Supplementary Material

Cost-Effectiveness Analysis of the Use of V116, a 21-Valent Pneumococcal Conjugate Vaccine, in Vaccine-Naïve Adults Aged ≥65 Years in the United States

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1. Demographic Inputs

Population Size and Mortality

Estimates of population size by single year of age representing the most recent year (2022) was obtained from the US census Bureau [1]. However, due to the impact of COVID on mortality rates, pre-COVID estimates (2019) of mortality rates obtained from National Vital Statistics Reports [2] were used. The estimates are presented in Table 1 below.

Table 1. Single Age Population Size and Annual Mortality Rate

Age	Population Size [1]	Mortality [2]	Age	Population Size [1]	Mortality [2]
19	4,295,710	0.000657	60	4,327,473	0.009090
20	4,438,006	0.000748	61	4,313,536	0.009808
21	4,723,644	0.000839	62	4,231,279	0.010518
22	4,663,473	0.000917	63	4,144,198	0.011202
23	4,483,807	0.000976	64	4,101,937	0.011890
24	4,396,849	0.001020	65	4,020,640	0.012621
25	4,346,308	0.001057	66	3,833,262	0.013499
26	4,351,553	0.001097	67	3,737,326	0.014468
27	4,419,629	0.001139	68	3,598,472	0.015571
28	4,503,844	0.001190	69	3,441,722	0.016804
29	4,571,830	0.001248	70	3,305,273	0.018143
30	4,672,812	0.001309	71	3,141,497	0.019683
31	4,739,263	0.001371	72	2,988,811	0.021193
32	4,751,526	0.001436	73	2,898,395	0.023529
33	4,614,523	0.001500	74	2,823,041	0.025583
34	4,530,012	0.001564	75	2,959,404	0.028288
35	4,476,550	0.001636	76	2,083,434	0.030996
36	4,483,170	0.001711	77	1,986,144	0.034485
37	4,478,749	0.001782	78	1,915,774	0.038071
38	4,383,099	0.001847	79	1,916,244	0.042153
39	4,446,381	0.001912	80	1,623,833	0.046589
40	4,438,786	0.001990	81	1,441,506	0.051588
41	4,375,219	0.002087	82	1,303,339	0.057742
42	4,356,125	0.002205	83	1,193,273	0.064540
43	4,175,926	0.002344	84	1,097,594	0.071641
44	4,081,360	0.002501	85	962,356	0.080529
45	4,029,138	0.002679	86	870,823	0.089744
46	3,891,868	0.002877	87	798,679	0.100480
47	3,935,451	0.003094	88	672,727	0.112250
48	3,859,402	0.003334	89	601,746	0.125094
49	3,908,239	0.003608	90	524,576	0.139038
50	4,094,089	0.003904	91	450,431	0.154096
51	4,334,593	0.004238	92	380,133	0.170257
52	4,265,282	0.004639	93	304,906	0.187494
53	4,102,135	0.005107	94	248,895	0.205752
54	4,011,448	0.005615	95	194,667	0.224954
55	4,021,403	0.006123	96	145,421	0.244995
56	4,075,771	0.006630	97	109,622	0.265747
57	4,228,510	0.007167	98	78,028	0.287060
58	4,322,714	0.007754	99	53,870	0.308767
59	4,318,616	0.008394	100+	88,988	1.000000

Risk Categories

The study population was stratified into three mutually exclusive risk groups—low-risk (LR), at-risk (AR), and high-risk (HR) adults based on the age group specific proportions and classifications reported by Pelton et al., 2019 [3] (see Table **2**).

Additionally, since there are no reported single age cohort risk distributions for the entire US population, a mathematical intra/interpolation algorithm was used to derive risk group transition probabilities for each age (Table **3**), and therefore the single age cohort risk distributions (Table **4**) based on the estimated multi-cohort (age-band) risk distributions reported by Pelton, 2019 [3]. For the purpose of this analysis, in this algorithm, the low-end age was assumed to have the reported distribution.

Table 2: Initial Split of Risk Groups by Age Groups

Age Group	LR	AR	HR
18-49	0.873	0.104	0.023
50-64	0.692	0.234	0.074
65-74	0.491	0.362	0.147
75+	0.353	0.425	0.222

LR = low risk; AR = at risk; HR = high risk
Source: Pelton et al. 2019 [3].

Table 3: Annual Transition Probability among Risk Groups

Age Group	LR to AR	LR to HR	AR to HR
18-49	0.005577	0.001645	0.001790
50-64	0.015194	0.007252	0.001790
65+	0.016198	0.015664	0.001790

LR = low risk; AR = at risk; HR = high risk
Source: Derived using risk distribution values from Pelton et.al. 2019 [3].

Table 4. Estimated Single Age Risk Distributions

Age	Low-risk	At-risk	High-Risk	Age	Low-risk	At-risk	High-Risk
18	**0.873**	**0.104**	**0.023**	61	0.538	0.333	0.129
19	0.867	0.109	0.025	62	0.526	0.340	0.134
20	0.860	0.113	0.026	63	0.514	0.348	0.138
21	0.854	0.118	0.028	64	0.502	0.355	0.143
22	0.848	0.122	0.029	**65**	**0.491**	**0.362**	**0.147**
23	0.842	0.127	0.031	66	0.475	0.369	0.155
24	0.836	0.131	0.033	67	0.460	0.377	0.164
25	0.830	0.136	0.034	68	0.445	0.383	0.172
26	0.824	0.140	0.036	69	0.431	0.390	0.179
27	0.818	0.145	0.038	70	0.417	0.396	0.187
28	0.812	0.149	0.039	71	0.403	0.403	0.194
29	0.806	0.153	0.041	72	0.390	0.408	0.202
30	0.800	0.157	0.042	73	0.377	0.414	0.209
31	0.794	0.162	0.044	74	0.365	0.420	0.215
32	0.789	0.166	0.046	**75**	**0.353**	**0.425**	**0.222**
33	0.783	0.170	0.047	76	0.341	0.430	0.228
34	0.777	0.174	0.049	77	0.330	0.435	0.235
35	0.772	0.178	0.050	78	0.319	0.440	0.241
36	0.766	0.182	0.052	79	0.309	0.444	0.247

37	0.761	0.186	0.054	80	0.298	0.449	0.253
38	0.755	0.190	0.055	81	0.288	0.453	0.259
39	0.750	0.194	0.057	82	0.279	0.457	0.264
40	0.744	0.198	0.058	83	0.269	0.461	0.270
41	0.739	0.201	0.060	84	0.260	0.465	0.275
42	0.733	0.205	0.061	85	0.251	0.468	0.280
43	0.728	0.209	0.063	86	0.242	0.472	0.286
Age	**Low-risk**	**At-risk**	**High-Risk**	**Age**	**Low-risk**	**At-risk**	**High-Risk**
44	0.723	0.213	0.065	87	0.234	0.475	0.291
45	0.718	0.216	0.066	88	0.226	0.479	0.296
46	0.712	0.220	0.068	89	0.218	0.482	0.301
47	0.707	0.223	0.069	90	0.210	0.485	0.306
48	0.702	0.227	0.071	91	0.202	0.488	0.310
49	0.697	0.231	0.072	92	0.194	0.491	0.315
50	**0.692**	**0.234**	**0.074**	93	0.187	0.493	0.320
51	0.676	0.244	0.079	94	0.179	0.496	0.325
52	0.661	0.254	0.085	95	0.172	0.498	0.329
53	0.646	0.264	0.090	96	0.165	0.501	0.334
54	0.632	0.273	0.095	97	0.158	0.503	0.339
55	0.617	0.282	0.100	98	0.151	0.506	0.343
56	0.603	0.291	0.105	99	0.144	0.508	0.348
57	0.590	0.300	0.110	100	0.138	0.510	0.353
58	0.576	0.308	0.115				
59	0.563	0.317	0.120				
60	0.551	0.325	0.125				

2. Epidemiological Inputs

IPD Incidence

IPD incidence was calculated as a 3-year (2017-2019) aggregated estimate—sum of cases divided by the sum of resident population over the 3-year period. The annual IPD incidence estimates were obtained from the Active Bacterial Core surveillance reports [46]. However, because the risk-specific estimates are not available, they were calculated by using the derived formulars shown below:

$$i_1 = \frac{I \cdot ri_{11}}{d_1 \cdot ri_{11} + d_2 \cdot ri_{21} + d_3 \cdot ri_{31}},\ i_2 = \frac{I \cdot ri_{21}}{d_1 \cdot ri_{11} + d_2 \cdot ri_{21} + d_3 \cdot ri_{31}},\ i_3 = \frac{I \cdot ri_{31}}{d_1 \cdot ri_{11} + d_2 \cdot ri_{21} + d_3 \cdot ri_{31}}$$

where I is the overall 3-year incidence, i_1, i_2 and i_3 are the incidence for subgroups 1 through 3 representing the risk-based subgroups (1 for LR; 2 for AR and 3 for HR using Pelton et al's 2019 [3] risk classification); d_1, d_2 and d_3 are the risk group's proportion and ri_{11}, ri_{21} and ri_{31} is the relative incidence with respect to risk group 1 (LR) [implies that $r_{11} = 1$]. The risk ratio or relative incidence were calculated from the risk-specific estimates for 2017-2018 presented by Charles Stoecker [5, 7], assuming that the relative risks were the same (Table **5**). The resulting risk specific estimates are presented in Table 6, and are what was used in this study.

