Published in final edited form as:

Vaccine. 2010 November 10; 28(48): 7620–7625. doi:10.1016/j.vaccine.2010.09.053.

Cost-effectiveness of dual influenza and pneumococcal vaccination in 50-year-olds

Kenneth J Smith, MD, MS, Bruce Y. Lee, MD, MBA, Mary Patricia Nowalk, PhD, RD, Mahlon Raymund, PhD, and Richard K. Zimmerman, MD, MPH

University of Pittsburgh School of Medicine, Pittsburgh, PA

Abstract

Influenza vaccination is now recommended for all ages; CDC pneumococcal polysaccharide vaccination (PPV) recommendations are comorbidity-based in nonelderly patients. We constructed a Markov model to estimate the cost-effectiveness of dual influenza and pneumococcal vaccination in 50-year-olds. Patients were followed for 10 years, with differing time horizons examined in sensitivity analyses. With 100% vaccine uptake, dual vaccination cost \$37,700/QALY gained compared to a CDC recommendation strategy; with observed vaccine uptake, dual vaccination cost \$5,300/QALY. Results were sensitive to shorter time horizons, favoring CDC recommendations. We found dual vaccination of all 50-year-olds economically reasonable. Shorter duration models may not fully account for PPV effectiveness.

Keywords

pneumococcal polysaccharide vaccine; influenza vaccine; cost-effectiveness; secondary pneumococcal pneumonia

1.0. Introduction

Pneumococcal infection (pneumococcal pneumonia, bacteremia, or meningitis) is a relatively common sequela of influenza infection, particularly among persons with underlying chronic illnesses [1]. Furthermore, an increasing proportion of adults ages 18–64 with invasive pneumococcal disease (IPD, bacteremia and meningitis) are individuals with an underlying chronic illness (52% in 1998–1999 and 59% in 2006–2007) [2]. In men and women of all ages, influenza and pneumonia continue to be a leading cause of death [3]. These outcomes can be prevented. Pneumococcal polysaccharide vaccine (PPV) prevents IPD and is universally recommended at age 65 and at any age >18 for those with underlying chronic medical conditions (HIV infection, malignancies, chronic renal disease, prior transplantation, immunodeficiency or immunosuppressive therapy, congestive heart failure, cardiomyopathy, atherosclerotic cardiovascular disease, chronic obstructive pulmonary disease, diabetes, cirrhosis, cerebrospinal fluid leak, alcohol abuse, asthma or smoking). Influenza vaccination prevents or reduces the severity of this common precursor to IPD and pneumonia.

Address correspondence to: Kenneth J. Smith, MD, MS, 200 Parkvale Building, 3520 Forbes Avenue, Pittsburgh, PA 15213; telephone: 412/647-4794; kjs8@pitt.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

U.S. PPV and influenza vaccination rates are suboptimal, particularly in persons with chronic medical conditions. For example in 2006, among persons with these conditions, only 32.5% for those aged 50–64 years and 13.5% for those aged 18–49 years [4] received pneumococcal polysaccharide vaccine (PPV) and 24.5% of 18–49 year-olds with these conditions received the influenza vaccine [5]. The relative success of age-based recommendations compared with those based on medical conditions led the Centers for Disease Control and Prevention (CDC) to recommend *universal* influenza vaccination for all persons in the United States ages 6 months and older [6]. This change in influenza vaccination policy, together with historically low vaccination rates among persons with underlying medical conditions, has raised questions regarding the suitability of current CDC recommendations for influenza vaccination (universal) and PPV (for persons with chronic medical conditions only at ages less than 65). Prior studies have shown that influenza [7] and PPV [8] individually, are reasonably cost effective at age 50. Conversely, the cost effectiveness of simultaneous administration of PPV and influenza at age 50 with continued annual influenza vaccination is unknown. In this analysis, we evaluate the cost effectiveness of PPV and influenza vaccination strategies at age 50 and compare them with current CDC recommendations.

