Economic Assessment of PCV20 for Adults Vaccinated with PCV13

Charles Stoecker
Tulane University
School of Public Health and Tropical Medicine

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Conflicts of Interest

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

Methods: Study Question

- **Evaluate cost effectiveness of using PCV20 after PCV13 in adults**

Methods: Evaluate:

- **Program cost/savings**
- **Changes in disease, medical costs, and nonmedical costs**
  - Societal perspective
- **Population**
  - Cohorts of 42+, 65+, or 75+ year olds who have had PCV13
  - Separate model reports for:
    - IC
      - Immunocompromised – HIV, Cancer, Organ Transplants, Dialysis
    - Healthy+CMC
      - Chronic Medical conditions – Diabetes, Heart Disease, Lung Disease, Liver Disease, Alcoholism
      - Others –"healthy"

Question 1: Use of PCV20 in adults who previously received PCV13 only

Comparator	Adding
PCV13 at Age 65 (Healthy/CMC)	**PCV20 at Age 66**
PCV13 at Age 75 (Healthy/CMC)	PCV20 at Age 76
PCV13 at Age 65 (IC)	PCV20 at Age 66
PCV13 at Age 75 (IC)	PCV20 at Age 76
PCV13 at Age 42 (IC)	PCV20 at Age 43

Question 2: Use of PCV20 in adults with IC aged 19-64 years who previously received PCV13 & PPSV23

Comparator	Adding
PCV13+PPSV23 at Age 42	**PCV20 at Age 47**
PCV13+PPSV23 at Age 42	PCV20 at Age 43

Question 3: Use of PCV20 in adults aged 65+ without IC (healthy/CMC) who previously received PCV13+PPSV23

Comparator	Adding
PCV13+PPSV23 at Age 65/66	**PCV20 at Age 71**
PCV13+PPSV23 at Age 65/66	PCV20 at Age 67
PCV13+PPSV23 at Age 65/66	PCV20 at Age 76
PCV13+PPSV23 at Age 75/76	PCV20 at Age 77
PCV13+PPSV23 at Age 75/76	PCV20 at Age 81

Question 3 (cont'd): Use of PCV20 in adults aged 65+ with IC who previously received PCV13+PPSV23

Comparator	Adding
PCV13+PPSV23 at Age 65	PCV20 at Age 66
PCV13+PPSV23 at Age 65	PCV20 at Age 70
PCV13+PPSV23 at Age 65	PCV20 at Age 75
PCV13+PPSV23 at Age 75	PCV20 at Age 76
PCV13+PPSV23 at Age 75	PCV20 at Age 80

