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Cost-Effectiveness of Pneumococcal and Influenza Vaccination Standing Order Programs

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Abstract

Objective—Despite the benefits of vaccination and guidelines for their use, influenza and pneumococcal vaccination rates remain below the 90% goal set by Healthy People 2010 for persons aged 65 years and older. Standing order programs (SOPs) authorize vaccination administration without physician orders. Here we examine the cost-effectiveness of SOPs to improve both pneumococcal and influenza vaccination rates in outpatient settings for individuals aged 65 years and older.

Study Design—Decision analysis-based cost-effectiveness analysis.

Methods—A Markov model was constructed to estimate the incremental cost-effectiveness of outpatient SOPs for PPSV and influenza vaccination in hypothetical 65-year-old and older US population cohorts. Vaccination rate improvement data were obtained from the medical literature. CDC Active Bacterial Core surveillance data and U.S. national databases were used to estimate costs and outcomes.

Results—SOPs cost $14,171 per quality adjusted life-year (QALY) gained compared to no program from a third-party payer perspective. In one-way sensitivity analyses, the SOP strategy cost less than $50,000/QALY if SOPs increased absolute vaccination rates by 4% or more (base case: 18%), annual SOP costs were less than $21 per person (base case: $4.60), or annual influenza incidence was 4% or more (base case: 10%). Model results were insensitive to other individual parameter variation, and were supported by a probabilistic sensitivity analysis.

Conclusions—SOP used to improve PPSV and influenza vaccination rates in outpatient settings is a promising and economically favorable investment, with cost-effectiveness analysis results remaining robust to parameter variation over clinically plausible ranges.

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Pneumonia and influenza continue to be among the leading causes of death in the United States (U.S.).[1] Influenza is estimated to cause an average of 200,000 hospitalizations and 36,000 deaths annually.[2] Because individuals 65 years and older are at increased risk for influenza complications, seasonal influenza vaccination is important. Invasive pneumococcal disease (IPD), which includes bacteremia and/or infection of the meninges, joints, bones, or body cavities, is a relatively common outcome following influenza, particularly among individuals with chronic illnesses.[3,4] Each year, pneumococcus causes about 500,000 cases of pneumonia, 50,000 cases of bacteremia, 3,000 cases of meningitis, and up to 7,000 - 12,500 deaths.[5]

The Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC) has recommended influenza vaccination for all persons aged six months and older; pneumococcal polysaccharide vaccine (PPSV) is recommended for all persons aged 65 years and older, and for persons with chronic medical conditions aged 18 years and older.[6] Among persons aged 65 years and older in 2010, the annual seasonal influenza vaccination rate was 63.6%,[7] while 59.4% reported ever receiving PPSV.[8] Despite the benefits of adult vaccination and the availability of usage guidelines, vaccination rates for seasonal influenza and PPSV remain below the Healthy People 2020 goal of 90% for each vaccine among persons aged 65 years and older.[9]

Standing orders authorize nurses and pharmacists to administer vaccinations according to a protocol approved by an institution or physician without an individual order or examination by the physician.[10] The Task Force on Community Preventive Services reviewed the evidence for standing orders and strongly recommended them.[11,12] Several studies have reported the successful use of SOPs.[13-15] Because both PPSV and influenza vaccination are recommended for persons aged 65 years and older, co-administration is another strategy to raise vaccination rates. Although Smith et al. found that dual PPSV and influenza vaccination of all 50-year olds was economically reasonable,[4] the cost-effectiveness of SOPs for vaccination of PPSV and influenza vaccine administered in outpatient settings for persons aged 65 years and older is unknown.

Methods

A Markov model was constructed to estimate, from the third-party payer and societal perspectives, the incremental cost-effectiveness of an SOP intervention for PPSV and influenza immunization. The intervention is implementation of SOPs in outpatient practice, and the comparison is between a base case of current practice (including some SOP-using practices) and broader SOP implementation in primary care practices for hypothetical cohorts of 65 year old and older patients in the U.S.

