GRADE:
15-valent and 20-valent Pneumococcal Conjugate Vaccine use in adults

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Policy Options for Cost-Effectiveness Analysis

After reviewing the results of the cost-effectiveness analysis and estimated public health impact from each policy option, the Work Group focused on **the following 4 options** for GRADE and EtR.

	Age 19–64 years with underlying conditions	**All aged ≥65 years**
Strategy a	**PCV15**	**PCV15**
Strategy b	**PCV20**	**PCV20**
Strategy c	**PCV15+PPSV23**	**PCV15+PPSV23**
Strategy d	PCV20+PPSV23	PCV20+PPSV23
	Age 19–49 years with underlying conditions	**All aged ≥50 years**
Strategy a	PCV15	PCV15
Strategy b	**PCV20**	**PCV20**
Strategy c	PCV15+PPSV23	PCV15+PPSV23
Strategy d	PCV20+PPSV23	PCV20+PPSV23

Methods

Outcomes

Outcome (Benefits)	Importance*	Description
Vaccine-type (VT) IPD	Critical	Studies on PCV15 or PCV20 assessing these clinical outcomes are currently not available → PCV15/PCV20 immunogenicity studies
VT non-bacteremic pneumococcal pneumonia	Critical	
VT death	Critical	

Outcome	Importance*	Description
Serious adverse events	Critical	Safety data for PCV15 and PCV20 are available.

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

PICO	Should PCV15 be routinely recommended to US adults ⩾65 years and older?	Should PCV15 be routinely recommended to US adults ⩾65 years and older in series with PPSV23?	Should PCV20 be routinely recommended to US adults ⩾65 years and older?	Should PCV20 be routinely recommended to US adults ⩾50 years and older?
Population	US adults aged ⩾65 years			US adults aged ⩾50 years
Intervention	One dose of PCV15	One dose of PCV15 followed by PPSV23	One dose of PCV20	
Comparison	1. PCV13 followed by PPSV23 (immunocompromised adults aged ⩾65 years*) 2. PPSV23 (immunocompetent or healthy adults aged ⩾65 years)** *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			1. PCV13 followed by PPSV23 (immunocompromised adults aged ≥50 years*) 2. PPSV23 only (adults 50–64 years with chronic medical conditions***, immunocompetent adults aged ≥65 years **) 3. No vaccination (adults 50–64 years without indications) *** CMC: includes chronic heart/lung/liver disease, cirrhosis, diabetes mellitus, alcoholism, and cigarette smoking
Outcome	Vaccine-type invasive pneumococcal disease, vaccine-type non-bacteremic pneumococcal pneumonia, deaths, serious adverse events			

GRADE Evidence Type

- Type 1 (high certainty): We are very confident that the true effect lies close to that of the estimate of the effect.
- Type 2 (moderate certainty): We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- Type 3 (low certainty): Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
- Type 4 (very low certainty): We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Note: Evidence type is not measuring the quality of individual studies, but how much certainty we have in the estimates of effect across each outcome.

GRADE Criteria

- **Initial evidence type** (certainty level) determined by study design
  - Initial evidence type 1 (high certainty): A body of evidence from randomized controlled trials
  - Initial evidence type 2 (low certainty): A body of evidence from observational studies
- **Risk of bias**: Can include failure to conceal allocation, failure to blind, loss to follow-up. Risk of bias may vary across outcomes.
- **Inconsistency**: Criteria for evaluating include similarity of point estimates, extent of overlap of confidence intervals, and statistical criteria including tests of heterogeneity and I^2
- **Indirectness**: Considers the generalizability of the evidence to the original PICO components*
- **Imprecision**: Considers the fragility of the relative and absolute effect measures based on the interpretation of the 95% CIs and the optimal information size.
- **Other considerations**: Includes publication bias or indications of dose-response gradient, large or very large magnitude of effect, and opposing residual confounding.

*Patients, Intervention, Comparison, or Outcomes differ from those of interest.

