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The Potential Economic Value of a "Universal" (Multi-Year) Influenza Vaccine

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SUMMARY

Background—Limitations of the current annual influenza vaccine have led to ongoing efforts to develop a "universal" influenza vaccine, i.e., one that targets a ubiquitous portion of the influenza virus so that the coverage of a single vaccination can persist for multiple years.

Objectives—To estimate the economic value of a "universal" influenza vaccine compared to the standard annual influenza vaccine, starting vaccination in the pediatric population (2–18 year olds), over the course of their lifetime.

Patient/methods—Monte Carlo decision analytic computer simulation model

Results—Universal vaccine dominates (i.e., less costly and more effective) the annual vaccine when the universal vaccine cost ≤$100/dose and efficacy ≥75% for both the 5 and 10 year duration. The universal vaccine is also dominant when efficacy is ≥50% and protects for 10 years. A $200 universal vaccine was only cost-effective when ≥75% efficacious for a 5 year duration when annual compliance was 25% and for a 10 year duration for all annual compliance rates. A universal vaccine is not cost-effective when it cost $200 and when its efficacy is ≤50%. The cost-effectiveness of the universal vaccine increases with the duration of protection.

Conclusions—Although development of a universal vaccine requires surmounting scientific hurdles, our results delineate the circumstances under which such a vaccine would be a cost-effective alternative to the annual influenza vaccine.

Keywords

Influenza Vaccine; Universal Vaccine; Economics; Pediatrics, Cost-effectiveness

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Background

The following limitations of the current annual influenza vaccine have led to ongoing efforts to develop a "universal" influenza vaccine, i.e., one that targets a ubiquitous portion of the influenza virus so that the coverage of a single vaccination can persist for multiple years:

- Annual vaccine administration: Administering influenza vaccine to the same patients each year incurs substantial costs and efforts. Persons must miss work. Maintaining influenza vaccination clinics and sites requires personnel time.
- Annual vaccine manufacturing: Every year influenza vaccine manufacturers must allocate significant resources to produce influenza vaccines. Due to varying viral strains every season and the limited production period, the timing and preparation of vaccine development might cause unnecessary delays.
- Patient compliance: Even when a person is recommended to be vaccinated, he or she may miss getting immunized certain years. According to the National Health Interview Survey and National Immunization Survey of United States for seasons 2005–2006, 2006–2007, and 2007–2008 and National Immunization Survey, influenza vaccination coverage levels ranged 31.8%–32.2% for ages 6–23 months, 26.4%–40.3% for ages 2–4 years, and 12.4%–21.1% for ages 5–17 years.[1] Estimation from the Behavioral Risk Factor Surveillance System (BRFSS) for influenza season 2008–2009 was 26.0%–38.7% for ages 2–4 year olds and 18.4%–23.4% for ages 5 to 17 year olds.[2]
- Changing influenza strains: Each year, different influenza strains emerge as the dominant circulating strains. Although each year, scientists attempt to predict these strains, their predictions are not always accurate.[3] Mutations may cause major antigenic drift every 2 to 5 years.[4]
- Emergence of novel influenza strain: As the 2009 influenza pandemic demonstrated, the annual vaccine may not cover new emergent strains.

Better understanding of the potential economic value of a "universal" vaccine can help guide investment and development for policy makers, manufacturers, insurance companies, investors, scientists, and other decision makers. Forecasting the impact of a vaccine early in its development when changes can still be made can increase the chances of a vaccine's success.[5]

Objectives

We developed a computational model to estimate the potential economic value of a "universal" influenza vaccine compared to the standard annual influenza vaccine in the pediatric population (ages 2 to 18 years), one of the Advisory Committee on Immunization Practices (ACIP) recommended high risk groups.[6]

Patients/methods

Model Structure

Figure 1 presents the general structure of the Markov decision analytic computer simulation model constructed using TreeAge Pro 2009 (TreeAge Software, Williamstown, Massachusetts). The model represents the decision from the societal perspective of whether a child (age 2 to 18 years old) should begin receiving a hypothetical universal influenza vaccine or the standard annual influenza vaccine The universal vaccine would have a certain duration of protection, therefore necessitating a periodic booster, and is assumed to be a single immunization. Each year the individual is scheduled to receive a vaccine, the

individual had a probability of complying. Additionally, we looked at the effects of vaccinating high-risk children. For these scenarios we assumed individuals were high-risk throughout their lifetime and had a twofold risk of hospitalization and mortality.

