National Center for Immunization & Respiratory Diseases

Adult Pneumococcal Vaccine Recommendations Updates

Miwako Kobayashi, MD, MPH

National Adult and Influenza Immunization Summit Call
December 1, 2022

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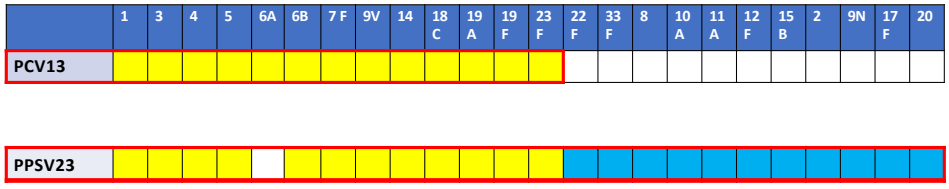
Two pneumococcal vaccines were licensed for use in U.S. adults before 2021.



23-valent pneumococcal polysaccharide vaccine (PPSV23)	Pneumovax23® Since 1983
13-valent pneumococcal conjugate vaccine (PCV13)	Prevnar13® Since 2011 (for adults)

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In 2021, 2 new pneumococcal conjugate vaccines were licensed for use among U.S. adults.

	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																								

23-valent pneumococcal polysaccharide vaccine (PPSV23) — Pneumovax23®

13-valent pneumococcal conjugate vaccine (PCV13) — Prevnar13®

15-valent pneumococcal conjugate vaccine (PCV15) — Vaxneuvance™

20-valent pneumococcal conjugate vaccine (PCV20) — Prevnar20™

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On October 20, 2021, the ACIP recommended use of new pneumococcal conjugate vaccines for adults.

Use of 15-Valent Pneumococcal Conjugate Vaccine and 20-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2022

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MMWR January 28, 2022

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New Adults Pneumococcal Vaccine Recommendations: No previous vaccination

Underlying conditions	Previous vaccination history	Age 19–64 years	Age ≥65 years
None	None	No vaccine recommendation	PCV20 OR PCV15 ≥1yr PPSV23
Chronic medical conditions	None	PCV20 OR PCV15 ≥8wks* PPSV23 / PCV15 ≥1yr PPSV23	
CSF leak, cochlear implant	None		
Immuno-compromised	None		

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

Use of 15-Valent Pneumococcal Conjugate Vaccine and 20-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2022 | MMWR (cdc.gov)

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Adults who started the series with PCV13 were recommended to complete with PPSV23

Underlying conditions	Age 19–64 years	Age ≥65 years
None	PCV13 Previously not recommended	PCV13 ≥1yr PPSV23
Chronic medical conditions		
CSF leak, cochlear implant	PCV13 ≥8wks PPSV23 ≥5yrs	PPSV23
Immuno-compromised	PCV13 ≥8wks PPSV23 ≥5yrs PPSV23	≥5yrs PPSV23

Use of 15-Valent Pneumococcal Conjugate Vaccine and 20-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2022 | MMWR (cdc.gov)

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Consideration 1: Adults who were previously recommended to receive PCV13

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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 (updated in 2019)
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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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 (**updated in 2019**)
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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Consideration 2: Immunologic advantage of PCV vs PPSV

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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

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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

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Consideration 3: Time since last pneumococcal vaccination

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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)

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Question: Should the groups of adults who started the previous recommendation with PCV13 receive PCV20 as an option to PPSV23 for added protection?

Underlying conditions	Age 19–64 years	Age ≥65 years
None	PCV13 Previously not recommended	PCV13 → ≥1yr → PPSV23
Chronic medical conditions		
CSF leak, cochlear implant	PCV13 → ≥8wks → PPSV23 → ≥5yrs → PPSV23	PPSV23
Immuno-compromised	PCV13 → ≥8wks → PPSV23 → ≥5yrs → PPSV23 → ≥5yrs → PPSV23	PPSV23

Use of 15-Valent Pneumococcal Conjugate Vaccine and 20-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2022 | MMWR (cdc.gov)

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What was the burden of pneumococcal disease in adults?

