Published in final edited form as:

Vaccine. 2013 August 20; 31(37): 3950–3956. doi:10.1016/j.vaccine.2013.06.037.

Cost-effectiveness of pneumococcal conjugate vaccination in immunocompromised adults

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Abstract

Objective—Pneumococcal disease is a significant problem in immunocompromised persons, particularly in HIV-infected individuals. The CDC recently updated pneumococcal vaccination recommendations for immunocompromised adults, adding the 13-valent pneumococcal conjugate vaccine (PCV13) to the previously recommended 23-valent pneumococcal polysaccharide vaccine (PPSV23). This analysis estimates the cost-effectiveness of pneumococcal vaccination strategies in HIV-infected individuals and in the broader immunocompromised adult group.

Design—Markov model-based cost-effectiveness analysis

Methods—The model considered immunocompromised persons aged 18–64 years and accounted for childhood PCV13 herd immunity; in a separate analysis, an HIV-infected subgroup was considered. PCV13 effectiveness was estimated by an expert panel; PPSV23 protection was modeled relative to PCV13 effectiveness. We assumed that both vaccines prevented invasive pneumococcal disease, but only PCV13 prevented nonbacteremic pneumonia.

Results—In all immunocompromised individuals, a single PCV13 cost \$70,937 per quality adjusted life year (QALY) gained compared to no vaccination; current recommendations cost \$136,724/QALY. In HIV patients, with a longer life expectancy (22.5 years), current recommendations cost \$89,391/QALY compared to a single PCV13. Results were sensitive to variation of life expectancy and vaccine effectiveness. The prior recommendation was not favored in any scenario.

Conclusions—One dose of PCV13 is more cost-effective for immunocompromised individuals than previous vaccination recommendations and may be more economically reasonable than

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Conflict of Interest

Richard Zimmerman and Mary Patricia Nowalk have a research grant from Merck, Inc., on HPV vaccine

Dr. Smith was responsible for the concept and design of the paper, acquisition, analysis, and interpretation of data, drafting and critical revision of the manuscript, statistical analysis, and obtaining the funding for the work.

Dr. Nowalk was responsible for concept and design of the paper, acquisition, analysis and interpretation of data, and the drafting and critical revision of the manuscript.

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current recommendations, depending on life expectancy and vaccine effectiveness in the immunocompromised.

Introduction

Streptococcus pneumoniae illness epidemiology is strikingly different between the general population and individuals with immunocompromising conditions. While invasive pneumococcal disease (IPD) incidence is low among young adults (3.8 cases per 100,000) and rises nearly 10-fold among adults over age 65 years (36.4/100,000), incidence increases dramatically among immunocompromised adults with hematological cancer or HIV infection (173–186/100,000).[1] Previously, the Advisory Committee on Immunization Practices (ACIP) recommended two doses of 23-valent pneumococcal polysaccharide vaccine (PPSV23) at least five years apart for immunocompromised individuals.[2] In June 2012, the ACIP issued new recommendations for immunocompromised adults, adding the 13-valent pneumococcal conjugate vaccine (PCV13) to the previously recommended PPSV23.[1]

The rationale for this change has 4 major components. First, comparable or greater antibody responses to PCV13 relative to PPSV23 were found in immunocompetent adults, indicating a reasonable likelihood of clinical benefit.[3] Interestingly, PCV13 antibody response was less when given 1 year after PPSV23 than when given *de novo*, which not seen when PCV13 immunization followed another PCV13 dose.[3] Second, the previously used 7-valent conjugate vaccine (PCV7), given in 2 doses 4 weeks apart, was 75% effective in preventing IPD in HIV infected adults not on highly active antiretroviral therapy in Malawi, [4] and provided similar antibody responses compared to PPSV23 in US and European HIV patients.[5, 6] In addition, when given vaccines in series, greater antibody responses were seen when PPSV23 was given after PCV7 and blunted response was not observed when PCV7 was given 5 years after PPSV23.[4, 6] Third, PPSV23 efficacy in preventing pneumococcal disease in the immunocompromised is questionable, with many experts believing it ineffective in this group.[7] Despite conflicting evidence on PPSV23 efficacy in HIV patients,[8, 9] the ACIP concluded that benefits of PPSV23 use outweighed its risks.[1] Finally, the strong indirect (herd immunity) effects due to childhood PCV7 observed in most population groups have not carried through to the immunocompromised, with high IPD rates from PCV7 serotypes seen in HIV-infected persons.[10] Also, PCV13 serotypes caused 50% of IPD in the immunocompromised in 2010, with an additional 21% caused by serotypes contained only in PPSV23.[1] Substantial replacement disease occurred in immunocompromised persons after widespread PCV7 use, especially an increase in serotype 19A.[11] The new recommendation includes both vaccines because PPSV23 contains 11 *S. pneumoniae* serotypes not found in PCV13, and PPSV23's known IPD protection in most populations.[1]

