



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

Almea Matanock, MD, MS

Advisory Committee on Immunization Practices

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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

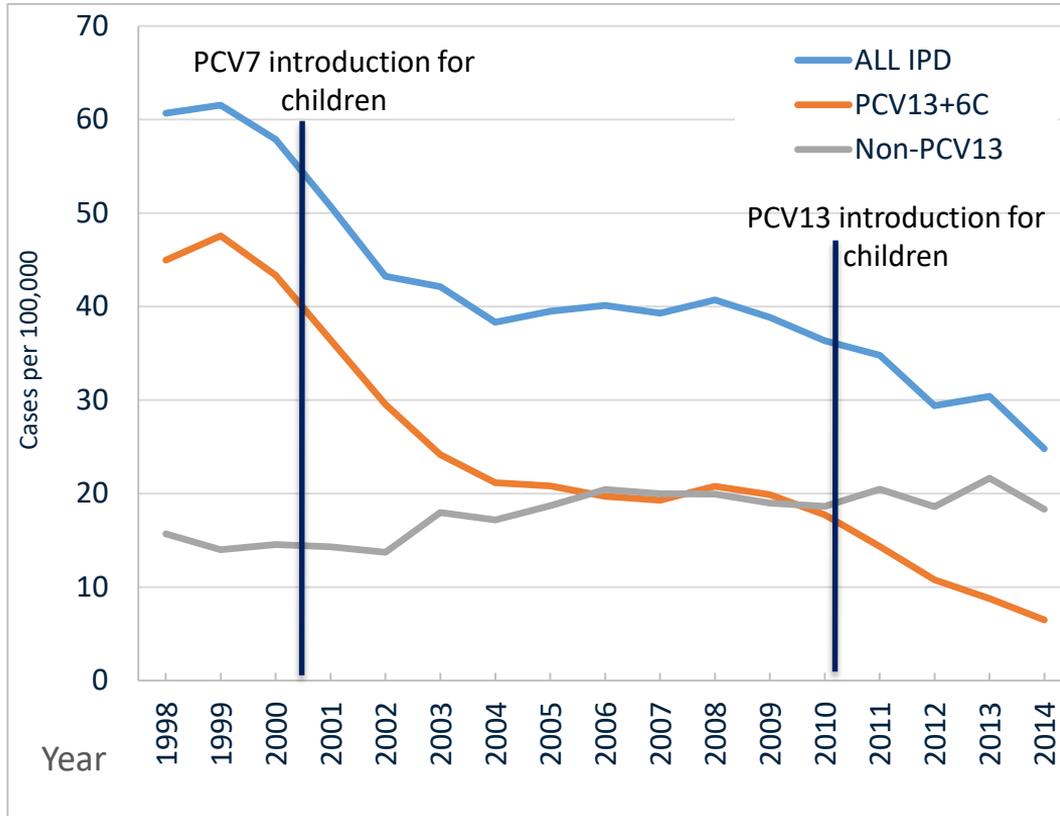
Not included in the current policy discussion:

- 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

IPD Incidence Among Adults ≥ 65 Years Old, 1998–2014¹



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)

¹Active Bacterial Core Surveillance, unpublished data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 2000¹
- Analysis of Healthcare Cost and Utilization Project (HCUP) data between 2010-2014 demonstrated²
 - 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