Table 5: 2017-2018 IPD Incidence by Risk Group

Age Group	Incidence (per 100,000 person-years)		
	LR	**AR**	**HR**
19 - 49	2.09	8.09	16.22
50 - 64	6.09	24.04	37.28
65 - 74	8.25	25.89	35.10
75 - 100	19.27	40.06	39.47

LR = low risk; AR = at risk; HR = high risk; IPD = invasive pneumococcal disease Source: ACIP 2021 Presentation by Charles Stoecker [5, 7]).

Table 6. 2017-2019 IPD Incidence by Risk Category

Age Group	Overall	LR	AR	HR
19 - 34	2.5	1.74	6.74	13.51
35 - 49	6.7	4.61	17.84	35.77
50 - 64	16.3	7.86	31.04	48.14

65 - 74	20.3	9.01	28.27	38.33
75 - 84	26.6	15.73	32.70	32.21
85 -100	39.4	23.31	48.46	47.74

LR = low risk; AR = at risk; HR = high risk; IPD = invasive pneumococcal disease
Source: calculated

IPD Case Fatality Rate

IPD case fatality rate and percent meningitis were obtained using the same 3-year aggregated estimate approach—summing up the cases and the corresponding year's denominators for 2017 through 2019 from the ABCs reports [4-6]. The 3-year estimates are presented in Table **7** below.

Table 7: IPD Case Fatality Rate and Percent Meningitis

Age Group	IPD case fatality rate	Percent Meningitis
19 - 34	0.04878	7.04%
35 - 49	0.07906	7.04%
50 - 64	0.11101	7.03%
65 - 74	0.12614	7.03%
75 - 84	0.11835	7.03%
85 -100	0.21522	7.03%

IPD = invasive pneumococcal disease

Outpatient and Inpatient NBPP Incidence

The incidence for outpatient NBPP were obtained from Tong et al., 2018 and adjusted as follows: The overall outpatient incidence rate for those aged 18-49 was calculated by applying the proportion of *S. pneumoniae* (Sp) in community-acquired pneumonia (11% [8]) and the proportion of the pneumonia cases that were outpatient (69.4% [9]) for those aged 18-49 from Tong et al., 2018 [9] (i.e., 51.9 = 680 x 0.694 x 0.11). Then, they were adjusted to obtain risk-specific incidence by using the derived formula presented in the preceding section. To do so, the relative risk ratios and respective risk group proportions for all-cause pneumonia from Pelton et al., 2019 [3] were assumed to be the same as those for outpatient NBPP. As an example, using the overall incidence of 51.9, the incidence for 18-49 LR was calculated as:

$$\frac{51.91}{873 + 0.104 \text{ x } 5.8 + 0.023 \text{ x } 19.7} \quad 0. \qquad = 26.91$$

The resulting incidences for all age/risk groups are presented in Table **8**.

Table 8: Outpatient NBPP Incidence by Risk Group

Age Group	Annual Incidence (per 100,000 person-years)		
	LR	AR	HR
19–49	26.91	156.06	530.06
50–64	34.33	168.20	477.14
65–74	43.23	211.81	479.81
75–84	133.78	387.96	561.87
85–100	227.30	659.17	954.66

LR = low risk; AR = at risk; HR = high risk
Source: Adjusted using data from Tong et al. 2018 [9] and Pelton et al. 2019 [3].

The inpatient NBPP incidence were obtained by applying the proportion of *S. pneumo* (11% [8]) to the hospitalized all-cause pneumonia cases reported by Pelton et al., 2019 [3]. The resulting incidence rates are presented in Table **9**.

Table 9: Inpatient NBPP Incidence by Risk Group

	Annual Incidence (per 100,000 person-years)		
Age Group	**LR**	**AR**	**HR**
19–49	3.85	22.77	77.11
50–64	9.68	47.19	134.86
65–74	21.01	103.51	233.64
75–100	105.27	301.95	439.12

LR = low risk; AR = at risk; HR = high risk
Source: Adjusted using data from Pelton et al. 2019 [3].

Inpatient NBPP Case Fatality Rate

Inpatient NBPP fatality rate was obtained from ACIP presentation in 2022 [10] and presented in Table **10** below.

Table 10: Inpatient NBPP Fatality Rate

Age Group	Fatality Rate
16–49	0.0160
50–64	0.0280
65–74	0.0350
75–84	0.0410
85–100	0.0530

NBPP = non-bacteremic pneumococcal pneumonia

Post-Meningitis Sequelae (PMS)

PMS included two specific sequalae—neurological disorder and hearing loss. The percentage of neurological disorder and hearing loss resulting from meningitis cases were 13% and 7%, respectively (Rubin et al., 2010 [11]).

IPD and NBPP Serotype Distribution

The serotype distribution data for IPD were obtained from the ABCs publicly available IPD serotype data [12]. For consistency, the same 3-year (2017-2019) aggregate estimate approach was adopted using a—sum of the serotype counts for both the numerators and denominators across the 3 years.

The serotype distribution for NBPP were estimated using data from our company's Pneumococcal pNeumonia, Mental Outcomes, Epidemiology and Urine serotyping (PNEUMO) US study [13]. The PNEUMO study uses our proprietary serotype specific urinary antigen detection (SSUAD) assays to detect the serotype prevalence. The assays detected the serotypes included in PCV15 and V116 for a total of 30 serotypes. The assays do not detect certain vaccine type (VT) serotypes (15B and 2), and do not identify non-vaccine types (NVT).

Because the aim was to determine the serotype distribution for non-invasive pneumococcal pneumonia, the culture positives from the PNEUMO Study could not be used since they were primarily blood cultures and classified as invasive cases. In addition, although the PNEUMO Study did include sputum cultures (which if positive, were classified as non-invasive), there were very few sputum cultures available from the study participants. For these reasons, the data from Isturiz et al., 2021 [14] were used to estimate the proportion of *S. pneumoniae* samples that were positive by culture diagnosis "only" (n=68; assuming the same proportion) to further inform the estimates of the serotype distribution in non-invasive pneumonia.

The details used in determining the serotype distribution for NBPP are outlined in the following step:

1. Estimating the prevalence of the three missing serotypes (15B and 2)
    a. Isturiz et al., 2021 [14] was used to estimate the expected counts of the three serotypes in the SSUAD study. Where two serotypes were reported for a particular serogroup, they were split evenly. For example, there were 7 counts reported for 15B/C among the 18-64 years age group in Isturiz et al., 2021 [14]. It was assumed that 15B and 15C accounted for a count of 3.5 each. A similar approach was applied to 6A/C.
    b. After estimating the expected counts for 15B and 2, they were then included to provide the total number of all VT serotypes in the PNEUMO study.

2. Estimating the number of *S. pneumoniae* cases in the SSUAD data
    a. *S. pneumoniae* cases (included those with VT and NVT etiology) were identified as the SSUAD+ and/or BINAX+ cases, as well as the expected SSUAD culture+ assuming the same positivity from Isturiz et al., 2021 [14] as described above.
    b. The total number of serotype counts that were attributable to *S. pneumoniae* cases were subsequently estimated by adjusting the number of *S. pneumoniae* subjects (cases) by a factor (>1). The factor derived from the SSUAD study is the average number of STs detected per subject/case.
    c. Finally, the distribution of serotypes was estimated using the ratio of individual serotype counts attributable to *S. pneumoniae* and the total serotype counts attributable to *S. pneumoniae*.

The estimated serotype distributions for IPD and NBPP used in the model are presented in the Table 11 below.

Table 11: IPD and NBPP Serotype Distribution

	IPD (2017-2019 [12])	NBPP (Adjusted SSUAD Data)

Serotype	18-49	50-64	65+	18-49	50-64	65+
ST 1	0.12%	0.00%	0.00%	0.00%	0.61%	3.95%
ST 3	12.02%	15.46%	16.33%	9.34%	12.86%	10.53%
ST 4	7.23%	3.24%	0.73%	0.00%	1.23%	0.66%
ST 5	0.00%	0.03%	0.00%	2.08%	1.23%	1.98%
ST 6A	0.06%	0.14%	0.15%	1.04%	0.31%	2.30%
ST 6C	2.60%	2.15%	3.26%	1.04%	0.31%	2.30%
ST 6B	0.06%	0.20%	0.21%	0.00%	1.23%	0.66%
ST 7F	1.97%	1.54%	0.53%	1.04%	2.45%	3.95%
ST 8	6.99%	5.22%	3.05%	3.11%	1.84%	3.29%
ST 9V	0.12%	0.31%	0.09%	3.11%	0.61%	1.32%
ST 10A	2.14%	1.88%	1.59%	0.00%	0.00%	0.66%
ST 11A	3.18%	4.03%	4.32%	2.08%	4.29%	3.95%
ST 12F	5.38%	4.71%	2.03%	1.04%	0.00%	0.00%
ST 14	0.06%	0.07%	0.21%	0.00%	0.61%	0.00%
ST 15B	1.21%	1.06%	1.79%	0.54%	0.36%	0.86%
ST 15C	0.87%	0.92%	1.35%	2.08%	0.61%	1.98%
ST 18C	0.00%	0.07%	0.03%	0.00%	0.00%	0.00%
ST 19A	3.18%	3.28%	2.58%	8.31%	4.90%	3.95%
ST 19F	3.29%	2.87%	2.67%	1.04%	5.51%	4.61%
ST 22F	9.13%	9.76%	10.16%	7.27%	9.80%	5.27%
ST 23F	0.00%	0.03%	0.03%	0.00%	0.00%	0.00%
ST 33F	3.47%	3.11%	4.35%	1.04%	1.23%	0.66%
ST 2	0.00%	0.00%	0.00%	0.00%	0.00%	0.34%
ST 9N	8.21%	6.96%	4.29%	6.23%	5.51%	1.98%
ST 17F	1.45%	1.37%	1.94%	3.11%	1.84%	3.29%
ST 20	4.68%	4.33%	2.32%	3.11%	2.45%	1.32%
ST 15A	2.66%	4.03%	5.81%	0.00%	3.06%	0.00%
ST 16F	2.66%	3.69%	4.52%	2.08%	0.61%	3.95%
ST 23A	3.93%	4.33%	5.79%	4.15%	2.45%	5.27%
ST 23B	3.41%	3.14%	2.79%	6.23%	2.45%	1.98%
ST 24F	0.06%	0.07%	0.21%	1.04%	1.23%	0.00%
ST 31	1.39%	1.88%	3.08%	0.00%	4.29%	2.63%
ST 35B	2.77%	3.41%	6.28%	7.27%	3.68%	3.95%
ST NVT	5.72%	6.72%	7.52%	22.63%	22.46%	22.42%

ST = serotype; SSUAD = Serotype-specific urinary antigen assay; IPD = invasive pneumococcal disease; NBPP = non-bacteremic pneumococcal pneumonia; NVT = non-vaccine type

3. Vaccine Effectiveness

The VEs and associated waning functions are presented in Table **12** and Figure 1, respectively below.