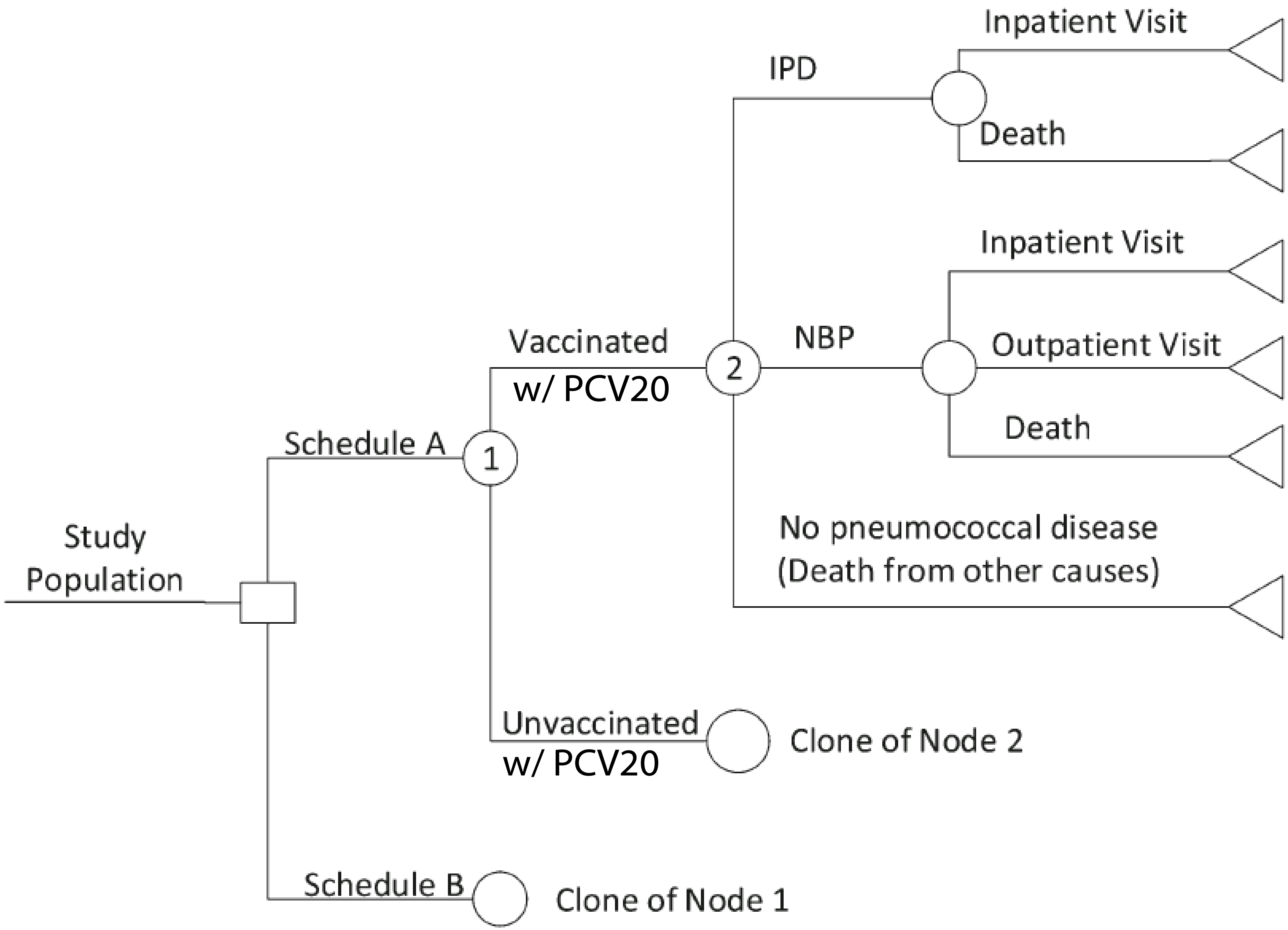
Methods: Economic Model

- **Cohort Model**
  - Cost per quality adjusted life year gained
  - Cost per life year gained
  - Cohort sizes depend on age and % vaccinated with PCV13 or PCV13+PPSV23
    - E.g.: Model size = # 75-IC-year-olds * % IC vaccinated with PCV13+PPSV23
  - All outcomes (case counts, deaths, QALYs, LYs, etc.) and costs discounted by 3%
  - All costs inflated to 2021$ using Consumer Price Index
  - Time horizon: 15 years
- **Compare each recommendation to status quo and calculate incremental cost effectiveness ratio**
  - Divide change in costs by change in Quality Adjusted Life Years (QALYs)
- **Probabilistic sensitivity 50,000 iterations**
  - CDF of $/QALY
  - 5^{th}, 95^{th} percentiles all outputs
  - "Tornado" of influential inputs

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 hospitalized NBP
- QALYs
- Life Years

Conceptual Model



CAP Hospitalization Rates per 100k 2013-2015

	19-49	50-64	65-74	75+
Healthy			191 (185, 197)	957 (938, 975)
CMC			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	75-84	85+
Healthy			8.25	13.90	33.06
CMC			25.89	33.34	58.57
IC	16.22	37.28	35.10	36.81	46.38

Source: Active Bacterial Core Surveillance System, 2017-2018

Case Fatality Rates

IPD			
	Healthy	CMC	IC
19-49			10.4
50-64			12.51
65-74	7.41	13.92	13.92
75-84	10.6	13.63	10.6
85+	19.37	23.72	19.97

Pneumonia			
	lower	base	upper
19-49	0.4	1.6	2.9
50-64	1.1	2.8	4.4
65-74	1.5	3.5	5.5
75-84	2.2	4.1	6.0
85+	3.3	5.3	7.2

IPD CFR from ABCs data. Pneumonia CFR from NIS 2018 lower bound: ICD-10 code J13 or J181 for primary diagnosis; upper bound: ICD-10 code J13 or J181 in any location; base estimate: mean of upper and lower.

Serotype Distributions, Healthy

% IPD (ABCs Data 2017-2018), Healthy

	65-74	75-84	85+
%PCV13 (+6C-3-19F)	7.99%	8.76%	9.19%
%serotype 3	15.45%	18.43%	11.01%
%serotype 19F	4.55%	1.77%	0.91%
% PCV15 only (ST 22F, 33F)	13.12%	15.82%	15.56%
% PCV 20 only (ST 8, 10A, 11A, 12F, 15B)	17.14%	6.14%	16.47%
% PPSV23 only (ST 2, 9N, 17F, 20)	10.26%	9.68%	6.46%

% Hospitalized All-Cause Pneumonia, Healthy & CMC

	65+
PCV13-ST3	3.5
ST3	1.1
PCV15only	1.2
PCV20only	2.8
PPSV23only	1.0

Serotype Distributions, CMC

% IPD (ABCs Data 2017-2018), CMC

	65-74	75-84	85+
%PCV13 (+6C-3-19F)	6.65%	5.88%	5.82%
%serotype 3	19.33%	15.08%	17.51%
%serotype 19F	2.87%	2.30%	1.93%
% PCV15 only (ST 22F, 33F)	12.09%	16.87%	15.16%
% PCV 20 only (ST 8, 10A, 11A, 12F, 15B)	14.19%	12.78%	10.11%
% PPSV23 only (ST 2, 9N, 17F, 20)	9.36%	6.65%	6.21%

Serotype Distributions, IC

% IPD (ABCs Data 2017-2018), IC

	19-49	50-64	65-74	75-84	85+
%PCV13 (+6C-3-19F)	11.26%	11.34%	9.84%	8.71%	12.71%
%serotype 3	8.79%	10.03%	12.32%	13.77%	8.17%
%serotype 19F	2.48%	2.38%	2.45%	1.85%	1.82%
% PCV15 only (ST 22F, 33F)	18.81%	12.41%	13.54%	16.98%	18.15%
% PCV 20 only (ST 8, 10A, 11A, 12F, 15B)	11.26%	13.72%	12.92%	10.56%	9.98%
% PPSV23 only (ST 2, 9N, 17F, 20)	10.02%	11.88%	7.39%	5.98%	2.72%

% Hospitalized All-Cause Pneumonia, IC

	19-49	65+
PCV13-ST3	4.1	3.2
ST3	1.1	0.6
PCV15only	1.3	1.4
PCV20only	3.4	2.3
PPSV23only	0.8	0.7

Vaccine Effectiveness

	Healthy/CMC	IC
PCV vs VT IPD	75 (41.4, 90.8)	25.0 (13.8, 30.3)
VE PCV vs VT IPD (Direct, ST3)	26 (0, 53.4)	8.7 (0, 17.8)
PCV vs VT (except ST3) NBP (Healthy)	66.7 (11.8, 89.3)	15 (4.7, 21.8)
PCV vs VT (except ST3) NBP (CMC)	40.3 (11,4, 60.2)	.
PCV vs ST3 NBP	15.6 (0, 32.04)	5.2 (0, 10.7)
PPSV vs VT IPD	59.7 (47.4, 69.1)	7.9 (0, 34.2)
PPSV vs VT NBP	20 (0, 40)	6.7 (0, 13.3)