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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

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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

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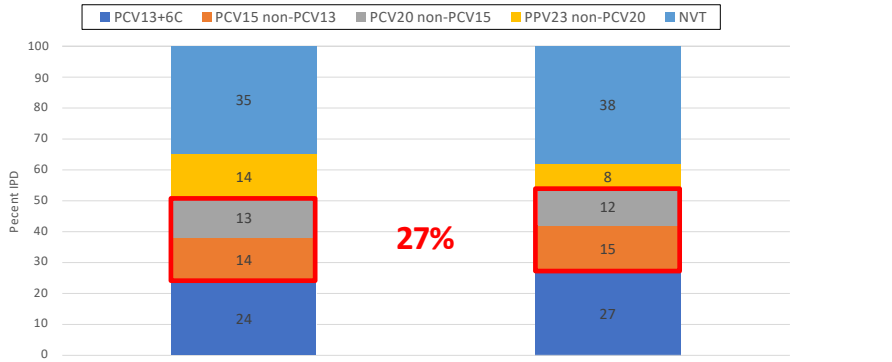
Pneumococcal serotypes contained in PCV20 but not in PCV13 caused 27% of Invasive Pneumococcal Disease in Adults in 2018–2019



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What was the impact of PCV13 use on adult pneumococcal disease burden?

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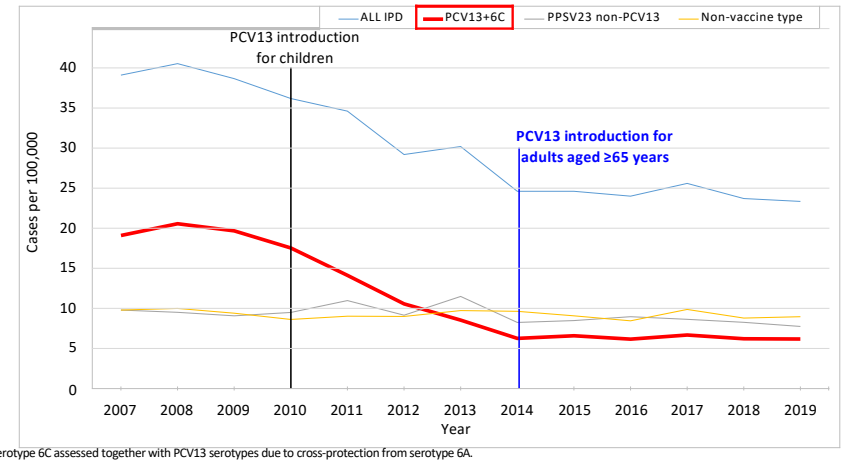
PCV13-type IPD incidence among adults aged ≥65 years decreased after PCV13 use in children but remained stable in 2014–2019



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

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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

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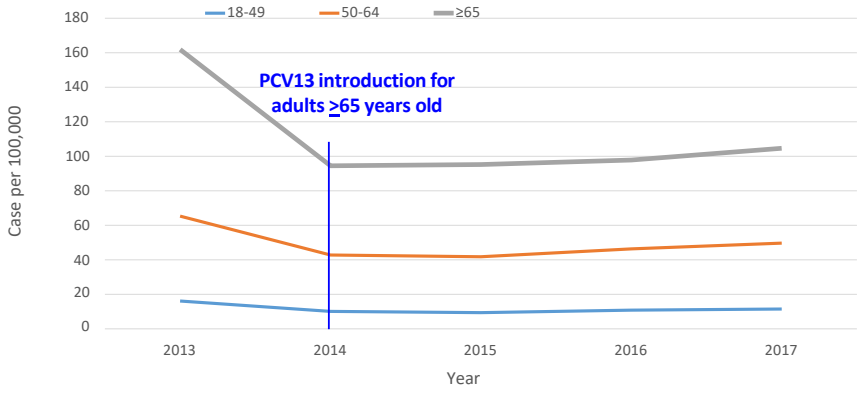
Hospitalized pneumococcal pneumonia incidence in adults did not decrease after routine PCV13 use among adults aged ≥65 years.



