Evidence to Recommendation Framework: Use of 15-valent and 20-valent Pneumococcal Conjugate Vaccines in Adults

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ACIP meeting

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Evidence to Recommendation (EtR) framework

- To provide **structure** for describing information considered in moving from evidence to ACIP vaccine recommendations.
- To provide **transparency** on the impact of additional factors on deliberations when considering recommendations.

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?
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?

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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=PCV15 or PCV20 use

Current ACIP Pneumococcal Vaccine Recommendations by Age and Risk Groups

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

PCV13: 13-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
Immunocompromising conditions **Immunocompromised adults**	Both PCV13* and PPSV23, repeat PPSV23 after 5 years	Both PCV13* and PPSV23

PCV13: 13-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
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Immunocompromising conditions	Both PCV13* and PPSV23, repeat PPSV23 after 5 years	Both PCV13* and PPSV23

Immunocompetent adults

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Current ACIP Pneumococcal Vaccine Recommendations by Age and Risk Groups

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None of the conditions listed below	No recommendation	PCV13* based on shared clinical decision making, PPSV23 for all
Chronic medical conditions† (CMC) Adults with CMC	PPSV23	PCV13* based on shared clinical decision making, PPSV23 for all
Cochlear implant, CSF leak	Both PCV13* and PPSV23	Both PCV13* and PPSV23
Immunocompromising conditions	Both PCV13* and PPSV23, repeat PPSV23 after 5 years	Both PCV13* and PPSV23

PCV13: 13-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
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Questions	1. Should PCV15 be routinely recommended to US adults ≥65 years? 2. Should PCV15 be routinely recommended to US adults ≥65 years in series with PPSV23?
Population	US adults aged ≥65 years
Intervention	**1. One dose of PCV15** **2. One dose of PCV15 followed by PPSV23**
Comparison	• PCV13 followed by PPSV23 (immunocompromised adults*) • PPSV23** (immunocompetent adults*)
Outcomes	VT-IPD, VT-NBPP, deaths, serious adverse events

VT: vaccine-type, IPD: invasive pneumococcal disease, NBPP: non-bacteremic pneumococcal pneumonia

*immunocompromised adults include adults with immunocompromising condition (chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, congenital or acquired asplenia, sickle cell disease, or other hemoglobinopathies), CSF leak, or cochlear implant; immunocompetent adults are those without these conditions.

**PCV13 recommended based on shared clinical decision making for immunocompetent adults ≥65 years

Questions	Should PCV20 be routinely recommended to US adults…	
	≥50 years?	≥65 years?
Population	US adults aged **≥50 years**	US adults aged **≥65 years**
Intervention	One dose of PCV20	
Comparison	PCV13 followed by PPSV23 (immunocompromised*)	
	PPSV23 only (immunocompetent* adults aged ≥65 years**)	
	PPSV23 only (50–64yrs, CMC†)	**NA**
	No vaccination (50–64yrs, no indications)	**NA**
Outcomes	VT-IPD, VT-NBPP, deaths, serious adverse events	

CMC: chronic medical conditions, VT: vaccine-type, IPD: invasive pneumococcal disease, NBPP: non-bacteremic pneumococcal pneumonia

*immunocompromised adults include adults with immunocompromising condition (chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, congenital or acquired asplenia, sickle cell disease, or other hemoglobinopathies), CSF leak, or cochlear implant; immunocompetent adults are those without these conditions.

†CMC includes chronic heart/lung/liver disease, cirrhosis, diabetes mellitus, alcoholism, and cigarette smoking

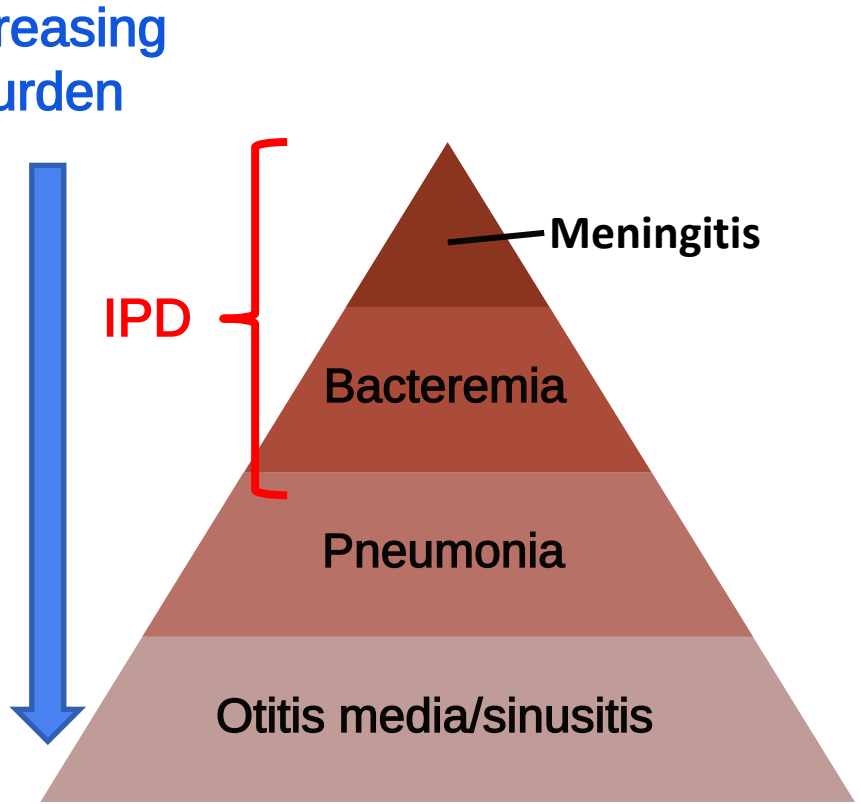
**PCV13 recommended based on shared clinical decision making for immunocompetent adults ≥65 years

Public Health Problem

Is pneumococcal disease of public health importance?

Pneumococcal disease

- Invasive pneumococcal disease (IPD)
  - e.g., meningitis, bacteremia, bacteremic pneumonia
- Non-invasive disease
  - e.g., non-bacteremic pneumonia



Estimated burden of pneumococcal disease in U.S. adults aged ≥19 years

- In 2018, **~30,000** IPD cases and **~3,500** IPD deaths occurred[1]
- In 2017, **~103,000** hospitalized pneumococcal pneumonia cases occurred[2]
  - **~40 to 55%** of the burden in adults aged **≥65 years**
  - **~80%** of the burden in adults aged **≥50 years**