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

Cohort Size Modifiers (Based on PCV13 & PPSV23 Coverage Data)

		42+	65+	75+
Healthy	PCV13 only	.	0.13	0.15
Healthy	PCV13+PPSV23	.	0.15	0.40
CMC	PCV13 only	.	0.18	0.15
CMC	PCV13+PPSV23	.	0.33	0.40
IC	PCV13 only	0.031	0.17	0.15
IC	PCV13+PPSV23	0.022	0.37	0.40

42+ IC coverage from Deb et al. "Pneumococcal vaccination coverage among adults aged 19 to 64 years with immuno-compromising conditions, cerebrospinal fluid (CSF) leaks, or cochlear implants in the US", Exp Rev Vac, 2021. All other coverage rates from CMS Claims 2020.

In-Model Coverage Rates

- **PCV13: 100%**
- **PPSV23: 100% (in scenarios that consider PPSV23)**
- **PCV20 (cohorts <75 years old): 63.8%[1]**
- **PCV20 (75 year old cohort): 72.7%[1]**

1 ratio of PPSV23 coverage to PCV13 coverage from CMS data

Methods: Inputs
Herd Effects from PCV15 or PCV20 in Children

- **Apply serotype group-specific declines previously observed in PCV13 types (+6C, -3) in adults after PCV13 introduction in children**
  - (No declines applied to PCV13 types in model)
- **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	Source
IPD	0.0709 (0.0509, 0.0909)	Mangen et al. 2015 Eur Respir J
IPT NBP	0.0709 (0.0509, 0.0909)	Mangen et al. 2015 Eur Respir J
OPT NBP	0.0045 (0.00399, 0.00501)	Mangen et al. 2015 Eur Respir J

Waning Immunity Assumptions

- **PCV13/20[a, b, c]**
  - No decline first five years
  - Linear decline over next 10 years
- **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.

Vaccine Price

- **PCV13 $257.99[a]**
- **PCV20 $283.72[a]**
- **PPSV23 $133.47[a]**
- **Administration+Time cost: $56.73[b]**

[a] Medicare maximum allowable reimbursement
[b] Medicare reimbursement for immunization administration (HCPCS code 90471) plus travel cost from Maciosek MV, Solberg LI, Coffield AB, Edwards NM, Goodman MJ. Influenza vaccination health impact and cost effectiveness among adults aged 50 to 64 and 65 and older. Am J Prev Med 2006;31(1):72-9.

Disease Cost

	Otherwise Healthy	CMC	IC		
Age	65+	65+	19-49	50-64	65+
IPD	$27,105	$25,454	$89,842	$120,355	$36,153
IPT NBP	$18,505	$16,043	$39,262	$35,982	$22,208
OPT NBP	$624	$583	$1,196	$1,052	$934

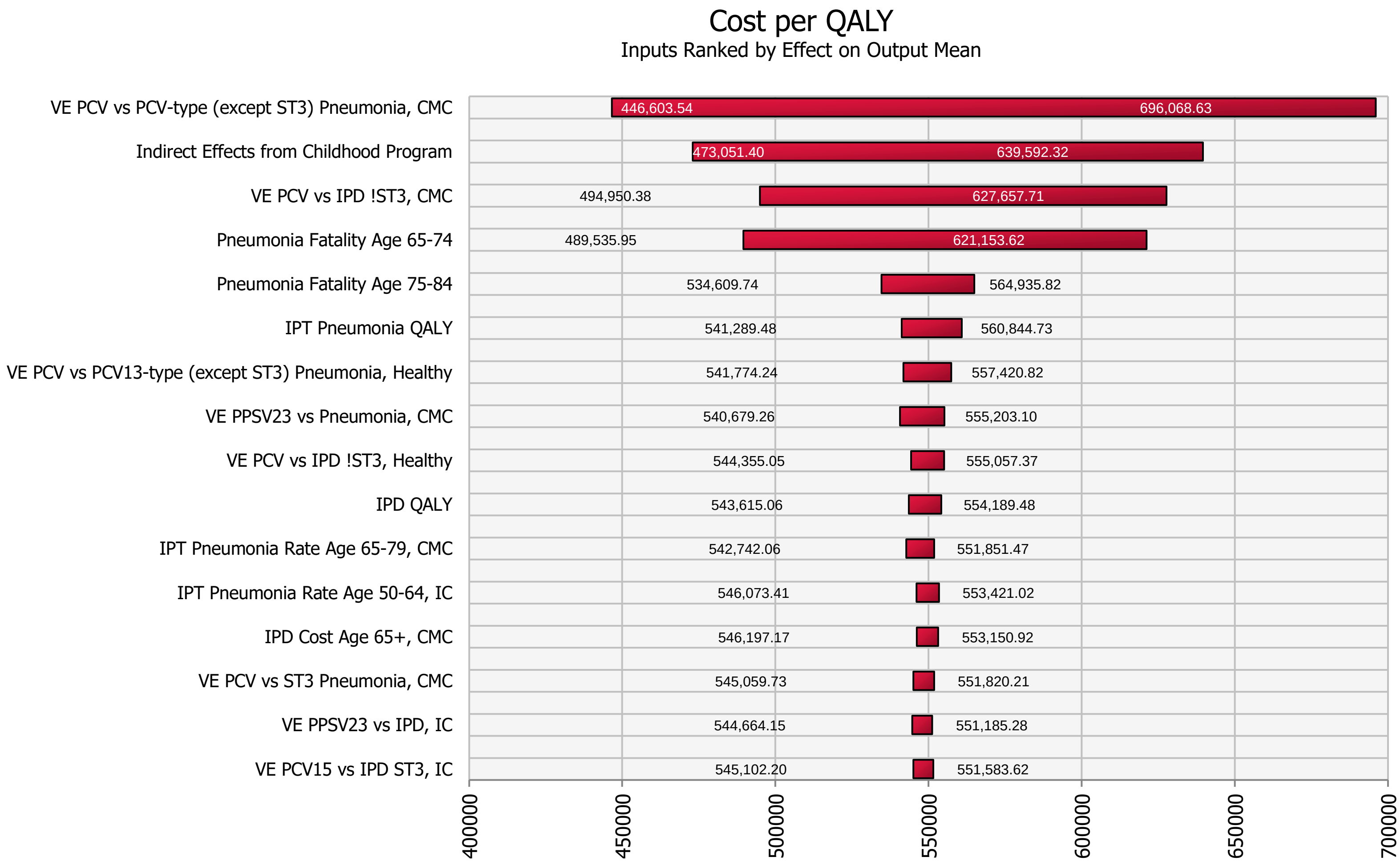
All costs from 2016-2019 data adjusted by Medical Care CPI. Costs for <65 come from MarketScan databases. Costs for 65+ from CMS Medicare Data

