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Cost-Effectiveness of Pneumococcal Vaccination and Uptake Improvement Programs in Underserved and General Population Adults Aged < 65 years

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Abstract

Introduction: In US adults aged <65 years, pneumococcal vaccination is recommended when high-risk conditions are present, but vaccine uptake is low. Additionally, there are race-based differences in illness risk and vaccination rates. The cost-effectiveness of programs to improve vaccine uptake or of alternative vaccination policies to increase protection is unclear.

Methods: A decision analysis compared, in US black and general population cohorts aged 50 years, the public health impact and cost-effectiveness of pneumococcal vaccination recommendations, without and with a vaccine uptake improvement program, and alternative population vaccine policies. Program-based uptake improvement (base case: 12.3% absolute increase, costing \$1.78/eligible patient) was based on clinical trial data. US data informed population-specific pneumococcal risk. Vaccine effectiveness was estimated using Delphi panel and trial data.

Results: In both black and general population cohorts, an uptake improvement program for current vaccination recommendations was favored, costing \$48,621 per QALY gained in black populations (\$54,929/QALY in the general population) compared to current recommendations without a program. Alternative vaccination policies largely prevented less illness and were economically unfavorable. In sensitivity analyses, uptake programs were favored, at a \$100,000/QALY threshold, unless they improved absolute vaccine uptake <2.1% in blacks or <2.6% in the general population. Results were robust in sensitivity analyses.

Conclusions: Programs to increase adult pneumococcal vaccination uptake are economically reasonable compared to change in vaccination recommendations, and more favorable in underserved minorities than in the general population. If addressing race-based health disparities is a priority, evidence-based programs to increase vaccination should be considered.

Introduction

Goals for the Healthy People 2020 prevention agenda include disease prevention, health equity, and disparity elimination. A specific objective for reducing vaccine-preventable disease is to increase pneumococcal vaccination rates in high-risk adults aged 18–64 years, due to poor uptake in this group.(US Dept. HHS. Healthy People 2020) In 2015, only 23% of this population had ever received pneumococcal vaccination.(Williams et al., 2017) Both white and underserved minority groups had similarly low rates, but increasing uptake trends were seen only in white adults.(Williams et al., 2017) Furthermore, underserved minority adults are at greater risk for pneumococcal disease, in part due to higher prevalence of chronic health conditions conferring high pneumococcal illness risk.(Nowalk et al., 2019) Thus, improvements in vaccination uptake are needed to protect these vulnerable populations. Efforts to do so might include interventions to improve uptake of current vaccination recommendations, such as the 4 Pillars™ Practice Transformation Program, which has increased adult vaccination rates in diverse US medical practices.(Lin et al., 2014)

Alternatively, changes to national vaccination recommendations could be an option. Current pneumococcal vaccination recommendations for US adults aged <65 years are based on chronic health conditions and, as a result, are cumbersome to implement. Among adults <65-years-old with conditions that confer high pneumococcal disease risk, the immunocompromised should receive both the 23-valent pneumococcal polysaccharide vaccine (PPSV23) and the 13-valent pneumococcal conjugate vaccine (PCV13), while the non-immunocompromised should receive only PPSV23.(CDC, 2016) Less cumbersome recommendations, such as vaccinating all adults 50-years-old with one or both vaccines, could be considered. In addition, adult pneumococcal vaccination policymaking is complicated by changes in pneumococcal disease epidemiology and by risk differences in population subgroups. Since the 2010 introduction of routine childhood PCV13 use and its resulting indirect effects (i.e., herd immunity), there has been substantially less pneumococcal illness in children and adults, particularly from pneumococcal serotypes contained in PCV13.(Pilishvili, 2018)

Prior analyses suggested that pneumococcal vaccination in all adults at age 50 years could be clinically and economically reasonable, while potentially improving overall protection compared to the current vaccination recommendations, particularly in the underserved.(Sisk et al., 2003; Smith et al., 2012; Wateska et al., 2019) Moreover, changes to general population vaccination recommendations for adults may have more substantial impact in minority adults compared to the general population due to greater pneumococcal disease risk in this group. However, reductions in adult pneumococcal disease due to routine childhood PCV13 use may reduce the potential benefits of adult pneumococcal vaccination. In this study, we use decision analysis modeling to estimate the cost-effectiveness of several pneumococcal vaccination strategies in adult cohorts aged <65 years, including an intervention program to increase uptake of the current recommendations. In addition, we examine alternative age-based general population vaccination policies that could be easier to implement than the current risk-based policies. Separate analyses compare outcomes in black and general population groups to determine if there are differences in potential strategy benefits between populations.

