Considerations for Pneumococcal 13-valent Conjugate and 23-valent Polysaccharide Vaccine Use among Adults

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Advisory Committee on Immunization Practices
Additional Meeting on Use of Pneumococcal Vaccines in Adults
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Outline

- Summary of evidence supporting routine PCV13 use among adults ≥65 years of age and GRADE conclusions
- Expected public health impact and cost-effectiveness
- Sequential use of PCV13 and PPSV23: intervals and rationale
- Indirect effects and long-term utility of routine PCV13 use among adults
- Proposed language

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
- GRADE evaluation demonstrated strong quality evidence (type 2)

[1]CAPITA, June 2014 ACIP

[2]Phase III trials, Pfizer, ACIP 2011, 2012

[2]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]

[1]Active Bacterial Core Surveillance, 2013

[2] Estimate based on studies using serotype-specific urine antigen test, Pfizer

Expected public health impact and cost-effectiveness

- **Various strategies considered and evaluated for expected public health impact and cost-effectiveness**
  - Vaccination at ages 50, 60, and 65 years
  - PCV13 instead of PPSV23
  - PCV13 in sequence with PPSV23

- **Adding PCV13 at age 65 years to existing PPSV23 recommendations likely the optimal strategy**
  - Health benefits for all outcomes
  - Cost-effectiveness comparable to other adult interventions accepted as cost-effective (base case)

Expected public health impact of adding PCV13 at age 65 years to existing PPSV23 recommendations (base case)

Health Outcomes	Change in outcome compared to existing PPSV23 recommendation
IPD	-226
Inpatient NBP	-4,961
Outpatient NBP	-7,252
Deaths (IPD)	-33
Deaths (NBP)	-332
QALYs	3,053
Life-years	4,627

Stoecker, ACIP June 2014

Cost-effectiveness of adding PCV13 at age 65 years to existing PPSV23 recommendations (base case)

Outcomes	Change in outcome compared to existing PPSV23 recommendation
Total Cost (Millions)	$189
Medical (Millions)	-$132
Vaccine total cost (Millions)	$321
Cost/QALY gained	$62,065
Cost/Life-year gained	$40,949

