Evidence to Recommendations Framework: PCV20 Use among Adults who Previously Received PCV13

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Advisory Committee on Immunization Practices

Pneumococcal Vaccines

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Serotypes Contained in Pneumococcal Vaccines

	1	3	4	5	6A	6B	7 F	9V	14	18 C	19 A	19 F	23 F	22 F	33 F	8	10 A	11 A	12 F	15 B	2	9N	17 F	20
PCV13																								
PCV15																								
PCV20																								
PPSV23																								

- **PCV15**: contains PCV13 serotypes and **22F and 33F**
- **PCV20**: contains PCV13 serotypes and **22F, 33F, 8, 10A, 11A, 12F, and 15B**
- **PPSV23 non-PCV20**: includes serotypes **2, 9N, 17F, and 20**

Adults Who Were Previously Recommended to Receive PCV13 and PPSV23

	19–64 years	≥65 years
None of the conditions listed below	No recommendation	PPSV23 and **PCV13*** based on shared clinical decision-making
Chronic medical conditions† (CMC)	PPSV23	
Cochlear implant, CSF leak	Both **PCV13*** and PPSV23	Both **PCV13*** and PPSV23
Immunocompromising conditions	Both **PCV13*** and PPSV23, repeat PPSV23 after 5 years	

PCV13: 13-valent pneumococcal conjugate vaccine, PCV15: 15-valent pneumococcal conjugate vaccine, PCV20: 20-valent pneumococcal conjugate vaccine, PPSV23: 23-valent pneumococcal polysaccharide vaccine

***If not previously given**; †Examples include alcoholism, chronic heart/liver/lung disease, diabetes, cigarette smoking

https://www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf

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Cochlear implant, CSF leak	Both **PCV13*** and PPSV23	Both **PCV13*** and PPSV23
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PCV13: 13-valent pneumococcal conjugate vaccine, PCV15: 15-valent pneumococcal conjugate vaccine, PCV20: 20-valent pneumococcal conjugate vaccine, PPSV23: 23-valent pneumococcal polysaccharide vaccine

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https://www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf

Policy Questions

Question 1	Question 2	Question 3
U.S. adults aged **≥19 years**	U.S. adults aged **19–64 years** with an immunocompromising condition, cerebrospinal fluid leak, or cochlear implant	U.S. adults aged **≥65 years**
Who previously received **PCV13 only**	Who previously received **both PCV13 and PPSV23**	Who previously received **both PCV13 and PPSV23**
Should they be recommended to receive a dose of PCV20 to complete their pneumococcal vaccine series?		Should they be recommended to receive a dose of PCV20?

PCV13=13-valent pneumococcal conjugate vaccine, PCV20=20-valent pneumococcal conjugate vaccine,

Policy Questions

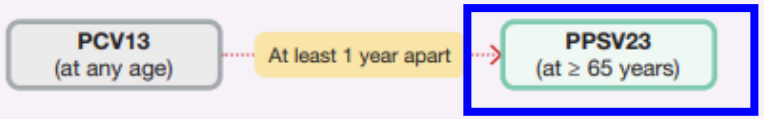
Adults who have NOT completed their recommended pneumococcal vaccine series

Group 1	Group 2	Group 3
U.S. adults aged **≥19 years**	U.S. adults aged **19–64 years** with an immunocompromising condition, cerebrospinal fluid leak, or cochlear implant	U.S. adults aged **≥65 years**
Who previously received **PCV13 only**	Who previously received **both PCV13 and PPSV23**	Who previously received **both PCV13 and PPSV23**
Should they be recommended to receive a dose of PCV20 to **complete** their pneumococcal vaccine series?		Should they be recommended to receive a dose of PCV20?

PCV13=13-valent pneumococcal conjugate vaccine, PCV20=20-valent pneumococcal conjugate vaccine,

Pneumococcal vaccine timing for adults who previously received PCV13
but who have not received all recommended doses of PPSV23

Adults 65 years or older without an immunocompromising condition, cerebrospinal fluid leak, or cochlear implant



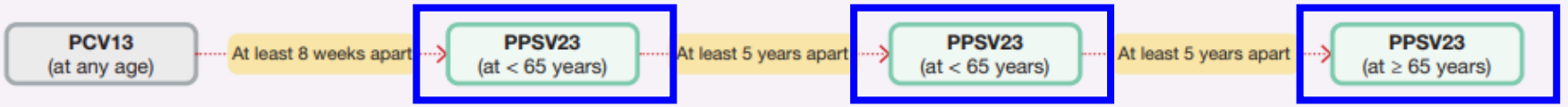
CDC recommends 1 dose of PPSV23 at age 65 years or older.**
Administer a single dose of PPSV23 at least 1 year after PCV13 was received. Their pneumococcal vaccinations are complete.

Adults 19 years or older with a cerebrospinal fluid leak or cochlear implant

CDC recommends 1 dose of PPSV23 before age 65 years and 1 dose of PPSV23** at age 65 years or older.**
Administer a single dose of PPSV23 at least 8 weeks after PCV13 was received.

- If the adult is 65 years or older, their pneumococcal vaccinations are complete.
- If the adult was younger than 65 years old when the first dose of PPSV23 was given, then administer a final dose of PPSV23 once they turn 65 years old and at least 5 years have passed since PPSV23 was first given. Their pneumococcal vaccinations are complete.

Adults 19 years or older with an immunocompromising condition



CDC recommends 2 doses of PPSV23 before age 65 years and 1 dose of PPSV23** at age 65 years or older.**
Administer a single dose of PPSV23 at least 8 weeks after PCV13 was received.

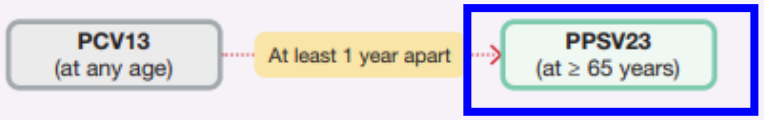
- If the patient was younger than 65 years old when the first dose of PPSV23 was given and has not turned 65 years old yet, administer a second dose of PPSV23 at least 5 years after the first dose of PPSV23. This is the last dose of PPSV23 that should be given prior to 65 years of age.
- Once the patient turns 65 years old and at least 5 years have passed since PPSV23 was last given, administer a final dose of PPSV23 to complete their pneumococcal vaccinations.

** For adults who have received PCV13 but have not completed their recommended pneumococcal vaccine series with PPSV23, one dose of PCV20 may be used if PPSV23 is not available. If PCV20 is used, their pneumococcal vaccinations are complete.

Pneumococcal Vaccine Timing for Adults-April 1, 2022 (cdc.gov)

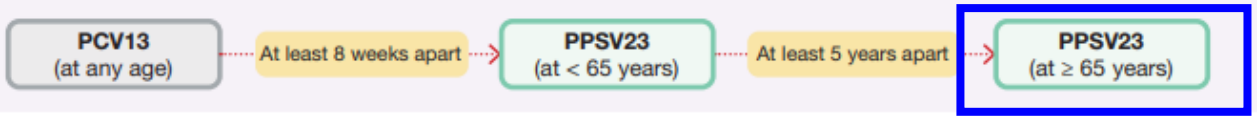
Pneumococcal vaccine timing for adults who previously received PCV13
but who have not received all recommended doses of PPSV23

Adults 65 years or older without an immunocompromising condition, cerebrospinal fluid leak, or cochlear implant



CDC recommends 1 dose of PPSV23 at age 65 years or older.**
Administer a single dose of PPSV23 at least 1 year after PCV13 was received. Their pneumococcal vaccinations are complete.

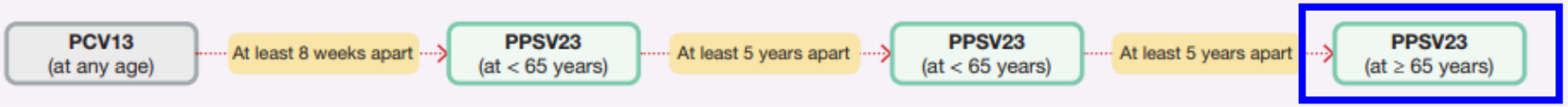
Adults 19 years or older with a cerebrospinal fluid leak or cochlear implant



CDC recommends 1 dose of PPSV23 before age 65 years and 1 dose of PPSV23** at age 65 years or older.**
Administer a single dose of PPSV23 at least 8 weeks after PCV13 was received.

- If the adult is 65 years or older, their pneumococcal vaccinations are complete.
- If the adult was younger than 65 years old when the first dose of PPSV23 was given, then administer a final dose of PPSV23 once they turn 65 years old and at least 5 years have passed since PPSV23 was first given. Their pneumococcal vaccinations are complete.

Adults 19 years or older with an immunocompromising condition



CDC recommends 2 doses of PPSV23 before age 65 years and 1 dose of PPSV23** at age 65 years or older.**
Administer a single dose of PPSV23 at least 8 weeks after PCV13 was received.

complete their pneumococcal vaccinations.

No more PPSV23 doses recommended after 1 dose at age 65 years or older.

** For adults who have received PCV13 but have not completed their recommended pneumococcal vaccine series with PPSV23, one dose of PCV20 may be used if PPSV23 is not available. If PCV20 is used, their pneumococcal vaccinations are complete.

[Pneumococcal Vaccine Timing for Adults-April 1, 2022 (cdc.gov)]

Policy Questions

Adults who have completed their recommended pneumococcal vaccine series

Group 1	Group 2	Group 3
U.S. adults aged **≥19 years**	U.S. adults aged **19–64 years** with an immunocompromising condition, cerebrospinal fluid leak, or cochlear implant	U.S. adults aged **≥65 years**
Who previously received **PCV13 only**	Who previously received **both PCV13 and PPSV23**	Who previously received **both PCV13 and PPSV23**
Should they be recommended to receive a dose of PCV20 to complete their pneumococcal vaccine series?		Should they be recommended to receive a dose of PCV20?

PCV13=13-valent pneumococcal conjugate vaccine, PCV20=20-valent pneumococcal conjugate vaccine,

Evidence to Recommendations (EtR) Framework

EtR Domain	Question
Public Health Problem	• Is the **problem** of public health importance?
Benefits and Harms	• How substantial are the desirable anticipated effects? • How substantial are the undesirable anticipated effects? • Do the desirable effects outweigh the undesirable effects? • What is the overall certainty of this evidence for the critical outcomes?
Values	• Does the target population feel the desirable effects are large relative to the undesirable effects? • Is there important variability in how patients value the outcomes?
Acceptability	• Is the **intervention** acceptable to key stakeholders?
Feasibility	• Is the **intervention** feasible to implement?
Resource Use	• Is the **intervention** a reasonable and efficient allocation of resources?
Equity	• What would be the impact of the **intervention** on health equity?

Problem: pneumococcal disease, **Intervention**: PCV20 use among adults who previously received PCV13

Public Health Problem

Is pneumococcal disease of public health importance for adults who have previously received PCV13?

1. Characteristics of the target population

Estimated number of adults who have already received ≥1 dose of PCV13

- **Adults aged ≥65 years: ~27 million**
  - Population size: **54.1** million[1]
  - Adults who received ≥1 dose of PCV13: **~50%[2]**

- **Adults aged 19–64 years with immunocompromising conditions: ~0.4 million**
  - Population size: **7.7** million[3]
  - Eligible adults who received ≥1 PCV13 dose:**~5%[4]**

1. United States Census Bureau
2. Hoehner et al. https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/pubs-resources/pcv13-medicare-beneficiaries-2010-2019.html
3. Estimated from census data and Pelton et al. CID 2019 to estimate the proportion with immunocompromising conditions
4. Deb et al. Expert Review of Vaccines 2021

Estimated incidence of pneumococcal disease in adults aged ≥65 years

Disease	Estimated incidence (per 100,000 population)
All-cause hospitalized pneumonia[1]	847–3,365
All-cause hospitalized noninvasive pneumococcal pneumonia[2]	105
Invasive pneumococcal disease (IPD)[3]	24

Case fatality ratio from IPD: 14%[3]

1. McLaughlin et al. Vaccine 2020 (limited to studies that collected data during or after 2010)
2. Gierke et al. IDweek 2020. CDC's **S**urveillance for **N**on**I**nvasive **P**neumococcal **P**neumonia (SNiPP), 2017
3. CDC ABCs, 2018–2019

Adults aged 19–64 years with immunocompromising conditions have 9–18 times the risk of pneumococcal disease compared with healthy adults.

