Economic Assessment of PCV15 & PCV20

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Conflicts of Interest

- Dr. Stoecker has no conflicts of interest to declare.

Methods: Study Question

- Evaluate cost effectiveness of using PCV15 or PCV20 in adults
  - Evaluate adding PPSV23 to either of these recommendations
- Evaluate
  - Program cost/savings
  - Changes in disease, medical costs, and nonmedical costs
    - Societal perspective
  - Population
    - Cohort of 4,256,608 19 year olds
    - Separate model buckets for:
      - Immunocompromised (IC) – HIV, Cancer, Organ Transplants, Dialysis
      - Chronic medical conditions (CMC)– Diabetes, Heart Disease, Lung Disease, Liver Disease, Alcoholism
      - Others –"healthy"

Methods: Interventions

- Eight strategies to evaluate
  - PCV15 at CMC/IC & Age 50
    - PCV15 at diagnosis of immunocompromising (IC) or chronic medical condition (CMC) for adults 19-49 plus PCV15 at age 50 (no PCV revaccination)
  - PCV20 at CMC/IC & Age 50
  - PCV15 at CMC/IC & Age 65
  - PCV20 at CMC/IC & Age 65
  - PCV15+PPSV at CMC/IC & Age 50
    - As above, but with PPSV at diagnosis of IC or CMC or age 50
  - PCV20+PPSV at CMC/IC & Age 50
  - PCV15+PPSV at CMC/IC & Age 65
  - PCV20+PPSV at CMC/IC & Age 65
- Compare to current recommendations
  - PCV13 at diagnosis of IC, PPSV23 eight weeks later, 2nd dose of PPSV23 5 years later if under age 65
  - PPSV23 at diagnosis of CMC
  - PCV13 under shared clinical decision making at age 65, PPSV23 one year later