Table 12: Vaccine Effectiveness

Disease	PCVs	PPSV23
Against IPD (Except ST3)	LR/AR: 75% (41.4%, 90.8%)[1] HR: 25.0% (13.8%, 30.3%)[2]	LR/AR: 59.7% (47.4%, 69.1%)[3] HR: 7.9% (0%, 34.2%)[3]
Against IPD (ST3 Only)	LR/AR: 26% (0%, 53.4%)[1] HR: 8.7% (0%, 17.8%)[2]	
Against NBPP (Except ST3)	LR: 66.7% (11.8%. 89.3%)[4] AR: 40.3% (11.4%, 60.2%)[4] HR: 15.0% (4.7%, 21.8%)[2]	LR/AR: 20% (0%, 40%)[5] HR: 6.7% (0%, 13.3%)[2]
Against NBPP (ST3 Only)	LR/AR: 15.6% (0%, 32.0%) HR: 5.2% (0%, 10.7%)[2]	

AR = at risk; IPD = invasive pneumococcal disease; LR = low risk; HR = high risk; NBPP = non-bacteremic pneumococcal pneumonia; PCV = pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine; ST = serotype

Source: Stoecker et al., 2021 [32] with adjustments based on:
1. Bonten et al. 2015 [15].
2. Assumed 1/3 of healthy/CMC adults, Cho et al. Vaccine 2013 [16].
3. Meta-analysis of Andrews 2012 [17], Rudnick 2013 [18], and Djennad 2018 [19] restricting to PPSV23 VE within 5 years of Vaccination 4. Suaya et al. Vaccine 2018 [20].
5. Lawrence et al. PLoS Med 2020 [21].

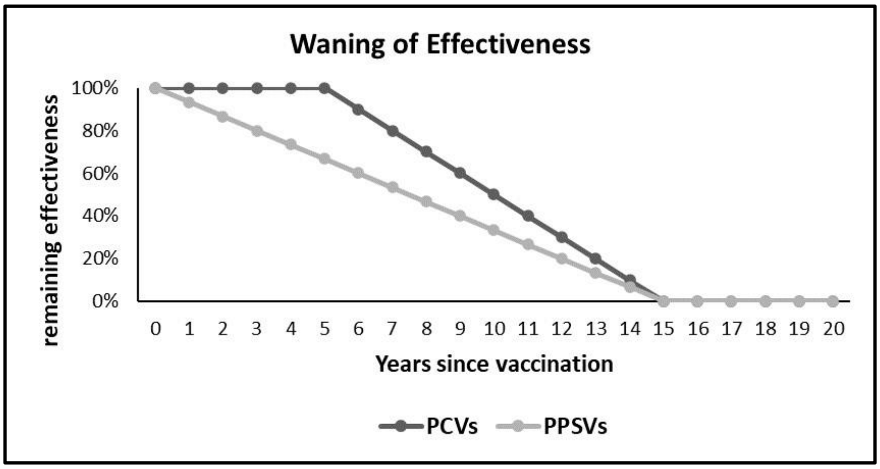

Figure 1: Waning of Effectiveness for Single Vaccine Strategy

PCV = pneumococcal conjugate vaccine; PPSV = pneumococcal polysaccharide vaccine. Source: Based on data from Bonten et al., 2015 [22].

4. Direct Costs

All costs were adjusted to reflect July 2023 US dollars, except vaccine acquisition costs.

Vaccine Acquisition and Administration Costs

Vaccine acquisition costs are the costs of acquiring the vaccine. Vaccine administration cost includes the associated materials and time needed to administer vaccine. Vaccine acquisition and administration costs are presented in Table **13** and Table **14**.

Table 13: Vaccine Acquisition Costs ($)

Vaccine	Acquisition cost	Source
PPSV23	117.08	Merck & Co., Inc., Rahway, NJ, USA
PCV15	221.80	Merck & Co., Inc., Rahway, NJ, USA
PCV20	260.81	Pfizer [23]
V116	287.75	Merck & Co., Inc., Rahway, NJ, USA

Table 14: Vaccine Administration Costs ($)

Age Group	Administration cost
19-49	30.52
50-64	30.52
65+	24.70

Source: Stoecker et al., 2021 [7].

Direct Treatment Costs

Direct treatment costs for IPD and NBPP are presented in Table **15** and Table **16** below.

Table 15: Direct Treatment Cost per IPD Case by Risk Group ($)

Age category	LR	AR	HR
19-49	59,953	56,023	94,966
50-64	57,996	51,678	127,220
65+	28,650	26,905	37,168

IPD = invasive pneumococcal disease. LR = low risk; AR = at risk; HR = high risk. Source: Stoecker et al., 2021 [7].

Table 16: Direct Treatment Cost per NBPP Case by Risk Group ($)

Age category	Inpatient NBPP			Outpatient NBPP		
	LR	AR	HR	LR	AR	HR
19-49	25,956	32,739	41,502	811	1,086	1,264
50-64	27,700	30,393	38,034	742	917	1,112

65+	19,561	16,959	23,474	659	615	987

NBPP = non-bacteremic pneumococcal disease; LR = low risk; AR = at risk; HR = high risk. Source:
Stoecker et al., 2021 [7].

Because PMS is a long-term condition, annualized costs were used (Table **17**) and were applied each year before death or end of the time horizon. In other words, individuals in the "post-meningitis sequelae" health state incur a treatment cost in each year/model cycle until they die or the end of the time horizon whichever comes first. For the default values, age group specific lifetime cost for PMS was obtained from Rubin et al., 2010 and are annualized based on the life expectancy. Table 17: Annual Direct Medical Costs for PMS ($)

Age Group	Neuro Disorder	Hearing Loss	Resulting Annual Direct Cost for PMS
19-34	23,686	4,591	11,274
35-49	22,639	4,388	10,776
50-64	21,660	4,198	10,309
65+	26,349	5,107	12,541

PMS = post-meningitis sequalae. Source:
Rubin et al., 2010 [24].

5. Indirect Costs

Indirect Treatment Costs

The indirect medical costs per case of IPD/NBPP and the annualized indirect medical cost of PMS are presented in Table **18** and Table **19** below. The annual indirect medical cost for PMS were derived the same way as the annual direct cost for PMS explained in section 4.

Table 18: Indirect Medical Costs per IPD and NBPP Case ($)

Age Category	IPD	Inpatient NBPP	Outpatient NBPP
16-34	3,322	2,684	1,277
35-49	1,333	1,076	513
50-64	886	715	341
65+	800	648	308

IPD = invasive pneumococcal disease; NBPP = non-bacteremic pneumococcal pneumonia.
Source: McLaughlin et al., 2015 [25].

Table 19: Annual Indirect Medical Costs for PMS Cases ($)

Age Group	Neuro Disorder	Hearing Loss	Resulting Annual Indirect Cost for PMS
16-34	13,006	0	4,552
35-49	12,431	0	4,351
50-64	11,893	0	4,162
65+	14,468	0	5,064

PMS = post-meningitis sequalae.
Source: Table 3 in Rubin et al., 2010 [24].

Travel Costs per Administration

The estimated patient time and travel cost per vaccination in the amount of $44.55 was obtained from Stoecker 2021 [7] and inflation-adjusted to 2023 US dollars.

Productivity Cost for Disease-Related Death

To account for the cost of PD-related deaths to society, the reported lifetime productivity costs [26] were annualized and used as a proxy (Table **20**). Specifically, based on the individual's age in each model cycle if they were still alive, the corresponding annual productivity is applied to each PD-related death until the end of the model time horizon or until the individual's rest lifetime if he/she didn't die due to the disease, whichever comes first. The default annual productivity is presented in Table **20** and derived using lifetime productivity loss from Grosse 2019 [26] and inflated to 2023.

Table 20: Annual Productivity Cost for Disease Related Death ($)

Age Category	Annual Cost
16-24	23,881
25-34	76,601
35-44	103,053
45-54	98,708
55-64	80,514
65-74	45,596
75-99	18,967

Source: Grosse et al., 2019 [26].

6. Utilities

Baseline Utility Values per Risk Group

The reported base case utility values by risk groups as well as those for PMS are presented in

Table 21 below.