Figure 1 presents a state transition diagram illustrating the Markov model, which was adapted from a prior study.[4] During each monthly cycle, a person may stay well, develop non-severe influenza, severe influenza, or IPD without influenza. Severe influenza was defined as requiring inpatient treatment while non-severe influenza was defined as those cases not requiring inpatient therapy. Inpatients with severe influenza may develop IPD, become disabled, or die due to influenza or other causes. We assumed that patients with

non-severe influenza would recover and not go on to worse outcomes, depicted by arrows from illness states to the well state. In the model, influenza occurs in 5-month seasons each year, with annual influenza vaccination at the start of each season, equal monthly incidence within that time frame, and constant yearly incidence over time. PPSV was given, based on the likelihood of vaccination, when patients entered the model; we assumed that no PPSV was given later in the model and no repeat PPSV vaccination. Patients who develop IPD may recover without disability, become disabled, or die. The cohort was followed monthly over their lifetimes until death. Age-specific mortality not associated with illness was based on U.S. mortality tables.[16]

Generally, U.S. national databases and published sources were used to estimate costs and outcomes, which were discounted at an annual rate of 3%.[17,18] PPSV effectiveness was estimated based on an expert panel, consisting of present and former CDC ACIP members or liaisons and other pneumococcal disease experts (Table 1), as described previously.[19] Because PPSV is generally thought to have little or no effectiveness against non-bacteremic pneumonia,[20,21] we conservatively assumed no PPSV effectiveness against pneumonia. IPD data were obtained from the CDC's Active Bacterial Core (ABC) surveillance data (Table 2).[22] Costs were derived from the medical literature, Medicare physician fees,[23] and 2006 Nationwide Inpatient Sample (NIS) data. Hospitalization charges from NIS data were adjusted using cost-to-charge ratios from the Medicare cost report.[24] Parameter values used in the model are summarized in Table 3. In addition, the following assumptions were included in the model: (1) equal likelihood and severity of side effects for each vaccine; (2) patients with immuno-compromising conditions gain no benefit from PPSV[4,19,25]; (3) 60.1% vaccine uptake for both vaccines, based on NHIS data[26], (4) yearly SOP costs remain constant through the lifetime of the modeled patient cohort, and (5) vaccination rates remain constant at the improved rate resulting from SOP use.

The numerator of the cost-effectiveness ratio represents per patient change in resources associated with the SOP including vaccine and administration costs, disease costs, and SOP costs. Details about the estimation of those costs are published elsewhere.[4,15,21,24,27,28] SOP costs are derived from time and motion studies of an inpatient program,[15] and thus may over- or under-estimate the costs of outpatient programs; for this reason, these costs were varied widely in sensitivity analyses. SOP costs in the model are per person in contact with the implemented program, not per person vaccinated. The denominator of cost-effectiveness ratio represents differences in adjusted quality of life years (QALYs) resulting from increased vaccination rates due to SOP use. QALYs account for changes in both duration and quality of life, and are the product of time spent in a health state and the quality of life utility value for that health state summed overall health states and over time.

In addition to the base case cost-effectiveness analysis, one-way sensitivity analyses and Monte Carlo probabilistic sensitivity analyses were performed to examine the robustness of cost-effectiveness estimates. One-way sensitivity analyses were conducted for all model parameters in Table 1 varying them over their listed ranges to evaluate influence on model results. In these analyses, the parameter of interest was varied while all other variables remained unchanged from their base case values. The probabilistic sensitivity analysis varied all input parameters simultaneously across their ranges; 10,000 model iterations were

performed over specific distributions selected based on the level of parameter value certainty. TreeAge Pro 2009 (TreeAge Software, Williamstown, MA) was used to perform the analysis.