2.0. Methods

We constructed a Markov deterministic cohort model to estimate the incremental cost effectiveness of five vaccination strategies in 50-year-old US population cohorts: no vaccination, influenza vaccination only, PPV only, vaccinate all with both vaccines (dual vaccination), and a CDC recommended strategy (influenza vaccination for all, PPV when comorbid conditions are present). Influenza vaccination only and PPV only strategies are not typical policies or recommendations; they are included for purposes of comparison only. The cohort was followed monthly for 10 years, with differing time horizons examined in sensitivity analyses. The analysis took a societal perspective. Costs are reported in 2006 US \$, and we discounted costs and effectiveness at 3% per year, as recommended by the Panel on Cost-Effectiveness in Health and Medicine [9].

Patients who receive influenza vaccine are vaccinated yearly; those receiving PPV receive it once at the start of the ten-year time frame of the model. Figure 1 is a schematic depiction of the Markov model. All individuals begin the model in the “Well” state. During each monthly cycle of the model, patients can: a) stay well or b) develop influenza or IPD without influenza, based on population risks for these illnesses and on the modification of those risks by influenza vaccine and/or PPV that may be received in a given strategy. We assumed that PPV affects only IPD, not noninvasive pneumonia. Patients may develop severe or non-severe influenza; we defined severe influenza as illness where hospitalization is required at some point during the illness, with risk based on population influenza hospitalization rates. We assumed that IPD only occurs after severe influenza, potentially biasing the model against PPV strategies. Patients with IPD can recover completely and return to Well, become disabled (based on meningitis rates), or die due to illness (not shown in the figure). Hospitalized patients with severe influenza can also become disabled; we assumed that this disability risk was the same as that seen with IPD. Patients may also die due to influenza or to other causes based on age-specific population data.

An expert panel, consisting of present and former CDC Advisory Committee on Immunization Practices members and other pneumococcal disease experts, estimated PPV effectiveness (Table 1). As previously described [8], we used the modified Delphi technique to elicit their estimates of age- and comorbidity-specific PPV effectiveness. The expert panel used case-control study data from Shapiro et al. [13] as a starting point and then extrapolated duration of effectiveness based on their judgment about likely antibody level decay. Other

probabilities and utilities were estimated from published sources and CDC data (Table 2); costs were derived from the medical literature and 2006 National Inpatient Survey data. Parameter values used in the model are summarized in Table 3. We assumed yearly influenza vaccination with 80% protection, 10% annual influenza incidence, 3.3% influenza hospitalization risk, and 10% IPD risk in hospitalized influenza patients. We also assumed equal likelihood and severity of side effects for each vaccine. For the CDC recommended vaccination strategy, we used 2006 National Health Interview Survey (NHIS) data to segment the cohort into patients with or without comorbid conditions, using methods described previously to designate patients as having immunocompromising conditions or other comorbid conditions as defined by the CDC [8]. Using these methods, 8.7% of 50-year-olds had immunocompromising conditions and 22.7% had other comorbid conditions, totaling 31.4% of 50-year-olds who were at high risk for pneumococcal disease. In the CDC recommendation strategy, only patients with these conditions receive PPV; we assumed that all persons with these conditions prior to the age of 50 were vaccinated at age 50, biasing toward CDC recommendations, and persons aged 50 to 60 who newly develop these conditions, based on age-related changes in NHIS data, are vaccinated when the condition occurs. In all strategies, we assumed that patients with immunocompromising conditions gain no benefit from PPV, consistent with published data and expert panel opinion [8;10]. This assumption was tested further in sensitivity analyses.

In the model, influenza occurs in 5-month seasons each year, with influenza vaccination yearly at the start of the season, equal monthly incidence within that time frame, and constant yearly incidence over the time horizon of the model. The base case analysis assumes 100% vaccine uptake for both vaccines; we also examine the effects of decreased uptake and differential adherence with age-based and comorbidity-based vaccine recommendations in 2006 (age-based coverage 57.1%, comorbidity-based coverage 32.5%) [4]. In these analyses, influenza vaccination was assumed to occur at age-based rates. PPV vaccination occurred at age-based rates in the dual vaccination strategy and at comorbidity-based rates in all other strategies.