Table 21: Baseline Utility Values per Risk Category

	"No Pneumococcal Disease" Health State			"PMS" Health State		
Age Category	**LR**	**AR**	**HR**	**Neurological disorder**	**Hearing loss**	**Resulting utility for PMS**
16–54	0.830	0.720	0.720	0.680	0.730	0.6975
55–59	0.810	0.690	0.690	0.680	0.730	0.6975
60–64	0.770	0.630	0.630	0.680	0.730	0.6975
65–69	0.760	0.570	0.570	0.680	0.730	0.6975
70–74	0.740	0.540	0.540	0.680	0.730	0.6975
75–79	0.700	0.520	0.520	0.680	0.730	0.6975
80–100	0.630	0.510	0.510	0.680	0.730	0.6975

LR = low risk; AR = at risk; HR = high risk; PMS = post-meningitis sequalae. Source: Sisk et al., 2003 [27]; Rubin 2010 [24].

Utility Decrement

IPD/NBPP utility decrements are presented in Table **22** below.

Table 22: Utility Decrement

Age Category	Utility Decrement	Duration (year)
IPD & NBPP inpatient	0.0709	0.089
NBPP outpatient	0.0045	0.041

IPD = invasive pneumococcal disease; NBPP = non-bacteremic pneumococcal pneumonia. Source: Mangen et al., 2015 [28].

7. Input Range and Distributions for PSA/DSA

Table 23. Input Range and Distributions

Parameter	Mean	LB	UB	Distribution	SD
PCV Efficacy					
Against IPD (all VT except ST3) for LR	0.750	0.414	0.908	Beta(8.1,2.7)	0.126
Against IPD (all VT except ST3) for AR	0.750	0.414	0.908	Beta(8.1,2.7)	0.126
Against IPD (all VT except ST3) for HR	0.250	0.138	0.303	Beta(8.1,2.7)	0.042
Against IPD due to ST3 for LR	0.260	0.000	0.534	Beta(26.21,78.62)	0.136
Against IPD due to ST3 for AR	0.260	0.000	0.534	Beta(2.44,6.93)	0.136
Against IPD due to ST3 for HR	0.087	0.000	0.178	Beta(2.44,6.93)	0.045
Against NBPP (all VT except ST3) for LR	0.667	0.118	0.893	Beta(3.26,34.26)	0.198
Against NBPP (all VT except ST3) for AR	0.403	0.114	0.602	Beta(3.12,1.56)	0.124
Against NBPP (all VT except ST3) for HR	0.150	0.047	0.218	Beta(5.85,8.67)	0.044
Against NBPP due to ST3 for LR	0.156	0.000	0.320	Beta(9.9,56.1)	0.082
Against NBPP due to ST3 for AR	0.156	0.000	0.320	Beta(2.93,15.83)	0.082
Against NBPP due to ST3 for HR	0.052	0.000	0.107	Beta(2.93,15.83)	0.027
PPSV Efficacy					
Against IPD for LR	0.597	0.474	0.691	Beta(46.27,31.24)	0.055
Against IPD for AR	0.597	0.474	0.691	Beta(46.27,31.24)	0.055
Against IPD for HR	0.079	0.000	0.342	Beta(0.68,7.88)	0.087
Against NBPP for LR	0.200	0.000	0.400	Beta(2.87,11.49)	0.102
Against NBPP for AR	0.200	0.000	0.400	Beta(2.87,11.49)	0.102
Against NBPP for HR	0.067	0.000	0.133	Beta(3.57,49.73)	0.034
IPD incidence					
LR; age 18-34	1.740	1.603	1.878	Gamma(2631.36,0)	0.034
LR; age 35-49	4.609	4.365	4.854	Gamma(4315.13,0)	0.070
LR; age 50-64	7.863	7.594	8.133	Gamma(3976.47,0)	0.125
LR; age 65-74	9.008	8.599	9.417	Gamma(4292.6,0)	0.137
LR; age 75-84	15.728	14.825	16.630	Gamma(5680.82,0)	0.209
LR; age 85+	23.309	21.655	24.964	Gamma(2562.18,0.01)	0.460
AR; age 18-34	6.737	6.205	7.269	Gamma(63.69,0.11)	0.844
AR; age 35-49	17.842	16.896	18.788	Gamma(4315.13,0)	0.272
AR; age 50-64	31.041	29.977	32.104	Gamma(4135.49,0.01)	0.483
AR; age 65-74	28.270	26.986	29.553	Gamma(2712.95,0.01)	0.543
AR; age 75-84	32.696	30.820	34.573	Gamma(2492.95,0.01)	0.655
AR; age 85+	48.457	45.018	51.896	Gamma(2562.18,0.02)	0.957
HR; age 18-34	13.507	12.440	14.574	Gamma(59.24,0.23)	1.755
HR; age 35-49	35.772	33.875	37.669	Gamma(4315.13,0.01)	0.545
HR; age 50-64	48.136	46.486	49.786	Gamma(2474.03,0.02)	0.968
HR; age 65-74	38.326	36.586	40.066	Gamma(2073.53,0.02)	0.842
HR; age 75-84	32.215	30.366	34.064	Gamma(1316.66,0.02)	0.888
HR; age 85+	47.743	44.355	51.132	Gamma(2562.18,0.02)	0.943
Proportion of menigitis	0.070	0.057	0.075	Beta(225,2971)	0.005
Proportion of PMS	0.200	0.160	0.240	Beta(76.63,306.53)	0.020
IPD fatality					
Age 18-34	0.049	0.033	0.067	Beta(5,185)	0.009
Age 35-49	0.079	0.065	0.094	Beta(37,436)	0.007
Age 50-64	0.111	0.100	0.122	Beta(112,933)	0.005
Age 65-74	0.126	0.111	0.142	Beta(80,551)	0.008
Age 75-84	0.118	0.100	0.137	Beta(44,342)	0.009
Age 85+	0.215	0.187	0.245	Beta(49,198)	0.015
NBPP-IP Incidence (per 100,000)					

LR; Age 18-24	3.850	3.850	3.960	Gamma(18823.84,0)	0.028
LR; Age 25-34	3.850	3.850	3.960	Gamma(18823.84,0)	0.028
LR; Age 35-44	3.850	3.850	3.960	Gamma(18823.84,0)	0.028
LR; Age 45-49	3.850	3.850	3.960	Gamma(18823.84,0)	0.028
LR; Age 50-54	9.680	9.570	9.900	Gamma(13221.93,0)	0.084
LR; Age 55-59	9.680	9.570	9.900	Gamma(13221.93,0)	0.084
LR; Age 60-64	9.680	9.570	9.900	Gamma(13221.93,0)	0.084
LR; Age 65-74	21.010	20.350	21.670	Gamma(3892.93,0.01)	0.337
LR; Age 75-84	105.270	103.180	107.250	Gamma(10279.99,0.01)	1.038
LR; Age 85-94	105.270	103.180	107.250	Gamma(10279.99,0.01)	1.038
LR; Age 95-100	105.270	103.180	107.250	Gamma(10279.99,0.01)	1.038
AR; Age 18-24	22.770	22.220	23.320	Gamma(6584.35,0)	0.281
AR; Age 25-34	22.770	22.220	23.320	Gamma(6584.35,0)	0.281

Parameter	Mean	LB	UB	Distribution	SD
LR; Age 18-24	26.907	24.697	28.458	Gamma(786.59,0.03)	0.959
LR; Age 25-34	26.907	24.697	28.458	Gamma(786.59,0.03)	0.959
LR; Age 35-44	26.907	24.697	28.458	Gamma(786.59,0.03)	0.959
LR; Age 45-49	26.907	24.697	28.458	Gamma(786.59,0.03)	0.959
LR; Age 50-54	34.326	32.668	35.935	Gamma(1696.63,0.02)	0.833
LR; Age 55-59	34.326	32.668	35.935	Gamma(1696.63,0.02)	0.833
LR; Age 60-64	34.326	32.668	35.935	Gamma(1696.63,0.02)	0.833
LR; Age 65-74	43.226	42.705	43.972	Gamma(17886.7,0)	0.323
LR; Age 75-84	133.779	131.366	136.728	Gamma(9565.62,0.01)	1.368
LR; Age 85-94	227.300	218.520	238.031	Gamma(2085.57,0.11)	4.977
LR; Age 95-100	227.300	218.520	238.031	Gamma(2085.57,0.11)	4.977
AR; Age 18-24	156.059	143.242	165.054	Gamma(786.59,0.2)	5.564
AR; Age 25-34	156.059	143.242	165.054	Gamma(786.59,0.2)	5.564
AR; Age 35-44	156.059	143.242	165.054	Gamma(786.59,0.2)	5.564
AR; Age 45-49	156.059	143.242	165.054	Gamma(786.59,0.2)	5.564
AR; Age 50-54	168.199	160.072	176.079	Gamma(1696.63,0.1)	4.083
AR; Age 55-59	168.199	160.072	176.079	Gamma(1696.63,0.1)	4.083
AR; Age 60-64	168.199	160.072	176.079	Gamma(1696.63,0.1)	4.083
AR; Age 65-74	211.810	209.253	215.462	Gamma(17886.7,0.01)	1.584
AR; Age 75-84	387.959	380.961	396.511	Gamma(9565.62,0.04)	3.967
AR; Age 85-94	659.169	633.708	690.289	Gamma(2085.57,0.32)	14.434
AR; Age 95-100	659.169	633.708	690.289	Gamma(2085.57,0.32)	14.434
HR; Age 18-24	530.063	486.528	560.614	Gamma(786.59,0.67)	18.900
HR; Age 25-34	530.063	486.528	560.614	Gamma(786.59,0.67)	18.900
HR; Age 35-44	530.063	486.528	560.614	Gamma(786.59,0.67)	18.900
HR; Age 45-49	530.063	486.528	560.614	Gamma(786.59,0.67)	18.900
HR; Age 50-54	477.135	454.082	499.490	Gamma(1696.63,0.28)	11.584
HR; Age 55-59	477.135	454.082	499.490	Gamma(1696.63,0.28)	11.584
HR; Age 60-64	477.135	454.082	499.490	Gamma(1696.63,0.28)	11.584

