Economic Assessment of PCV21 in U.S. Adults

Charles Stoecker

Tulane University

School of Public Health and Tropical Medicine

ACIP

June 27, 2024

Conflicts of Interest

❏ **Dr. Stoecker has no conflicts of interest to declare.**

Acronyms

- PCV: pneumococcal conjugate vaccine
- PCV20: 20 valent PCV
- PCV21: 21 valent PCV
- VE: vaccine effectiveness
- VT: vaccine type
- ST: serotype
- NBP: non-bacteremic pneumonia
- IPD: invasive pneumococcal disease
- IPT: inpatient
- OPT: outpatient
- QALY: quality adjusted life year
- IC: immunocompromised
- CMC: chronic medical conditions, but not IC
- NIS: National Immunization Survey
- ABCs: Active Bacterial Core Surveillance System

Methods: Study Question

❑ **Evaluate cost effectiveness of using PCV21 in adults**

❑ **Evaluate**

- Program cost/savings
- Changes in disease, medical costs, nonmedical costs, and work productivity costs
  - Limited societal perspective
- Population
  - Separate cohorts of 4,256,608 19-year-olds, 3,990,700 42-year-olds, 4,051,078 50-year-olds, or 3,567,978 65-year-olds for specific questions
  - Separate model buckets for:
    - ○ Immunocompromised (IC) – HIV, Cancer, Organ Transplants, Dialysis
    - ○ Chronic medical conditions (CMC)– Diabetes, Heart Disease, Lung Disease, Liver Disease, Alcoholism
    - ○ Others –"General"

Methods: Interventions

❑ **Five strategies to evaluate**

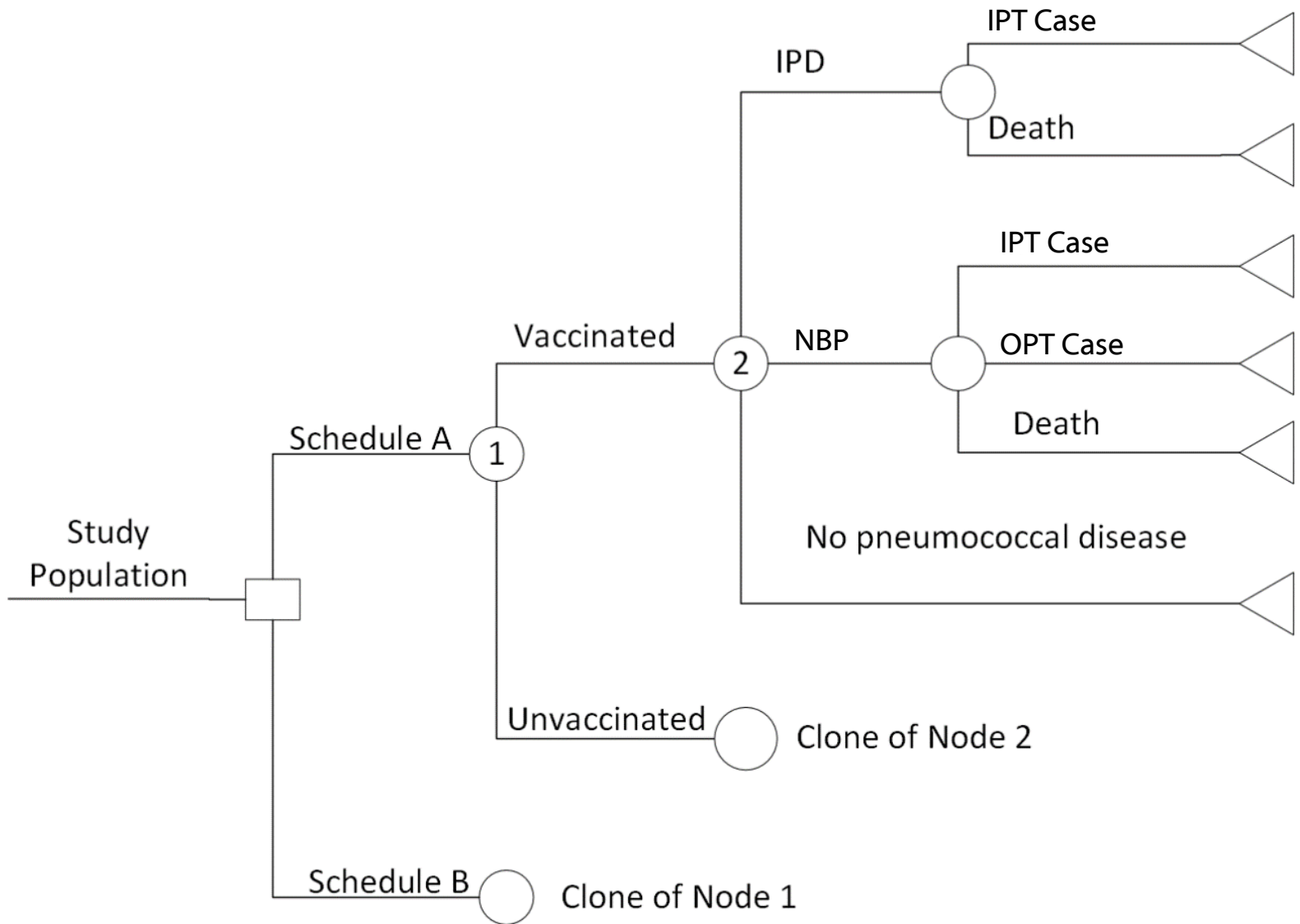|	Intervention	Comparator
Question 1a	Age-based vaccination at 65 with PCV21	Age-based vaccination at 65 with PCV20
Question 1b	Risk-based vaccination with PCV21	Risk-based vaccination with PCV20
Question 2	Age-based vaccination at 50 with PCV21	Age-based vaccination at 65 with PCV21
Question 3	Age-based vaccination at 19 with PCV21	Age-based vaccination at 50 with PCV21
	<u>Supplemental PCV21 Dose after PCV20</u>	
	Vaccination at 65 with PCV20 and 66 with PCV21 (all)	Age-based vaccination at 65 with PCV20
	Vaccination at 65 with PCV20 and 70 with PCV21 (all)	Age-based vaccination at 65 with PCV20
	Risk-based vaccination with PCV20 and vaccination after 1 year with PCV21 (CMC/IC)	Risk-based vaccination with PCV20
	Risk-based vaccination with PCV20 and vaccination after 5 years with PCV21 (CMC/IC)	Risk-based vaccination with PCV20

