Budget-Impact Analysis of Alternative Herpes Zoster Vaccine Strategies: A U.S. HMO Perspective

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ABSTRACT

BACKGROUND: A herpes zoster vaccine has been approved by the FDA for use in prevention of herpes zoster in individuals who are aged 50 years or older. The Advisory Committee on Immunization Practices (ACIP) recommends vaccination only in individuals who are aged 60 years and older.

OBJECTIVES: To (a) estimate the overall budget and health impact of either the introduction of a new vaccination strategy (individuals over the age of 50 years vs. individuals over the age of 60 years) within a hypothetical health plan or simply an increase in coverage within the population aged 60 years and over and (b) discern what effect copayments and changes to copayments have on the health plan's budget.

METHODS: A decision-analytic economic model was developed to inform managed care decision makers of the potential effect on costs and outcomes associated with the use of the herpes zoster vaccine for prevention of herpes zoster (i.e., simple zoster or shingles). The model took a U.S. payer perspective. The number of eligible patients entering the model was estimated by considering the age distribution of the plan population and the percentage of patients contraindicated for vaccination (i.e., those who were immunocompromised or who had a history of anaphylactic/anaphylactoid reaction to gelatin, neomycin, or any other component of the vaccine). Eligible patients were vaccinated based on the projected uptake rates among the unvaccinated population in 2 possible vaccination scenarios: (1) a vaccination strategy in which only individuals over age 60 years can be vaccinated and (2) a vaccination strategy in which individuals over age 50 years can be vaccinated. Vaccination was assumed to reverse the age-related decline in immunity against zoster. The population vaccinated each year was estimated based on the uptake rates (percentage of the eligible unvaccinated that are vaccinated) required to reach a target annual coverage (percentage ever vaccinated). Patients could experience costs and outcomes related to vaccination or related to herpes zoster. Specifically, vaccination could cause adverse events that would require the use of health care resources. Patients who developed zoster could experience postherpetic neuralgia or develop nonpain complications that would require the use of health care resources. Vaccine costs, zoster cases (with and without postherpetic neuralgia or nonpain complication), and vaccine-related adverse events for the 2 vaccination scenarios were estimated for each budget year.

RESULTS: For a managed care organization population of 5 million members, the model estimated that a vaccination program that included patients over age 50 years instead of a program limiting vaccination to those over age 60 years was associated with a decrease in the number of patients developing zoster (2,372-3,392 cases avoided over 5 years). Annual incremental per-member-per-month (PMPM) costs associated with this vaccination program change were estimated to range from $0.08 to $0.14. When the vaccination program was kept at age 60 years and over and coverage was increased, the model estimated that the annual incremental PMPM costs ranged from $0.04 to $0.06. Differences in costs were driven primarily by vaccination costs. The results of the scenario analyses showed that lower vaccination costs because of the application of copayments for a managed care organization reduced the magnitude of the total cost increase associated with the increase in uptake.

CONCLUSIONS: Vaccinating individuals aged 50 to 59 years with the herpes zoster vaccine would likely have an impact on a health plan's budget because of the expected increase in the total number of individuals being vaccinated in the population, with limited cost savings because of fewer cases of herpes zoster. Higher coverage of vaccinations resulted in a greater increase in total costs each year. However, increasing coverage would also result in a decrease in the number of individuals developing zoster and associated postherpetic neuralgia and nonpain complications over the next 5 years.

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What is already known about this subject

- The herpes zoster vaccine has been approved by the FDA for use in prevention of zoster in individuals aged 50 years or older.
- The Advisory Committee on Immunization Practices (ACIP) recommends vaccination in individuals aged 60 years and older. ACIP continues to evaluate new duration of protection data to make recommendations for the optimal age of vaccination and the need for revaccination.
- Coverage rates for herpes zoster vaccination are slightly above 20% among adults aged over 60 years (20.1% in 2012) and are negligible among adults aged 65 years and over.

What this study adds

- This study estimates that the budget impact of vaccinating individuals for herpes zoster prevention at age 60 years and above (ACIP recommendation) or age 50 years and above (based on FDA approval), as well as the likely clinical outcomes from a health plan perspective.
- The base-case findings provide evidence that changes in herpes zoster vaccine uptake results in an annual budget impact ranging from $2,601,963 to $8,9696,715 ($0.04-$0.14 per member per month) for health plans with 5 million members.
- Over a 5-year period, the changes in herpes zoster vaccine uptake would result in the number of cases of herpes zoster avoided ranging from 1,020 to 3,392.

Herpes zoster, also known as zoster or shingles, is a painful blistering rash that can occur in individuals who have previously been infected with the varicella zoster virus, which causes chicken pox. The varicella zoster virus reactivates later in an individual's life as herpes zoster. The most common complication is postherpetic neuralgia (PHN), which can last for several months to years.[1] Other nonpain (e.g., ocular, neurologic, and dermatologic) complications can also occur.[2]

Zoster and its complications are associated with medical care costs and losses in quality of life.[3] Yawn et al. (2009) found that the average direct medical cost to treat herpes zoster was $707 for individuals aged < 50 years and $2,006 for individuals aged ≥ 70 years (2006 U.S. dollars), resulting in an estimated $1.1 billion in direct medical costs to treat zoster in the United States.[2] Quality of life losses for individuals with zoster are associated with the severity of pain.[4] Estimates from van Hoek et al. (2009) predicted that individuals with mild, moderate, and severe pain have reduction in quality of life of 9%, 29%, and 68%, respectively.[5]

Zostavax is a live-attenuated single dose varicella zoster virus (herpes zoster vaccine) vaccine and is currently the only vaccine available for the prevention of zoster. The Shingles Prevention Study demonstrated that a single dose of zoster vaccine significantly reduced the incidence of herpes zoster by 51.3% and the incidence of PHN by 66.5% in adults aged 60 years or older over a 4-year period.[6] A recent study by Morrison et al. (2014) presented additional years of efficacy (up to 11 years), showing that efficacy does not completely wane until after year 10.[7] In the Zoster Efficacy and Safety Trial, a single dose of zoster vaccine significantly reduced the incidence of herpes zoster by 69.8% in adults aged 50-59 years over a 2-year period.[8] The herpes zoster vaccine has been approved by the U.S. Food and Drug Administration (FDA) for use in prevention of zoster in individuals aged 50 years and older. However, in 2011 the Advisory Committee on Immunization Practices (ACIP) recommended vaccination in individuals aged 60 years and older. This decision was reaffirmed in 2013. ACIP considered all available evidence (epidemiology, duration of protection, supply, and cost-effectiveness) at the time of its decisions.[9] Cost-effectiveness analysis has shown that vaccination for herpes zoster becomes more cost-effective as the age of vaccination increases.[10] ACIP continues to evaluate new evidence, including new duration of protection data, in order to make recommendations for the optimal age of vaccination and the need for revaccination.[9]

More recent data, however, indicate that the incidence of zoster has increased over time across all ages. In comparison with incidence rates from about 10 years ago and a more recent study, incidence rates have increased from 4.2 to 6.7 per 1,000 persons among adults aged 50-59 years.[3,11] Similarly, the incidence rate of herpes zoster in the placebo group of the Zoster Efficacy and Safety Trial (conducted from 2007 to 2010) was 6.6 per 1,000 persons among adults aged 50-59 years.[8]

Managed care organizations in the United States need to make coverage decisions informed by health economic studies that depict the potential impact on costs and outcomes associated with the use of vaccines. In this study, a budget-impact model has been developed to inform managed care decision makers of the potential impact on costs and outcomes associated with the use of vaccination for prevention of zoster when offering zoster vaccination at age 60 years and above (ACIP recommendation) and at age 50 years and above (based on FDA approval).[9]

