitus</td>
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<td>Cerebrospinal fluid leak</td>
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<td>Alcoholism</td>
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<td>Chronic liver disease, cirrhosis</td>
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<td>Cigarette smoking</td>
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<td>Persons with functional or anatomic asplenia</td>
<td>Sickle cell disease/other hemoglobinopathy</td>
<td>✓</td>
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<tr>
<td>Immunocompromised persons</td>
<td>Congenital or acquired immunodeficiency§</td>
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<td>Human immunodeficiency virus infection</td>
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<td>Iatrogenic immunosuppression**</td>
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<td>Solid organ transplant</td>
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* All adults aged ≥65 years should receive a dose of PPSV23, regardless of previous history of vaccination with pneumococcal vaccine.
† Including congestive heart failure and cardiomyopathies, excluding hypertension.
§ Including chronic obstructive pulmonary disease, emphysema, and asthma.
¶ Includes B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease).
** Diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy.
Prevention of pneumococcal disease among adults with immunocompromising conditions

Recommendation for PPSV23-naïve adults

Adults 19 years of age or older with immunocompromising conditions, functional or anatomic asplenia, CSF leaks, or cochlear implants, and who have not previously received PCV13 or PPSV23 should receive a dose of PCV13 first followed by currently recommended doses of PPSV23

(PCV13) + (PPSV23) + (PPSV23*) + (PPSV23 (@ ≥65 years))

>8 weeks

>5 years

*Second PPSV dose before age 65 years NOT recommended for adults with CSF leaks or those with cochlear implants
Prevention of pneumococcal disease among adults with immunocompromising conditions

Integrating PCV13 recommendation for adults previously vaccinated with PPSV23 (red indicates previously received doses)

1) PPSV23 + PCV13 + PPSV23* + PPSV23 (@ ≥65 years)
   - ≥5 years
   - >8 weeks
   - ≥1 year

2) PPSV23 + PPSV23* + PCV13 + PPSV23 (@ ≥65 years)
   - ≥5 years
   - ≥1 year

3) PPSV23 + PPSV23* + PPSV23 (@ ≥65 years) + PCV13
   - ≥5 years
   - ≥1 year

*Second PPSV dose @<65 years NOT recommended for adults with CSF leaks or cochlear implants
Conclusions

• PCV13 is effective against invasive disease and pneumonia among adults $\geq 65$ years.
• Combined regimen of PCV13 followed by PPSV23 provides optimal coverage of disease causing serotypes.
• PCV13 is now recommended in series with PPSV23 for all adults $\geq 65$ years and adults $<65$ with immunocompromising conditions, CSF leaks, and cochlear implants.
• PPSV23 only is recommended for adults $<65$ with chronic conditions (e.g. heart disease, diabetes)