Question 1

PCV13 @65, PCV20 @66

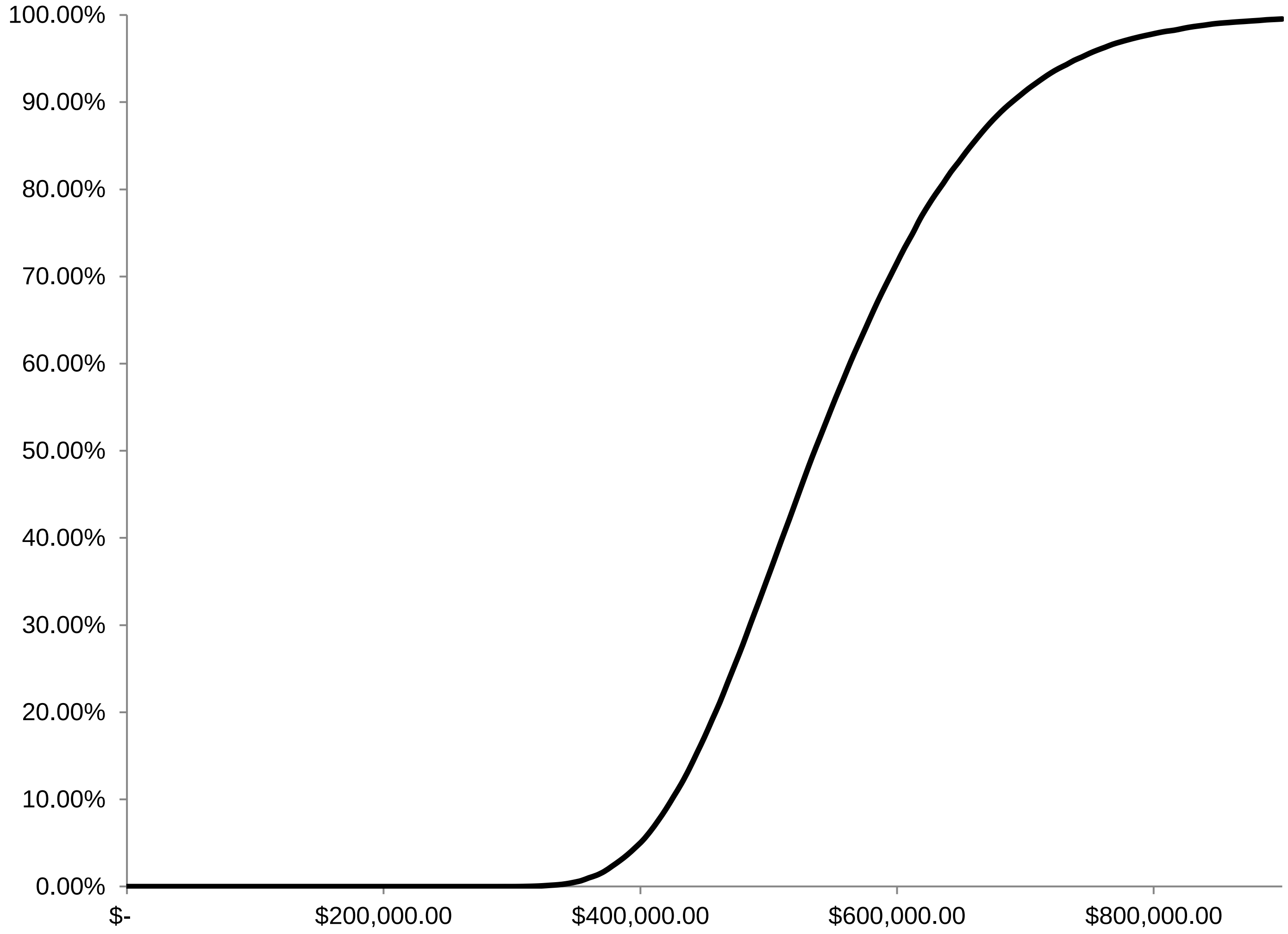
	Base	(5th, 95th)
IPD Cases	-97	(-112,-68)
Hospitalized Pneumonia Cases	-343	(-454,-189)
Non-hospitalized Pneumonia Cases	-719	(-939,-402)
Deaths due to IPD	-13	(-15,-9)
Deaths due to Pneumonia	-13	(-18,-6)
QALYs	196	(134,237)
Life-years	313	(213,381)
Costs (million $)		
Total Cost	$97	(95,100)
Medical Costs	-$9	(-11,-6)
Vaccine Costs	$105	(105,105)
Cost Ratios ($)		
Cost/QALY	493,242	(399,996, 741,184)
Cost/Life-year	308,781	(249,669, 465,368)
Initial Population	422,781	

Question 1
PCV13 @65, PCV20 @66
Sensitivity to Model Inputs



Note: Input distributions are not all symmetrical around the mean, thus base case $/QALY results will not equal mean $/QALY.