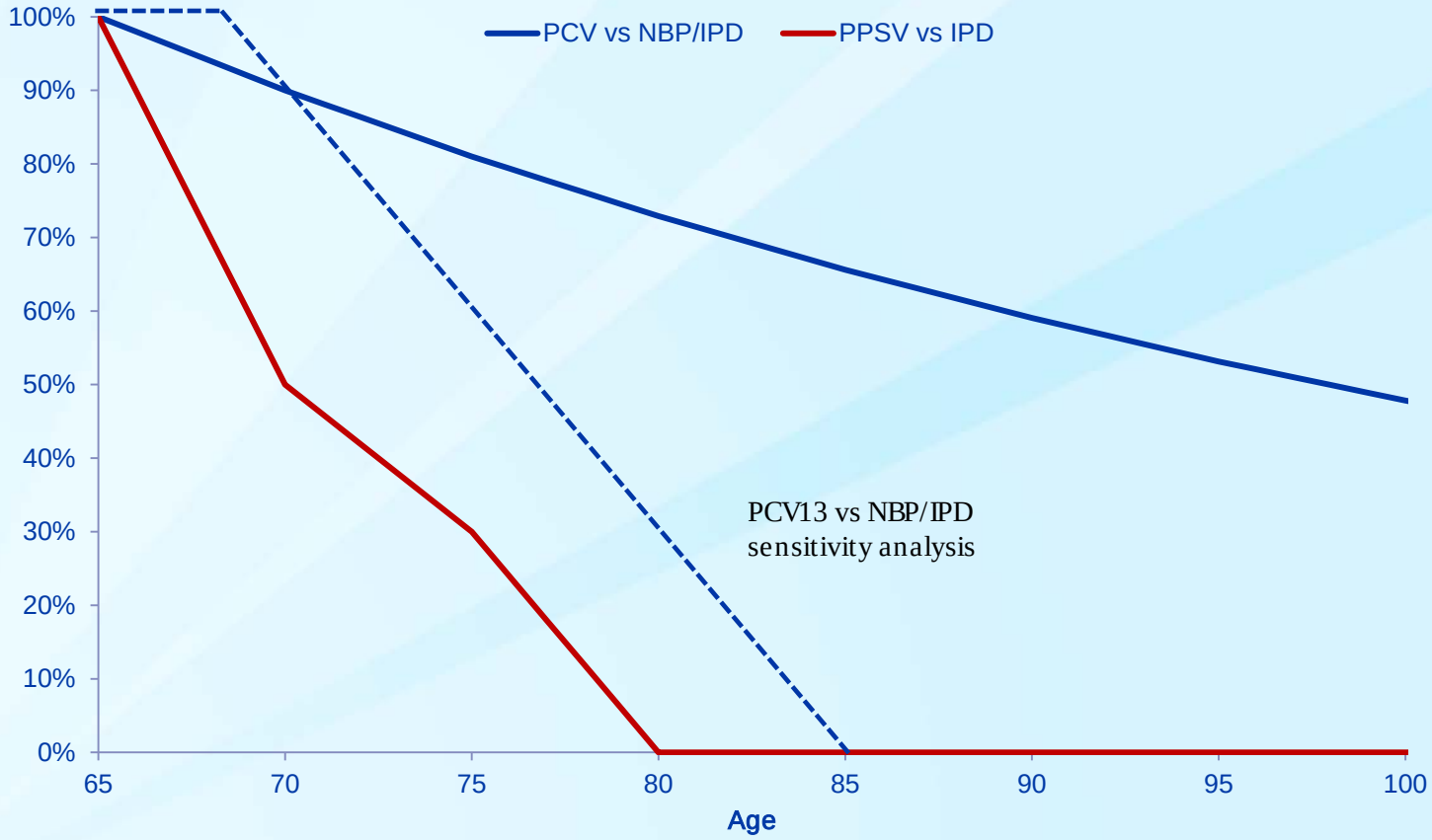
Stoecker, ACIP June 2014

Suggestions for sensitivity analysis

- Shorter duration of protection for PCV13 against IPD and non-bacteremic pneumonia
- PPSV23 efficacy against non-bacteremic pneumonia
- CMS price for vaccine doses

Sensitivity analysis: waning of PCV13 protection

- PCV13 waning of protection against IPD and NBP:
  - No change during 5 years post-vaccination (CAPiTA)
  - Linear decline to 0% efficacy over 20 years



Sensitivity analysis: waning of PCV13 protection

Strategy: Adding PCV13 to the current schedule at age 65 vs. current strategy	June 2014 (base case)	PCV13 waning to VE 0% over 20 years
Change in Health Outcomes		
IPD	-226	-173
Hospitalized non-bacteremic pneumonia	-4,961	-4,687
Non-hospitalized non-bacteremic pneumonia	-7,252	-6,850
Deaths due to IPD	-33	-25
Deaths due to non-bacteremic pneumonia	-332	-314
Discounted QALYs	3,053	3,014
Discounted Life-years	4,627	4,526
Total Cost (Millions)	$189	$198
Medical	-$132	-$123
Vaccine total cost	$321	$321
Cost Ratios		
Cost/QALY gained	62,065	65,681
Cost/Life-year gained	40,949	43,736

Sensitivity analysis: PPSV23 VE vs. NBP

- **PPSV23 VE against non-bacteremic pneumonia**
  - Efficacy of 73% in meta-analysis based on studies using previous formulation of PPSV[1]; the only PPSV23 study showed no effect[2]
  - No efficacy in another meta-analysis[3]
  - Recent studies reported VE 64% in RCT among long-term care residents[4] and VE 48% in a large cohort study[5]
    - Limited generalizability
    - Methodological concerns (e.g. % bacteremic, analytic methods)
- **Evaluated 45% VE for PPSV23 vs NBP in sensitivity analysis**