PCV13 costs considerably more than PPSV23. An analysis from the UK found PCV13 use for persons with immunocompromising and other high-risk conditions unlikely to be cost effective.[12] The CDC also performed a cost-effectiveness analysis, but only examined the new vaccination recommendation for the immunocompromised compared to the prior recommendation[1, 13]. Given doubts regarding PPSV23 effectiveness in the immunocompromised, the cost effectiveness of using only PCV13 in this group is germane. Here we consider several vaccination strategies, specifically examining the cost-effectiveness of the previous ACIP recommendation (two PPSV23 vaccines separated by at least 5 years), the current ACIP recommendation using both PCV13 and PPSV23, and regimens using only PCV13.

Methods

We used a Markov state-transition model to estimate the cost effectiveness of 6 vaccination strategies in immunocompromised persons aged 19–64 years: no vaccine, a single PPSV23, two PPSV23 doses separated by 5 years (the previous CDC recommendation[2]), a single PCV13 alone, two PCV13 doses separated by 5 years, and the current CDC recommendation for PPSV23 naïve patients, PCV13 followed by PPSV23 at least 8 weeks later then a second PPSV23 in 5 years.[1] In a sensitivity analysis, we also examined the recommended strategy for patients previously vaccinated with PPSV23, PCV13 at least 1 year after the PPSV23, then a second PPSV23 vaccination 5 years after the first. To account for changes in both duration and quality of life, we used quality adjusted life years (QALYs), the product of time in a health state and that state's quality of life utility, which can range from 0 (death) to 1 (perfect health).

In the model, hypothetical cohorts of immunocompromised persons could become ill due to nonbacteremic pneumococcal pneumonia or invasive pneumococcal disease during each yearly cycle of the model. Once ill, they could recover, become disabled, or die. If they became disabled, they could not return to a non-disabled state. Patients could die from pneumococcal illness, or due to other causes based on the cohort's life expectancy.

The model considered, over a 15-year time horizon, immunocompromised persons aged 19–64 years with an average life expectancy of 11.7 years, based on SEER data on the 5-year cause-specific survival for all malignant cancers.[14] We used CDC definitions for immunocompromising conditions, which include HIV infection, Hodgkin disease, leukemia, lymphoma, myeloma, generalized malignancy, chronic renal failure, nephrotic syndrome, solid organ or bone marrow transplant, immunoglobulin deficiency, asplenia, sickle cell disease, or current immunosuppressive therapy (including radiation, systemic steroids, or chemotherapy).[1] In a separate analysis, we only considered HIV positive individuals, who have a 22.5-year life expectancy (95% CI 22.2–22.7 years).[15] In each cohort, life expectancy was used to calculate yearly mortality risk, which was applied over the 15-year time horizon of the model. A 15-year time horizon assumes no vaccination health effects after 15 years.