	Rate per 100,000 person-years, 2013–2015		
	Healthy[1]	**High-risk[2]**	**Rate Ratio**
18–49 years			
Hospitalized IPD	0.6 (0.5, 0.7)	8.6 (6.7, 11.2)	**15.4 (11.3, 20.9)**
Hospitalized pneumococcal pneumonia	1.2 (1.1, 1.3)	21.1 (17.9, 24.9)	**17.6 (14.4, 21.5)**
50–64 years			
Hospitalized IPD	1.9 (1.6, 2.1)	16.4 (14.4, 18.7)	**8.8 (7.4, 10.6)**
Hospitalized pneumococcal pneumonia	3.9 (3.5, 4.2)	43.0 (39.7, 46.6)	**11.1 (9.9, 12.6)**

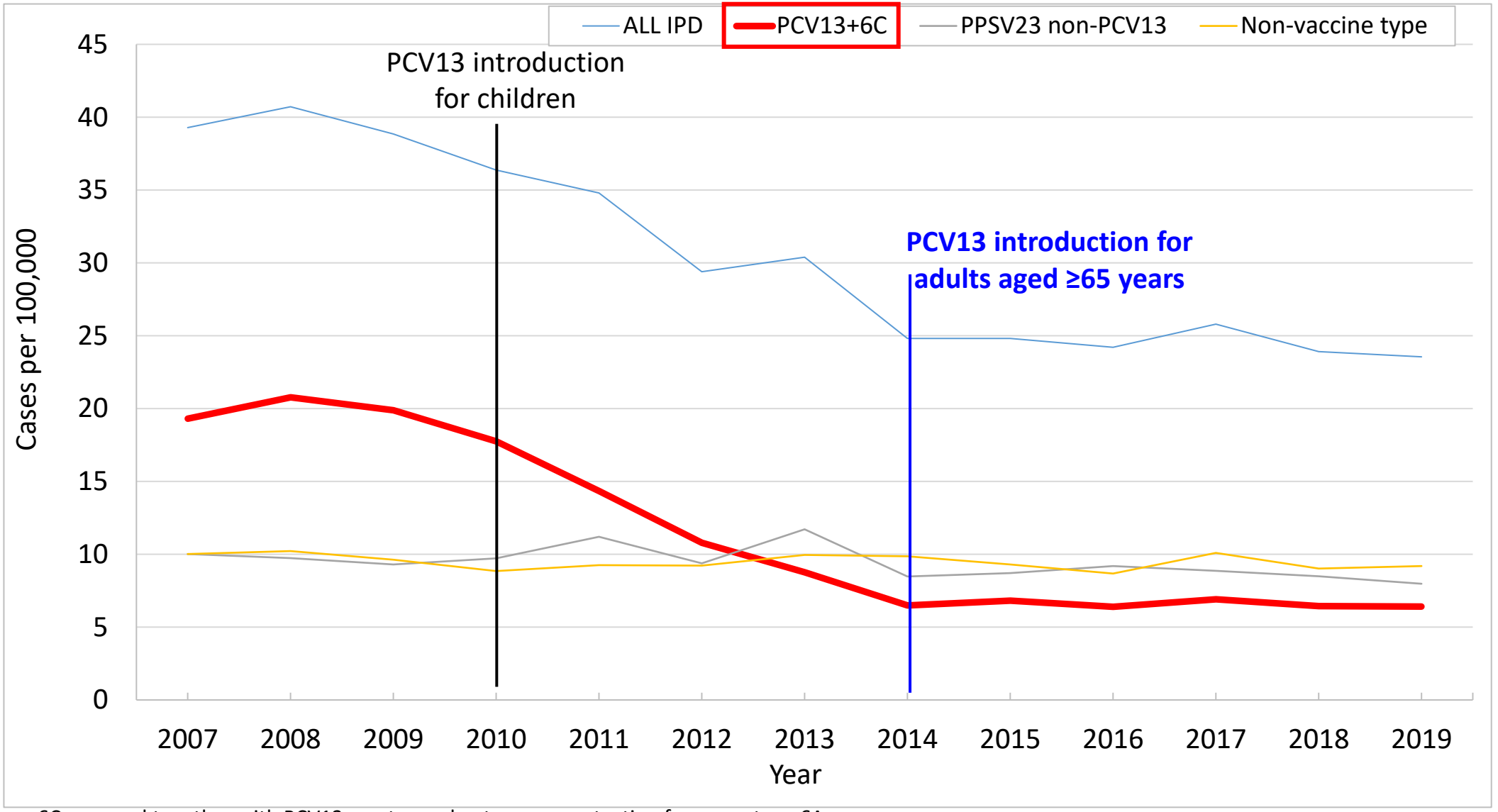
Reference: Pelton et al. CID 2019

IPD=invasive pneumococcal disease

1. Adults without any conditions with risk-based pneumococcal vaccine indications
2. Adults with immunocompromising condition or with cochlear implant

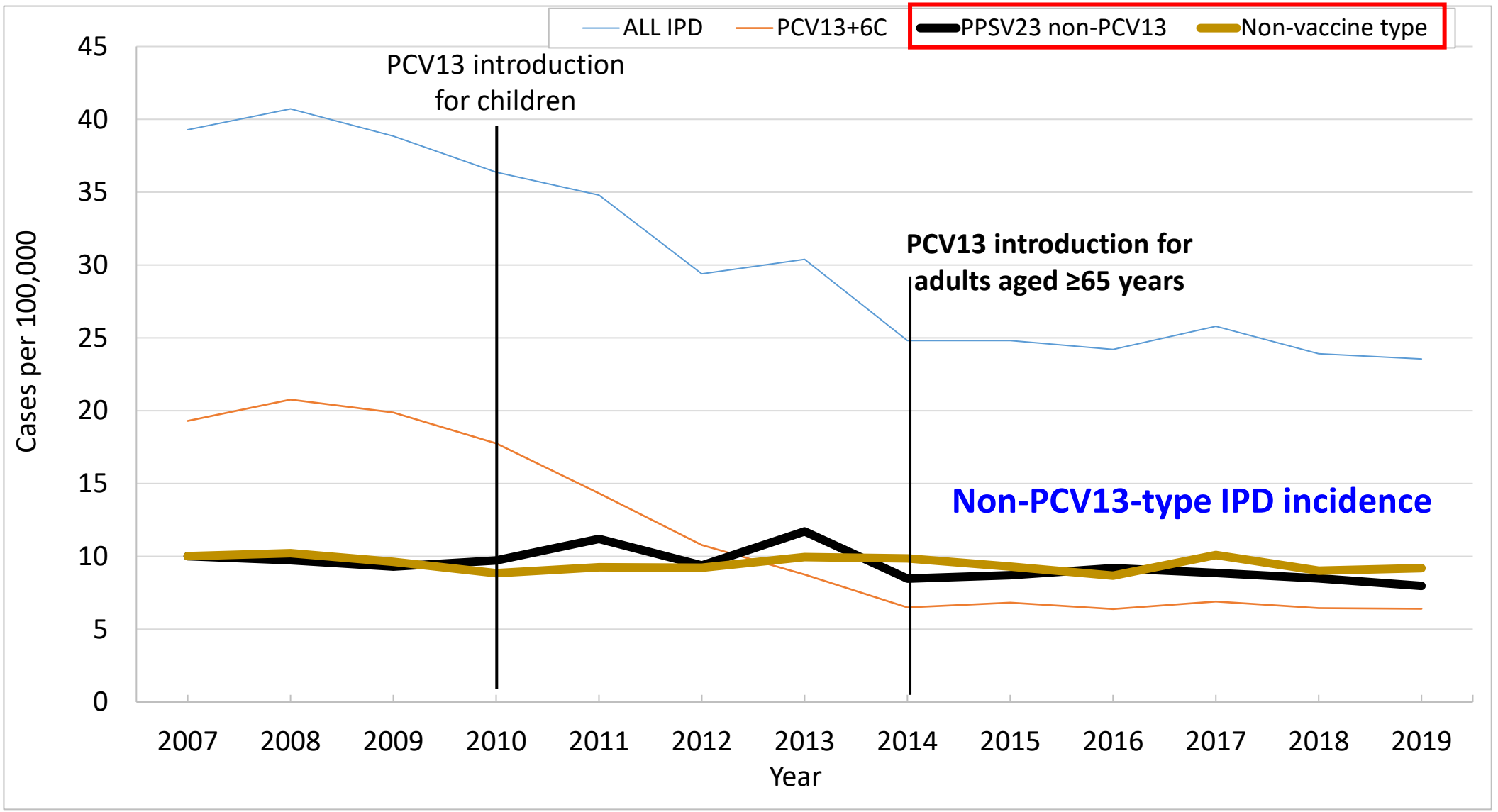
2. Impact of PCV13 use against pneumococcal disease in adults

PCV13-type IPD incidence among adults aged ≥65 years decreased after PCV13 use in children but remained stable in 2014–2019



Serotype 6C assessed together with PCV13 serotypes due to cross-protection from serotype 6A.
CDC Active Bacterial Core surveillance, 2007–2019

Non-PCV13-type IPD incidence among adults aged ≥65 years remained stable.



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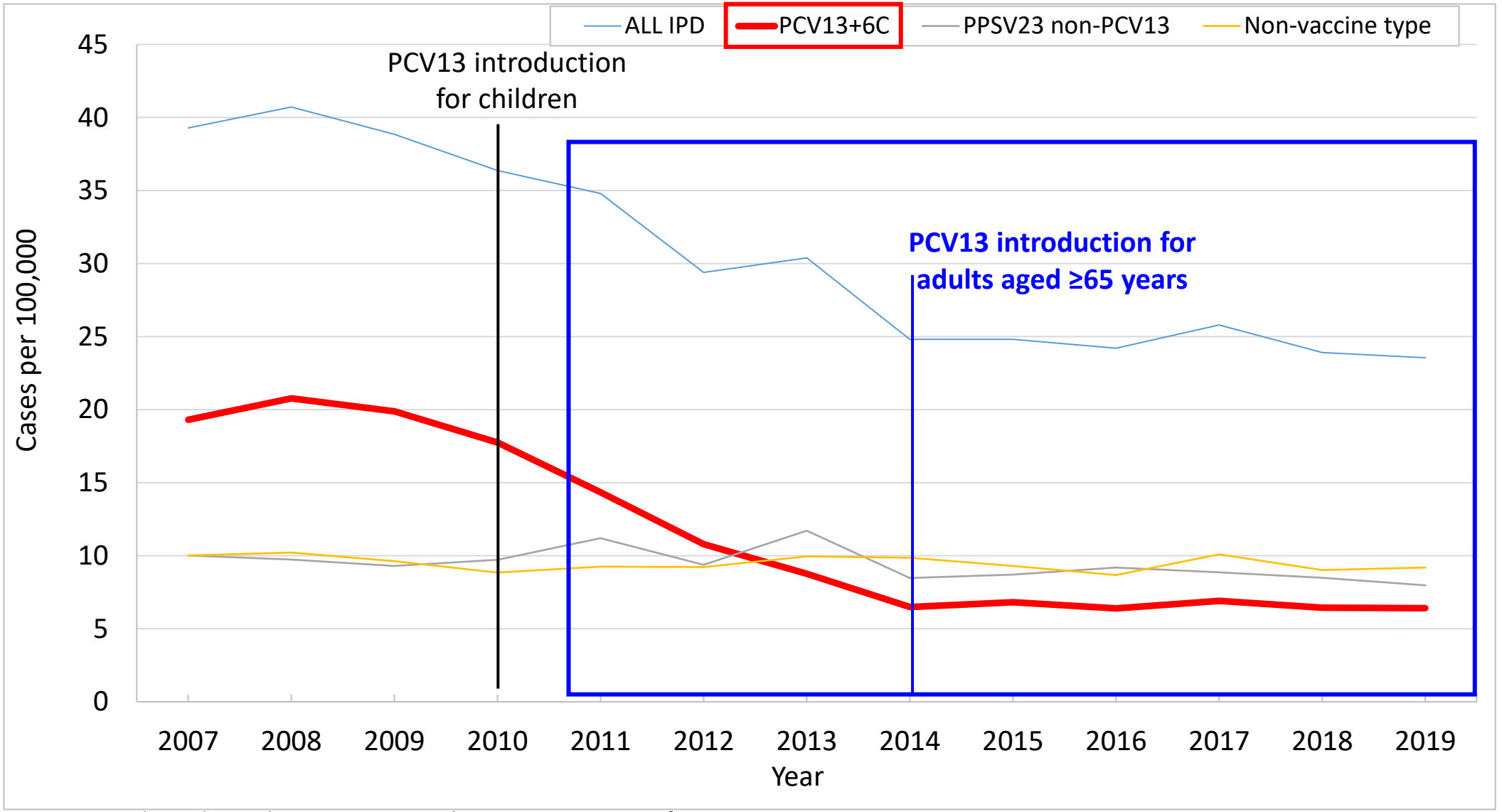
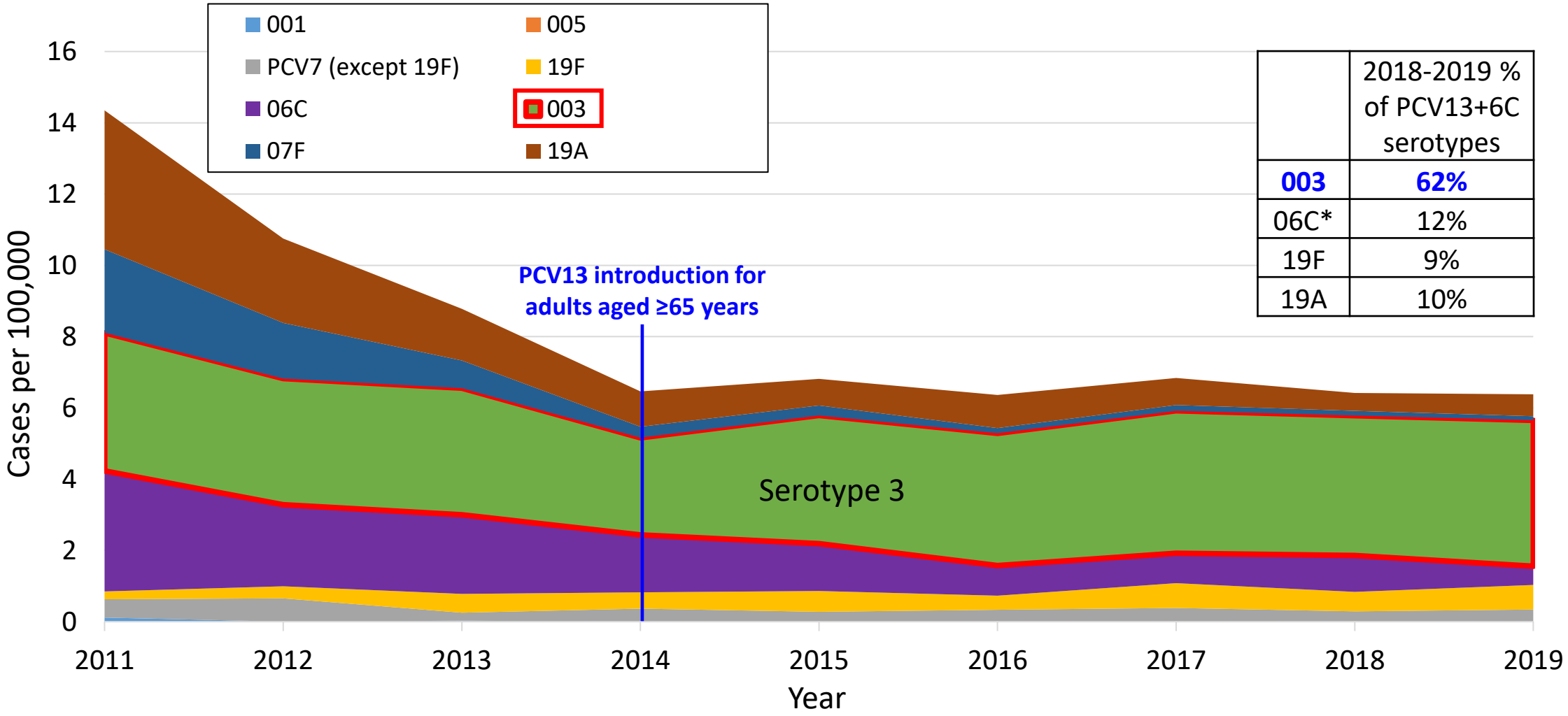