Results

From a third-party payer perspective, SOPs cost $14,171 per QALY gained compared to no SOP when the SOP-related absolute increase in vaccination rate was at its base case level, 18% (Table 4, top). When the societal perspective taken, which adds costs that patients incur while seeking or receiving care,[18] SOPs cost $12,718 per QALY gained. We report all subsequent results from the third-party payer perspective.

In one-way sensitivity analyses, individual variation of the vaccination rate increase due to SOPs (Table 4) showed that the incremental cost-effectiveness ratio remained less than $50,000 per QALY gained if absolute vaccination rates increased ≥4%. The effects of varying other selected parameter values in one-way sensitivity analyses are shown in Figure 2. Of these, program costs and annual influenza probability had the greatest effects on results, however SOPs cost less than $50,000/QALY if program costs were not greater than $21 per person per year (base case = $4.60[15]) or annual influenza incidence was ≥4% (base case 10%). Varying PPSV effectiveness had little impact on model results, given the relatively low incidence of invasive pneumococcal disease when compared to influenza incidence. With PPSV effectiveness at its low range estimate (Table 1), SOPs cost $14,694/QALY gained, $523 more than the base case value; if PPSV was completely ineffective, SOPs cost $15,577/QALY. Individual variation of the other listed parameters had little effect on model results.

In the probabilistic sensitivity analysis, which varied all parameter values simultaneously over distributions, SOPs were favored in greater than 82% of model iterations if the willingness-to-pay acceptability threshold was $50,000/QALY or more. In this analysis, SOPs were cost saving in 9.6% of iterations and were more costly and less effective than no program in 0.7% of the model iterations.

Discussion

We found that SOPs for influenza and pneumococcal vaccination were cost-effective under a wide range of assumptions. When using the frequently cited $50,000 per QALY gained acceptability threshold, which probably underestimates willingness to pay for health care gains in the US,[19,29,30] $21 per person spent on program costs or 4% absolute increases in vaccination rates would still meet this criterion. The analysis was relatively insensitive to variation of other parameters, and simultaneous variation of all parameters in a probabilistic sensitivity analysis showed a high likelihood that SOPs would be favored.

Missed opportunities for vaccination during outpatient visits contribute to low vaccination rates and unnecessary disease burden. Failure to assess and offer vaccines at visits, as well as low rates of preventive care visits contribute to missed opportunities to vaccinate.[31,32] SOPs are a powerful way to reduce missed opportunities and to raise immunization rates. The CDC has recommended SOPs for adult vaccination since 2000.[10] However, the Center

for Medicare & Medicaid Services (CMS) prohibited SOPs for all medications until 2002 when CMS allowed SOPs for influenza and pneumococcal polysaccharide vaccines.[33] The ACIP,[10] the Task Force for Community Preventive Services,[12] and the Southern California Evidence-Based Practice Center-RAND[34] have endorsed SOPs for improving immunization rates.

However, only 42% of primary care physicians who immunized adults in their practices reported consistent use of SOPs.[35] Factors associated with consistent use of SOPs include awareness about CDC/CMS stance on standing orders policies, physician perception about the power of SOPs, staffing levels (i.e., number of assistants to help each clinician), and use of electronic medical records (EMRs).[35,36] Record keeping and tracing of vaccination status is facilitated by the EMR. In some settings, the EMR can send alerts, make ordering and billing of vaccinations easy, or pull the most recent vaccination status into the nursing, thereby facilitating the use of SOP protocols by nursing personnel.[36] CMS has incentives for EMR usage which may further facilitate SOPs.

Given the SOPs are effective in raising vaccination rates and economically reasonable, why are they not used more? Physicians and practice managers may be unaware of the economics of SOPs, which we estimate will cost less than $5 per person per year to implement; in contrast, the administration fee by Medicare for influenza and pneumococcal vaccines is about $21, depending on the locale.[37] Several benefits can occur through SOP use, including reduced office visits for respiratory infections, decreasing both patient illness burden and strains on office manpower and flow during the influenza season. Another benefit is that adult immunization is a quality measure that can lead to bonus payments[38] in some settings. The balance between SOP cost and the reimbursement that can occur through their use appears sufficient to justify SOPs.