Invasive pneumococcal disease rates for the immunocompromised were obtained from 2007–2008 CDC Active Bacterial Core surveillance (ABCs) data,[16] which also supplied case-fatality rate and IPD serotype distribution data (Table 1, top). Meningitis risk given IPD was used as a proxy for disability risk given IPD, understanding that not all meningitis patients are disabled but some with non-meningitis IPD are. NPP rates were calculated from National Hospital Discharge Survey data[17] under the assumption that 30% of all hospitalized pneumonia cases are caused by pneumococci (Table 1, bottom).[18, 19] As previously, we assumed that the serotype distribution of NPP was similar to IPD and that NPP and IPD case rate ratios were the same among comorbidity groups.[16] Disability after hospitalized NPP was modeled as 50% of the IPD value and varied widely in sensitivity analyses. Indirect (herd immunity) effects due to childhood PCV13 use were modeled as both changes in pneumococcal illness rates and in serotype distributions among disease cases, as previously described.[16]

In the immunocompromised, PPSV23 has limited effectiveness, with many experts feeling it is not protective.[7] PCV13 may be more effective in these patients, albeit based on limited evidence.[4, 5, 8, 9] We used PCV13 effectiveness in the immunocompromised as estimated by a pneumococcal disease expert panel using the modified Delphi technique (Table 2). Since PPSV23 effectiveness in the immunocompromised is controversial, we modeled PPSV23 effectiveness as a value relative to PCV13 effectiveness against IPD, examining

how effective the vaccines would need to be for strategies to be considered cost-effective. In the model, both vaccines were assumed to be effective against their respective serotypes in preventing IPD, but only PCV13 prevented nonbacteremic pneumococcal pneumonia (NPP), consistent with published data.[20–22] As we have previously described,[16] pneumococcal disease risk was modeled as a function of the projected infection risk and accounting for the indirect effects of childhood PCV13, the projected likelihood of infection from a vaccine serotype, the probability of vaccination, and the probability the vaccine is effective against its contained serotypes. The probability of pneumococcal vaccination in the immunocompromised aged 19–64 was 33.9%.[23]

Table 3 shows other model parameter values. Quality of life utilities were obtained from the medical literature and illness costs came from the Nationwide Inpatient Sample. A societal perspective was taken, using 2006 US\$ and discounting future costs and effectiveness at 3% per year.[24] There is no US cost-effectiveness criterion, but \$50,000 per QALY gained is a frequently cited but poorly justified benchmark.[25] Recent work suggests that \$100,000/QALY gained is more realistic,[26] and we use this as our cost-effectiveness criterion.

We performed 1-way sensitivity analyses, varying all parameters individually over the ranges listed in Table 3. Then, 2-way sensitivity analyses of selected parameters were performed. A probabilistic sensitivity analysis, varying all parameter values and herd immunity scenarios simultaneously 3000 times over distributions, was carried out; its results are summarized as an acceptability curve, depicting the likelihood that strategies would be considered cost-effective over a range of societal willingness-to-pay (or acceptability) thresholds. Parameter distributions were chosen based on data characteristics and the uncertainty surrounding a parameter value. In a separate analysis, we examined the effects of using alternative parameter values from the CDC cost-effectiveness analysis performed at the ACIP's request.[1, 13]

Results

Table 4 (top) shows base case results, using an 11.7 year life expectancy for the immunocompromised cohort. In this analysis, strategies using only PPSV23 had higher incremental cost-effectiveness ratios (ICERs) than more effective strategies and are eliminated from further consideration, as recommended,[24] due to extended dominance. A single dose PCV13 strategy costs \$70,937 per quality adjusted life year (QALY) gained compared to no vaccination. The current CDC recommendation, when compared to a single PCV13, costs almost \$137,000/QALY gained. Compared to the prior recommendation, the current recommendation prevented 58 more NPP cases, 9 more IPD cases, and 9 more deaths per 100,000 immunocompromised persons over 15 years.

Results for the HIV infected subgroup, with an average life expectancy of 22.5 years, are shown in Table 4 (bottom). Strategies using PPSV23 alone are again eliminated by extended dominance, but the current recommendation costs about \$89,000 per quality adjusted life year (QALY) gained compared to a single PCV13. In this scenario, the current recommendation prevented 74 more NPP cases, 11 more IPD cases, and 12 more deaths per 100,000 HIV-infected persons than the prior recommendation. In both the base case and HIV scenarios, giving 2 PCV13 doses separated by 5 years was more costly and less effective than the current recommendation.