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

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Data on safety and effectiveness of PCV20 use among adults who previously received PCV13

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Summary of Evidence

- Systematic review of literature
  - **No PCV20 efficacy or effectiveness data**
  - 2 Phase 3 clinical trials on PCV20 among adults who previously received PCV13 were identified
    - Immunogenicity: 2 studies[1,2]
    - Safety: 1 study[1]
    - Adults aged ≥65 years **without** immunocompromising conditions
- Summary: **Immunogenicity**
  - Compared with adults who previously received PPSV23 1–5 years prior, adults who received PCV13 ≥6 months prior had **comparable or improved immune response to PCV20**
- Summary: **Safety**
  - Proportion of serious adverse events among PCV13+PCV20 group was **comparable** to PCV13+PPSV23 group

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

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Summary of cost-effectiveness analysis

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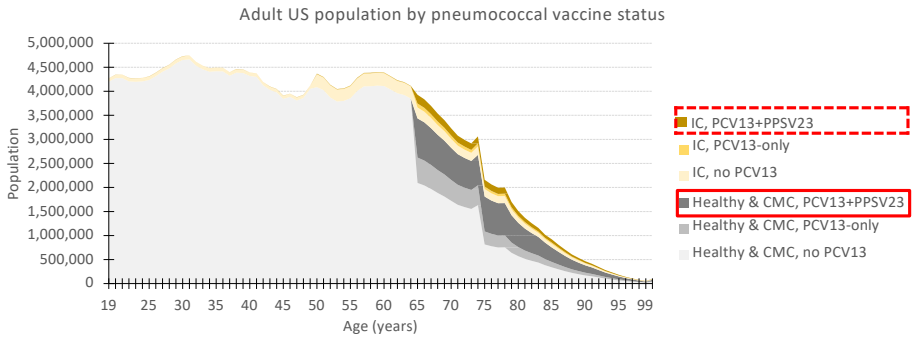
Comparison will focus on assessment of PCV20 use among adults aged ≥65 years who previously received PCV13 and PPSV23.



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.

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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).

QALY: quality-adjusted life year

[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.

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Cost-effectiveness ratios, PCV20

65+, PCV13+PPSV23, single cohort

	CDC[a]	Pfizer[b]	Merck[c]
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$/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

a. The CDC model as
b. The Pfizer model a
herd effects.
c. The Merck model

ER estimate includes

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

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Additional Considerations

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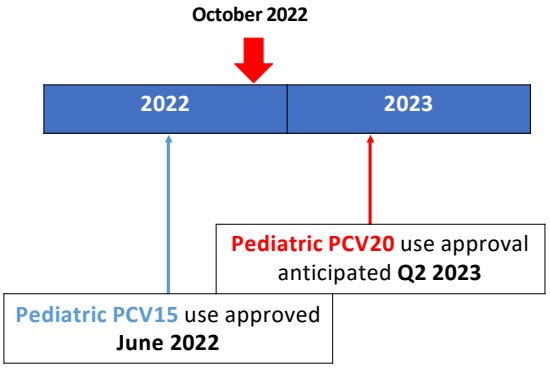
Context: Approval of PCV20 use among Children Anticipated in 2023



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Context: New Adult Pneumococcal Vaccines in Advanced Stages of Development

	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	22F	33F	8	10A	11A	12F	15B	2	9N	17F	20	20B	15A	15C	16F	23A	23B	24F	31	35B
PCV13																																	
PCV15																																	
PCV20																																	
PPSV23																																	
AFX3772																																	
V116																																	

24-valent pneumococcal vaccine — **AFX3772, GSK**

- Completed phase 1/2 study for adults[1]

21-valent pneumococcal conjugate vaccine — **V116, Merck**

- Completed phase 1/2 study for adults[2]
- Phase 3 immunobridging studies in adults are currently ongoing

1. Chichili et al. Vaccine 2022; 2. Platt et al. Lancet ID 2022.

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Updated ACIP Recommendations

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Group 1: Immunocompromised adults who received PCV13+PPSV23 but have not completed their series

- Adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak who have received both PCV13 and PPSV23 with incomplete vaccination status are recommended to complete their pneumococcal vaccine series by receiving either a dose of PCV20 at least 5 years after the last pneumococcal vaccine dose or PPSV23 as previously recommended.