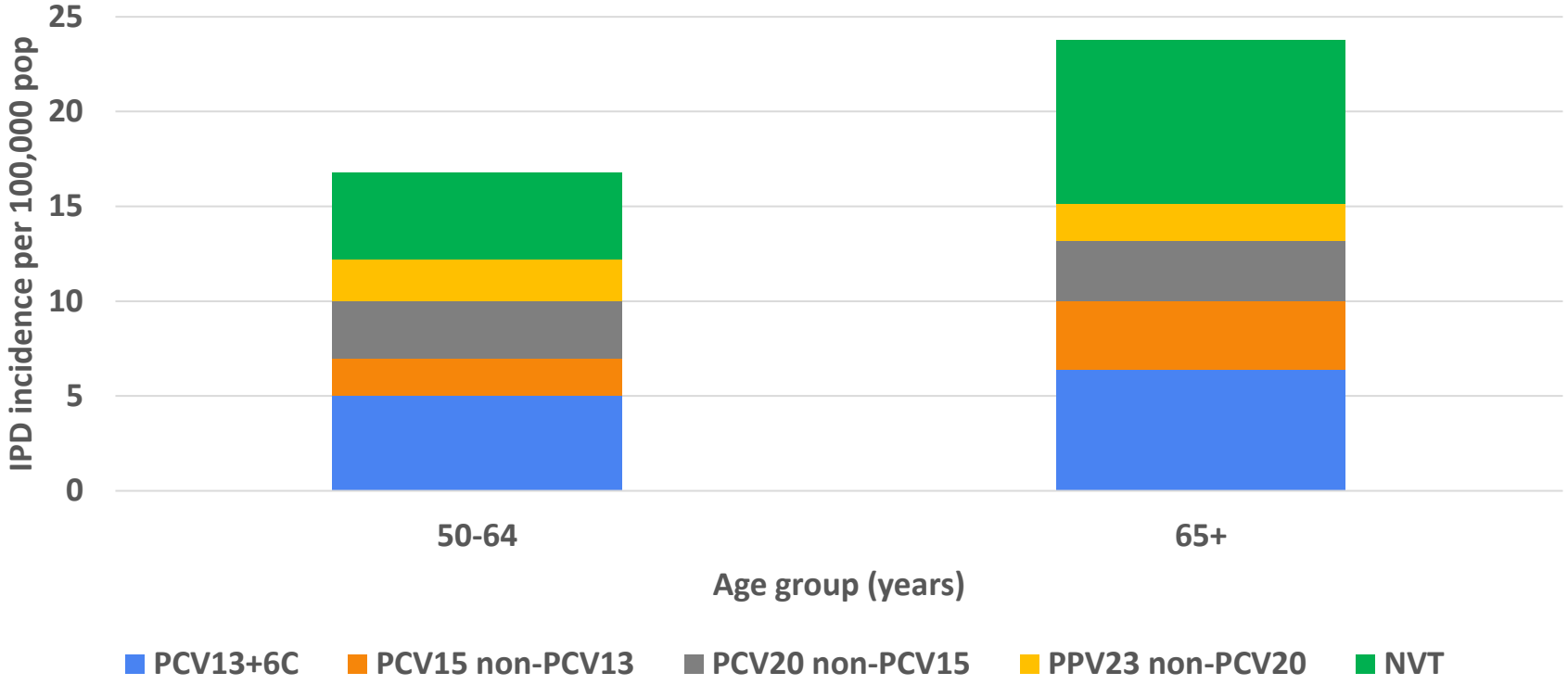
1. CDC ABCs, 2018, 2. CDC SNiPP, 2017

Impact of Pneumococcal Conjugate Vaccine (PCV) Use in the United States to date

- Introduction of **PCV in children** reduced vaccine-preventable pneumococcal disease burden in adults
  - Includes adults at increased risk of pneumococcal disease

- Population level impact after PCV13 was recommended for all adults aged ≥65 years in 2014:
  - Reductions in PCV13-type **pneumococcal pneumonia** incidence documented
  - No impact on PCV13-type **invasive pneumococcal disease (IPD)** observed
  - Most common remaining PCV13-type disease is due to **serotype 3**

IPD Incidence by Serotype Group and Age Group, ABCs 2018–2019



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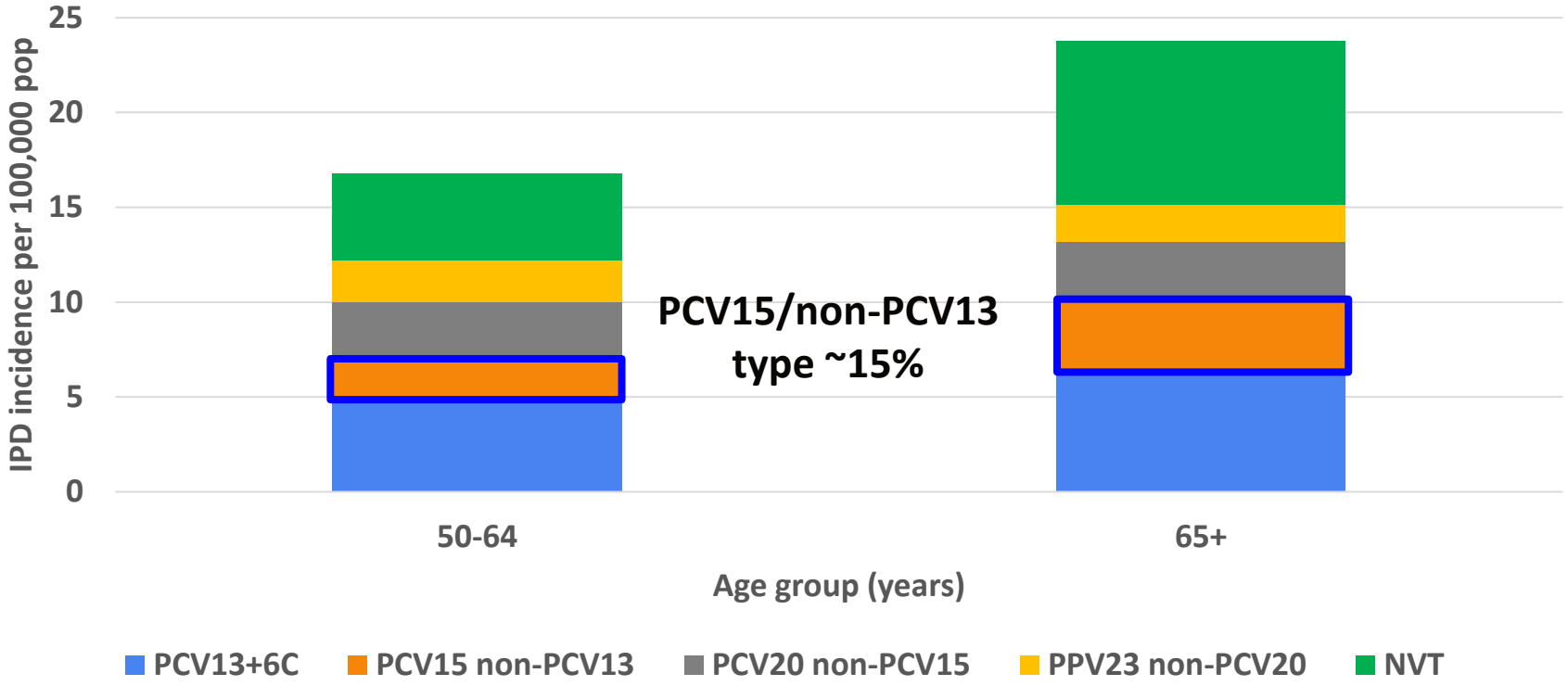