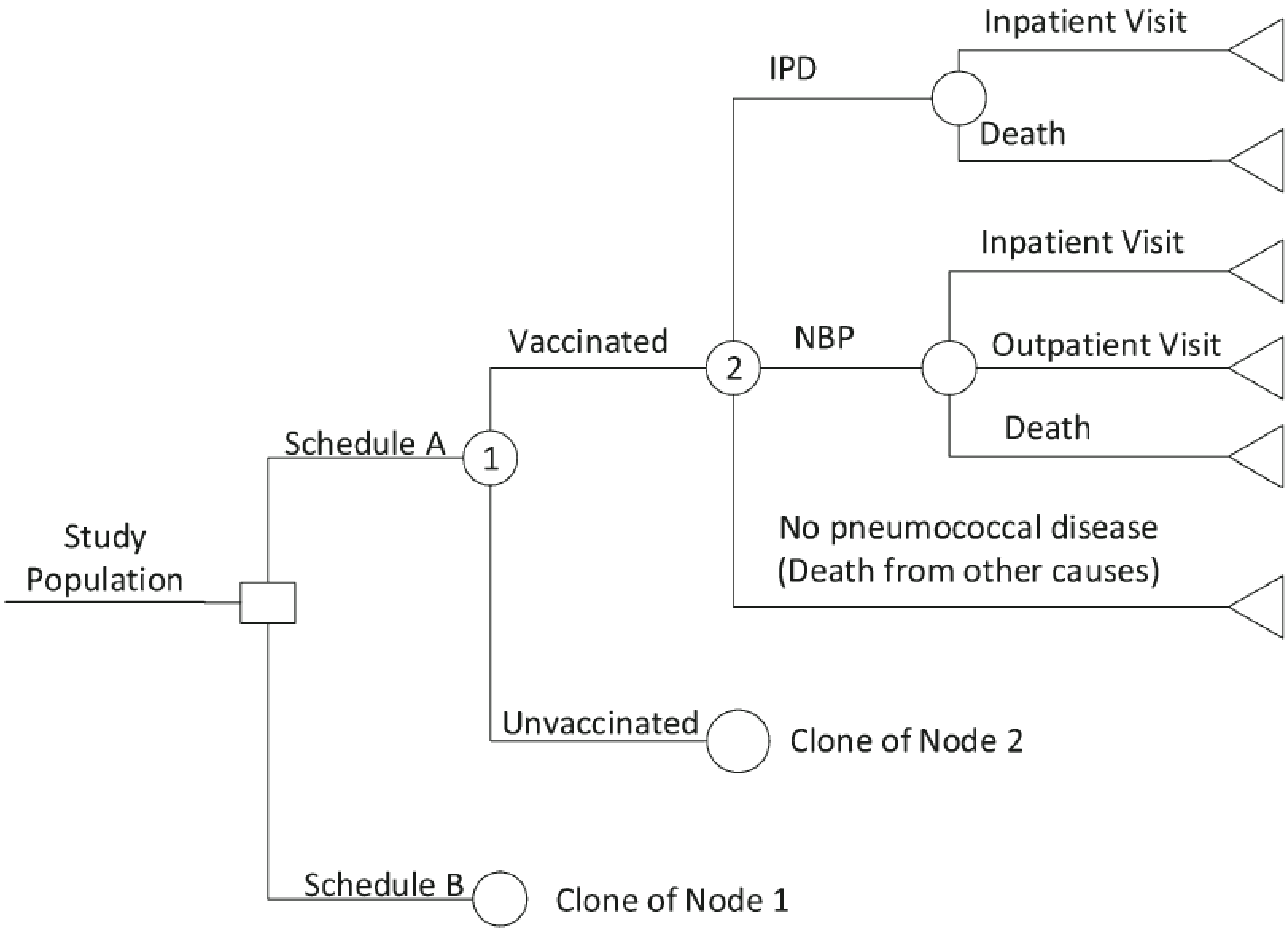
Methods: Economic Model

- **Cohort Model**
  - Cost per quality adjusted life year gained
  - Cost per life year gained
  - Use a cohort of 19-year-olds
- **Compare each recommendation to status quo and calculate incremental cost effectiveness ratio**
  - Divide change in costs by change in Quality Adjusted Life Years (QALYs)
- **Costs in April, 2021$**
  - Inflated by the Health Care component of Personal Consumption Expenditures
- **Outcomes Discounted by 3%**

Methods: Health Outcomes

- Cases of Invasive Pneumococcal Disease (IPD)
- Cases of hospitalized Nonbacteremic Pneumonia (NBP)
- Cases of outpatient NBP
- Deaths due to IPD
- Deaths due to NBP
- QALYs
- Life Years

Conceptual Model



CAP Hospitalization Rates per 100k 2013-2015

	19-49	50-64	65-74	75+
Healthy	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)	3676 (3623,3730)

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

IPD Rates per 100k

	19-49	50-64	65-74	75+
Healthy	2.09	6.09	8.25	19.27
CMC	8.09	24.04	25.89	40.06
IC	16.22	37.28	35.10	39.47

Source: Active Bacterial Core Surveillance System, 2017-2018

Serotype Distributions, Healthy

% IPD (ABCs Data 2017-2018), Healthy	50-64	65-74	75+
%PCV13 (+6C-3-19F)	10.41%	7.99%	8.98%
%serotype 3	14.53%	15.45%	14.79%
%serotype 19F	3.57%	4.55%	1.34%
% PCV15 only (ST 22F, 33F)	17.53%	13.12%	15.23%
% PCV20 only (ST 8, 10A, 11A, 12F, 15B/C)	19.74%	18.84%	12.54%
% PPSV23 only (ST 2, 9N, 17F, 20)	11.23%	10.26%	8.07%

% Hospitalized All-Cause Pneumonia, Healthy	50-64	65+
PCV13-ST3	1.97	2.22
ST3	1.87	1.88
PCV15only	0.93	1.03
PCV20only	2.9	2.22
PPSV23only	2.39	1.2