Methods

Model Structure

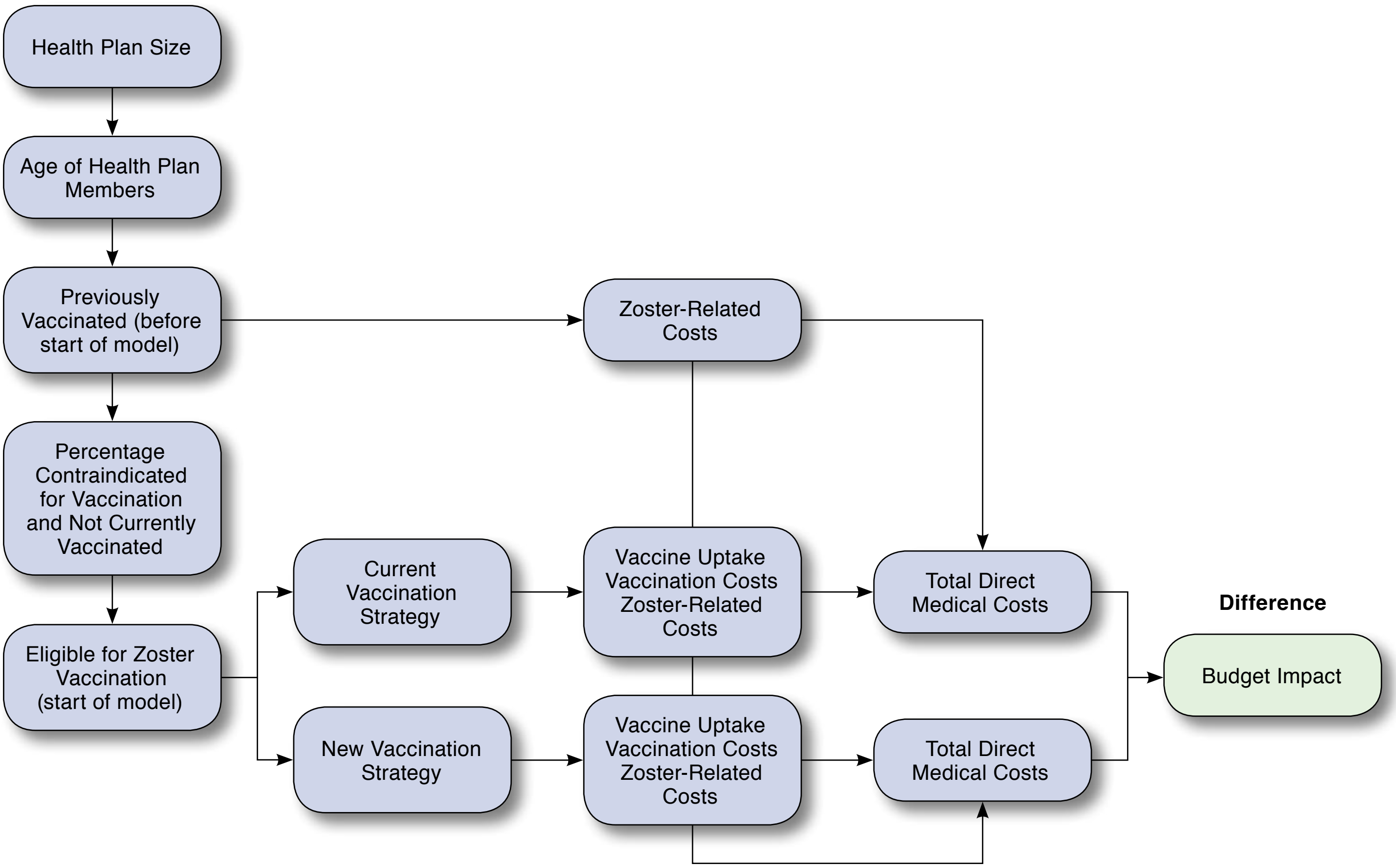
A budget-impact model was constructed in Microsoft Excel (Microsoft Corp., Redmond, WA) to estimate the effect on costs and health outcomes from a potential change in the recommended age of vaccination for the prevention of zoster from age 60 years and older to age 50 years and older. The model allowed for a comparison of 2 vaccination strategies: (1) individuals over age 60 years were eligible for vaccination and (2) individuals over age 50 years were eligible for vaccination. The model estimated the costs and outcomes of each strategy for a hypothetical health plan of 5 million individuals (Figure 1).

The model analyzed the annual zoster vaccination-related and zoster treatment-related expenditures of the hypothetical health plan over a 5-year period. Specifically, the model estimated the vaccine-specific effect on (a) vaccine acquisition and administration costs, (b) vaccine-related adverse events experienced and their related costs, and (c) zoster-related events (zoster cases, PHN, and nonpain complications) and their related costs. Population-level costs and outcomes then were estimated on the basis of the distribution of individuals by vaccination status (unvaccinated or vaccinated, time since vaccination, and age at vaccination); costs; resource use; adverse events; and mortality for the 2 vaccination strategies, using the methods described in the following subsections.

Population

The size of the health plan was assumed to be 5 million members in order to represent a large U.S. insurer.[12] The model used age groups to define the age distribution of the plan (e.g., ages 45-49 and ages 50-54). The age distribution was estimated using the breakdown for private insurers that is seen in the Medical Expenditure Panel Survey (MEPS) 2011 Full Year Person-Level File and the population estimates from the U.S. Census Bureau.[13,14] The population within each age group was assumed to be evenly distributed among the ages in that range to distribute the population into individual ages from these age groups. For example, there was the same number of individuals who were aged 45 years as there were aged 46 years. Table 1 presents the population parameters used by the model.

FIGURE 1 Budget-Impact Model Structure



Each year, those individuals in the eligible-for-vaccination population were either vaccinated (based on vaccine uptake rates) or remained unvaccinated. The population eligible for vaccination in year 1 was estimated by considering the following:

- Current age of the health plan members (to estimate number of members over age 50 years).
- Percentage of individuals who were contraindicated for the herpes zoster vaccine.
- Percentage of health plan members who were already vaccinated.

For subsequent years, the population eligible for vaccination was estimated by considering the following:

- Aging within the health plan (e.g., individuals who were aged 49 years in year 1 would be aged 50 years in year 2 of the model).
- Deaths within the health plan.
- Number of individuals already vaccinated.

Vaccine Uptake Scenarios

Table 2 presents the annual vaccine uptakes among the unvaccinated individuals that were used to estimate the number of individuals being vaccinated each year. The model compared the budget impact of 4 hypothetical vaccine uptake scenarios for the currently available herpes zoster vaccine: 3 for the ACIP recommendation of vaccinating only individuals over age 60 years (steady coverage 60+, higher uptake 60+, and lower uptake 60+) and 1 for the vaccination strategy based on FDA approval in which individuals over age 50 years can be vaccinated (lower uptake 50+). A scenario with higher uptakes for the 50+ analysis was omitted because of the unrealistic coverage of vaccine that would result from higher uptakes (35% coverage for 50+).

For each uptake scenario, the yearly uptakes were derived using the following steps:

1. Yearly vaccine coverages were estimated for all 5 years using a linear estimate between the current coverage (percentage already vaccinated) for each age group (20%

TABLE 1 Model Inputs

Parameter	Value	Sources and/or Assumptions
Population inputs		
Plan members	5,000,000	Assumption
Current percentage of lives covered, by age group in years		Derived based on the private insured population seen in the 2011 Full Year Person-Level File of the AHRQ Medical Expenditure Panel Survey.[13] Estimates of the U.S. population from the U.S. Census Bureau are used to split the AHRQ population in the modeled age groups.[14]
≤44	51.85	
45-49	7.44	
50-54	8.42	
55-59	7.67	
60-64	5.32	
65-69	4.72	
70-74	2.45	
74-79	1.84	
80-84	1.42	
85-89	0.93	
90-94	0.54	
99-99	0.15	
Percentage contraindicated for the herpes zoster vaccine	0.0952	Estimated based on the prevalence of immunodeficiency in a general population from Boyle and Buckley (2007)[27] and the percentage having an anaphylactic reaction as seen in the Zostavax prescribing information (2016).[28] Assume same percentage for all age groups
Percentage already vaccinated		
Aged 50-59 years	0.0	Based on Williams et al. (2014)[29]
Aged 60+ years	20.0	Based on Williams et al. (2014)[29]
Average number of years since a vaccination for those vaccinated before year 1 of the model	3 years	Assumption
Probability of zoster-related death, %		
Age group		
50-59	0.0	CDC's compressed mortality file, Series 20, 1999-2012[19]
60-69	0.007	
70-74	0.013	
75-79	0.039	
80-84	0.031	
85+	0.186	
Vaccination cost, $		
Vaccine price	173.98	CDC's vaccine price list (2014)[20]
Administration fee	25.08	The Essential RBRVS; CPT 90471 (immunization administration)[21]
Patient copayment for vaccine	0.00	Assumption
Vaccine adverse event rates and costs		
Injection-site reaction		
Probability, %		
50-59	63.60	Zostavax prescribing information (2016)[28]
60+	48.00	Zostavax prescribing information (2016)[28]
Cost to treat	$0.00	Assumption[a]
Headache		
Probability, %		
50-59	9.40	Zostavax prescribing information (2016)[28]
60+	1.40	Zostavax prescribing information (2016)[28]
Cost to treat	$0.00	Assumption[a]
Allergic reaction[b]		
Probability, %		
50-59	0.01	Assumption[b]
60+	0.01	Zostavax prescribing information (2016)[28]
Cost to treat	$7,219.70	Healthcare Cost and Utilization Project,[22] adjusted to 2014 dollars using medical component of Consumer Price Index[23]