Another possible reason for limited SOP use is unfamiliarity with resources. Peer-reviewed SOP toolkits, suggested related resources and protocols are available at www.immunizationed.org [39] and protocols for SOP for various vaccines are available at www.immunize.org/standingorders.

Strengths and Limitations

Although inpatient SOP costs have been published for PPSV,[15] to our knowledge, this is the first paper examining the cost-effectiveness of outpatient SOPs for both PPSV and influenza vaccination. The results of our study should facilitate planning by health care providers and administrators, office managers, insurers and government officials.

Limitations include a number of estimated variables as well as SOP cost and cost-effectiveness estimates that may not remain stable during these times of substantial change in health care. In addition, certain parameters, such as vaccine effectiveness estimates, are controversial.[40-45] For these reasons, we varied all parameters in sensitivity analyses, finding, in particular, that PPSV effectiveness values had little influence on model results. Models based on national data provide estimates but do not necessarily reflect the costs in a particular locale. We assume that yearly SOP costs, and the improved vaccination rates that occur through their use, remain constant, thus our analysis will not be correct if SOP costs or

effects change significantly over time. Finally, although a new vaccine, the pneumococcal conjugate vaccine is now licensed in the United States,[46] the ACIP has thus far declined to make recommendations for its routine use in adults; for this reason we have not considered it in our analysis.

With these limitations in mind, we conclude that SOP implementation for both PPSV and influenza vaccination in outpatient settings, targeting patients aged 65 and older, is a promising and economically favorable investment, with cost-effectiveness analysis results remaining robust to parameter variation over clinically plausible ranges.

Take-Away Points

We examined the cost-effectiveness of using standing order programs, which allow influenza and pneumococcal vaccination without a physician order, to improve the suboptimal vaccination rates in older US populations

- Administering pneumococcal and influenza vaccines in outpatient settings under standing order programs was economically favorable and can impact public health through higher vaccination rates.
- Results were robust to parameter variation over clinically plausible ranges.
- In a time of health care reform and physician shortages, our results support wider use of standing order programs.

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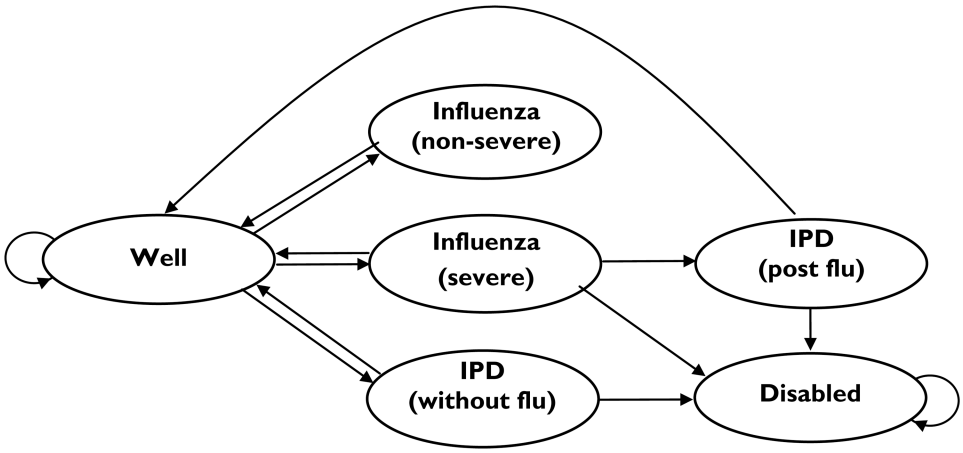

Figure 1. Web Archive

The State Diagram of Markov Model for Influenza and Pneumococcal Polysaccharide Vaccines in Persons ≥65 Years of Age. Not shown in the diagram: patients in all states can transition to the Dead stage, based on age- and/or disease-specific mortality.