Question 1
PCV13 @65, PCV20 @66
Cumulative Distribution Function

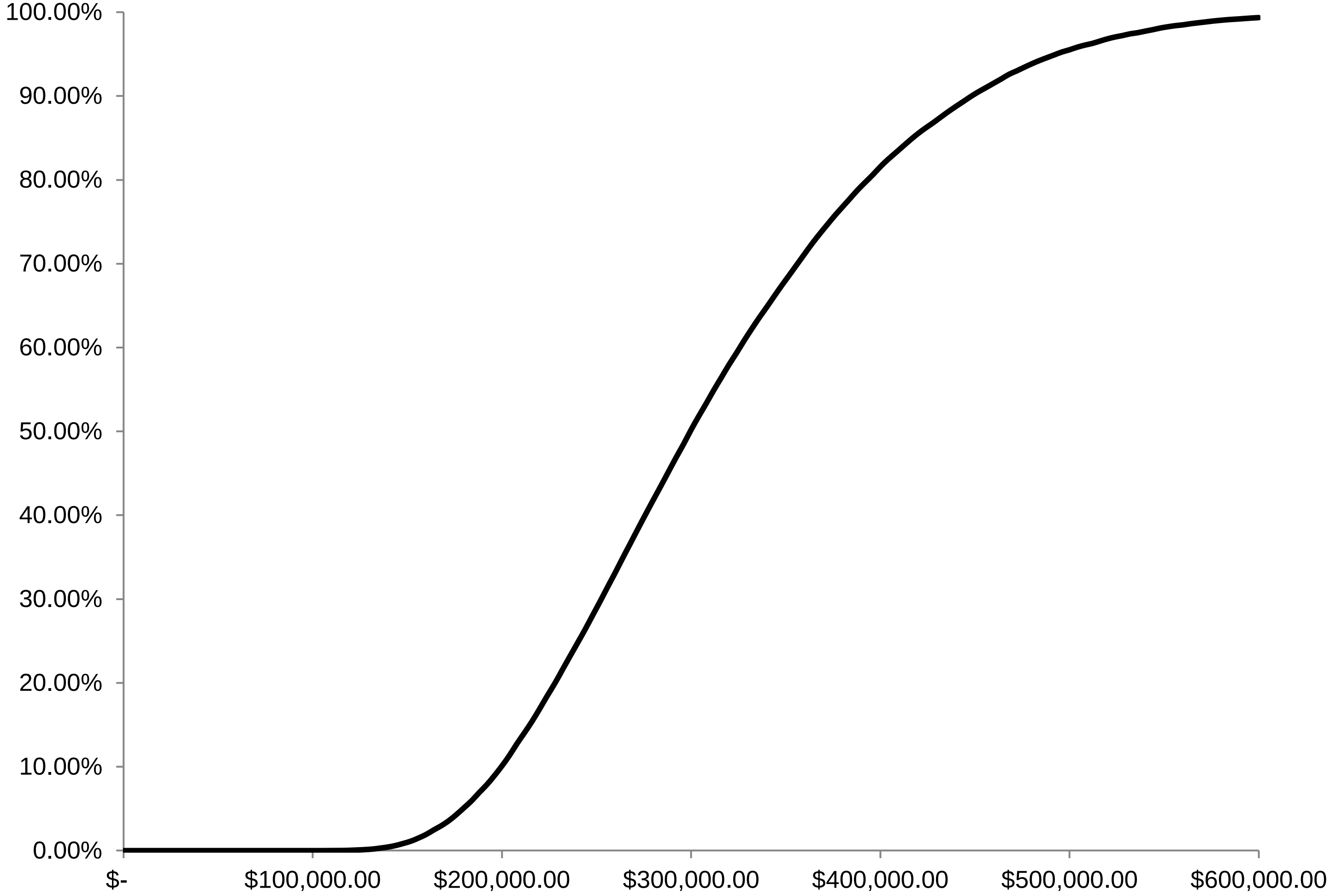


Question 2

PCV13 @42, PPSV @42, PCV20 @47

	Base	(5^{th}, 95^{th})
IPD Cases	-3	(-3,-2)
Hospitalized Pneumonia Cases	-11	(-16,-5)
Non-hospitalized Pneumonia Cases	-59	(-84,-28)
Deaths due to IPD	0	(0,0)
Deaths due to Pneumonia	0	(0,0)
QALYs	10	(6,12)
Life-years	12	(7,16)
Costs (million $)		
Total Cost	$2	(2,3)
Medical Costs	-$1	(-1,0)
Vaccine Costs	$3	(3,3)
Cost Ratios ($)		
Cost/QALY	254,555	(179,473, 493,296)
Cost/Life-year	200,500	(141,889, 385,642)
Initial Population	12,609	