Sensitivity analysis

In one-way sensitivity analyses, variation of cohort life expectancy and vaccine effectiveness estimates caused substantial changes in results. Both PCV13 alone and the current recommendation strategy cost >\$100,000 per QALY when life expectancy was 8

years, and cost <\$100,000/QALY when life expectancy was 19 years. Individual variation of other parameter values had less substantial effects on results. Substituting the regimen recommended for individuals who had previously received PPSV23 for the PPSV23 naïve regimen left results essentially unchanged. Similarly, varying vaccine uptake had minimal effects on results. When examining older immunosuppressed cohorts aged 75 years, PCV13 alone cost \$141,366/QALY gained and the current recommendation cost \$465,494/QALY gained.

In 2-way sensitivity analyses, we simultaneously varied 2 vaccine effectiveness parameters whose true values are unclear: PPSV23 effectiveness in preventing IPD caused by its component serotypes relative to PCV13's serotype-specific IPD preventive effectiveness and PCV13 effectiveness against NPP relative to its IPD effectiveness. In all immunocompromised persons (Figure 1, top), 1) a single PPSV23 dose strategy was favored, using a \$100,000/QALY gained willingness to pay threshold, when PPSV23 relative effectiveness was high and PCV13 relative effectiveness against NPP was low; 2) a single PCV13 was favored when PPSV23 effectiveness was low and PCV13 effectiveness against NPP was high; 3) the current recommendation was favored when both vaccines were highly effective; and 4) the previously recommended strategy was never favored. In HIV patients, with their longer life expectancy (Figure 1, bottom), the area where the current recommendation was favored is much larger, and was favored if PPSV23 relative effectiveness was >49% and PCV13 relative effectiveness against NPP was >52% (expert panel estimate: 70%).

In all immunocompromised persons, the probabilistic sensitivity analysis (Figure 2, top), varying all parameter values over distributions, showed that the no vaccination strategy was most likely to be considered cost-effective if the willingness-to-pay (or acceptability) threshold was \$100,000/QALY gained, a single PCV13 was favored when the threshold was \$110,000 to \$140,000/QALY, and the current recommendation favored at higher thresholds. In HIV patients (Figure 2, bottom), the current recommendation was favored if the acceptability threshold was \$100,000/QALY gained.

In a separate analysis, we re-ran our model using many of the model parameters and assumptions used by the CDC to estimate the cost-effectiveness of the newly recommended vaccination strategy in the immunocompromised, compared to the prior recommendation. [13] As in our analysis, they assumed no PPSV23 effectiveness against NPP. However, unlike ours, they compared only those 2 strategies and considered both hospitalized and outpatient pneumonia. [13] In addition, they assumed slightly higher initial PCV13 effectiveness against IPD in the immunocompromised, lower PPSV23 effectiveness against IPD, lower PCV13 effectiveness against NPP, a maximum 5 year preventive duration for both vaccines, and boosting of PCV13 effectiveness with PPSV23 revaccination. They found the current vaccination recommendation to be cost-saving and more effective than the previous recommendation. Our model, which considered only hospitalized pneumonia, when otherwise modified to use other CDC assumptions and considering only the current and former recommendations as they did, found that the current recommendation cost \$39,242 per QALY gained compared to the prior recommendation.

Discussion

PCV13 use in immunocompromised adults may prevent more pneumococcal disease than strategies using only PPSV23, prompting the CDC to recommend both vaccines despite uncertainty regarding their effectiveness, either alone or in combination, in the immunocompromised. This analysis builds on our prior work examining PCV13 use in all adults 50 years old [16] and accounts for unknown pneumococcal vaccine effectiveness and

uncertain herd immunity effects from childhood PCV13. We found that using PCV13 in the immunocompromised aged 19–64 years will likely be more beneficial and economically reasonable compared to regimens using only PPSV23. Our analysis strongly supports replacement of the former ACIP recommendation for two PPSV23 doses separated by 5 years in the immunocompromised, which was not favored in any scenario.