TABLE 1 Model Inputs *(continued)*

Parameter	Value	Sources and/or Assumptions
Pain in the extremity		
Probability, %		
50-59	1.30	Zostavax prescribing information (2016)[28]
60+	0.80	Zostavax prescribing information (2016)[28]
Cost to treat	$0.00	Assumption[a]
Acute zoster-only treatment cost per case, $		
Age group		
50-54	660.22	Yawn et al. (2009),[2] adjusted to 2014 dollars using medical component of Consumer Price Index[23]
55-59	651.41	
60-64	643.34	
65-69	873.95	
70-74	870.92	
75-79	875.68	
80-84	922.31	
85+	1,734.26	
PHN treatment cost per case, $		
Age group		
50-54	1,254.40	Yawn et al. (2009)[2], adjusted to 2014 dollars using medical component of Consumer Price Index[23]
55-59	1,254.40	
60-64	2,765.07	
65-69	2,765.07	
70-74	6,437.81	
75-79	6,437.81	
80-84	6,437.81	
85+	6,437.81	
Nonpain complications treatment cost per case, $		
Age group		
50-54	6,493.45	Yawn et al. (2009),[2] adjusted to 2014 dollars using medical component of Consumer Price Index[23]
55-59	6,493.45	
60-64	5,976.43	
65-69	5,976.43	
70-74	6,735.19	
75-79	6,735.19	
80-84	6,423.56	
85+	6,423.56	

[a]Cost to treat injection-site reactions, headache, and pain in the extremity were assumed to be negligible to the health plan and therefore set to zero.
[b]Rate for individuals aged 60+ years was assumed to be the same as the rate for individuals aged 50-59 years.
AHRQ = Agency for Health Care Research and Quality; CDC = Centers for Disease Control and Prevention; CPT = Current Procedural Terminology; PHN = postherpetic neuralgia; RBRVS = Resource-Based Relative Value Scale.

for the age 60 and over group; 0% for the age 50 and over group) and the hypothetical coverage by year 5 of the model for each age group.

2. Yearly uptake rates were estimated by calibrating the model. Microsoft Excel's built-in solver function was used to determine the uptake rates needed to equate the coverages (percentage of patients who had never received the herpes zoster vaccine) assumed for each year.

The budget impact of a change in vaccination recommendation (60+ to 50+) was estimated by comparing the outcomes of each 60+ uptake scenario with the 50+ uptake scenario. These comparisons gave a range of possible budget impacts that a change to the vaccination recommendation could have on a health plan. Comparisons of the 60+ uptake scenarios (steady coverage 60+ vs. lower uptake 60+ and higher uptake 60+ vs. lower uptake 60+) were also analyzed to estimate what effect changes in uptake would have on a health plan's budget in the absence of a change in vaccination age strategy.

TABLE 2 Vaccine Uptake Among Those Unvaccinated and Overall Coverage

Age Group (Years)	Age-Specific Vaccine Uptake for Each Modeled Year Among the Unvaccinated (Resulting Overall Coverage[a])[22]				
	Year 1	Year 2	Year 3	Year 4	Year 5
Projected Steady Coverage Age 60+ Years (Steady Coverage 60+)					
Represents a steady level of vaccine coverage in the population aged 60 years and older in absence of vaccination recommendation for population aged 50 years and older (ACIP recommendation)					
Derivation: 20% currently vaccinated and remains steady at 20% over 5 years; same percentage of unvaccinated individuals who are vaccinated each year (uptake) is applied for every age group for a specific year					
50-59[b]	0.00% (0.00%)	0.00% (0.00%)	0.00% (0.00%)	0.00% (0.00%)	0.00% (0.00%)
60+[b]	1.51% (20.00%)	2.08% (20.00%)	2.01% (20.00%)	1.95% (20.00%)	1.89% (20.00%)
Total coverage 50+	10.38%	10.67%	10.94%	11.19%	11.42%
Projected Higher Uptake, Age 60 Years and Over (Higher Uptake 60+)					
Represents an increase in vaccine coverage in the population aged 60 years and older in absence of vaccination recommendation for population aged 50 years and older (ACIP recommendation)					
Derivation: 20% currently vaccinated and 35% vaccinated by year 5 (coverage rate is assumed to increase linearly); same percentage of unvaccinated individuals who are vaccinated each year (uptake) is applied for every age group for a specific year					
50-59[b]	0.00% (0.00%)	0.00% (0.00%)	0.00% (0.00%)	0.00% (0.00%)	0.00% (0.00%)
60+[b]	5.21% (23.00%)	6.27% (26.00%)	6.72% (29.00%)	7.19% (32.00%)	7.68% (35.00%)
Total coverage 50+	11.94%	13.89%	15.90%	17.97%	20.08%
Projected Lower Uptake, Age 60 Years and Over (Lower Uptake 60+)					
Represents a lower increase in vaccine coverage in the population aged 60 years and older than in the higher uptake 60+ scenario in the absence of vaccination recommendation for population aged 50 years and older (ACIP recommendation)					
Derivation: 20% currently vaccinated and 28% vaccinated by year 5 (coverage rate is assumed to increase linearly); same percentage of unvaccinated individuals who are vaccinated each year (uptake) is applied for every age group for a specific year					
50-59[b]	0.00% (0.00%)	0.00% (0.00%)	0.00% (0.00%)	0.00% (0.00%)	0.00% (0.00%)
60+[b]	3.48% (21.60%)	4.27% (23.20%)	4.44% (24.80%)	4.60% (26.40%)	4.77% (28.00%)
Total coverage 50+	11.21%	12.39%	13.60%	14.82%	16.06%
Projected Lower Uptake, Age 50 Years and Over (Lower Uptake 50+)					
Represents the introduction of vaccination in the population aged 50-59 years (FDA approval)					
Derivation: Assumes overall coverage for all those aged 50 years and over will reach 28% by year 5 (increasing linearly). Assumes that additional coverage will come from uptake in vaccination in the population aged 50-59 years					
50-59[b]	5.61% (5.61%)	5.50% (10.30%)	6.09% (14.81%)	6.75% (19.13%)	7.49% (23.27%)
60+[b]	3.48% (21.60%)	4.27% (23.65%)	4.44% (26.01%)	4.60% (28.65%)	4.77% (31.52%)
Total coverage 50+	13.90%	17.43%	20.95%	24.48%	28.00%

[a]*Overall coverage is for the populations within each age range (50-59 and 60+).*
[b]*Percentage presented for an age group is applied to each individual age within that age group. For example, the uptake rate for an individual aged 60 years is 5.21%, and the uptake for an individual aged 61 years is 5.21% in year 1 for both vaccination strategies.*
ACIP = Advisory Committee on Immunization Practices; FDA = U.S. Food and Drug Administration.

Incidence of Herpes Zoster and Herpes Zoster-Related Complications

The model estimated the number of zoster-related events for unvaccinated individuals by applying an age-specific incidence rate for each event. For the vaccinated population, the model used age-specific and time-since-vaccination-specific efficacy parameters that were applied to the incidence rates of the unvaccinated population to estimate the number of zoster-related events for vaccinated individuals.

The age-specific natural unvaccinated incidence of zoster was estimated by using a linear extrapolation of the incidence data, grouped by ages, presented by Johnson et al. (2015).[11] This study looked at the burden of zoster in an immunocompetent population. Similarly, the age-specific probabilities of PHN, obtained from Yawn et al. (2007) were estimated using a linear extrapolation of age-group specific data.[15] The linear extrapolation was completed by using a "step" method in which the age-group value was used for each age within the age group to create a dataset. A linear curve was then fit to these data. Probabilities of nonpain complications for individuals with zoster were taken from Yawn et al.[15] For the current study, these probabilities were not extrapolated further. The age-specific risk estimates are presented in Appendix A (available in online article). The equations used to estimate these incidences are as follows:

- Zoster incidence by age

$$Z_{Age} = 0.00017 \times Age - 0.00209$$

- PHN incidence by age

$$PHN_{Age} = Z_{Age} \times (Age \times 0.0049 - 0.2086)$$

- Nonpain complications incidence by age

$$Nonpain\ Comp_{Age} = \begin{cases} Z_{Age} \times 0.081\ if\ 50 \le Age \le 69 \\ Z_{Age} \times 0.121\ if\ 70 \le Age \le 79 \\ Z_{Age} \times 0.157\ if\ Age \ge 80 \end{cases}$$

The equation key is as follows: Z_{Age} is the incidence of zoster at the current age of an individual; *Age* is the current age of an individual; PHN_{Age} is the probability of PHN at the current age of an individual; and $Nonpain\ Comp_{Age}$ is the probability of nonpain complications at the current age of an individual.