Methods: Economic Model

❑ **Cohort Model**
  - Cost per quality adjusted life year (QALY) gained
  - Cost per life year gained

❑ **Compare each intervention to comparator strategy and calculate incremental cost effectiveness ratio**
  - Divide change in costs by change in QALYs

❑ **Costs in 2023$**
  - Inflated by the Medical Care component of Consumer Price Index

❑ **Future costs and outcomes discounted by 3% annually**

Methods: Health Outcomes

- ❑ **Cases of Invasive Pneumococcal Disease (IPD)**
- ❑ **Cases of Hospitalized (IPT) Nonbacteremic Pneumonia (NBP)**
- ❑ **Cases of outpatient (OPT) NBP**
- ❑ **Deaths due to IPD**
- ❑ **Deaths due to IPT NBP**
- ❑ **QALYs**
- ❑ **Life Years**

Conceptual Model

Background mortality from non-pneumococcus related illness is included in all branches, but not displayed in the model for brevity.

Model Inputs

- **IPD rates, all-cause IPT and OPT NBP rates, IPD cases resulting in fatality were estimated by age- and risk group (general/CMC/IC).**

- **Age-group specific IPT NBP case fatality rates were applied to all risk groups**

- **Vaccine effectiveness (VE) was estimated by risk group and outcome (IPD/NBP).**
    - VE against serotype 3 was lower than other VT
    - VE was the same across PCV20 and PCV21

- **Vaccine coverage was estimated by age group (19–49, 50–64, 65+) and scenario (risk based, supplemental)**

- **Herd inputs updated from previous iteration**
    - New baseline estimation strategy
    - Bigger initial effect
    - Plateau after 6 years

See supplemental slides for the specific estimates used in the model.

IPD Serotype Distributions, General

Serotype Group	18-49 Years	50-64 Years	65-74 Years	75-84 Years	85+ Years
% PCV20 only -4-19F (1, 5, 6B, 9V, 14, 18C, 23F, 15B, including isolates reported as 15BC)	1.99%	1.52%	3.09%	1.01%	1.08%
% PCV20 & PCV21 -3 (6A, 7F, 19A, 22F, 33F, 8, 10A, 11A, 12F) +6C	34.44%	41.95%	32.72%	32.32%	33.33%
% PCV21 only -35B (9N, 17F, 20, 15A, 15C, 16F, 23A, 23B, 24F, 31)	30.13%	30.70%	31.48%	29.29%	35.48%
% serotype 3	13.91%	12.46%	17.28%	21.21%	14.25%
% serotype 4	4.97%	2.43%	1.23%	0.00%	0.00%
% serotype 19F	4.97%	4.56%	3.70%	3.03%	3.01%
% serotype 35B	2.65%	0.91%	4.32%	5.05%	3.23%
Ratio PCV21 only:PCV20 only serotypes	2.75	3.71	4.46	8.50	9.46

Source: Active Bacterial Core Surveillance 2018-2019. For multivariate sensitivity analyses distributions are beta-pert with -/+20% for low and high.

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IPD Serotype Distributions, CMC

Serotype Group	18-49 Years	50-64 Years	65-74 Years	75-84 Years	85+ Years
% PCV20 only -4-19F (1, 5, 6B, 9V, 14, 18C, 23F, 15B, including isolates reported as 15BC)	0.49%	0.71%	1.88%	2.17%	1.81%
% PCV20 & PCV21 -3 (6A, 7F, 19A, 22F, 33F, 8, 10A, 11A, 12F) +6C	36.99%	33.62%	30.36%	32.79%	28.62%
% PCV21 only -35B (9N, 17F, 20, 15A, 15C, 16F, 23A, 23B, 24F, 31)	30.33%	32.67%	30.83%	32.52%	33.70%
% serotype 3	11.34%	17.96%	21.91%	17.07%	17.39%
% serotype 4	9.99%	4.35%	1.25%	0.27%	0.72%
% serotype 19F	3.08%	2.45%	2.66%	2.44%	2.17%
% serotype 35B	2.59%	3.01%	4.23%	5.15%	6.88%
Ratio PCV21 only:PCV20 only serotypes	2.43	4.75	6.06	7.72	8.63

Source: Active Bacterial Core Surveillance 2018-2019. For multivariate sensitivity analyses distributions are beta-pert with -/+20% for low and high.

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IPD Serotype Distributions, IC

Serotype Group	18-49 Years	50-64 Years	65-74 Years	75-84 Years	85+ Years
% PCV20 only -4-19F (1, 5, 6B, 9V, 14, 18C, 23F, 15B, including isolates reported as 15BC)	6.02%	3.92%	3.30%	2.88%	0.00%
% PCV20 & PCV21 -3 (6A, 7F, 19A, 22F, 33F, 8, 10A, 11A, 12F) +6C	28.92%	31.63%	30.03%	37.50%	48.31%
% PCV21 only -35B (9N, 17F, 20, 15A, 15C, 16F, 23A, 23B, 24F, 31)	31.33%	33.73%	33.99%	26.44%	25.84%
% serotype 3	15.66%	8.43%	11.55%	10.10%	4.49%
% serotype 4	1.20%	1.20%	1.32%	0.00%	0.00%
% serotype 19F	3.61%	3.61%	3.30%	1.44%	5.62%
% serotype 35B	6.02%	6.63%	8.91%	9.62%	5.62%
Ratio PCV21 only:PCV20 only serotypes	3.45	4.62	5.42	8.35	5.60

Source: Active Bacterial Core Surveillance 2018-2019. For multivariate sensitivity analyses distributions are beta-pert with -/+20% for low and high.