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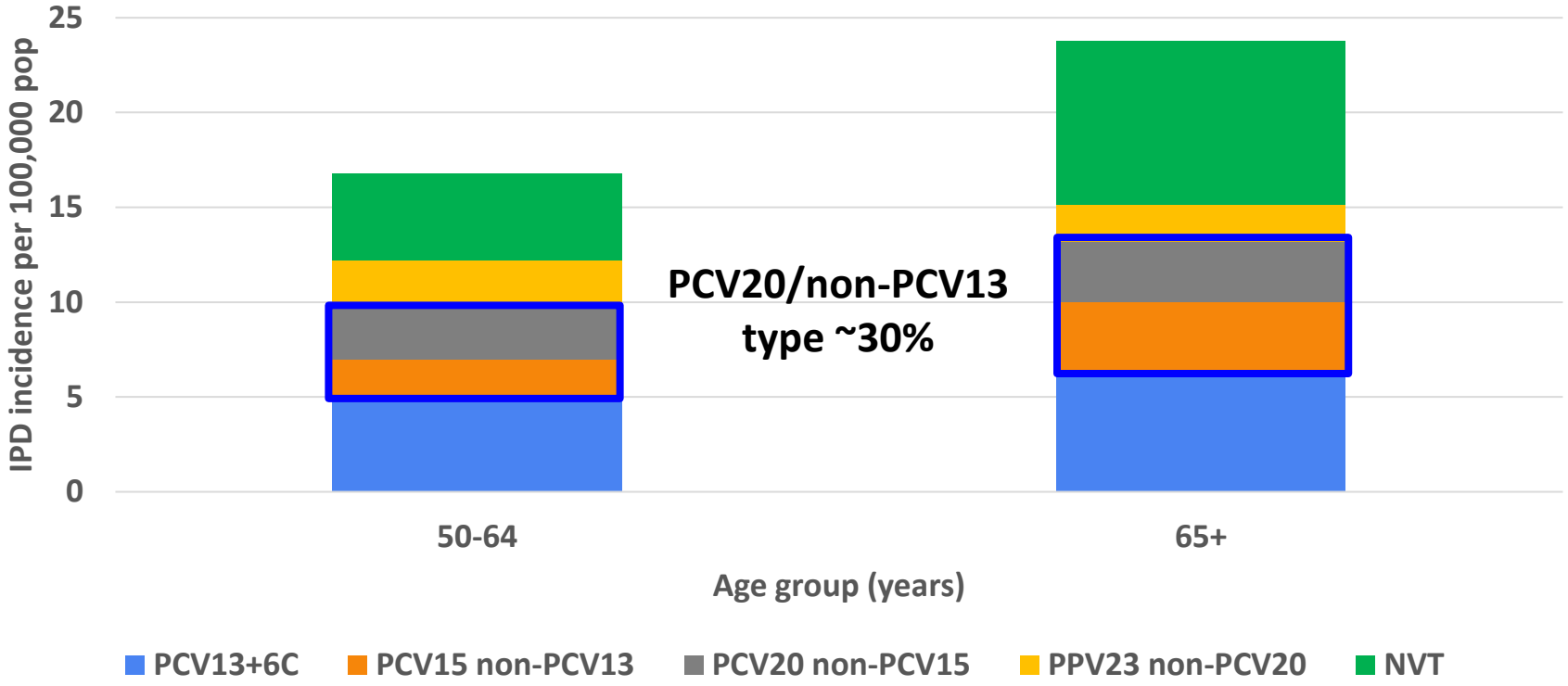


Public Health Problem

Is pneumococcal disease of public health importance in adults aged ≥50 years?

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

Benefits and Harms

How substantial are the desirable anticipated effects?

- How substantial is the anticipated effect for:

    Vaccine-type IPD

    Vaccine-type non-bacteremic pneumococcal pneumonia

    Vaccine-type death?

Benefits and Harms

How substantial are the undesirable anticipated effects?

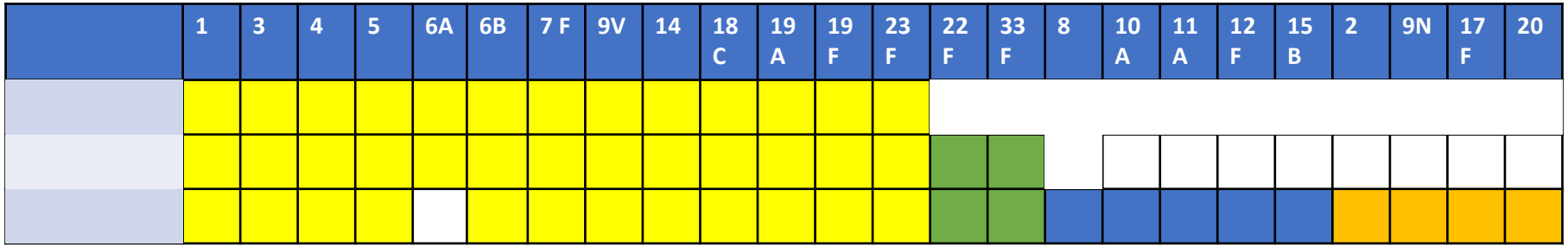
- How substantial is the anticipated effect for serious adverse events?

Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

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

Serotypes Contained in Pneumococcal Vaccines



Shared serotypes:

- PCV15 vs. PCV13=13 serotypes
- PCV15 vs. PPSV23=14 serotypes

Summary of Available Evidence from PCV15 studies: Benefits

- **PCV15 vs. PCV13**:
  - GMTs and % seroresponders higher for PCV15 recipients for some serotypes shared with PCV13
  - In one phase 3 RCT, PCV15 met non-inferiority criteria for 13/13 serotypes based on GMT ratio; serotype 3 response met the superiority criteria.

Moderate certainty of evidence

- **PCV15 vs. PPSV23**: In one phase 2 RCT, PCV15 met non-inferiority criteria for 14/14 serotypes based on GMT ratios

Moderate certainty of evidence

Please see GRADE summary tables for details

Benefits and Harms

How substantial are the desirable anticipated effects?

- PCV15 use for persons aged ≥65 years

□ Minimal
□ Small
□ Moderate
□ Large
□ Varies
□ Don’t know

Benefits and Harms

How substantial are the desirable anticipated effects?

- PCV15 use for persons aged ≥65 years

□ Minimal
□ Small
□ Moderate
□ Large
□ Varies
□ Don't know

- PCV15 contains 2 additional serotypes vs. PCV13
- No PPSV23→ lose coverage for 9 serotypes
- Recommendation with a single vaccine may achieve higher vaccine coverage

Summary of Available Evidence, PCV15-PPSV23 series

- **PCV15-PPSV23 vs. PCV13-PPSV23 immunogenicity**:
  - In three phase 3 RCTs, GMTs and % seroresponders were higher in PCV15-PPSV23 recipients for some shared serotypes

Moderate certainty of evidence

Please see GRADE summary tables for details

Benefits and Harms

How substantial are the desirable anticipated effects?

- PCV15 use for persons aged ≥65 years in series with PPSV23

□ Minimal
□ Small
□ Moderate
□ Large
□ Varies
□ Don't know

- PCV15 contains 2 additional serotypes vs. PCV13

Summary of Available Evidence from PCV15 studies: Harms

- **PCV15 vs. PCV13, PPSV23 Serious Adverse Events (SAEs):**
  - No SAEs were associated with the vaccines

Moderate certainty of evidence

- **PCV15-PPSV23 vs. PCV13-PPSV23 SAEs**:
  - No SAEs were associated with the vaccines

Moderate certainty of evidence

Please see GRADE summary tables for details

Benefits and Harms

How substantial are the undesirable anticipated effects?

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

- PCV15 use for persons aged ≥65 years
- PCV15 use for persons aged ≥65 years in series with PPSV23

Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

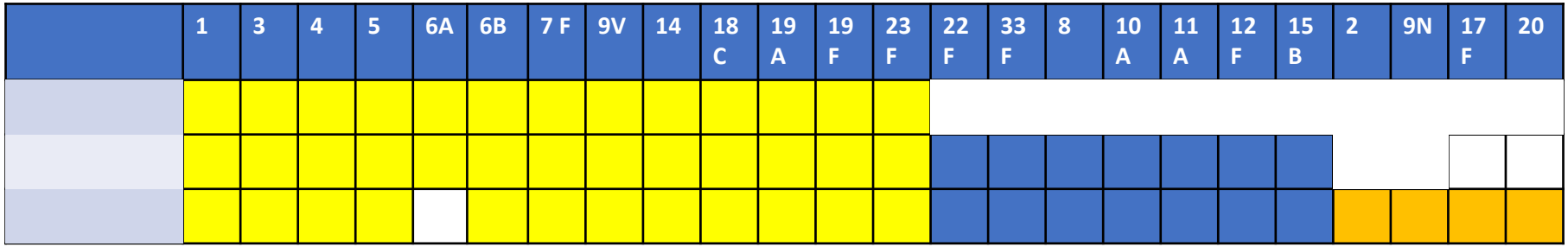
- What is the balance between the desirable effects relative to the undesirable effects?

