Summary of Work Group Interpretation of EtR and Policy Options

PCV Use in Adults aged ≥50 years

October 23, 2024

Miwako Kobayashi, MD, MPH

PICO for WG discussion through October 2024

Policy question:	Should a single dose of pneumococcal conjugate vaccine (PCV) be recommended for all PCV-naïve adults aged 50–64 years?
Population	PCV-naïve adults aged 50–64 years in the United States
Intervention	One dose of PCV15*, PCV20, or PCV21 *In series with PPSV23
Comparison	Current risk-based vaccine recommendation (CMC or IC)
Outcomes	Vaccine type (VT)-IPD, VT-non-bacteremic pneumococcal pneumonia, VT-pneumococcal mortality, serious adverse events

CMC=chronic medical conditions (i.e., alcoholism; chronic heart disease, including congestive heart failure and cardiomyopathies; chronic liver disease; chronic lung disease, including chronic obstructive pulmonary disease, emphysema, and asthma; cigarette smoking; or diabetes mellitus); IC=immunocompromising condition(i.e., chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, HIV infection, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplant, congenital or acquired asplenia, or sickle cell disease or other hemoglobinopathies). Those with a cerebrospinal fluid leak and a cochlear implant are also included among those with a risk-based vaccine indication.

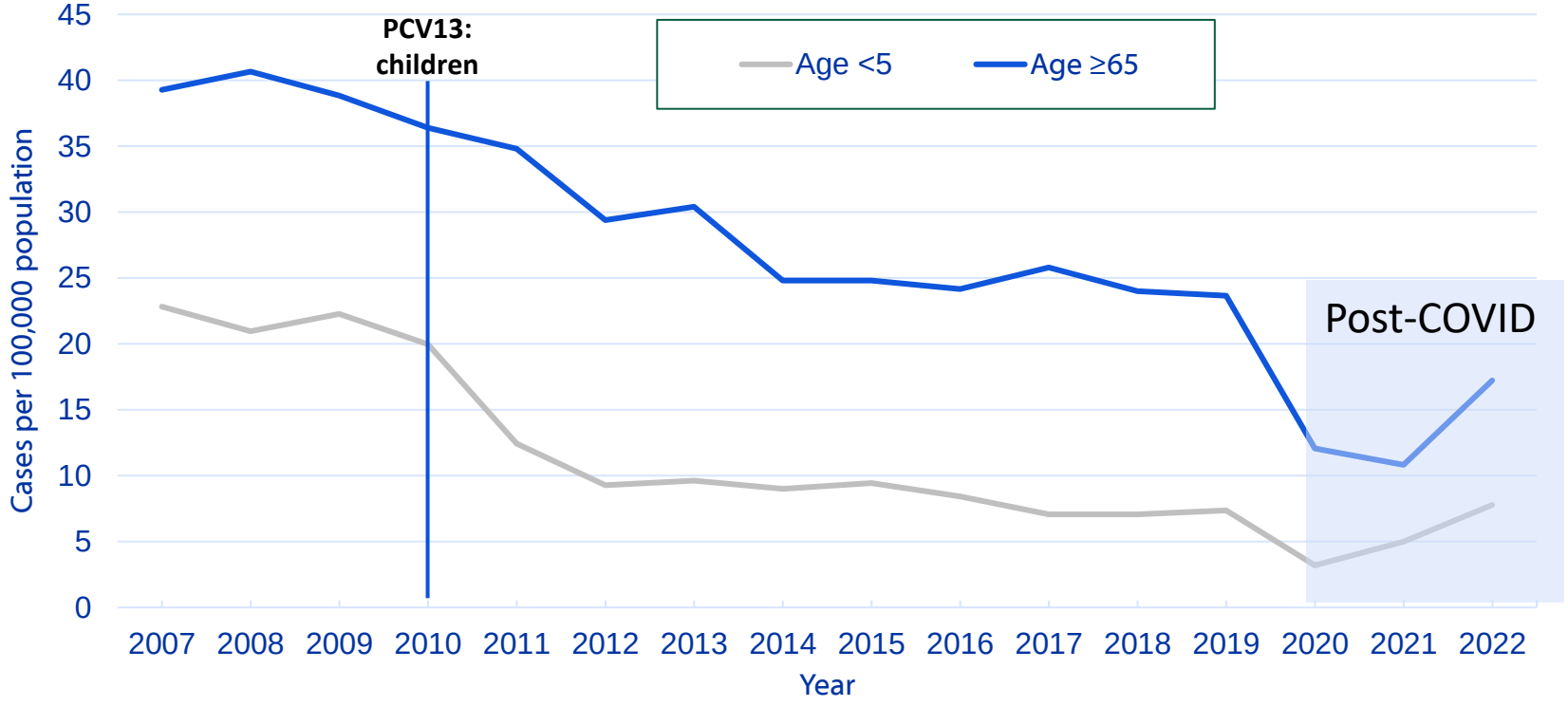
Evidence to Recommendations (EtR) framework

EtR Domain	Question
Public Health Problem	• Is the problem of public health importance?
Equity	• What would be the impact of the intervention on health equity?
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?
Resource Use	• Is the intervention a reasonable and efficient allocation of resources?
Feasibility	• Is the intervention feasible to implement?

Public Health Problem

Is pneumococcal disease of public health importance for adults aged 50–64 years?

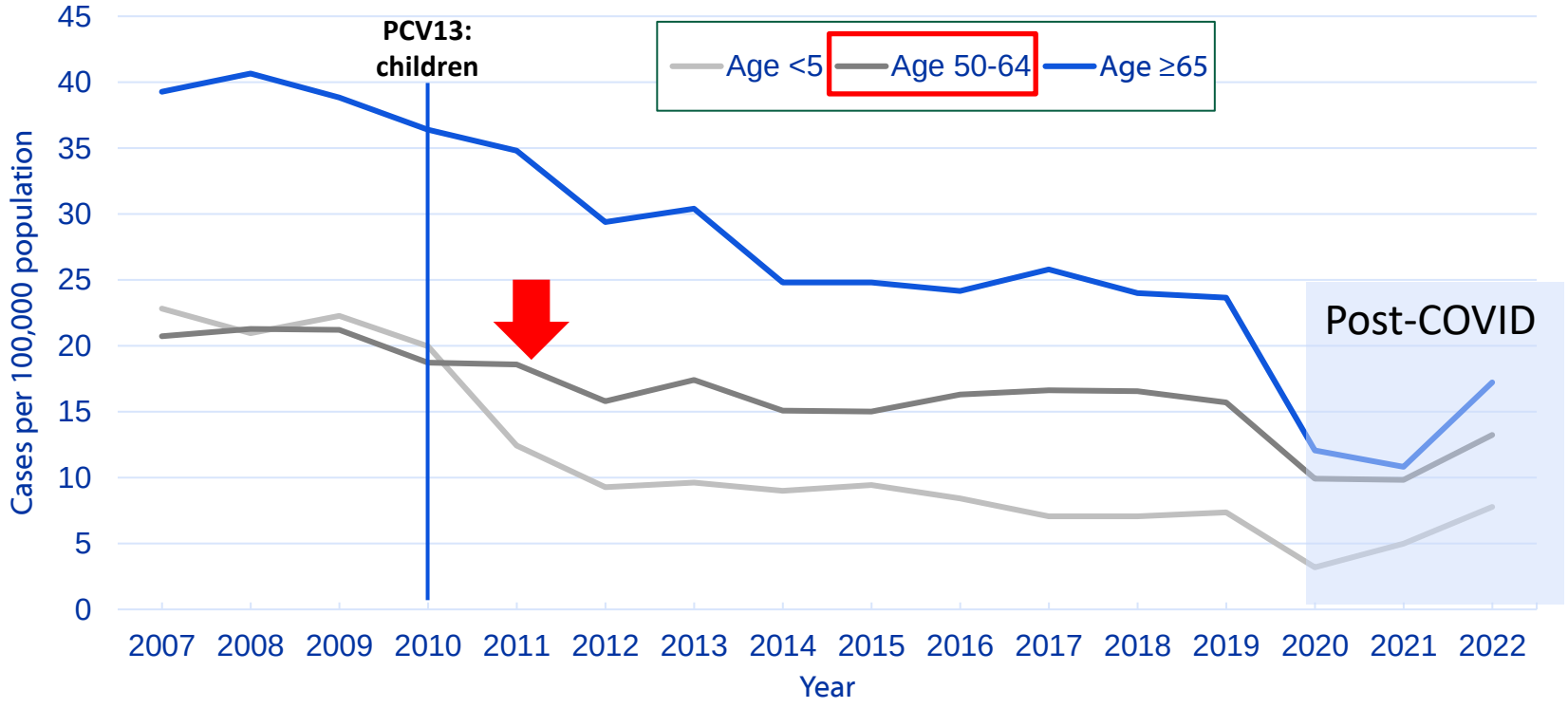
Invasive pneumococcal disease (IPD) incidence rates, by age group, 2007–2022