Age-specific vaccine efficacy rates against zoster were taken from clinical trial data.[6,8,16] Vaccine efficacy against PHN and nonpain complications was not assumed beyond the protection afforded by reducing the incidence of herpes zoster. The durability of efficacy was modeled by assuming that efficacy wanes over time. The methods used to estimate vaccine waning efficacy over time have been described previously by Li et al. (2015), whose models were estimated based on data from individuals aged ≥60 years.[17] For the purpose of this budget-impact model, the equations were recalculated to include data from those individuals aged ≥50 years.[8] Model A assumes a decline in vaccine efficacy as a function of aging and time since vaccination. Model B assumes the initial decline in vaccine efficacy observed during the first year, with subsequent decline because of aging only. Models A and B fit the data equally well. There is no clear biological evidence as to whether Model A or Model B may be more plausible. Therefore, an average of these 2 models was used as a base-case scenario to attempt to alleviate uncertainty, since the resulting vaccine durability model falls between Model A and Model B. Model A and Model B were examined separately in the sensitivity analysis. The models are as follows:

- Model A (assumes an accelerated waning over time)

$$VE = 1 - e^{-1.5945 + 0.0349 \times (Age - 49) + 0.0344 \times YearSinVac}$$

- Model B (assumes a drop in year 1 waning only)

$$VE = 1 - e^{-1.3713 + (0.0405 \times YearSinVac + 0.205 \times I_{>1Year})VacAge > 60}$$

Alternative assumptions for vaccine efficacy and durability were considered in scenario analysis. The equation key is as follows: *VE* is vaccine efficacy; *Age* is the current age of an individual; *YearSinVac* is the number of years since vaccination; $_{VacAge} > 60$ limits use of parameter to only when current age is greater than 60; and $I > 1\ year$ is if first year of vaccination then value is 0, otherwise the value is 1.

Adverse Events

Because of the risk of adverse events from vaccination, adverse events and the costs of treating them were estimated and included in the model. Specifically, those adverse events that could be directly linked to the vaccine were included, such as injection-site reaction, headache, allergic reaction (anaphylaxis), and pain in the extremity (Table 1). All adverse events and the costs associated with treating them were assumed to occur during the year of vaccination.

Mortality

The model considered mortality for the zoster-free population and the population with zoster (increased risk of mortality). All-cause mortality rates from the National Vital Statistics Life Tables (2011 data) were used to estimate age-specific probability of death for the zoster-free population.[18] The probability of zoster death was derived from the death rates for zoster-related death as seen in the Centers for Disease Control and Prevention's (CDC) compressed mortality file "Underlying Cause-of-Death."[19] The probabilities of zoster-related death are presented in Table 1. The probability estimates for all-cause mortality were applied to the zoster-free population. The increased risk of mortality for the population with zoster was estimated by additively applying the probability of zoster-related death to the all-cause mortality estimates.

Costs

The cost of the herpes zoster vaccine was obtained from the CDC vaccine price list.[20] An administration fee also was added to each administration. The fee was the price of immunization administration from the Essential Resource-Based Relative Value Scale (RBRVS), Current Procedural Terminology (CPT) 90471.[21] For the main analyses, the patient copayment was assumed to be zero. Alternative copayments were considered in sensitivity analyses.

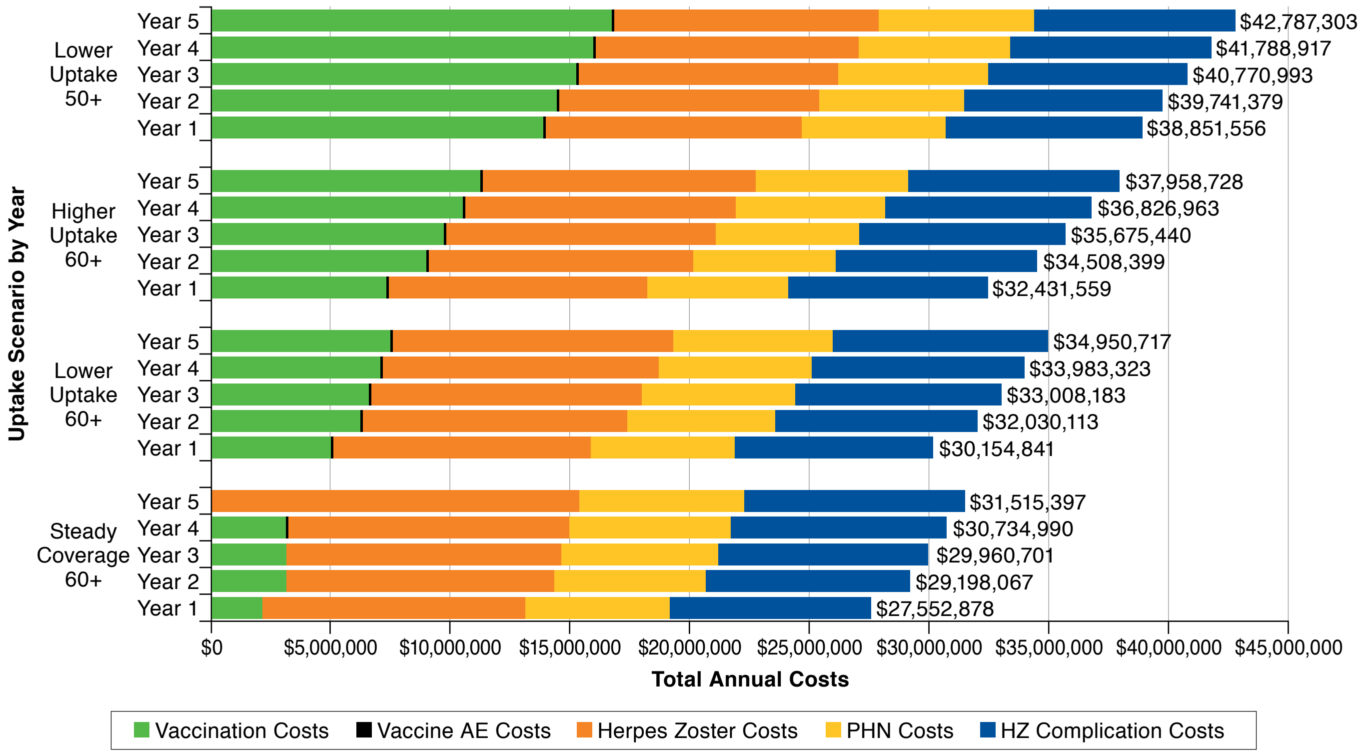
The costs of treating injection-site reactions, headache, and pain in the extremity were assumed to be negligible to the health plan; therefore, these costs were set to zero in the main analyses. In sensitivity analyses, a cost to treat these adverse events was applied to analyze the effect on the budget. A one-time cost of treating allergic reaction was assumed and was obtained through publicly available cost estimates.[22]

The age-specific costs of treating zoster, PHN, and nonpain complications were taken from Yawn et al. (2009), which looked at the health care utilization and costs for herpes zoster using data from Olmsted County, Minnesota.[2] Costs were inflated to 2014 U.S. dollars using the medical care component of the Consumer Price Index.[23] Treatment costs were applied to the proportion of the population experiencing each event. Cost and outcomes were undiscounted, as recommended for budget-impact analyses.[24] Per-case costs are presented in Table 1.

Model Outcomes

The primary outcomes of interest from the budget-impact analysis included total annual and per-member-per-month (PMPM) costs. Total annual and PMPM costs were reported for vaccination strategies and for all uptake scenarios. Total annual and PMPM costs for the current vaccination strategy then were

FIGURE 2 Total Annual Costs



AE = adverse event; HZ = herpes zoster; PHN = postherpetic neuralgia.

subtracted from the total annual and PMPM costs for the new vaccination strategy to estimate the change in costs (i.e., the budget impact for the payer) each year over the next 5 years. The annual impacts on health outcomes (adverse events and zoster-related events) are also presented.

Scenario Analyses

To test the robustness of the results to variations in the assumptions and for uncertainty in the estimates of specific parameters, the effects of varying model parameter estimates in a series of analyses were examined. Alternative copayments, alternative assumptions for vaccine efficacy and durability, and alternative adverse reaction costs were tested.