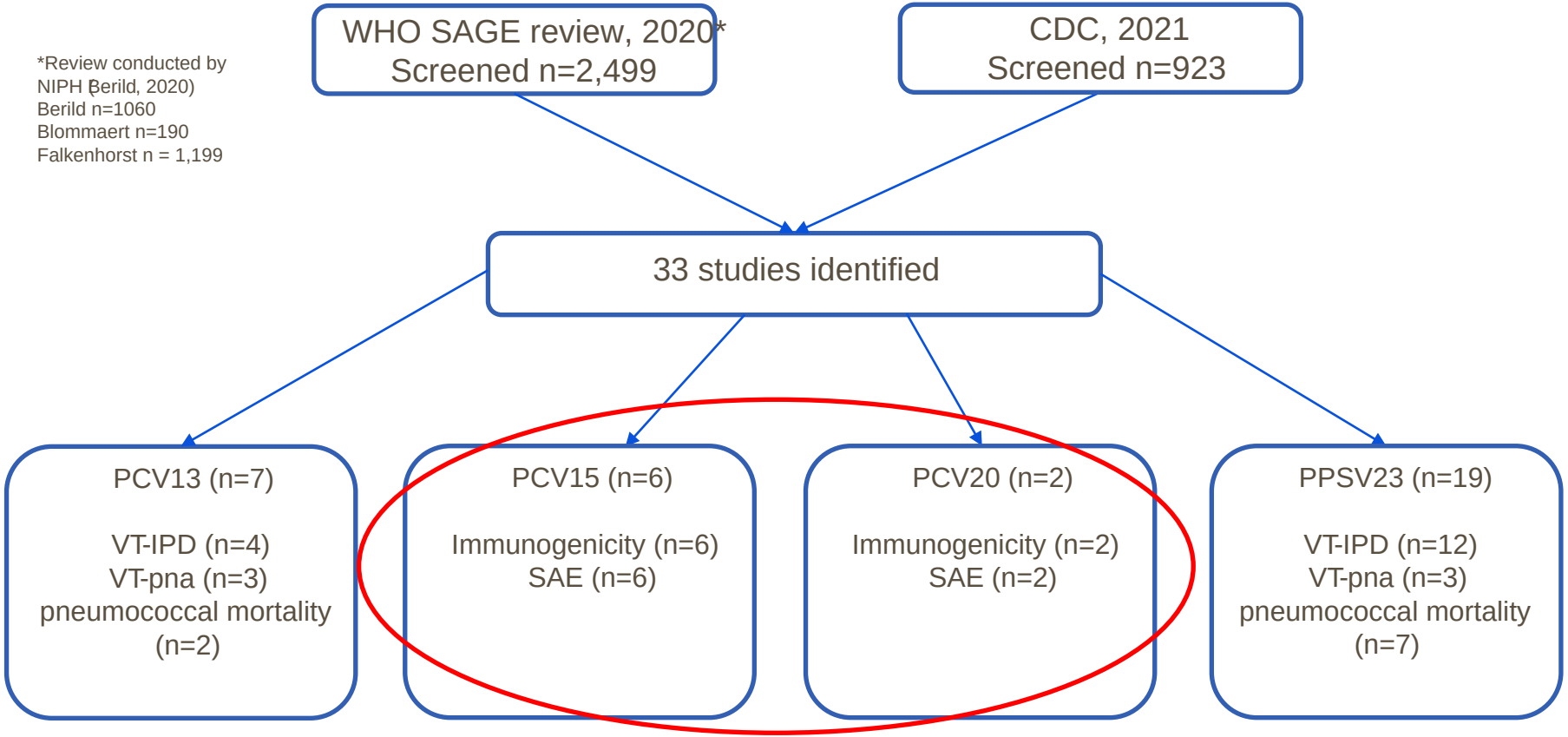
Guyatt GH, Oxman AD, Kunz R et al. GRADE guidelines: 8. Rating the quality of evidence —indirectness. *J Clin Epidemiol*. 2011.