Source: CDC's Active Bacterial Core surveillance

Adapted from Gierke Feb 2024 ACIP meeting presentation

Invasive pneumococcal disease (IPD) incidence rates, by age group, 2007–2022



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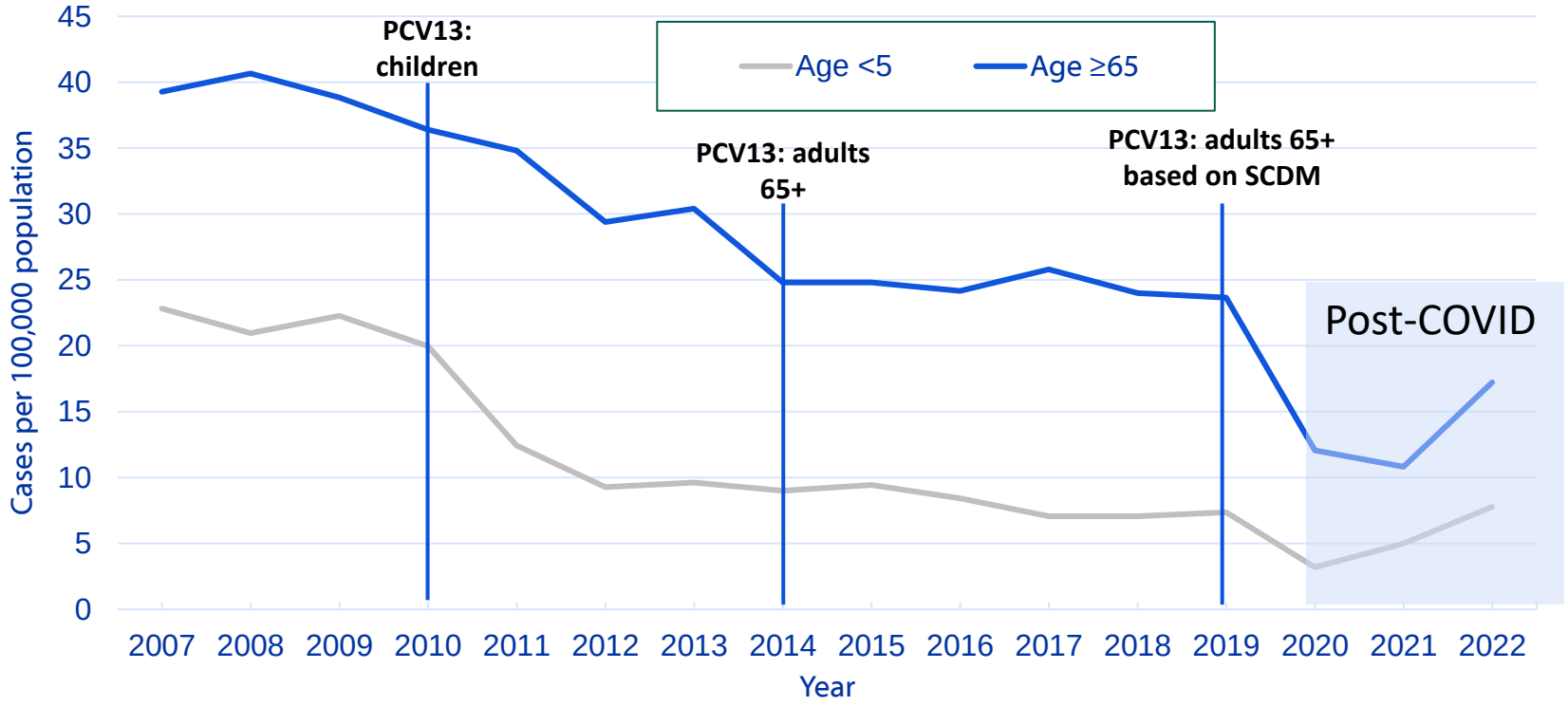
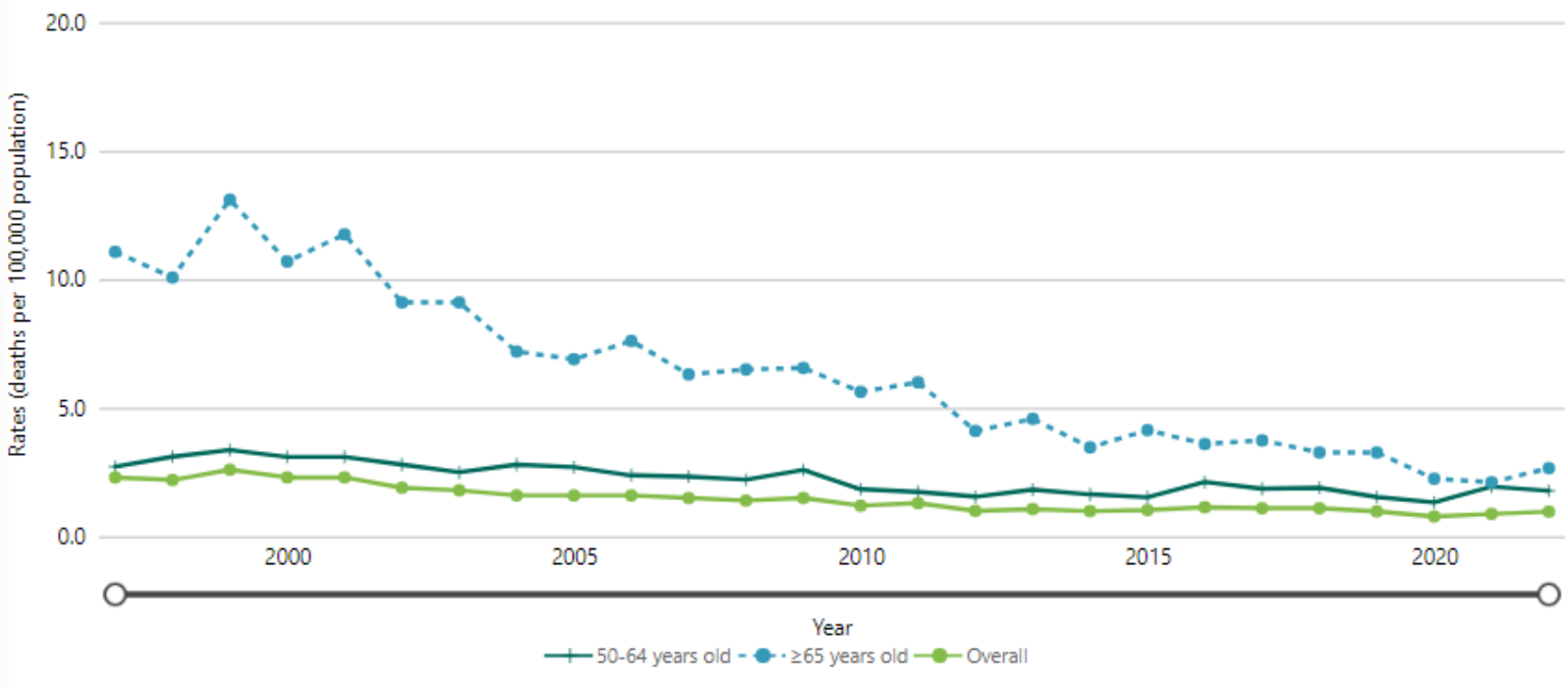


SCDM: shared clinical decision-making

Source: CDC's Active Bacterial Core surveillance

Adapted from Gierke Feb 2024 ACIP meeting presentation

IPD mortality rate* in adults aged ≥65 years has become closer to that in adults aged 50–64 years



ABCs Bact Facts Interactive Data Dashboard | ABCs | CDC. *deaths from IPD per 100,000 population

Adults aged 50–64 years at increased risk of pneumococcal disease

- Among adults aged 50–64 years with **pneumococcal disease** (IPD[1], hospitalized pneumococcal pneumonia[2])**, a high proportion (88%)** of adults had **≥1 condition with a risk-based pneumococcal vaccine indication (risk condition)**

1. CDC ABCs 2018–2021 data
2. Self et al. PNEUMO study unpublished data

Is pneumococcal disease of public health importance?

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

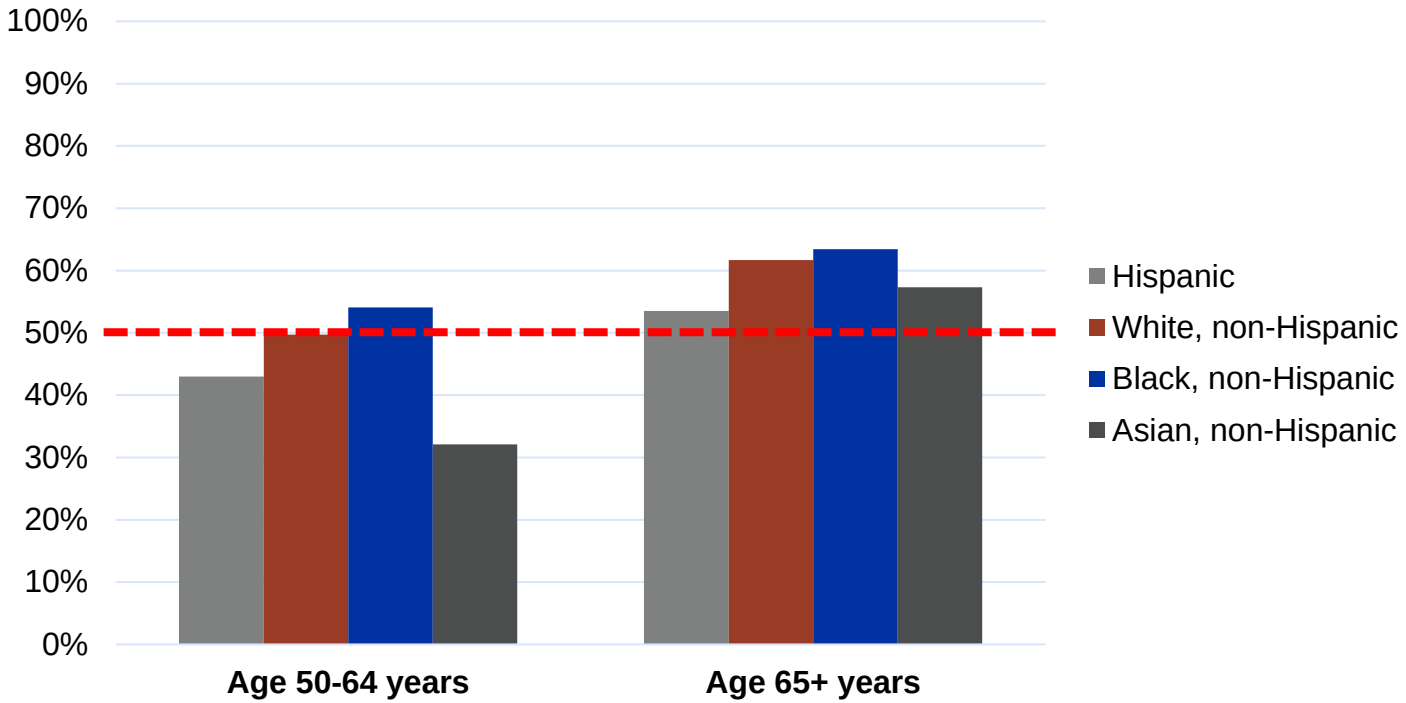
- Success of pediatric PCV program increased the relative burden of pneumococcal disease in adults aged 50–64 years, especially in those with risk conditions*.
- **Additional Work Group comment:**
  - Should consider the absolute rate of disease (rather than relative burden compared with other age groups). IPD rates have come down significantly compared with pre-PCV era rates.