Serotype Distributions, CMC

% IPD (ABCs Data 2017-2018), CMC

	19-49	50-64	65-74	75+
%PCV13 (+6C-3-19F)	18.54%	11.09%	6.65%	5.72%
%serotype 3	10.84%	17.27%	19.33%	16.05%
%serotype 19F	2.65%	2.61%	2.87%	2.16%
% PCV15 only (ST 22F, 33F)	11.98%	11.68%	12.09%	16.20%
% PCV20 only (ST 8, 10A, 11A, 12F, 15B/C)	20.69%	18.00%	15.41%	13.12%
% PPSV23 only (ST 2, 9N, 17F, 20)	16.02%	13.69%	9.36%	6.48%

% Hospitalized All-Cause Pneumonia, CMC & IC

	19-49	50+
PCV13-ST3	2.81	1.94
ST3	2.8	2.29
PCV15only	2.34	1.41
PCV20only	6.07	4.59
PPSV23only	2.34	3.35

Serotype Distributions, IC

% IPD (ABCs Data 2017-2018), IC

	19-49	50-64	65-74	75+
%PCV13 (+6C-3-19F)	11.26%	11.34%	9.84%	9.75%
%serotype 3	8.79%	10.03%	12.32%	11.59%
%serotype 19F	2.48%	2.38%	2.45%	1.83%
% PCV15 only (ST 22F, 33F)	18.81%	12.41%	13.54%	17.38%
% PCV20 only (ST 8, 10A, 11A, 12F, 15B/C)	13.74%	15.84%	17.25%	10.97%
% PPSV23 only (ST 2, 9N, 17F, 20)	10.02%	11.88%	7.39%	4.88%

Vaccine Effectiveness

	Healthy/CMC	IC
PCV vs VT IPD	75 (41.4, 90.8)	27.1 (15, 32.8)
VE PCV vs VT IPD (Direct, ST3)	26 (0, 53.4)	9.4 (0, 19.3)
PCV vs VT (except 3) NBP (Healthy)	66.7 (11.8, 89.3)	16.3 (5.1, 23.6)
PCV vs VT (except 3) NBP (CMC)	40.3 (11.4, 60.2)	.
PCV vs ST3 NBP	15.6 (0, 32.04)	6 (0, 11)
PPSV vs VT IPD	33 (27.3, 38.3)	11.9 (9.9, 13.8)
PPSV vs VT NBP	20 (0, 40)	7 (0, 14)

PCV vs VT (except ST3) IPD: Bonten NEJM 2015 (per protocol)
PCV vs ST3 IPD: Point estimate from Pilishvili et al. ISPPD2018 abstract, lower bound set to 0, upper bound from Lewis 2020 ISPPD poster
PCV vs VT (except 3) NBP: Suaya Vaccine 2018; 1477-1483.
PCV vs ST3 NBP: applied the ratio of IPD VE/Pneumonia VE for all PCV13 types to the point estimate for ST3 IPD VE.
PPSV vs VT IPD: CDC meta-analysis of 7 studies using indirect cohort methods 4/15/2021
PPSV vs VT NBP: Lawrence, 2020 (meta-analysis of 3 studies, Kim, Suzuki and Lawrence: 19.2% (0-39.1)
All IC estimates: Apply ratio of VE for IC in Djennad 2018 to estimates for Healthy/CMC
PCV15 & PCV20 VE: Hurley CID 2020; Stacy Human Vaccines & Immunotherapeutics 2019

Coverage Rates

- **Risk-based recommendation 23.3% (21.8, 24.3)**
  - NHIS 2018
- **Age-based recommendation at 50 38.83% (22.5, 55.15)**
  - Mean of NHIS 2018 coverage for Zoster 60-64 (22.5%) and age-based recommendation at age 65 below (55.15%)
- **Age-based recommendation at 65 PCV 46.15% (43.3, 49)**
  - Mean of McLaughlin et al. 2019. (43.3%) and any PCV13 coverage in Medicare beneficiaries (49%)
- **Age-based recommendation at 65 PPSV 55.15% (49, 61.3)**
  - Mean of NHIS 2014 data for any pneumococcal vaccine (49%) and any PPSV23 coverage data in Medicare beneficiaries aged ≥65 years, 2019 (61.3%)