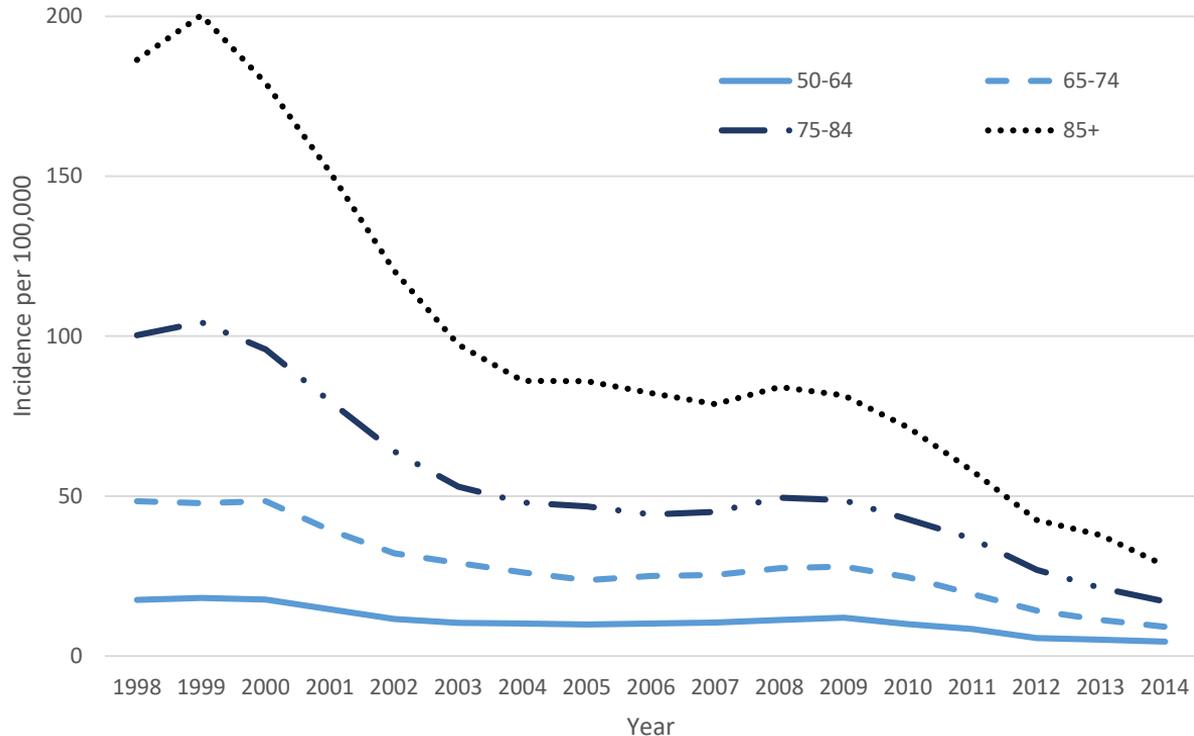
¹Tsaban et al. 2017

²Lessa 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, 1998–2014¹

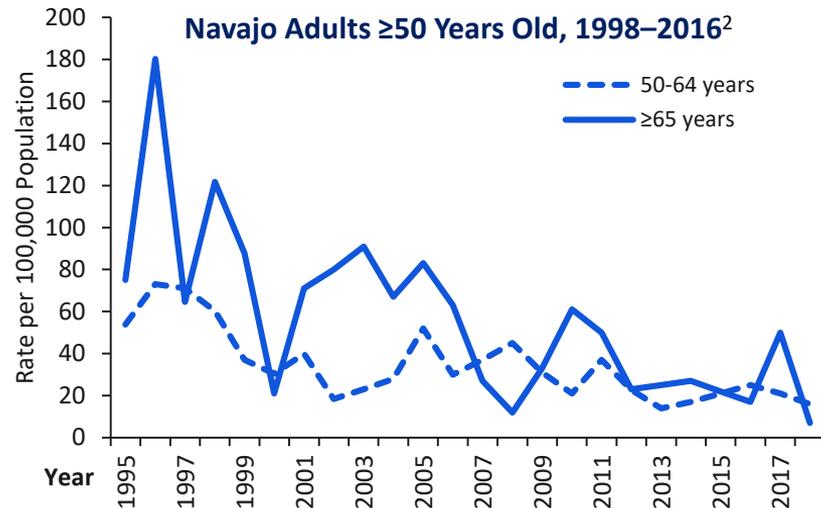
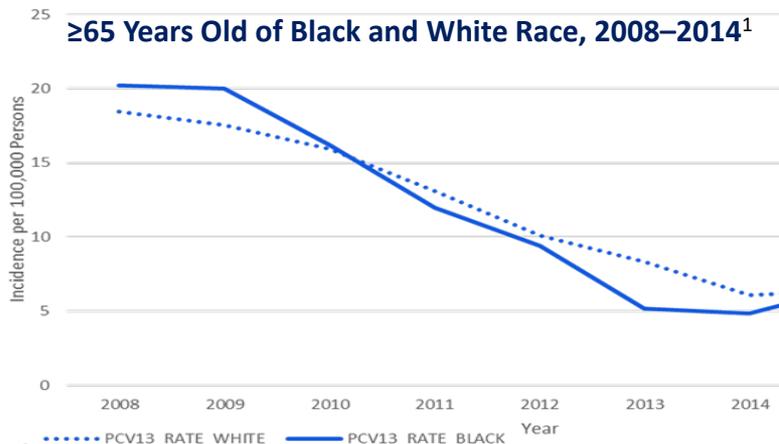