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

***Intervention:**

- PCV15 use for persons aged ≥65 years
- PCV15 use for persons aged ≥65 years in series with PPSV23

Serotypes Contained in Pneumococcal Vaccines



Shared serotypes:

- PCV20 vs. PCV13=13 serotypes
- PCV20 vs. PPSV23=7 serotypes not included in PCV13

Summary of Available Evidence from PCV20 studies: Benefits

- **PCV20 vs. PCV13**:
  - In one phase 2 RCT, GMT and % seroresponders in PCV20 recipients lower for some shared serotypes.
  - In one phase 3 RCT, PCV20 met noninferiority criteria for all 13/13 shared serotypes by GMT ratio. ***Moderate certainty of evidence***

- **PCV20 vs. PPSV23**:
  - In one phase 2 RCT, GMT and % seroresponders in PCV20 recipients higher for some shared serotypes.
  - In one phase 3 RCT, PCV20 met noninferiority criteria for 6/7 shared serotypes (not met for serotype 8) based on GMT ratio; higher %seroresponders in 6/7 serotypes. ***Moderate certainty of evidence***

Please see GRADE summary tables for details

Summary of Available Evidence from PCV20 studies: Benefits

- **Age 50–59 years vs. 60–64 years**:
  - Noninferiority criteria met for all 20 serotypes in phase 3 RCT.

Please see GRADE summary tables for details

Benefits and Harms

How substantial are the desirable anticipated effects?

- PCV20 use for persons aged ≥50 years

□ Minimal
□ Small
□ Moderate
□ Large
□ Varies
□ Don't know

- Some concerns about lower immunogenicity observed in PCV20 vs. PCV13
- Noninferiority criteria largely met
- Recommendation with single vaccine likely to improve vaccine coverage
- Improved vaccine coverage in 50–64-year-olds

Benefits and Harms

How substantial are the desirable anticipated effects?

- PCV20 use for persons aged ≥65 years

□ Minimal
□ Small
□ Moderate
□ Large
□ Varies
□ Don't know

- Public health impact from the cost-effectiveness analysis deemed to be large
- Some concerns about lower immunogenicity observed in PCV20 vs. PCV13
- Additional impact from this age-based recommendation alone may not be large

Summary of Available Evidence from PCV20 studies: Harms

- **PCV20 vs. PCV13**
  - No vaccine-related SAEs reported.

Moderate certainty of evidence

- **PCV20-saline vs. PCV13-PPSV23**
  - No vaccine-related SAEs reported.

Moderate certainty of evidence

Please see GRADE summary tables for details

Benefits and Harms

How substantial are the <u>undesirable</u> anticipated effects?

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

- PCV20 use for persons aged ≥50 years
- PCV20 use for persons aged ≥65 years

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:**

- PCV20 use for persons aged ≥50 years
- PCV20 use for persons aged ≥65 years

Work Group Interpretation: Benefits and Harms

EtR Domains	PCV15, ≥65 years	PCV15 +PPSV23, ≥65 years	PCV20, ≥50 years	PCV20, ≥65 years
Public Health Problem	Yes			
Benefits and Harms				
a. Benefits	Small	Small	Large	Moderate-Large
b. Harms	Minimal			
c. Benefit>Harm?	Favors intervention			
d. Overall certainty: effectiveness	Moderate			
e. Overall certainty: safety	Moderate			

Note: Each policy question is compared to the current vaccine recommendation

Work Group Interpretation: Benefits and Harms

EtR Domains	PCV15, ≥65 years	PCV15 +PPSV23, ≥65 years	PCV20, ≥50 years	PCV20, ≥65 years
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d. Overall certainty: effectiveness	Moderate			
e. Overall certainty: safety	Moderate			

Note: Each policy question is compared to the current vaccine recommendation

Values and Preferences

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

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

Values: Characteristics of Included Studies

Study	Study period	Methods	Population
Albright 2017	2015	12 focus group discussions	Adult patients of a safety net system including 8 FQHCs in Denver metropolitan area (N=687, **78% White, 66% Hispanic**)
Lu 2017	2017	Internet panel survey	Nationally representative sample of U.S. adults aged ≥19 years (N=2,683)
Brown 2017*	2012	Mixed-method telephone survey	Northwestern Medical Faculty Foundation General Internal Medicine Clinic, **Black patients** aged ≥65 years with a **documented refusal** of PPSV23 (N=40)
Kaljee 2017*	2013-2014	8 focus group discussions	Patients aged ≥65 years, patients at primary care clinics that are part of the Henry Ford Health System (N=48, 92.9% female, **100% Black**)

*Included in 2019 EtR; FQHC= Federally Qualified Health Center

Key Findings and Limitations

- Awareness of pneumococcal vaccines lower compared to influenza vaccines, and may be variable by age or race/ethnicity
- Awareness of pneumonia* high, but perceived susceptibility may be low
- None were on PCV15 or PCV20
- Findings may not be generalizable to the US population

*used as an example of disease that the vaccine prevents

Values and Preferences

Criterion 1: Do adults feel that the desirable effects from vaccination are large relative to undesirable effects?

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

- PCV15 use for persons aged ≥65 years
- PCV15 use for persons aged ≥65 years in series with PPSV23
- PCV20 use for persons aged ≥50 years
- PCV20 use for persons aged ≥65 years

Values and Preferences

Criterion 1: Do adults feel that the desirable effects from vaccination are large relative to undesirable effects?

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

- Pneumococcal vaccines have been available and have achieved moderate coverage
- Pneumococcal disease can result in serious consequences

Values and Preferences

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

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

Work Group Interpretation: Values and Preferences

EtR Domains	PCV15, ≥65 years	PCV15 +PPSV23, ≥65 years	PCV20, ≥50 years	PCV20, ≥65 years
Public Health Problem	Yes			
Benefits and Harms				
a. Benefits	Small	Small	Large	Moderate-Large
b. Harms	Minimal			
c. Benefit>Harm?	Favors intervention			
d. Overall certainty: effectiveness	Moderate			
e. Overall certainty: safety	High			
Values				
a. Desirable >Undesirable?	**Probably yes**			
b. Uncertainty?	**Probably not important uncertainty or variability**			

Note: Each policy question is compared to the current vaccine recommendation

Acceptability

Is the option acceptable to key stakeholders?