The time horizon for the model is the child's lifetime. The model has a cycle length of 1 year. The Markov states are mutually exclusive; an individual can only be in one state in a given year. Each year, an individual had a probability of becoming infected with influenza. Vaccination attenuates this probability by the vaccine-related efficacy. Each time an individual is vaccinated, he or she has a probability of developing vaccine side effects.[7] Individuals who contract influenza have probabilities of developing symptoms or remaining asymptomatic. Symptomatic individuals then have a probability of visiting an outpatient setting and a probability of requiring hospitalization. Each individual with influenza has a probability of surviving or dying from influenza. Those who die from influenza or other unrelated causes enter the death state. The model concludes its run when an individual enters this state, otherwise known as the absorptive state.

Each simulation run sends 1,000 individuals 1,000 times through the model for a total of 1,000,000 trials of an individual's lifetime. For each simulation, the following equation calculates the incremental cost-effectiveness ratio (ICER) of the “universal” vaccine versus the annual vaccine:

$$= \frac{\text{Cost}_{\text{Utilizing Universal Vaccine}} - \text{Cost}_{\text{Utilizing Annual Vaccine}}}{\text{Effectiveness}_{\text{Utilizing Universal Vaccine}} - \text{Effectiveness}_{\text{Utilizing Annual Vaccine}}}$$

where effectiveness is expressed in quality-adjusted life-years (QALYs). ICER values less than $50,000 per quality-adjusted life-year (QALY) identified the strategy as cost-effective.[8–9] The model was from the societal perspective, and therefore accounted for both direct (i.e., outpatient and hospitalization costs) and indirect costs (i.e., cost of productivity losses due to missed work (e.g., parent losses for child care) and influenza-attributable mortality of expected lifetime earnings).

Budget Impact Analysis

We also calculated the potential economic value of a universal influenza vaccine from the societal perspective for the U.S. pediatric population. The U.S. Census bureau estimate in July 2009 was used to provide the age stratified population: 21.3 million (under 5 years), 20.6 million (5–9 years), 20.0 million (10–14 years), and 21.5 million (15–19 years).[10]

Data Inputs

Table 1 lists the probabilities, costs, durations, and utilities used in the model along with their corresponding distributions and sources. Costs of annual vaccination are based on the average whole sale price and administration cost.[11] Mortality values are from the CDC National Vital Statistics Reports of Number of Deaths and Death Rates, by Age, Race, and Sex: United States 2007.[12] A 3% discount rate converted costs and QALYs from other years into 2010 values.[13] Death resulted in a QALY loss based on the QALY-adjusted life expectancy of the person's age.[14] Each influenza episode resulted in age-adjusted QALY decrements for the duration of the condition.[8]

Sensitivity Analyses

Sensitivity analyses systematically varied the cost of the universal vaccine ($100, $200), universal vaccine efficacy (range: 50%–75%), probability of influenza infection being symptomatic (50% or 67%), initial age of the individual (range: 2–18 years), compliance

with annual vaccine (range: 25%, 50%, 75%, and 100%), and the duration of universal vaccine protection (5 or 10 years).[15–16] Probabilistic sensitivity analyses simultaneously varied the values of each parameter across the ranges listed in Table 1.