Evidence Retrieval (PCV13, PCV15, PCV20)

- Leveraged systematic review presented to WHO/SAGE in 2020
  - Searched literature up to March 2019
- Additional search of literature published during April 2019–Feb 2021
  - **Databases**: Pubmed, Medline, Embase, CINAHL, Web of Science, Scopus, Epistemonikos and Cochrane library databases
  - **Inclusion for PCV13**: data on 1)human subjects, 2) adults, 3) relevant to vaccine efficacy or effectiveness against vaccine-type invasive pneumococcal disease, vaccine-type pneumonia, or death
  - **Inclusion for PCV15, PCV20**: data on 1) human subjects, 2) formulation considered for licensure, 3) adults aged ≥50 years or adults with underlying conditions
- Contacted manufacturers for unpublished and other relevant data
- Title and abstracts were screened independently by two separate reviewers

Evidence Retrieval

*Review conducted by NIPH (Berild, 2020)
Berild n=1060
Blommaert n=190
Falkenhorst n = 1,199



Review of evidence

- Review of evidence on clinical outcomes
  - PCV13 data against VT-IPD, VT-pneumonia, VT-mortality
  - PPSV23 data against VT-IPD, VT-pneumonia, VT-mortality
- Evidence for PCV15 (immunogenicity and SAE data)
- Evidence for PCV20 (immunogenicity and SAE data)

Vaccine effectiveness against clinical outcomes

Background

PCV13 VE against VT-IPD

Study	Population	Method	VE	(95%CI)
Bonten* Dutch adults ≥65 years old		Community Acquired Pneumonia Immunization Trial in Adults (CAPiTA) RCT (PCV13 vs placebo) (n=84,496); per protocol	75%	(41, 91)
		CAPiTA RCT (PCV13 vs placebo) (n=84,496) [+]	76%	(48, 89)[+]
Pilishvili	US adults ≥65 years old	Case-control; Active Bacterial Core Surveillance (ABCs) IPD cases and age- and zip code matched population-based controls (n=1,530)	59%	(11, 81)[¶]
Pilishvili	US adults ≥65 years old	Case-control; ABCs IPD cases enrolled in Medicare part B matched to controls on age group, census tract, and length of enrollment in part B (n=10,851)	47%	(4, 71)[¶]
Lewis*	Kaiser Permanente Northern California members, ≥65 years	Cohort study; KPNC members with no record of prior receipt of PPSV23, 2014 – 2018	68%	(28, 84)

[+]All episodes of PCV13-type IPD using modified intent-to-treat (mITT); [¶]VE estimate for PCV13+6C types
*Pfizer funded studies

PCV13 against VT-pneumonia

Study	Population	Method	VE	(95%CI)
Bonten*	Dutch adults ≥65 years old	CAPiTA RCT, non-bacteremic pneumonia, per-protocol (PCV13 vs placebo) (n=84,496)	45%	(14, 65)
McLaughlin*	U.S. adults ≥65 years old	Louisville cohort study nested test negative design case-control; any non-PCV13-type non-bacteremic pneumonia as controls (n=2,014)	71%	(-6, 90) [i]
Prato*	Italian adults ≥65 years old	Test-negative design case-control; any non-PCV13-type pneumonia as controls (n=186)	38%	(-131, 89) [ii]

[i]In the primary analysis, reported here, the controls were defined as all non-PCV13-type pneumonia. In a sensitivity analysis, where controls were defined as non-PCV13-type pneumococcal pneumonia, the VE was 69% (-47, 94).
[ii]*S. pneumoniae* confirmed in nasopharyngeal, sputum, bronchoalveolar-lavage, or sterile site on polymerase chain reaction (PCR) or culture. The controls were defined as all non-PCV13-type pneumonia.

*Pfizer funded study

PCV13 against VT-disease deaths

Study	Population	Method	Outcome	VE	(95%CI)
Bonten*	Dutch adults ≥65 years old	RCT (PCV13 vs placebo) (n=84,496)	PCV13-type disease mortality	0%	(-1280, 93)
Vila-Corcoles 2020	Spanish (Catalonia), ≥50 years	Population-based cohort (EPIVAC study), 2015-2016	Death from pneumococcal pneumonia	adjHR= 1.67	(0.61–4.60)

