Economic Analysis of Sustaining the Current Recommendation for PCV13 use Among Adults 65 Years or Older in the Context of Continued Indirect Effects from the Pediatric PCV13 Program

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Conflicts of Interest

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

Methods: Study Question

- **Evaluate cost-effectiveness of continuing to recommend PCV13 at age 65 for all adults**
  - How well does the direct protection offered by PCV13 match the current and projected disease burden?
  - Incorporate updated estimates of indirect (herd) impacts from the pediatric immunization program
- **Evaluate**
  - Program cost vs changes in medical and nonmedical costs
  - Changes in disease
  - Aggregate disease endpoints to quality-adjusted life years (QALYs)

Methods: Intervention

- **Continue age-based recommendations for PCV13 at 65 (introduced in 2014)**
  - PPSV23 for those with underlying medical conditions 19-64 and PCV13 at age 65 years followed by PPSV23 ≥ 1 year later (or when at least 5 years have passed since previous dose)
  - Immunocompromised excluded from this model
    - (Keep vaccine recommendation from 2012)
- **Comparison strategy:**
  - PPSV23 for those with underlying medical conditions 19-64 and PPSV23 (only) at age 65 years
  - Immunocompromised excluded from this model
    - (Keep vaccine recommendation from 2012)

See https://www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf for a full description of current recommendations

Methods: Time Frame

- Track 65 year olds in 2019 through life expectancy (or until age 100)
- Incorporate disease rates prior to 2014 PCV13 recommendation for adults aged 65 years and older with PCV13
- Project indirect impacts from pediatric PCV13 immunization program ahead through lifetime of cohort
- All outcomes and costs discounted by 3%
- All costs in 2017$

Methods: Economic Model

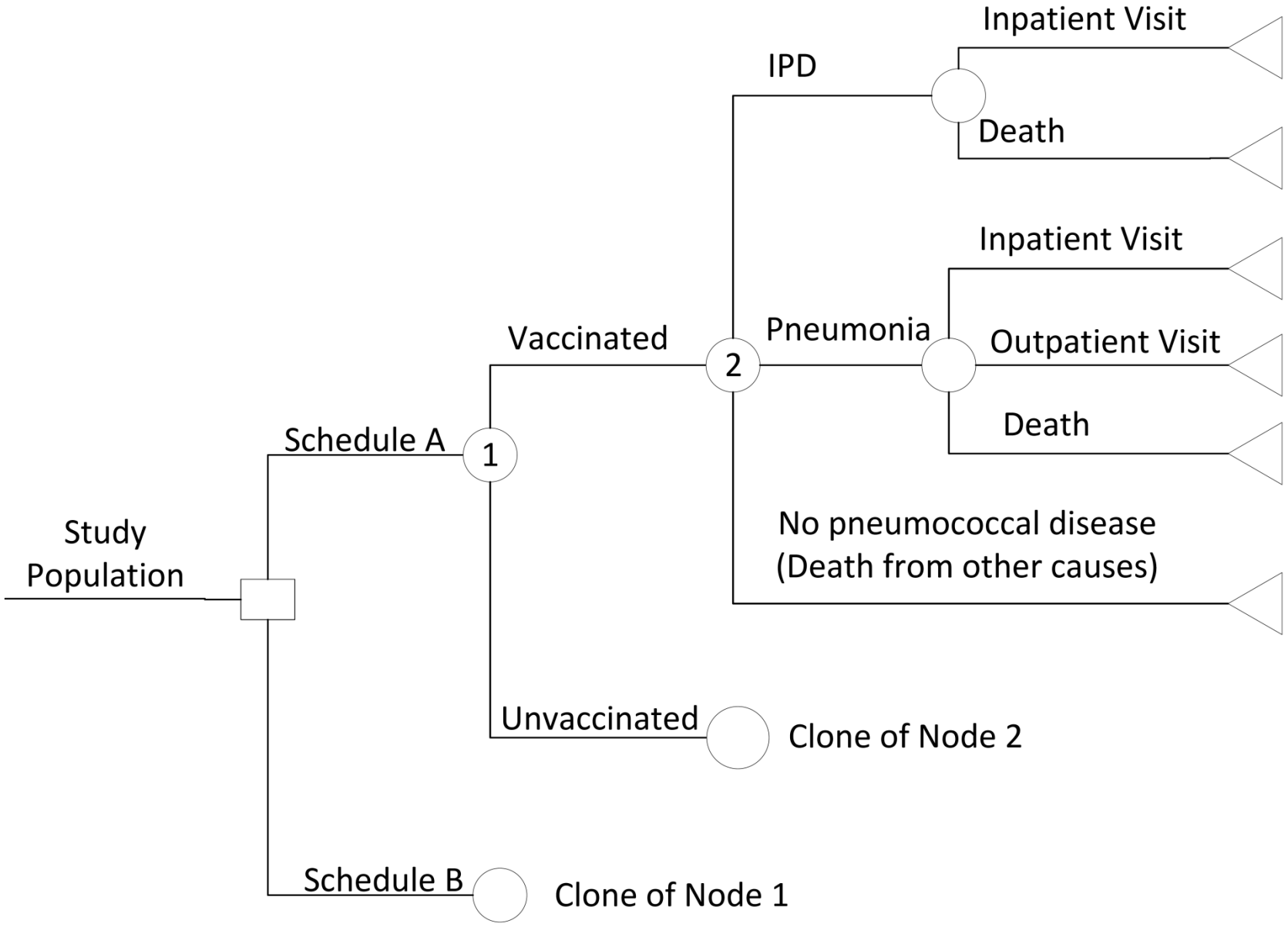
- **Cohort Model**
  - 2,676,090 adults at age 65
  - 43.8% with Chronic Medical Conditions (CMC)*
  - (Excluding immunocompromised)
- **Calculate incremental cost -effectiveness ratio of two recommendations**
  - Divide change in costs by change in QALYs
- **Societal perspective**