Key Points

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

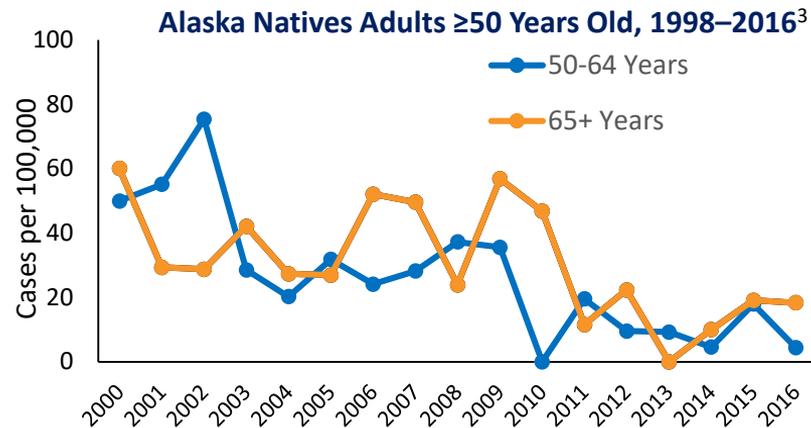
¹Active Bacterial Core Surveillance, unpublished data

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 race¹, Navajos², and Alaska Natives³
- 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

IPD Incidence per 100,000 Adults ≥65 Years Old¹

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

*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

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

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

Key Points

- Post licensure observational studies demonstrate that PCV13 is safe and effective
- GRADE analysis consistent with 2014 findings