All parameter values were varied individually in 1-way sensitivity analyses. Selected parameters were varied jointly in multi-way sensitivity analyses, and all parameters were varied simultaneously over distributions (as shown in Table 3) in a probabilistic sensitivity analysis. Parameter distributions were chosen based on data characteristics and level of certainty regarding that parameter value.

3.0 Results

Base case results, assuming 100% compliance with all vaccination strategies, are shown in Table 4 (top section). Total costs (i.e., vaccination and downstream illness costs) were higher and effectiveness was lower for no vaccination, influenza vaccination only and PPV only compared with CDC recommended strategy, and thus were dominated. Compared to the CDC recommended strategy, dual vaccination for all cost \$2.60 more while gaining 0.00024 QALYs (~0.1 day), or \$37,700/QALY gained. The large increase in costs for strategies not using influenza vaccine is due to costs associated with influenza disease.

Table 4 (bottom section) depicts results when observed age- and comorbidity-based vaccination rates are incorporated into the model. Greater costs for vaccination strategies are seen (\$521 vs. \$326), reflecting more illness due to decreased vaccination compliance, but there is a decrease in incremental costs between the CDC recommendation and the dual vaccination strategies, due to more PPV uptake in the dual vaccination strategy. The incremental effectiveness between these strategies is unchanged, resulting in an incremental cost-effectiveness ratio (ICER) of about \$5300 per QALY gained.

Results were most sensitive to time horizon variation, with the ICER of dual vaccination for all strategies $> \$100,000$ per QALY if the time horizon was 6 years or fewer. Results were less affected by changes in the yearly probability of influenza and in the probability of IPD with severe influenza. The effect of varying these three parameters simultaneously is shown in Figure 2. Areas within each segment depict where vaccination strategies would be favored for each of three cost-effectiveness acceptability thresholds, that is, the maximum that society would be willing to pay for a quality adjusted life year, for time horizons of 1, 5 or 10 years. The $\$50,000$ per QALY threshold is a commonly cited but controversial benchmark [10], while ratios less than $\$20,000/\text{QALY}$ are commonly considered to be a “good buy” and ratios greater than $\$100,000/\text{QALY}$ are often considered to be an expensive use of health care resources [11;12]. With 100% vaccine uptake, at any of these cost-effectiveness thresholds, dual vaccination would not be considered cost-effective at a time horizon of 5 years or fewer. Dual vaccination would be favored at a 10-year time horizon and $\$50,000$ – $\$100,000$ cost-effectiveness thresholds if the yearly influenza probability were at least 1% (Figure 2, top). When observed vaccine uptake is used in the model (Figure 2, bottom), dual vaccination is more economically favorable at 5-year horizons.

In probabilistic sensitivity analyses, we varied all parameters simultaneously, using 5000 random draws from distributions representing parameters and calculating incremental cost-effectiveness ratios from each set of values chosen. These results, depicted in Figure 3 as cost-effectiveness acceptability curves for a range of acceptability (or willingness to pay) thresholds, mirror those of the multi-way sensitivity analysis above. When a 5-year time horizon is considered, dual vaccination is unlikely to be considered cost-effective when 100% compliance is assumed but is favored more than 50% of the time at a $\$100,000/\text{QALY}$ threshold when observed vaccination rates are assumed. Over a 10-year time horizon, dual vaccination is favored in more than 97% of iterations at a $\$100,000/\text{QALY}$ threshold regardless of vaccine uptake assumptions.