The cost-effectiveness of adding PPSV23 to a PCV13 regimen depends, in part, on life expectancy. Due to the competing risk of mortality, the currently recommended strategy, using both vaccines, is favored in this analysis only when life expectancy was ≥ 19 years if the cost-effectiveness acceptability threshold is \$100,000 per QALY gained and PPSV23 effectiveness against IPD in the immunocompromised was greater than many experts predict. However, current CDC recommendations are reasonable both clinically and economically for HIV-infected populations, due to high pneumococcal disease rates and evidence of increasing life expectancy and immune function maintenance resulting from highly active antiretroviral therapy. Persons with other immunocompromising conditions associated with shorter life spans and poorer immune responsiveness may benefit less than the HIV infected from adding PPSV23 to PCV13. Due to PPSV23's relatively small impact on illness prevention and considerable incremental cost, PCV13 alone might be economically favored for these patients. This strategy also meets the policy criteria of simplicity. However, if life expectancy falls below 8 years, any vaccination strategy becomes less favorable economically, echoing recommendations to consider limiting preventive interventions in persons with severe comorbidities who might not benefit from them.[27–29]

Results are also sensitive to variation of PPSV23 effectiveness, relative to that of PCV13, and of PCV13 effectiveness against NPP. When the effectiveness of both vaccines is high, then the recent recommendation is favored. When PCV13 effectiveness is high and that of PPSV23 is low, then a single dose of PCV13 is favored. When PPSV23 effectiveness is high and PCV13 effectiveness is low, a single dose of PPSV23 is favored. Unfortunately, data on the immunogenicity or effectiveness of PCV13 in immunocompromised adults are not available.[1] In addition, PCV13 effectiveness against pneumonia in either healthy or immunocompromised adults is unknown at present and awaits results from the CAPITA study, a randomized controlled trial of 85,000 immunocompetent patients in the Netherlands, scheduled to finish data collection in August 2013.[30] This trial excluded the immunocompromised, thus PCV13 effects on NPP in this group will remain unclear.

The indirect effects of childhood PCV7 on carriage and IPD rates among adults are well established.[31–33] Hence, we expect childhood PCV13-related herd immunity for the 6 additional serotypes added to PCV13 to further reduce adult pneumococcal disease rates. However, pneumococcal epidemiology in immunocompromised persons is more complex than that of healthy adults. Furthermore, replacement disease (i.e., increased pneumococcal disease from nonvaccine serotypes) may preferentially occur in the immunocompromised. In addition, it is possible that PCV13 might lead to serotype shift, including novel serotypes.[34]

The results of the CDC's unpublished cost-effectiveness analysis influenced the decision to add PCV13 to the recommended regimen for immunocompromised persons.[1, 13] That analysis found the newly recommended regimen to be cost saving compared to the prior recommendation while preventing more disease. However, this analysis did not consider vaccinating with PCV13 alone. In addition, compared to our model, they modeled a greater magnitude of PCV13 effectiveness over a shorter duration and a boosting of PCV13 effectiveness with subsequent PPSV23 vaccination. Finally, they modeled decreases in both hospitalized and outpatient pneumonia, while our analysis was limited to hospitalized

pneumonia due to problems with estimating pneumococcal disease likelihood and serotype distributions in outpatient pneumonia and the relatively low cost of outpatient pneumonia compared to hospitalized pneumococcal disease.[16, 35] Their modeling choices tend to favor PCV13 more than our model's parameter values and vaccination strategies considered, accounting for the differences in results seen between analyses.

The UK analysis of PCV13 in high-risk groups, including the immunocompromised, found PCV13 unlikely to be cost-effective, driven by their base-case assumption that PCV13 did not prevent NPP.[12] If this is true, we agree that PCV13 strategies will not be favored, as shown in Figure 1. In that analysis, if PCV13 is fully effective against vaccine serotype NPP in the immunocompromised, PCV13 costs £24,296 (or ~\$38,874) per QALY gained. Our model assumes intermediate NPP effectiveness and PCV13 costs \$70,937/QALY.