Methods

We developed a Markov decision analysis model to estimate the public health impact and cost-effectiveness of pneumococcal vaccination strategies in hypothetical 50-year-old US black and general population cohorts throughout their remaining lifetimes. Black population data were used as a proxy for underserved minorities due to a high proportion of blacks among US underserved minorities and suboptimal accounting for underserved minority status in US epidemiologic data.(See et al., 2017) The modeled strategies included: 1) no vaccination; 2) PPSV23 for all at age 50 years; 3) PPSV23 only for individuals with immunocompromising and other high-risk conditions; 4) both PCV13 and PPSV23 for those with immunocompromising and other high-risk conditions; 5) both PCV13 and PPSV23 for all at age 50 years; 6) current Centers for Disease Control and Prevention (CDC) recommendations (both PCV13 and PPSV23 for immunocompromised individuals and sole PPSV23 use for individuals with other high-risk conditions); and 7) current CDC recommendations plus an intervention program to increase vaccination coverage. The modeled immunization intervention program was based on the 4 Pillars™ Practice Transformation Program (whose components are: convenient vaccination, patient communication, enhanced office systems, and an office immunization champion), which increased absolute adult pneumococcal vaccination rates in high-risk adults aged <65 years by 12.3% in a clinical trial.(Wateska et al., 2018)

In the cost-effectiveness analysis, the effectiveness term was quality-adjusted life-years (QALY), the product of quality-of-life utilities associated with health states and health state durations. The cost year was 2014, taking a health care system perspective and discounting future costs and effectiveness by 3% per year over a lifetime horizon.

Modeled population cohorts were segmented by chronic health status, using the 2013–14 National Health Interview Survey (NHIS) data and CDC health state definitions. CDC definitions of immunocompromising conditions include: HIV infection, immunodeficiency disorders, anatomical or functional asplenia, and chronic renal failure and nephrotic syndrome. We used CDC estimates for population likelihood of these conditions.(Harpaz et al., 2016) CDC defines other high-risk pneumococcal disease conditions as: chronic heart disease (excluding hypertension), chronic lung disease, chronic liver disease, alcoholism, diabetes mellitus, and cigarette smoking. Cigarette smokers with immunocompromising or other high-risk conditions were assigned to the appropriate health state based on the presence of those conditions. Smokers without other conditions were considered in a separate health state due to lower pneumococcal disease risk than the other high-risk illnesses, but greater than average risk. Average risk group individuals had none of those conditions. Thus, four chronic health states were modeled: average risk, average risk smoker, immunocompromised, and other conditions conferring high pneumococcal disease risk. Further detail on cohort segmentation is included in the Supplemental Material.

A schematic depiction of the Markov model is shown in Figure 1. The Markov cycle length was 1 year. For each strategy, cohorts were segmented by health status at age 50 years (as above), with yearly updates in health state distributions, accounting for death, based on NHIS data and NCHS life tables.(Arias et al., 2016) For cohorts vaccinated at age 50 years,

the vaccinated portion was assumed to be 23%, the current US pneumococcal vaccine uptake in high-risk groups.(Williams et al., 2017) This vaccination rate was also used for patients who moved from average risk to other health states, thus potentially becoming newly eligible for vaccination (in risk-based vaccination strategies) during the transition year. Regardless of initial vaccination strategy, once cohorts reached age 65 years, they received CDC-recommended vaccinations at that age (both PCV13/PPSV23) at reported uptake levels (63.6%). Cohorts had a yearly pneumococcal disease risk that was modified, if vaccinated, by age- and health state-specific vaccine effectiveness (VE) and time since vaccination. Not shown in the model diagram is a disabled health state, which could occur as a result of invasive pneumococcal disease (IPD) or hospitalized nonbacteremic pneumococcal pneumonia (NBP). Also not shown are transitions between health states and mortality due to pneumococcal disease or other causes.