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NBP Serotype Distributions

| Serotype Group	18-49 Years	50-64 Years	65+ Years
% PCV20 only -4-19F (1, 5, 6B, 9V, 14, 18C, 23F, 15B)	0.6%	0.7%	1.1%
% PCV20 & PCV21 -3 (6A, 7F, 19A, 22F, 33F, 8, 10A, 11A, 12F) +6C	3.0%	4.5%	3.9%
% PCV21 only -35B (9N, 17F, 20, 15A, 15C, 16F, 23A, 23B, 24F, 31)	3.2%	4.2%	2.4%
% serotype 3	1.1%	2.0%	1.4%
% serotype 4	0.0%	0.2%	0.2%
% serotype 19F	0.1%	0.9%	0.7%
% serotype 35B	0.8%	0.6%	0.7%
Ratio PCV21 only:PCV20 only serotypes	5.7	2.7	1.6

Source: Merck adjusted SSUAD serotype distribution data.
Note that the serotype distribution is among all community-acquired pneumonia, not limited to pneumococcal pneumonia.
For multivariate sensitivity analyses distributions are beta-pert with -/+20% for low and high.

Waning Immunity Assumptions

❑ **No decline in effectiveness for first five years [a]**

❑ **Wane to zero over next 10 years [b]**
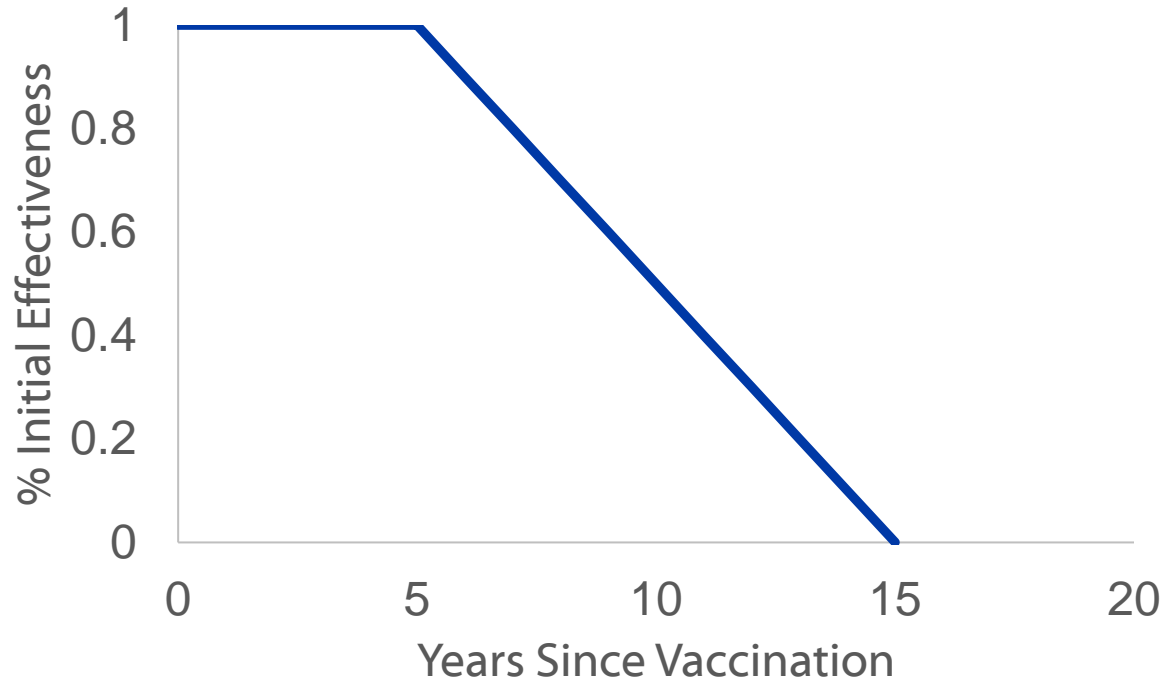
[a]Patterson S, Webber C, Patton M, Drews W, Huijts SM, Bolkenbaas M, et al. A post hoc assessment of duration of protection in CAPiTA (Community Acquired Pneumonia immunization Trial in Adults). Trials in Vaccinology. 2016;5.:92-96.
[b] van Werkhoven CH, Huijts SM, Bolkenbaas M, Grobbee DE, Bonten MJ. The Impact of Age on the Efficacy of 13-valent Pneumococcal Conjugate Vaccine in Elderly. Clin Infect Dis 2015;61(12):1835-8.

Vaccine Price

- ❑ **PCV20 $288.66[a]**

- ❑ **PCV21 $319.43[b]**
  - ▪ Sensitivity analysis with PCV21 price 5% higher ($335.60)

- ❑ **Administration 19-64 years: $30.49[c]**

- ❑ **Administration 65+ years: $21.07[d]**

- ❑ **Travel + patient time cost: $44.46[e]**

[a] Payment Allowance Limits for Medicare Part B for PCV20.
[b] Applied ratio of PCV21 to PCV20 price from manufacturer model and applied to PCV20 Medicare price. Sensitivity analysis uses upper bound of manufacturer PCV21 price range.
[c] Tsai et al. AJPM 2019. Updated to 2023 dollars.
[d] Average Medicare maximum allowable reimbursement for immunization administration (HCPCS code 90471) across all Medicare Administrative Contractors, 2023.
[e] Travel cost from Maciosek et al. Am J Prev Med 2006. Updated to 2023 dollars.