This analysis has limitations. Data are lacking on PCV13 effectiveness against NPP in the immunocompromised, which may never be known from randomized trials. The magnitude of herd effects from childhood PCV13 among immunocompromised persons is also currently unknown and replacement disease is challenging to predict in this population. Surveillance data over the next several years should provide those answers.

Conclusions

This analysis suggests that one dose of PCV13 is more cost-effective for immunocompromised individuals than the previous ACIP recommendations of two doses of PPSV23 and may be more economically reasonable than the 2012 ACIP recommendations, depending on the life expectancy of the cohort. Our conclusions are sensitive to assumptions regarding PCV13 effectiveness against NPP and PPSV23 effectiveness against IPD in the immunocompromised.

Acknowledgments

Funding

This work is supported by the National Institute of Allergy and Infectious Diseases at the National Institutes of Health [R01 AI076256]

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Figure 1.

Two-way sensitivity analysis.

Graphs depict areas where vaccination strategies are favored using a \$100,000 per quality adjusted life year gained threshold for the base case analysis considering all immunocompromised persons (top) and for HIV-infected individuals (bottom) when both PPSV23 effectiveness against invasive pneumococcal disease (IPD) relative to PCV13 effectiveness (x-axis) and PCV13 effectiveness against nonbacteremic pneumococcal pneumonia (NPP) relative to its IPD effectiveness (y-axis) are simultaneously varied. PPSV23 = 23-valent pneumococcal polysaccharide vaccine, PCV13 = 13-valent pneumococcal conjugate vaccine.

Figure 2.**Probabilistic sensitivity analysis**

Cost-effectiveness acceptability curves show the likelihood that vaccination strategies will be considered cost-effective over a range of willingness-to-pay (or acceptability) thresholds when parameters are simultaneously varied over distributions in the base case scenario (all the immunocompromised, top) and in the HIV infected (bottom).

Table 1

Characteristics of Pneumococcal Disease in the Immunocompromised

Invasive Pneumococcal Disease*	Ages 18–49	Ages 50–59	Ages 60–69	Ages 70–79	Ages 80+
Invasive disease rate (per 100,000)	71.85	67.08	58.52	54.1	64.3
PPSV23 vaccine serotype coverage (%)	78.0%	73.3%	74.1%	65.8%	62.9%
PCV13 vaccine serotype coverage (%)	51.9%	48.3%	48.7%	40.8%	40.8%
Probability of outcome given invasive disease					
Meningitis	6.8%	7.2%	6.2%	3.8%	2.1%
Mortality	7.0%	10.5%	11.3%	11.6%	19.7%
Hospitalized Nonbacteremic Pneumococcal Pneumonia					
	Ages 18–44	Ages 45–64	Ages 65+		
Rate (per 100,000)	204.3	343.6	868.0		

* Source: CDC Acute Bacterial Core surveillance data, 2007–8

Table 2

Expert panel estimates of 13-valent pneumococcal conjugate vaccine effectiveness in the immunocompromised.

Years post vaccination	Invasive pneumococcal disease		Nonbacteremic pneumococcal pneumonia	
	Base	Range	Base	Range
1	50	0–80	35	0–80
3	45	0–60	32	0–60
5	35	0–50	25	0–45
10	25	0–40	18	0–36
15	5	0–35	4	0–32