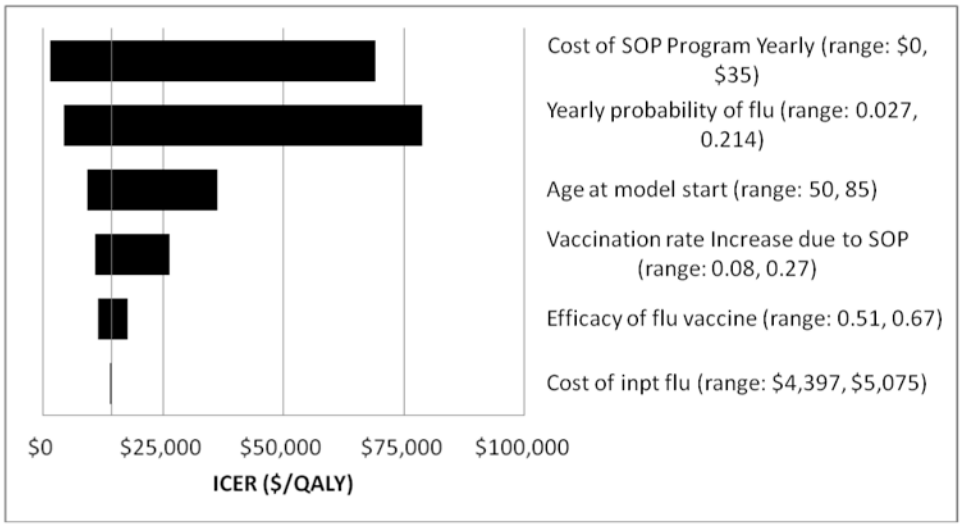

Figure 2. Tornado Diagram at SOP vs. No SOP for Influenza and Pneumococcal Polysaccharide Vaccines in Persons ≥65 Years of Age

Table 1

Expert panel estimates of PPSV effectiveness against susceptible pneumococcal serotypes

Years post vaccination		Range	
	Base Case (%)	Low (%)	High (%)
1	80	60	90
3	73	50	83
5	58	31	80
7	33	13	48
10	0	0	10
15	0	0	10

Table 2

Characteristics of invasive pneumococcal infections based on active bacterial core surveillance system (ABC)

	Age 65-69	Age 70-79	Age 80+	Source
IPD rates (per 100,000 per year)	38.7	38.7	38.7	2009 ABCs
IPD outcome rates (per 100,000 per year)				
Mortality	6.56	6.56	6.56	2009 ABCs
Meningitis	1.61	1.27	1.26	2007-8 ABCs
PPSV vaccine serotype coverage (%)	74.1	65.8	62.9	2007-8 ABCs

Source: Centers for Disease Control and Prevention. Active Bacterial Core surveillance (ABCs).[22]