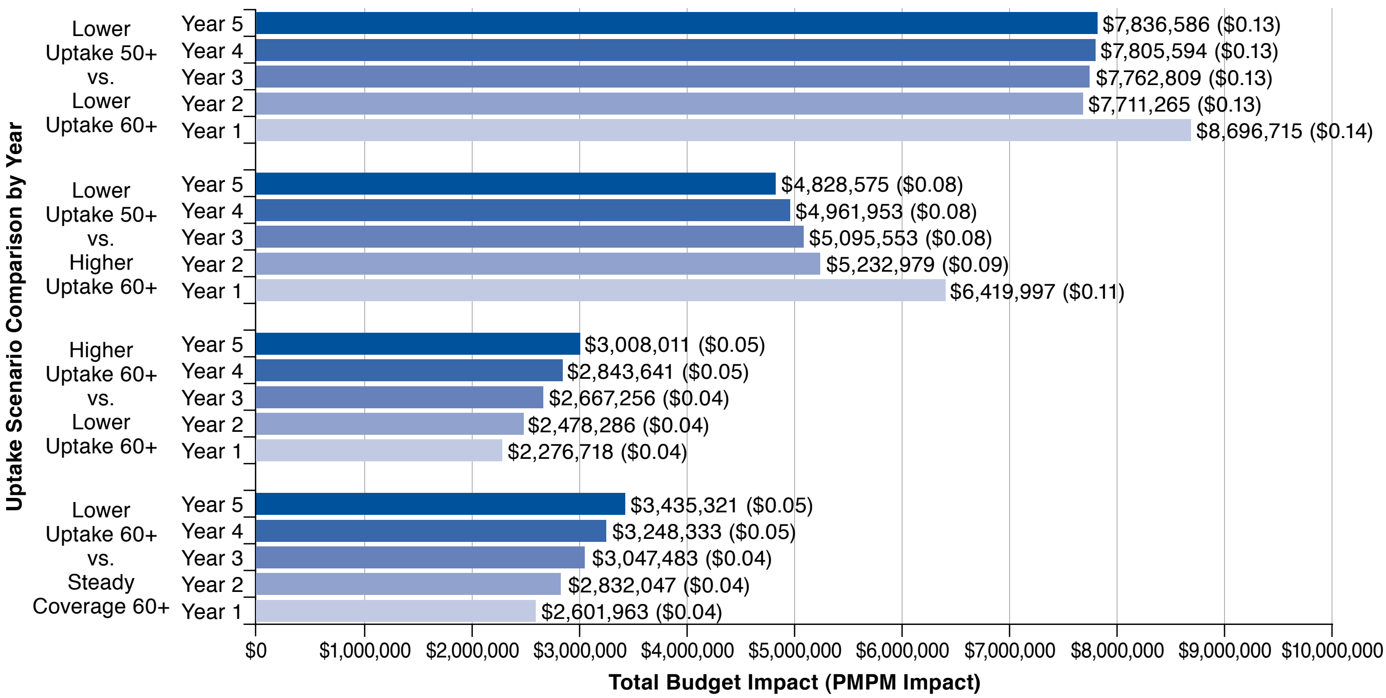
In the base-case analyses, no copayments were assumed for all uptake scenarios. Two types of alternative copayment analyses were implemented to see what effect copayments and changes to copayments had on the health plan's budget. Because these scenarios reduced the costs borne by the payer, they are useful in understanding possible affects that other cost-reducing schemes (discounts and rebates) would have on a health plan's budget. The first copayment analysis applied the same copayment to both uptake scenarios being compared. This type of copayment analysis was done first with a $25 copayment, then with a $50 copayment, and finally with a $75 copayment.

The second copayment analysis applied a $50 copayment as the current copayment within the plan and estimated the budget impact of not only a change in the uptake but a change in copayment to $25. The same was done for a $75 copayment with a change to a $50 copayment. This analysis represents an added reason for possible increases in uptake (lowering the copayment could influence more individuals to get vaccinated).

The effect of efficacy durability on the results was tested by running the modeling using Model A (accelerated waning over time) and Model B (drop in year 1 waning only) individually to estimate the vaccine efficacy over time, instead of the base case, which used the midpoint between the 2 models.

Efficacy durability was additionally tested by using only the observed efficacy data from the long-term persistence study and then further limited by using only the efficacy presented in the prescribing information.[7] For the observed efficacy, individuals who were vaccinated between the ages of 50 and 59 years received a 69.8% reduction in probability of zoster for the first 2 years after vaccination. After 2 years, efficacy for

FIGURE 3 Budget Impact



PMPM = per member per month.

these patients was 0%. Individuals who were vaccinated at age 60 years and above received the following reductions in probability of zoster for years 1 through 11 after vaccination: 62.0%, 48.9%, 46.8%, 44.6%, 43.1%, 30.6%, 46.0%, 31.1%, 6.8%, 14.1%, and -1.7%. After 11 years, efficacy for these patients was 0%.

Based on the efficacy presented in the prescribing information, the vaccine efficacy was analyzed over 2 years for individuals aged 50-59 years (69.8% efficacy) and over 4 years for individuals aged 60 years and older (51.3% efficacy). Because of the trial length, the model assumed in the base-case scenario that vaccine efficacy lasted for the analyzed period (2 years for age 50-59 years and 4 years for age 60 years and older). After these periods, the vaccine efficacy was 0%.

Results

Base-Case Results

For all uptake scenarios, the costs associated with vaccination (vaccine costs and administration costs), adverse events, and zoster (zoster-only costs, PHN costs, and nonpain complication costs) are presented in Figure 2 for the hypothetical health plan of 5 million members. Full tables of results for all the budget-impact comparisons are presented in Appendices B-E (available in online article).

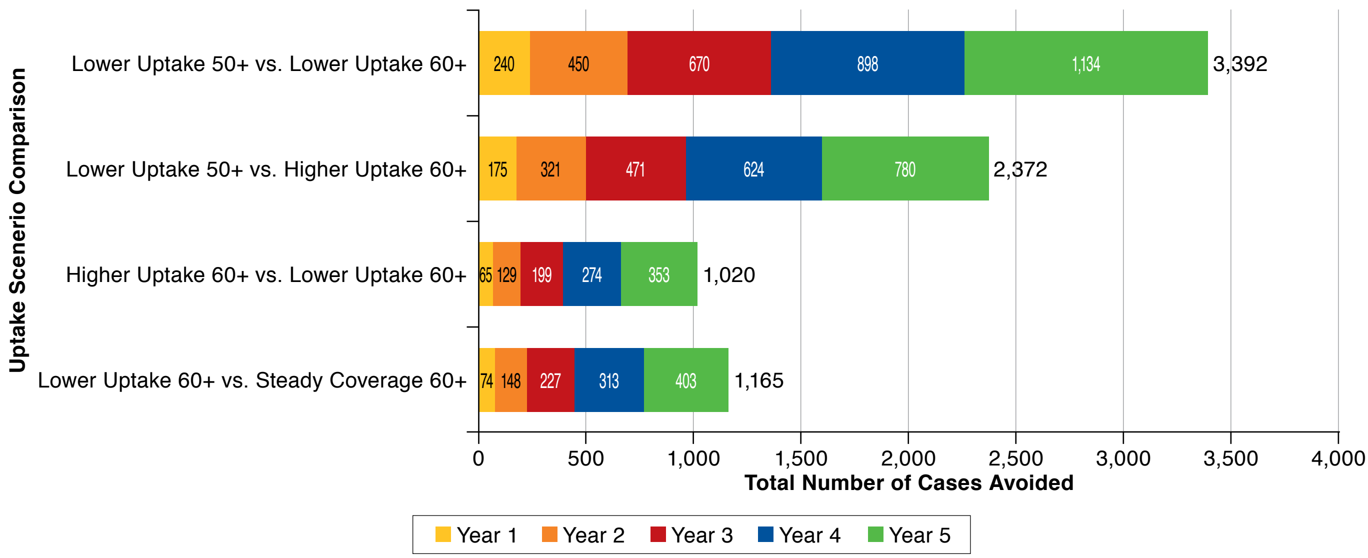
The estimated total annual costs when vaccine coverage remained steady at 20% for the population aged 60 years and older were $27,552,878, $29,198,067, $29,960,701, $30,734,990, and $31,515,397 for years 1-5, respectively. The estimated numbers of zoster cases per year were 13,471, 13,812, 14,165, 14,523, and 14,884 for years 1 through 5, respectively.

ACIP Recommendation-Based Uptake Comparison (60+ Eligible)

Assuming a cumulative vaccine uptake of 28% by year 5 for the population aged 60 years and older only (lower uptake 60+) resulted in higher direct medical cost (Figure 3) than when coverage remained steady at 20% for the same population: increases of $2,601,963, $2,832,046, $3,047,482, $3,248,332, and $3,435,320 in years 1 through 5, respectively. These increases in total annual costs resulted in PMPM budget increases of $0.04 in year 1, $0.05 in years 2-4, and $0.06 in year 5. For the 5-year time frame, the total number of zoster cases avoided was 1,165 when uptake increased over the 5 years to a cumulative uptake of 28%.