Table 3

Parameter Values and Ranges Examined in Sensitivity Analyses

Description	Range			Distribution	Source
	Base case	Low	High		
Vaccine effectiveness (Delphi estimates)					
PCV13 against IPD	Base	Low range	High range	Triangular	Expert panel (Table 2)
PCV13 against NPP	Base	Low range	High range	Triangular	Expert panel (Table 2)
PPSV23 effectiveness in preventing:					
IPD	50% of base	0%	100%	Beta	Estimated
NPP	0% of base	0%	90%	Beta	Expert panel
Relative risk of infection with vaccine serotypes	1	0.9	1.1	Uniform	Table 1
Vaccine adverse events					
Duration of symptoms (days)	3	1	8	Exponential	[36]
Probability per vaccinee after first vaccination	3.2%	2.2%	4.6%	Beta	[36]
Relative risk after subsequent vaccinations	3.3	2.1	5.1	Log normal	[36]
Disability					
Excess mortality per year	0.1	0	1	Uniform	Estimated
Risk relative to base case risk	1	0.5	1.5	Uniform	Table 1 *
Risk in noninvasive pneumonia relative to IPD	0.5	0	1	Uniform	Estimated
Case-fatality odds ratio	1.5	1.3	1.8	Log normal	
Utility weights					
Immunocompromised population				Uniform	[37]
50–55 y	0.72	0.67	0.77		
55–60 y	0.69	0.64	0.74		
60–65 y	0.63	0.58	0.68		
65–70 y	0.57	0.52	0.62		
70–75 y	0.54	0.49	0.59		
75–80 y	0.52	0.47	0.57		
80–85 y	0.51	0.46	0.56		
> 85 y	0.51	0.46	0.56		
Invasive pneumococcal disease	0.2	0.1	0.5	Uniform	[37]
Hospitalized noninvasive pneumonia	0.2	0.1	0.5	Uniform	Estimate [37]

Description	Range			Source
	Base case	Low	High	
Disabled	0.4	0.2	0.6	Estimate [38]
Vaccine adverse event	0.9	0.8	0.99	Estimate [38]
Costs				
Vaccine and administration				
PPSV23	\$43	\$25	\$67	[39, 40]
PCV13	\$128	\$73	\$196	[39, 40]
Invasive pneumococcal disease				
Discharged alive				
50–64	\$24,519	base	base	[41]
65–74	\$20,416	base	base	[41]
>74	\$17,166	base	base	[41]
Died				
50–64	\$33,778	base	base	[41]
65–74	\$29,263	base	base	[41]
>74	\$20,750	base	base	[41]
Nonbacteremic pneumonia				
Discharged alive				
50–64	\$19,396	base	base	[41]
65–74	\$16,925	base	base	[41]
>74	\$13,258	base	base	[41]
Died				
50–64	\$35,408	base	base	[41]
65–74	\$28,288	base	base	[41]
>74	\$21,560	base	base	[41]

* Using meningitis rates as a proxy for disability incidence

PPSV23 = pneumococcal polysaccharide vaccine, PCV13 = pneumococcal conjugate vaccine, IPD = invasive pneumococcal disease, NPP = nonbacteremic pneumococcal pneumonia

Table 4

Cost Effectiveness Analysis Results

Base Case (life expectancy 11.7 years)					
Strategy	Incremental			Incremental Effectiveness	Incremental CE Ratio
	Cost	Effectiveness			
No vaccination	\$577.10	-	4.91677	-	-
PPSV23– 1 dose	\$586.60	\$9.50	4.91690	0.00013	(Ext Dom)
Prior recommendation	\$593.90	\$7.30	4.91691	0.00001	(Ext Dom)
PCV13 – 1 dose	\$606.10	\$12.20	4.91718	0.00041	\$70,937
Current recommendation	\$623.20	\$17.00	4.91731	0.00012	\$136,724
PCV13 – 2 doses	\$627.50	\$4.30	4.91722	–0.00009	(Dominated)

HIV Infected (life expectancy 22.5 years)					
Strategy	Incremental			Incremental Effectiveness	Incremental CE Ratio
	Cost	Effectiveness			
No vaccination	\$753.00	-	6.2088	-	-
PPSV23– 1 dose	\$761.50	\$8.50	6.20899	0.00019	(Ext Dom)
Prior recommendation	\$770.30	\$8.80	6.20900	0.00001	(Ext Dom)
PCV13 – 1 dose	\$778.90	\$8.60	6.20938	0.00058	\$44,316
Current recommendation	\$795.90	\$17.00	6.20957	0.00019	\$89,391
PCV13 – 2 doses	\$804.30	\$8.40	6.20945	–0.00013	(Dominated)