Serotype 6C assessed together with PCV13 serotypes due to cross-protection from serotype 6A.
CDC Active Bacterial Core surveillance, 2007–2019

Among remaining PCV13 serotypes*, serotype 3 caused >60% of IPD among adults ≥65 years old in 2018–2019

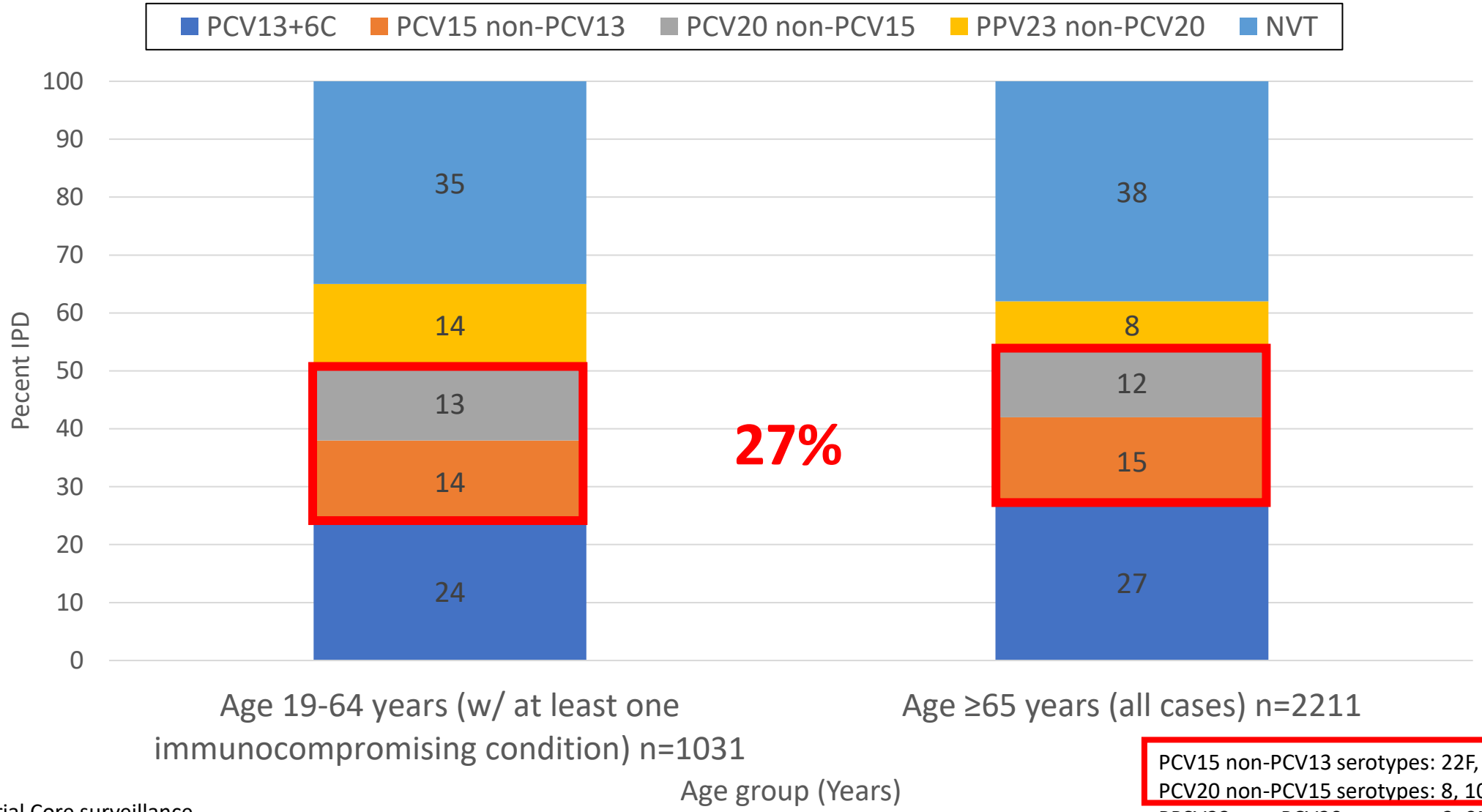


	2018-2019 % of PCV13+6C serotypes
003	**62%**
06C*	12%
19F	9%
19A	10%

*Serotype 6C assessed together with PCV13 serotypes due to cross-protection from serotype 6A.

CDC Active Bacterial Core surveillance, 2007–2019

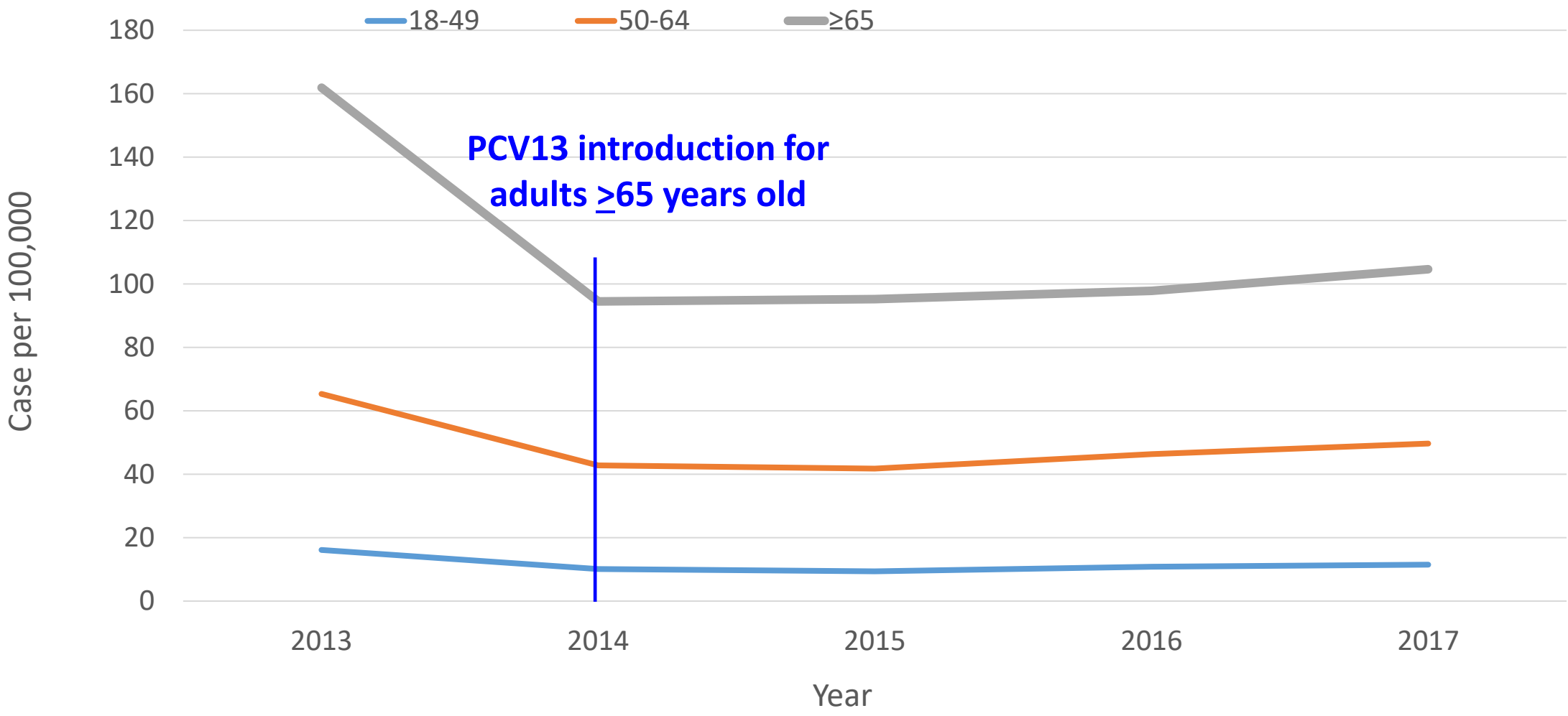
Pneumococcal serotypes contained in PCV20 but not in PCV13 caused 27% of Invasive Pneumococcal Disease in Adults in 2018–2019



PCV15 non-PCV13 serotypes: 22F, 33F
PCV20 non-PCV15 serotypes: 8, 10A, 11A, 12F, 15B
PPSV23 non-PCV20 serotype: 2, 9N, 17F ,20

CDC Active Bacterial Core surveillance

Hospitalized pneumococcal pneumonia incidence in adults did not decrease after routine PCV13 use among adults aged ≥65 years.



Gierke et al. IDweek 2020. CDC's **S**urveillance for **N**on**I**nvasive **P**neumococcal **P**neumonia (SNiPP), 2013–2017

Reduction in incidence of hospitalized PCV13-type pneumococcal pneumonia was observed after routine PCV13 use among a cohort of adults aged ≥65 years.

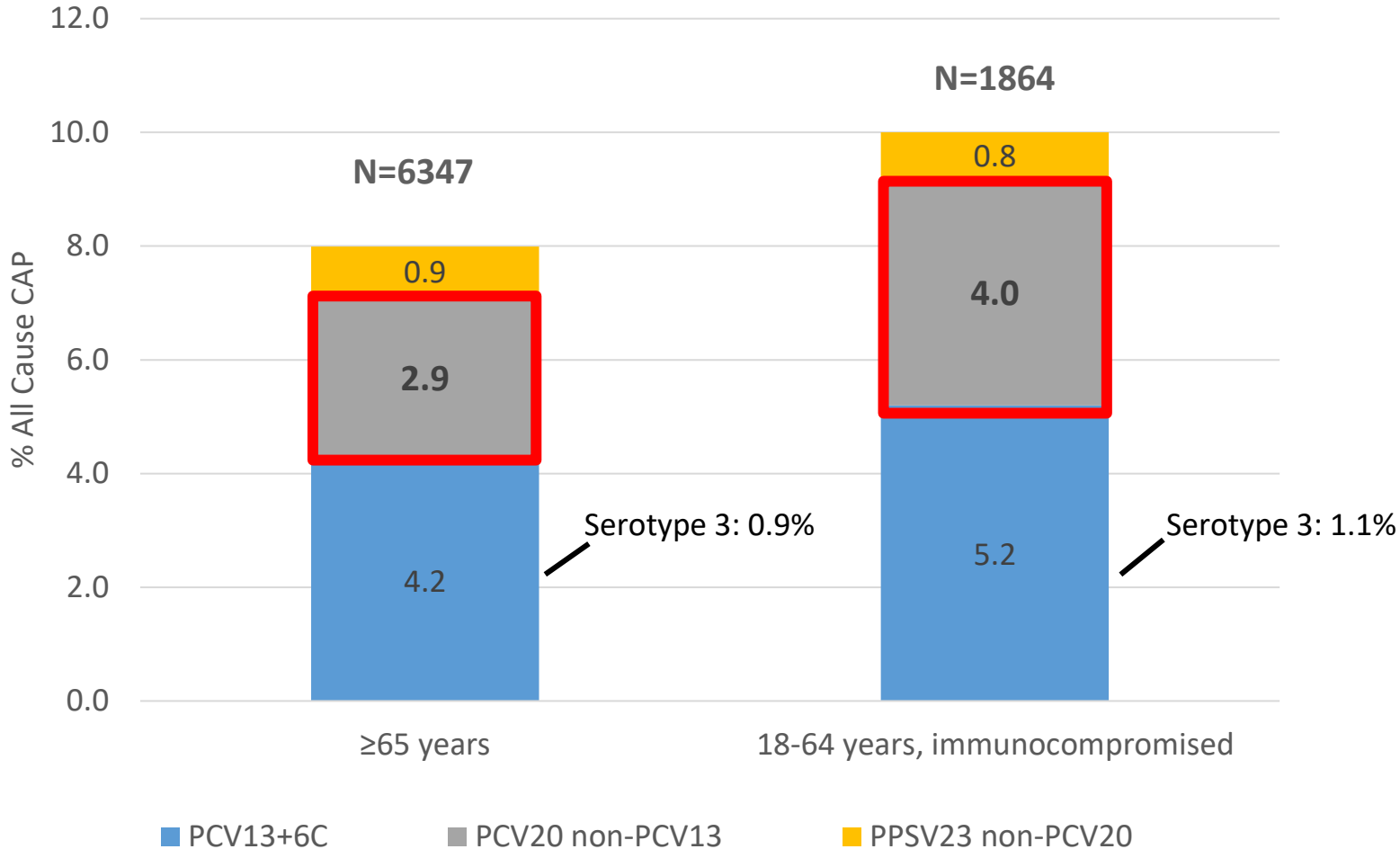
Louisville cohort study: among ≥65 years old, 2014-2016

- **31.5% reduction** (95%CI: 8.3, 48.9) in PCV13-type hospitalized pneumococcal pneumonia[1*]

Swerdlow Jun 2018 ACIP meeting presentation*

*Pfizer funded study

In 2013–2016, additional serotypes contained in PCV20 but not in PCV13 caused 3–4% of all-cause hospitalized community-acquired pneumonia in adults.