Parameter	Mean	LB	UB	Distribution	SD
HR; Age 65-74	479.814	474.023	488.087	Gamma(17886.7,0.03)	3.588
HR; Age 75-84	561.871	551.737	574.257	Gamma(9565.62,0.06)	5.745
HR; Age 85-94	954.659	917.783	999.728	Gamma(2085.57,0.46)	20.904
HR; Age 95-100	954.659	917.783	999.728	Gamma(2085.57,0.46)	20.904
Vaccine Administration Cost					
	30.522	24.417	36.626	Gamma(96.04,0.32)	3.114
AR; Age 35-44	22.770	22.220	23.320	Gamma(6584.35,0)	0.281
AR; Age 45-49	22.770	22.220	23.320	Gamma(6584.35,0)	0.281
AR; Age 50-54	47.190	46.530	47.850	Gamma(19639.22,0)	0.337
AR; Age 55-59	47.190	46.530	47.850	Gamma(19639.22,0)	0.337
AR; Age 60-64	47.190	46.530	47.850	Gamma(19639.22,0)	0.337
AR; Age 65-74	103.510	102.850	105.270	Gamma(28112.92,0)	0.617
AR; Age 75-84	301.950	298.870	305.140	Gamma(35637.49,0.01)	1.599
AR; Age 85-94	301.950	298.870	305.140	Gamma(35637.49,0.01)	1.599
AR; Age 95-100	301.950	298.870	305.140	Gamma(35637.49,0.01)	1.599
HR; Age 18-24	77.110	74.910	79.310	Gamma(4719.42,0.02)	1.122
HR; Age 25-34	77.110	74.910	79.310	Gamma(4719.42,0.02)	1.122
HR; Age 35-44	77.110	74.910	79.310	Gamma(4719.42,0.02)	1.122
HR; Age 45-49	77.110	74.910	79.310	Gamma(4719.42,0.02)	1.122
HR; Age 50-54	134.860	132.770	136.840	Gamma(16871.34,0.01)	1.038
HR; Age 55-59	134.860	132.770	136.840	Gamma(16871.34,0.01)	1.038
HR; Age 60-64	134.860	132.770	136.840	Gamma(16871.34,0.01)	1.038
HR; Age 65-74	233.640	229.570	237.820	Gamma(12324.2,0.02)	2.105
HR; Age 75-84	439.120	433.840	444.400	Gamma(26571.17,0.02)	2.694
HR; Age 85-94	439.120	433.840	444.400	Gamma(26571.17,0.02)	2.694
HR; Age 95-100	439.120	433.840	444.400	Gamma(26571.17,0.02)	2.694
NBPP-IP Case Fatality					
Age 18-24	0.016	0.004	0.029	Gamma(6.18,379.91)	0.006
Age 25-34	0.016	0.004	0.029	Gamma(6.18,379.91)	0.006
Age 35-44	0.016	0.004	0.029	Gamma(6.18,379.91)	0.006
Age 45-49	0.016	0.004	0.029	Gamma(6.18,379.91)	0.006
Age 50-54	0.028	0.011	0.044	Gamma(10.72,372.31)	0.008
Age 55-59	0.028	0.011	0.044	Gamma(10.72,372.31)	0.008
Age 60-64	0.028	0.011	0.044	Gamma(10.72,372.31)	0.008
Age 65-74	0.035	0.015	0.055	Gamma(11.32,312.06)	0.010
Age 75-84	0.041	0.022	0.060	Gamma(17.11,400.3)	0.010
Age 85-94	0.053	0.033	0.072	Gamma(26.82,479.25)	0.010
Age 95-100	0.053	0.033	0.072	Gamma(26.82,479.25)	0.010
NBPP-OP Incidence					
Age 18-49					

Parameter	Mean	LB	UB	Distribution	SD
Age 50-64	30.522	24.417	36.626	Gamma(96.04,0.32)	3.114
Age 65+	24.702	19.762	29.643	Gamma(96.04,0.26)	2.521
Travel cost for administration	44.550	22.275	74.257	Gamma(11.29,3.95)	13.261
Direct Treatment Cost for IPD					
LR: Age 18-49	59,953	52,490	68,195	Gamma(223.94,267.72)	4,006
LR: Age 50-64	57,996	54,169	62,006	Gamma(841.59,68.91)	1,999
LR: Age 65+	28,650	28,258	29,054	Gamma(19879.98,1.44)	203
AR: Age 18-49	56,023	33,524	82,924	Gamma(19.76,2834.79)	12,602
AR: Age 50-64	51,678	41,898	63,200	Gamma(90.44,571.4)	5,434
AR: Age 65+	26,905	24,898	29,091	Gamma(632.68,42.53)	1,070
HR: Age 18-49	94,966	56,160	151,312	Gamma(15.31,6204.39)	24,274
HR: Age 50-64	127,220	98,339	156,222	Gamma(74.23,1713.89)	14,766
HR: Age 65+	37,168	36,434	40,180	Gamma(1512.69,24.57)	956
Direct Treatment Cost for PMS					
Age 16-34	11,274	9,019	13,529	Gamma(96.04,117.39)	1,150
Age 35-49	10,776	8,621	12,931	Gamma(96.04,112.2)	1,100
Age 50-64	10,309	8,248	12,371	Gamma(96.04,107.34)	1,052
Age 65+	12,541	10,033	15,050	Gamma(96.04,130.59)	1,280
Direct Treatment Cost for NBPP - IP					
LR: Age 18-49	25,956	25,387	26,527	Gamma(7968.01,3.26)	291
LR: Age 50-64	27,700	27,211	28,239	Gamma(11159.9,2.48)	262
LR: Age 65+	19,561	19,530	19,589	Gamma(1711282.59,0.01)	15
AR: Age 18-49	32,739	28,869	37,255	Gamma(234.19,139.8)	2,139
AR: Age 50-64	30,393	28,640	32,259	Gamma(1083.49,28.05)	923
AR: Age 65+	16,959	16,837	17,082	Gamma(73667.8,0.23)	62
HR: Age 18-49	41,502	34,377	50,665	Gamma(99.77,415.99)	4,155
HR: Age 50-64	38,034	34,875	41,485	Gamma(508.77,74.76)	1,686
HR: Age 65+	23,474	23,317	23,640	Gamma(81472.88,0.29)	82
Direct Treatment Cost for NBPP - OP					
LR: Age 18-49	811	801	821	Gamma(25566.33,0.03)	5
LR: Age 50-64	742	734	749	Gamma(34330.65,0.02)	4
LR: Age 65+	659	658	662	Gamma(677658.24,0)	1
AR: Age 18-49	1,086	1,000	1,180	Gamma(559.64,1.94)	46
AR: Age 50-64	917	868	966	Gamma(1334.52,0.69)	25
AR: Age 65+	615	610	621	Gamma(53128.41,0.01)	3
HR: Age 18-49	1,264	1,152	1,391	Gamma(431.36,2.93)	61
HR: Age 50-64	1,112	1,041	1,188	Gamma(884.23,1.26)	37
HR: Age 65+	987	979	996	Gamma(47282.2,0.02)	5
Indirect cost for IPD - LR					
LR: Age 16 - 64	3,322	2,657	3,986	Gamma(96.04,34.59)	339
LR: Age 65 - 74	1,333	1,066	1,599	Gamma(96.04,13.88)	136
LR: Age 75 - 84	886	709	1,063	Gamma(96.04,9.22)	90
LR: Age 85 - 100	800	640	960	Gamma(96.04,8.33)	82
AR: Age 16 - 64	3,322	2,657	3,986	Gamma(96.04,34.59)	339
AR: Age 65 - 74	1,333	1,066	1,599	Gamma(96.04,13.88)	136
AR: Age 75 - 84	886	709	1,063	Gamma(96.04,9.22)	90
AR: Age 85 - 100	800	640	960	Gamma(96.04,8.33)	82
HR: Age 16 - 64	3,322	2,657	3,986	Gamma(96.04,34.59)	339
HR: Age 65 - 74	1,333	1,066	1,599	Gamma(96.04,13.88)	136