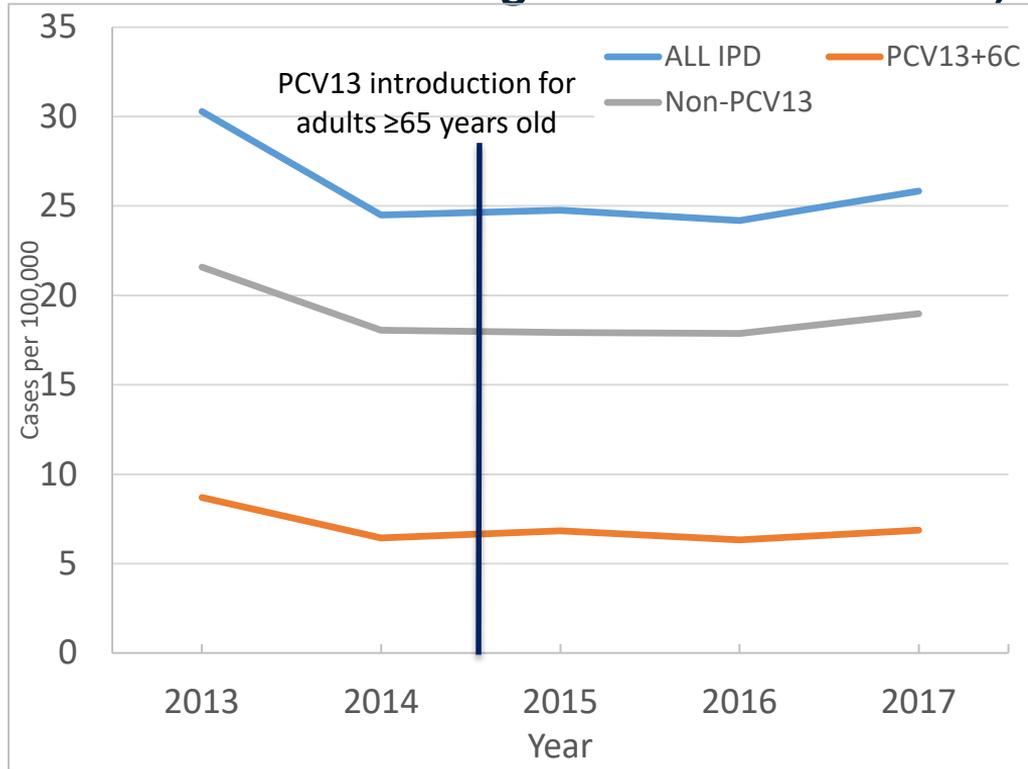
PCV13 uptake among adults ≥ 65 years

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, 2013–2017¹



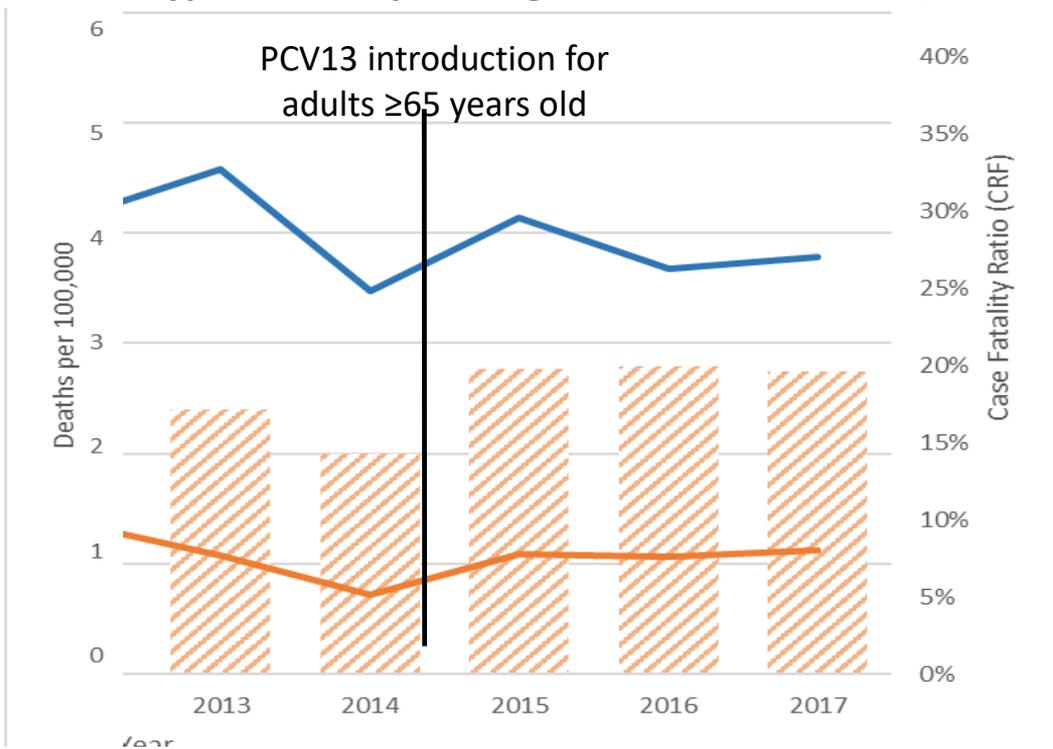
Key Point

- 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, 2013-2017¹



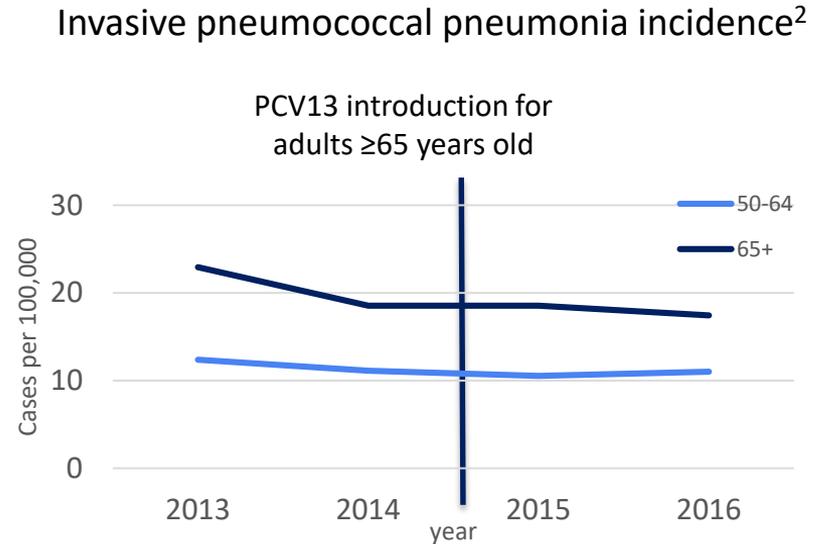
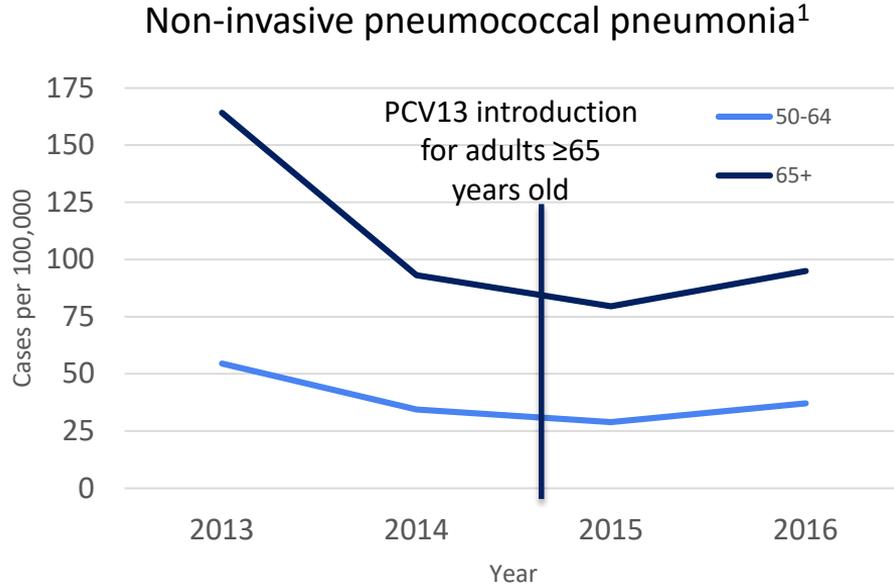
Key Points