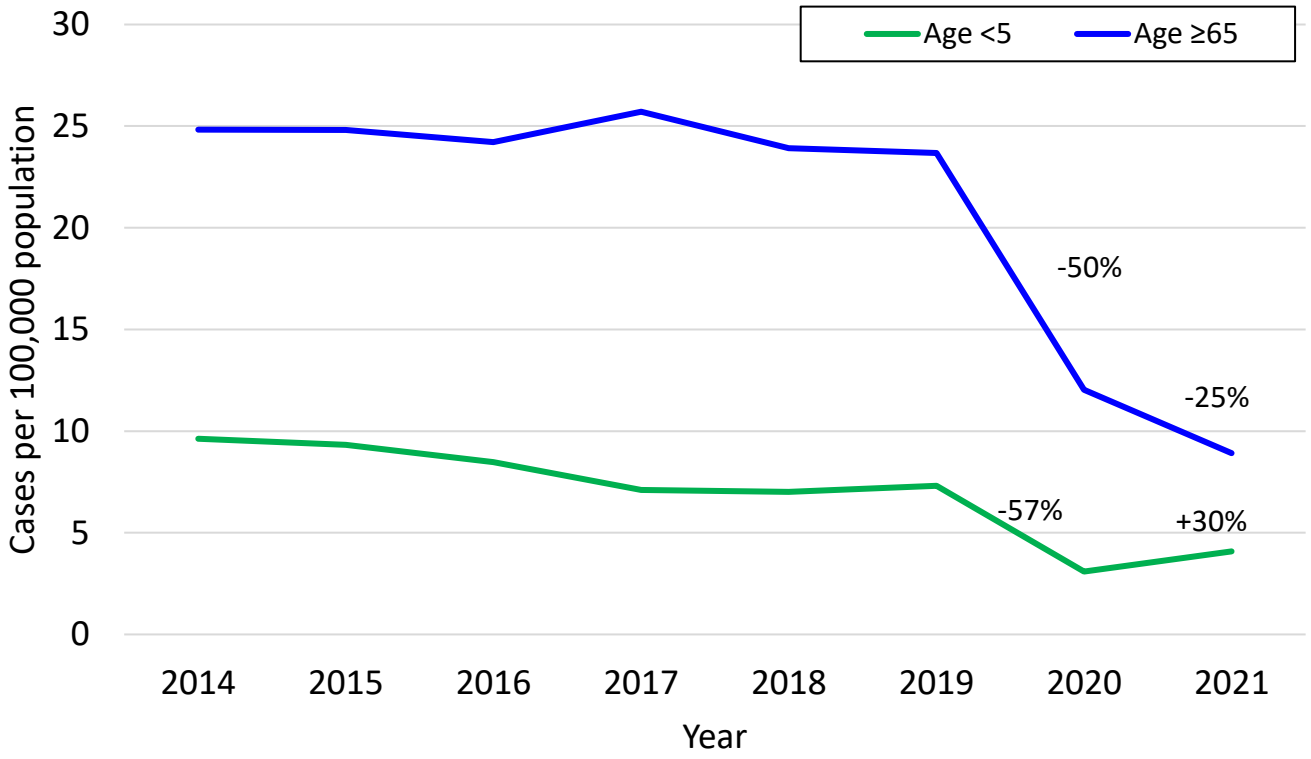
Isturiz et al. CID 2021

PCV15 non-PCV13 serotypes: 22F, 33F
PCV20 non-PCV15 serotypes: 8, 10A, 11A, 12F, 15B/15C (15B and C are identified together in the assay)
PPSV23 non-PCV20 serotype: 2, 9N, 17F ,20

*Pfizer funded study

3. Impact of the COVID-19 pandemic on pneumococcal disease incidence

Overall Invasive Pneumococcal Disease (IPD) incidence decreased in both adults and children early during the COVID-19 pandemic.



Children < 5 years

57% decline in overall IPD in 2020,
30% increase in 2021

Adults ≥ 65 years

50% decline in overall IPD in 2020,
additional 25% decline in 2021

CDC Active Bacterial Core surveillance unpublished data

Incidence of pneumococcal pneumonia hospitalizations among adults may have decreased during the COVID-19 pandemic.

Year	Location	Association with COVID-19 pandemic	Hospitalizations per 100,000 adult population per year (95% CI)	
			All-cause pneumonia	Pneumococcal pneumonia
Sep 2018–Aug 2019	Nashville	Before pandemic	470 (422-517)	43 (39-47)
Sep 2019–Aug 2020	Nashville	During pandemic	613 (524-702)	**27 (23-32)**
Nov 2020–Oct 2021	Nashville	During Pandemic	484 (411-557)	**9 (8-11)**

Self et al. ISPPD 2022, study funded by Merck

Public Health Problem

Is pneumococcal disease of public health importance in adults who received PCV13?

- ☐ No
- ☐ Probably no
- ☐ Probably yes
- ☐ Yes
- ☐ Varies
- ☐ Don’t know

Public Health Problem

- Vaccine-preventable pneumococcal disease burden remains (especially pneumonia)
- Reduction in pneumococcal disease incidence due to COVID-19 is likely time-limited[1]
- **Group 1. Adults who have received PCV13 only**:
  - Protection against limited serotype coverage
- **Group 2. Adults aged 19–64 years with immunocompromising conditions**:
  - Protection from PPSV23 in this group may be limited
- **Group 3. Adults aged ≥65 years**:
  - Population size is substantial
  - Significance depends on factors that determine the risk of pneumococcal disease, such as time since last pneumococcal vaccination, underlying conditions, or age

1. Perniciaro et al. CID 2022

Benefits and Harms

Pneumococcal Vaccines: PCVs vs. PPSV23

	1	3	4	5	6A	6B	7 F	9V	14	18 C	19 A	19 F	23 F	22 F	33 F	8	10 A	11 A	12 F	15 B	2	9N	17 F	20
PCV13																								
PCV15																								
PCV20																								
PPSV23																								

	PCV	PPSV23
Basic Vaccine Composition	Capsular polysaccharides conjugated to **CRM197 Carrier Protein**	Capsular polysaccharide antigens
Mechanism of action	T-cell **dependent**	T-cell **independent**
Memory B cell production	**Yes**	**No**

PCV: pneumococcal conjugate vaccine, PPSV23: 23-valent pneumococcal polysaccharide vaccine

Pneumococcal Vaccines: PCVs vs. PPSV23

	PCV	PPSV23
Duration of protection	**No decline for 5 yrs**[1]	Variable findings, waning reported as early as **2 years** since vaccination[2]
Vaccine Effectiveness vs. Vaccine-type IPD	Supported by clinical efficacy/effectiveness data	Supported by clinical efficacy/effectiveness data; limited effectiveness reported in immunocompromised adults[3]
Vaccine Effectiveness vs. Vaccine-type non-invasive/non-bacteremic pneumonia	Supported by clinical efficacy data • **Moderate** protection (45%: 95% CI 14 to 63)[4]	**Variable** clinical effectiveness data • Modest protection (18%: 95% CI -4 to 35%) from a meta-analysis[5]

1. Patterson et al. Trials in Vaccinology 2016.
2. World Health Organization. Strategic Advisory Group of Experts on Immunization 5-7 October 2020. https://terrance.who.int/mediacentre/data/sage/SAGE_eYB_October_2020.pdf?ua=1
3. French et al. NEJM 2000; Andrews et al. Vaccine 2012; Rudnick et al. Vaccine 2013; Djennad et al. EClinicalMedicine 2018
4. Bonten et al. NEJM 2015
5. Farrar et al. https://www.medrxiv.org/content/10.1101/2022.10.06.22280772v1.full

Estimated time since PCV13 or PPSV23 vaccination: Medicare beneficiaries aged ≥65 years, June 2022

- **Time since last PCV13 vaccination (with/without PPSV23):**
  - **Median 5.6** (range 0–8.5) years

- **Time since last PPSV23 vaccination (adults who received PCV13 → PPSV23):**
  - **Median 3.1** (range 0–8.4) years

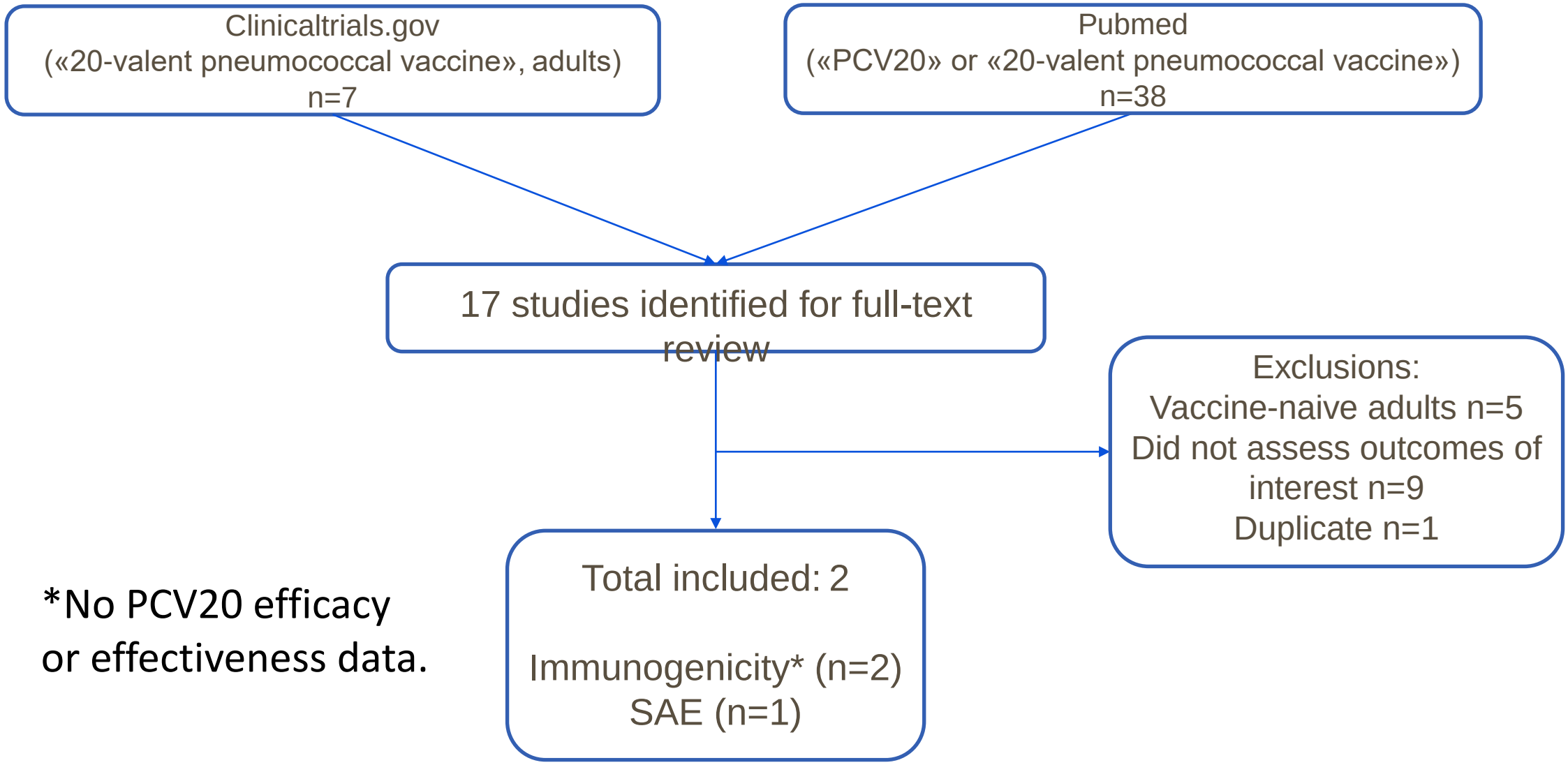
CMS unpublished Fee-For-Service data (available on August 1, 2022)

PICO Questions for GRADE

Population	U.S. adults aged **19–64 years** with an immunocompromising condition, cerebrospinal fluid leak, or cochlear implant	U.S. adults aged **≥65 years**
	Who previously received **PCV13**	
Intervention	One dose of PCV20	
Comparison	Use of PPSV23 based on currently recommended dosing and schedule	
Outcomes (critical)	VT-IPD, VT-nonbacteremic pneumococcal pneumonia, VT-pneumococcal mortality, SAE following vaccination	

PCV13=13-valent pneumococcal conjugate vaccine, PCV20=20-valent pneumococcal conjugate vaccine, PPSV23=23-valent pneumococcal polysaccharide vaccine, SAE= serious adverse events, VT=vaccine type

Evidence Retrieval



*No PCV20 efficacy or effectiveness data.