Bounds of beta-pert distributions in parenthesis

Methods: Inputs
Herd Effects from PCV15 or 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 PCV15 starting in 2023
- Apply to additional types in PCV20 starting in 2024
- Run versions of the model with and without these herd effects to assess importance

Methods: Inputs
Utility Decrements

Variable	QALYs	Healthy Days Lost
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

Implied duration of hospitalization: 32.4 days

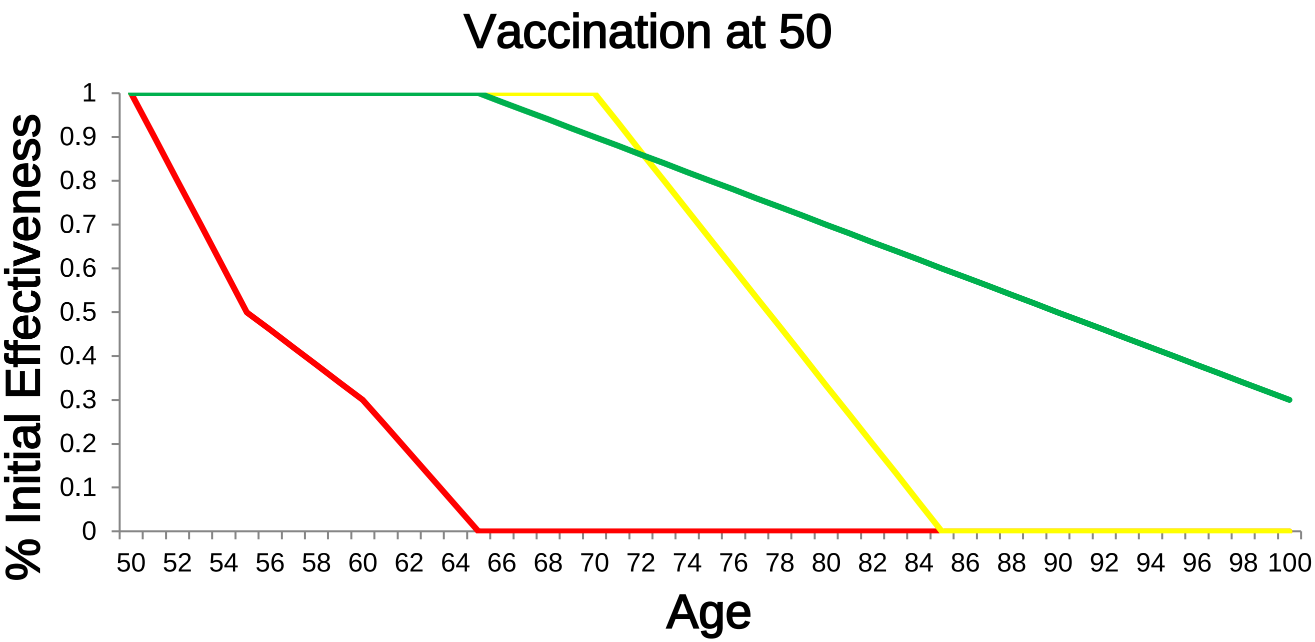
QALY values from Mangen et al. 2015 Eur Respir J (95% CIs in parenthesis)
Duration of illness calculations assume a day in the hospital is worth 20% of a healthy day (Sisk et al. 2003 Ann. Intern. Med.)