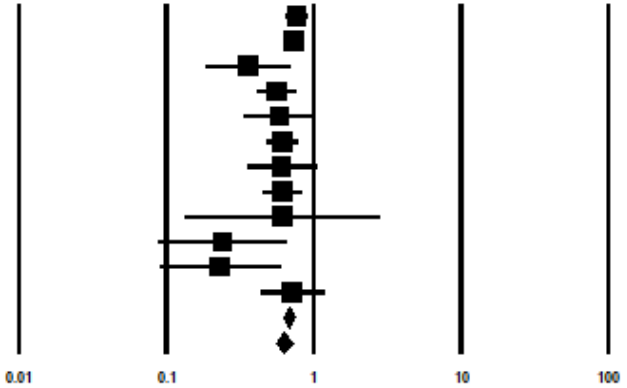
*Pfizer funded study

PPSV23 effectiveness data

PPSV23 against VT-IPD : pooled VE estimate of observational studies

PPSV23 vs VT-IPD, Observational Studies

Model	Subgroup within study	Study name	Outcome	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
	>=65 years, all	Andrews 2012	VT IPD	0.760	0.641	0.901	-3.155	0.002
	>=65 years, all	Djennad 2018	VT IPD	0.730	0.641	0.831	-4.746	0.000
	>=65 years	Dominguez 2005	VT IPD	0.360	0.184	0.705	-2.980	0.003
	>=60 years	Gutierrez-Rodriguez 2014	VT IPD	0.555	0.404	0.762	-3.637	0.000
	>=65 years	Kim 2019	VT IPD	0.581	0.332	1.016	-1.905	0.057
	>=65 years	Rudnick 2013	VT IPD	0.611	0.469	0.796	-3.651	0.000
	>=65 years	Shimbashi 2020	VT IPD	0.606	0.347	1.060	-1.757	0.079
	>=75 years	Su 2021	VT IPD	0.610	0.441	0.844	-2.980	0.003
	>=65 years	Vila-Corcoles 2006	VT IPD	0.610	0.132	2.811	-0.634	0.526
	>=50 years	Vila-Corcoles 2009	VT Bacteremic PP	0.240	0.089	0.650	-2.808	0.005
	>=60 years	Vila-Corcoles 2010	VT IPD	0.230	0.089	0.594	-3.037	0.002
	>=65 years	Wright 2013	VT IPD	0.715	0.435	1.175	-1.325	0.185
Fixed				0.676	0.621	0.735	-9.176	0.000
Random				0.624	0.543	0.716	-6.711	0.000



Pooled VE: 38% (28, 46)

Favours PPSV23 Favours no vaccine

Model	Effect size and 95% interval			Test of null (2-Tail)		Heterogeneity				Tau-squared			
Model	Number Studies	Point estimate	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed	12	0.676	0.621	0.735	-9.176	0.000	18.573	11	0.069	40.774	0.019	0.022	0.000	0.136
Random	12	0.624	0.543	0.716	-6.711	0.000								

PPSV23 against VT-Pneumonia

Study	Population	Method	VE	(95%CI)
Kim 2019	South Korean hospitalized adults, ≥65 years	Case-control, hospital-based; cases: non-bacteremic pneumococcal pneumonia	-2%	(-40, 26)
Lawrence 2020	British hospitalized adults, ≥65 years	Test-negative design case-control; non-PPV23 serotype pneumococcal pneumonia or nonpneumococcal pneumonia as control (n=993)	20%	(-5, 40)[i]
Suzuki 2017	Japanese adults, ≥65 years	Test-negative design case-control; patients who tested negative for pneumococcal infection as controls (n=1617)	34%	(6, 53)

[i]Secondary analysis from a prospective cohort study of adults (aged ≥16 years) with CAP hospitalized in Nottingham, England, from September 2013 to August 2018

PPSV23 against pneumococcal mortality

Study	Population	Method	Outcome	Measure	(95%CI)
Maruyama 2010	Japanese adults, ≥55 years	RCT, nursing home residents	death from pneumococcal pneumonia	Rate: 35.1% (placebo) vs. 0% (vaccine)	P<0.01
Vila-Corcoles 2020	Spanish (Catalonia), ≥50 years	Population-based cohort (EPIVAC study), 2015-2016	death from pneumococcal pneumonia	adjHR=1.47	(0.96–2.26)
Vila-Corcoles 2006	Spanish (Tarragona), ≥65 years	Prospective cohort (1999 – 2001	death due to pneumococcal infection	adjHR=0.50	(0.13–2.02)
Su 2021	Taiwanese adults, ≥75 years	Screening method	death from any pneumococcal infection	VE = 32.5%	(17.5, 44.7)
Christenson 2004	Swedish adults, ≥65 years	Prospective cohort (1998 – 2000)	in-hospital mortality due to pneumonia	VE = 7%	(-19, 28)
Rose 2020	German adults, ≥60 years	Retrospective cohort among those insured in a large statutory health insurance (2008 – 2014)	30-day mortality due to pneumonia	VE = 29.6%	(-60.9, 69.2)
Song 2018	South Korean adults, ≥65 years	Multicenter prospective cohort study (2014 – 2017)	30-day mortality among ILI patients	VE = -29%	(-136, 29)