Results

Cost Effectiveness Analysis when Universal Protection Duration is 5 years

Table 2 shows how the ICER of universal vaccination compares to annual vaccination varying with differing universal vaccine efficacy, cost, and annual vaccine compliance when the duration of universal vaccine protection is 5 years. Universal vaccine is the dominant strategy (i.e., saves costs and provides health benefits) when vaccine cost is ≤$100/dose and vaccine efficacy is ≥75% for all scenarios tested. The annual vaccine dominates the $100 universal vaccine, only when the universal is 50% efficacious and annual compliance is 100%. When increasing the cost to $200/dose, universal vaccine is cost-effective only when annual compliance is ≤25% and universal vaccine efficacy ≥75% for both symptomatic rates. A $200 universal vaccine with an efficacy ≤50% was not cost-effective for any annual compliance rate. For high-risk children, a $100 universal vaccine dominated the annual vaccine or had ICER values ≥$185,060/QALY for all probabilities of annual compliance.

Budget Impact Analysis when Universal Protection Duration is 5 years

Switching from the annual vaccine to the universal vaccine can yield cost savings from the societal perspective. A $100/dose universal vaccine with a vaccine efficacy ≥75% will provide cost savings per pediatric patient vaccinated: $1–$104 (ages below 5 years), $5–$102 (5–9 years), $6–$96 (10–14 years), and $168–$266 (15–18 years). Therefore, switching the entire pediatric population to universal vaccination could generate cost savings of $15 million - $2.2 billion for those below 5 years, $101 million - $2.1 billion for 5–9 years, $121 million - $1.9 billion for 10–14 years, and $3.6 billion - $5.7 billion for 15–18 years over their lifetimes. Increasing the proportion of developing symptomatic influenza from 50% to 67% will provide more cost savings.

Cost Effectiveness Analysis when Universal Protection Duration is 10 years

Table 3 demonstrates the incremental cost-effectiveness ratio when duration of protection by the universal vaccine increases from 5 to 10 years. Universal vaccine is optimal (i.e., economically dominant) compared to annual vaccine when its efficacy ≥50% and cost ≤ $100/dose for all annual compliance and symptomatic rates explored.

Figure 2 shows acceptability curves for the universal and annual vaccine when the universal protects for 10 years and costs $100. The universal vaccine consistently has a higher probability of being cost-effective, even with an increasing willingness to pay. A $200/dose universal vaccine is cost-effective only when its efficacy is ≥75%. At an efficacy of 50%, a $200 universal vaccine is not cost-effective compared to the annual vaccine. Figure 2b shows the curves for this change in cost.

Budget Impact Analysis when Universal Protection Duration is 10 years

Increasing the duration of universal protection to 10 years further augments the potential cost savings to society. A $100/dose universal vaccine with ≥75% efficacy can provide cost savings of $295 – $398 per pediatric patients (ages below 5 years), $284 – $388 (5–9 years), $274 – $377 (10–14 years), and $261–$364 (15–18 years) vaccinated. Therefore, switching the entire pediatric population to universal vaccination could generate cost savings of $6.2 billion - $8.5 billion for those below 5 years, $5.9 billion - $8.0 billion for 5–9 years, $5.5 billion - $7.5billion for 10–14 years, and $5.6 billion - $7.8 billion for 15–18 years over

their lifetimes. As before, increasing the probability of being symptomatic will provide even more cost savings.

Discussion

Our results suggest that a universal vaccine could provide substantial economic value by overcoming the annual vaccine's current drawbacks. This favors investment in universal vaccine development, helps establish efficacy and duration of protection targets for developers, and prepares policy makers for reimbursement questions. Addressing these issues early in a vaccine's development when changes are easier to make could help avoid considerable problems in the future.[5]

In many ways, our study underestimates the potential value of a universal vaccine. Not only is compliance with the annual vaccine far less than 100%, many children do not get vaccinated until later into the influenza season, i.e., after October or even November. As previous studies have demonstrated the value of annual influenza vaccine drops the later in the season the vaccine is administered, because the longer the patient remains unvaccinated, the more susceptible they are to being infected.[17–18] Moreover, our model did not account for how the universal vaccine may prevent the vaccinated individual from transmitting the influenza virus to others. Unvaccinated individuals are not only more susceptible to infection but may shed more virus when infected compared to vaccinated individuals. Our model focuses on the individual and does not consider influenza transmission and herd immunity. If the universal vaccine were to results in a greater proportion of the populations protected, then it could more substantially reduce transmission than the standard annual vaccine and therefore would be more cost effective. Finally, in our model, individuals are healthy children without co-morbidities that may worsen influenza outcomes.