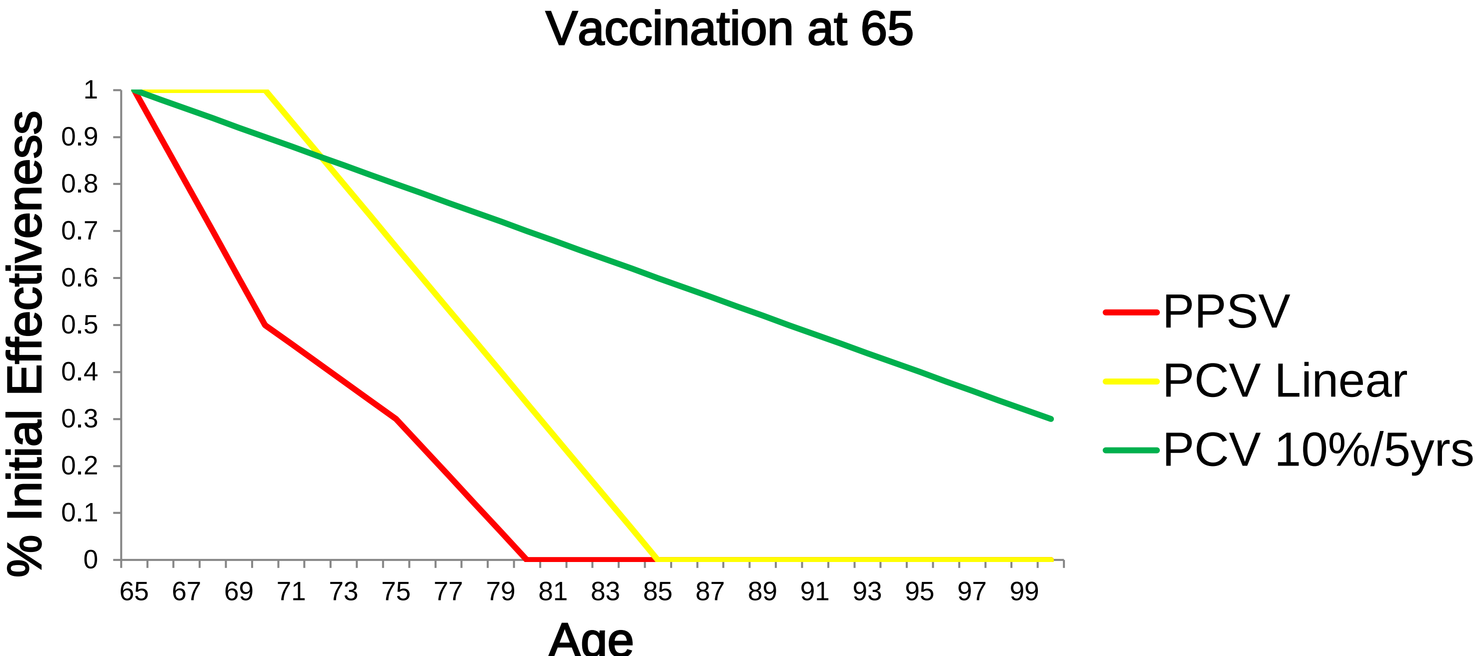
Waning Immunity Assumptions

- **PCV13/15/20**
  - No decline in effectiveness until age 65[a]
  - Scenario 1:
    - 10% every 5 years starting at age 65[b]
  - Scenario 2:
    - Linear decline to zero between 70 and 85[c]
- **PPSV23**[d]
  - Declines in effectiveness start at vaccination
  - Linear decline to 50% of initial over first 5 years
  - Linear decline to 30% of initial over next 5 years
  - Linear decline to 0% of initial over next 5 years

[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]By assumption.
[c]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.
[d]Fry AM, Zell ER, Schuchat A, Butler JC, Whitney CG. Comparing Potential Benefits of New Pneumococcal Vaccines with the Current Polysaccharide Vaccine in the Elderly. Vaccine 2002;21:303-311.