Sensitivity Analyses

- **Higher PCV21 Price**
  - 5% higher: $335.60 vs $319.43
- **No PCV20 type indirect protections for adults from childhood program**
- **Serotype 4 disease at 30% of pneumococcal disease**
  - Decrease other serotypes proportionally to preserve overall disease rates
- **Fix disease QALY decrements by age**
  - Only for moving age-based recommendation to 19 or 50 years
  - Set QALY decrements to age 19 decrements for all ages
- **Alternate QALY decrements**

PCV21 Overview

Health Outcomes	Question 1a PCV1 @Age 65	Question 1b PCV21 @CMC/IC	Question 2 PCV21 @Age 50	Question 3 PCV21 @Age 19
IPD Cases	-889 (-1099,-624)	-194 (-233,-139)	215 (-101,534)	223 (112,339)
Hospitalized Pneumonia Cases	-1630 (-2210,-929)	-368 (-489,-207)	1050 (423,1751)	350 (159,544)
Non-hospitalized Pneumonia Cases	-3663 (-5050,-2082)	-1427 (-1927,-801)	247 (-1732,2421)	926 (77,1911)
Deaths due to IPD	-108 (-137,-74)	-23 (-28,-16)	36 (-3,75)	28 (16,42)
Deaths due to Pneumonia	-60 (-90,-31)	-11 (-16,-6)	48 (14,86)	11 (4,20)
QALYs	1302 (926,1613)	363 (265,435)	52 (-633,744)	-507 (-759,-261)
Life-years	2082 (1476,2591)	513 (376,614)	-389 (-1331,564)	-682 (-1010,-360)
Costs (million $)				
Total Cost	5 (-12,30)	-29 (-38,-17)	-5 (-119,121)	185 (111,254)
Medical Costs	-60 (-74,-42)	-26 (-31,-18)	-34 (-74,9)	35 (18,51)
Vaccine Costs	90 (79,101)	12 (12,13)	75 (-108,258)	129 (40,219)
Work Loss	-24 (-30,-17)	-16 (-20,-11)	-47 (-78,-16)	21 (9,33)
Cost Ratios ($)				
Cost/QALY	4,132 (C-S, 18,599)	C-S (C-S, C-S)	C-S (187,994*, 162,634)	D (D, D)
Cost/Life-year	2584 (C-S, 11,579)	C-S (C-S, C-S)	13,675* (89,406*, 214,539)	D(D, D)

95% CI in parenthesis; * Indicates dollars saved per QALY or Life-year lost; C-S indicates cost-saving; D indicates dominated.

Question 1a: Vaccination at age 65 with PCV21

Cohort of 65-year-olds. Comparator is PCV20 at age 65.

	Base	PCV21 @ $335.60	PCV20 Child Indirect 0%	Serotype 4 @ 30%	Tang QALY Values
Health Outcomes					
IPD Cases	-889	-889	-855	152	-889
Hospitalized Pneumonia Cases	-1,630	-1,630	-1,019	-422	-1,630
Non-hospitalized Pneumonia Cases	-3,663	-3,663	-2,320	-807	-3,663
Deaths due to IPD	-108	-108	-104	18	-108
Deaths due to Pneumonia	-60	-60	-37	-16	-60
QALYs	1,302	1,302	1,098	-45	1,321
Life-years	2,082	2,082	1,771	-74	2,082
Costs (million $)					
Total Cost	$5	$37	$24	$85	$5
Medical Costs	-$60	-$60	-$46	-$5	-$60
Vaccine Costs	$90	$121	$90	$90	$90
Work Loss	-$24	-$24	-$20	$1	-$24
Cost Ratios ($)					
Cost/QALY	4,132	28,061	21,947	Dominated	4,073
Cost/Life-year	2,584	17,549	13,602	Dominated	2,584

Question 1b: Vaccination at CMC/IC with PCV21

Cohort of 42-year-olds. Comparator is PCV20 at CMC/IC.

	Base	PCV21 @ $335.60	PCV20 Child Indirect 0%	Serotype 4 @ 30%	Tang QALY Values
Health Outcomes					
IPD Cases	-194	-194	-188	29	-194
Hospitalized Pneumonia Cases	-368	-368	-265	-190	-368
Non-hospitalized Pneumonia Cases	-1,427	-1,427	-1,128	-694	-1,427
Deaths due to IPD	-23	-23	-22	3	-23
Deaths due to Pneumonia	-11	-11	-8	-6	-11
QALYs	363	363	324	29	361
Life-years	513	513	458	32	513
Costs (million $)					
Total Cost	-$29	-$22	-$24	$3	-$29
Medical Costs	-$26	-$26	-$22	-$7	-$26
Vaccine Costs	$12	$19	$12	$12	$12
Work Loss	-$16	-$16	-$14	-$3	-$16
Cost Ratios ($)					
Cost/QALY	Cost-Saving	Cost-Saving	Cost-Saving	111,812	Cost-Saving
Cost/Life-year	Cost-Saving	Cost-Saving	Cost-Saving	98,126	Cost-Saving

Question 1b: Vaccination at CMC/IC with PCV21

Cohort of 42-year-olds. Comparator is PCV20 at CMC/IC.

	Serotype 4 @ 5%	Serotype 4 @ 10%	Serotype 4 @ 15%	Serotype 4 @ 20%	Serotype 4 @ 25%	Serotype 4 @ 30%	Serotype 4 @ 35%
Health Outcomes							
IPD Cases	-184	-141	-99	-56	-13	29	72
Hospitalized Pneumonia Cases	-345	-314	-283	-252	-221	-190	-159
Non-hospitalized Pneumonia Cases	-1,327	-1,201	-1,074	-947	-821	-694	-567
Deaths due to IPD	-21	-16	-11	-6	-2	3	8
Deaths due to Pneumonia	-11	-10	-9	-8	-7	-6	-5
QALYs	345	282	218	155	92	29	-35
Life-years	486	395	304	214	123	32	-58
Costs (million $)							
Total Cost	-27	-21	-15	-9	-3	3	9
Medical Costs	-24	-21	-17	-14	-10	-7	-3
Vaccine Costs	12	12	12	12	12	12	12
Work Loss	-15	-13	-10	-8	-5	-3	0
Cost Ratios ($)							
Cost/QALY	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	111,812	Dominated
Cost/Life-year	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	98,126	Dominated

Base case serotype 4 distributions are age, risk, and disease condition specific as displayed earlier in the slides. They range from 0 to 9.99%

Question 2: Vaccination at age 50
Cohort of 50-year-olds. Comparator is PCV21 at CMC/IC or age 65.