Acceptability: Review of Available Evidence

- Healthcare Provider (HCP) Surveys
  - Vaccine Policy Collaborative Initiative (VPCI) Survey on **PCV13 shared clinical decision-making (SCDM)** recommendation (internet and mail)[1]
    - Primary care internists and family practice physicians
  - Pfizer's survey on HCP preferences web-based survey[2]
    - Primary care physicians, physician assistants, nurse practitioners, pharmacists
    - Asked to rank **hypothetical vaccine recommendations** for adults aged ≥65 years and adults 19–64 years with underlying conditions

1. Hurley et al. 2021; 2. Pfizer HCP preference survey 2021

Acceptability: Review of Available Evidence

- Association of Immunization Managers (AIM) web-based survey
    - Primarily immunization program managers/directors
    - Option to provide narrative responses

Key Findings

- Confusion about current **shared clinical decision-making** for PCV13 use[1,2]
- Preference for a **simplified** pneumococcal vaccine recommendation[2,3]
  - Same recommendation across age- and risk-groups[3]
- Mixed responses on use of **PCV in series with PPSV23**
  - Routine PCV-PPSV23 use was the most preferred among provided options in one survey[3]
  - Implementation/communication challenges, health equity issues (in hard-to-reach population) expressed in another[2]

1. Hurley et al. 2021; 2. AIM survey 2021; 3. Pfizer HCP preference survey 2021

Key Findings

- Mixed responses on **lowering age-based recommendation**
  - Respondents supportive of lowering the age-based recommendation in one survey[3]
  - Communication challenges, concerns for lower coverage in adults 50–64 yrs (less likely to seek primary health care) and potential for disparity by insurance status expressed in another[2]

1. Hurley et al. 2021; 2. AIM survey 2021; 3. Pfizer HCP preference survey 2021

Acceptability

Is recommending PCV15 for persons aged ≥65 years acceptable to key stakeholders?

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

Acceptability

Is recommending PCV15 for persons aged ≥65 years in series with PPSV23 acceptable to key stakeholders?

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

Acceptability

Is recommending PCV15 for persons aged ≥65 years in series with PPSV23 acceptable to key stakeholders?

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

- PCV has been recommended in series with PPSV23
- Logistical challenges associated with use of 2 different vaccines in series

Acceptability

Is recommending PCV20 for persons aged ≥50 years acceptable to key stakeholders?

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

- Changing the target age may cause some initial implementation challenges
- May provide an opportunity to improve coverage in adults aged <65 years with underlying conditions
- Recommendation consisting of one vaccine is likely more acceptable than the current recommendation

Acceptability

Is recommending PCV20 for persons aged ≥65 years acceptable to key stakeholders?

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

Work Group Interpretation: Acceptability

EtR Domains	PCV15, ≥65 years	PCV15 +PPSV23, ≥65 years	PCV20, ≥50 years	PCV20, ≥65 years
Public Health Problem	Yes			
Benefits and Harms				
a. Benefits	Small	Small	Large	Moderate-Large
b. Harms	Minimal			
c. Benefit>Harm?	Favors intervention			
d. Overall certainty: effectiveness	Moderate			
e. Overall certainty: safety	High			
Values				
a. Desirable>Undesirable?	Probably yes			
b. Uncertainty?	Probably not important uncertainty or variability			
Acceptability	**Probably yes**	**Varies**	**Probably yes**	**Yes**

Note: Each policy question is compared to the current vaccine recommendation

Resource Use

Is the option a reasonable and efficient allocation of resources?

Cost-Effectiveness Analysis on PCV15 Policy Questions

	19–64 years with CMC and immunocompromising conditions	All ≥65 years
Option 1 **"PCV15, ≥65 years"**	**PCV15**	**PCV15**
Option 2 **"PCV15 + PPSV23, ≥65 years"**	**PCV15+PPSV23**	**PCV15+PPSV23**

Cost-Effectiveness Analysis on PCV20 Policy Questions

	19–49 years with CMC and immunocompromising conditions	All ≥50 years
Option 1 "PCV20, ≥50 years"	**PCV20**	**PCV20**
	19–64 years with CMC and immunocompromising conditions	**All ≥65 years**
Option 2 "PCV20, ≥65 years"	**PCV20**	**PCV20**

- Options compared to current pneumococcal vaccine recommendations.

Cost $/QALY Saved by Scenarios (Stoecker Model)

	PCV15, ≥65 years	PCV15 + PPSV23, ≥65 years (ICER)	PCV20, ≥50 years	PCV20, ≥65 years
Base Case	**158,025**	**+462,604**	**Cost-saving**	**Cost-saving**
One-way sensitivity analyses				
Indirect effects from children	507,445	+483,075	24,625	Cost-saving
PCV VE=0% vs. ST 3 disease	Dominated*	+330,183	Cost-saving	Cost-saving
Improved PCV15 VE vs. ST 3 disease	117,066	+476,768	NA	NA

*Dominated: the new option is more costly and less effective compared to the current recommendation.
ICER: incremental cost-effectiveness ratio compared to PCV15 only age ≥65 years

Cost $/QALY Saved by Scenarios (Stoecker Model)

	PCV15, ≥65 years	PCV15 + PPSV23, ≥65 years (ICER)	PCV20, ≥50 years	PCV20, ≥65 years
Base Case	158,025	+462,604	Cost-saving	Cost-saving
One-way sensitivity analyses				
Indirect effects from children	**507,445**	**+483,075**	**24,625**	**Cost-saving**
PCV VE=0% vs. ST 3 disease	Dominated*	+330,183	Cost-saving	Cost-saving
Improved PCV15 VE vs. ST 3 disease	117,066	+476,768	NA	NA

*Dominated: the new option is more costly and less effective compared to the current recommendation.
ICER: incremental cost-effectiveness ratio compared to PCV15 only age ≥65 years

Cost $/QALY Saved by Scenarios (Stoecker Model)

	PCV15, ≥65 years	PCV15 + PPSV23, ≥65 years (ICER)	PCV20, ≥50 years	PCV20, ≥65 years
Base Case	158,025	+462,604	Cost-saving	Cost-saving
One-way sensitivity analyses				
Indirect effects from children	507,445	+483,075	24,625	Cost-saving
PCV VE=0% vs. ST 3 disease	**Dominated***	**+330,183**	**Cost-saving**	**Cost-saving**
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*Dominated: the new option is more costly and less effective compared to the current recommendation.
ICER: incremental cost-effectiveness ratio compared to PCV15 only age ≥65 years

Resource Use

Is recommending PCV15 for persons aged ≥65 years a reasonable and efficient allocation of resources?

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

Resource Use

Is recommending PCV15 for persons aged ≥65 years in series with PPSV23 a reasonable and efficient allocation of resources?

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

Resource Use

- **Is recommending PCV20 for persons aged ≥50 years a reasonable and efficient allocation of resources?**
- **Is recommending PCV20 for persons aged ≥65 years a reasonable and efficient allocation of resources?**

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

Work Group Interpretation: Resource Use

EtR Domains	PCV15, ≥65 years	PCV15 +PPSV23, ≥65 years	PCV20, ≥50 years	PCV20, ≥65 years
Public Health Problem	Yes			
Benefits and Harms				
a. Benefits	Small	Small	Large	Moderate-Large
b. Harms	Minimal			
c. Benefit>Harm?	Favors intervention			
d. Overall certainty: effectiveness	Moderate			
e. Overall certainty: safety	High			
Values				
a. Desirable>Undesirable?	Probably yes			
b. Uncertainty?	Probably not important uncertainty or variability			
Acceptability	Probably yes	Varies	Probably yes	Yes
Resource use	**Probably no**	**No**	**Yes**	**Yes**

Note: Each policy question is compared to the current vaccine recommendation

Equity

What would be the impact on health equity?