Model parameters are summarized in Table 1. Age-, race-, and health state-specific IPD incidence and the likelihood of vaccine serotype-specific illness came from 2013–2014 CDC Active Bacterial Core surveillance (ABCs) data. IPD is a pneumococcal disease with a positive culture from typically sterile sites (e.g., blood and cerebrospinal fluid). ABCs data on a component of IPD, bacteremic pneumonia, were used to estimate hospitalized NBP rates using the method of Said et al.(Said et al., 2013) This method assumes that 3 cases of hospitalized NBP occur for each case of bacteremic pneumonia. Non-hospitalized or outpatient NBP was estimated under the prior assumption that 30% of all cause outpatient pneumonia is pneumococcal pneumonia.(Stoecker et al., 2016) This estimate was updated with a further risk reduction of 35.1% resulting from childhood vaccination-based herd immunity effects.(Pilishvili et al., 2017) Thus, the model assumes that 19.5% of outpatient all-cause pneumonia (i.e., $30\% * (1-31.5\%)$) is pneumococcal. Vaccine serotype likelihoods for IPD were assumed to be the same for hospitalized and outpatient NBP. Race- and health state-specific hospitalized NBP rates were derived using IPD rate ratios between health states (Supplemental Tables 1 and 2). Race-specific outpatient NBP risk was assumed to be the same across all health states (Supplemental Table 3). Hospitalized NBP mortality was assumed to be half that of IPD, and varied in sensitivity analyses.

Vaccine effectiveness was estimated from Delphi panel data (Supplemental Tables 4 & 5). In a sensitivity analysis, the PCV13 effectiveness value was adjusted using results from a randomized clinical trial evaluating its effectiveness in adults aged 65 years and older (Bonten et al., 2015) under the assumption that VE was similar in both age groups (Supplemental Table 6). Additionally, in the base case analysis, it was assumed that PPSV23 was ineffective in preventing hospitalized and outpatient NBP.(Smith et al., 2012) As this is a controversial area, scenarios where PPSV23 was effective against NBP were also performed, assuming that PPSV23 effectiveness against NBP was half that of PPSV23 effectiveness against IPD (Supplemental Table 7).

Utility values came from medical literature,(Gold et al., 1998; Jackson et al., 1999; Mangen et al., 2017; Sisk et al., 2003; Stoecker et al., 2016) pneumococcal disease costs came from the 2013–14 Nationwide Inpatient Sample (NIS), and vaccine costs were CDC private sector costs.(CDC Vaccine Price List, 2014) The intervention program cost, estimated from 4

Pillars clinical trial data, was \$1.78 (range \$0.70 - \$2.26) per eligible patient per year.(Smith et al. 2017)

In addition to the sensitivity analyses described above, one-way sensitivity analyses, individually varying parameter values over ranges shown in Table 1, and probabilistic sensitivity analyses, simultaneously varying all parameters over distributions 3000 times, tested the robustness of model results. In the probabilistic sensitivity analyses, parameter distributions were based on individual parameter characteristics. Cost parameters were fitted to gamma distributions, and probabilities and costs were fitted to beta distributions to mimic Table 1 ranges. All models and sensitivity analyses were run for the general population and the black population subgroup. Due to substantial uncertainty regarding outpatient NBP risk, we also performed analyses where outpatient NBP was not considered.

Results

Table 2 displays model public health results for vaccination strategies and their resulting frequency of cases and deaths in 50-year-old single-year cohorts over their remaining lifetimes. Compared with other strategies, current recommendations plus an intervention program to increase vaccine uptake prevented the most IPD cases and deaths in both black and general populations, regardless of assumptions regarding PPSV23 effectiveness in preventing NBP. Giving both vaccines to all 50-year-olds resulted in the fewest NBP cases in both populations, with fewer NBP cases occurring when PPSV23 was assumed effective against NBP.

In the cost-effectiveness analysis where PPSV23 was assumed ineffective against NBP (Table 3, top), current recommendations had the lowest incremental cost-effectiveness ratio, about \$44,000-\$47,000 per QALY gained for both black and general populations compared to no vaccination. Adding a program to increase current recommendation uptake modestly increased the cost per QALY gained compared to current recommendations without a program, to about \$49,000 and \$55,000/QALY gained. Compared to the uptake intervention strategy, giving all 50- year-olds both PCV13 and PPSV23 cost >\$750,000/QALY gained. Other strategies were eliminated from consideration, as recommended, due to being less effective and more expensive than other strategies or having higher incremental cost-effectiveness ratios than more effective strategies.(Cantor, 1994; Neumann et al., 2017) Health interventions costing <\$100,000/QALY gained are generally considered economically reasonable in the US.(Braithwaite et al., 2008; Neumann et al., 2014) When PPSV23 was assumed protective against NBP (Table 3, bottom), current recommendations with an uptake intervention were more strongly favored, costing \$24,000-\$27,000/QALY gained compared to competing strategies, with PCV13/PPSV23 for all 50-year-olds costing >\$1 million/QALY gained.