[1]Moberly et al 2008 [2]Ortquist et al [3]Huss et al 2009 [4]Muruyama et al 2010 [5]Ochoa-Gondar et al 2014

Sensitivity analysis: PPSV23 VE vs. NBP

Strategy: Adding PCV13 to the current schedule at age 65 vs. current strategy	June 2014 (base case)	PPSV23 VE against NBP = 45%
Change in Health Outcomes		
IPD	-226	-226
Hospitalized non-bacteremic pneumonia	-4,961	-1,547
Non-hospitalized non-bacteremic pneumonia	-7,252	-2,261
Deaths due to IPD	-33	-33
Deaths due to non-bacteremic pneumonia	-332	-104
Discounted QALYs	3,053	892
Discounted Life-years	4,627	1,449
Total Cost (Millions)	$189	$276
Medical	-$132	-$46
Vaccine total cost	$321	$321
Cost Ratios		
Cost/QALY gained	62,065	309,211
Cost/Life-year gained	40,949	190,286

Sensitivity analysis: vaccine costs

- CMS prices instead of CDC contract price

Vaccine	CDC Cost/ Dose	CMS price (95%AWP)**
PPSV23	$44.50	$78.00
PCV13	$89.75	$154.00

- Analysis done from societal perspective
- Costs intended to reflect value of resources used to produce intervention
  - CMS figure represents reimbursements, not likely resource value
- Applied CMS price in sensitivity analysis only

	CDC Cost/ Dose (base case)	CMS price (95%AWP)** (sensitivity analysis)
Cost/QALY	62,065	110,284
Cost/Life-year saved	40,949	72,763

*PRIVATE SECTOR PRICES ARE THOSE REPORTED BY VACCINE MANUFACTURERS ANNUALLY TO CDC

**95% OF AVERAGE WHOLESALE PRICE

Summary of evidence: Sequence and intervals for PCV13 and PPSV23 use

- Immune response improved when PCV13 given as the first dose [1,2]
- No studies designed to evaluate the length for an optimal interval between PCV13 and PPSV23
- Intervals of 2, 6, or 12 months, and 3-4 years[1,2,3,4]
  - Improved immune response compared to baseline for all
  - Non-inferior response post-PCV/PPSV23 vs. post-PCV alone
  - Comparisons across studies difficult to make
- One study with direct comparison of intervals[4]
  - Immune response equivalent between 2 months vs. 6 months
  - Increased reactogenicity with a 2 month interval

[1]Phase III studies (004, 3005, 3010), February 2011 ACIP
[2]DeRoux et al. CID 2008
[3]Goldblatt et al. CID 2009
[4]Myernik et al. CID 2008

Considerations for selection of intervals

- Immune response and safety
- Risk window for PPSV23-only serotypes
- Practical aspects (timing for the next visit)
- Programmatic (quality measures, immunization systems)

WG Conclusions: Sequence and intervals for PCV13 and PPSV23 use

- PCV13 should be given first when possible
- Interval between PCV13 followed by PPSV23:

  6-12 months
- Interval for PCV13 when given post-PPSV23:

  ≥1 year
- Include flexibility in the guidance if doses cannot be administered within the recommended window:

  If a second dose cannot be given during this time window, a dose can be given later during the next visit

Indirect Effects and Long-term Utility of PCV13

- Indirect effects of PCV7 introduction on PCV7-type IPD and pneumonia among adults of all age groups
- Indirect effects of PCV13 program have further reduced the proportion of adult IPD caused by PCV13 types and pneumonia disease burden
  - Additional reductions likely in the next 3-5 years (if similar to post-PCV7 experience)
  - The largest impact may have already been observed due to rapid PCV13 uptake

Key point: The expected benefits of PCV13 use among adults will likely decline over time