PCV20=20-valent pneumococcal conjugate vaccine, SAE= serious adverse events, VT=vaccine type

Summary of included studies

- Both from Phase 3 clinical trials among adults aged ≥65 years **without IC**
- **Cannon et al. 2021 (safety and immunogenicity)[1]**
  - **Immunogenicity**:
    - Response to PCV20 by prior vaccine status (PCV13, PPSV23, PCV13+PPSV23)
    - No PCV20 vs PPSV23 comparison
  - **Safety**: PCV20 vs PPSV23 in PCV13 group; PCV20 in PCV13+PPSV group
- **B7471004 post-hoc analysis (immunogenicity), unpublished[2]**
  - Post-hoc analysis of a phase 3 trial assessing PCV20 and QIV coadministration
  - Response to PCV20 stratified by previous vaccination status

See GRADE tables in appendix for details.

IC=immunocompromising conditions; QIV=quadrivalent inactivated influenza vaccine

1. Cannon et al. Vaccine 2021. Funded by Pfizer.

2. Safety and Immunogenicity of 20vPnC Coadministered With SIIV in Adults ≥65 Years of Age - Full Text View - ClinicalTrials.gov. Funded by Pfizer

GRADE Summary of Findings: Immunogenicity

- **OPA GMT ratios[1]**
  - Previous **PCV13** > previous **PPSV23** for all 20 serotypes
  - Previous **PCV13+PPSV23** > previous **PPSV23** for 15 to 19 (of 20) serotypes

- **% seroresponders[2]**
  - Previous **PCV13** > previous **PPSV23** for 13 to 18 (of 20) serotypes
  - Previous **PCV13+PPSV23** > previous **PPSV23** for 3 to 6 (of 20) serotypes

OPA GMT=opsonophagocytic activity geometric mean titer

1. Defined as [GMT (PCV20, previous PCV13 with or without PPSV23)]/[GMT (PCV20, previous PPSV23 only)]; blood draws occurred 1-month post-dose
2. Defined as percentage of participants with a ≥4-fold rise in OPA titers from before to 1 month after vaccination

GRADE Summary of Findings: Safety

- Proportion reporting serious adverse events (SAEs) through 6 months after vaccination was similar across groups
  - PCV13 + **PCV20** (n=246) vs. PCV13 + **PPSV23** (n=127)
    - **2.4% vs 1.6%**
  - PCV13 + PPSV23 + **PCV20** (n=325, no comparator group)
    - **1.6%**
- No vaccine-related SAEs
- No deaths reported

Cannon et al. Vaccine 2021. Funded by Pfizer

Benefits and Harms

How substantial are the desirable anticipated effects?

Group 1. Adults with PCV13 only
Group 2. Adults aged 19–64 years with IC with PCV13+PPSV23

- ☐ Minimal
- ☐ Small
- ☐ Moderate
- ☐ Large
- ☐ Varies
- ☐ Don’t know

Group 3. Adults aged ≥65 years with PCV13+PPSV23

- ☐ Minimal
- ☐ Small
- ☐ Moderate
- ☐ Large
- ☐ Varies
- ☐ Don’t know

Benefits and Harms

How substantial are the desirable anticipated effects?

Group 1. Adults with PCV13 only
Group 2. Adults aged 19–64 years with IC with PCV13+PPSV23

- ☐ Minimal
- ☐ Small
- ☐ Moderate
- ☐ Large
- ☐ Varies
- ☐ Don't know

- These adults have not completed the recommended PPSV23 series
- Immunologic benefits of PCV vs PPSV23
  - **Group 1. Adults with PCV13 only**:
    - Depends on type of underlying risk of disease
  - **Group 2. Adults aged 19 –64 years with IC**:
    - May have inadequate response to PPSV23 and shorter duration of protection

IC= immunocompromising conditions

Benefits and Harms

How substantial are the desirable anticipated effects?

Small anticipated effects

- Incremental benefits of PCV20 use among these adults is likely modest

Moderate anticipated effects

- Based on understanding of immunologic benefits of PCV vs PPSV23

Others

- Depends on factors such as:
  - time since vaccination
  - age of patient
  - presence of underlying medical conditions
  - indirect effects of pediatric PCV20 vaccination

Group 3. Adults aged ≥65 years with PCV13+PPSV23

Benefits and Harms

How substantial are the undesirable anticipated effects?

- ☐ Minimal
- ☐ Small
- ☐ Moderate
- ☐ Large
- ☐ Varies
- ☐ Don’t know

Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

- What is the balance between the desirable effects relative to the undesirable effects?

- ☐ Favors intervention*
- ☐ Favors current recommendation
- ☐ Favors both
- ☐ Favors neither
- ☐ Varies
- ☐ Don’t know

***Intervention: a dose of PCV20**

Benefits and Harms

What is the overall certainty of this evidence for the critical outcomes?

	Group 1. Adults with PCV13 only	Group 2. IC adults aged 19–64 years PCV13+PPSV23	Group 3. Adults aged ≥65 years PCV13+PPSV23
Effectiveness	3 (low)	3 (low)	2 (moderate)
Safety	3 (low)	3 (low)	2 (moderate)

GRADE Summary of Findings (Adults Aged ≥65 years)

Certainty assessment							№ of patients		Results		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PCV20 following previous PCV13**	**Previous PPSV23 receipt**	**Relative (95% CI)**	**Absolute (95% CI)**		
VT-IPD, VT-nonbacteremic pneumococcal pneumonia, VT-pneumococcal mortality Outcome (Assessed with: Immunogenicity)												
2	Randomized studies	Not serious	Not serious	**Serious[a]**	Not serious	Not serious	754 - 898	296 - 340	**OPA GMT ratios** •Previous PCV13 > previous PPSV23 for all 20 serotypes •Previous PCV13+PPSV23 > previous PPSV23 for 15 to 19 (of 20) serotypes **% seroresponders** •Previous PCV13 > previous PPSV23 for 13 to 18 (of 20) serotypes •Previous PCV13+PPSV23 > previous PPSV23 for 3 to 6 (of 20) serotypes		**2 (moderate)**	Critical
Serious adverse events following immunization												
1	Randomized studies	Not serious	Not serious	Not serious	**Serious[b]**	Not serious	**8/371**	**2/127**	--	0.8 to 1.6%	**2 (moderate)**	Critical

a. These are all immunogenicity studies and there are no correlates of protection for the critical outcomes considered

b. Few vaccine-related serious adverse events reported do not meet the optimal information size

GRADE Summary of Findings (IC Adults Aged 19–64 years)

Certainty assessment							№ of patients		Results		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PCV20 following previous PCV13**	**Previous PPSV23 receipt**	**Relative (95% CI)**	**Absolute (95% CI)**		
VT-IPD, VT-nonbacteremic pneumococcal pneumonia, VT-pneumococcal mortality Outcome (Assessed with: Immunogenicity)												
2	Randomized studies	Not serious	Not serious	**Very serious[a,b]**	Not serious	Not serious	754 - 898	296 - 340	**OPA GMT ratios** •Previous PCV13 > previous PPSV23 for all 20 serotypes •Previous PCV13+PPSV23 > previous PPSV23 for 15 to 19 (of 20) serotypes **%seroresponders** •Previous PCV13 > previous PPSV23 for 13 to 18 (of 20) serotypes •Previous PCV13+PPSV23 > previous PPSV23 for 3 to 6 (of 20) serotypes		**3 (low)**	Critical
Serious adverse events following immunization												
1	Randomized studies	Not serious	Not serious	**Serious[b]**	**Serious[c]**	Not serious	**8/371**	**2/127**	--	0.8 to 1.6%	**3 (low)**	Critical

a. These are all immunogenicity studies and there are no correlates of protection for some critical outcomes considered
b. No studies among adults 19 – 64 years of age with underlying medical conditions; study populations are adults 65 years of age and older without immunocompromising conditions
c. Few vaccine-related serious adverse events reported do not meet the optimal information size

Values

Values and Preferences

Criterion 1: Do adults who previously received PCV13 (with or without PPSV23) feel that the desirable effects from PCV20 vaccination are large relative to undesirable effects?

- □ No
- □ Probably no
- □ Probably yes
- □ Yes
- □ Varies
- □ Don’t know

No research evidence identified

Values and Preferences

Criterion 1. Does the target population feel that the desirable effects are large relative to undesirable effects?

- These are adults who have already received PCV13 (with or without PPSV23):
  - Likely to have some understanding of the importance of receiving pneumococcal vaccines
- Additional Work Group comments:
  - Not enough information to make the decision
  - Interpretation will vary among the target population

Values and Preferences

Criterion 2: Is there important uncertainty about, or variability in, how much adults value the main outcomes?

Group 1. Adults who received PCV13 only?
Group 2. Adults aged 19–64 years with IC who received both PCV13 and PPSV23?

- ☐ Important uncertainty or variability
- ☐ Probably important uncertainty or variability
- ☐ Probably not important uncertainty or variability
- ☐ No important uncertainty or variability
- ☐ No known undesirable outcomes

- No research evidence
- Previously vaccinated adults probably do not have important uncertainty or variability

Values and Preferences

Criterion 2: Is there important uncertainty about, or variability in, how much adults value the main outcomes?

No research evidence identified.

- **Adults aged ≥65 years who received both PCV13 and PPSV23?**

Variable responses by Work Group members

- □ Important uncertainty or variability
- □ Probably important uncertainty or variability
- □ Probably not important uncertainty or variability
- □ No important uncertainty or variability
- □ No known undesirable outcomes

Values and Preferences

Criterion 2. Is there important uncertainty about or variability in how much people value the main outcomes?

- These are adults who have already received PCV13 (with or without PPSV23):
  - Probably no important uncertainty or variability about receiving another dose of a pneumococcal vaccine

- There could be uncertainty or variability depending on the age, life expectancy, time since the last vaccination, or perceived severity of pneumococcal disease among adults aged ≥65 years who have completed their recommended vaccine series.

Acceptability

Is the option acceptable to key stakeholders?

Findings from Healthcare Provider (HCP) Surveys

- **Two web-based HCP surveys using a commercial survey panel**
  - Limited to HCPs who administer pneumococcal vaccines to adults
- **≥65% of respondents approved use (strongly/somewhat) of higher-valent PCV for prior PCV13 recipients[1]**

- **Providers were more agreeable to administering PCV20 for[2]:**

IC adults aged 19–64 years, PCV13 only > **Adults aged ≥65 years, PCV13 only** > **IC adults aged 19–64 years, PCV13 +PPSV23** > **Adults aged ≥65 years PCV13 + PPSV23**

IC=immunocompromised

1. Pfizer HCP preference survey 2021
2. University of Iowa HCP preference survey 2022. Respondents were asked if they “Strongly disagree”, “Disagree”, “Neither agree or disagree”, “Agree”, or “Strongly agree” with administering PCV20 for adults who were previously vaccinated.

Acceptability

Is recommending PCV20 for adults who previously received PCV13 (with or without PPSV23) acceptable to key stakeholders?

- □ No
- □ Probably no
- □ Probably yes
- □ Yes
- □ Varies
- □ Don’t know

Resource Use

Is recommending PCV20 for adults who previously received PCV13 a reasonable and efficient allocation of resources?

Acknowledgements

- Informed by work conducted by three modeling groups
  - CDC Team
    - Charles Stoecker[a], Miwako Kobayashi[b], Bo-Hyun Cho[b], Namrata Prasad[b]
  - Merck Team
    - Kwame Owusu-Edusei[c], Elamin Elbasha[c]
    - Arijita Deb[c], Kelly Johnson[c], Oluwaseun Sharomi[c], Thomas Weiss[c], Temi Folaranmi[c], Craig Roberts[c], Donald Yin[c], Richard Haupt[c], Tufail Malik[c]
  - Pfizer Team
    - Derek Weycker[d], Ahuva Averin[d], Mark Atwood[d], Melody Shaff[d], Reiko Sato[e], Erica Chilson[e], Vincenza Snow[e], Alejandro Cane[e], Raymond Farkouh[e]

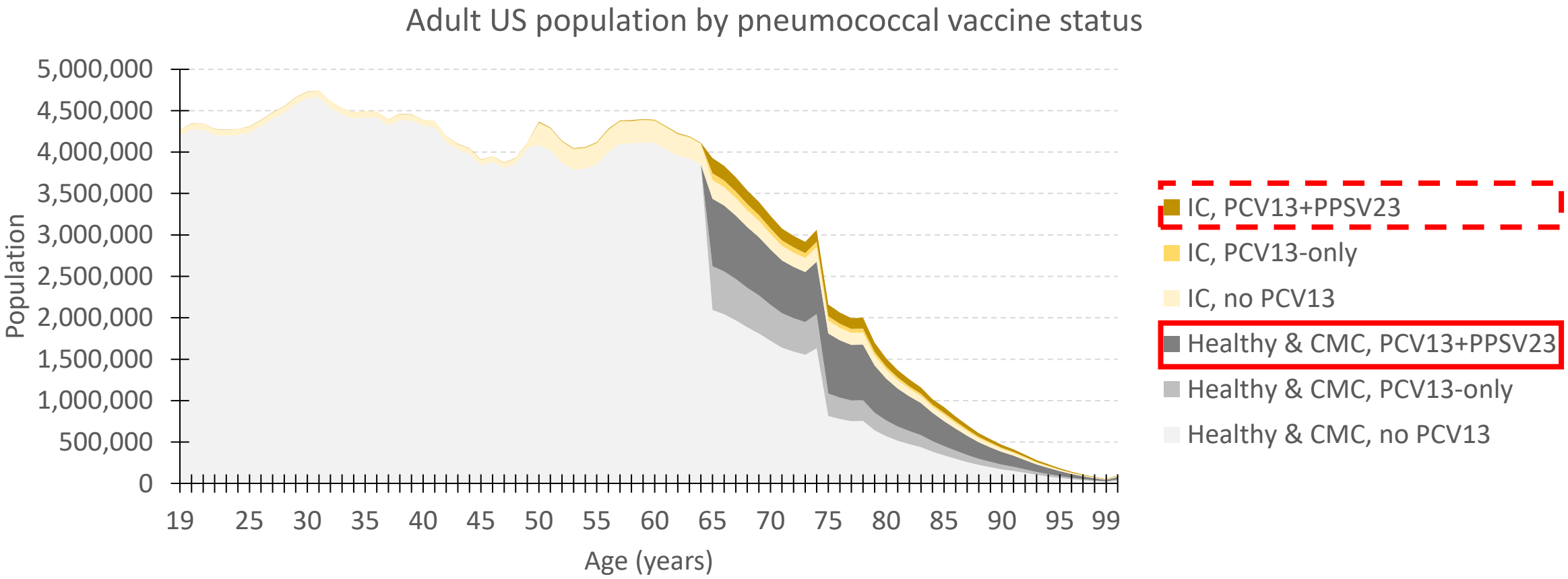
Slide courtesy of Andrew Leidner, CDC

[a.] Tulane University; [b.] CDC; [c.] Merck; [d.] Policy Analysis Inc (PAI); [e.] Pfizer;

Conflict of interest statements

- Andrew J. Leidner: None.
- CDC team: None.
- Pfizer team:
  - Pfizer manufacturers the PCV13 and PCV20 vaccines.
  - PAI team members are funded by Pfizer, other team members are employed by Pfizer.
- Merck team:
  - Merck manufacturers the PPSV23 and PCV15 vaccines.