*Adults with certain underlying medical conditions or other risk factors

Equity

What would be the impact of recommending PCV for all PCV-naïve adults aged 50–64 years on **health equity?**

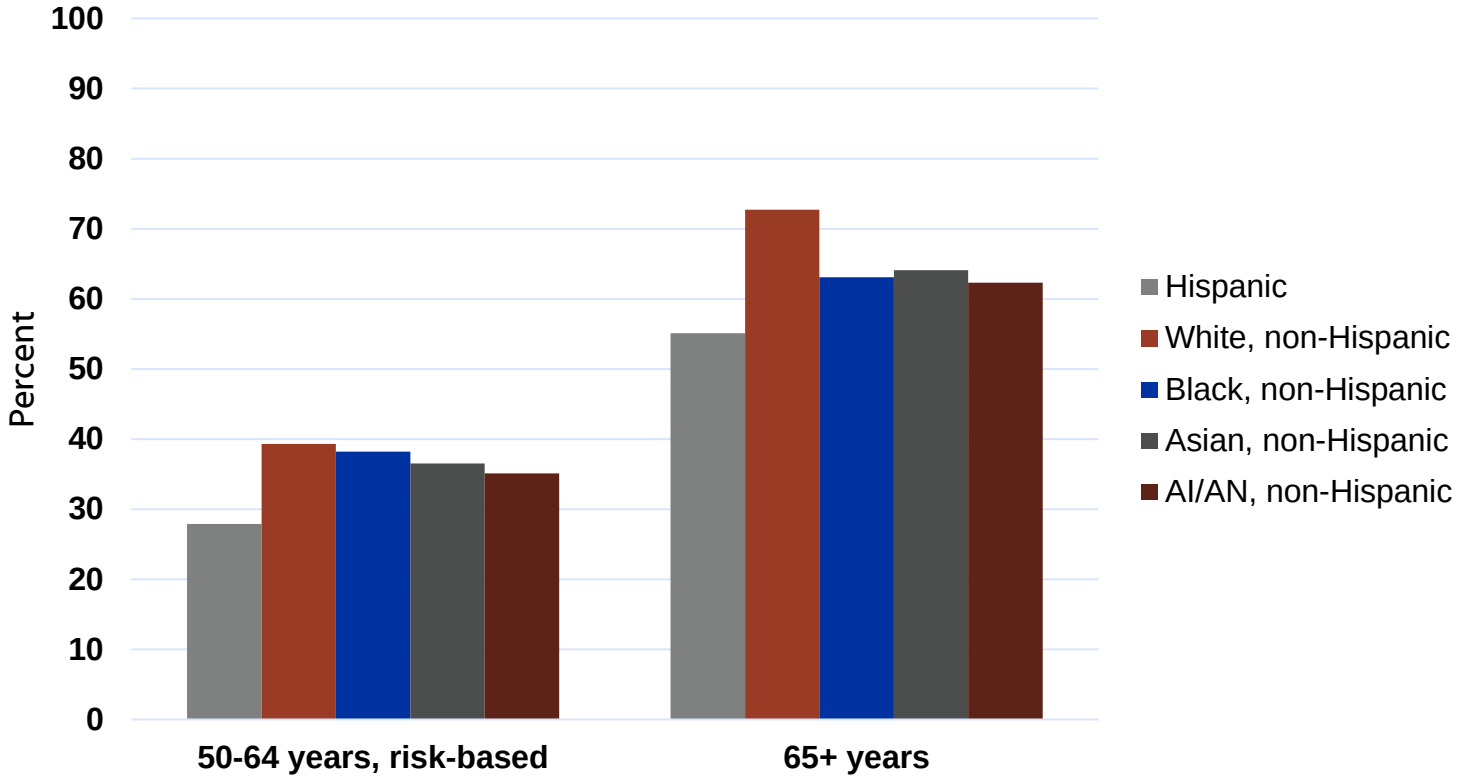
About 32–54% of adults aged 50–64 years have underlying conditions with risk-based pneumococcal vaccine indication*



Source: NHIS 2020 data

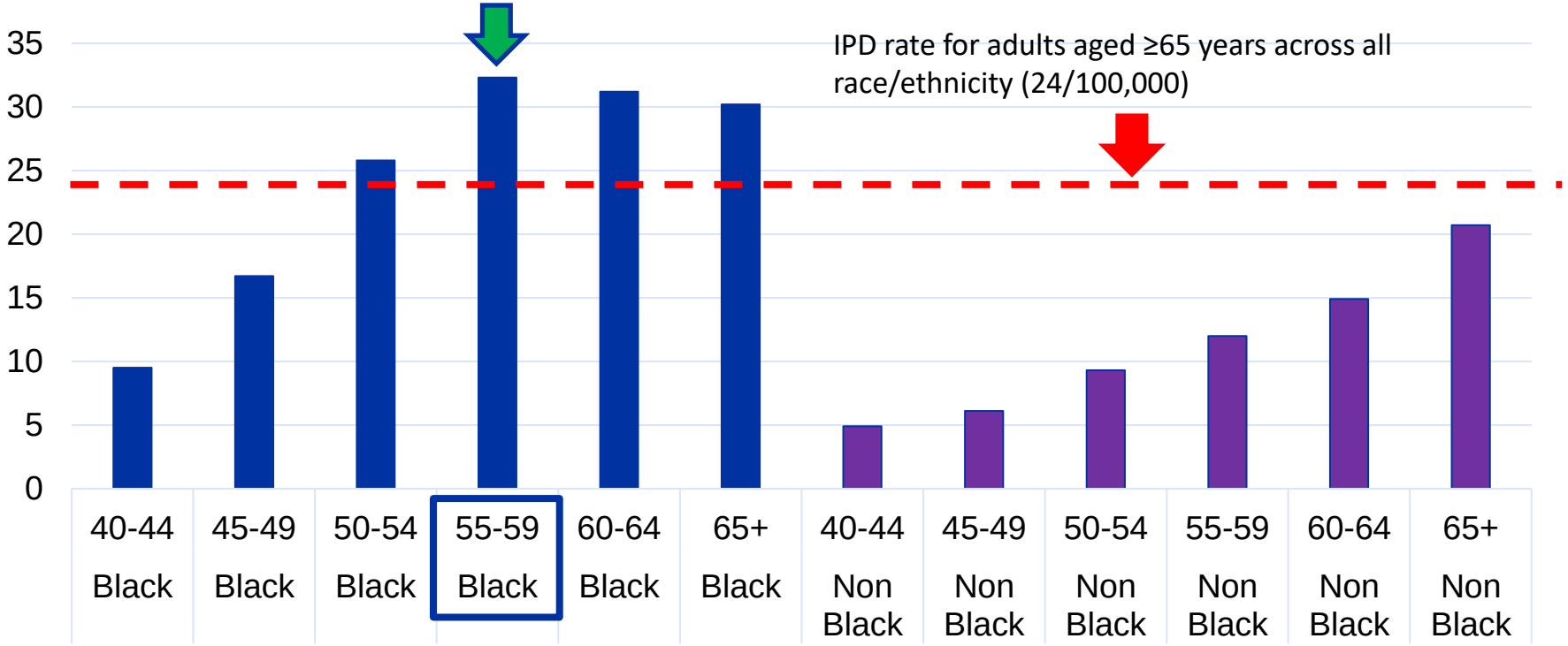
*chronic heart disease, chronic lung disease, chronic liver disease, diabetes, smoking, alcoholism, weakened immune system due to prescriptions, weakened immune system due to health condition, solid cancer (not including non-melanoma skin cancer or unknown type of skin cancer) and blood cancer

Disparities in pneumococcal vaccine coverage by race/ethnicity exist for both age-based and risk-based indications