	Base	PCV21 @ $335.60	PCV20 Child Indirect 0%	Serotype 4 @ 30%	Fix QALY Decrements	Tang QALY Decrements
Health Outcomes						
IPD Cases	215	215	398	131	215	215
Hospitalized Pneumonia Cases	1,050	1,050	2,220	775	1,050	1,050
Non-hospitalized Pneumonia Cases	247	247	2,175	282	247	247
Deaths due to IPD	36	36	62	23	36	36
Deaths due to Pneumonia	48	48	93	35	48	48
QALYs	52	52	-283	45	-3	17
Life-years	-389	-389	-1,061	-257	-389	-389
Costs (million $)						
Total Cost	-$5	-$3	-$4	$19	-$5	-$5
Medical Costs	-$34	-$34	-$25	-$23	-$34	-$34
Vaccine Costs	$75	$78	$75	$75	$75	$75
Work Loss	-$47	-$47	-$54	-$33	-$47	-$47
Cost Ratios ($)						
Cost/QALY	Cost-Saving	Cost-Saving	15,489*	429,479	1,739,015*	Cost-Saving
Cost/Life-year	13,675*	6,916*	4,138*	Dominated	13,675*	13,675*

* Dollars saved per QALY or Life-year lost.

Question 2 Modeling Strategies

- ❑ **"Moving age-based recommendation from 65 to 50"**
  - ▪ Shifts disease burden from younger to older adults
  - ▪ Save the cost of vaccinating 65-year-olds
- ❑ **"Adding vaccination at 50 in addition to 65"**
  - ▪ Isolates disease burden reduction from 50– to 64-year-olds
    - • Convenient since we assume 15-year vaccine duration
  - ▪ Clinicians may be unwilling to not re-vaccinate at age 65 in above recommendation

Question 2: Vaccination at age 50 and 65
Cohort of 50-year-olds. Comparator is PCV21 at CMC/IC or age 65.

	Base	PCV21 @ $335.60	PCV20 Child Indirect 0%	Serotype 4 @ 30%	Fix QALY Decrements	Tang QALY Decrements
Health Outcomes						
IPD Cases	-424	-424	-560	-307	-424	-424
Hospitalized Pneumonia Cases	-462	-462	-412	-306	-462	-462
Non-hospitalized Pneumonia Cases	-3,202	-3,202	-3,835	-2,184	-3,202	-3,202
Deaths due to IPD	-41	-41	-53	-30	-41	-41
Deaths due to Pneumonia	-8	-8	-3	-5	-8	-8
QALYs	1,105	1,105	1,408	780	1,096	1,074
Life-years	1,262	1,262	1,574	895	1,262	1,262
Costs (million $)						
Total Cost	$298	$317	$253	$344	298	$298
Medical Costs	-$84	-$84	-$110	-$59	-84	-$84
Vaccine Costs	$450	$468	$450	$450	450	$450
Work Loss	-$67	-$67	-$87	-$47	-67	-$67
Cost Ratios ($)						
Cost/QALY	269,932	286,553	179,685	440,518	272,038	277,778
Cost/Life-year	236,322	250,873	160,744	384,319	236,322	236,322

Question 3: Vaccination at age 19
Cohort of 19-year-olds. Comparator is PCV21 at CMC/IC or age 50.

	Base	PCV21 @ $335.60	PCV20 Child Indirect 0%	Serotype 4 @ 30%	Fix QALY Decrements	Tang QALY Decrements
Health Outcomes						
IPD Cases	223	223	373	158	223	223
Hospitalized Pneumonia Cases	350	350	564	244	350	350
Non-hospitalized Pneumonia Cases	926	926	1,649	659	926	926
Deaths due to IPD	28	28	46	20	28	28
Deaths due to Pneumonia	11	11	17	8	11	11
QALYs	-507	-507	-835	-358	-509	-498
Life-years	-682	-682	-1,113	-481	-682	-682
Costs (million $)						
Total Cost	$185	$190	$222	$168	$185	$185
Medical Costs	$35	$35	$57	$25	$35	$35
Vaccine Costs	$129	$134	$129	$129	$129	$129
Work Loss	$21	$21	$35	$15	$21	$21
Cost Ratios ($)						
Cost/QALY	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
Cost/Life-year	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated

Supplemental PCV21 One Year after PCV20 (all)

Cohort of 66-year-olds. Comparator is no additional vaccine.

	Base	PCV21 @ $335.60	PCV20 Child Indirect 0%	Serotype 4 @ 30%	Tang QALY Decrements
Health Outcomes					
IPD Cases	-847	-847	-866	-525	-847
Hospitalized Pneumonia Cases	-1,875	-1,875	-1,973	-1,276	-1,875
Non-hospitalized Pneumonia Cases	-3,981	-3,981	-4,065	-2,690	-3,981
Deaths due to IPD	-104	-104	-107	-65	-104
Deaths due to Pneumonia	-70	-70	-74	-48	-70
QALYs	1,261	1,261	1,285	808	1,286
Life-years	2,059	2,059	2,110	1,325	2,059
Costs (million $)					
Total Cost	$557	$584	$555	$587	$557
Medical Costs	-$65	-$65	-$67	-$43	-$65
Vaccine Costs	$644	$671	$644	$644	$644
Work Loss	-$23	-$23	-$23	-$15	-$23
Cost Ratios ($)					
Cost/QALY	442,010	463,475	431,656	726,607	433,172
Cost/Life-year	270,614	283,756	262,879	443,207	270,614

Supplemental PCV21 Five Years after PCV20 (all)

Cohort of 70-year-olds. Comparator is no additional vaccine.