Waning


Vaccination at 50
% Initial Effectiveness
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
50 52 54 56 58 60 62 64 66 68 70 72 74 76 78 80 82 84 86 88 90 92 94 96 98 100
Age


Vaccination at 65
% Initial Effectiveness
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
65 67 69 71 73 75 77 79 81 83 85 87 89 91 93 95 97 99
Age
PPSV
PCV Linear
PCV 10%/5yrs

Vaccine Price

- PCV13 $211.86[a]
- PCV15 $228.81[a]
- PCV20 $233.05[a]
- PPSV23 $110.45[a]

- Administration 19 -64 $29.16[b]
- Administration 65+ $23.60 [c]
- Travel + Patient Time cost: $42.52[d]

[a] Communication with manufacturers
[b] Tsai et al. AJPM 2019.
[c] Average Medicare maximum allowable reimbursement for immunization administration (HCPCS code 90471) across all MACs
[d] travel cost from Maciosek et al. Am J Prev Med 2006.

Disease Cost ($)

	Otherwise Healthy			CMC			IC		
Age	19-49	50-64	65+	19-49	50-64	65+	19-49	50-64	65+
IPD	57,278 (50,148, 65,152)	55,408 (51,752, 59,239)	27,372 (26,997, 27,758)	53,523 (32,028, 79,224)	49,372 (40,029, 60,380)	25,705 (23,787, 27,793)	90,729 (53,654, 144,561)	121,544 (93,951, 149,252)	35,510 (34,808, 38,387)
IPT NBP	24,798 (24,254, 25,343)	26,464 (25,997, 26,979)	18,688 (18,659, 18,715)	31,278 (27,581, 35,593)	29,037 (27,362, 30,820)	16,202 (16,086, 16,320)	39,650 (32,843, 48,404)	36,337 (33,319, 39,634)	22,427 (22,277, 22,585)
OPT NBP	775 (765, 784)	709 (701, 716)	630 (629, 632)	1,038 (955, 1,127)	876 (829, 923)	588 (583, 593)	1,208 (1,101, 1,329)	1,062 (995, 1,135)	943 (935, 952)

All costs from 2016-2019 inflated to April 2021. Costs for <65 come from MarketScan databases. Costs for 65+ from CMS Medicare Data.
Bootstrapped 95% CIs shown in parenthesis and used as inputs in normal distribution.

Scenarios

- Base Case
- PCV 0 VE vs ST3
  - Assume all PCVs have no effectiveness against serotype 3
- Short Run Herd Effects
  - Model 4.1% decline per year in PCV15/PCV20 unique types
  - Start PCV15 decline at age 53 for vaccination at age 50
  - Start PCV20 decline at age 54 for vaccination at age 50
  - Start PCV15 decline at age 68 for vaccination at age 65
  - Start PCV20 decline at age 69 for vaccination at age 65
- PCV Steeper Waning
  - Assume PCVs have linear decline in effectiveness between age 70 and 85
- Enhanced PCV15 VE vs ST3
  - Healthy/CMC: 41.6% vs IPD; 24.96% vs NPB
  - IC: 15 vs IPD; 9 vs NPB

Summary of Findings Across One-Way Sensitivity Analyses ($/QALY)

	(1) PCV15, 50	(2) PCV20, 50	(3) ICER (1) +PPSV	(4) ICER (2) +PPSV	(5) PCV15, 65	(6) PCV20, 65	(7) ICER (5) +PPSV	(8) ICER (6) +PPSV
Base Case	282,711	Cost-Saving	574,871	1,635,228	158,025	Cost-Saving	462,604	1,313,935
PCV0 VE vs ST3	1,133,404	Cost-Saving	403,527	792,145	Dominated	Cost-Saving	330,183	658,782
Short Run Herd Effects	817,889	24,625	595,673	1,635,228	507,445	Cost-Saving	483,075	1,313,935
Steeper Waning	603,452	4,951	574,871	1,635,228	1,164,689	Cost-Saving	464,388	1,326,755
Enhanced PCV15 VE	231,267		583,149		117,066		476,768	