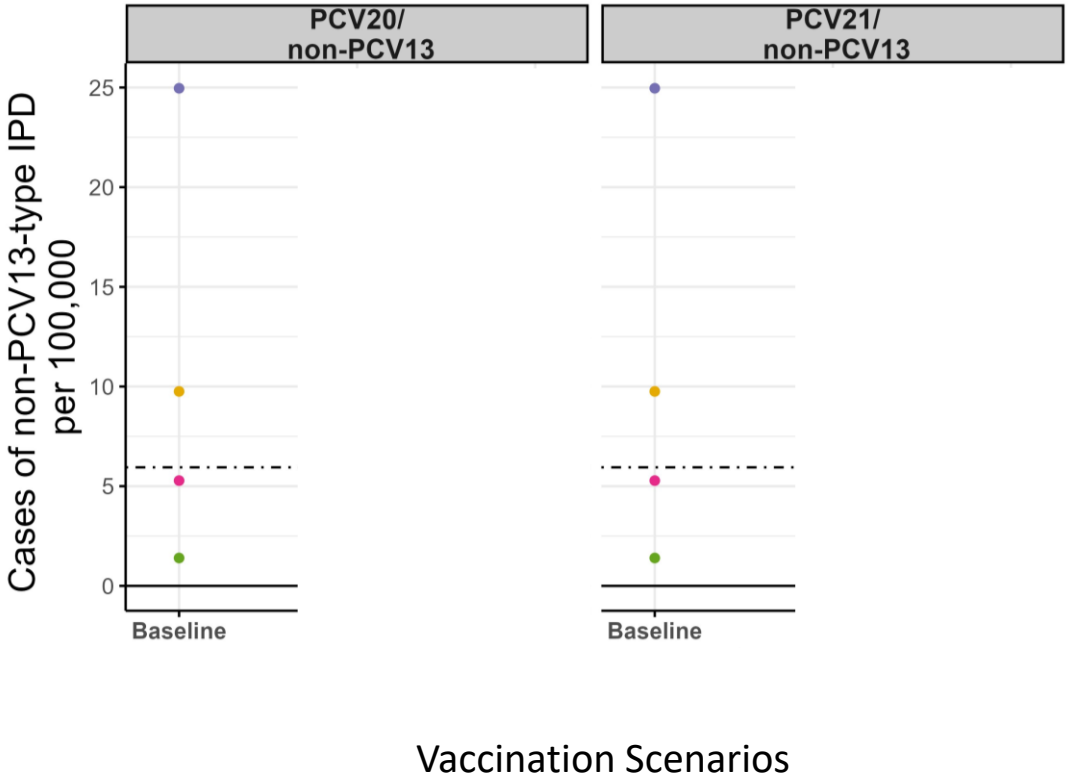
Source: BRFSS 2022; AI/AN=American Indian and Alaska Native

IPD rates (any pneumococcal serotype) in Black adults peak at a younger age compared with Non-Black adults



ABCs 2018 –2019 unpublished data

Impact of hypothetical PCV20/PCV21 vaccination scenarios on non-PCV13-type IPD rates in adults aged ≥19 years



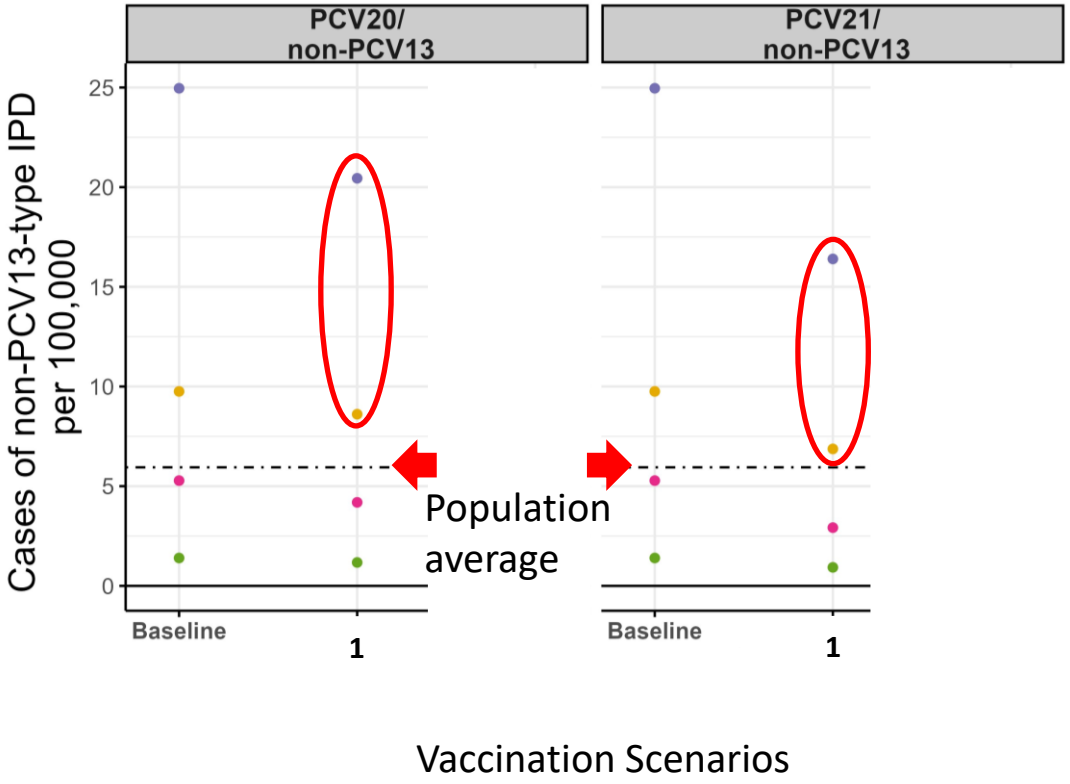
Race and ethnicity

- AI/AN (American Indian and Alaska Native)
- Asian
- Black
- White

- **For simplicity, assumes vaccine protects against 100% of vaccine-type disease**
- **Vaccine coverage is applied to adults who developed non-PCV13-type IPD in 2014–2019**

CDC ABCs 2014–2019 unpublished data.

Impact of hypothetical PCV20/PCV21 vaccination scenarios on non-PCV13-type IPD rates in adults aged ≥19 years



Race and ethnicity

- AI/AN (American Indian and Alaska Native)
- Asian
- Black
- White

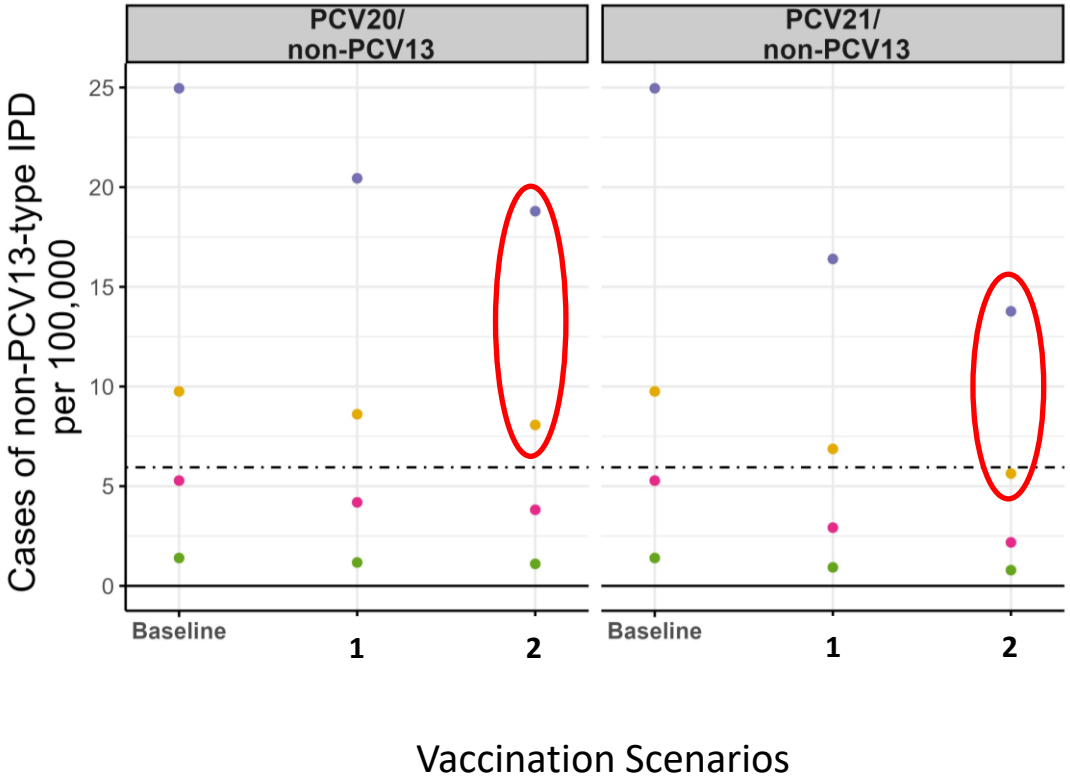
Vaccination Scenarios:

1. **Current risk-based (19–64 years) and age-based (≥65 years) recommendations with observed vaccine coverage by race**

- For simplicity, assumes vaccine protects against 100% of vaccine-type disease
- Vaccine coverage is applied to adults who developed non-PCV13-type IPD in 2014–2019

CDC ABCs 2014–2019 unpublished data.

Impact of hypothetical PCV20/PCV21 vaccination scenarios on non-PCV13-type IPD rates in adults aged ≥19 years



Race and ethnicity

- AI/AN (American Indian and Alaska Native)
- Asian
- Black
- White

Vaccination Scenarios:

1. Current risk-based and age-based recs with observed vaccine coverage by race
2. **Lower age-based recs to ≥50 years using current coverage for adults aged ≥65 years; risk-based for 19–49 years**

CDC ABCs 2014–2019 unpublished data.

What would be the impact of recommending PCV for all PCV-naïve adults aged 50–64 years on health equity?