In one-way sensitivity analyses, the uptake intervention strategy remained favored at a \$100,000/QALY threshold with individual variation of all Table 1 parameters throughout their listed ranges. Intervention programs were favored, at a \$100,000/QALY threshold, unless they improved absolute vaccine uptake <2.1% (base case: 12.3%) in the black population or <2.6% in the general population. Removing consideration of outpatient NBP,

due to its uncertainty, had little effect on analysis results, increasing the incremental cost-effectiveness ratio of the uptake intervention strategy by about \$8000/QALY in all scenarios. Assuming PCV13 effectiveness was similar to that observed in 65+ year olds led to unchanged cost-effectiveness ratios for current recommendation strategies and higher ratios for routine PCV13 use in 50-year-olds.

In a probabilistic sensitivity analysis for the black population when PPSV23 was ineffective against NBP (Figure 2), current recommendations with the intervention program was favored if the acceptability threshold was \$50,000/QALY gained, and was favored in 92% of the model iterations at a \$100,000/QALY threshold. In similar analyses in all population and PPSV effectiveness scenarios, current recommendations with the program was favored in >50% of model iterations at thresholds \$60,000/QALY gained.

In separate analyses, the effects of more easily implemented strategies (e.g., pneumococcal vaccination for all 50-year-olds) were explored, compared to the current, more complicated, recommendations. In black populations, if vaccinating all 50-year-olds increased absolute uptake by 10% (from 23% to 33%) and PPSV23 does not prevent NBP, PPSV23 for all 50-year-olds cost \$127,000/QALY gained and PCV13/PPSV23 for all cost \$450,000/QALY. If PPSV23 prevents NBP, PPSV23 for all cost \$57,000/QALY gained and PCV13/PPSV23 for all cost >\$1 million/QALY in black populations. In the general population, assuming a 10% absolute uptake increase with age-based strategies, both PPSV23 for all and PCV13/PPSV23 for all cost slightly >\$360,000/QALY when PPSV23 was ineffective against NBP. If PPSV23 prevents NBP, PPSV23 for all cost \$120,200/QALY gained and PCV13/PPSV23 for all cost \$769,000/QALY in the general population under this scenario's assumptions.

Another scenario examined situations where an uptake intervention program was not considered due to potential infeasibility. In this analysis, PPSV23 for all at age 50 became more reasonable economically, costing \$83,300/QALY in blacks and \$139,000/QALY in the general population when giving PPSV23 to all 50-year-olds increased absolute uptake by 10%. PCV13/PPSV23 for all cost >\$360,000/QALY gained for either population in this scenario.

Discussion

This analysis found that intervention programs to increase uptake of current adult pneumococcal vaccination recommendations in adults <65 years old (PCV13 and PPSV23 for the immunocompromised; PPSV23 for other high-risk adults) were clinically and economically favorable compared to current recommendations without a program. These findings were seen regardless of the population considered and were unaffected by PPSV23 effectiveness assumptions. The intervention program strategy was more favorable in analyses limited to the black population, and its favorability was robust in sensitivity analyses. When compared to the intervention program, giving all 50-year-olds either PPSV23 alone or both PPSV23 and PCV13 were found to be unfavorable in most scenarios, either because they were more expensive and less effective than other strategies or had high costs per QALY gained.

Prior work suggested that pneumococcal vaccination for all 50-year-olds could be economically reasonable (Sisk et al., 2003; Smith et al., 2012; Smith et al., 2008) but our current analysis shows, that under most circumstances, this is no longer the case. Previous analyses were performed before changes in pneumococcal epidemiology resulting from routine childhood PCV13 vaccination occurred. Since 2010, when childhood PCV13 was first recommended, indirect effects have substantially decreased pneumococcal disease rates and markedly diminished the likelihood of PCV13 serotype disease in both children and adults. As a result, the potential public health impact of pneumococcal vaccination for all adults is less than previously projected and, from a cost-effectiveness standpoint, is less favorable. Adult vaccination now prevents less disease than previously, while vaccination costs have risen.