Base Case Vax at 50

	PCV15 at CMC/IC & Age 50	PCV20 at CMC/IC & Age 50	ICER Adding PPSV to Column 1	ICER Adding PPSV to Column 2
Health Outcomes				
IPD Cases	-153	-500	-54	-24
Hospitalized Pneumonia Cases	-194	-2,914	-175	-51
Non-hospitalized Pneumonia Cases	-225	-7,401	-1,069	-312
Deaths due to IPD	-22	-67	-6	-3
Deaths due to Pneumonia	-10	-110	-4	-1
QALYs	193	1,378	156	59
Life-years	274	1,976	199	76
Costs (million $)				
Total Cost	$55	-$16	$90	$96
Medical Costs	-$11	-$85	-$9	-$3
Vaccine Costs	$66	$69	$99	$99
Cost Ratios ($)				
Cost/QALY	282,711	Cost-Saving	574,871	1,635,228
Cost/Life-year	199,968	Cost-Saving	451,630	1,265,201

Base Case Vax at 65

	PCV15 at CMC/IC & Age 65	PCV20 at CMC/IC & Age 65	ICER Adding PPSV to Column 1	ICER Adding PPSV to Column 2
Health Outcomes				
IPD Cases	-116	-435	-106	-48
Hospitalized Pneumonia Cases	-155	-2,822	-692	-227
Non-hospitalized Pneumonia Cases	-55	-7,000	-2,076	-669
Deaths due to IPD	-18	-60	-13	-6
Deaths due to Pneumonia	-9	-107	-23	-8
QALYs	113	1,224	352	133
Life-years	181	1,801	516	196
Costs (million $)				
Total Cost	$18	-$50	$163	$175
Medical Costs	-$8	-$79	-$19	-$6
Vaccine Costs	$26	$28	$182	$182
Cost Ratios ($)				
Cost/QALY	158,025	Cost-Saving	462,604	1,313,935
Cost/Life-year	98,566	Cost-Saving	315,857	893,281

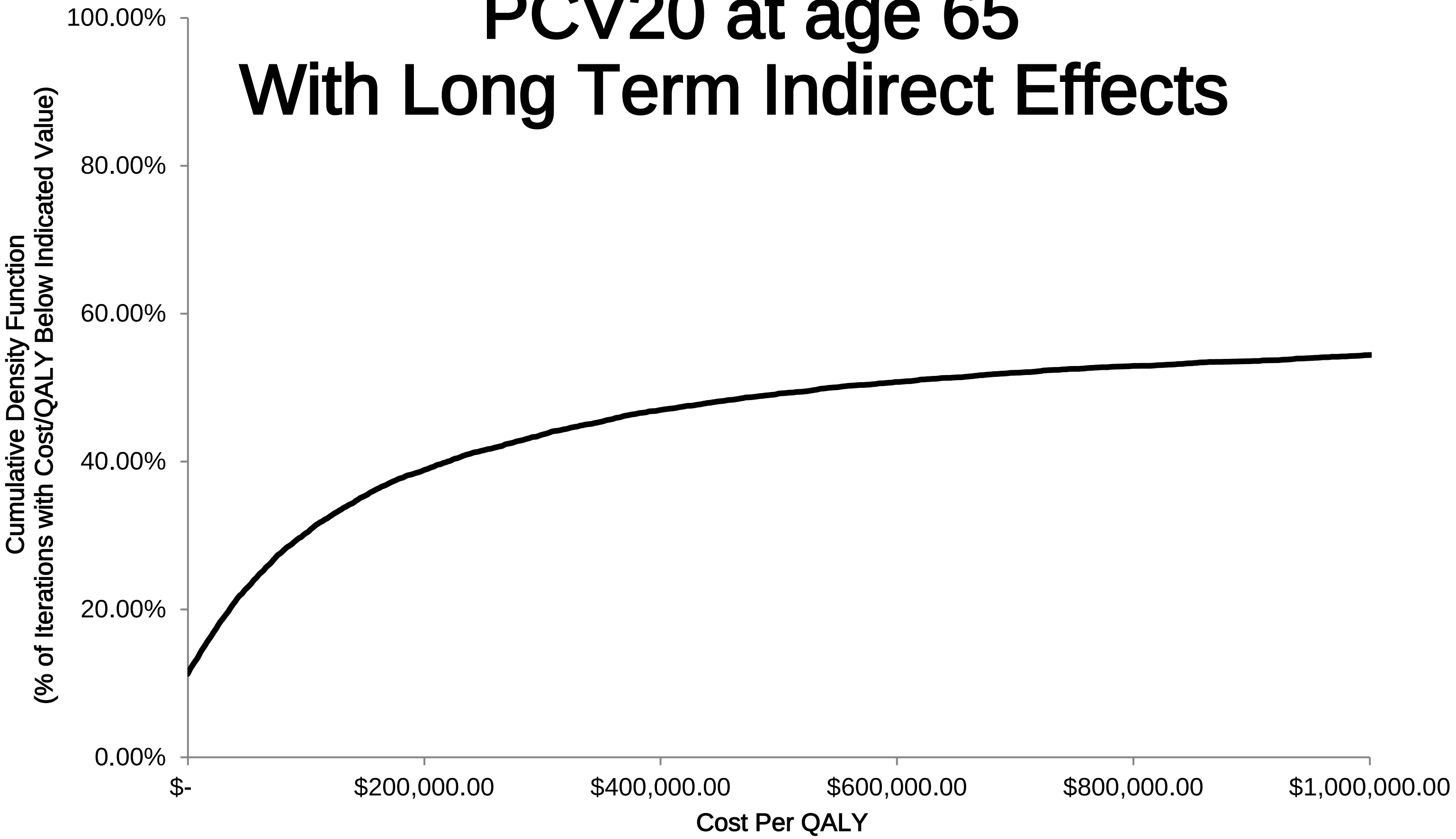
Number Needed to Vaccinate to Avert… Base Case (No Herd Effects)