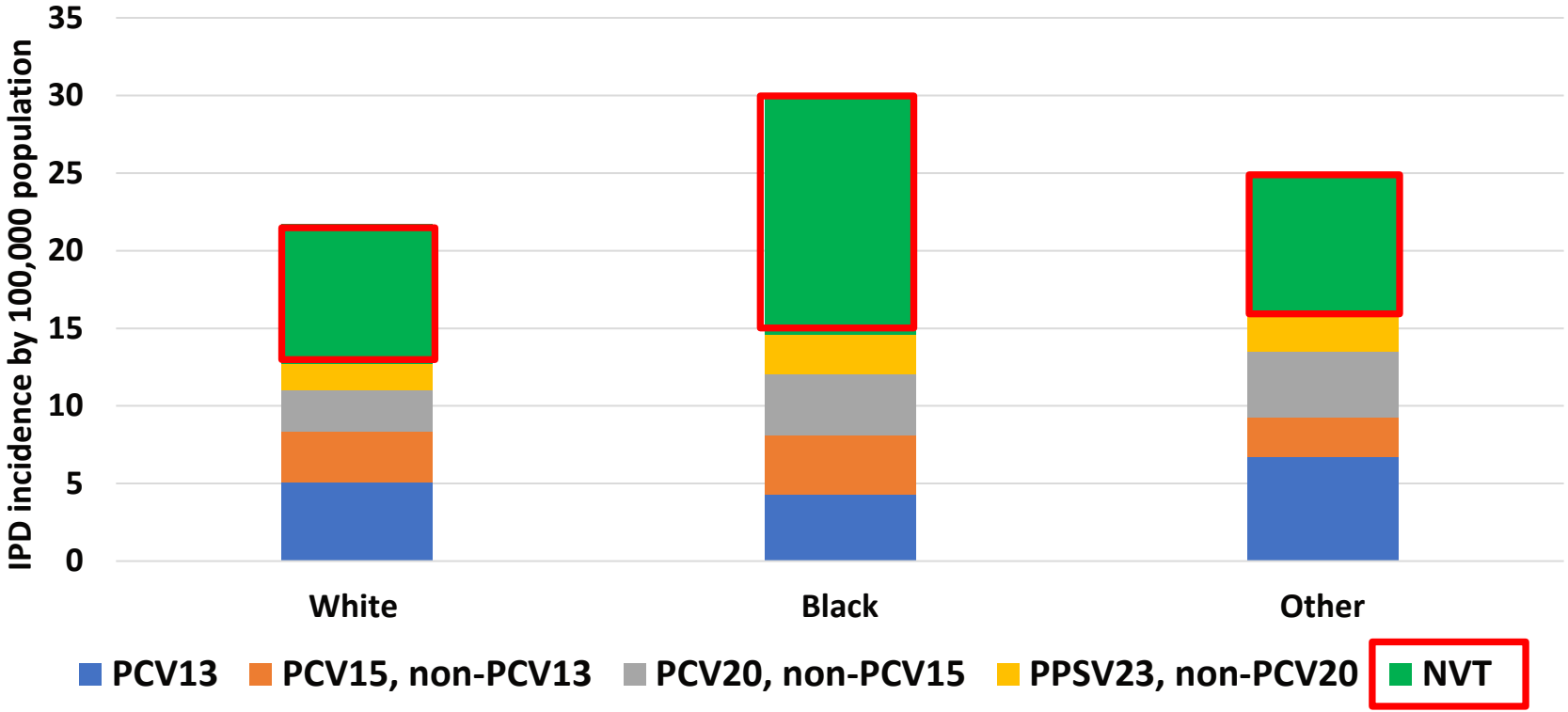
Groups or settings that might be disadvantaged in relation to pneumococcal disease burden

- Older adults[1]
- Adults with certain underlying medical conditions[2]
- Black population (vs. non-Black population)[2]
- American Indian (AI)/Alaska Native (AN) population[3]
- Adults living in impoverished census tracts[4]

Indirect effects from pediatric PCV vaccination reduced disparities in vaccine-type pneumococcal disease.

1. ABCs, 2. ABCs and NHIS, 3. June 2019 ACIP meeting presentation, 4. Burton et al. AJPH 2010

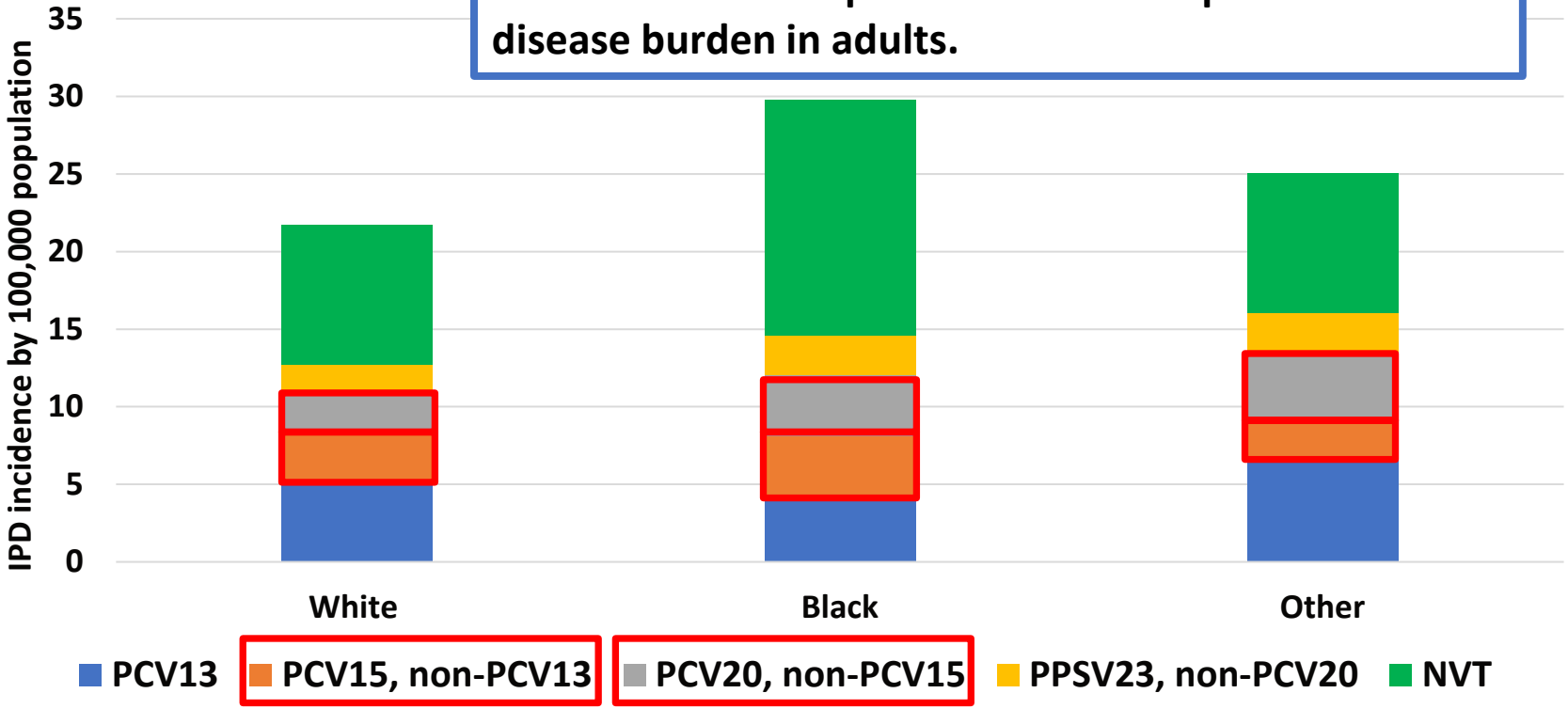
IPD Incidence by Serotype Group in Adults Aged ≥65 Years by Race, 2017–2018



CDC ABCs, 2017–2018

IPD Incidence by Serotype Group in Adults Aged ≥65 Years by Race, 2017–2018

Use of PCV15 or PCV20 in adults may reduce, but not eliminate racial disparities in invasive pneumococcal disease burden in adults.