Evidence for PCV15

Immunogenicity and safety

Summary of Phase 2/3 Immunogenicity Study Results

- **Outcomes summarized:**
  - Ratio of opsonophagocytic activity (OPA) geometric mean titer (GMT)
  - % Seroresponders[1]
  - Point estimates used for descriptive comparison

- **Statistical interpretation:**
  - Statistical non-inferiority[2] reported whenever assessed
  - If non-inferiority not assessed, “statistical significance” was defined as:
    - 95% CI of GMT ratio did not cross 1
    - 95% CI of % ≥4-fold rise in OPA GMT in the PCV15/20 vs comparator group did not overlap

1. Defined as subjects with ≥4-fold rise in OPA GMT titer post-vaccination compared to pre-vaccination
2. Noninferiority declared if the lower bound of the 2-sided 95% CI for the GMT ratio for that serotype was >0.5

Immunogenicity in healthy adults who received PCV15 only

		N (PCV15)	N (Comparison)	Comparison	GMT ratios[1]	% Seroresponders[2]
Ermlich 2018	Phase 2 RCT, adults ≥50 years	230	230	PCV13	• PCV15>PCV13 in 7/13 serotypes • Significantly higher for 5/13 serotypes	• PCV15>PCV13 in 9/13 serotypes • Non-significant for all serotypes (9/9)
		230	231	PPSV23	• PCV15>PPSV23 in 12/13 serotypes • Non-inferior[3] for all 13 serotypes	• PCV15>PPSV23 in 10/13 serotypes • Significantly higher for 3/10 serotypes (3, 6B, 23F)
V114-019	Phase 3 RCT (Pivotal Trial), adults ≥50 years	596-598	597-598	PCV13	• PCV15>PCV13 in 5/13 serotypes • Non-inferior[4] for the 13 serotypes • Superiority[5] criteria met for ST3	• PCV15>PCV13 in 5/13 shared serotypes • Significantly higher for 1/5 serotypes (ST3)
Peterson 2019	Phase 2 RCT, adults ≥65 years, h/o PPSV23	127	126	PCV13 (in those with previous PPSV23)	• PCV15>PCV13 in 7/13 serotypes	• PCV15>PCV13 in 8/13 shared serotypes • Non-significant for all serotypes (8/8)

1. Ratio calculated as [GMT (PCV15)]/[GMT (comparator vaccine)].
2. Seroresponse: subjects with >=4-fold rise in OPA GMT titer post-vaccination compared to pre-vaccination.
3. Non-inferiority was declared if lower bound of two-sided 95% CI of between-group ratio (PCV15/PPV23) of OPA GMTs for each shared serotype was >0.33 (3-fold non-inferiority margin). GMC/GMT ratio estimation
4. The statistical criterion for noninferiority requires the lower bound of the 2-sided 95% confidence interval (CI) of the OPA GMT ratio (V114/ Prevnar 13™) to be greater than 0.5
5. The statistical criterion for superiority requires the lower bound of the 2-sided 95% CI of the OPA GMT ratio [V114/ Prevnar 13™] to be greater than 2.0.

Immunogenicity in adults with underlying conditions, PCV15 only

		N (PCV15)	N (Comparison)	Comparison	GMT ratios[1]	% Seroresponders[2]
V114-017	Immunocompetent adults 18-49 years of age at risk of pneumococcal disease, Phase 3	1004-1019	320-343	PCV13	• PCV15>PCV13 in 6/13 serotypes	• PCV15>PCV13 in 6/13 shared serotypes • Significantly higher in 1/6 serotype (ST18C)
V114-018	Adults ≥18 years of age with HIV, Phase 3	126-131	116-131	PCV13	• PCV15>PCV13 in 10/13 serotypes	• PCV15>PCV13 in 9/13 serotypes

1. Ratio calculated as [GMT (PCV15)]/[GMT (comparator vaccine)].
2. Seroresponse: subjects with >=4-fold rise in OPA GMT titer post-vaccination compared to pre-vaccination.