Under current model assumptions, the ACIP recommendation of age 60 years and older with higher uptake was estimated to be more costly in all modeled years than with the lower uptake. The total annual budget for the higher uptake

FIGURE 4 Total Cases of Zoster Avoided over 5 Years



scenario ranged from $2,278,718 to $3,008,011 higher than the lower uptake. The increase in total budget when comparing the uptake scenarios produced an increase in yearly PMPM costs of $0.04 in the first 3 years and $0.05 in years 4 and 5. With increased coverage resulting from the higher uptake scenario, a decrease in the number of zoster cases was estimated to occur each year compared with the lower uptake scenario. By the end of year 5, 1,020 cases of zoster were avoided when comparing the higher uptake with the lower uptake scenario for age 60 years and older (Figure 4).

FDA Approval-Based Uptake Results (50+ Eligible) Versus ACIP Recommendation-Based Uptake Comparison (60+ Eligible)

When comparing a change from vaccination strategies based on the ACIP recommendation (higher and lower uptake 60+ scenarios) to strategies based on FDA approval (lower uptake 50+ scenario), vaccinating individuals who were aged 50 years and older was estimated to increase the total budget because of increased vaccination costs and adverse event costs (Figure 2 and Figure 3). Increases in the budget for vaccination were partially offset by the decrease in cost to treat zoster because of the reduction in cases (Figure 4).

Comparing a low uptake in a vaccination program for those aged 50 years and older (lower uptake 50+) to a low uptake in a vaccination program for those aged 60 years and older (lower uptake 60+), the total annual direct medical costs were always higher for vaccination in those aged 50 years and older: incremental cost of $8,696,715, $7,711,265, $7,762,809, $7,805,594, and $7,836,586 for years 1 through 5, respectively. These increases in total costs resulted in PMPM budget increases of $0.14 in year 1 and $0.13 in years 2-5. For the 5-year time frame, the total number of zoster cases avoided when comparing these 2 scenarios (lower uptake 50+ to lower uptake 60+) was 3,392 with vaccination in those aged 50 years and older.

Comparing a low uptake in a vaccination program for those aged 50 years and older (lower uptake 50+) to a higher uptake in a vaccination program for those aged 60 years and over (higher uptake 60+), the total annual direct medical costs were always higher for vaccination in those aged 50 years and older: incremental cost of $6,419,997, $5,232,97, $5,095,553, $4,961,953, and $4,828,575 for years 1-5, respectively. These increases in total costs resulted in PMPM budget increases of $0.11 in year 1, $0.09 in year 2, and $0.08 in years 3-5. For the 5-year time frame, the total number of zoster cases avoided when comparing these 2 scenarios (lower uptake 50+ to higher uptake 60+) was 2,372 with vaccination in those aged 50 years and older.

Vaccine Efficacy Scenario Analyses

Using the vaccine efficacy models (Model A, accelerated waning over time, and Model B, drop in year 1 waning only) separately, instead of using the midpoint between the models, had minimal effect on the budget estimates (Table 3). Limiting the durability of the vaccine efficacy by using observed efficacy or label efficacy (see footnote of Table 3 for more detail) increased the budget impact and lowered the number of zoster cases avoided when comparing a 50+ scenario to a 60+ scenario.

TABLE 3 Scenario Analysis Results: Cumulative 5-Year Estimates

Alternative Scenario	Lower Uptake 60+ vs. Steady Coverage 60+	Higher Uptake 60+ vs. Lower Uptake 60+	Lower Uptake 50+ vs. Higher Uptake 60+	Lower Uptake 50+ vs. Lower Uptake 60+
Cumulative 5-year impact on total direct medical costs, $				
Base case	15,165,146	13,273,912	26,539,057	39,812,969
$25 copay	12,943,663	11,330,632	22,958,089	34,288,721
$50 copay	10,722,180	9,387,352	19,377,121	28,764,473
$75 copay	8,500,696	7,444,072	15,796,153	23,240,224
Efficacy Model A[a]	15,054,066	13,177,502	26,543,626	39,721,129
Efficacy Model B[a]	15,273,849	13,368,257	26,536,553	39,904,810
Observed efficacy[b]	14,713,364	12,886,717	28,752,698	41,639,415
Label efficacy[c]	15,795,142	13,828,510	28,740,763	41,635,818
Adverse event costs[d]	18,424,987	16,125,513	35,749,936	51,875,449
Cumulative 5-year zoster cases avoided, n				
Base case	1,165	1,020	2,372	3,392
$25 copay	1,165	1,020	2,372	3,392
$50 copay	1,165	1,020	2,372	3,392
$75 copay	1,165	1,020	2,372	3,392
Efficacy Model A[a]	1,185	1,038	2,427	3,465
Efficacy Model B[a]	1,144	1,003	2,316	3,319
Observed efficacy[b]	1,225	1,070	904	1,975
Label efficacy[c]	793	692	475	1,166
Adverse event costs,[d] $	1,165	1,020	2,372	3,392

Note: All presented impacts were calculated as the first listed scenario minus the second listed.

[a]*Model A assumed a decline in vaccine efficacy as a function of aging and time since vaccination. Model B assumed the initial decline in vaccine efficacy observed during the first year, with subsequent decline because of aging only.*

[b]*Observed efficacy against zoster from available clinical studies was used as the vaccine efficacy. Individuals who were vaccinated between the ages of 50 and 59 years received a 69.8% reduction in probability of zoster for the first 2 years after vaccination. After 2 years, efficacy for these patients was 0%. Individuals who were vaccinated at the age of 60 years and older received the following reductions in probability of zoster for years 1 through 11 after vaccination: 62.0%, 48.9%, 46.8%, 44.6%, 43.1%, 30.6%, 46.0%, 31.1%, 6.8%, 14.1%, and -1.7%. After 11 years, efficacy for these patients was 0%.*

[c]*As per the prescribing information, the vaccine efficacy was analyzed over 2 years for individuals aged 50-59 years and older and 4 years for individuals aged 60 years and older. Vaccine efficacy (per label): 50-59 = 69.8%, 60 and older = 51%. Because of the trial length, the model assumed in the base case that vaccine efficacy lasted for the analyzed period (2 years for age 50-59 and 4 years for 60 and older). After these periods, the vaccine efficacy was 0%.*

[d]*In the base case, no costs were assumed for injection-site reactions, headache, and pain in the extremity. For this scenario, the cost of a physician's visit at a price of $73.08 was assumed to be the treatment costs for these adverse events.*[21]

Copayment Scenario Analyses

In the base-case analyses, no copayment was assumed for all uptake scenarios. Two types of alternative copayment analyses were implemented to see what effect copayments and changes to copayments had on the health plan's budget.

Results of the copayment scenario analysis that applied the same copayment to both uptake scenarios being compared (Table 4) showed that, under a $25 copayment, the cumulative 5-year total budget impact would be about 14% less than when no copayment was applied. When a $50 copayment was applied, this reduction increased to around 28%. Finally, when a $75 copayment was applied, the cumulative 5-year total budget impact was about 42% less than when no copayment was applied.

Results of the copayment scenario analyses that included a combined reduction in copayment from $50 to $25, with an associated increase in vaccine uptake (Table 4), showed that these scenarios result in a more than 9% increase in the budget impact for all comparisons (ranging from 9.87% to 24.59% increases depending on the uptake scenario comparison). Similarly, combining a reduction of copayment from $75 to $50, with the same increase in vaccine uptake, showed that the budget impact increases by more than 8% (ranging from 8.76% to 21.61% increases depending on the uptake scenario comparison).

Adverse Event Costs Analysis

In the base-case analyses, no costs to the health plan were assumed for injection site reactions, headaches, and pain in the extremity. In an alternative scenario, a treatment cost of $73.08 for a physician's visit was assumed to be the treatment costs for these adverse events. Results of this analysis showed that the budget impact would further increase because of the added treatment costs of these adverse events.