Parameter	Mean	LB	UB	Distribution	SD
HR: Age 75 - 84	886	709	1,063	Gamma(96.04,9.22)	90
HR: Age 85 - 100	800	640	960	Gamma(96.04,8.33)	82
Indirect cost for IPD – NBPP IP					
LR: Age 16 - 64	2,684	2,147	3,220	Gamma(96.04,27.94)	274
LR: Age 65 - 74	1,076	861	1,291	Gamma(96.04,11.21)	110
LR: Age 75 - 84	715	572	859	Gamma(96.04,7.45)	73
LR: Age 85 - 100	648	518	777	Gamma(96.04,6.75)	66
AR: Age 16 - 64	2,684	2,147	3,220	Gamma(96.04,27.94)	274
AR: Age 65 - 74	1,076	861	1,291	Gamma(96.04,11.21)	110
AR: Age 75 - 84	715	572	859	Gamma(96.04,7.45)	73
AR: Age 85 - 100	648	518	777	Gamma(96.04,6.75)	66
HR: Age 16 - 64	2,684	2,147	3,220	Gamma(96.04,27.94)	274
HR: Age 65 - 74	1,076	861	1,291	Gamma(96.04,11.21)	110
HR: Age 75 - 84	715	572	859	Gamma(96.04,7.45)	73
HR: Age 85 - 100	648	518	777	Gamma(96.04,6.75)	66
Indirect cost for IPD – NBPP OP					
LR: Age 16 - 64	1,277	1,022	1,533	Gamma(96.04,13.3)	130
LR: Age 65 - 74	513	410	615	Gamma(96.04,5.34)	52
LR: Age 75 - 84	341	273	409	Gamma(96.04,3.55)	35
LR: Age 85 - 100	308	246	370	Gamma(96.04,3.21)	31
AR: Age 16 - 64	1,277	1,022	1,533	Gamma(96.04,13.3)	130
AR: Age 65 - 74	513	410	615	Gamma(96.04,5.34)	52
AR: Age 75 - 84	341	273	409	Gamma(96.04,3.55)	35
AR: Age 85 - 100	308	246	370	Gamma(96.04,3.21)	31
HR: Age 16 - 64	1,277	1,022	1,533	Gamma(96.04,13.3)	130
HR: Age 65 - 74	513	410	615	Gamma(96.04,5.34)	52
HR: Age 75 - 84	341	273	409	Gamma(96.04,3.55)	35
HR: Age 85 - 100	308	246	370	Gamma(96.04,3.21)	31
Indirect cost for PMS					
Age 16 - 64	4,552.00	3,642	5,462	Gamma(96.04,47.4)	464
Age 65 - 74	4,350.81	3,481	5,221	Gamma(96.04,45.3)	444
Age 75 - 84	4,162.48	3,330	4,995	Gamma(96.04,43.34)	425
Age 85 - 100	5,063.74	4,051	6,076	Gamma(96.04,52.73)	517
Baseline utility for “No Pneumococcal Disease” health state					
LR: Age 16–54	0.830	0.780	0.880	Beta(179.13,36.69)	0.026
LR: Age 55–59	0.810	0.760	0.860	Beta(190.75,44.74)	0.026
LR: Age 60–64	0.770	0.720	0.820	Beta(208.78,62.36)	0.026
LR: Age 65–69	0.760	0.710	0.810	Beta(212.26,67.03)	0.026
LR: Age 70–74	0.740	0.690	0.790	Beta(218.04,76.61)	0.026
LR: Age 75–79	0.700	0.650	0.750	Beta(225.19,96.51)	0.026
LR: Age 80–100	0.630	0.580	0.680	Beta(225.03,132.16)	0.026
AR: Age 16–54	0.720	0.670	0.770	Beta(222.33,86.46)	0.026
AR: Age 55–59	0.690	0.640	0.740	Beta(226.1,101.58)	0.026
AR: Age 60–64	0.630	0.580	0.680	Beta(225.03,132.16)	0.026
AR: Age 65–69	0.570	0.520	0.620	Beta(214.11,161.52)	0.026
AR: Age 70–74	0.540	0.490	0.590	Beta(205.58,175.12)	0.026
AR: Age 75–79	0.520	0.470	0.570	Beta(198.92,183.62)	0.026
AR: Age 80–100	0.510	0.460	0.560	Beta(195.33,187.67)	0.026
HR: Age 16–54	0.720	0.670	0.770	Beta(222.33,86.46)	0.026
HR: Age 55–59	0.690	0.640	0.740	Beta(226.1,101.58)	0.026
HR: Age 60–64	0.630	0.580	0.680	Beta(225.03,132.16)	0.026
HR: Age 65–69	0.570	0.520	0.620	Beta(214.11,161.52)	0.026

Parameter	Mean	LB	UB	Distribution	SD
HR: Age 70–74	0.540	0.490	0.590	Beta(205.58,175.12)	0.026
HR: Age 75–79	0.520	0.470	0.570	Beta(198.92,183.62)	0.026
HR: Age 80–100	0.510	0.460	0.560	Beta(195.33,187.67)	0.026
Baseline utility for "PMS" health state					
Age 16–54	0.698	0.424	0.971	Beta(6.87,2.98)	0.140
Age 55–59	0.698	0.424	0.971	Beta(6.87,2.98)	0.140
Age 60–64	0.698	0.424	0.971	Beta(6.87,2.98)	0.140
Age 65–69	0.698	0.424	0.971	Beta(6.87,2.98)	0.140
Age 70–74	0.698	0.424	0.971	Beta(6.87,2.98)	0.140
Age 75–79	0.698	0.424	0.971	Beta(6.87,2.98)	0.140
Age 80–100	0.698	0.424	0.971	Beta(6.87,2.98)	0.140
Utility decrement					
For IPD	0.071	0.051	0.091	Beta(44.78,586.86)	0.010
For inpatient NBPP	0.071	0.051	0.091	Beta(44.78,586.86)	0.010
For outpatient NBPP	0.005	0.004	0.005	Beta(297.74,65865.85)	0.000
Duration of utility decrement					
For IPD	0.089	0.054	0.123	Gamma(25,0)	0.018
For inpatient NBPP	0.089	0.054	0.123	Gamma(25,0)	0.018
For outpatient NBPP	0.041	0.025	0.057	Gamma(25,0)	0.008
Discount rate for costs	0.030	0.000	0.050		
Discount rate for QALYs	0.030	0.000	0.050		

AR = at risk; HR = high risk; IP = inpatient; IPD = invasive pneumococcal disease; LB = lower bound; LR = low risk; NBPP = nonbacteremia pneumococcal pneumonia; PCV = pneumococcal conjugate vaccine; OP = outpatient; QALY = quality adjusted life years; SD = standard deviation; ST3 = serotype 3; UB = upper bound; VT = vaccine type.

8. Scenario Analyses Results

Scenario 1

From the health sector perspective, as shown in Table 3 of the manuscript, the total direct costs for V116, PCV20, and PCV15+PPSV23 arms are $14,652,926,275, $14,637,142,617, and 15,736,808,401 respectively. The incremental cost of V116 vs. PCV20 or vs. PCV15+PPSV23 became $15,783,658, and -$1,083,882,127. This leads to an ICER of V116 vs PCV20 at $3,873 per QALY gained. The ICER of V116 vs. PCV15+PPSV23 remained cost-saving as in the base case.

Scenario 2

Detailed results from a single 65-year-old cohort approach were reported in Table **24**. In this case, ICERs remained cost-saving for both comparisons as in the base case.

Table 24. Scenario 2 - Summary Outcome Results and Estimated ICERs for PCV-Naïve Adults Aged 65 Years Old

Age & Risk Cohorts Included = LR/AR/HR; 65 year old only; Cohort Size = 1,375,059			
Outcomes	V116 [a]	PCV20 [a]	Incremental (V116 vs. PCV20)
IPD cases	6,255	6,591	-336
PMS cases	75	79	-4
NBPP-IP cases	49,494	49,843	-349
NBPP-OP cases	84,119	84,750	-632
IPD deaths	944	986	-42
NBPP deaths	2,138	2,151	-13
Life years	26,832,771	26,831,928	843
QALYs (discounted)	11,724,891	11,724,575	316
Total Costs ($; Discounted)	1,658,584,325	1,674,569,313	-15,984,988
Vaccine acquisition cost	217,842,328	197,963,267	19,879,061
Vaccine admin cost	18,749,742	18,749,742	0
Direct disease treatment cost	802,902,164	817,213,054	-14,310,890
Indirect disease treatment cost	52,363,063	53,438,265	-1,075,202
Indirect disease related death cost	532,912,195	553,390,152	-20,477,957
Travel cost for vaccination	33,814,832	33,814,832	0

ICER ($/QALY gained)			Cost Saving

Age & Risk Cohorts Included = LR/AR/HR; 65 year old only; Cohort Size = 1,375,059

Outcomes	V116 [a]	PCV15+PPSV23 [a]	Incremental (V116 vs. PCV15+PPSV23)
IPD cases	6,255	6,544	-289
PMS cases	75	78	-4
NBPP-IP cases	49,494	49,874	-380
NBPP-OP cases	84,119	84,817	-698
IPD deaths	944	980	-36
NBPP deaths	2,138	2,152	-14
Life years	26,832,771	26,831,991	780
QALYs (discounted)	11,724,891	11,724,597	294
Total Costs ($; Discounted)	1,658,584,325	1,780,551,501	-121,967,176
Vaccine acquisition cost	217,842,328	254,632,560	-36,790,232
Vaccine admin cost	18,749,742	36,953,375	-18,203,633
Direct disease treatment cost	802,902,164	816,801,179	-13,899,015
Indirect disease treatment cost	52,363,063	53,434,077	-1,071,014
Indirect disease related death cost	532,912,195	552,085,543	-19,173,348
Travel cost for vaccination	33,814,832	66,644,767	-32,829,934
ICER ($/QALY gained)			Cost Saving

[a]: the vaccine coverage rate is 55.2%.