IPD: invasive pneumococcal disease; PPSV: pneumococcal polysaccharide vaccine

Table 3

Parameter values and ranges examined in sensitivity analyses

Description	Base Case	Range		Distribution	Source
		Low	High		
Yearly influenza risk (%)	10	2.7	21.4	Beta	[45,47-50]
Hospitalization risk with influenza (%)	3.1	1.7	5.7	Beta	[51]
IPD risk in hospitalized influenza patients (%)	10	7.5	12.5	Beta	[47]
Influenza vaccine effectiveness (%)	59	51	67	Beta	[50]
PPSV effectiveness	Table 1	Table 1 low range	Table 1 high range	Triangular	Table 1
Relative risk of pneumococcal infection with PPSV serotypes[b]	1	0.9	1.1	Uniform	Table 2
Impact of SOP on vaccination rate (%)	18	8	27	Beta	[52]
Vaccine adverse events					
Duration of symptoms (days)	3	1	8	Exponential	[40]
Probability (%)	3.2	2.2	4.6	Beta	[40]
Disability					
Excess mortality per year	0.1	0	1	Uniform	Estimated
Relative risk[b]	1	0.5	1.5	Uniform	Table 2[a]
IPD case-fatality odds ratio for patients with immunocompromising or other comorbid conditions	1.5	1.3	1.8	Log normal	[53]
Utility weights					
Age ≥ 65 years	0.84	0.68	1	Uniform	[54]
Invasive pneumococcal disease (applied for 34 days)	0.2	0.1	0.5	Uniform	[27]
Influenza – hospitalized (applied for 14 days)	0.2	0.1	0.5	Uniform	Estimate [27]
Influenza – outpatient (applied for 5 days)	0.8	0.7	0.9	Uniform	Estimate [54]
Disabled (applied for remaining lifetime)	0.4	0.2	0.6	Uniform	Estimate [54]
Vaccine adverse event (applied for 3 days)	0.9	0.8	0.99	Uniform	Estimate [54]
Costs (in 2006 US Dollars)					
Influenza vaccine and administration	$32	$26	$40	Gamma	[21,28]
PPSV and administration	$43	$33	$60	Gamma	[27]
Standing order program cost per patient (per year)	$4.60	$0	$35	Gamma	Estimate [15]
Influenza					

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Description	Base Case	Range		Distribution	Source
		Low	High		
Hospitalized	$4,723	$4,397	$5,075	Gamma	NIS
Outpatient	$167	$129	$209	Gamma	NIS
Invasive pneumococcal disease					
Discharged alive					
Age 65-74 years	$20,416	$18,374	$22,458	Gamma	NIS
Age ≥ 75 years	$17,166	$15,449	$18,883	Gamma	NIS
Died					
Age 65-74 years	$29,263	$26,337	$32,189	Gamma	NIS
Age ≥ 75 years	$20,750	$18,675	$22,825	Gamma	NIS
Disability (per year)	$10,000	$8,000	$10,000	Gamma	Estimate [4]

IPD: invasive pneumococcal disease; PPSV: pneumococcal polysaccharide vaccine; NIS, National Inpatient Survey.

[a] Using meningitis rates as a proxy for disability incidence;

[b] Relative risk compared to Table 2 values.

Table 4

Incremental Cost-Effectiveness Ratios for SOP by Base Case (18%) and in Sensitivity Analyses on Vaccination Rate Increases for Influenza and Pneumococcal Polysaccharide Vaccines in Persons ≥65 Years of Age

Strategy	Increase in Vaccination Rate (%)	Cost (C)	Incremental Cost (ΔC)	Effectiveness (E, QALY)	Incremental Effectiveness (ΔE)	ICER (ΔC/ΔE)
No SOP	18	$740.47		11.4605		
SOP		$831.45	$90.99	11.4669	0.0064	$14,171
No SOP	0	$740.47		11.4605		
SOP		$803.25		11.4605		(Dominated)
No SOP	1	$740.47		11.4605		
SOP		$804.80	$64.33	11.4608	0.0004	$180,429
No SOP	2	$740.47		11.4605		
SOP		$806.36	$65.89	11.4612	0.0007	$92,395
No SOP	3	$740.47		11.4605		
SOP		$807.92	$67.45	11.4615	0.0011	$63,052
No SOP	5	$740.47		11.4605		
SOP		$811.04	$70.57	11.4623	0.0018	$39,579
No SOP	10	$740.47		11.4605		
SOP		$818.86	$78.40	11.464	0.0036	$21,982
No SOP	20	$740.47		11.4605		
SOP		$834.62	$94.15	11.4676	0.0071	$13,196

QALY: quality adjusted life year; ICER: Incremental cost-effectiveness ratio ($/QALY); SOP: standing order program.