Discussion

In the United States, where vaccination for individuals aged 60 years and over has been universally recommended, the results of this budget-impact analysis indicated that including

TABLE 4 Copayment Change Scenario Analysis Results: Cumulative 5-Year Estimates

Uptake with Copayment Comparison	Difference in Total Cumulated 5-Year Costs[a]
Lower uptake 60+ ($25 copay) vs. steady coverage 60+ ($50 copay)	$14,791,768
Higher uptake 60+ ($25 copay) vs. lower uptake 60+ ($50 copay)	$15,400,220
Lower uptake 50+ ($25 copay) vs. lower uptake 60+ ($50 copay)	$28,970,957
Lower uptake 50+ ($25 copay) vs. higher uptake 60+ ($50 copay)	$38,358,309
Lower uptake 60+ ($50 copay) vs. steady coverage 60+ ($75 copay)	$12,570,284
Higher uptake 60+ ($50 copay) vs. lower uptake 60+ ($75 copay)	$13,456,940
Lower uptake 50+ ($50 copay) vs. lower uptake 60+ ($75 copay)	$25,389,989
Lower uptake 50+ ($50 copay) vs. higher uptake 60+ ($75 copay)	$32,834,061

[a]*All presented differences are calculated as the first listed scenario minus the second list.*

individuals aged 50-59 years (based on FDA approval) as eligible for vaccination will increase a health plan's budget, especially when assuming an increased uptake for the herpes zoster vaccine. Compared with the current strategy in which individuals aged 60 years and older can be vaccinated (ACIP recommendation), a strategy that includes vaccinating individuals aged 50-59 years was estimated to result in an average budget increase of $0.08 to $0.14 PMPM in the first 5 years. The total increase in direct medical costs ranged from $26,539,057 to $39,812,969 in the same period. The increased vaccine coverage when individuals aged 50-59 years are included would result in a 3.5%-6.2% reduction in zoster cases (2,372-3,392 cases avoided) in the health plan population over the 5-year modeled period. Annual incremental PMPM estimates were driven by the hypothetical projected annual uptake rates for the unvaccinated population and the price of the vaccine.

Even without including individuals aged 50-59 years as eligible for vaccination, small increases in vaccine coverage will still have an impact on a health plan's budget. Compared with a steady coverage of 20% over 5 years, a scenario in which coverage reaches 28% by year 5 will increase annual budgets by about 10%. If coverage were to instead reach 35% by year 5, the annual budgets would increase an additional 9% on average.

The hypothetical annual uptakes and the comparisons analyzed provide decision makers with estimates of the possible budget impact with vaccination recommendation changes and changes in uptake in vaccination at all ages, as well as copayment options. The increases in uptake could occur because of various factors apart from a recommendation change by the CDC, including an increase in marketing of the vaccine to the consumer and the health care community. These reasons could be enough to overcome the barriers that are keeping the overall vaccination rates low for adults in the United States. A survey of U.S. physicians found that the reason for low vaccination rates among adults were mostly financial barriers, such as low reimbursement rates for a vaccine, lack of reimbursement for a vaccine, or coverage under Medicare Part D (which typically includes high out-of-pocket costs).[25]

Age of vaccination and the durability of vaccine protection have an effect on the treatment cost because of the number of zoster cases per year. If vaccine protection were to wane faster, then the total costs would be higher, resulting in higher PMPM impact. This was seen in the scenario analyses where only observed efficacy data were applied for the years in which the observational data were available, with vaccine protection stopping after the last observation. The PMPM impact increased another $0.01 to $0.03 from the base-case estimates when the predicted efficacy based on the 2 efficacy models were analyzed separately. The copay analyses showed that a 5-year budget for a health maintenance organization could be reduced by 14%, 28%, and 42% when copays of $25, $50, and $75 are applied, respectively. These budget reductions are likely to be the maximums values, ranging from 9% to 24%, given that as copays amounts increase vaccine uptake rates are likely to be reduced. Based on the scenario analyses regarding copayment changes and the effect on uptake, the magnitude of cost impact was found to be linked to how the copayment changes and the effect this change would have on uptake. However, real-word evidence on the association between copay level and vaccine uptake are warranted.

An additional benefit of earlier vaccination would be reduced indirect costs. Even though zoster is likely to be less severe in younger ages, individuals still miss work (absenteeism) and are also less productive while at work (presenteeism) because of zoster symptoms. A study by Singhal et al. (2011) estimated that individuals with zoster who are aged 50-59 years will miss 3.3 days of work and will have an additional 71.4 hours (8.9 days) of presenteeism.[26] As the incidence in zoster increases in younger age groups, missed work could become an additional burden that has not been captured in this budget-impact analysis, since loss of work productivity would not be associated with costs to a health plan.

Limitations

Multiple predictive models were used, as described in Li et al. (2015), to predict the durability of vaccine efficacy for an individual after vaccination.[17] The base analyses utilized the midpoint of 2 predictive models to estimate the vaccine efficacy over time: accelerated waning over time (Model A, as labeled in the cost-effectiveness model) and drop in year 1 waning only (Model B).

The Shingles Prevention Study demonstrated that zoster vaccine not only reduced the incidence of herpes zoster but also reduced the severity and duration of zoster-associated pain and the risk of PHN in patients who developed herpes zoster.[6] However, we did not assume vaccine efficacy against PHN beyond the protection afforded by reducing the incidence of herpes zoster. Therefore, the offsetting costs from zoster might be underestimated.

Costs to treat events were assumed to fall entirely within the budget year. Adverse event costs were applied in the year of vaccination. Zoster, PHN, and nonpain complication costs were applied in the year that the zoster case occurred.

Changes to the health plan demographics were limited to only aging and death. We did not explicitly model additional members joining the plan or attrition of members.

In the base-case analysis, copayment was not assumed, and the effect of change to copayments and the downstream effect on uptake were analyzed through simple methods. Given the uncertainty of the effect of copayments on uptake rates and the sensitivity of this study's results to this effect, future analyses using alternative methods for estimating this correlation are warranted to improve the precision around this study's estimates.

The analysis was also limited to assume no costs to the health plan for treating injection-site reactions, headache, and pain in the extremity. This decision was made because such treatment costs are minimal and may be paid for by the patient.

Because inputs from different sources and several model assumptions were used in creating the model, the results were validated against recent publications in the literature. In this study, a similar population to that in the study by Le et al. (2015)—vaccinating a single 50 year old and comparing with no vaccination—was analyzed.[10] The model horizon in our analysis was extended to 10 years, and the model estimated that after 10 years there would be incremental costs of $164 and 0.0208 herpes zoster cases prevented when compared with no vaccination. Le et al. found that over a lifetime the incremental costs was $137 with 0.0251 herpes zoster cases prevented. The results of these 2 models were very close even though there are differing parameter and structural assumptions between the models.

Also, we compared the estimated annual zoster incidence for the population aged 50 years and over from our model with the Johnson et al. study,[11] which was used for age specific incidence, to see if our model predicted a similar overall incidence for this population. Johnson et al. found the incidence of zoster among adults aged 50 years and older to be 8.46 (95% confidence interval = 8.39-8.52) per 1,000 person years. Our model predicted that the incidence in year 1 for those aged 50 years and older was 8.52 per 1,000 person years.

Conclusions

Vaccinating individuals aged 50-59 years with the herpes zoster vaccine will have an effect on a health plan's budget because of the expected increase in the total number of individuals being vaccinated in the population, with some offsetting cost savings because of fewer cases of zoster. Adopting a strategy of vaccination for individuals aged 50 years and older and/or higher coverage rates for those aged 60 years and older within a plan is estimated to result in a decrease in the number of zoster cases and associated PHN and nonpain complications over the next 5 years.

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DISCLOSURES

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Graham and Mauskopf were primarily responsible for the design and programming of the economic model, identification and final selection of the input parameter values, interpretation of the study results, and preparation of the study report. Johnson, Kawai, Xu, and Acosta contributed to model design, input parameter estimation, interpretation of the results, and review of and revisions to the study report. All authors had access to the data, participated in the development of this manuscript, and gave final approval before submission. All authors have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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APPENDIX A Incidence of Events Per Individual

Age (Years)	Zoster[a]	Postherpetic Neuralgia[b]	Nonpain Complications[b]
50	0.00636	0.00023	0.00052
51	0.00653	0.00027	0.00053
52	0.00670	0.00031	0.00054
53	0.00687	0.00035	0.00056
54	0.00704	0.00039	0.00057
55	0.00721	0.00044	0.00058
56	0.00738	0.00049	0.00060
57	0.00755	0.00053	0.00061
58	0.00771	0.00058	0.00062
59	0.00788	0.00063	0.00064
60	0.00805	0.00069	0.00065
61	0.00822	0.00074	0.00067
62	0.00839	0.00080	0.00068
63	0.00856	0.00086	0.00069
64	0.00873	0.00092	0.00071
65	0.00890	0.00098	0.00072
66	0.00907	0.00104	0.00073
67	0.00924	0.00111	0.00075
68	0.00941	0.00117	0.00076
69	0.00957	0.00124	0.00078
70	0.00974	0.00131	0.00118
71	0.00991	0.00138	0.00120
72	0.01008	0.00145	0.00122
73	0.01025	0.00153	0.00124
74	0.01042	0.00160	0.00126
75	0.01059	0.00168	0.00128
76	0.01076	0.00176	0.00130
77	0.01093	0.00184	0.00132
78	0.01110	0.00193	0.00134
79	0.01127	0.00201	0.00136
80	0.01144	0.00210	0.00180
81	0.01160	0.00219	0.00182
82	0.01177	0.00227	0.00185
83	0.01194	0.00237	0.00187
84	0.01211	0.00246	0.00190
85	0.01228	0.00255	0.00193
86	0.01245	0.00265	0.00195
87	0.01262	0.00275	0.00198
88	0.01279	0.00285	0.00201
89	0.01296	0.00295	0.00203
90	0.01313	0.00305	0.00206
91	0.01330	0.00315	0.00209
92	0.01346	0.00326	0.00211
93	0.01363	0.00337	0.00214
94	0.01380	0.00348	0.00217
95	0.01397	0.00359	0.00219
96	0.01414	0.00370	0.00222
97	0.01431	0.00382	0.00225
98	0.01448	0.00393	0.00227
99	0.01465	0.00405	0.00230