Comparison will focus on assessment of PCV20 use among adults aged ≥65 years who previously received PCV13 and PPSV23.



Note(s): Population levels by year of age come from US Census, 2021 projections. Portions of population in a risk status (Healthy, CMC, IC) by year of age come from the Pfizer model report. Portions of population with a past pneumococcal vaccinations come from the CDC model report.

Selected key assumptions that can impact Incremental Cost Effectiveness Ratios (ICERs)

Model characteristics	CDC	Pfizer	Merck
Indirect effects from pediatric vaccination	Yes[a]	Yes[a]	**No**
PCV VE vs. serotype 3 disease	9-26%[b]	**60-75%[b]**	5-26%[b]
PPSV23 VE vs NBP	7-20%[c]	**0%**	3-67%[c]
Inpatient NBP case fatality ratios among 65+	3-5%[d]	3-11%[d]	**7-12%[d]**
QALY loss for IPD and inpatient NBP	0.071[e]	**0.130[e]**	0.071[e]

IPD: invasive pneumococcal disease, NBP: non-bacteremic pneumococcal pneumonia, IPD: invasive pneumococcal disease, QALY: quality-adjusted life-year, VE: vaccine effectiveness

a. The CDC and Pfizer models included scenarios where no herd effects from pediatric vaccinations occurred.
b. The PCV ST3 VE assumptions could vary by age, risk group, and disease outcome (IPD, NBP), depending on the model. The CDC model investigated PCV ST3 VE = 0% in scenarios.
c. The CDC model varied PPSV23 NBP VE across 2 risk groups. The Merck model varied PPSV23 NBP VE across 3 risk groups and 23 serotypes of disease.
d. The CDC and Merck model varied inpatient NBP CFRs by age. The Pfizer model varied inpatient NBP CFRs by age and risk group.
e. For added context, a QALY losses of 0.071 and 0.130 could be considered as representing a 32-day hospitalization 59-day hospitalization, respectively, where 20% health-related quality of life is experienced for the duration of hospitalization.

Averted disease burden, PCV20 use[a] vs. no vaccine

65+, PCV13+PPSV23, single cohort

	CDC	Pfizer[b]	Merck[c]
Age of PCV20 vaccination	71 years	72 years	73 years
Time since last vaccination	5 years	7 years	5 years
QALYs gained	375	876	584
Deaths averted	65	293[b]	131
Hospitalization averted	1,252	3,318[b]	1,444
Cases averted	2,628	6,269[b]	3,143

- All models find that health outcomes improve with use of PCV20 (vs. no vaccination).
- Differences in estimated averted outcomes appear to be due to differences in assumptions on VE, CFRs, QALY loss, discounting, and population size.

QALY: Quality-Adjusted Life Year

[a.] These scenarios presented assume a PCV20 vaccination coverage rate of 73% in the CDC and Merck models, and 69% in the Pfizer model.

[b.] In the Pfizer model, QALYs were discounted, but deaths, hospitalizations, and cases were not discounted; QALY losses per hospitalized disease episode were greater than in the other models.

[c.] The Merck model did not assume herd effects.

Cost-effectiveness ratios, PCV20

65+, PCV13+PPSV23, single cohort

	CDC[a]	Pfizer[b]	Merck[c]
Age of PCV20 vaccination	71 and 81 years	72 years	73 years
Time since last vaccination	5 years	7 years	5 years
$/QALYs	**153,000 to 414,000**	**81,000 to 159,000**	**217,000**

- Models appear to be somewhat consistent across several summary measures.
- Lower $/QALY were found in the Pfizer model, which assumed higher PCV-ST3-VE, lower PPSV23-NBP-VE, and higher QALY loss from IPD and inpatient NBP (more severe disease).

[a.] The CDC model assumed PPSV23 was moderately protective against NBP. Range are due to different assumptions on herd effects, and age at PCV20 vaccination (71, 81).

[b.] The Pfizer model assumed QALY losses per IPD and hospitalized NBP case were greater than the other models. Range of estimates is with and without herd effects, higher ICER estimate includes herd effects.

[c.] The Merck model assumed no herd effects. If herd effects were included, the ICER would likely be higher.

Cost-effectiveness ratios, PCV20

65+, PCV13+PPSV23, single cohort

	CDC[a]	Pfizer[b]	Merck[c]
Age of PCV20 vaccination	71 and 81 years	72 years	73 years
Time since last vaccination	5 years	7 years	5 years
$/QALYs	**153,000 to 414,000**	**81,000 to 159,000**	**217,000**

Cost-effectiveness ratios for previous policy questions among adults aged ≥65 years:

- Continuing routine PCV13 + PPSV23 use, 2019[1]
  - CDC model: **$562,000**/QALY
  - Pfizer model: **$199,000**/QALY
- Use of PCV20 only or PCV15 + PPSV23 vs previous recommendations, 2021[2]
  - **Cost-saving** in most scenarios

1. Leidner February 2019 ACIP meeting presentation
2. Leidner September 2021 ACIP meeting presentation

a. The CDC model as

b. The Pfizer model a

herd effects.

c. The Merck model

R estimate includes

Resource Use

- **Is recommending PCV20 for adults who previously received PCV13 a reasonable and efficient allocation of resources?**

Group1. Adults with PCV13 only

- ☐ No
- ☐ Probably no
- ☐ Probably yes
- ☐ Yes
- ☐ Varies
- ☐ Don't know

Yes/Probably Yes

- Benefits of recommending PCV20 still outweigh the cost for adults who have received PCV13 only

Probably No

- The cost-effectiveness analysis findings do not justify the use of resources except for the immunocompromised

Resource Use

- **Is recommending PCV20 for adults who previously received PCV13 a reasonable and efficient allocation of resources?**

Yes/Probably Yes

- Anticipated benefits from adding PCV20 outweigh the cost.

Probably No

- Anticipated added benefits from recommending PCV20 instead of PPSV23 for adults who have already received PCV13 and PPSV23 are not large enough to justify the use of resources.

Varies

- Depends on the time since the last vaccination, age, and underlying conditions.

IC= immunocompromising conditions

Group 2. Adults aged 19–64 years with IC with PCV13+PPSV23

Group 3. Adult… PPSV23

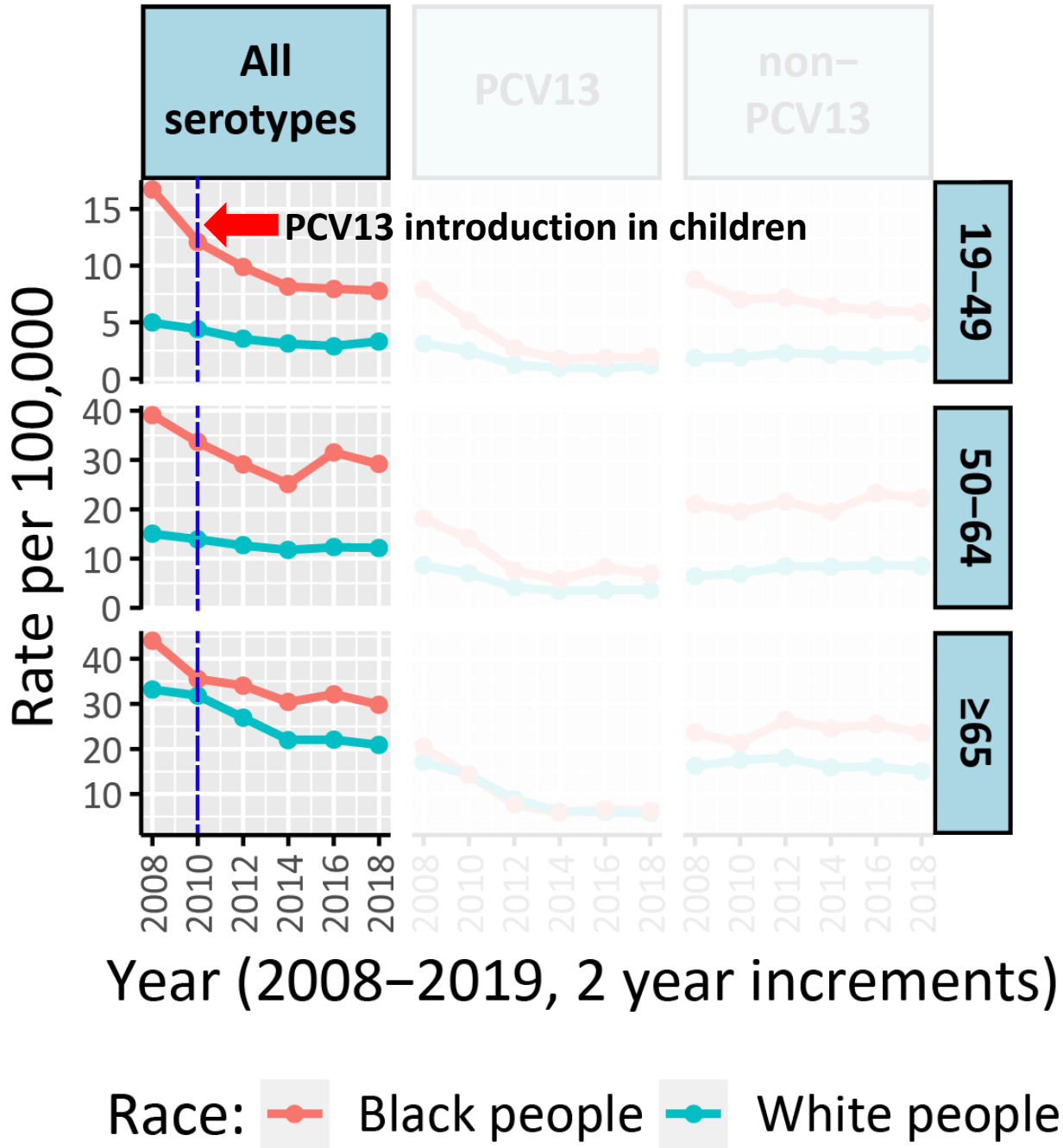
- ☐ No
- ☐ Probably no
- ☐ Probably yes
- ☐ Yes
- ☐ Varies
- ☐ Don't know

Variable responses among Work Group members

Equity

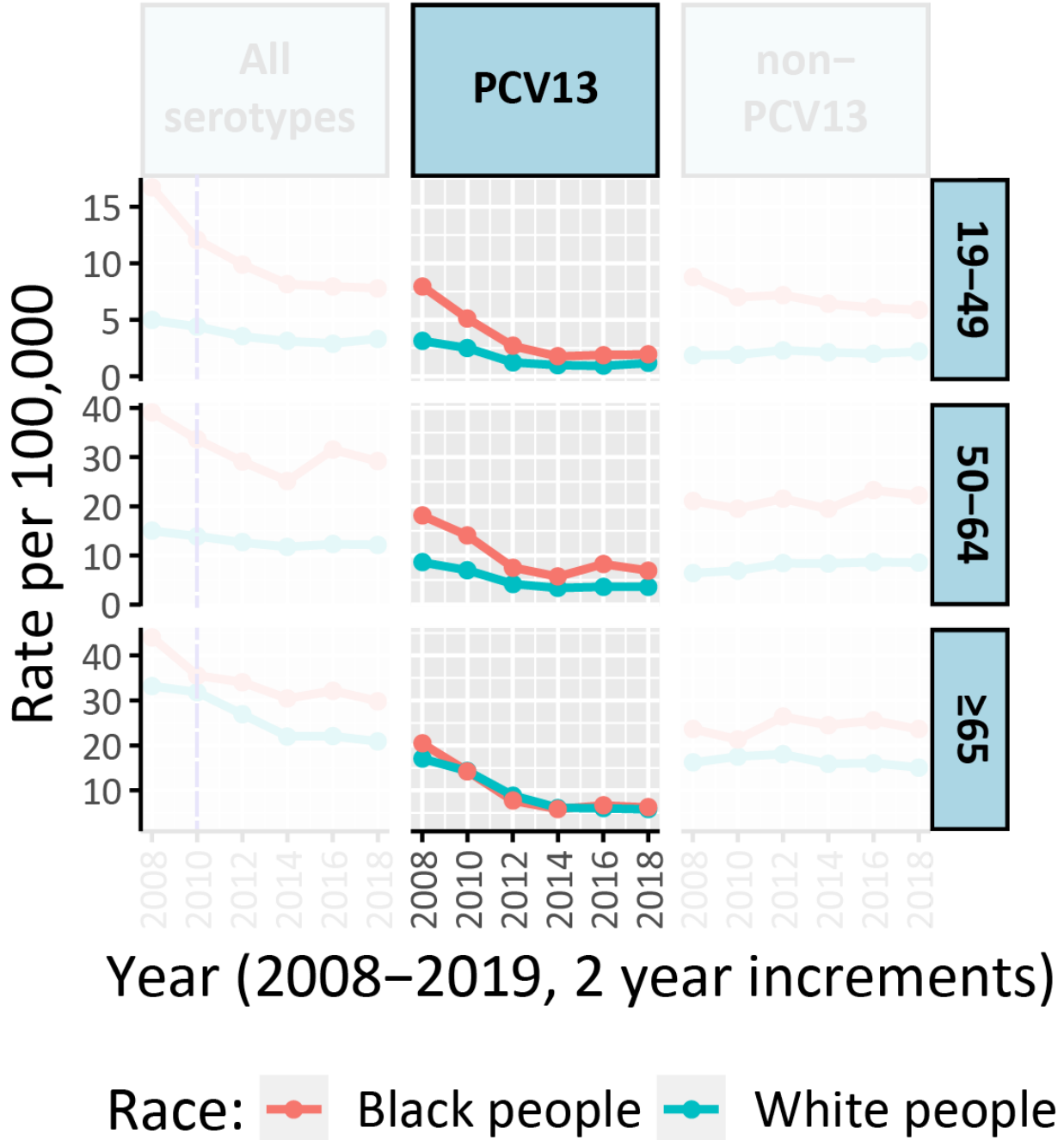
What would be the impact on health equity?