- □ Reduced
- □ Probably reduced
- □ Probably no impact
- □ Probably increased
- □ Increased
- □ Varies
- □ Don’t know

Work Group comments

- **The intervention could help improve health equity by:**
  - Improving vaccine coverage for those with known or unknown risk conditions
  - Providing protection at an earlier age when certain populations (e.g., Black adults, AI adults) are already experiencing elevated disease rates
  - Simplifying the recommendation, which could improve implementation across all populations
- **Acknowledged that the overall impact on health equity is complex and would depend on how the recommendation is implemented and any underlying disparities in healthcare access.**

Benefits and Harms

Outcomes considered were specified in PICO

Outcome (Benefits)	Importance*	Data sources
VT-IPD	Critical	PCV clinical trial data (immunogenicity)
VT-non-bacteremic pneumococcal pneumonia	Critical	
VT-pneumococcal deaths	Critical	
Serious adverse events (SAE)	Critical	PCV clinical trial data; post-licensure safety data (PCV20)

*Rated on a 1 to 9 scale, where 7–9 are critical, 4–6 are important, 1–3 are of limited importance

Updated targeted literature search

- **Previously conducted systematic review of literature and presented summary of findings and GRADE for PCV15[1], PCV20[2], PCV21[3]**
- **Updated literature search (August and September, 2024) based on current PICO question**
- **6 PCV15 trials, 3 PCV20 trials, and 7 PCV21 trials included in the updated review (list of studies available in supplemental slides)**

1. Presented summary of literature search through February 18, 2021
2. Presented summary of literature search through March 31, 2022
3. Presented summary of literature search through October 17, 2023

PCV clinical trial data (immunogenicity)

Conclusions remain unchanged

- PCV15: **Noninferior**[1] to PCV13 for all shared serotypes; had statistically significantly greater response[2] for non-PCV13 serotypes 22F and 33F vs. PCV13
- PCV20: **Noninferior**[3] to PCV13 for all shared serotypes; **noninferior**[3] to PPSV23 for 6/7 non-PCV13 serotypes (not met for serotype 8)
- PCV21: **Noninferior**[4] to PCV20 for 10/10 shared serotypes; had statistically significantly greater response[5] for 10/11 PCV21-unique serotypes (except serotype 15C)

1. Noninferiority defined as the lower bound of the 2-sided 95% CI of the OPA GMT ratio (PCV15/PCV13) to be >0.5.
2. Statistically significantly greater response for unique serotypes (22F and 33F) defined as the lower bound of the 2-sided 95% CI of the OPA GMT ratio (PCV15/PCV13) to be >2.0 and the lower bound of the 2-sided 95% CI of the differences (PCV15-PCV13) between the proportions of participants with a ≥4-fold rise to be >0.1 (or 10 percentage points)
3. Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the OPA GMT ratio (PCV20/comparator vaccine) for that serotype was greater than 0.5 (2-fold criterion).
4. Noninferiority for GMT ratio was defined as the lower bound of the 2-sided 95% CI of the OPA GMT ratio [PCV21 / (Comparator Vaccine)] to be >0.5.
5. Statistically significantly greater response for GMT ratio was defined as the lower bound of the 2-sided 95% CI of the OPA GMT ratio [PCV21 / (Comparator Vaccine)] to be >2.0. Statistically significantly greater response for difference in proportions of participants with a ≥4-fold rise in serotype-specific OPA responses from baseline to 30 days postvaccination was defined as the lower bound of the 2-sided 95% CI of the differences [PCV21 – (Comparator Vaccine)] between the proportions of participants with a ≥4-fold rise from baseline to 30 days postvaccination to be >0.1.

1. How substantial are the desirable anticipated effects* of PCV vaccination?

Intervention: Recommending PCV for all PCV-naïve adults aged 50–64 years
Comparator: Risk-based recommendation for adults with CMC/IC

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

***Desirable anticipated effects for the following outcomes as specified in the PICO:**
Vaccine-type (VT) IPD, VT non-bacteremic pneumococcal pneumonia, VT pneumococcal mortality

Certainty of evidence (February 2024 ACIP meeting): Moderate

CMC: chronic medical conditions, IC=immunocompromising conditions

PCV clinical trial data (safety)

Conclusions remain unchanged

- **No vaccine-related serious adverse events reported for PCV15 and PCV20**
- **Two vaccine-related serious adverse events reported among PCV21 recipients (previously presented)**
  - Bronchospasm (V116-005): 50-year-old female in the sequential group with bronchospasm within 30 minutes after the 2nd vaccination (V116); duration 23 hours; resolved
  - Injection site cellulitis (V116-006): 67-year-old female in Cohort 1 (prior PPSV23) with injection site cellulitis on Day 6; duration 1.57 weeks; resolved

Post-licensure PCV20 safety data

What we presented during the February 2024 ACIP meeting

- **October 2021–December 2023: 1,976 VAERS reports after PCV20 in adults***
- **Most reports were classified as non-serious**
- **Data mining alert for disproportional reporting of Guillain-Barré Syndrome (GBS) after PCV20 vaccine**
  - **11 reports** for GBS after PCV20 vaccine, verified by chart review
  - The reporting rate for GBS after PCV20 vaccine was **0.5 cases** per million doses distributed
- **FDA also presented preliminary FDA-CMS partnership data at the meeting**
  - Near real-time monitoring in Medicare beneficiaries aged ≥65 years had not identified a safety signal for GBS

*adults defined as individuals aged ≥19 years

Post-licensure PCV20 safety data

Updated data

- **October 2021–August 2024: 2,767 VAERS reports after PCV20 in adults***
  - **18 reports** for Guillain-Barré Syndrome (GBS) after PCV20 vaccine, verified by chart review
  - The reporting rate for GBS after PCV20 vaccine was **0.7 cases** per million doses distributed
- **Updated data findings from FDA-CMS partnership (data through May 31, 2024)**
  - A statistically significant signal **(IRR>1[†]) for GBS following PCV20 vaccination** in Medicare beneficiaries aged ≥65 years identified when using the primary GBS definition
    - GBS events were not chart confirmed (based on claims)
    - Findings were not statistically significant when using a different GBS definition or adjusting for positive predictive value
    - Incidence was low (<10 GBS cases per 100K person-years), resulting in wide credible intervals

*adults defined as individuals aged ≥19 years

[†]Bayesian Poisson Regression was used to estimate the posterior distribution of incidence rate ratio (IRR) between pre-specified risk and comparison windows

Summary: Post-licensure PCV20 safety data

- Potential Guillain-Barré Syndrome (GBS) signal for PCV20 in VAERS
- GBS signal in Medicare sequential monitoring for primary definition, but not for alternate definition or when adjusted for positive predictive value
- Significant uncertainty because of the small number of GBS cases observed
- CDC and FDA will continue to monitor post-licensure PCV safety

2. How substantial are the *undesirable* anticipated effects* of PCV vaccination?

Intervention: Recommending PCV for all PCV-naïve adults aged 50–64 years
Comparator: Risk-based recommendation for adults with CMC/IC

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

***Desirable unanticipated effects for the following outcome as specified in the PICO:** Serious adverse events

Certainty of evidence (February 2024 ACIP meeting): Moderate

CMC: chronic medical conditions, IC=immunocompromising conditions

3. Do the desirable effects of PCV vaccination outweigh the *un*desirable anticipated effects?

Intervention: Recommending PCV for all PCV-naïve adults aged 50–64 years
Comparator: Risk-based recommendation for adults with CMC/IC

- □ Favors intervention
- □ Favors current (risk-based for CMC/IC only)
- □ Favors both
- □ Favors neither
- □ Varies
- □ Don't know

Additional Work Group comment:

- Some members believed that the interpretation would vary by the PCV product

CMC: chronic medical conditions, IC=immunocompromising conditions

Values and Preferences

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

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

Work Group comments

- Members with experience serving underserved populations, with many underinsured or self-pay individuals, noted that these groups can be comfortable with pneumococcal vaccines if benefits are clearly explained.
- The effectiveness of communication about benefits depends significantly on who delivers the message and how much time is spent explaining it.
- There was discomfort in asserting what the target population thinks without more evidence.
- Average populations may prioritize concerns about undesirable effects over perceived benefits.
- Increased vaccine hesitancy observed in recent times makes the interpretation challenging.

2. Is there important uncertainty about or variability in how much people 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

*Vaccine-type (VT) IPD, VT-non-bacteremic pneumococcal pneumonia, VT-pneumococcal deaths, serious adverse events

Acceptability

Is the intervention acceptable to key stakeholders?

Is it acceptable to recommend PCV for all PCV-naïve adults aged 50–64 years?

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

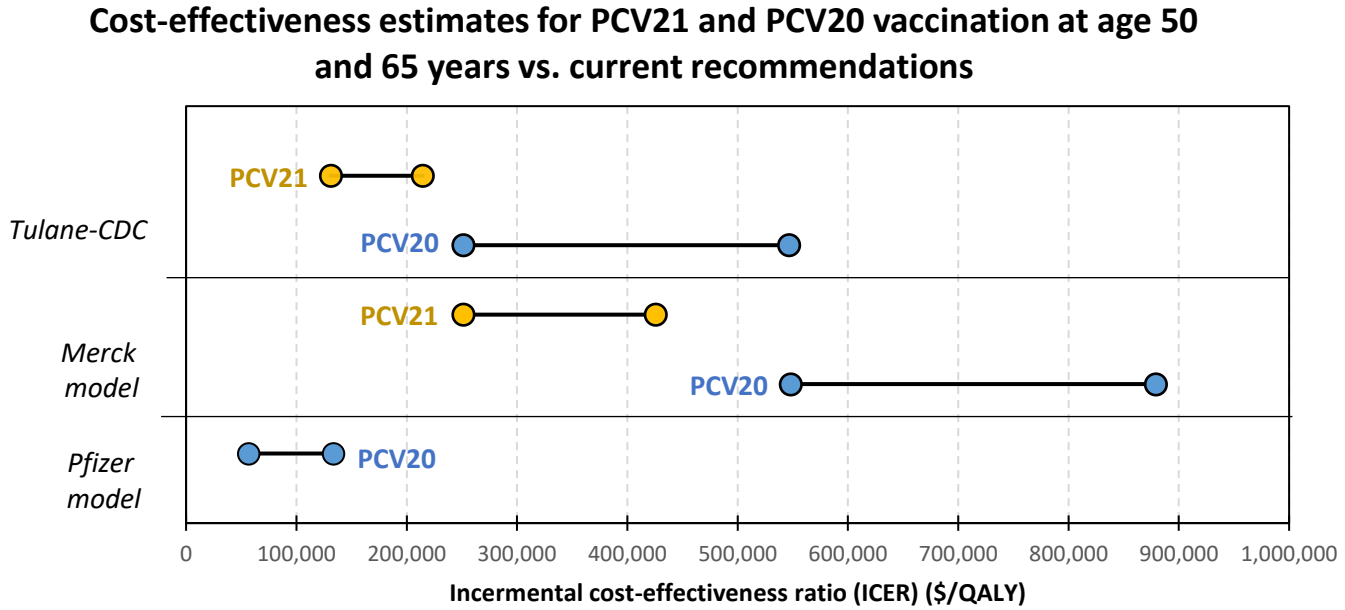
- **At the June ACIP meeting, presented findings from Merck-funded healthcare provider surveys[1,2]:**
  - challenges with implementing risk-based vaccine recommendations (e.g., time constraints, difficulties in identifying vaccination history or underlying health condition of the patient)
  - support for lowering the age threshold of the current age-based recommendation