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

PCV13 CFR % All IPD Mortality Incidence PCV13 Mortality Incidence

¹Active Bacterial Core Surveillance, unpublished data

Population-Level Impact on Non-Invasive and Invasive Pneumonia



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

¹Gierke. ACIP October 2018. Surveillance for Non-Invasive Pneumococcal Pneumonia (SNIpp), unpublished data

²Active Bacterial Core Surveillance (ABCs), unpublished data

Population-Level Impact on PCV13-type Pneumonia¹

	Jun 2014 – May 2015 Incidence per 100,000 (95%CI ^x)	Jun 2015 – May 2016 Incidence per 100,000 (95%CI ^x)	Absolute Difference	% Relative Reduction
≥65y All	Indirect Effects PCV13 coverage 11%, May 2015 [†]	Indirect and Direct Effects PCV13 coverage 36%, May 2016 [†]		
All-cause CAP	2412 (2317, 2511)	2080 (1992, 2172)	332	13.8 (8.5, 18.7)
PCV13-type CAP	112 (93, 135)	76 (61, 96)	36	31.5 (8.3, 48.9)
% of CAP Caused by PCV13 Serotypes	4.6%	3.7%		

^x95% 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 $\sim 17^b$ – 76^c /100,000 ($\sim 4\%$ of all pneumonia)
 - Common PCV13 serotypes (% of PCV13-types): 3 (37%), 19A (28%), 6A (12%), 5 (9%), 7F (7%)^c

^aActive Bacterial Core Surveillance (ABCs), unpublished data

^bGierke. ACIP October 2018. Surveillance for Non-Invasive Pneumococcal Pneumonia (SNIIPP), unpublished data

^cSwerdlow. 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)

Health Outcomes

	CDC 2018 (PCV13 VE for ST3 IPD and ST3 pneumonia 0%)	CDC 2018 (PCV13 VE for ST3 IPD 26% and ST3 pneumonia 45%)	Pfizer 2018 (PCV13 VE for ST3 IPD 26% and ST3 pneumonia 45%)
IPD Cases	-76	-84	-175
Hospitalized Pneumonia Cases	-2,047	-5,262	-2,826
Non-hospitalized Pneumonia Cases	-2,205	-5,611	-2,965
Deaths due to IPD	-10	-11	-25
Deaths due to Pneumonia	-79	-207	-199

Estimated Public Health Impact: Cases Averted and Cost Over the Lifetime of the Cohort (2.7 Million Adults 65 Years Old)

		CDC 2018 (PCV13 VE for ST3 IPD and ST3 pneumonia 0%)	CDC 2018 (PCV13 VE for ST3 IPD 26% and ST3 pneumonia 45%)	Pfizer 2018 (PCV13 VE for ST3 IPD 26% and ST3 pneumonia 45%)
Health Outcomes	IPD Cases	-76	-84	-175
	Hospitalized Pneumonia Cases	-2,047	-5,262	-2,826
	Non-hospitalized Pneumonia Cases	-2,205	-5,611	-2,965
	Deaths due to IPD	-10	-11	-25
	Deaths due to Pneumonia	-79	-207	-199
	QALYs	709	1,624	1,542
	Life-years	1,101	2,611	1,865
Costs (million \$)	Medical Costs	-\$25	-\$63	-\$51
	Vaccine Costs	\$423	\$423	\$357
	Total Cost	\$398	\$361	\$306
Cost effectiveness Ratios (\$)	Cost/QALY	\$561,417	\$222,132	\$199,000