Effect of PCV13 on racial disparities in IPD burden



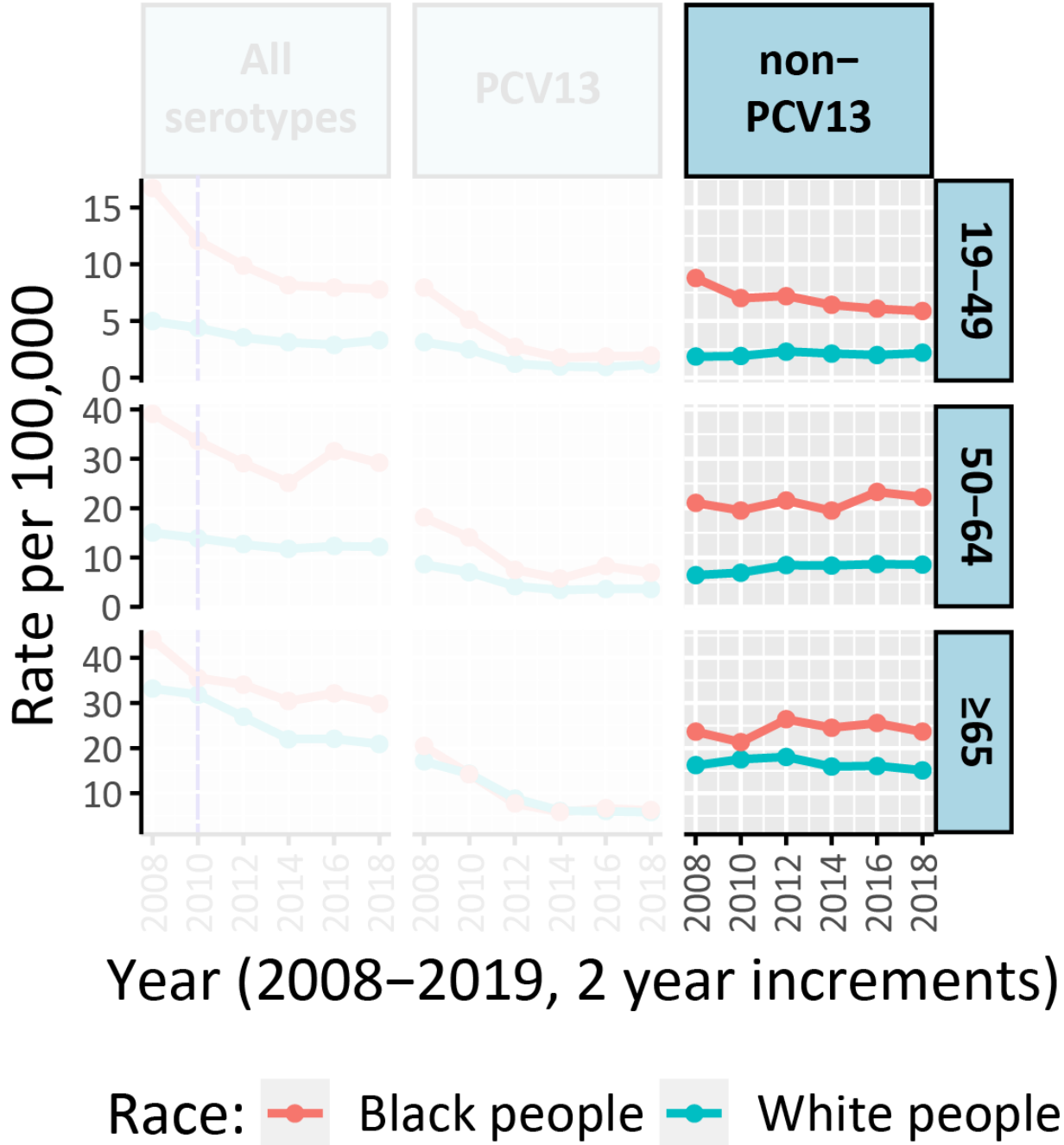
CDC Active Bacterial Core surveillance

Racial disparities in PCV13-type IPD incidence were reduced



CDC ABCs

Racial disparities in non-PCV13-type IPD incidence remain

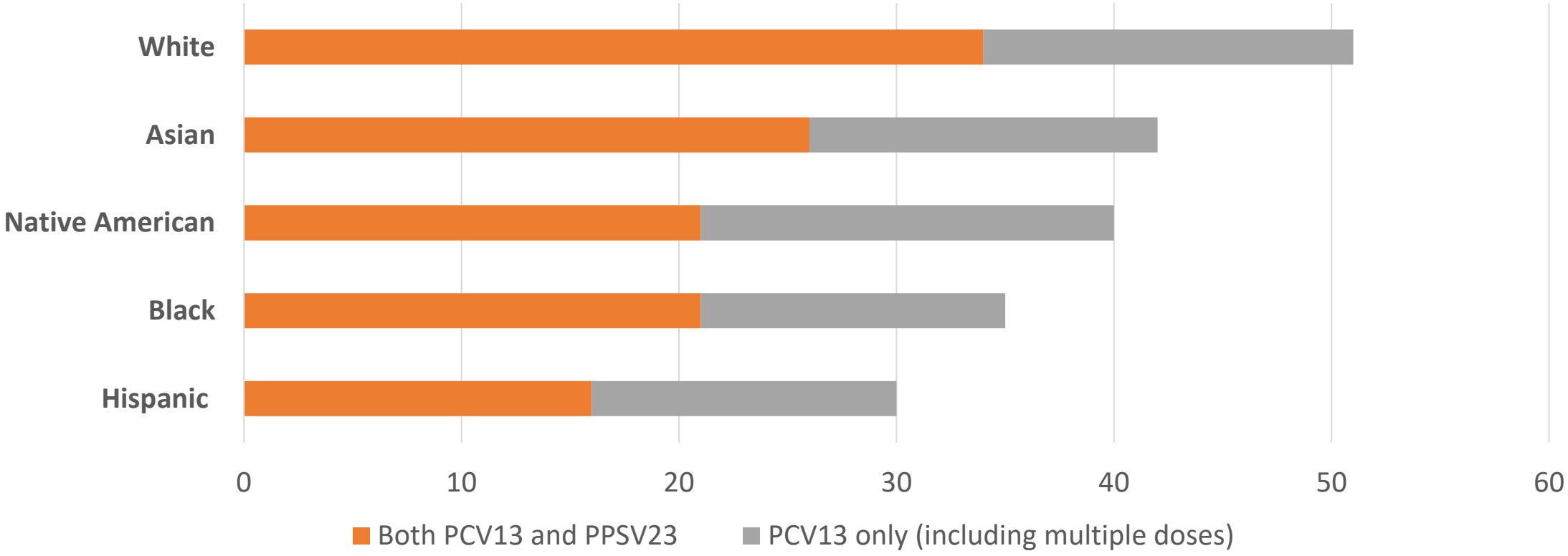


The proportion receiving any pneumococcal vaccine was significantly lower among Hispanics and Asians compared with Whites among adults aged 19–64 years with risk-based pneumococcal vaccine indications[1]

	Sample size	%	(95% CI)
Overall	5,202	23.9	(22.4-25.3)
White	3,514	26.3	(24.5-28.1)
Black	699	23.3	(19.5-27.7)
Hispanic	624	16.7	(13.4-20.6)*
Asian	179	13.8	(8.8-21.2)*
Other	186	23.5	(16.8-31.7)

1. Includes adults without immunocompromising conditions such as diabetes, chronic heart/lung disease, or smokers
*p<0.05 for comparisons with White as the reference.
Vaccination Coverage among Adults in the United States, National Health Interview Survey, 2019–2020 | CDC

Compared to Whites, PCV13 and PCV13 + PPSV23 coverage were lower in other racial/ethnic groups among Medicare beneficiaries aged ≥65 years.



Adapted from https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/pubs-resources/pcv13-medicare-beneficiaries-2010-2019.html

Equity

What would be the impact of recommending PCV20 for adults who previously received PCV13 on health equity?

- ☐ Reduced
- ☐ Probably reduced
- ☐ Probably no impact
- ☐ Probably increased
- ☐ Increased

Variable Work Group interpretation and divided between “probably reduced” and “probably no impact”.

Equity

Increased or probably increased health equity

- Conditions that increase risk of pneumococcal disease are more prevalent in non-White populations
- PCV20 use will decrease remaining disparities in pneumococcal disease burden
- Access to vaccines is likely better for minority populations compared with access to care for the disease

Equity

Probably no impact on health equity

- Vaccine access and utilization are likely to follow existing patterns.
- Limited impact at the population level due to small number of adults aged 19–64 years with IC who received both PCV13 and PPSV23
- Small incremental benefits of PCV20 among adults who already received PCV13 and PPSV23

Reduced/probably reduced health equity

- PCV20 uptake will likely be higher among those with good access to care and could worsen existing disparities

IC=immunocompromising conditions

Feasibility

Are the options feasible to implement?

Feasibility

- **Is recommending PCV20 for adults who previously received PCV13 feasible to implement?**

Group 1. Adults with PCV13 only
Group 2. Adults aged 19–64 years with IC with PCV13+PPSV23

- ☐ No
- ☐ Probably no
- ☐ Probably yes
- ☐ Yes
- ☐ Varies
- ☐ Don't know

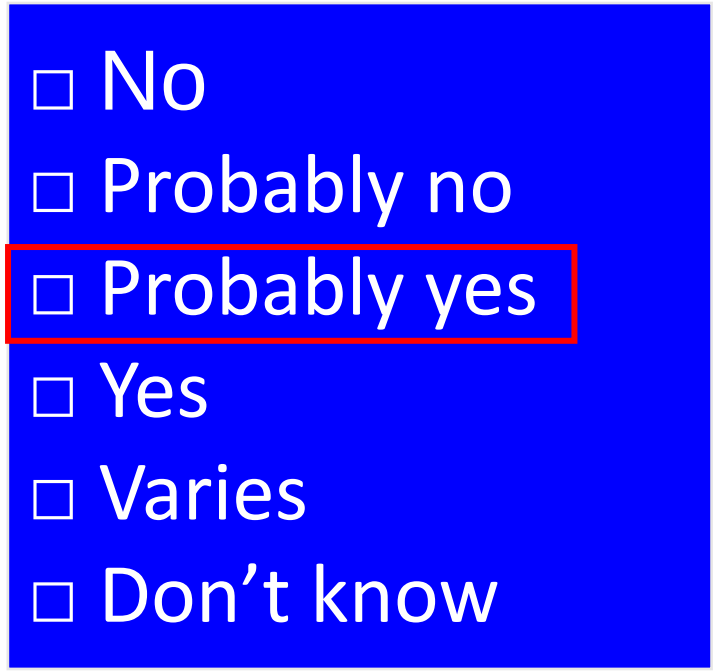
- These are adults who have **not completed** the recommended vaccine series with PPSV23:
  - May simplify recommendations if adults can complete the recommended vaccine series with a dose of PCV20
  - May reduce need to determine vaccination status of patients
- May reduce need to stock multiple types of vaccines

Feasibility

- **Is recommending PCV20 for adults who previously received PCV13 feasible to implement?**

Group 3. Adults aged ≥65 years with PCV13+PPSV23

- These are adults who have **completed** the recommended vaccine series:
  - Adding a dose of PCV20 may complicate the recommendation
  - Compliance with the recommendation may be an issue



Feasibility: additional considerations

- Access to PCV20
  - Poll among Association of Immunization Managers (AIM) members*, Sept 2022:
    - 7 of 22 jurisdictions currently offer PCV20 through their adult immunization program

- Vaccine coverage by insurance
  - Under the Affordable Care Act, new ACIP recommendations required to be covered without cost-sharing starting **one year after** the date the recommendation is issued

*Members are primarily state, local, and territorial immunization program managers/directors