Pneumococcal disease risk is greater in the black population, our proxy for underserved minorities. Potential responses to address racial disparities in adult pneumococcal disease incidence could include changes in general population vaccination recommendations that disproportionately favor underserved minorities or strategies to increase vaccination rates. This analysis found that changes in recommendations (i.e., vaccination with one or both vaccines for all 50-year-olds) were economically unfavorable under base case assumptions that assume identical vaccine uptake in all strategies. However, changing from current chronic illness-based recommendations to less complex age-based recommendations could lead to increased uptake. In this scenario, if age-based vaccination increased absolute uptake by 10%, giving PPSV23 to all at age 50 had more moderate cost-effectiveness results (\$127,000/QALY, black population analysis; \$361,000/QALY, general population). However, this strategy's costs remained >\$100,000/QALY gained when compared to programs to increase current recommendation uptake, unless PPSV23 was effective against NBP.

With increasing racial diversity and less clear racial distinctions, vaccination recommendations directed along racial lines would be problematic. However, the benefit of improved implementation and uptake of public health recommendations to higher risk groups is clear. While there is some evidence that targeted interventions may be more successful in raising adult vaccination rates among specific population subgroups, (McLaughlin et al., 2019) several intervention studies have indicated that efforts to improve vaccination rates (such as through primary care practices) increased vaccine uptake and reduced racial disparities. (Humiston et al., 2011; Nowalk et al., 2008; Schwartz et al., 2006)

Our analysis has vaccination policy implications. The effectiveness and cost-effectiveness of pneumococcal vaccination strategies in adults <65 years are directly related to vaccine uptake. Intervention programs to improve current recommendation uptake are the optimal solution, with greatest public health impact at reasonable cost, if they can be broadly deployed. If broad use of intervention programs is not feasible, then changing from complex chronic illness-based vaccination to easier to implement age-based recommendations may be an option to increase pneumococcal vaccine uptake, if age-based vaccination substantially increases uptake. In scenarios where intervention programs are not considered due to potential infeasibility, PPSV23 for all at age 50 cost \$83,300/QALY gained in the black population and \$139,000/QALY in the general population if this strategy increased absolute

uptake by 10%. It is not clear if widespread use of programs to increase vaccine uptake is feasible or if age-based recommendations can increase pneumococcal vaccine uptake in adults aged <65 years. Further study of these questions is warranted.

Our findings have limitations. Mathematical models are simulations of reality and cannot replace randomized trials, which would be difficult and expensive in this situation. PCV13 effectiveness is not uniform across all serotypes, with its effectiveness against serotype 3 under debate. This analysis did not account for this variability, but if PCV13 effectiveness against serotype 3 is low, results for routine PCV13 use would be more economically unfavorable. Finally, the percentage of community-acquired pneumonia attributable to PCV13 and PPSV23 serotypes is unclear; as a result, we conducted extensive sensitivity analyses to examine broad potential ranges.

Conclusion

Low pneumococcal vaccination rates among high-risk adults <65 years of age and changing pneumococcal disease epidemiology from childhood vaccination programs have prompted reevaluation of current adult pneumococcal vaccination recommendations. Decision analysis modeling suggests that increasing adult pneumococcal vaccine uptake is important and indicates that current recommendations enhanced with programs to increase vaccination are economically reasonable, particularly for US underserved minorities. If addressing race-based health disparities is a priority, evidence-based programs to increase vaccination in underserved minorities should be strongly considered.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflict of interest: Dr. Zimmerman has no current conflicts of interest but within 3 years had research grants from Sanofi Pasteur, Merck & Co., and Pfizer on unrelated topics. Drs. Nowalk and Lin have an active research grant from Merck & Co. on an unrelated topic, and had research grants within 3 years from Pfizer and Sanofi Pasteur on unrelated topics that are no longer active. Dr. Schaffner is a member of data safety monitoring boards for Merck and Pfizer, and has served as a consultant for Dynavax, Novavax, GSK, Sanofi-Pasteur and Seqirus. Dr. Harrison is on a scientific advisory board for GSK. Other authors have no competing interests to disclose.

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Figure 1. Schematic Depiction of the Markov Model.