1. Online survey conducted in February 2024 by ZS, funded by Merck. 502 HCPs (physicians, NP/PAs, pharmacists who vaccinate) participated; majority (70%) physicians
2. Online survey conducted from March–May 2024 by OPEN Health, funded by Merck. Included a total of 340 HCPs consisting of physicians, nurse practitioners, physician assistants, and pharmacists

Resource Use

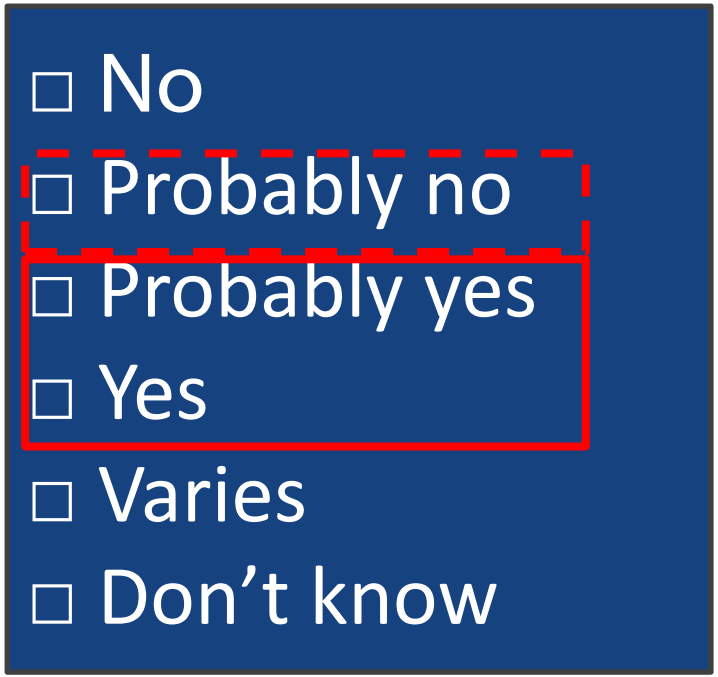
Is the intervention a reasonable and efficient allocation of resources?

Summary of model findings, “adding” strategies



- From the “adding” comparisons, all strategies improved health, but none were cost-saving
- Cost per QALY gained estimates for PCV20 had a wider range, more uncertainty than PCV21
- In two of three models, PCV21 had lower costs per QALY gained than PCV20

Is PCV use for PCV-naïve adults aged 50–64 years a reasonable and efficient allocation of resources?



- **Probably yes/yes:**
  - Despite the higher economic costs, members valued the opportunity to prevent more disease, particularly among racial and ethnic groups who currently have higher disease burden

Work Group comments

Probably No/Varies:

- Some Work Group members expressed concerns about the less favorable economic analysis for PCV20 compared to PCV21.
- Improved vaccination coverage among those with risk-based pneumococcal vaccine indications could diminish the need for broader age-based vaccination, while acknowledging that there has been insufficient success
- The decision varies when considering projections over the next 15 years, e.g., indirect effects of pediatric vaccination, availability of new higher-valency vaccines, data on duration of protection from vaccination, and considerations of whether or not to give booster doses.

Feasibility

Is the intervention feasible to implement?

Is it feasible to implement PCV for all PCV-naïve adults aged 50–64 years?

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

Vaccine coverage tends to be lower in younger adults even with an age-based recommendation

	50–64 yrs		≥65 yrs
COVID-19[1]	25.2%		40.6%
Influenza[2]	51.5%		73.8%
Recombinant Zoster Vaccine[3]	12.2% (50–59)	20.1% (60–64)	22.8%
Pneumococcal[4]	37.3%*		69.7%

*Receipt of any pneumococcal vaccine dose among those with risk-based indications

1. Week ending May 11, 2024. Vaccine coverage with the updated 2023-2024 COVID-19 vaccine, defined as receipt of at least one vaccination since September 2023.
2. Week ending May 11, 2024. Vaccine coverage for the 2023-2024 influenza season
3. Vaccination Coverage among Adults in the United States, National Health Interview Survey, 2021 | CDC, % represents those who received at least 2 doses
4. BRFSS 2022 data, % represents receipt of any pneumococcal vaccine dose

Compared with vaccine coverage in adults aged ≥65 years, pneumococcal vaccine coverage in adults aged 50–64 years with risk-based indication was disproportionately lower

	50–64 yrs		≥65 yrs	(50–64 yrs)/ (≥65 yrs)
COVID-19[1]	25.2%		40.6%	0.62
Influenza[2]	51.5%		73.8%	0.70
Recombinant Zoster Vaccine[3]	12.2% (50–59)	20.1% (60–64)	22.8%	
Pneumococcal[4]	37.3%*		69.7%	0.54

*Receipt of any pneumococcal vaccine dose among those with risk-based indications

1. Week ending May 11, 2024. Vaccine coverage with the updated 2023-2024 COVID-19 vaccine, defined as receipt of at least one vaccination since September 2023.
2. Week ending May 11, 2024. Vaccine coverage for the 2023-2024 influenza season
3. Vaccination Coverage among Adults in the United States, National Health Interview Survey, 2021 | CDC, % represents those who received at least 2 doses
4. BRFSS 2022 data, % represents receipt of any pneumococcal vaccine dose

Work Group comments

- Age-based recommendations are generally easier to implement than risk-based recommendations
- Lower vaccine coverage in younger adults is likely due to multiple factors, such as healthcare access, perceived risk of disease or benefits from vaccination.
  - There is a larger proportion of adults aged 50–64 years without health insurance compared with adults aged ≥65 years[1].
- Having a different age-based recommendation by vaccine product (e.g., PCV20, PCV21) will be more challenging to implement.
- Variability in health insurance coverage might keep PCV20 as the only practical option for some individuals in the short term since PCV21 is new.

1. Health Insurance Coverage in the United States: 2022 (census.gov)

Summary of Work Group Interpretations of EtR Domains

EtR Domains	Work Group Interpretation
Public Health Problem	Yes
Equity	Probably increased
Benefits and Harms	
a. Benefits	Moderate
b. Harms	Minimal
c. Benefit>Harm?	Favors intervention
Values and Preferences	
a. Desirable>Undesirable?	Probably yes/yes
b. Uncertainty?	Probably not important uncertainty or variability
Acceptability	Yes
Resource Use	Probably yes/Yes
Feasibility	Probably yes/Yes

Key considerations: factors supporting lowering the PCV age-based recommendation to age ≥50 years

1. The relatively high burden of pneumococcal disease in adults aged 50–64 years, particularly among those with risk conditions
2. Potential for improved vaccine uptake through an age-based recommendation, which is easier to implement compared with the current risk-based recommendation
3. Potential to reduce pneumococcal disease incidence in demographic groups experiencing the highest burden
4. Projected health benefits from economic models* despite increased net costs

*Note that these are models that assumed that another vaccine dose is given later in life to ensure older adults are protected from disease

Key considerations: potential implications

1. Economic concerns: While our models showed health benefits, there were significant concerns about the cost of lowering the age recommendation for both PCV20 and PCV21 when considering overall health benefits to society
2. Market availability and insurance coverage: Concerns were raised that variability in health insurance coverage might keep PCV20 as the only practical option for some individuals in the short term, given that PCV21 is a newer vaccine
3. Ease of implementation: The Work Group agreed that having different age-based recommendations by vaccine would be challenging to implement

Key considerations: uncertainties

1. How long is the duration of protection from a dose of PCV in adults?
2. What is the magnitude of indirect effects from pediatric PCV15/20 vaccination?
3. What might be the impact of higher-valency vaccines under development?

Summary: Work Group Interpretation

- **Should a single dose of pneumococcal conjugate vaccine be recommended for all PCV-naïve adults aged 50–64 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

Should a single dose of pneumococcal conjugate vaccine be recommended for all PCV-naïve adults aged 50–64 years?

- **Policy options for ACIP consideration**
  - The majority recommended, but about a quarter said “do not recommend the intervention”
    - The higher cost/QALY gained for PCV20 compared to PCV21 in economic analyses
    - Uncertainties around key assumptions like the impact of pediatric PCV use and duration of protection
    - Concerns about the implications of a broad recommendation given the differences in serotype coverage between PCV20 and PCV21

Should a single dose of pneumococcal conjugate vaccine be recommended for all PCV-naïve adults aged 50–64 years?