4.0. Discussion

Compared to current CDC recommendations, we found that universal dual PPV and influenza vaccination at age 50 costs about $\$38,000$ per QALY gained, a value typically considered an economically reasonable use of health care resources, when 100% compliance with both age- and comorbidity-based vaccination recommendations was assumed. Due to low uptake by high risk groups, the cost of a dual vaccination strategy decreased to only $\$5,300/\text{QALY}$ when observed age- and comorbidity-based vaccination rates were included in the model. Advisory committees are moving away from comorbidity-based recommendations, as demonstrated by the recent universal influenza vaccine recommendation [6]; our work supports extending age-based vaccine recommendations to adult PPV.

We found that dual vaccination was more favorable at longer time horizons and less favorable as the model time horizon was reduced. While PPV is generally efficacious at age 50 years and effectiveness appears to persist at least 5 years [13;14], the exact duration of protection is unknown. Shapiro et. al., found the effectiveness in those vaccinated at age < 55 years to be 93% within 3 years of vaccination, 89% for 3 to 5 years after vaccination and 85% after 5 years [14]. Studies of antibody response to pneumococcal vaccination show an initial substantial rise, followed by a decline over the first year, generally reaching a plateau between 2 and 5 years later for most serotypes; the plateau value is higher than that found in vaccine-naïve persons [15]. This analysis highlights the importance of considering longer-term vaccination effects; models considering relatively short time horizons, which do not account for the entire duration of PPV effectiveness, will overestimate the incremental cost-

effectiveness ratio of combined PPV and influenza vaccination strategies, therefore biasing analyses against dual vaccination strategies.

Effects of revaccination are a concern that arises when considering initial PPV at age 50 potentially followed by revaccination at age 65 years. Data show a good safety profile for PPV revaccination, although local reactions increase modestly over initial vaccination rates [15;16]. Revaccination effectiveness is unknown in the general population. The immunogenicity of PPV revaccination is controversial because of the potential for tolerance to the vaccine [13;15;17–19]. If tolerance develops, it is likely to decrease as the revaccination interval increases. Whether tolerance is a significant factor at a 15-year vaccination interval (age 50 to 65 years) is unknown. Revaccination was not considered in our model, a potential limitation, because our cohort begins at age 50 and is followed for 10 years.

Our analysis has several other limitations. Because PPV effectiveness in pneumococcal disease prevention is unclear, we used an expert panel to estimate age-, duration-, and comorbidity-specific vaccine effectiveness. For IPD rates, we used CDC ABCs data, thus the validity of the model results depends on how closely these rates correspond to true population rates; our results may not apply to populations at higher or lower risk. Secondly, childhood vaccination with the 7-valent pneumococcal conjugate vaccine has caused significant declines in adult illness from pneumococcal serotypes contained in that vaccine [20]. We used ABCs data to model decreased PPV serotype coverage as each cohort ages; future work using dynamic transmission modeling or agent-based models could provide more reliable estimates and account for future vaccine developments, including use of the 13-valent pneumococcal conjugate vaccine recently licensed for children. The possibility exists that 13-valent pneumococcal conjugate vaccination might reduce both IPD and noninvasive pneumonia, and not including this possibility in our analysis is a limitation. However, including adult pneumococcal conjugate vaccination strategies in future analyses awaits further data on its protective efficacy in adults, including efficacy against noninvasive pneumonia. It should also be noted that the adult conjugate vaccination, due to its effects on pneumococcal colonization, could have herd immunity effects that decrease pneumococcal disease incidence, while PPV was no such effect.

Our analysis is consistent with prior work by ourselves and others showing that PPV is clinically and economically reasonable in 50-year-olds regardless of the presence or absence of comorbid conditions [8;21–23]. Despite these data, recommendations to routinely vaccinate 50 year- olds have not been made. This study further strengthens consideration of routine PPV use in these individuals.