Blue box denotes a decision node in the model whereby a decision is made among the 7 different vaccination strategies. The green circles represent chance nodes where there are probabilities of being in a certain health state, probabilities of vaccination based on strategy and health state, and subsequently, pneumococcal disease outcomes.

immuno = immunocompromising conditions, IPD = invasive pneumococcal disease, NBP = nonbacteremic pneumococcal pneumonia

Figure 2. Probabilistic Sensitivity Analysis for Adult Pneumococcal Vaccination Strategies in the Black Population.

Results shown as a cost-effectiveness acceptability curve under the assumption that the pneumococcal polysaccharide vaccine (PPSV) is not effective against nonbacteremic pneumococcal pneumonia. The y-axis shows the likelihood that strategies would be considered cost-effective over a range of willingness-to-pay (or acceptability) thresholds on the x-axis.

immuno = immunocompromising conditions, PCV = pneumococcal conjugate vaccine, QALY = quality adjusted life year.

Table 1.

Parameter values examined in the decision model

Parameter	Value	Range	Source
Probabilities			
Vaccine Coverage			
Baseline - without program	23%	17.9% – 27.7%	(Williams, 2017)
Additional coverage with program	12.3%	0% – 25%	(Smith, 2017)
PCV13 serotype coverage			
Black population	18.6%	12.7% – 25.2%	CDC ABCs
General population	24.5%	21.1% – 28.5%	CDC ABCs
PPSV23 serotype coverage			
Black population	57.5%	47.8% – 69.6%	CDC ABCs
General population	66.9%	57.7% – 78.1%	CDC ABCs
Vaccine Effectiveness			
PCV13 against IPD	Supplemental Table 4		
PCV13 against NBP	Supplemental Table 4		
PPSV23 against IPD	Supplemental Table 5		
IPD yearly risk per 100,000			
Black population	29.5	26.2 – 33.0	CDC ABCs
General population	17.1	15.9 – 18.4	CDC ABCs
Non-bacteremic pneumonia yearly risk per 100,000			
Inpatient			
Black population	82.6	27.7 – 143.0	Estimate (Said, 2013)
General population	48.2	20.9 – 108.0	Estimate (Said, 2013)
Outpatient			
Black population	200.9	30.4 – 309.4	Estimate (Pilishvili, 2017; Stoecker, 2016)
General population	117.9	23.2 – 235.8	Estimate (Pilishvili, 2017; Stoecker, 2016)
IPD case fatality			
Black population	8%	5.7% – 10.5%	CDC ABCs
General population	10%	9.1% – 11.8%	CDC ABCs
Disability post IPD			
Black population	6%	4.5% – 8.8%	CDC ABCs
General population	6%	4.7% – 6.7%	CDC ABCs
Costs			
Vaccine			
PPSV23	\$94.51	\$48.78 – \$152.45	(CDC, 2014)
PCV13	\$180.05	\$103 – \$277	(CDC, 2014)
Administration	\$25.84	\$21.33 – \$31.18	(US HHS, 2014)
Implementation program (per eligible patient)	\$1.78	\$0.70 – \$2.26	(Smith, 2017)
Vaccine side effects (per occurrence)	\$0.76	\$0 – \$2	Estimate
IPD-discharged alive	\$26,001	\$13,000 – \$39,001	NIS
IPD-death	\$49,066	\$24,533 – \$73,599	NIS

Parameter	Value	Range	Source
Pneumonia- discharged alive	\$19,984	\$9,992 – \$29,976	NIS
Outpatient pneumonia	\$131.23	\$65.62 – \$196.85	NIS
Pneumonia-death	\$46,647	\$23,323 – \$69,970	NIS
Initial IPD symptom treatment	\$5	\$0 – \$10	Estimate
Disability (per yr)	\$14,239	\$7,947 – \$21,763	(Anderson, 2010)
Utility weights			
Disability	0.4	0.21 – 0.59	Estimate (Gold, 1998)
Hospitalization	0.2	0.11 – 0.30	(Sisk, 2003; Mangen, 2017)
Vaccine side effects	0.9	0.77 – 0.97	Estimate (Gold, 1998)
Well	0.83	0.78 – 0.88	(Sisk, 2003)
Disutility- outpatient NBP	0.004	0.002 – 0.006	(Stoecker, 2016)
Illness durations (days)			
IPD	34	17 – 51	(Sisk, 2003; Mangen, 2017)
Hospitalized pneumonia	34	17 – 51	(Sisk, 2003; Mangen, 2017)
Vaccine side effects	3	1 – 8	(Jackson, 1999)

Table 2.