Estimating cases potentially preventable annually among adults 65 years or older

Outcome (PCV13 type)	2015 • **20%** reduction due to herd effects* • PCV13 direct effects** • Coverage **10% (5%-30%)**	2019 • **86%** reduction due to herd effects* • PCV13 direct effects** • Coverage **30% (20%-60%)**
IPD	160 (80-480)	80 (50-170)
Inpatient CAP	2,030 (1,020-6,090)	1,070 (700 -2,130)
Outpatient CAP	2,970 (1,480-8,900)	1,560 (1,040 – 3,120)
Total CAP	5,000 (2,500-14,990)	2,630 (1,740 – 5,250)

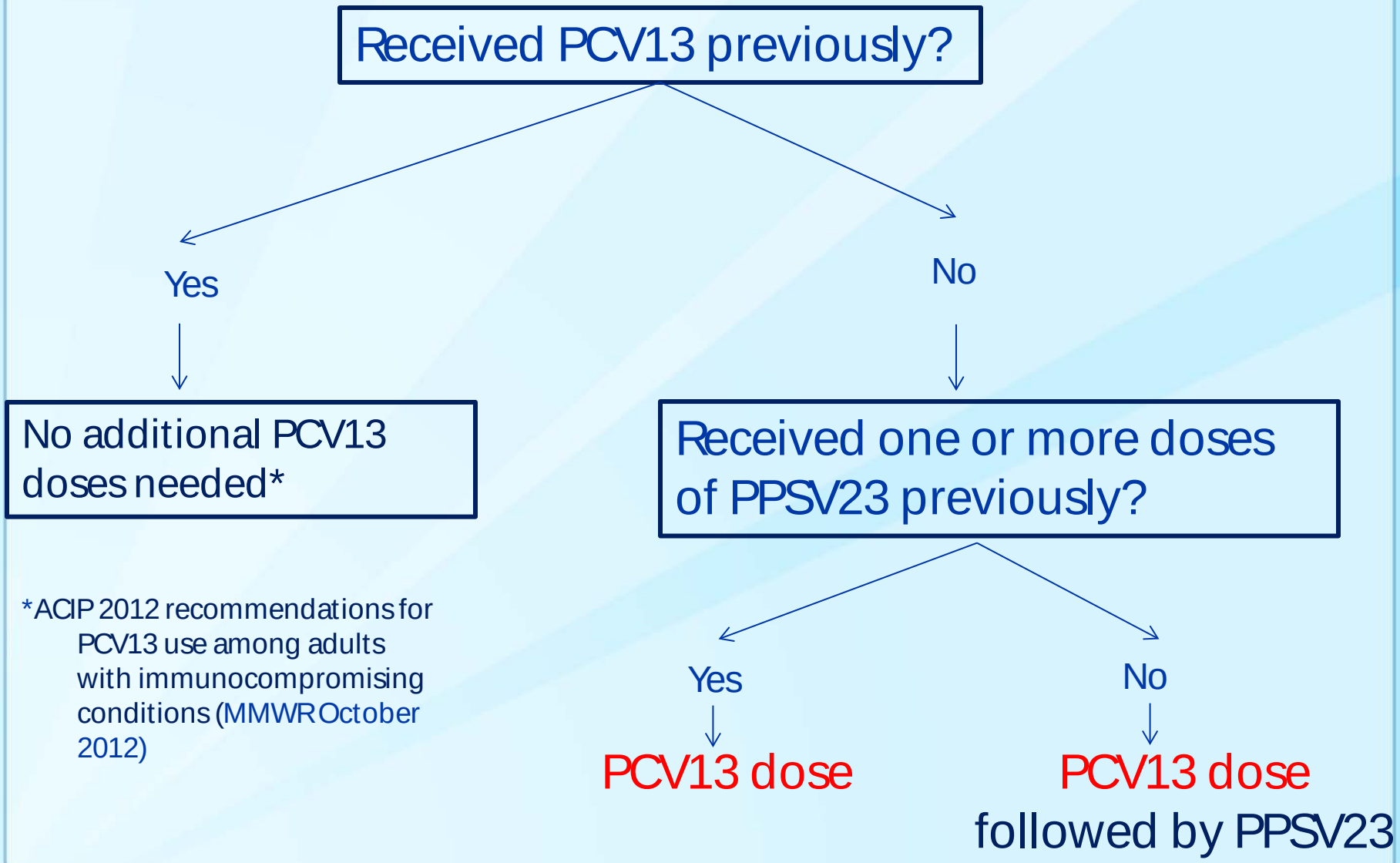
*Based on post-PCV7 reductions observed between 2003 and 2009
**Assume PCV13 VE = 75% (IPD) and 45% (CAP)