IPD = invasive pneumococcal disease; NBPP = non-bacteremic pneumococcal pneumonia; OP = outpatient; IP = inpatient; PMS = postmeningitis sequelae; V116 = 21-valent pneumococcal conjugate vaccine; PCV15 = 15-valent pneumococcal conjugate vaccine; PCV20 = 20-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine; CS = cost-saving; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life years

Scenario 3

Age & Risk Cohorts Included = LR/AR/HR; 65+; Cohort Size = 19,735,405

Outcomes	V116	PCV20	Incremental (V116 vs. PCV20)
IPD cases	66,758	71,962	-5,204
PMS cases	784	846	-63
NBPP-IP cases	590,660	598,887	-8,227
NBPP-OP cases	1,013,893	1,027,067	-13,174
IPD deaths	11,009	11,761	-751
NBPP deaths	26,792	27,143	-351
Life years	260,988,047	260,977,729	10,318
QALYs (discounted)	116,064,090	116,060,014	4,075
Total Costs ($; Discounted)	21,007,786,365	21,246,368,938	-238,582,573

Vaccine acquisition cost	3,126,561,879	2,841,249,490	285,312,389
Vaccine admin cost	269,103,939	269,103,939	0
Direct disease treatment cost	10,733,967,610	11,003,521,976	-269,554,367
Indirect disease treatment cost	633,089,480	648,967,100	-15,877,620
Indirect disease related death cost	5,759,739,202	5,998,202,177	-238,462,976
Travel cost for vaccination	485,324,255	485,324,255	0
ICER ($/QALY gained)			Cost Saving

When herd effects of PCV20 vaccination in the pediatric population was accounted for, the ICERs remained cost saving for both comparisons. The incremental clinical and economic outcomes between the intervention and comparators only changed slightly compared to the base case results. Table **25** showed the detailed outcomes.

Table 25. Summary Outcome Results and Estimated ICERs for PCV-Naïve Adults Aged 65+
Years When Herd Immunity of PCV20 Pediatric Vaccination is Included

Age & Risk Cohorts Included = LR/AR/HR; 65+; Cohort Size = 19,735,405 Outcomes	V116	PCV15+PPSV23	Incremental (V116 vs. PCV15+PPSV23)
IPD cases	66,758	71,286	-4,527
PMS cases	784	838	-54
NBPP-IP cases	590,660	599,876	-9,216
NBPP-OP cases	1,013,893	1,028,653	-14,760
IPD deaths	11,009	11,661	-652
NBPP deaths	26,792	27,184	-393
Life years	260,988,047	260,978,180	9,867
QALYs (discounted)	116,064,090	116,060,166	3,923
Total Costs ($; Discounted)	21,007,786,365	22,787,809,005	-1,780,022,640
Vaccine acquisition cost	3,126,561,879	3,654,590,279	-528,028,400
Vaccine admin cost	269,103,939	530,369,900	-261,265,960
Direct disease treatment cost	10,733,967,610	11,007,243,327	-273,275,718
Indirect disease treatment cost	633,089,480	649,458,982	-16,369,502
Indirect disease related death cost	5,759,739,202	5,989,633,665	-229,894,463
Travel cost for vaccination	485,324,255	956,512,853	-471,188,597
ICER ($/QALY gained)			Cost Saving

IPD = invasive pneumococcal disease; NBPP = non-bacteremic pneumococcal pneumonia; OP = outpatient; IP = inpatient; PMS = postmeningitis sequelae; V116 = 21-valent pneumococcal conjugate vaccine; PCV15 = 15-valent pneumococcal conjugate vaccine; PCV20 = 20-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine; CS = cost-saving; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life years

Scenario 4A

Table 26. Scenario 4A - Summary Outcome Results and Estimated ICERs for PCV-Naïve Adults Aged 65+ Years

Age & Risk Cohorts Included = LR/AR/HR; 65+; Cohort Size = 19,735,405

Outcomes	V116	PCV20	Incremental (V116 vs. PCV20)
IPD cases	70,526	76,598	-6,072
PMS cases	828	901	-73
NBPP-IP cases	610,409	620,163	-9,754
NBPP-OP cases	1,048,489	1,064,177	-15,688
IPD deaths	11,650	12,546	-895
NBPP deaths	27,698	28,119	-421
Life years	260,977,045	260,965,272	11,773
QALYs (discounted)	116,060,339	116,055,795	4,545
Total Costs ($; Discounted)	21,645,868,960	21,950,521,470	-304,652,510
Vaccine acquisition cost	3,126,561,879	2,841,249,490	285,312,389
Vaccine admin cost	269,103,939	269,103,939	0
Direct disease treatment cost	11,130,134,927	11,437,147,665	-307,012,738
Indirect disease treatment cost	655,210,334	673,052,328	-17,841,994
Indirect disease related death cost	5,979,533,625	6,244,643,792	-265,110,167
Travel cost for vaccination	485,324,255	485,324,255	0
ICER ($/QALY gained)			Cost saving

Age & Risk Cohorts Included = LR/AR/HR; 65+; Cohort Size = 19,735,405

Outcomes	V116	PCV15+PPSV23	Incremental (V116 vs. PCV15+PPSV23)

IPD cases	70,526	76,552	-6,026
PMS cases	828	900	-72
NBPP-IP cases	610,409	623,223	-12,814
NBPP-OP cases	1,048,489	1,069,112	-20,623
IPD deaths	11,650	12,546	-896
NBPP deaths	27,698	28,253	-554
Life years	260,977,045	260,964,242	12,803
QALYs (discounted)	116,060,339	116,055,426	4,913
Total Costs ($; Discounted)	21,645,868,960	23,568,509,709	-1,922,640,749
Vaccine acquisition cost	3,126,561,879	3,654,590,279	-528,028,400
Vaccine admin cost	269,103,939	530,369,900	-261,265,960
Direct disease treatment cost	11,130,134,927	11,485,069,541	-354,934,614
Indirect disease treatment cost	655,210,334	676,105,710	-20,895,377
Indirect disease related death cost	5,979,533,625	6,265,861,427	-286,327,801
Travel cost for vaccination	485,324,255	956,512,853	-471,188,597
ICER ($/QALY gained)			Cost saving

IPD = invasive pneumococcal disease; NBPP = non-bacteremic pneumococcal pneumonia; OP = outpatient; IP = inpatient; PMS = postmeningitis sequelae; V116 = 21-valent pneumococcal conjugate vaccine; PCV15 = 15-valent pneumococcal conjugate vaccine; PCV20 = 20-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine; CS = cost-saving; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life years

Age & Risk Cohorts Included = LR/AR/HR; 65+; Cohort Size = 19,735,405			
Outcomes	V116	PCV20	Incremental (V116 vs. PCV20)
IPD cases	67,820	75,089	-7,269
PMS cases	796	883	-87
NBPP-IP cases	600,954	612,885	-11,931
NBPP-OP cases	1,033,689	1,052,783	-19,094
IPD deaths	11,229	12,311	-1,082
NBPP deaths	27,277	27,795	-518
Life years	260,983,374	260,969,501	13,873
QALYs (discounted)	116,062,459	116,057,209	5,250
Total Costs ($; Discounted)	21,326,899,551	21,729,738,076	-402,838,526
Vaccine acquisition cost	3,126,561,879	2,841,249,490	285,312,389
Vaccine admin cost	269,103,939	269,103,939	0
Direct disease treatment cost	10,942,107,916	11,304,379,761	-362,271,845
Indirect disease treatment cost	644,716,194	665,481,439	-20,765,245
Indirect disease related death cost	5,859,085,366	6,164,199,191	-305,113,825
Travel cost for vaccination	485,324,255	485,324,255	0
ICER ($/QALY gained)			Cost saving

Age & Risk Cohorts Included = LR/AR/HR; 65+; Cohort Size = 19,735,405			
Outcomes	V116	PCV15+PPSV23	Incremental (V116 vs. PCV15+PPSV23)
IPD cases	67,820	75,559	-7,739
PMS cases	796	888	-92

NBPP-IP cases	600,954	617,392	-16,438
NBPP-OP cases	1,033,689	1,059,984	-26,294
IPD deaths	11,229	12,391	-1,162
NBPP deaths	27,277	27,993	-716
Life years	260,983,374	260,967,384	15,990

Scenario 4B

Table 27. Scenario 4B - Summary Outcome Results and Estimated ICERs for PCV-Naïve Adults Aged 65+ Years

QALYs (discounted)	116,062,459	116,056,475	5,984
Total Costs ($; Discounted)	21,326,899,551	23,401,145,704	-2,074,246,153
Vaccine acquisition cost	3,126,561,879	3,654,590,279	-528,028,400
Vaccine admin cost	269,103,939	530,369,900	-261,265,960
Direct disease treatment cost	10,942,107,916	11,383,251,027	-441,143,111
Indirect disease treatment cost	644,716,194	670,238,316	-25,522,122
Indirect disease related death cost	5,859,085,366	6,206,183,329	-347,097,963
Travel cost for vaccination	485,324,255	956,512,853	-471,188,597
ICER ($/QALY gained)			Cost saving

IPD = invasive pneumococcal disease; NBPP = non-bacteremic pneumococcal pneumonia; OP = outpatient; IP = inpatient; PMS = postmeningitis sequelae; V116 = 21-valent pneumococcal conjugate vaccine; PCV15 = 15-valent pneumococcal conjugate vaccine; PCV20 = 20-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine; CS = cost-saving; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life years

Scenario 4C

Table 28. Scenario 4C - Summary Outcome Results and Estimated ICERs for PCV-Naïve Adults Aged 65+ Years