	Base	PCV21 @ $335.60	PCV20 Child Indirect 0%	Serotype 4 @ 30%	Tang QALY Decrements
Health Outcomes					
IPD Cases	-1,035	-1,035	-1,300	-673	-1,035
Hospitalized Pneumonia Cases	-3,360	-3,360	-4,852	-2,355	-3,360
Non-hospitalized Pneumonia Cases	-5,770	-5,770	-8,028	-4,015	-5,770
Deaths due to IPD	-129	-129	-163	-84	-129
Deaths due to Pneumonia	-132	-132	-193	-93	-132
QALYs	1,580	1,580	2,099	1,064	1,600
Life-years	2,608	2,608	3,460	1,757	2,608
Costs (million $)					
Total Cost	$485	$510	$439	$524	$485
Medical Costs	-$102	-$102	-$142	-$70	-$102
Vaccine Costs	$608	$634	$608	$608	$608
Work Loss	-$22	-$22	-$28	-$15	-$22
Cost Ratios ($)					
Cost/QALY	306,901	323,076	209,103	492,194	302,891
Cost/Life-year	185,860	195,656	126,871	298,071	185,860

Supplemental PCV21 1/5 years after PCV20 Among Adults with CMC/IC
Comparator is no additional vaccine.

	1 Year Cohort @41	1 Year Cohort @45	1 Year Cohort @55	5 Years Cohort @41	5 Years Cohort @45	5 Years Cohort @55
Health Outcomes						
IPD Cases	-508	-532	-514	-553	-580	-584
Hospitalized Pneumonia Cases	-933	-990	-1,056	-1,049	-1,119	-1,239
Non-hospitalized Pneumonia Cases	-3,593	-3,504	-3,031	-3,903	-3,823	-3,448
Deaths due to IPD	-57	-62	-63	-63	-68	-73
Deaths due to Pneumonia	-29	-32	-37	-34	-37	-44
QALYs	936	981	897	1,004	1,053	1,010
Life-years	1,320	1,394	1,332	1,424	1,506	1,504
Costs (million $)						
Total Cost	$314	$291	$199	$314	$287	$208
Medical Costs	-$66	-$68	-$61	-$71	-$73	-$69
Vaccine Costs	$421	$399	$289	$428	$402	$309
Work Loss	-$41	-$40	-$28	-$44	-$42	-$31
Cost Ratios ($)						
Cost/QALY	335,330	296,483	221,736	312,933	272,520	206,191
Cost/Life-year	237,779	208,572	149,339	220,664	190,605	138,491

Alternate Efficiency Measures
(Does not account for overlap between measures)

Number needed to vaccinate to prevent…

	PCV21 @65	PCV21 @CMC/IC	PCV21 @50 & @65	PCV21 Suppl @66	PCV21 Suppl @70
Hospitalization	643	572	7,127	512	300
Case	263	180	974	209	130
Death	9,758	9,026	155,708	8,087	5,109

$ per averted…

	PCV21 @65	PCV21 @CMC/IC	PCV21 @50 & @65	PCV21 Suppl @66	PCV21 Suppl @70
Hospitalization	$2,227	Cost-Saving	$335,952	$205,491	$111,219
Case	$906	Cost-Saving	$72,898	$83,279	$47,910
Death	$33,521	Cost-Saving	$6,139,249	$3,220,043	$1,879,564

Limitations

- ❑ **Sequelae from IPD not modeled explicitly**

- ❑ **Ranges on serotype distributions and other IPD data from ABCs are +/- 25% by assumption**

- ❑ **Uncertainties about the pneumococcal disease trends due to pneumococcal serotypes that are no longer included in PCV21 (e.g., serotype 4, 19F)**

- ❑ **Uncertainties about the indirect effects from pediatric PCV20 use**

- ❑ **Disruption from changing pneumococcal schedule not modeled**

- ❑ **Disease rates are constant within specified age bins as single-year of age disease estimates are unlikely to be precise.**

Summary

- **Replacing PCV20 with PCV21 at age 65 increases QALYs with modest increases in cost**
    - Simulations range from $4,000 to $28,000 / QALY in several scenarios
    - Replacing PCV20 with PCV21 is dominated (lower QALYs and more costs) in a scenario where serotype 4 disease accounts for 30% of pneumococcal disease
- **Replacing PCV20 with PCV21 at diagnosis of IC or CMC before age 65 is cost-saving**
    - Cost is $110,000/QALY in a scenario where serotype 4 disease accounts for 30%
    - At serotype 4 disease rates at 35% or above it results in decreased QALYs
- **Moving PCV21 vaccination from age 65 to age 50 increases case counts and deaths, but also results in gains in QALYs**
    - Disease burden is shifted from younger adults to older adults who have lower background QALY values
- **Vaccinating at both age 50 and age 65 costs $300,000/QALY**
    - Sensitivity analyses range from $200,000/QALY to $400,000/QALY
- **Vaccinating with PCV21 at age 19 instead of age 50 is dominated**
    - Less health (both lower QALYs and more cases) and increased costs
- **Supplemental PCV21 at age 65 that includes all adults that previously had PCV20 (at age 65 or at CMC/IC) costs $400,000/QALY**
    - If the supplemental dose is delayed until age 70 the cost drops to $300,000/QALY
- **Supplemental PCV21 for the CMC/IC population ranges from $200,000 to $300,000 per QALY in the base case**
    - Cost per QALY is 5-30% lower if PCV21 is delayed 5 years after PCV20 vaccination rather than 1 year afterward
    - Assuming no herd immunity from childhood PCV20 program is associated with the lowest cost per QALYs

Thank you!