* CMC is defined as those with chronic heart disease, chronic lung disease, diabetes mellitus, alcoholism, and chronic liver disease .

Methods: Health Outcomes

- Cases of Invasive Pneumococcal Disease (IPD)
- Cases of inpatient non -invasive pneumococcal pneumonia (henceforth “pneumonia”)
- Cases of outpatient pneumonia
- Deaths due to IPD
- Deaths due to pneumonia
- QALYs
- Life Years

Conceptual Model



Methods: Inputs
IPD Disease Burden

	Healthy 65+	CMC 65+
IPD Rate (per 100,000)	15.38	36.73
% IPD Cases Resulting in Fatality	14.11%	14.80%
%PCV13 (+6C-3-19F)	14.32%	14.67%
% Serotype 3	12.03%	11.20%
% Serotype 19F	2.48%	1.09%
% PPSV23 (not in PCV13)	36.31%	36.61%
% PPSV23 (all)	60.39%	55.33%

Averages of 2013-2014 ABCs data.

Methods: Inputs
Pneumonia Disease Burden

	Age 65-74		Age 75-84		Age 85+	
	base	95% ci	base	95% ci	base	95% ci
Inpatient All-Cause Pneumonia Rate (per 100,000), Healthy[c]	402.50	(262.4, 542.6)	739.15	(684.4, 793.9)	1053.5	(684.4, 1422.6)
Inpatient All-Cause Pneumonia Rate (per 100,000), CMC[c]	1216.10	(792.8, 1639.4)	2233.20	(2067.7, 2398.7)	3182.9	(2067.7, 4298.1)
% All-Cause Pneumonia Cases Resulting in Fatality[d]	3.9	(3.8, 4.1)	3.9	(3.8, 4.1)	3.9	(3.8, 4.1)
Outpatient All-Cause Pneumonia Rate (per 100,000), Healthy[e]	443		724		1048	
Outpatient All-Cause Pneumonia Rate (per 100,000), CMC[e]	1338		2187		3166	
% All-Cause Pneumonia due to PCV13 types[f]	5.1	(3.4, 6.8)	5.1	(3.4, 6.8)	5.1	(3.4, 6.8)

[c] The lower bound of All-Cause Pneumonia disease burden comes from Jain et al. 2015. The upper bounds come from Ramirez et al. These bounds were then split into healthy and CMC specific rates using the ratio of disease in these two groups from Weycker et al. 2016 weighted by the prevalence of the healthy and CMC populations from NHIS data. To obtain the base case we take the midpoint between the upper bound and lower bound.