[a] *Derived from Johnson et al. (2015).*[11]
[b] *Derived from Yawn et al. (2007).*[15]

APPENDIX B Budget-Impact Results: Costs to Health Plan—Lower Uptake 60+ Versus Steady Coverage 60+

Outcome	Year 1		Year 2		Year 3		Year 4		Year 5	
	Lower Uptake 60+	Steady Coverage 60+	Lower Uptake 60+	Steady Coverage 60+	Lower Uptake 60+	Steady Coverage 60+	Lower Uptake 60+	Steady Coverage 60+	Lower Uptake 60+	Steady Coverage 60+
Cost outcomes ($)										
Vaccine[a]	4,884,452	2,119,579	6,236,794	3,082,862	6,669,513	3,128,639	7,095,638	3,171,286	7,515,983	3,212,389
Zoster	30,154,841	25,426,425	32,030,113	26,105,207	33,008,183	26,821,915	33,983,323	27,553,419	34,950,717	28,292,589
AE	15,841	6,873.93	20,226	9,997.92	21,630	10,146.38	23,012	10,284.68	24,375	10,417.98
Total	30,154,841	27,552,878	32,030,113	29,198,067	33,008,183	29,960,701	33,983,323	30,734,990	34,950,717	31,515,397
Difference	2,601,963		2,832,046		3,047,482		3,248,332		3,435,320	
PMPM impact	0.04		0.05		0.05		0.05		0.06	
Health outcomes										
Zoster only	74 (13,471-13,397)		147 (13,812-13,665)		227 (14,165-13,938)		313 (14,523-14,210)		403 (14,884-14,481)	
PHN	13 (1,446-1,433)		24 (1,485-1,461)		36 (1,529-1,493)		49 (1,576-1,527)		62 (1,626-1,564)	
Nonpain complication	8 (1,312-1,304)		14 (1,346-1,332)		22 (1,382-1,360)		30 (1,418-1,388)		40 (1,455-1,415)	

[a]*Includes vaccine cost and administration costs.*

AE = adverse event; PHN = postherpetic neuralgia; PMPM = per member per month.

APPENDIX C Budget-Impact Results: Costs to Health Plan—Higher Uptake 60+ Versus Lower Uptake 60+

Outcome	Year 1		Year 2		Year 3		Year 4		Year 5	
	Higher Uptake 60+	Lower Uptake 60+	Higher Uptake 60+	Lower Uptake 60+	Higher Uptake 60+	Lower Uptake 60+	Higher Uptake 60+	Lower Uptake 60+	Higher Uptake 60+	Lower Uptake 60+
Cost outcomes ($)										
Vaccine[a]	7,303,715	4,884,452	8,996,483	6,236,794	9,767,520	6,669,513	10,528,372	7,095,638	11,278,837	7,515,983
Zoster	25,104,158	30,154,841	25,482,740	32,030,113	25,876,244	33,008,183	26,264,448	33,983,323	26,643,313	34,950,717
AE	23,686	15,841	29,176	20,226	31,677	21,630	34,144	23,012	36,578	24,375
Total	32,431,559	30,154,841	34,508,399	32,030,113	35,675,440	33,008,183	36,826,963	33,983,323	37,958,728	34,950,717
Difference	2,276,718		2,478,286		2,667,256		2,843,641		3,008,011	
PMPM impact	0.04		0.04		0.04		0.05		0.05	
Health outcomes										
Zoster only	64 (13,397-13,333)		130 (13,665-13,535)		199 (13,938-13,739)		274 (14,210-13,936)		354 (14,481-14,127)	
PHN	11 (1,433-1,422)		22 (1,461-1,439)		32 (1,493-1,461)		43 (1,527-1,484)		54 (1,564-1,510)	
Nonpain complication	6 (1,304-1,298)		13 (1,332-1,319)		20 (1,360-1,340)		27 (1,388-1,361)		35 (1,415-1,380)	

[a]*Includes vaccine cost and administration costs.*

AE = adverse event; PHN = postherpetic neuralgia; PMPM = per member per month.

APPENDIX D Budget-Impact Results: Costs to Health Plan—Lower Uptake 50+ Versus Higher Uptake 60+

Outcome	Year 1		Year 2		Year 3		Year 4		Year 5	
	Higher Uptake 60+	Lower Uptake 50+	Higher Uptake 60+	Lower Uptake 50+	Higher Uptake 60+	Lower Uptake 50+	Higher Uptake 60+	Lower Uptake 50+	Higher Uptake 60+	Lower Uptake 50+
Cost outcomes ($)										
Vaccine[a]	7,303,715	13,853,061	8,996,483	14,489,111	9,767,520	15,254,357	10,528,372	16,016,907	11,278,837	16,773,442
Zoster	25,104,158	24,953,569	25,482,740	25,205,279	25,876,244	25,467,165	26,264,448	25,720,066	26,643,313	25,959,463
AE	23,686	44,926	29,176	46,989	31,677	49,471	34,144	51,944	36,578	54,397
Total	32,431,559	38,851,556	34,508,399	39,741,379	35,675,440	40,770,993	36,826,963	41,788,917	37,958,728	42,787,303
Difference	6,419,997		5,232,979		5,095,553		4,961,953		4,828,575	
PMPM impact	0.11		0.09		0.08		0.08		0.08	
Health outcomes										
Zoster only	-175 (13,158-13,333)		-321 (13,215-13,535)		-471 (13,267-13,739)		-624 (13,312-13,936)		-780 (13,347-14,127)	
PHN	-3 (1,419-1,422)		-6 (1,433-1,439)		-11 (1,450-1,461)		-16 (1,468-1,484)		-23 (1,487-1,510)	
Nonpain complication	-13 (1,285-1,298)		-24 (1,295-1,319)		-35 (1,306-1,340)		-46 (1,315-1,361)		-57 (1,323-1,380)	

[a]*Includes vaccine cost and administration costs.*

AE = adverse event; PHN = postherpetic neuralgia; PMPM = per member per month.

APPENDIX E Budget-Impact Results: Costs to Health Plan—Lower Uptake 50+ Versus Lower Uptake 60+

Outcome	Year 1		Year 2		Year 3		Year 4		Year 5	
	Lower Uptake 60+	Lower Uptake 50+	Lower Uptake 60+	Lower Uptake 50+	Lower Uptake 60+	Lower Uptake 50+	Lower Uptake 60+	Lower Uptake 50+	Lower Uptake 60+	Lower Uptake 50+
Cost outcomes ($)										
Vaccine[a]	4,884,452	13,853,061	4,884,452	13,853,061	4,884,452	13,853,061	4,884,452	13,853,061	4,884,452	13,853,061
Zoster	30,154,841	24,953,569	30,154,841	24,953,569	30,154,841	24,953,569	30,154,841	24,953,569	30,154,841	24,953,569
AE	15,841	44,926	15,841	44,926	15,841	44,926	15,841	44,926	15,841	44,926
Total	30,154,841	38,851,556	30,154,841	38,851,556	30,154,841	38,851,556	30,154,841	38,851,556	30,154,841	38,851,556
Difference	8,696,715		7,711,265		7,762,809		7,805,594		7,836,586	
PMPM impact	0.14		0.13		0.13		0.13		0.13	
Health outcomes										
Zoster only	-240 (13,158-13,397)		-450 (13,215-13,665)		-670 (13,267-13,938)		-898 (13,312-14,210)		-1,134 (13,347-14,481)	
PHN	-14 (1,419-1,433)		-27 (1,433-1,461)		-42 (1,450-1,493)		-59 (1,468-1,527)		-77 (1,487-1,564)	
Nonpain complication	-19 (1,285-1,304)		-36 (1,295-1,332)		-54 (1,306-1,360)		-73 (1,315-1,388)		-92 (1,323-1,415)	

[a]*Includes vaccine cost and administration costs.*

AE = adverse event; PHN = postherpetic neuralgia; PMPM = per member per month.