PCV13 for adults ≥65 years of age: Work Group Conclusions

- In the short-term, a recommendation for universal PCV13 use is warranted
- In the long-term, continued herd effects may limit the utility of a universal recommendation
  - The magnitude of indirect effects unknown
  - Uncertainty around the burden of vaccine preventable non-bacteremic pneumonia
- Opportunity to prevent disease during the 2014-2015 respiratory season

ACIP WG Proposal for Pneumococcal Vaccine Use among Adults

Categories of adults ≥65 years old to consider



*ACIP 2012 recommendations for PCV13 use among adults with immunocompromising conditions (MMWR October 2012)

Adults ≥65 years of age with no previous pneumococcal vaccine (PCV13 or PPSV23)

Proposed language:

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 ≥65 years of age with no previous pneumococcal vaccine (PCV13 or PPSV23)

Proposed guidance on intervals for sequential use:

A dose of PPSV23 should be given 6 to 12 months following a dose of PCV13. If PPSV23 can not be given during this time window, a dose of PPSV23 should be given during the next visit. The two vaccines should not be co-administered.

PCV13 (@65 years or later) + PPSV23

6-12 months

PCV13-naïve adults ≥65 years of age previously vaccinated with PPSV23

Proposed language:

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.

PCV13-naïve adults ≥65 years of age previously vaccinated with PPSV23

Proposed 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

1) PPSV23 + PCV13

(@65 years or later)

≥1 years

≥5 years

2) PPSV23 + PCV13 + PPSV23

(< 65 years old) (@65 years or later) (@65 years or later)

≥1 years

6-12 months

Potential time-limited utility of routine PCV13 use among adults ≥65 years

Proposed language:

The recommendations for routine PCV13 use among adults ≥65 years old* should be re-evaluated in 2018 and revised as needed

*if approved by ACIP and CDC Director

Potential time-limited utility of routine PCV13 use among adults ≥65 years

- **Monitoring of the impact of the new recommendation in the target population of adults ≥65 years old**
  - Vaccine uptake of PCV13 and PPSV23
  - PCV13-type IPD burden and serotype distribution for IPD cases
  - PCV13-type and all CAP burden
- **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**
  - PCV13-type IPD burden and serotype distribution for IPD cases among unvaccinated
  - Changes in PCV13-type CAP burden among individuals younger than 65 years

*if approved by ACIP and CDC Director

Potential time-limited utility of routine PCV13 use among adults ≥65 years

- **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**
  - Declining burden of PCV13-type disease among adults <65 years old due to indirect effect of vaccinating children may signal that PCV13 is no longer needed
  - Revised cost effectiveness evaluation incorporating changes in disease burden, uptake, and the cost of the vaccines will help align this recommendation with other adult vaccines in use

ACIP vote

Adults ≥65 years of age with no previous pneumococcal vaccine (PCV13 or PPSV23)

Proposed language:

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

PCV13-naïve adults ≥65 years of age previously vaccinated with PPSV23

Proposed language:

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.

Potential time-limited utility of routine PCV13 use among adults ≥65 years

Proposed language:

The recommendations for routine PCV13 use among adults ≥65 years old* should be re-evaluated in 2018 and revised as needed

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