Age & Risk Cohorts Included = LR/AR/HR; 65+; Cohort Size = 19,735,405

Outcomes	V116	PCV20	Incremental (V116 vs. PCV20)
IPD cases	64,988	73,510	-8,521
PMS cases	764	865	-101
NBPP-IP cases	592,373	606,277	-13,905
NBPP-OP cases	1,017,090	1,040,001	-22,911
IPD deaths	10,674	12,001	-1,327
NBPP deaths	26,850	27,466	-616
Life years	260,988,738	260,973,001	15,737
QALYs (discounted)	116,063,969	116,058,194	5,774
Total Costs ($; Discounted)	21,086,722,102	21,565,343,763	-478,621,661
Vaccine acquisition cost	3,126,561,879	2,841,249,490	285,312,389
Vaccine admin cost	269,103,939	269,103,939	0
Direct disease treatment cost	10,795,693,710	11,201,756,408	-406,062,698
Indirect disease treatment cost	636,662,226	659,660,920	-22,998,694
Indirect disease related death cost	5,773,376,092	6,108,248,750	-334,872,658
Travel cost for vaccination	485,324,255	485,324,255	0

Indirect disease treatment cost	636,662,226	665,670,295	-29,008,069
Indirect disease related death cost	5,773,376,092	6,163,874,178	-390,498,086
Travel cost for vaccination	485,324,255	956,512,853	-471,188,597
ICER ($/QALY gained)			Cost saving

ICER ($/QALY gained) Cost saving

Age & Risk Cohorts Included = LR/AR/HR; 65+; Cohort Size = 19,735,405

Outcomes	V116	PCV15+PPSV23	Incremental (V116 vs. PCV15+PPSV23)
IPD cases	64,988	74,445	-9,456
PMS cases	764	876	-112
NBPP-IP cases	592,373	612,099	-19,726
NBPP-OP cases	1,017,090	1,049,743	-32,653
IPD deaths	10,674	12,172	-1,498
NBPP deaths	26,850	27,729	-879
Life years	260,988,738	260,970,030	18,708
QALYs (discounted)	116,063,969	116,057,220	6,749
Total Costs ($; Discounted)	21,086,722,102	23,274,589,137	-2,187,867,035
Vaccine acquisition cost	3,126,561,879	3,654,590,279	-528,028,400
Vaccine admin cost	269,103,939	530,369,900	-261,265,960
Direct disease treatment cost	10,795,693,710	11,303,571,633	-507,877,923

IPD = invasive pneumococcal disease; NBPP = non-bacteremic pneumococcal pneumonia; OP = outpatient; IP = inpatient; PMS = postmeningitis sequelae; V116 = 21-valent pneumococcal conjugate vaccine; PCV15 = 15-valent pneumococcal conjugate vaccine; PCV20 = 20-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine; CS = cost-saving; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life years

9. REFERENCES

1. United States Census Bureau. *Annual Estimates of the Resident Population by Single Year of Age and Sex for the United States for year 2022*. 2023 [cited 2024 March 6]; Available from: https://www.census.gov/data/tables/timeseries/demo/popest/2020s-national-detail.html.
2. Arias, E. and J.Q. Xu, *United States Life Table, 2019*, in *National Vital Statistics Report*. 2022, National Center for Health Statistics (U.S.): Hyattsville, MD.
3. Pelton, S.I., R. Bornheimer, R. Doroff, et al., *Decline in Pneumococcal Disease Attenuated in Older Adults and Those With Comorbidities Following Universal Childhood PCV13 Immunization.* Clin Infect Dis, 2019. **68**(11): p. 1831-1838.
4. Centers for Disease Control and Prevention, *Active Bacterial Core Surveillance Report, Emerging Infections Program Network, Streptococcus pneumoniae, 2017*. 2017, Centers for Disease Control and Prevention,: Atlanta, GA.
5. Centers for Disease Control and Prevention, *Active Bacterial Core Surveillance Report, Emerging Infections Program Network, Streptococcus pneumoniae, 2018*. 2018, Centers for Disease Control and Prevention: Atlanta, GA.
6. Centers for Disease Control and Prevention, *Active Bacterial Core Surveillance Report, Emerging Infections Program Network, Streptococcus pneumoniae, 2019*. 2019, Centers for Disease Control and Prevention: Atlanta, GA.
7. Stoecker, C., *Economic Assessment of PCV15 & PCV20: Presentation to the ACIP June 25, 2021*. 2021, Centers for Disease Control and Prevention.
8. World Health Organisation (WHO), *Strategic Advisory Group of Experts on Immunization* 2020, World Health Organization: Geneva, Switzerland.
9. Tong, S., C. Amand, A. Kieffer, M.H. Kyaw, *Trends in healthcare utilization and costs associated with pneumonia in the United States during 2008-2014.* BMC Health Serv Res, 2018. **18**(1): p. 715.
10. Stoecker, C., *Economic Assessment of PCV20 for Adults Vaccinated with PCV13: Presented at ACIP, October 19, 2022*. 2022, Centers for Disease Control and Prevention.
11. Balsells, E., R. Dagan, I. Yildirim, et al., *The relative invasive disease potential of Streptococcus pneumoniae among children after PCV introduction: a systematic review and meta-analysis.* J Infect, 2018. **77**(5): p. 368-378.
12. Centers for Disease Control and Prevention, *2016-2021 Serotype Data for Invasive Pneumococcal Disease Cases by Age Group from Active Bacterial Core surveillance*. 2023, Active Bacterial Core Surveillance: Atlanta, GA.
13. Self, W.H., K.D. Johnson, J.J. Resser, et al., *Prevalence, Clinical Severity, and Serotype Distribution of Pneumococcal Pneumonia Among Adults Hospitalized With Community-Acquired Pneumonia in Tennessee and Georgia, 2018-2022.* Clinical Infectious Diseases, 2024.

14. Isturiz, R., L. Grant, S. Gray, et al., *Expanded Analysis of 20 Pneumococcal Serotypes Associated With Radiographically Confirmed Community-Acquired Pneumonia in Hospitalized US Adults.* Clin Infect Dis, 2021.
15. Bonten, M.J., S.M. Huijts, M. Bolkenbaas, et al., *Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults.* New England Journal of Medicine, 2015. **372**(12): p. 1114-1125.
16. Cho, B.H., C. Stoecker, R. Link-Gelles, M.R. Moore, *Cost-effectiveness of administering 13-valent pneumococcal conjugate vaccine in addition to 23-valent pneumococcal polysaccharide vaccine to adults with immunocompromising conditions.* Vaccine, 2013. **31**(50): p. 6011-21.
17. Andrews, N.J., P.A. Waight, R.C. George, M.P. Slack, E. Miller, *Impact and effectiveness of 23-valent pneumococcal polysaccharide vaccine against invasive pneumococcal disease in the elderly in England and Wales.* Vaccine, 2012. **30**(48): p. 6802-8.
18. Rudnick, W., Z. Liu, A. Shigayeva, et al., *Pneumococcal vaccination programs and the burden of invasive pneumococcal disease in Ontario, Canada, 1995-2011.* Vaccine, 2013. **31**(49): p. 5863-71.
19. Djennad, A., M.E. Ramsay, R. Pebody, et al., *Effectiveness of 23-Valent Polysaccharide Pneumococcal Vaccine and Changes in Invasive Pneumococcal Disease Incidence from 2000 to 2017 in Those Aged 65 and Over in England and Wales.* EClinicalMedicine, 2018. **6**: p. 42-50.
20. Suaya, J.A., Q. Jiang, D.A. Scott, et al., *Post hoc analysis of the efficacy of the 13valent pneumococcal conjugate vaccine against vaccine-type community-acquired pneumonia in at-risk older adults.* Vaccine, 2018. **36**(11): p. 1477-1483.
21. Lawrence, H., H. Pick, V. Baskaran, et al., *Effectiveness of the 23-valent pneumococcal polysaccharide vaccine against vaccine serotype pneumococcal pneumonia in adults: A case-control test-negative design study.* PLoS Med, 2020. **17**(10): p. e1003326.
22. Bonten, M.J., S.M. Huijts, M. Bolkenbaas, et al., *Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults.* N Engl J Med, 2015. **372**(12): p. 111425.
23. Pfizer Inc. *Statutory Price Disclosure For Connecticut Prescribers*. 2024 [cited 2024 March 6]; Available from: https://cdn.pfizer.com/pfizercom/products/ctprescribers/PREVNAR20CTPriceDisclosureShortForm01112024.pdf.
24. Rubin, J.L., L.J. McGarry, D.R. Strutton, et al., *Public health and economic impact of the 13-valent pneumococcal conjugate vaccine (PCV13) in the United States.* Vaccine, 2010. **28**(48): p. 7634-43.
25. McLaughlin, J.M., J.J. McGinnis, L. Tan, A. Mercatante, J. Fortuna, *Estimated Human and Economic Burden of Four Major Adult Vaccine-Preventable Diseases in the United States, 2013.* J Prim Prev, 2015. **36**(4): p. 259-73.

26. Grosse SD, Krueger KV, Pike J, *Estimated annual and lifetime labor productivity in the United States, 2016: implications fro economic evaluations.* J Med Econ, 2019. **22**(6): p. 501-508.
27. Sisk, J.E., W. Whang, J.C. Butler, V.-P. Sneller, C.G. Whitney, *Cost-effectiveness of vaccination against invasive pneumococcal disease among people 50 through 64 years of age: role of comorbid conditions and race.* Annals of internal medicine, 2003. **138**(12): p. 960-968.
28. Mangen, M.-J.J., M.H. Rozenbaum, S.M. Huijts, et al., *Cost-effectiveness of adult pneumococcal conjugate vaccination in the Netherlands.* European Respiratory Journal, 2015. **46**(5): p. 1407-1416.