**Please send comments to:
cfstoecker@tulane.edu**

Contributors:

**Andrew Leidner
Miwako Kobayashi
Bo-Hyun Cho
Yin Wang
Cheryl Ward**

IPD Rates per 100k

Risk Group	19-49 Years	50-64 Years	65-74 Years	75-84 Years	85+ Years
General	2.09	6.09	8.25	13.90	33.06
CMC	8.09	24.04	25.89	33.34	58.57
IC	16.22	37.28	35.10	36.81	46.38

NBP Hospitalization Rates per 100k

Risk Group	19-49 Years	50-64 Years	65-74 Years	75+ Years
General	35 (35, 36)	88 (87, 90)	191 (185, 197)	957 (938, 975)
CMC	207 (202, 212)	429 (423, 425)	941 (925, 957)	2745 (2717, 2774)
IC	701 (681, 721)	1226 (1207, 1244)	2124 (2087, 2162)	3992 (3944, 4040)

Source: MarketScan & Optum databases. 2013-2015 data. (Pelton et al. CID 2019) (95% CIs in parenthesis)

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NBP Outpatient Rates per 100k

Risk Group	19-49 Years	50-64 Years	65-74 Years	75-84 Years	85+ Years
General	322.92	385.04	491.98	1366.22	2378.97
CMC	1872.91	1886.72	2410.70	3962.03	6899.00
IC	6361.40	5352.10	5461.00	5738.10	9991.70

IPD Cases Resulting in Fatality

Risk Group	19-49 Years	50-64 Years	65-74 Years	75-84 Years	85+ Years
General	5.54%	8.73%	7.93%	11.25%	17.30%
CMC	7.24%	11.06%	12.22%	12.82%	22.97%
IC	10.04%	14.27%	13.97%	11.33%	17.62%

IPT NBP Cases Resulting in Fatality

	Base	Low	High
18-49 Years	1.6	0.4	2.9
50-64 Years	2.8	1.1	4.4
65-74 Years	3.5	1.5	5.5
75-84 Years	4.1	2.2	6.0
85+ Years	5.3	3.3	7.2

Source: NIS2018 (lower bound: ICD-10 code J13 or J181 for primary diagnosis; upper bound: ICD-10 code J13 or J181 in ANY location; base: mean of LB and UB).
Low and High parameters used in beta-pert distribution

Vaccine Effectiveness

	General	CMC	IC
PCV vs VT (-ST3) IPD[a]	75.0 (41.4, 90.8)	75.0 (41.4, 90.8)	25.0 (13.8, 30.3)
PCV vs ST3 IPD[b]	26.0 (0, 53.4)	26.0 (0, 53.4)	8.7 (0, 17.8)
PCV vs VT (-ST3) NBP[c]	66.7 (11.8, 89.3)	40.3 (11.4, 60.2)	15.0 (4.7, 21.8)
PCV vs ST3 NBP[d]	15.6 (0, 32.0)	15.6 (0, 32.0)	5.2 (0, 10.7)

a. Bonten NEJM 2015 (per protocol)
b. Point estimate from Pilishvili et al. ISPPD2018 abstract, lower bound set to 0, upper bound from Lewis 2020 ISPPD poster
c. Suaya Vaccine 2018; 1477-1483.
d. Applied the ratio of IPD VE/Pneumonia VE for all PCV13 types to the point estimate for ST3 IPD VE.

Coverage Rates

	Base	Low[e]	High[e]
PCV Age-based 19-49[a]	22.2	17.76	26.64
PCV Age-based 50-64[b]	39.65	23.3	56
PCV, Age-based 65+[c]	56	49	63
Risk-based (at development of CMC/IC)[a]	22.2	21	23.5
PCV21 supplemental dose[d]	40.7	11.2	63.4

a. NHIS 2021 data https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/pubs-resources/vaccination-coverage-adults-2021.html ; Low and high in age-based 19-49 context are -/+20% of base case; low and high in risk-based context are bounds of the 95% CI for coverage among individuals eligible for risk-based vaccination
b. Low: NHIS 2021 for Zoster Vaccine in adults 60-64 years; high: base estimate for PCV15/PCV20 coverage in adults 65 years and older; base: mean
c. High: NHIS 2021 any pneumococcal coverage; low: any PCV13 coverage data in Medicare beneficiaries aged ≥65 years, 2019; base: mean
d. % of PCV20 recipients who received PCV13 among Medicare Parts A/B beneficiaries as of Jan 17, 2024; low: coverage at age 66 years; high: coverage at age 80-84 years
e. Parameters for beta-pert distribution

Herd Effects from PCV20 in Children

❑ **Apply serotype group-specific declines observed in PCV13 types (+6C, -3, -19F) in adults after PCV13 introduction in children**

❑ **Apply to additional types in PCV20**

❑ **Run versions of the model with and without these herd effects to assess importance**

Remaining Share of Disease

Year	Base	Lower	Upper
1	0.755161	0.707483	0.813869
2	0.496227	0.459737	0.53535
3	0.339094	0.312705	0.372755
4	0.244074	0.220786	0.268572
5	0.187125	0.166702	0.206661
6	0.156599	0.138492	0.177142
7+	No further declines		

Source: Unpublished CDC model.

Utility Decrements

Variable	QALY Decrements[a]	Implied Healthy Days Lost[b]
IPD	0.0709 (0.0509, 0.0909)	25.9
IPT NBP	0.0709 (0.0509, 0.0909)	25.9
OPT NBP	0.0045 (0.00399, 0.00501)	1.6

Alternate Utility Decrements[c]

Pneumococcal Disease Treatment Intensity, Age	QALY Decrement
Outpatient, 19-64	0.0094
Inpatient, 19-64	0.0396
Outpatient, 65+	0.0586
Inpatient, 65+	0.0087

[a] QALY values from Mangen et al. 2015 Eur Respir J (95% CIs in parenthesis)
[b] Health days lost were include on this slide to illustrate in relatable terms the magnitude of health loss associated with QALY decrements. Healthy days lost calculated by multiplying QALY decrement by 365.
[c] Alternate values are inverse variance weighted values from Tang et al. 2021 J Pub Health. Source material places higher decrement on outpatient disease than inpatient disease for age 65+.