We conclude that both the current CDC recommendations and dual vaccination with annual influenza vaccine and PPV, starting at age 50 years for all persons, are reasonably cost effective. Under certain conditions, such as a short time horizon and 100% vaccine uptake, the current CDC policy is most favored from clinical and economic standpoints. However, given the duration of protection likely afforded by PPV and less-than-perfect vaccine recommendation compliance, longer time horizons should be considered and observed vaccination rates should be accounted for. With these considerations in place, dual vaccination with PPV at age 50 years and influenza annually is quite favorable economically, supporting a change in vaccination policy.

Acknowledgments

This study was supported by the National Institute of Allergy and Infectious Diseases, Grant No. R01AI076256. Its contents are the responsibility of the authors and do not necessarily reflect the official views of the NIH.

Abbreviations

PPV	Pneumococcal polysaccharide vaccine/vaccination
CDC	Centers for Disease Control and Prevention
IPD	Invasive pneumococcal disease
ABCs	Active Bacterial Core Surveillance
NIS	National Inpatient Survey

Reference List

1. McCullers JA. Insights into the Interaction between Influenza Virus and Pneumococcus. *Clinical Microbiology Reviews*. 2006 Jul; 19(3):571–82. [PubMed: 16847087]
2. Pilishvili T, Lexau C, Farley MM, et al. Sustained Reductions in Invasive Pneumococcal Disease in the Era of Conjugate Vaccine. *The Journal of Infectious Diseases*. 2010 Jan 10; 201(1):32–1. [PubMed: 19947881]
3. Deaths, percent of total deaths, and death rates for the 15 leading causes of death in 5-year age groups, by race and sex. 2006. http://www.cdc.gov/nchs/data/dvs/LCWK1_2006pdf
4. Center for Disease Control and Prevention. Self-reported pneumococcal vaccination coverage trends 1989 – 2008 among adults by age group, risk group, race/ethnicity, health-care worker status, and pregnancy status, United States, National Health Interview Survey (NHIS). http://www.cdc.gov/flu/professionals/vaccination/pdf/NHIS89_08ppvxtrendtabpdf 2008 Available from: URL: http://www.cdc.gov/flu/professionals/vaccination/pdf/NHIS89_08ppvxtrendtab.pdf
5. Centers for Disease Control and Prevention. Self-reported influenza vaccination coverage trends 1989 – 2008 among adults by age group, risk group, race/ethnicity, health-care worker status, and pregnancy status, United States, National Health Interview Survey (NHIS). http://www.cdc.gov/flu/professionals/vaccination/pdf/NHIS89_08fluvxtrendtabpdf 2008 Available from: URL: http://www.cdc.gov/flu/professionals/vaccination/pdf/NHIS89_08fluvxtrendtab.pdf
6. Centers for Disease Control and Prevention. ACIP Provisional Recommendations for the Use of Influenza Vaccines. <http://www.cdc.gov/vaccines/recs/provisional/downloads/flu-vac-mar-2010-508pdf> 2010 March 2 [cited 2010 Mar 9]; Available from: URL: <http://www.cdc.gov/vaccines/recs/provisional/downloads/flu-vac-mar-2010-508.pdf>
7. Maciosek MV, Solberg LI, Coffield AB, Edwards NM, Goodman MJ. Influenza vaccination health impact and cost effectiveness among adults aged 50 to 64 and 65 and older. *Am J Prev Med*. 2006 Jul.;72–9. [PubMed: 16777545]
8. Smith KJ, Zimmerman RK, Lin CJ, et al. Alternative strategies for adult pneumococcal polysaccharide vaccination: a cost-effectiveness analysis. *Vaccine*. 2008 Jan.26:1420–31. [PubMed: 18272262]
9. Gold, M.; Siegel, J.; Russell, L.; Weinstein, M. *Cost-Effectiveness in Health and Medicine*. New York: Oxford University Press; 1996.
10. Jackson, LA.; Neuzil, KM. Pneumococcal polysaccharide vaccines. In: Plotkin, SA.; Orenstein, WA.; Offit, PA., editors. *Vaccines*. 5. Saunders Elsevier Inc; 2008. p. 569–604.
11. Braithwaite RS, Meltzer DO, King JT Jr, Leslie D, Roberts MS. What does the value of modern medicine say about the \$50,000 per quality-adjusted life-year decision rule? *Med Care*. 2008; 46(4):349–56. [PubMed: 18362813]
12. Laupacis A, Feeny D, Detsky AS, Tugwell PX. How attractive does a new technology have to be to warrant adoption and utilization? Tentative guidelines for using clinical and economic evaluations. *CMAJ*. 1992 Feb 15; 146(4):473–81. [PubMed: 1306034]
13. Jackson, LA.; Neuzil, KM. Pneumococcal polysaccharide vaccines. In: Plotkin, SA.; Orenstein, WA.; Offit, PA., editors. *Vaccines*. 5. Saunders Elsevier Inc; 2008. p. 569–604.
14. Shapiro ED, Berg AT, Austrian R, et al. The protective efficacy of polyvalent pneumococcal polysaccharide vaccine. *N Engl J Med*. 1991; 325(21):1453–60. [PubMed: 1944423]