The 2009 influenza pandemic identifies another possible benefit of the universal vaccine. A universal vaccine that provides protection against novel strains may circumvent the need to develop a specific vaccine against an emerging pandemic strain. As computer simulation studies have suggested, timely and effective vaccination of the population may be the most important mitigation intervention.[17–20]

Bringing a universal vaccine to market requires surmounting numerous hurdles. First, the vaccine must contain an appropriate antigen common to all possible circulating influenza viruses. Second, the antigen should be stable and not prone to mutation. Third, the antigen must not occur in other common human tissues. Fourth, the antigen needs to generate an adequate immune response. Fifth, the vaccine must remain effective and not wane for the duration of vaccine coverage.

Du and colleagues describe the possible approaches in developing a universal influenza vaccine which focus on the conserved sequences of M2e, HA (HA1, HA2), NP, and epitopes from different influenza viral proteins.[21] These sequences occur across many known subtypes of influenza virus making them ideal universal vaccine targets. Some candidates use a combination of these conserved epitopes from different viral proteins, potentially offering further cross-protection across varying subtypes.[21] Other candidates focus on the sequences of major structural proteins of the virus surface, ectodomain of matrix protein 2.[22–23] Scientists have also targeted human antibodies that could cross-react with and neutralize several different hemagglutinin viral subtypes.[24–27] Several candidate “universal” influenza vaccines are currently at different stages of development based on these targets. Five companies, Acambis Inc. (Cambridge, UK), Cytos Biotechnology (Schlieren, Switzerland), Merck & Co Inc. (NJ,USA), and VaxInnate Corp.

(NJ,USA) have reported promising preliminary Phase 1 clinical study results.[3, 28] BiondVax's (Ness Ziona, Israel) Mulitmeric-001 Universal Flu Vaccine successfully navigated through phase I/II trials and will enter Phase II trials in 2010.[29–30] BiondVax is currently recruiting patients 55 to 75 years old for its next study.[31]

A recently published article reports significant human B cell responses towards the 2009 pandemic H1N1 influenza.[32] Most of the neutralizing antibodies induced by the virus are able to cross-react against epitopes in the hemagglutinin head and stalk of various influenza strains. Tested antibodies show broad protection against H1N1 and H5N1 influenza strain with abundantly stalk-reactive antibodies in H1N1 patients. Such universal vaccine may have a stronger cross-protection to divergent virus subtypes, reduced production time and cost. This advantage may serve as an important direction in the development of a universal influenza vaccine.

Another study provides evidence that a universal vaccine which covers all influenza strains is achievable. This novel influenza vaccine is able to reactivate and induce T-cell responses (CD8+ and CD4+) towards NP and M1 proteins of the virus that is common in all influenza type A strains.[33] It proves to be safe and well tolerated with less local side effects. Extensive protection against seasonal and pandemic influenza is promising. According to researchers, introduction of such a vaccine would provide protection for at least 5–10 years. [34]

Limitations

In addition to the limitations identified earlier, all models are simplifications of real life. A model cannot represent all possible influenza outcomes and the heterogeneity that exist among the patient population. Rather than make decisions, a model provides information for decision makers such as public health officials, scientists, insurance companies, investors, manufacturers, and clinicians. Models are designed to elucidate relationships, raise questions, and approximate orders of magnitude instead of providing exact answers. Although our model does not explicitly represent natural immunity from infection, which may persist for several years, especially when occurring in children, the various outcome probabilities (e.g., risk of influenza) did draw from studies where natural immunity was present.