- **Is there sufficient information to move forward with a recommendation**
  - Yes
- **Policy options for ACIP consideration**
  - Recommend the intervention

Proposed policy option

- **ACIP recommends a pneumococcal conjugate vaccine (PCV) for all PCV-naïve adults aged ≥50 years**

Clinical considerations

Proposed language

PCV-naïve adults* (or adults with unknown history)

DRAFT

- **A single dose of PCV (PCV15, PCV20, or PCV21) is recommended for all adults aged ≥50 years and for adults aged 19–49 years with certain underlying conditions or risk factors[†] who have not received a PCV or whose vaccination history is unknown.**
- **If PCV15 is administered, a single dose of PPSV23 [§] should be administered ≥1 year after the PCV15 dose. A minimum interval of 8 weeks can be considered if PCV15 is used in adults with an immunocompromising condition[¶], cochlear implant, or CSF leak.**

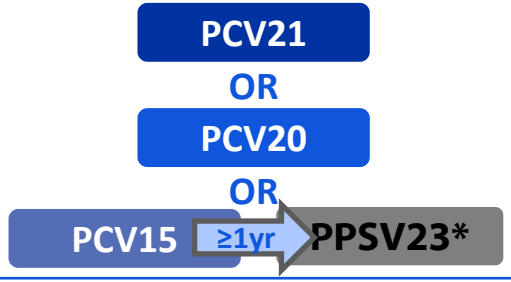
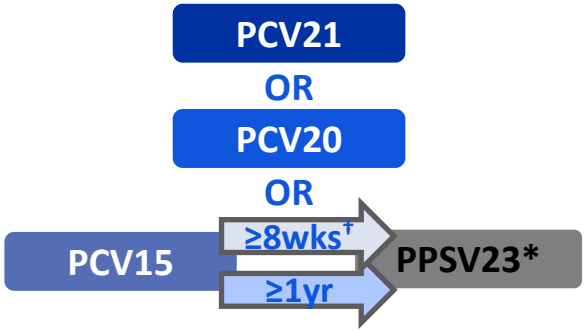
*Includes adults who received PCV7 only

[†] Alcoholism; chronic heart, liver, or lung disease; chronic renal failure; cigarette smoking; cochlear implant; congenital or acquired asplenia; cerebrospinal fluid leak; diabetes mellitus; generalized malignancy; HIV; Hodgkin disease; immunodeficiency; iatrogenic immunosuppression; leukemia, lymphoma, or multiple myeloma; nephrotic syndrome; solid organ transplant; sickle cell disease; or other hemoglobinopathies.

[§] For adults who have received PCV15 but have not completed their recommended pneumococcal vaccine series with PPSV23, 1 dose of PCV21 or PCV20 may be used if PPSV23 is not available.

[¶]Chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, HIV infection, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplant, congenital or acquired asplenia, or sickle cell disease or other hemoglobinopathies.

PCV-naïve adults (or adults with unknown history) DRAFT

<table>
<tr><th>Underlying conditions</th><th>Previous vaccination history</th><th>Age 19–49 years</th><th>Age ≥50 years</th></tr>
<tr><td>None</td><td>None</td><td>No vaccine recommendation</td><td> 
</td></tr>
<tr><td>Chronic medical conditions</td><td>None</td><td rowspan="3" colspan="2"> 

*If adults previously received PPSV23 before receiving a dose of PCV15, it need not be followed by another dose of PPSV23
†A minimum interval of 8 weeks can be considered for adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak</td></tr>
<tr><td>CSF leak, cochlear implant</td><td>None</td></tr>
<tr><td>Immuno-compromised</td><td>None</td></tr>
</table>

Use of 21-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2024 | MMWR

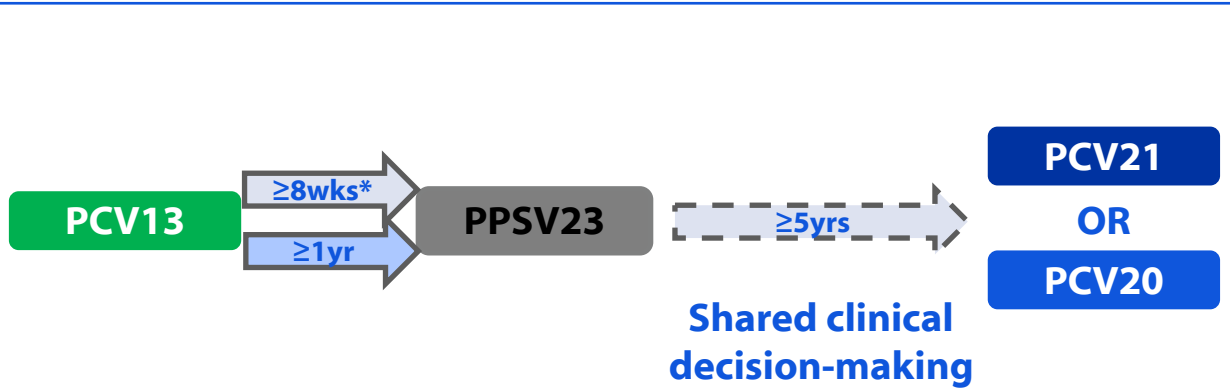
PCV13-experienced adults who completed the recommended vaccine series DRAFT (no change from current)

- **Shared clinical decision-making is recommended regarding use of a supplemental PCV20 or PCV21 dose for adults aged ≥65 years who have completed their recommended vaccine series with both PCV13 and PPSV23.**

Rationale:

- **No change is proposed to the age threshold. Under the previous recommendation, PCV13-vaccinated adults were only considered to have "completed" their recommended vaccine doses after receiving one and final dose of PPSV23 at or after age 65 years. Therefore, this scenario only applies to adults aged ≥65 years who received both PCV13 and PPSV23 at or after age 65 years.**

PCV13-experienced adults who completed the recommended vaccine series DRAFT (no change from current)

Underlying conditions	Age ≥65 years
None	
Chronic medical conditions	
CSF leak, cochlear implant	
Immuno-compromised	

*A minimum interval of 8 weeks can be considered for adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak

Use of 21-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2024 | MMWR

PCV13-experienced adults who have not completed the recommended vaccine series DRAFT

- **A single dose of either PCV20 or PCV21 is recommended for adults aged ≥19 years who have started their pneumococcal vaccine series with PCV13 but have not received all recommended pneumococcal vaccine doses.**

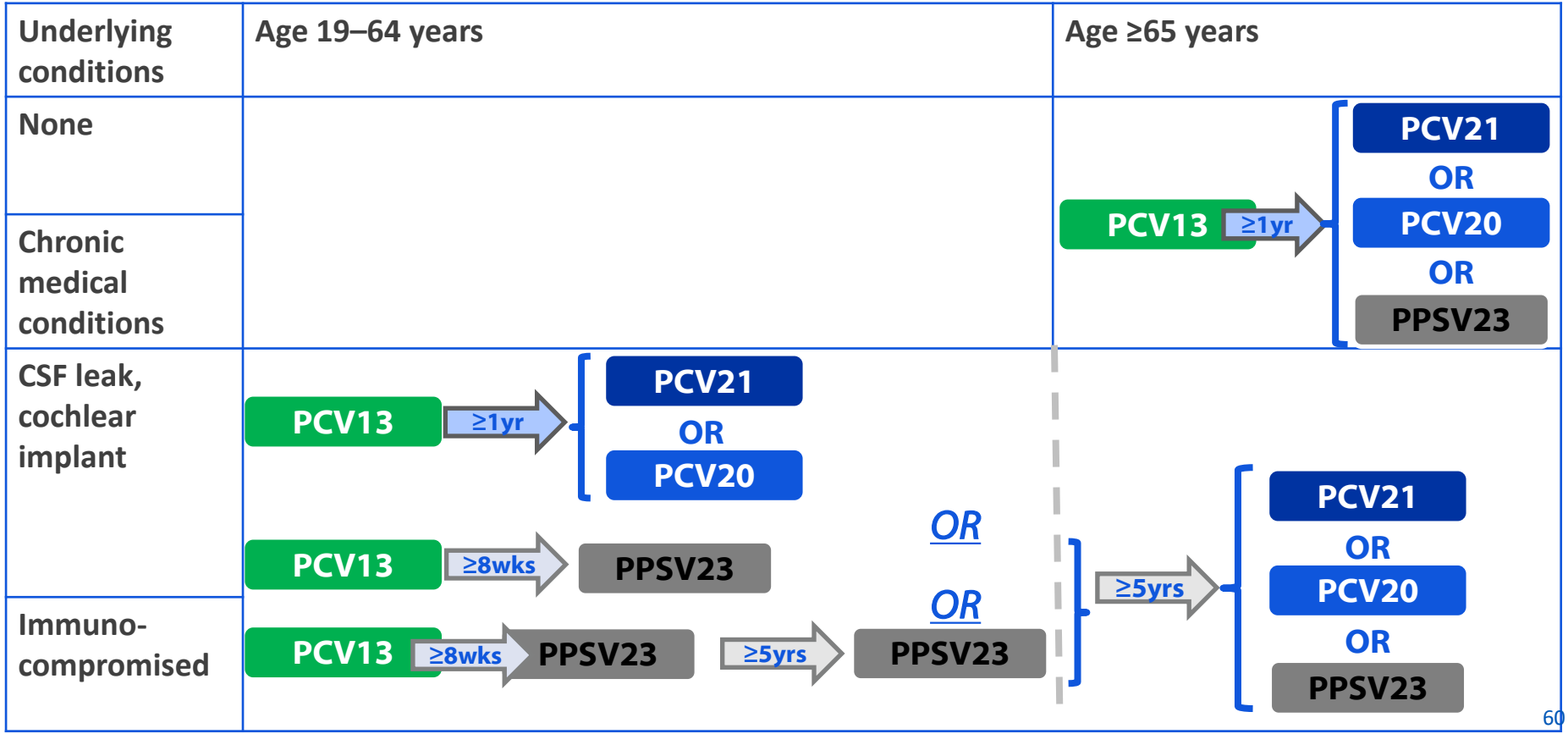
Change:

- **Removed the option to complete vaccine series with PPSV23 for PCV13-experienced adults**