15. Musher DM, Manoff SB, Liss C, et al. Safety and Antibody Response, Including Antibody Persistence for 5 years, after Primary Vaccination or Revaccination with Pneumococcal Polysaccharide Vaccine in Middle-Aged and Older Adults. *The Journal of Infectious Diseases*. 2010 Feb 15; 201(4):516–24. [PubMed: 20092407]
16. Jackson LA, Benson P, Sneller VP, et al. Safety of revaccination with pneumococcal polysaccharide vaccine. *Journal of the American Medical Association*. 1999; 281:243–4. [PubMed: 9918479]
17. O'Brien KL, Hochman M, Goldblatt D. Combined schedules of pneumococcal conjugate and polysaccharide vaccines: is hyporesponsiveness an issue? *Lancet Infect Dis*. 2007; 7(9):597–606. [PubMed: 17714673]
18. Davidson M, Bulkow LR, Grabman J, et al. Immunogenicity of pneumococcal revaccination in patients with chronic disease. *Arch Intern Med*. 1994; 154(19):2209–14. [PubMed: 7944842]
19. Manoff SB, Liss C, Caulfield MJ, et al. Revaccination with 23-Valent Pneumococcal Polysaccharide Vaccine Induces Elevated and Persistent Functional Antibody Responses in Adults Aged >65 Years. *J Infect Dis*. 2010 Feb 15; 201(4):525–33. [PubMed: 20088694]
20. Lexau CA, Lynfield R, Danila R, et al. Changing epidemiology of invasive pneumococcal disease among older adults in the era of pediatric pneumococcal conjugate vaccine. *Journal of the American Medical Association*. 2005 Oct 26; 294(16):2043–51. [PubMed: 16249418]
21. Sisk JE, Whang W, Butler JC, Sneller VP, Whitney CG. 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):960–8. [PubMed: 12809452]
22. Gable CB, Holzer SS, Engelhart L, et al. Pneumococcal vaccine: Efficacy and associated cost savings. *Journal of the American Medical Association*. 1990; 264(22):2910–5. [PubMed: 2232086]
23. Plans-Rubio P. Pneumococcal polysaccharide vaccine: cost-effectiveness recommendations in adults. *Expert review of pharmacoeconomics & outcomes research*. 2005; 5(5):541. [PubMed: 19807582]
24. Khazeni N, Hutton DW, Garber AM, Hupert N, Owens DK. Effectiveness and cost-effectiveness of vaccination against pandemic influenza (H1N1) 2009. *Ann Intern Med*. 2009; 151(12):829–39. [PubMed: 20008759]
25. Lee BY, Brown ST, Cooley PC, et al. A computer simulation of employee vaccination to mitigate an influenza epidemic. *Am J Prev Med*. 2010; 38(3):247–57. [PubMed: 20042311]
26. Lee BY, Tai JH, Smith KJ. The timing of influenza vaccination for older adults (65 years and older). *Vaccine*. 2009; 27(50):7110–5. [PubMed: 19786135]
27. Jefferson TO, Rivetti D, DiPietrantonj C, Rivetti A, Demicheli V. Vaccines for preventing influenza in healthy adults. *Cochrane Database of Systematic Review*. 2007:2.
28. IOM report: patient safety--achieving a new standard for care. *Acad Emerg Med*. 2005 Oct; 12(10):1011–2. [PubMed: 16204148]
29. Gold MR, Franks P, McCoy KI, Fryback DG. Toward consistency in cost-utility analyses: using national measures to create condition-specific values. *Med Care*. 1998 Jun; 36(6):778–92. [PubMed: 9630120]
30. Sisk JE, Whang W, Butler JC, Sneller VP, Whitney CG. Cost-effectiveness of vaccination against invasive pneumococcal disease among people 50 through 64 years of age: role of comorbid conditions and race. *Ann Intern Med*. 2003; 138(12):960–8. [PubMed: 12809452]
31. Centers for Disease Control and Prevention National Immunization Program Vaccines for Children. CDC price list. 2010. www.cdc.gov/nip/vfc/cdc_vac_price_list.htm [cited 2010 May 27]