CDC ABCs, 2017–2018

The new PCVs may reduce the higher IPD burden in AI/AN adults aged ≥50 years.

In adults aged ≥50 years,

- From 2011–2019, IPD incidence in AN[1] was approximately **3x** higher compared to non-AN adults in Alaska.
- In 2019, IPD incidence in AI[2] adults was approximately **4x** higher compared to general US population[3].
  - Additional PCV15 serotypes*: **6-7%** (AI) to **9-13%** (AN) of IPD
  - Additional PCV20 serotypes*: **28–31%** (AN) to **31–35%** (AI) of IPD

AI: American Indian, AN: Alaska Native

[1] John Hopkins Center for American Indian Health, unpublished data; [2]CDC, Arctic Investigations Program, unpublished data; 3. CDC ABCs

*serotypes included in PCV15 or PCV20, but not in PCV13. serotype distribution data represents 2015–2020 for AI, 2011–2019 for AN

Pneumococcal Vaccine Coverage in adults aged 19–64 years with indications has been low.

	Sample size	%	(95% CI)
Overall	5,851	23.3%	(22.0, 24.6)
White	4,048	23.6%	(22.1, 25.2)
Black	696	25.7%	(21.8, 30.0)
Hispanic	656	18.5%	(15.2, 22.4)*
Asian	192	25.0%	(17.3, 34.5)
Other	259	25.8%	(19.3, 33.5)

National Health Interview Survey, 2018

*p<0.05 for comparisons with white as the reference.

Compared to Whites, Hispanics had significantly lower proportion of those who ever received pneumococcal vaccines.

	Sample size	%	(95% CI)
Overall	5,851	23.3%	(22.0, 24.6)
White	4,048	23.6%	(22.1, 25.2)
Black	696	25.7%	(21.8, 30.0)
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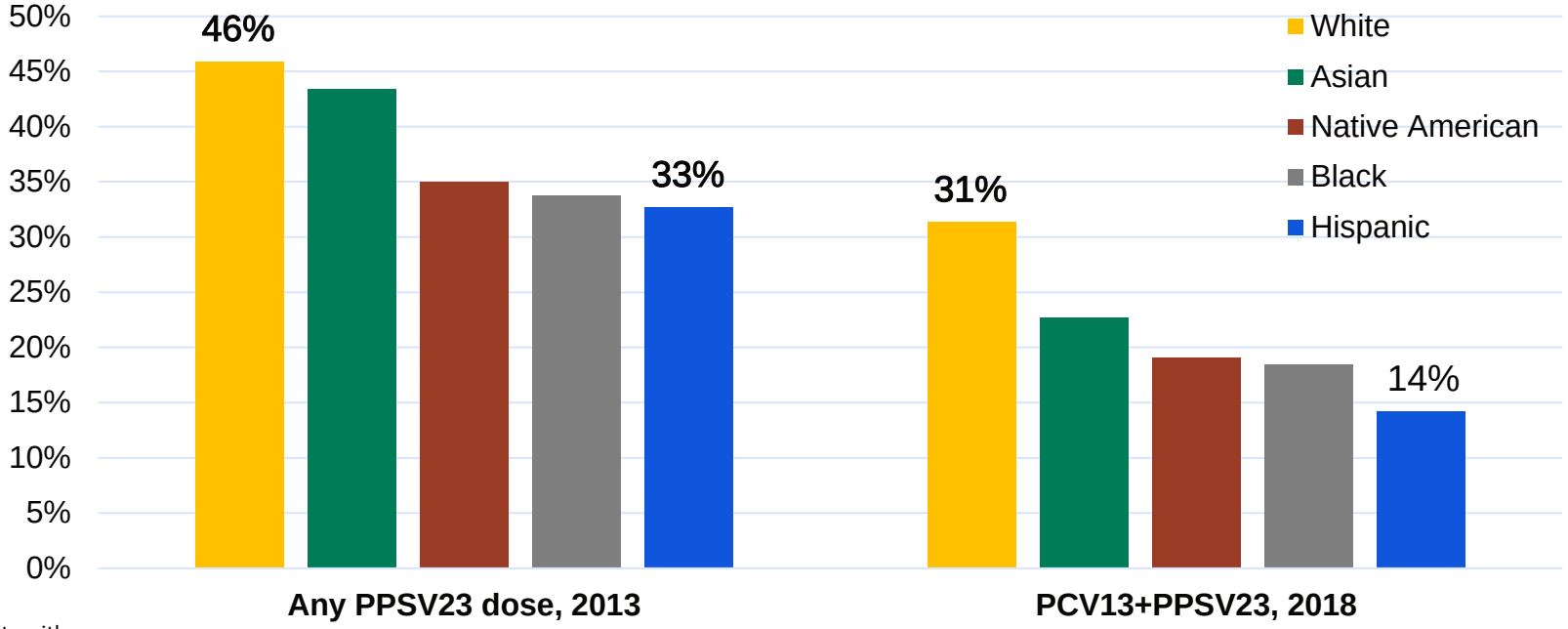
Asian	192	25.0%	(17.3, 34.5)
Other	259	25.8%	(19.3, 33.5)

National Health Interview Survey, 2018

*p<0.05 for comparisons with white as the reference.

Coverage of recommended pneumococcal vaccines was lower in Medicare beneficiaries aged ≥65 years when both PCV13 and PPSV23 were recommended, and racial disparities existed.



*except for adults with immunocompromising conditions

CDC Unpublished Data

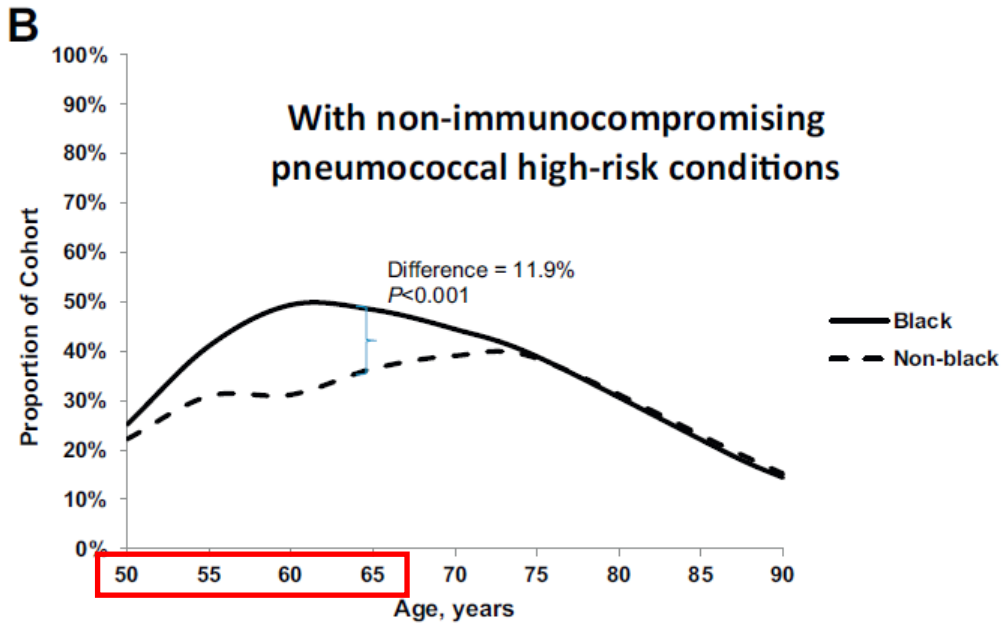
PPSV23 only recommended*

PCV13+PPSV23 recommended

Lowering the age-based recommendation may disadvantage those who are uninsured.