Baseline QALY Values

Age	General	CMC/IC
50-55	0.83 (0.78,0.88)	0.72 (0.67,0.77)
56-60	0.81 (0.76,0.86)	0.69 (0.64,0.74)
61-65	0.77 (0.72,0.82)	0.63 (0.58,0.68)
66-70	0.76 (0.71,0.81)	0.57 (0.52,0.62)
71-75	0.74 (0.69,0.79)	0.54 (0.49,0.59)
76-80	0.7 (0.65,0.75)	0.52 (0.47,0.57)
81-85	0.63 (0.58,0.68)	0.51 (0.46,0.56)
86+	0.51 (0.46,0.56)	0.51 (0.46,0.56)

Sisk, 2003.

Disease Cost (2023$)

	Disease	Setting	Cost	95% CI	
19-64 Years	IPD	IPT	$64,018.10	$61,559.31	$66,424.61
	NBP	IPT	$58,423.99	$55,923.53	$60,908.13
	NBP	OPT	$362.38	$339.44	$385.24
65+ Years	IPD	IPT	$27,564.22	$27,039.18	$28,149.20
	NBP	IPT	$21,300.64	$20,825.64	$21,800.98
	NBP	OPT	$318.22	$308.06	$328.70

ICD-10 Codes for Medical Cost Extraction

Disease	ICD-10 Codes
IPD	A40.3, A40.9+B95.3, A41.9+B95.3, R78.81+B95.3, G00.1, G00.2+B95.3, G00.9+B95.3, G03.9+B95.3, J86.x+B95.3, J85.1+B95.3, A40.3 + at least one code from "All-cause", A40.9+B95.3 + at least one code from "All-cause", A41.9+B95.3 + at least one code from "All-cause", R78.81+B95.3 + at least one code from "All-cause", A40.9 & J13, A41.9 & J13, R78.81 & J13, M00.1x, K65.8+B95.3, I30.1+B95.3, I33.0+B95.3, I33.9 +B95.3, K65.2+B95.3, M86.1x/M86.2x/M86.9+B95.3, M00.0x, M00.2x, M00.8x, M00.9 + B95.3
NBP	J13, J15.9+B95.3, J18.0/J18.1+B95.3, J18.8/J18.9+B95.3
All-cause (for satisfying some definitions of IPD)	J12.x (J12.0, J12.1, J12.2, J12.3, J12.81, J12.89, J12.9), J13, J18.1, A48.1, J14, J15.0, J15.1, J15.2x (J15.20, J15.211, J15.212, J15.29), J15.3, J15.4, J15.5, J15.6, J15.8, J15.9, J15.7, J16.x (J16.0, J16.8), A22.1, A37.X1, B25.0, B44.0, J17, J18.0, J18.2, J18.8, J18.9, J09.X1, J10.0x (J10.00, J10.01, J10.08), J11.0x (J11.00, J11.08)

Work Loss

Labor Force Participation and Daily Wage

Age	Labor Force Participation Rate (%)[a]	Median Daily Wage ($)[b]
19 to 24	71	99.71
25 to 34	83.2	148.86
35 to 44	83	175.57
45 to 54	81.1	176.14
55 to 64	65.2	169.43
65 to 74	26.6	157.29
75+	8.2	157.29

Duration of Work Loss

	Base	High	Low
Inpatient[c]	34	17	51
Outpatient[d]	26.4	13.2	39.7

[a] US Bureau of Labor Statistics.
[b] Current Population Survey, 2023.
[c] Altawalbeh SM, Wateska AR, Nowalk MP, Lin CJ, Harrison LH, Schaffner W, Zimmerman RK, Smith KJ. Societal cost of racial pneumococcal disease disparities in US adults aged 50 years or older. Applied Health Economics and Health Policy. 2024 Jan;22(1):61-71.
[d] Used ratio of days of work loss from outpatient (14) to inpatient pneumonia (18) allowed by Marine Corps policy and applied to inpatient durations of illness from Altawalbeh 2024. Vold Pepper P, Owens DK. Cost-effectiveness of the pneumococcal vaccine in the United States Navy and Marine Corps. Clinical infectious diseases. 2000 Jan 1;30(1):157-64.

Question 1a: Vaccination at age 65 with PCV21
Cohort of 65-year-olds. Comparator is PCV20 at age 65.

	Serotype 4 @ 5%	Serotype 4 @ 10%	Serotype 4 @ 15%	Serotype 4 @ 20%	Serotype 4 @ 25%	Serotype 4 @ 30%	Serotype 4 @ 35+%
Health Outcomes							
IPD Cases	-749	-569	-389	-209	-28	152	
Hospitalized Pneumonia Cases	-1,498	-1,282	-1,067	-852	-637	-422	
Non-hospitalized Pneumonia Cases	-3,350	-2,841	-2,333	-1,824	-1,316	-807	
Deaths due to IPD	-91	-69	-47	-25	-4	18	
Deaths due to Pneumonia	-55	-47	-39	-32	-24	-16	
QALYs	1,132	897	661	426	191	-45	
Life-years	1,808	1,431	1,055	679	302	-74	
Costs (million $)							
Total Cost	15	29	43	57	71	85	
Medical Costs	-54	-44	-34	-24	-15	-5	
Vaccine Costs	90	90	90	90	90	90	
Work Loss	-21	-17	-12	-8	-4	1	
Cost Ratios ($)							
Cost/QALY	13,436	32,640	65,513	134,710	374,763	Dominated	Dominated
Cost/Life-year	8,412	20,443	41,059	84,543	236,327	Dominated	Dominated

Base case serotype 4 distributions are age, risk, and disease condition specific as displayed earlier in the slides. They range from 0 to 9.99%