Question 2
PCV13 @42, PPSV @42, PCV20 @47
Cumulative Distribution Function

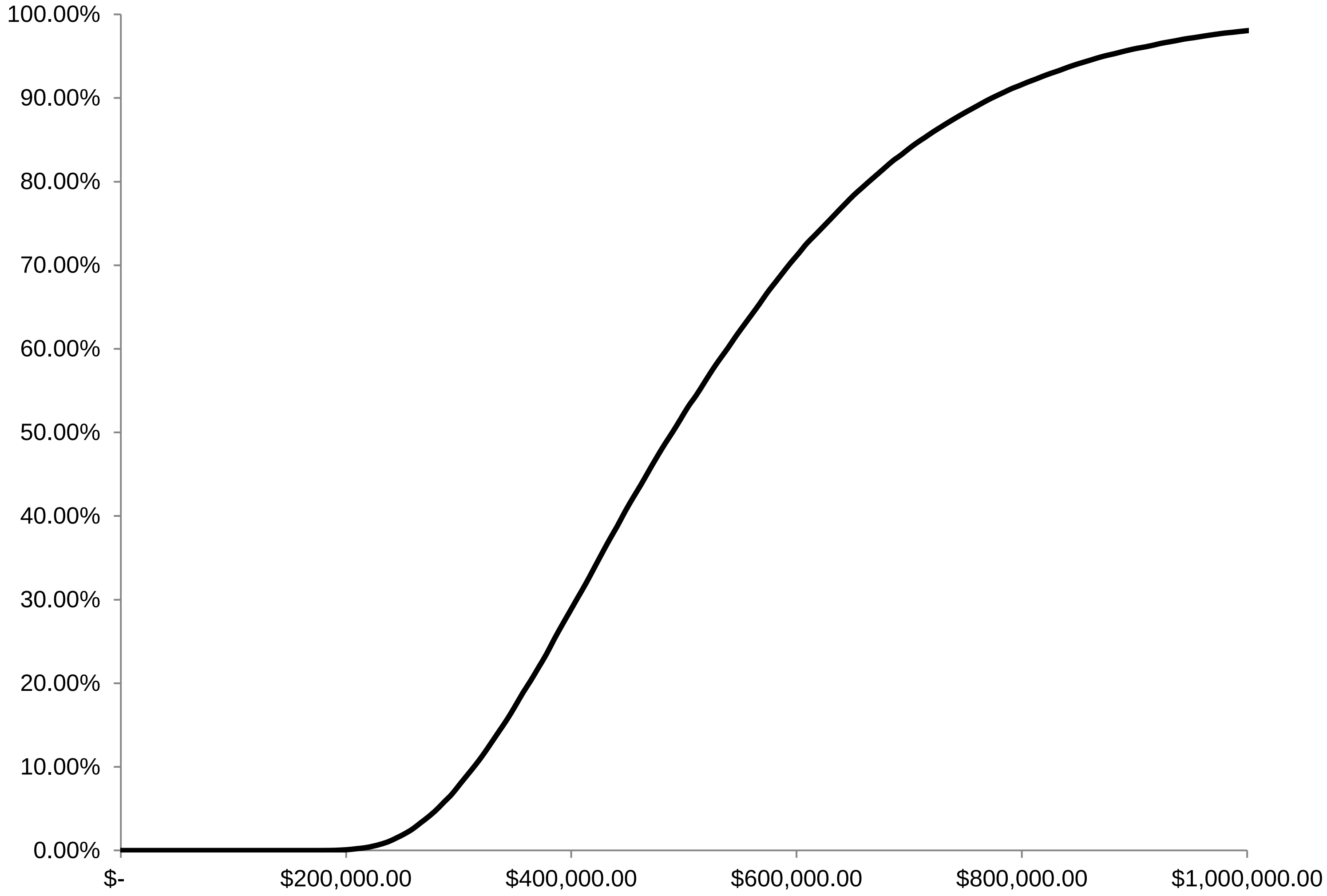


Question 3

PCV13 @65, PPSV23 @66, PCV20 @71

	Base	(5th, 95th)
IPD Cases	-115	(-151,-67)
Hospitalized Pneumonia Cases	-870	(-1276,-372)
Non-hospitalized Pneumonia Cases	-1,095	(-1609,-465)
Deaths due to IPD	-16	(-21,-9)
Deaths due to Pneumonia	-35	(-54,-14)
QALYs	294	(150,409)
Life-years	477	(244,666)
Costs (million $)		
Total Cost	$122	(114,131)
Medical Costs	-$18	(-25,-9)
Vaccine Costs	$140	(140,140)
Cost Ratios ($)		
Cost/QALY	414,166	(281,250, 872,758)
Cost/Life-year	255,192	(173,032, 534,378)
Initial Population	556,234	