[d] Source: National Inpatient Sample 2014.

[e] Source: Nelson et al. 2008

[f] Source: Pfizer Inc. Study B1851147 (Oct 2013-Sept 2014), lower bound from Oct 2015-Sept 2016), upper bound created to be symmetrical

Methods: Inputs
Vaccine Effectiveness

Vaccine	Disease	Rate (95% CI)	Source
PCV13	PCV13-type IPD	67 (11, 88)	Pilishvili et al. ISPPD2018 abstract
PCV13	ST3 IPD	0 (0, 26)	Pilishvili et al. ISPPD2018 abstract
PCV13	PCV13-type (except ST3) pneumonia, healthy	41.1 (12.7, 60.7)	Bonten NEJM 2015 (CAPITA)
PCV13	PCV13-type (except ST3) pneumonia, CMC	32.5 (3.9, 53)	Suaya Vaccine 2018
PCV13	ST3 pneumonia	0 (0, 45)	Adapted from ISPPD2018 abstract & Bonten NEJM 2015 (CAPITA)
PPSV23	PPSV23-type IPD	67 (37, 73)	Falkenhorst et al. 2017
PPSV23	PPSV23-type pneumonia	0 (0, 50)	Schiffner-Rohe 2016, Falkenhorst 2017, Tin Tin Htar 2017

Original PCV13 serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F
We include 6C and exclude 3 as "VT" for this study:
VT: 1, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 6C

Methods: Inputs
Indirect Effects from PCV13 in Children

- 4.1% (95% CI = 0, 7%) reduction in serotype disease per year
  - Serotypes: 1, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 23F, 6C
  - Applies to both pneumonia and IPD
  - Results from the direct vs indirect effects model presented to ACIP
- We assume no further indirect (herd) effects on serotypes 19F and 3

Methods: Inputs
Coverage Rate

Vaccine	Coverage	Source
PPSV23	61.3% (59.9%, 62.7%)	NHIS 2014 (MMWR 2016)
PCV13	40% (39.6, 41%)	Lower bound: CMS Coverage data Upper bound: Pfizer IMS Claims data (Sept 2017) Midpoint by calculation

Methods: Inputs
Vaccine Cost ($)

Variable	Price	Source
PCV13	$192.637	95% AWP; Medicare Part B (Dec 2017)
PPSV23	$98.849	95% AWP; Medicare Part B (Dec 2017)
Vaccine Administration	$26.61	Medicare Reimbursement Rate
Travel+ time cost	$30.12	Maciosek et al 2006 Am J Prev Med

Methods: Inputs
Disease Cost (2017$)

	base	95% CI
IPD	20,842	(20,673, 21,020)
Inpatient (IPT) Pneumonia	11,258	(11,232, 11,288)
Outpatient (OPT) Pneumonia	275	(274, 276)

Source: Medicare Claims, 2010-2015, inflated to 2017 with Consumer Price Index.

Methods: Inputs
Utility Decrements

Variable	QALYs	Healthy Life Lost (Days)	Implied Average Duration of Illness (Days)	Source
IPD	0.008665	3.2	21	Melagaro & Edmunds 2004 Vaccine
IPT Pneumonia	0.006	2.2	15	Melagaro & Edmunds 2004 Vaccine
OPT Pneumonia	0.004	1.5	15	Melagaro & Edmunds 2004 Vaccine

Implied duration of illness based off of an IPD or IPT pneumonia day being 85% of a healthy day, and an OPT pneumonia day being 90% of a healthy day (Vold et al 2000 Clin Infect Dis)