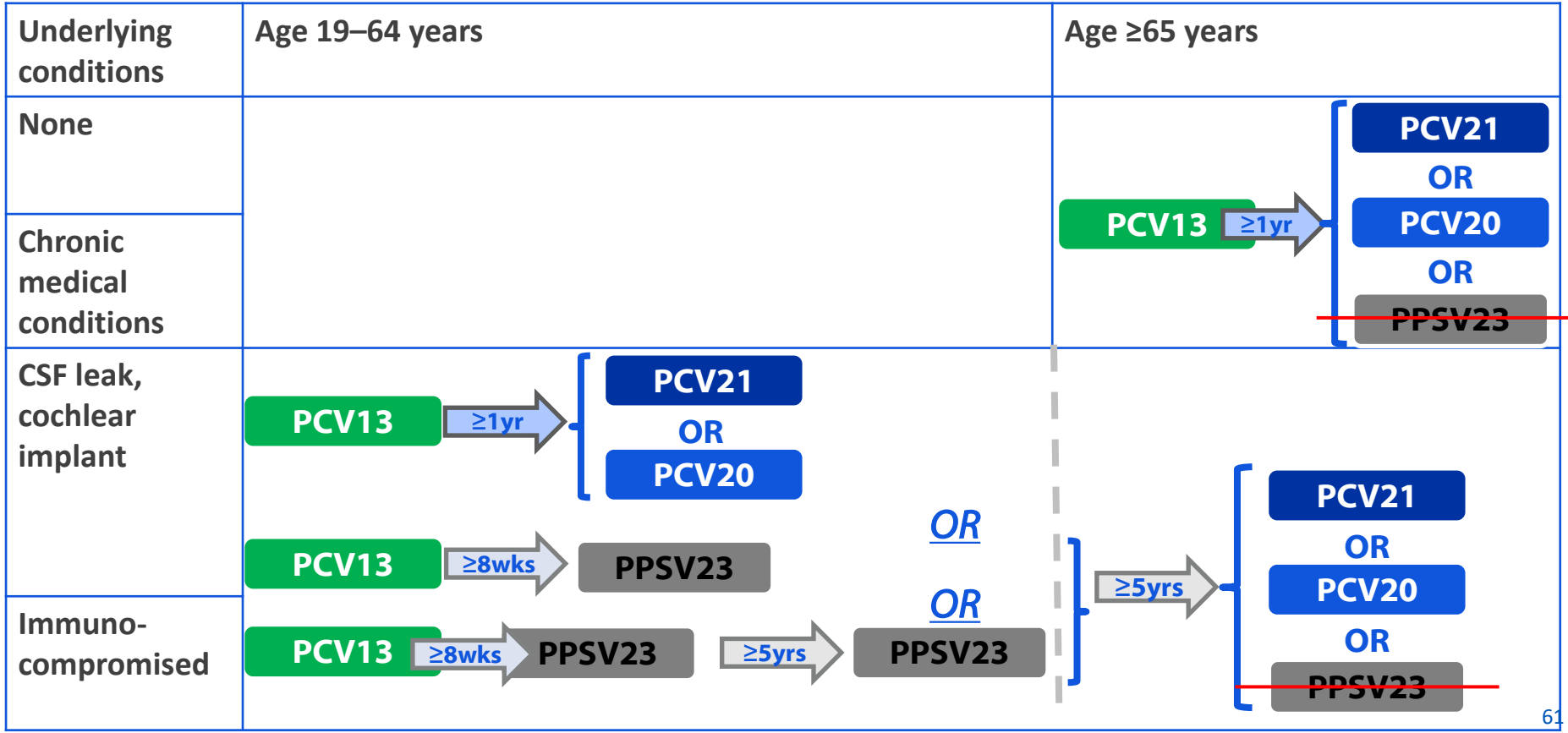
Rationale:

- **The potential need for repeated PPSV23 doses in adults who received PCV13 was one of the reasons for the complexity of the recommendation.**

PCV13-experienced adults who have not completed the recommended vaccine series (current recommendation)



PCV13-experienced adults who have not completed the recommended vaccine series (proposed)



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Supplementary Slides

Search strategy

Database	Strategy	Run Date	Records
PubMed	(PCV15 OR PCV20 OR "15-valent pneumococcal conjugate vaccine" OR "20-valent pneumococcal conjugate vaccine") AND adult; Filters applied: English, Humans, from 2021/2/19 - Present.	August 3, 2024	94
PubMed	(PCV21 OR V116 OR "pneumococcal conjugate vaccine 21" OR "pneumococcal conjugate vaccine 21-valent") AND ("2023/09/19"[Date - Publication] : "3000"[Date - Publication])	September 8, 2024	66
Clinicaltrials.gov	V114, Filter: "Adult (18-64)", "Phase 3"	August 17, 2024	8
Clinicaltrials.gov	20vPnc, PCV20, 20-valent PCV, 20-valent pneumococcal conjugate vaccine; Filter: "Adult (18-64)", "Phase 3"	August 17, 2024	18
Clinicaltrials.gov	1. Intervention: “V116”, filter: “Adult (18–64)”, “Phase 3” 2. “PCV21”, filter: “Adult (18–64)”, “Phase 3” 3. “21 valent pneumococcal conjugate vaccine”, filter: “Adult (18–64)”, “Phase 3”	September 8, 2024	1. 7 2. 0 3. 7 (all duplicate with 1)

PCV15 studies included in the review of evidence

Study	Study design	Country (or more detail, if needed)	Age (range	Total population	N Intervention	N comparison	Outcomes	Funding source
Song 2021	Phase III randomized controlled trial	US, Korea, Spain, Taiwan	Adults ≥50 years of age, PCV followed by PPSV23 12 months later	627	325	302	Immunogenicity, Safety	Merck
Mohapi 2022	Phase III randomized controlled trial	US	Adults ≥18 years of age with HIV, PCV followed by PPSV23 8 weeks later	298	150	148	Immunogenicity, Safety	Merck
Platt 2022	Phase III randomized controlled trial	US, Japan, Spain, Canada, Taiwan	Adults ≥50 years of age	1202	602	600	Immunogenicity, Safety	Merck
Simon 2022	Phase III randomized controlled trial	US, Australia, Chile, Denmark, Finland, UK	Adults ≥50 years of age	2340	2107	233	Immunogenicity, Safety	Merck
Severance 2022	Phase III randomized controlled trial	US	Adults ≥50 years of age	1200	600 (concomitant with QIV)	600 (sequential QIV administration)	Immunogenicity, Safety	Merck
V110-911	Phase III randomized controlled trial	US, Puerto Rico	Adults ≥50 years of age	850 (includes 426 who received PPSV23	214 (concomitant with mRNA-1273)	210 (sequential mRNA-1273 administration)	Immunogenicity and safety	Merck

PCV20 studies included in the review of evidence

Study	Study design	Country (or more detail, if needed)	Age (range	Total population	N Intervention	N comparison	Outcomes	Funding source
Essink, 2022	Phase III randomized controlled trial	US and Sweden	Adults ≥ 18-49 years (34.0, SD 8.8)	448	336 (PCV20)	112 (PCV13)	Immunogenicity, Safety	Pfizer
			Adults ≥ 50-59 years (54.9, SD 2.8)	445	334 (PCV20)	111 (PCV13)		
			Adults ≥ 60 years (64.6, SD 4.8)	2997	1507 (PCV20)	1490 (PCV13+PPSV23)		
Hurley, 2021	Phase II randomized controlled trial	US	Adults 60 - 64 years (62.0, SD 1.4)	444	222	222	Immunogenicity, Safety	Pfizer
Haranaka, 2024	Phase III randomized controlled trial	Japan, South Korea, and Taiwan	Adults aged ≥60 years (66.1, SD 4.7)	1421	711 (PCV20)	710 (PCV13+PPSV23)	Immunogenicity, Safety	Pfizer

PCV21 studies included in the review of evidence

Study	Study design	Country	Age	Total population	N Intervention*	N comparison	Outcomes	Funding source
Platt, 2023	RCT (Phase II)	US	Adults ≥50 years	508	254	PPSV23: 254	Immunogenicity and Safety	Merck
Platt, 2024	RCT (Phase III); pivotal study	US, Australia, Belgium, Chile, Germany, Korea, New Zealand, Puerto Rico, Sweden, Taiwan, Turkey	Healthy adults ≥50 years, pneumococcal vaccine – naïve	2,663	1, 179	PCV20: 1,177	Immunogenicity and Safety	Merck
			Healthy adults 18 - 49 years, pneumococcal vaccine – naïve		200	PCV20: 100		
V116-005	RCT (Phase III)	US	Adults ≥50 years	1,080	(V116 + QIV, coadministered): 536	(QIV followed by V116): 536	Immunogenicity and Safety	Merck
Scott, 2024	RCT (Phase III)	US, Canada, Israel, France, Italy, Japan, Korea, Spain, Taiwan	Adults ≥50 years, previous PPSV23 ≥1 year prior to enrollment	350	229	PCV15, n=117	Immunogenicity and Safety	Merck
			Adults ≥50 years, previous PCV13 ≥1 year prior to enrollment	261	174	PPSV23 N=85		
			Adults ≥50 years, PCV13+PPSV23, PCV15+PPSV23, PCV15, PCV20, or PPSV23+PCV13 ≥1 year prior to enrollment	106	105	None		
V116-007	RCT (Phase III)	Belgium, Chile, France, South Africa, Thailand, United States	Adults ≥18 years living with HIV; 36% prior PCV13 or PPSV23*	313	155	PCV15+PPSV23, n=156	Immunogenicity and Safety	Merck
V116-008	RCT (Phase III)	United States, Australia, Canada, Chile, Japan, South Korea, New Zealand, Poland,	Adults aged 18–64 years with increased risk for pneumococcal disease†	518	386	PCV15+PPSV23, n=130	Immunogenicity and Safety	Merck
V116-010	RCT (Phase III)	Argentina, Australia, Colombia, Germany, Israel, South Korea, New Zealand, Spain, Taiwan, Turkey, United Kingdom	Adults aged ≥50 years, pneumococcal vaccine-naïve	1,484	739	PPSV23: 741	Immunogenicity and Safety	Merck

*participants who received at least one dose of study intervention