Annual Number Needed to Vaccinate (NNV) Among Adults ≥65 Years Old*

Outcome	Incidence per	Vaccine			
PCV13-type:	100,000	Effectiveness (VE)	(95%CI)	NNV	(range)
IPD	5 ^a	76% ^b	(48, 89)	26,300	(22,500, 41,700)
Inpatient Pneumonia	17 ^c –76 ^d	43% ^e	(12, 63)	3,000–14,000	(2,100, 50,200)
Outpatient Pneumonia	88 ^f	43% ^e	(12, 63)	2,600	(1,800, 9,500)

*Calculation: $NNV = 1 / (\text{incidence rate} \times VE)$

^a Active Bacterial Core Surveillance, unpublished data

^b Bonten et al. CAPiTA. 2015.

^c 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

^d Swerdlow. ACIP June 2018. Pfizer, unpublished data

^e Webber et al. CAPiTA. 2017.

^f 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 illness¹⁻³
 - Low perceived personal susceptibility to pneumonia¹⁻²
- Workgroup perspective: Potential protection against pneumonia likely outweighs the side effects of PCV13 for older adults

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 providers¹
 - Providers recommended continuing with current recommendation²
 - Keeping the current recommendations may be best programmatically if new conjugate vaccines available soon³
 - Reimbursement for vaccine is still a programmatic issue³
- 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

Element	Favoring <u>Continued</u> PCV13 Use	Favoring <u>No Longer</u> using PCV13
Burden of Disease	<ul style="list-style-type: none"> PCV13-type disease reduced, but not eliminated through indirect effects from pediatric PCV use 	<ul style="list-style-type: none"> Indirect effects from pediatric PCV use have reduced the burden of PCV13-type disease to historic lows
Benefits	<ul style="list-style-type: none"> PCV13 effective in preventing PCV13-type pneumococcal disease 	<ul style="list-style-type: none"> 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 Benefits from continued PCV13 use are expected to be minimal
Acceptability	<ul style="list-style-type: none"> Frequent changes in recommendations may negatively impact the perceived importance of future adult vaccine recommendations 	<ul style="list-style-type: none"> Credibility comes from evidence-based recommendations
Resources Used	<ul style="list-style-type: none"> A recommendation change would incur a cost to update electronic medical records, decision support tools, etc. 	<ul style="list-style-type: none"> Economic analyses results do not favor continued PCV13 use
Feasibility	<ul style="list-style-type: none"> Universal prevention strategies are easier to implement effectively than risk-based ones Frequent changes in recommendations present implementation challenges 	<ul style="list-style-type: none"> Simplifies the recommendations—current recommendations have been confusing and difficult to implement

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

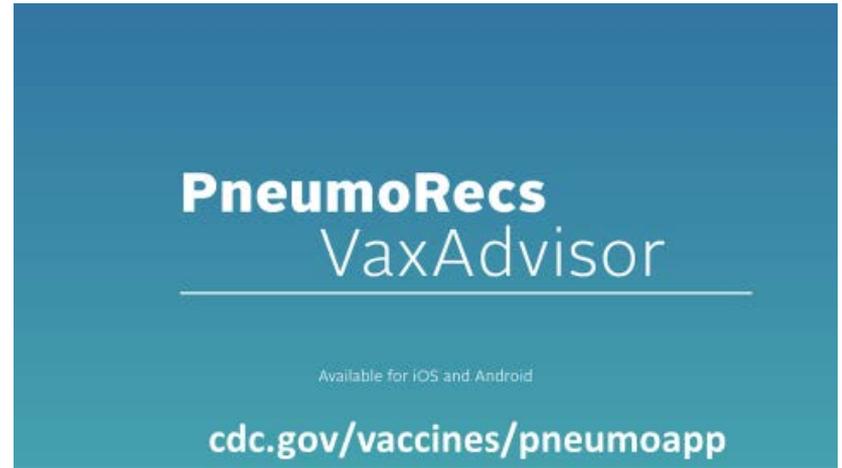
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C. **No longer recommend PCV13:** “ACIP no longer recommends PCV13 for adults 65 years or older who do not have an immunocompromising condition. All adults 65 years or older should receive a dose of PPSV23.”

Thank you!

For more information, contact CDC
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