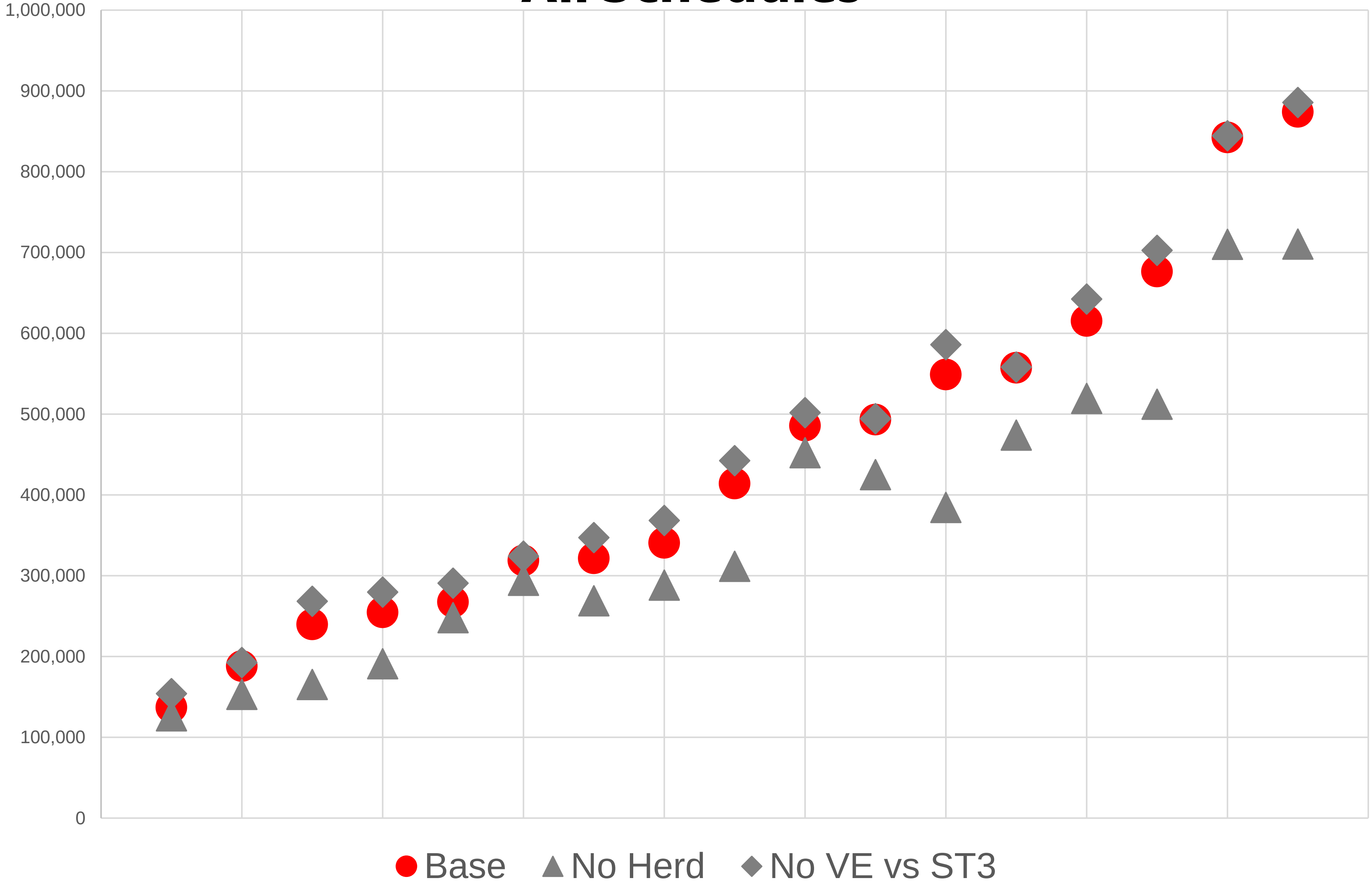
Question 3
PCV13 @65, PPSV23 @66, PCV20 @71
Cumulative Distribution Function



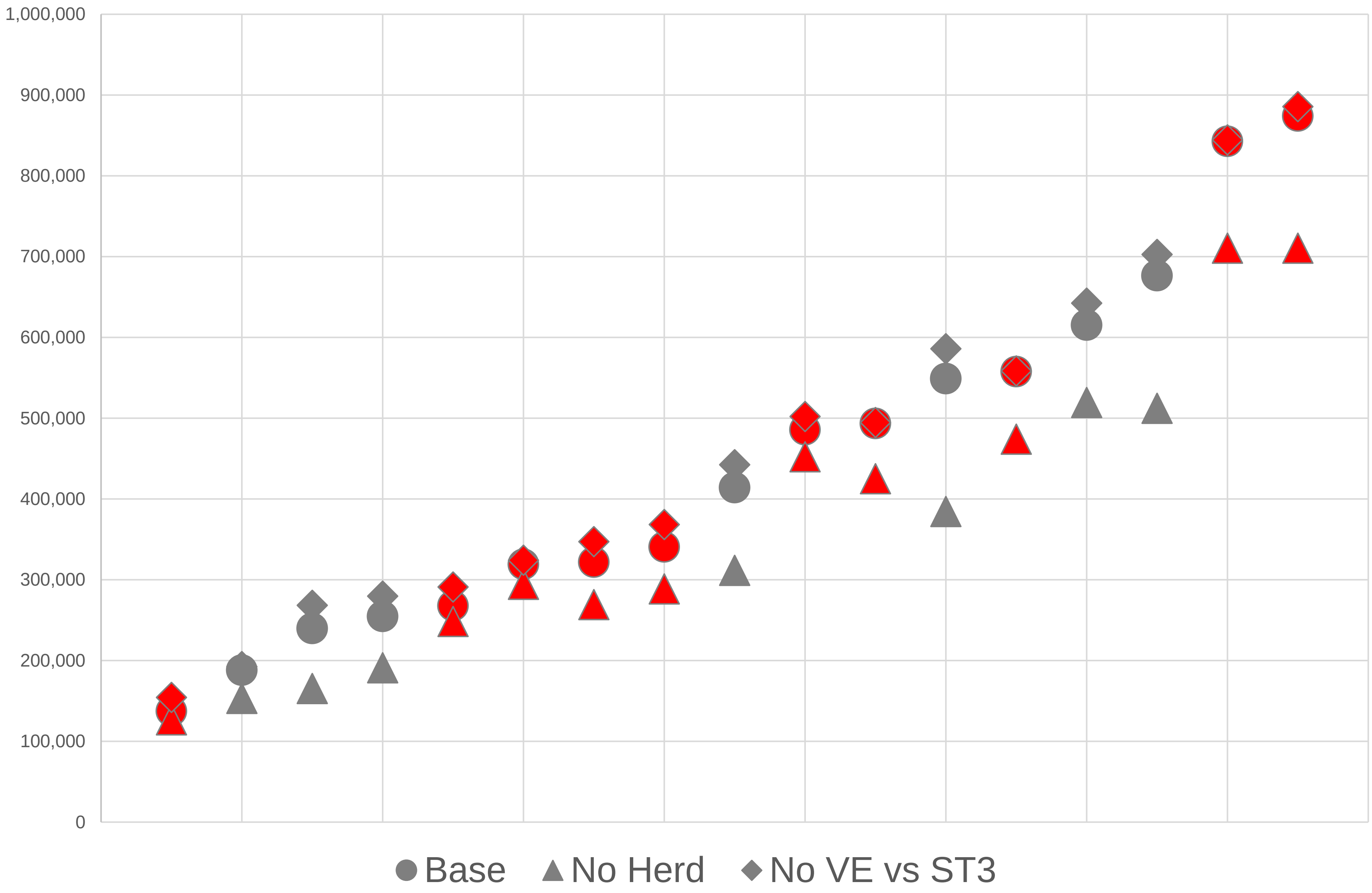
One-way Alternate Scenarios

- Zero herd effects from childhood program
- PCVs have zero effectiveness against ST3