https://www.cdc.gov/vaccines/acip/index.html

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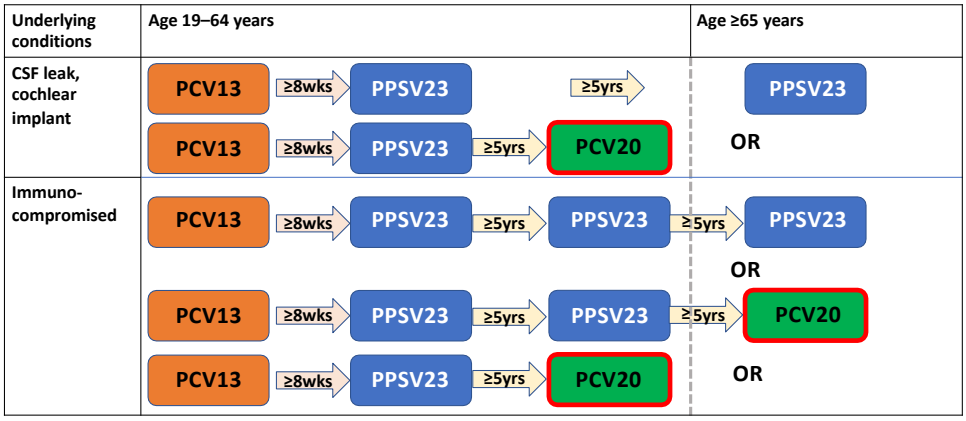
Group 1: Immunocompromised adults who received PCV13+PPSV23 but have not completed their series



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Group 2: Adults aged ≥65 yrs who completed the series with PCV13+PPSV23

- Shared clinical decision-making is recommended regarding administration of PCV20 for adults aged ≥65 years who completed their vaccine series with both PCV13 and PPSV23. If a decision to administer PCV20 is made, a dose of PCV20 is recommended at least 5 years after the last pneumococcal vaccine dose.

https://www.cdc.gov/vaccines/acip/index.html

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Group 2: Adults aged ≥65 yrs who completed the series with PCV13+PPSV23

Underlying conditions	Age 19–64 years	Age ≥65 years
None	PCV13 Previously not recommended	PCV13 → ≥1yr → PPSV23 AND ≥5yrs → PCV20
Chronic medical conditions		
CSF leak, cochlear implant	PCV13 → ≥8wks → PPSV23 → ≥5yrs	Shared clinical decision-making
Immuno-compromised	PCV13 → ≥8wks → PPSV23 → ≥5yrs → PPSV23	≥5yrs → PPSV23

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Group 3: Adults who started the series with PCV13 but have not received PPSV23

Adults who have received PCV13 only are recommended to receive a dose of PCV20 at least 1 year after the PCV13 dose or PPSV23 as previously recommended to complete their pneumococcal vaccine series.

https://www.cdc.gov/vaccines/acip/index.html

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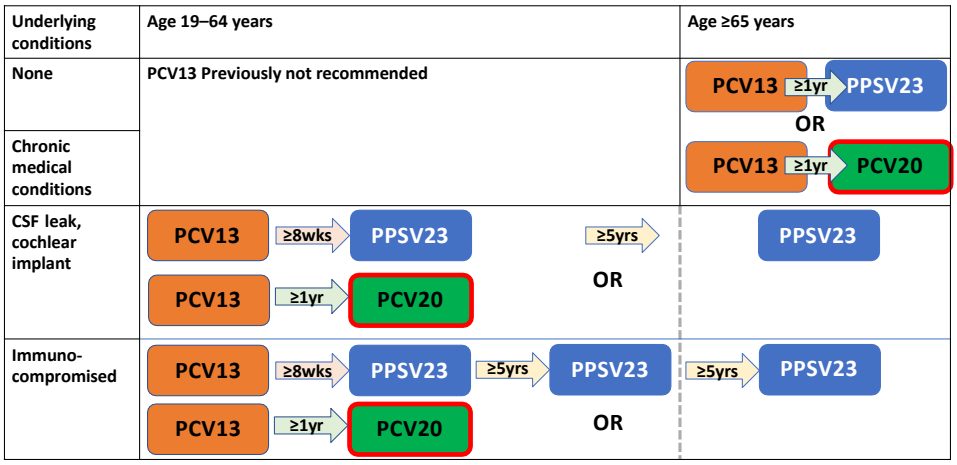
Group 3: Adults who started the series with PCV13 but have not received PPSV23



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Proposed Timeline for Publication of the Updated Recommendations

- New pneumococcal vaccine recommendations will be reflected in the new Adult Immunization Schedule: scheduled for publication early 2023
- New recommendations, along with updated recommendations related to implementation, will be published as MMWR Recommendations and Reports later in 2023

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- ACIP and the Pneumococcal Vaccines Work Group
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1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

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