Methods: Inputs
Alternate Larger Utility Decrements

Variable	QALYs	Healthy Life Lost (Days)	Implied Average Duration of Illness (Days)	Source
IPD	0.074521	27.2	181	Sisk et al 2003 Ann Intern Med
IPT Pneumonia	0.051601	18.8	125	Taking ratio of IPT Pneumonia to IPD in Melagaro and applying to Sisk
OPT Pneumonia	0.034401	12.6	125	Taking ratio of OPT Pneumonia to IPD in Melagaro and applying to Sisk

Implied duration of illness based off of an IPD or IPT pneumonia day being 85% of a healthy day, and an OPT pneumonia day being 90% of a healthy day (Vold et al 2000 Clin Infect Dis)

Waning Immunity Assumptions

- PCV13
  - Scenario 1:
    - Linear decline to zero between 70 and 85
  - Scenario 2:
    - 10% every 5 years starting at age 65
    - Linear declines within 5 year increments
- PPSV23
  - 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

Base Case Table

	Base Case	95% CI
Health Outcomes		
IPD Cases	-82	(-104, -57)
Inpatient Pneumonia Cases	-1,772	(-3,148, -343)
Outpatient Pneumonia Cases	-1,907	(-3,286, -374)
Deaths due to IPD	-11	(-14, -8)
Deaths due to Pneumonia	-69	(-122, -13)
QALYs	618	(214, 1,392)
Life-years	986	(273, 1,598)
Costs (million $)		
Total Cost	$401	($385, $419)
Medical Costs	-$22	(-$38, -$6)
Vaccine Costs	$423	($419, $428)
Cost Ratios ($)		
Cost/QALY	648,845	(277,338, 1,951,526)
Cost/Life-year	406,521	(241,096, 1,529,489)

Sensitivity Analyses

- **PPSV vs Pneumonia**
  - Base: 0%
  - Sensitivity: 45%
- **PCV vs ST3 Disease**
  - Base: 0% vs IPD & 0% vs pneumonia
  - Sensitivity 26% vs IPD & 45% vs pneumonia
- **Large QALY Decrements**
  - Base: IPD = 0.009 (3 days of perfect health)
    IPT Pneumonia = 0.006 (2 days)
    OPT Pneumonia = 0.004 (1 day)
  - Sensitivity: IPD = 0.075 (27 days of perfect health)
    IPT Pneumonia = 0.052 (19 days)
    OPT Pneumonia = 0.034 (13 days)
- **Slow PCV13 Waning**
  - Base: Linear decline to zero between 70-85
  - Sensitivity: 10% every 5 years