Figure 1.
The Markov model. *For simplicity of illustration, transitions for deaths in the model due to illness or other causes are not shown.*

Figure 2. Multi-way sensitivity analysis

The top portion depicts results when 100% compliance with vaccination strategies is assumed; the bottom depicts results using observed age-based (57.1%) and comorbidity-based (32.5%) vaccine uptake. In each portion, graph segments depict areas where vaccination strategies are favored with variation of yearly influenza risk and the risk of developing IPD while hospitalized with influenza for the listed cost-effectiveness thresholds and model time horizons.

Figure 3. Probabilistic sensitivity analysis

Cost-effectiveness acceptability curves for the dual vaccination strategy at 5-year and 10-year time horizons. Each plot depicts the likelihood (on the y-axis) that dual vaccination would be considered cost-effective given a cost-effectiveness willingness to pay (or acceptability) criterion (on the x-axis) for the time horizon and vaccine uptake assumptions shown.

Expert Panel Estimates of PPV Effectiveness (%) in Preventing Vaccine-Susceptible Invasive Pneumococcal Disease

Table 1

Vaccinee age/health:	Healthy 50-year-olds *		Immunocompromised (all ages)	
	Base case	Range Low High	Base case	Range Low High
Years post vaccination				
1	93	80 95	0	0 25.5
3	89	74 94.5	0	0 18
5	85	66 90	0	0 5
7	60	40 75	0	0 5
10	20	0 30	0	0 2.5
15	0	0 20	0	0 2.5

* Patients with other comorbid conditions vaccinated at these ages had the same base case and high range values, low range was decreased 25% relative to listed values

Table 2

Characteristics of Invasive Pneumococcal Infections Based on the Active Bacterial Core Surveillance System*

	Age 50–54	Age 55–59	Age 60–64
Invasive pneumococcal disease rates (per 100,000 population per year)			
Total	15.8	19.1	21.2
No comorbid or immunocompromising conditions	5.9	8.1	9.9
≥1 comorbid conditions	50.2	52.6	42.7
≥1 immunocompromising conditions	82.7	55.3	53.3
Disease outcome rates (per 100,000 population per year)			
Meningitis	1.3	1.4	1.5
Mortality	2.4	2.6	3.1
PPV vaccine serotype coverage (%)			
Total	77.3%	75.2%	77.9%
No comorbid or immunocompromising conditions	82.5%	78.8%	84.6%
≥1 comorbid conditions	78.1%	75.8%	78.0%
≥1 immunocompromising conditions	72.4%	65.4%	68.5%

* Source: Active Bacterial Core Surveillance 2003–04, Centers for Disease Control and Prevention