Conclusion

Limitations of the current annual influenza vaccine have led to ongoing efforts to develop a “universal“ influenza vaccine, i.e., one that targets a conserved portion of the influenza virus so that the coverage of a single vaccination can persist for multiple years. Our results suggest that a universal vaccine could provide substantial economic value by overcoming the annual vaccine's current drawbacks. This favors investment in universal vaccine development, helps establish efficacy and duration of protection targets for developers, and prepares policy makers for reimbursement questions. Addressing these issues early in a vaccine's development when changes are easier to make could help avoid considerable problems in the future. Although development of a universal vaccine requires surmounting scientific hurdles, our results delineated the circumstances under which such a vaccine would be a cost-effective alternative to the annual influenza vaccine.

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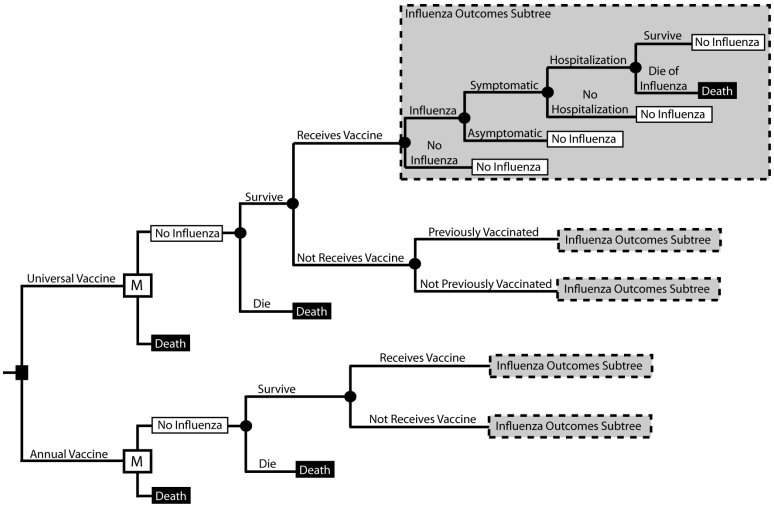

Figure 1.
Model Structure State Diagram

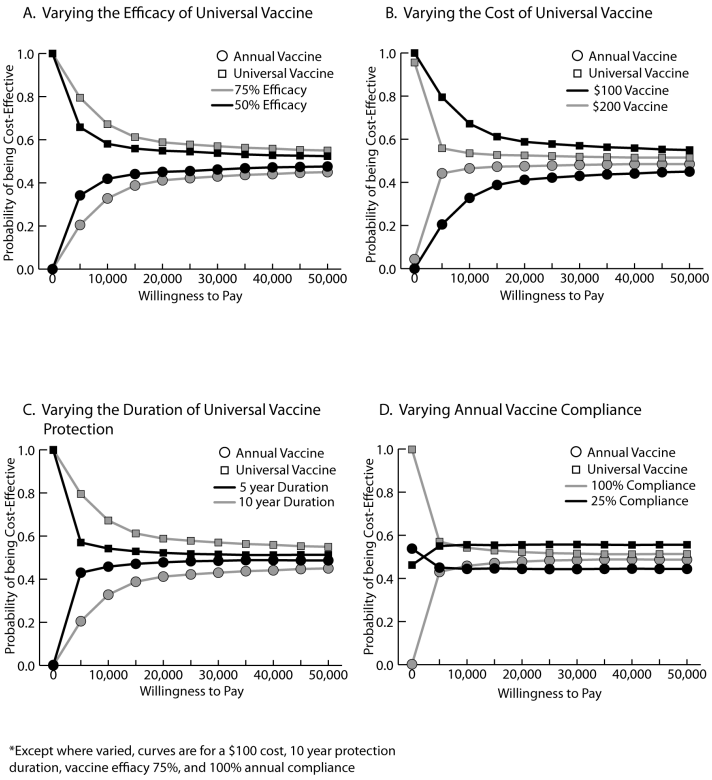

Figure 2.