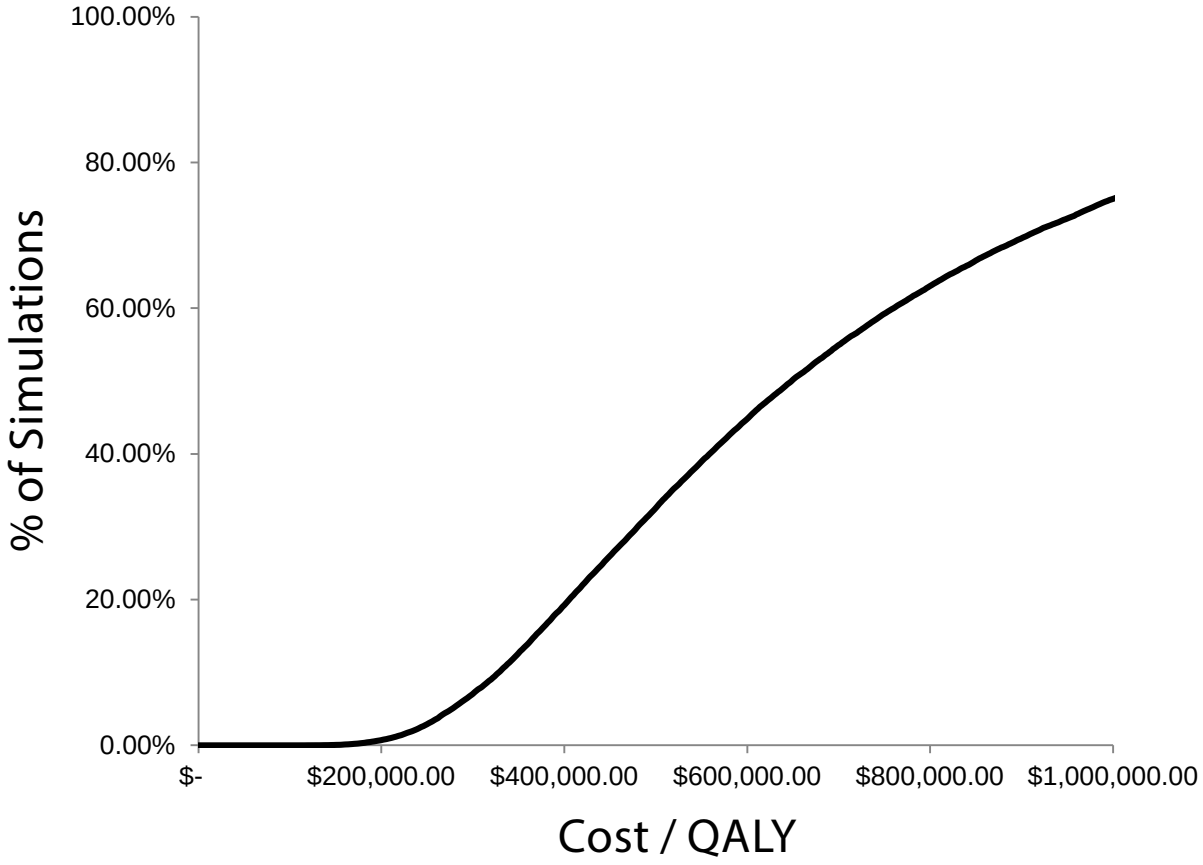
One-way Sensitivity Analyses

	Base Case	PPSV vs Pneumonia 45%	PCV vs ST3: 26% vs IPD 45% vs pneumonia
Health Outcomes			
IPD Cases	-82	-82	-90
Inpatient Pneumonia Cases	-1,772	-180	-4,754
Outpatient Pneumonia Cases	-1,907	-181	-5,066
Deaths due to IPD	-11	-11	-12
Deaths due to Pneumonia	-69	-7	-183
QALYs	618	111	1,462
Life-years	986	187	2,364
Costs (million $)			
Total Cost	$401	$419	$366
Medical Costs	-$22	-$4	-$57
Vaccine Costs	$423	$423	$423
Cost Ratios ($)			
Cost/QALY	648,845	3,776,021	250,655
Cost/Life-year	406,521	2,242,347	154,971