	PCV15 at CMC/IC & Age 50	PCV15 at CMC/IC & Age 65	PCV20 at CMC/IC & Age 50	PCV20 at CMC/IC & Age 65
To Avert 1 Hospitalization	573	581	79	75
To Avert 1 Case	322	356	29	28
To Avert 1 Death	6,968	6,920	1,472	1,393

Cost per Outcome Averted
Base Case (No Herd Effects)

	PCV15 at CMC/IC & Age 50	PCV15 at CMC/IC & Age 65	PCV20 at CMC/IC & Age 50	PCV20 at CMC/IC & Age 65
To Avert 1 Hospitalization	$157,895	$65,890		
To Avert 1 Case	$95,680	$54,718	Cost Saving	
To Avert 1 Death	$1,736,968	$672,283		

Vaccine Acceptability Curve
PCV20 at age 65
With Long Term Indirect Effects



- **Substantial uncertainty introduced by potential herd effects**
  - 69.7% of model iterations cost more than $100k/QALY
  - 61.1% more than $200k/QALY
  - 56.3% more than $300k/QALY
- **38.8% of model iterations were dominated by current recommendations**
  - (Led to decreases in health and increases in cost)

Existing Study

- Evaluation of PCV20 or PCV15 at age 65 (Smith et al. 2021 AJPM)
  - PCV20 $173k/QALY without indirect effects
  - PCV20 $449k/QALY with indirect effects
  - PPSV23 and PCV15 even less economically viable
- Key difference
  - This evaluation includes risk-based recommendations bundled with age-based

Limitations

- Work loss not considered
- Model assumed no vaccine adverse events
- Substantial uncertainty remains around the influence of
  - Serotype 3 VE
  - A PCV15/PCV20 childhood immunization program
  - Vaccine waning
  - Vaccine-preventable pneumonia burden

Conclusions

(Given these assumptions and Limitations)

- Modeling indicated PCV20 was economically efficient at both ages 50 and 65 under several alternative scenarios
- PCV15 model findings were mixed even under optimistic assumptions about PCV15 VE vs serotype 3
- Adding PPSV23 to either PCV15 or PCV20 incurred high costs for minimal health gains in the model
- PCV20 less likely to be economically efficient under predicted indirect protection from the childhood program over the long term as modeled

Thank you!

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