Affordable Care Act Implementation FAQs - Set 12 | CMS

Summary of Work Group Interpretation

EtR Domains	Group1. Adults with PCV13 only	Group 2. IC adults aged 19–64 years PCV13+PPSV23	Group 3. Adults aged ≥65 years PCV13+PPSV23
Public Health Problem	Yes		
Benefits and Harms			
a. Benefits	Moderate		Small/Moderate
b. Harms	Minimal		
c. Benefit>Harm?	Favors intervention		
d. Certainty: effectiveness	3 (low)		2 (moderate)
e. Certainty: safety	3 (low)		2 (moderate)
Values			
a. Desirable>Undesirable?	Probably Yes		
b. Uncertainty?	Probably not important uncertainty or variability		Variable responses among WG members
Acceptability	Probably Yes		
Resource Use	Probably Yes/Yes, but with variability	Variable responses by WG members	
Equity	Split between “probably no impact” and “probably increased health equity”		
Feasibility	Yes		Probably Yes

Summary: Work Group Interpretations

Should PCV20 be recommended for:

Group 1. adults aged ≥19 years who previously received PCV13 only

Group 2. adults aged 19–64 years with IC who previously received PCV13+PPSV23

Group 3. adults aged ≥65 years who previously received PCV13+PPSV23

Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences is *closely balanced* or *uncertain*	Desirable consequences *probably* outweigh undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings	There is insufficient evidence to determine the balance of consequences

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For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

GRADE Summary of Studies: Immunogenicity

Author, year	Study design; population and age	Intervention	N intervention	N comparison	Comparator vaccine	OPA GMT ratios [range (serotype)][1]	Absolute difference in % seroresponders (serotype)[2]	Interpretation	Study limitations (Risk of Bias)
Cannon 2021	RCT (Phase III); U.S. and Swedish adults ≥65 years with prior pneumococcal vaccination	PCV20 (1 dose) after previous PCV13	201 - 243	216 - 246	PCV20 (1 dose), previous PPSV23 vaccine	1.30 (11A) to 2.97 (23F)	-5.10 (6A) to 34.90 (33F)	OPA GMT ratios • Previous PCV13 > previous PPSV23 for all 20 serotypes; significantly higher for 17/20 serotypes %seroresponders • Previous PCV13 > previous PPSV23 for 18/20 serotypes (not for 6A or 19A); significantly higher for 8/18 serotypes	Low
		PCV20 (1 dose) after previous PCV13+PPSV23	102 -121	216-246	PCV20 (1 dose), previous PPSV23 vaccine	0.91 (7F) to 1.93 (23F)	-19.40 (11A) to 1.00 (15B)	OPA GMT ratios • Previous PCV13+PPSV23 > previous PPSV23 for 19/20 serotypes (not for 7F); significantly higher for 23F %seroresponders • Previous PCV13+PPSV23 > previous PPSV23 for 3/20 serotypes (14, 15B, 33F); none significantly higher	
B7471004	RCT (Phase III); U.S. adults ≥65 years with prior pneumococcal vaccination; received influenza vaccination 1 month prior to PCV20	PCV20 (1 dose) after previous PCV13	123 - 146	80 – 94	PCV20 (1 dose), previous PPSV23 vaccine	1.15 (5) to 2.60 (23F)	-10.4 (4) to 22.7 (15B)	OPA GMT ratios • Previous PCV13 > previous PPSV23 for all 20 serotypes; significantly higher for 6/20 serotypes %seroresponders • Previous PCV13 > previous PPSV23 for 13/20 serotypes; significant for 15B	
		PCV20 (1 dose) after previous PCV13+PPSV23	328 -388	80 - 94	PCV20 (1 dose), previous PPSV23 vaccine	0.83 (11A) to 2.26 (23F)	-12.90 (4) to 7.40 (23F)	OPA GMT ratios • Previous PCV13+PPSV23 > previous PPSV23 for 15/20 serotypes; significantly higher for 6B, 18C, and 23F %seroresponders • Previous PCV13+PPSV23 > previous PPSV23 for 6/20 serotypes; none significantly higher	Low

1. Ratio calculated as [GMT (PCV20)]/[GMT (comparator vaccine)]; blood draws occurred 1 month post-dose.
2. Seroresponse: percentage of participants with ≥4-fold rise in pneumococcal OPA titers from before to after 1 month vaccination.

GRADE Summary of Studies: Safety

Author, year	Study Design; population and age	N intervention	N comparison	Comparator vaccine	Absolute % difference (% SAE PCV20 – % SAE comparator)*	N related to vaccine	Study limitations (Risk of Bias)
Cannon 2021	RCT (Phase III); U.S. and Swedish adults ≥65 years with previous PCV13 vaccination	246	127	PPSV23, previous PCV13	0.8%	0	Low
	RCT (Phase III); U.S. and Swedish adults ≥65 years with previous PCV13 + PPSV23 vaccination	125	0	none	1.6%	0	

*Reported serious adverse events include those that occurred after dose 1 through completion of study participation.

Model overview, selected key assumptions

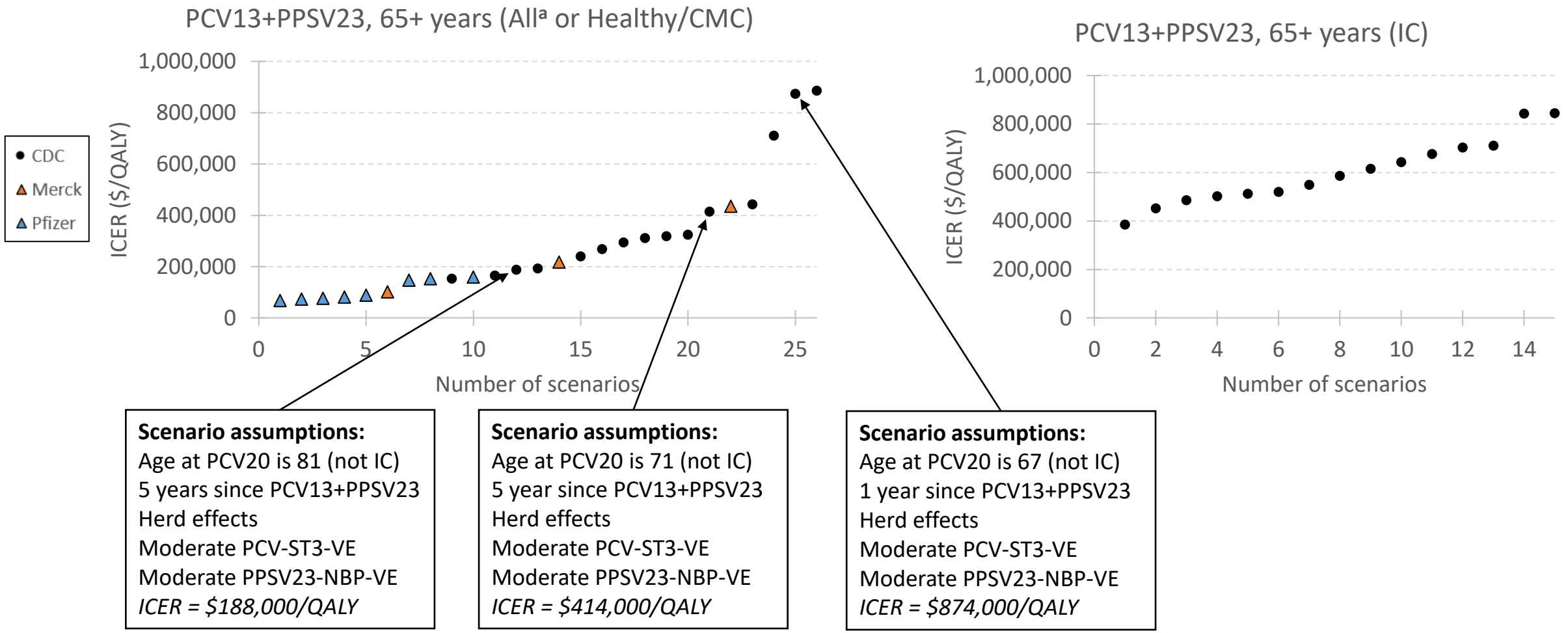
Model characteristics	CDC	Merck	Pfizer
Model type	Single cohort[a], lifetime	Single cohort[a], lifetime	Multi-cohort[b], lifetime (SA: Single cohort)
Perspective	Societal[c]	Health care[c]	Health care
Adverse events	No	No	No
Sensitivity analyses	Univariate, scenario & probabilistic sensitivity analyses	Univariate, scenario & probabilistic sensitivity analyses	Univariate & scenario analyses
Time since previous vaccination	1, 5, 10 years	5 years (SA: 1 and 8 years)	7 years (SA: 5 and 9 years)
Age in years at PCV20 vaccination	65+ cohort: 66, 71, 75, 76, 77, 80, 81	65+ cohort: 73	All ages (65+ average: 75)

[a.] In any given scenario, the CDC and Merck models start the model with a single-aged cohort of individuals, not a full population composed of many different ages. For this reason, these models have one specific starting age. For example, a 70-year-old cohort may be used to represent and estimate values in the 65+ age group.

[b.] The Pfizer model base case used a multi-cohort, but single cohort results were provided in a scenario.

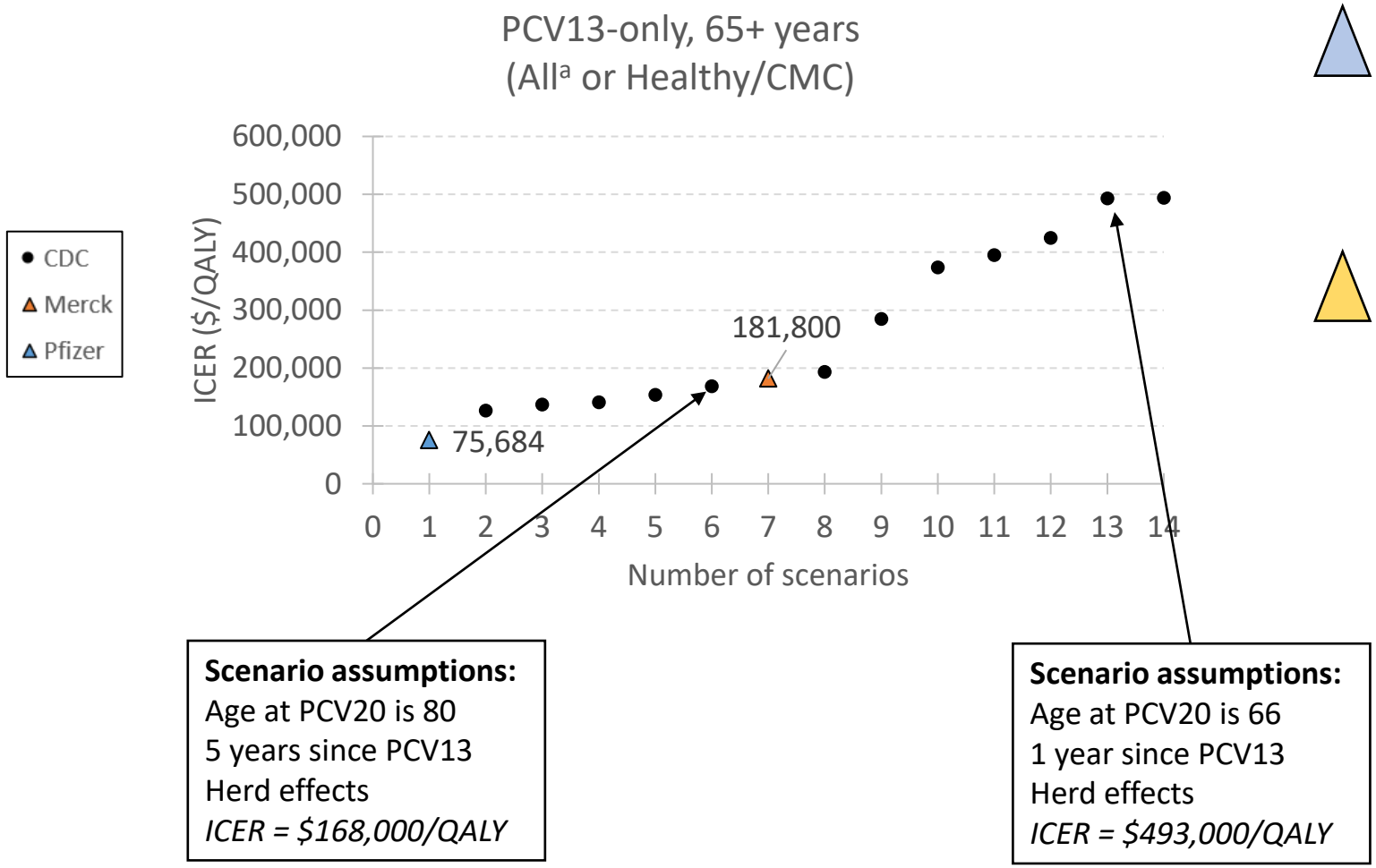
[c.] The CDC model includes one societal perspective component, travel cost added to the cost of vaccine administration. The Merck model provide a scenario using the societal perspective that was similar to the CDC model.

PCV13+PPSV23, summary of economic analyses among 65+ population



[a] Most results from the Pfizer model did not separate IC and healthy/CMC populations, and did not separate 19-64 and 65+ populations. So the Pfizer scenarios capture an average ICER that is weighted by the population size of the different subgroups, where the largest of the subgroups is PCV13+PPSV23 recipients who are 65+ years.

PCV20 for adults aged ≥65 years with **PCV13 only** ICER range: **$76,000** to **$493,000** per QALY gained



Pfizer model: $75,684/QALY
- Includes adults aged 19–64 years with IC
- PCV20 given 7 years after PCV13 vs. no additional vaccine

Merck model: $181,800/QALY
- PCV20 given at age 73 years, 5 years after PCV13 vs. no additional vaccine

[a.] Most results from the Pfizer model did not separate IC and healthy/CMC populations, and did not separate 19-64 and 65+ populations. These results represent an average ICER that is weighted by the population size of the different subgroups, where the largest of the subgroups is PCV13+PPSV23 recipients who are 65+ years.