Immunogenicity in adults, PCV15-PPSV23 series

		N (PCV15)	N (Comparison)	Comparison	GMT ratios[1]	% Seroresponders[2]
V114-017	Immunocompetent adults 18-49 years of age at risk of pneumococcal disease, Phase 3	830-844	276-283	PCV13 +PPSV23 (6 month interval)	• PCV15+PPSV23>PCV13+PPSV23 in 9/13 serotypes	• PCV15+PPSV23>PCV13+PPSV23 in 5/13 serotypes • Non-significant for all 5/5
V114-018	Adults ≥18 years of age with HIV, Phase3	118-123	113-117	PCV13 +PPSV23 (8 week interval)	• PCV15+PPSV23>PCV13+PPSV23 in 11/13 serotypes	• PCV15+PPSV23>PCV13+PPSV23 in 10/13 shared serotypes
V114-016	Adults ≥50 years of age, Phase 3	320-321	322-323	PCV13+PPSV23 (12 month interval)	• PCV15+PPSV23>PCV13+PPSV23 in 13/13 serotypes • Significantly higher for 3/13 serotypes (ST1, 14, 23F)	• PCV15+PPSV23>PCV13+PPSV23 in 11/13 shared serotypes • Non-significant for all 11/11

1. Ratio calculated as [GMT (PCV15)]/[GMT (comparator vaccine)].
2. Seroresponse: subjects with >=4-fold rise in OPA GMT titer post-vaccination compared to pre-vaccination.

SAE in healthy adults who received PCV15 only

		N (PCV15)	N (Comparison)	Comparison	Observation period	%SAE PCV15	%SAE Comparator group	Absolute % difference	N related to vaccine
Ermlich 2018 Phase 2 RCT, adults ≥50 years		229	230	PCV13	6 months	1.7	2.2	-0.5	0
		229	230	PPSV23	6 months	1.7	3	-1.3	0
Peterson 2019	Phase 2 RCT, adults ≥65 years, h/o PPSV23	127	126	PCV13 (in those with h/o PPSV23)	30 days	0	1.6	-1.6	0
V114-019	Phase 3 RCT (Pivotal Trial), adults ≥50 years	602	600	PCV13	6 months	1.5	2.2	-0.7	0

SAE in adults with underlying conditions, PCV15 only

		N (PCV15)	N (Comparison)	Comparison	Observation period	%SAE PCV15	%SAE Comparator group	Absolute % diference	N related to vaccine
V114-017	Immunocompetent adults 18-49 years at risk of pneumococcal disease	1134	378	PCV13	6 months	4.3	3.2	1.1	0
V114-018	Adults ≥18 years with HIV	152	150	PCV13	6 months	2	0	2	0

SAE in adults, PCV15-PPSV23 series

		N (PCV15)	N (Comparison)	Comparison	Observation period	%SAE PCV15	%SAE Comparator group	Absolute % difference	N related to vaccine
V114-016	Adults ≥50 years of age	298	302	PCV13+PPSV23	1 month post-PPSV23 (13 months post-first dose)	0.3	0.7	-0.4	0
V114-017	Immunocompetent adults 18-49 years at risk of pneumococcal disease	1036	345	PCV13+PPSV23	1 month post-PPSV23 (7 months post-first dose)	0.3	0.9	-0.6	0
V114-018	Adults ≥18 years with HIV	150	148	PCV13+PPSV23	6 months post first dose	1.3	4.1	-2.8	0