Public health results of strategy options in 50-year-old cohorts over their remaining lifetimes (ordered by invasive pneumococcal disease [IPD] cases, lowest nonbacteremic pneumococcal disease [NBP] cases in bold)

Assuming PPSV23 is NOT effective vs. non-bacteremic pneumonia	IPD cases	IPD deaths	NBP cases	NBP deaths
Black Population (cohort size = 550,782)				
No vaccination	7,205	854	67,872	565
High-risk & immunocompromised get PPSV23	7,116	845	67,811	565
Current recommendations*	7,104	844	67,781	564
High-risk & immunocompromised get PCV13/PPSV23	7,104	844	67,594	562
All get PPSV23	7,077	841	67,812	565
All get PCV13/PPSV23	7,063	840	67,361	561
Current recommendations* with program to increase vaccination rates	7,060	840	67,732	563
General Population (cohort size = 4,041,014)				
No vaccination	32,802	3,813	423,270	4,389
High-risk & immunocompromised get PPSV23	32,330	3,766	423,036	4,389
Current recommendations*	32,276	3,761	422,889	4,384
High-risk & immunocompromised get PCV13/PPSV23	32,269	3,760	421,914	4,367
All get PPSV23	32,141	3,747	423,041	4,389
All get PCV13/PPSV23	32,062	3,740	420,426	4,358
Current recommendations* with program	32,027	3,736	422,684	4,381
Black Population (cohort size = 550,782)				
No vaccination	7,205	854	67,722	560
High-risk & immunocompromised get PPSV23	7,117	845	67,268	555
Current recommendations*	7,105	844	67,238	554
High-risk & immunocompromised get PCV13/PPSV23	7,105	892	67,191	553
All get PPSV23	7,078	841	66,932	553
All get PCV13/PPSV23	7,063	840	66,745	550
Current recommendations* with uptake program	7,061	840	67,031	551
General Population (cohort size = 4,041,014)				
No vaccination	32,803	3,813	422,230	4,342

Assuming PPSV23 is NOT effective vs. non-bacteremic pneumonia	IPD cases	IPD deaths	NBP cases	NBP deaths
High-risk & immunocompromised get PPSV23	32,331	3,766	420,099	4,309
Current recommendations*	32,277	3,761	419,951	4,303
High-risk & immunocompromised get PCV13/PPSV23	32,270	3,760	419,670	4,299
All get PPSV23	32,142	3,748	418,103	4,295
All get PCV13/PPSV23	32,063	3,740	416,911	4,281
Current recommendations* with uptake program	32,028	3,736	418,873	4,285

PPSV23 = 23-valent pneumococcal polysaccharide vaccine, PCV13 = 13-valent pneumococcal conjugate vaccine

* Immunocompromised get PCV13/PPSV23, other high-risk get PPSV2

Table 3.
Cost-effectiveness analysis results of policy and implementation program options*

<i>Assuming PPSV23 is NOT effective vs. non-bacteremic pneumonia</i>	Incremental Cost-Effectiveness (per QALY gained)
Black Population	
Current recommendations [†]	\$44,532
Current recommendations [†] with program to increase vaccination rates	\$48,621
AllgetPCV13/PPSV23	\$751,589
General Population	
Current recommendations [†]	\$46,706
Current recommendations [†] with program to increase vaccination rates	\$54,929
AllgetPCV13/PPSV23	\$878,556
Assuming PPSV23 IS effective vs. non-bacteremic pneumonia	
Black Population	
Comorbid, immunocompromised get PPSV23	\$20,084
Current recommendations [†]	\$21,976
Current recommendations [†] with program to increase vaccination rates	\$24,371
AllgetPCV13/PPSV23	\$1.87 million
General Population	
Comorbid, immunocompromised get PPSV23	\$19,046
Current recommendations [†] with program to increase vaccination rates	\$27,537
AllgetPCV13/PPSV23	\$162.7 million

PPSV23 = 23-valent pneumococcal polysaccharide vaccine, PCV13 = 13-valent pneumococcal conjugate vaccine

* Dominated strategies not shown

[†] Immunocompromised get PCV13/PPSV23, other high-risk get PPSV23