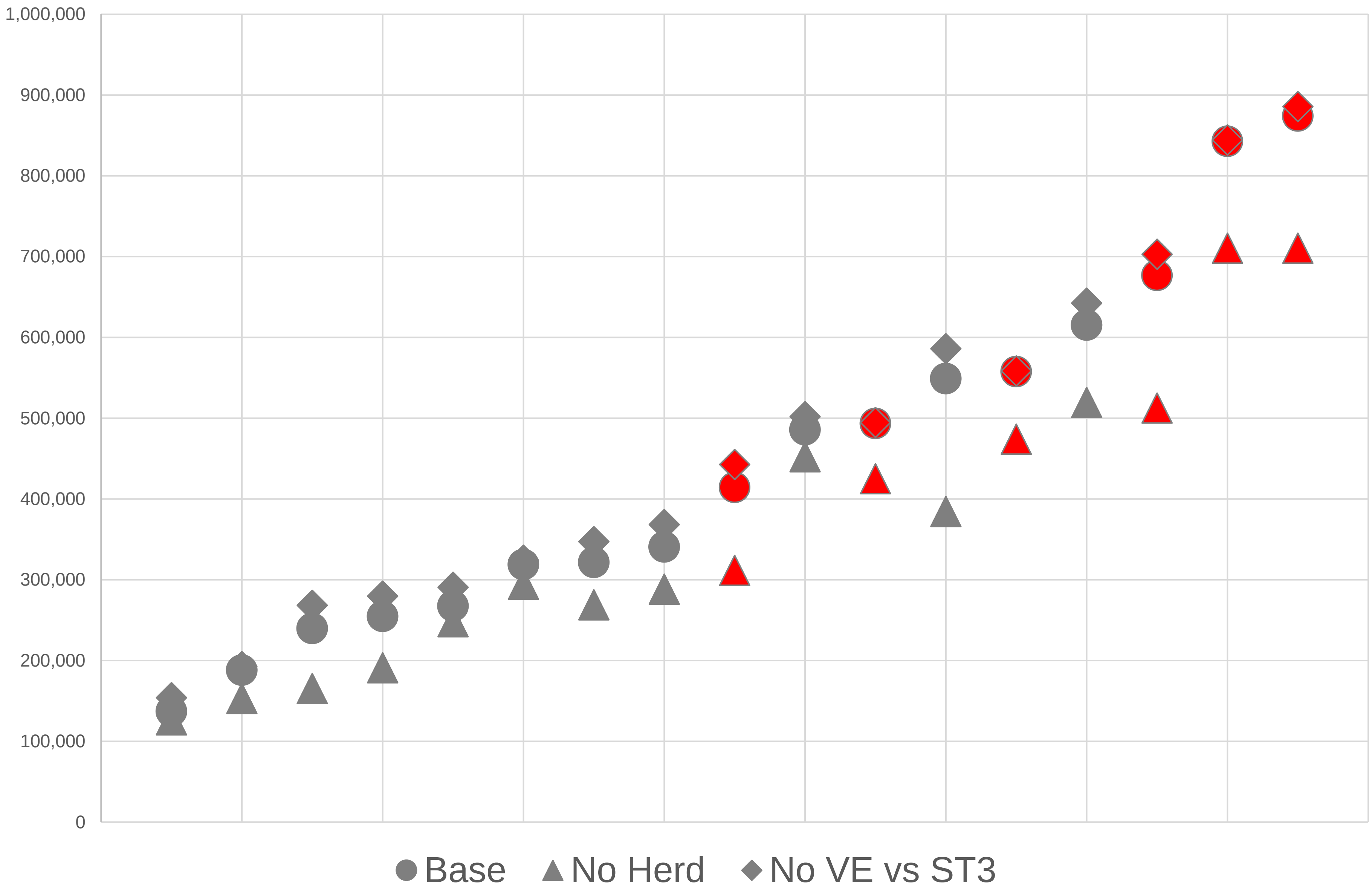
One-Way Sensitivity Results
All Schedules



One Year Delay Schedules



PCV20 @ Age 66-71 Schedules



Limitations

- Substantial uncertainty around effects from childhood program
- Uncertainty around vaccine effectiveness against non-invasive disease

Summary

- **No policies or model simulations below <$126,640 / QALY**
- **Q1: Adults 19+ who previously received PCV13 only**
  - 137k – 557k / QALY (Base case)
- **Q2: IC adults 19-64 who previously received PCV13+PPSV23**
  - 255k - 341k / QALY (Base case)
- **Q3: Adults 65+ who previously received PCV13+PPSV23**
  - 188k – 874k / QALY (Base case)
- **Context from recent PCV modeling for adults at age 65:**
  - Replacing PPSV23(all)+PCV13(shared clinical decision-making)
    - With PCV20(all): cost-saving
    - With PCV15(all)+PPSV23(all): cost-saving
  - Continuing to recommend PCV13(all) in 2019: $562k/QALY

Thank you!

Please send comments to:
cfstoecker@tulane.edu

Contributors:

Miwako Kobayashi
Namrata Prasad
Andrew Leidner
Bo-Hyun Cho