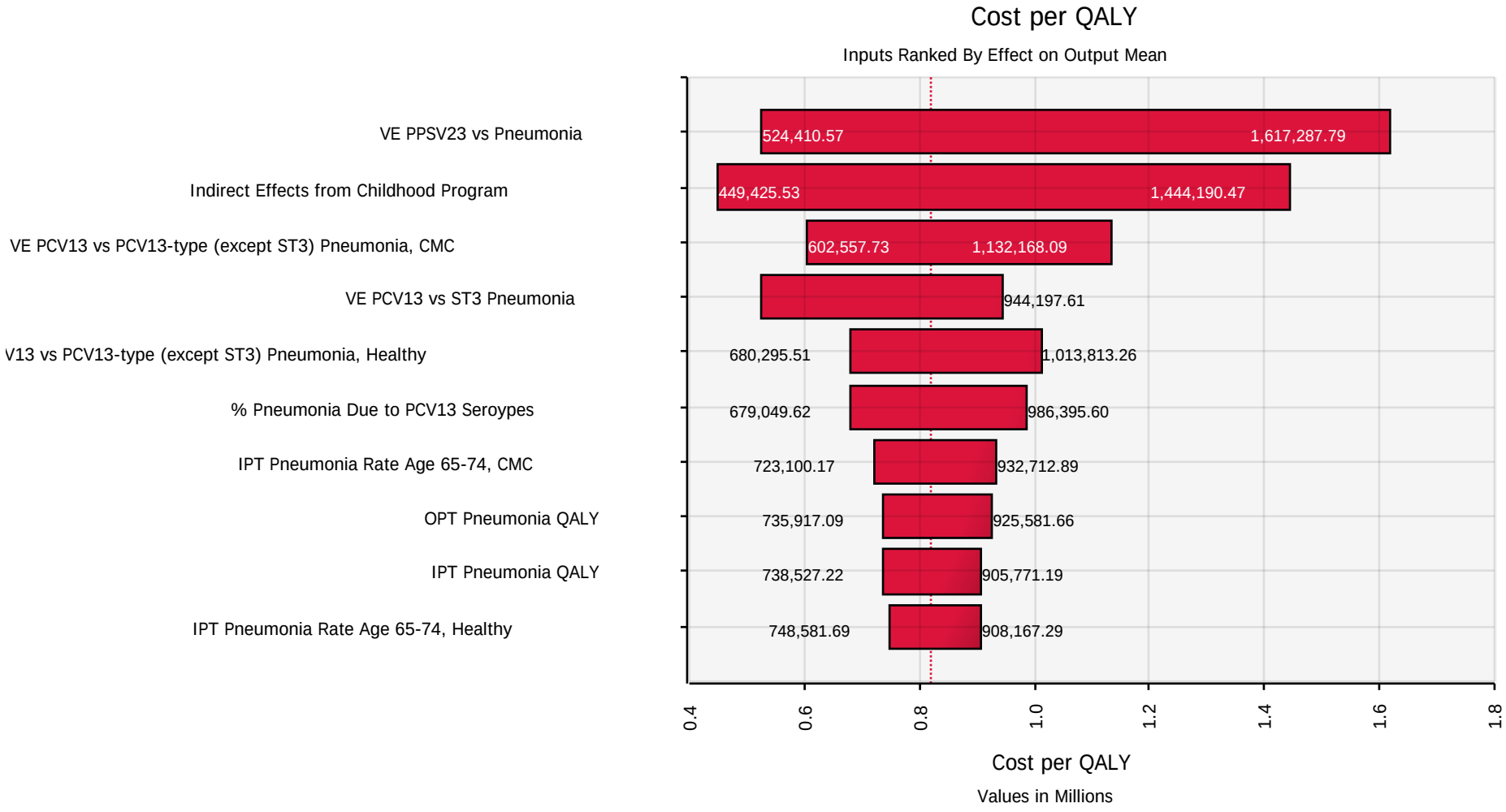
One-way Sensitivity Analyses

	Base Case	Large QALY Decrements	Slow PCV13 Waning
Health Outcomes			
IPD Cases	-82	-82	-176
Inpatient Pneumonia Cases	-1,772	-1,772	-2,022
Outpatient Pneumonia Cases	-1,907	-1,907	-2,148
Deaths due to IPD	-11	-11	-23
Deaths due to Pneumonia	-69	-69	-78
QALYs	618	707	698
Life-years	986	986	1,137
Costs (million $)			
Total Cost	$401	$401	$396
Medical Costs	-$22	-$22	-$27
Vaccine Costs	$423	$423	$423
Cost Ratios ($)			
Cost/QALY	648,845	567,511	567,962
Cost/Life-year	406,521	406,521	348,515

Vaccine Schedule Acceptability Curve



Tornado Diagram



Comparisons between 2018 and 2014 Analyses

- **2014 Analysis (converted to 2017$)**
  - $64,880 / QALY in 2014
  - Projected $286,855 / QALY in 2019
- **2018 Analysis (2017$)**
  - $648,845 / QALY in 2019
- **Chief assumption differences in 2018 study**
  - Indirect effects half the size
  - PCV13 assumed ineffective against ST3 (in the base case)
  - % of PCV13-type pneumonia disease half the size
  - Decompose pneumonia burden by risk status

Source: Medicare Claims, 2010-2015.

Thank you!

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