- In 2019, the National Health Interview Survey[1] reported that:
  - **14.7%** aged 18–64 years vs. **0.9%** aged ≥65 years uninsured
- Among adults aged 18–64 years, groups more likely to be uninsured were:
  - Those who were **poor/near poor** (<200% of the federal poverty level)
  - **Hispanics**
- Section 317-funded vaccines can be used to vaccinate the uninsured[2]

1. https://www.cdc.gov/nchs/data/nhis/earlyrelease/insur202009-508.pdf
2. https://www.cdc.gov/vaccines/imz-managers/guides-pubs/qa-317-funds.html



Lowering the age-based recommendation may improve vaccine coverage in population with higher prevalence of conditions that increase the risk of pneumococcal disease at a younger age.

Non-immunocompromising pneumococcal high-risk conditions: chronic heart, lung, or liver disease; diabetes mellitus; alcoholism; asthma; cirrhosis

Nowalk et al. Journal of the National Medical Association 2019.

Equity

What would be the impact of recommending PCV15 in persons aged ≥65 years be on health equity?

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

- A simplified recommendation may improve overall vaccine coverage
- No PPSV23→ lose coverage for 9 serotypes

Equity

What would be the impact of recommending PCV15 in persons aged ≥65 years in series with PPSV23 be on health equity?

□ Reduced
□ Probably reduced
□ Probably no impact
□ Probably increased
□ Increased

- A vaccine recommendation with 2 different vaccines is more likely to disadvantage those with challenges with healthcare access

Equity

What would be the impact of recommending PCV20 in persons aged ≥50 years be on health equity?

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

- May potentially disadvantage uninsured adults
- May improve vaccine coverage in adults with underlying conditions before age 65 years

Equity

What would be the impact of recommending PCV20 in persons aged ≥65 years be on health equity?

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

- May potentially disadvantage adults with limited access
- A simplified recommendation may improve overall vaccine coverage

Work Group Interpretation: Equity

EtR Domains	PCV15, ≥65 years	PCV15 +PPSV23, ≥65 years	PCV20, ≥50 years	PCV20, ≥65 years
Public Health Problem	Yes			
Benefits and Harms				
a. Benefits	Small	Small	Large	Moderate-Large
b. Harms	Minimal			
c. Benefit>Harm?	Favors intervention			
d. Overall certainty: effectiveness	Moderate			
e. Overall certainty: safety	High			
Values				
a. Desirable>Undesirable?	Probably yes			
b. Uncertainty?	Probably not important uncertainty or variability			
Acceptability	Probably yes	Varies	Probably yes	Yes
Resource use	Probably no	No	Yes	Yes
Equity	**Probably no impact**	**Probably reduced**	**Probably increased**	**Probably increased**

Note: Each policy question is compared to the current vaccine recommendation

Feasibility

Are the options feasible to implement?

Feasibility: Summary of Work Group Interpretation

- PCV-PPSV23 series has been recommended: feasible
  - May disadvantage people with challenges with access to vaccines
- A recommendation that consists of a single vaccine dose is easier to implement and is likely to achieve coverage in a larger population.

Feasibility

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

- **Is recommending PCV15 for persons aged ≥65 years feasible to implement?**
- **Is recommending PCV20 for persons aged ≥50 years feasible to implement?**
- **Is recommending PCV20 for persons aged ≥65 years feasible to implement?**

Feasibility

Is recommending PCV15 for persons aged ≥65 years in series with PPSV23 feasible to implement?

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

Work Group Interpretation: Feasibility

EtR Domains	PCV15, ≥65 years	PCV15 +PPSV23, ≥65 years	PCV20, ≥50 years	PCV20, ≥65 years
Public Health Problem	Yes			
Benefits and Harms				
a. Benefits	Small	Small	Large	Moderate-Large
b. Harms	Minimal			
c. Benefit>Harm?	Favors intervention			
d. Overall certainty: effectiveness	Moderate			
e. Overall certainty: safety	High			
Values				
a. Desirable>Undesirable?	Probably yes			
b. Uncertainty?	Probably not important uncertainty or variability			
Acceptability	Probably yes	Varies	Probably yes	Yes
Resource use	Probably no	No	Yes	Yes
Equity	Probably no impact	Probably reduced	Probably increased	Probably increased
Feasibility	**Yes**	**Probably yes**	**Yes**	**Yes**

Note: Each policy option is compared to the current vaccine recommendation

Summary of Work Group Interpretation

EtR Domains	PCV15, ≥65 years	PCV15 +PPSV23, ≥65 years	PCV20, ≥50 years	PCV20, ≥65 years
Public Health Problem		Yes		
Benefits and Harms				
a. Benefits	**Small**	**Small**	**Large**	**Moderate-Large**
b. Harms		Minimal		
c. Benefit>Harm?		Favors intervention		
d. Overall certainty: effectiveness		Moderate		
e. Overall certainty: safety		High		
Values				
a. Desirable>Undesirable?		Probably yes		
b. Uncertainty?		Probably not important uncertainty or variability		
Acceptability	**Probably yes**	**Varies**	**Probably yes**	**Yes**
Resource use	**Probably no**	**No**	**Yes**	**Yes**
Equity	**Probably no impact**	**Probably reduced**	**Probably increased**	**Probably increased**
Feasibility	Yes	Probably yes	Yes	Yes

Note: Each policy option is compared to the current vaccine recommendation, not across options

Summary: Work Group Interpretations

Should Merck PCV15 be recommended for persons aged ≥65 years?

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

- Cost-effectiveness analysis showed some benefits in preventing disease.
- Concerns about losing coverage for 9 serotypes that are included in PPSV23.

Summary: Work Group Interpretations

Should Merck PCV15 be recommended for persons aged ≥65 years in series with 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

- PCV15-PPSV23 may prevent additional disease but added benefit likely small.
- Potential undesirable consequences related to resource use, feasibility, and equity may outweigh the desirable consequences.
- Some patients currently receive PCV13-PPSV23 series.

Summary: Work Group Interpretations

Should Pfizer PCV20 be recommended for persons aged ≥50 years?

Should Pfizer PCV20 be recommended for persons aged ≥65 years?

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

Next Steps

- Additional **cost-effective analyses** underway
- GRADE and EtR for **risk-based recommendation** for younger adults not targeted by the age-based recommendation
  - To be presented at the **September ACIP meeting**

- Refine policy options on **age- and risk- based recommendations** on PCV15 and PCV20 use in adults for a vote at the **October ACIP meeting**
  - PCV15 and PCV20 will be reviewed separately

Questions for ACIP members

- Are there other age-based policy options we should be considering for GRADE and EtR?
- Are there policy options we should not be considering for a vote?
- Are there additional data the Committee would like to see before deciding on policy options?

PCV15:

Should Merck PCV15 be recommended for persons aged ≥65 years?

Should Merck PCV15 be recommended for persons aged ≥65 years in series with PPSV23?

PCV20:

Should Pfizer PCV20 be recommended for persons aged ≥50 years?

Should Pfizer PCV20 be recommended for persons aged ≥65 years?

Acknowledgements

- ACIP and the Pneumococcal Work Group
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Thank you

For more information, contact CDC
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