Evidence for PCV20

Immunogenicity and safety

Immunogenicity in healthy adults aged ≥50 years, PCV20 only

	N (PCV20)	N (Comparison)	Comparison	GMT ratios[1]	% Seroresponders[2]
B7471007 Phase 3 RCT, adults ≥60 years	1435	1420	PCV13	• PCV20<PCV13 in 12/13 serotypes • Noninferiority criteria[3] met for all 13/13 serotypes	• PCV20<PCV13 in 12/13 serotypes • Significantly lower for 1/12 (ST3)
	1433	1383	PPSV23 (7 common st)	• PCV20>PPSV23 in 6/7 serotypes • Noninferiority criteria[3] met for 6/7 serotypes (not met for ST8)	• PCV20>PPSV23 in 6/7 serotypes (all significant) • PCV20<PPSV23 ST8 (significant)
Hurley 2020 Phase 2 RCT, adults 60-64 years	195-210	194-208	PCV13	• PCV20<PCV13 in 13/13 serotypes • CI did not overlap in 4/13	• PCV20<PCV13 in 12/13 shared serotypes (all non-significant)
	185-207	181-204	PPSV23 (7 common st)	• PCV20>PPSV23 in 6/7 shared serotypes (CI did not overlap in 3/6) • PSV20<PPSV23 for ST8 (CI did not overlap)	• PCV20>PPSV23 in 6/7 shared serotypes (significantly higher in 2/6) • PCV20<PPSV23 for ST8 (non-significant)

1. Ratio calculated as [GMT (PCV20)]/[GMT (comparator vaccine)]. Range of GMT ratios for the common serotypes is shown.
2. Seroresponse: subjects with >=4-fold rise in OPA GMT titer post-vaccination compared to pre-vaccination. Absolute difference calculated as [% seroresponders (PCV20)]-[%seroresponders (comparator vaccine)]; positive results favor PCV20. Range of absolute differences for common serotypes is shown.
3. Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the geometric mean ratio (GMR) for that serotype was greater than 0.5 (2-fold criterion).

Immunogenicity in healthy adults aged 50-59 years vs older adults

		N (PCV20)	N (Comparison)	Comparison	GMT ratios[1]	% Seroresponders[2]
B7471007	Phase 3 RCT, adults 50-59 years vs **60-64 years**	321	946	PCV20	• 50-59>60-64 years in 15/20 serotypes • Non-inferiority criteria[3] met for all 20 serotypes	
	Phase 3 RCT, adults 50-59 years vs **≥60 years**	321	1435	PCV20		• 50-59>60+ years group in 18/20 serotypes (significantly higher in 1/18)

1. Ratio calculated as [GMT (PCV20)]/[GMT (comparator vaccine)]. Range of GMT ratios for the common serotypes is shown.
2. Seroresponse: subjects with >=4-fold rise in OPA GMT titer post-vaccination compared to pre-vaccination.
3. Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the geometric mean ratio (GMR) for that serotype was greater than 0.5 (2-fold criterion).

SAE in healthy adults in healthy adults aged ≥50 years

	N (PCV20)	N (Comparison)	Comparison	Observation period	%SAE PCV20	%SAE Comparator group	Absolute % diference	N related to vaccine
B7471007 Phase 3 RCT, adult	1461	1445	PCV13 or PCV13+PPSV23 (60 years or older)	within 6 months	2.4	1.9	0.5 (CI overlaps)	0
	334	111	PCV13 (50-59 years)	within 6 months	0.3	0.9	-0.6 (CI overlaps)	0
Hurley 2020 Phase 2 RCT, adults 60-64 years	221	222	PCV13	within 1 month following PCV20 or PCV13	0	0.5	-0.5 (CI overlaps)	0
	213	214	PCV13+PPSV23	Throughout the 12-mo study period, PCV20+saline vs PCV13+PPSV23)	4.1	5	-0.9 (CI overlaps)	0

Summary GRADE tables

Should PCV15 be routinely recommended to US adults ≥65 years and older?
Should PCV15 be routinely recommended to US adults ≥65 years and older in series with PPSV23?

Type	Outcome	Importance	Included in evidence profile	Certainty of evidence
Benefits	VT- IPD	Critical	Yes	2
	VT-pneumonia	Critical	Yes	2
	VT- mortality	Critical	Yes	2
Harms	Serious adverse events	Critical	Yes	2

Should PCV20 be routinely recommended to US adults ≥50 years and older?
Should PCV20 be routinely recommended to US adults ≥65 years and older?

Type	Outcome	Importance	Included in evidence profile	Certainty for healthy individuals
Benefits	VT- IPD	Critical	Yes	2
	VT-pneumonia	Critical	Yes	2
	VT- mortality	Critical	Yes	2
Harms	Serious adverse events	Critical	Yes	2

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For more information, contact CDC
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TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.