Table 3

Parameter Values and Ranges Examined in Sensitivity Analyses

Description	Range			Distribution	Source
	Base case	Low	High		
Yearly influenza risk	10%	2.7%	21.4%	Beta	[24–27]
Hospitalization risk with influenza	3.3%	1.7%	5.7%	Beta	[24]
IPD risk in hospitalized influenza patients	10%	7.5%	12.5%	Beta	[24]
Influenza vaccine effectiveness	80%	56%	96%	Beta	[27]
PPV effectiveness	Base	Low range	High range	Triangular	Table 1
Relative risk of pneumococcal infection with PPV serotypes [†]	1	0.9	1.1	Uniform	Table 2
Vaccine adverse events					
Duration of symptoms (days)	3	1	8	Exponential	[16]
Probability	3.2%	2.20%	4.6%	Beta	[16]
Disability					
Excess mortality per year	0.1	0	1	Uniform	Estimated
Relative risk [†]	1	0.5	1.5	Uniform	Table 2 *
IPD case-fatality odds ratio for patients with immunocompromising or other comorbid conditions	1.5	1.3	1.8	Log normal	[28]
Utility weights					
50–54 y	0.92	0.86	0.98	Uniform	[29]
≥55 y	0.88	0.82	0.94	Uniform	[29]
Invasive pneumococcal disease	0.2	0.1	0.5	Uniform	[30]
Influenza - severe	0.2	0.1	0.5	Uniform	Estimate [30]
Influenza – non-severe	0.8	0.7	0.9	Uniform	Estimate [29]
Disabled	0.4	0.2	0.6	Uniform	Estimate [29]
Vaccine adverse event	0.9	0.8	0.99	Uniform	Estimate [29]
Costs					
Influenza vaccine and administration	\$15	\$9	\$23	Gamma	[31]
PPV and administration	\$30	\$15	\$50	Gamma	[30]
Influenza					
Hospitalized	\$4,723	\$4,397	\$5,075	Gamma	NIS
Outpatient	\$167	\$129	\$209	Gamma	NIS

Description	Range			Distribution	Source
	Base case	Low	High		
Invasive pneumococcal disease					
Discharged alive	\$24,519	\$22,607	\$26,971	<i>Gamma</i>	NIS
Died	\$33,778	\$30,400	\$37,156	<i>Gamma</i>	NIS
Disability (per year)	\$10,000	\$8,000	\$10,000	<i>Gamma</i>	Estimate

*

Using meningitis rates as a proxy for disability incidence

†

Relative risk compared to Table 2 values

IPD = invasive pneumococcal disease, PPV = pneumococcal polysaccharide vaccine, NIS = National Inpatient Survey, NA = not applicable

Table 4
Cost, Effectiveness, and Incremental Cost-Effectiveness Ratios for Vaccination Strategies*

Strategy	Cost	Incremental Cost	Effectiveness (QALY)	Incremental Effectiveness (QALY)	Incremental Cost Effectiveness Ratio (ICER)
<i>100% vaccine uptake</i>					
CDC recommendations	\$325.85	-	7.58793	-	-
Flu only	\$328.44	\$2.59	7.58758	-0.00035	(Dominated)
Flu and PPV	\$335.12	\$9.28	7.58817	0.00024	\$37,700
PPV only	\$765.80	\$430.68	7.56878	-0.01939	(Dominated)
None	\$779.31	\$444.19	7.56806	-0.02011	(Dominated)
<i>Age- and comorbidity-based actual vaccine uptake</i>					
CDC recommendations	\$521.49		7.57926		
Flu and PPV	\$522.79	\$1.31	7.57950	0.00024	\$5,312
Flu only	\$523.96	\$1.17	7.57914	-0.00036	(Dominated)
PPV only	\$771.60	\$248.80	7.56847	-0.0103	(Dominated)
None	\$779.31	\$256.51	7.56806	-0.01144	(Dominated)

* All values are per person affected by the decision