Acceptability Curves a) varying the efficacy of universal vaccine, b) varying the cost of universal vaccine, c) varying the duration of universal vaccine protection, d) varying annual vaccine compliance

Table 1

Data inputs

Description (units)	Distribution	Mean	Standard Deviation or Range	Source
COSTS ($US)				
Annual vaccine	Point Estimate	20	-	[11,35]
Influenza Treatment:				
Outpatient Visit				
Pediatric Outpatient Visit	Point Estimate	74.90		[36]
Adult Outpatient Visit	Triangular	104.77	69.14 – 140.39	[37]
Elderly Outpatient visit	Triangular	155.92	118.39 – 193.44	[37]
Hospitalization				
Age 1 to 4	Gamma	5992	515	[38]
Age 5 to 9	Gamma	5761	561	[38]
Age 10 to 14	Gamma	8735	1231	[38]
Age 15 to 17	Gamma	6559	816	[38]
Age 18 to 44	Gamma	6506	461	[38]
Age 45 to 64	Gamma	7580	759	[38]
Age 65 to 84	Gamma	7568	234	[38]
Age 85 and Over	Gamma	7698	240	[38]
General death	Triangular	6921	5191 – 9025	[39]
Treatment of vaccine side effects	Triangular	0.79	0.70 – 3.93	[11]
Median hourly wage	Point Estimate	15.57	-	[35]
DURATIONS				
Work hours per day	-	8	-	Assumption
Absenteeism from influenza (days)	Uniform	3.2	1.5 – 4.9	[40]
Time being sick from the flu	Uniform	6	5 – 7	[41–42]
Time after having vaccine side effects	Uniform	0.75	0.5 – 1	[43]
UTILITIES (QALYs)				
One year of life				
Age 0 to 17	Point Estimate	1	-	[8]
Age 18 to 64	Point Estimate	0.92	-	[8]
Age 65 and Over	Point Estimate	0.84	-	[8]
Influenza with no hospitalization	Triangular	0.65	0.49 – 0.81	[44–45]
Influenza with hospitalization	Triangular	0.50	0.38 – 0.63	[44,46]
Vaccine side effects	Triangular	0.95	0.71 – 1.00	[46]
PROBABILITIES				
Clinical Outcomes without Vaccination				
Influenza throughout the year	Triangular	0.125	0.05 – 0.2	[7]
Outpatient Visit given influenza				

Description (units)	Distribution	Mean	Standard Deviation or Range	Source
Age 0 to 4	Beta	0.455	0.098	[47]
Age 5 to 17	Beta	0.318	0.061	[47]
Age 18 to 64	Beta	0.313	0.014	[47]
Age 65 and Over	Beta	0.620	0.027	[47]
Age 0 to 4 (High-risk)	Beta	0.910	0.250	[47]
Age 5 to 17 (High-risk)	Beta	0.635	0.167	[47]
Age 18 to 64 (High-risk)	Beta	0.625	0.118	[47]
Age 65 and Over(High-risk)	Beta	0.850	0.093	[47]
Hospitalization given influenza				
Age 0 to 4	Beta	0.0141	0.0047	[47]
Age 5 to 17	Beta	0.0006	0.0002	[47]
Age 18 to 49	Beta	0.0042	0.0014	[47]
Age 50 to 64	Beta	0.0193	0.0064	[47]
Age 65 and Over	Beta	0.0421	0.0140	[47]
Mortality given influenza				
Age 0 to 4	Beta	0.00004	0.00001	[47]
Age 5 to 17	Point Estimate	0.00001		[47]
Age 18 to 49	Beta	0.00009	0.00003	[47]
Age 50 to 64	Beta	0.00134	0.00045	[47]
Age 65 and Over	Beta	0.01170	0.00390	[47]
Vaccine efficacy	Triangular	0.45	0.56 – 0.68	[7]
Vaccine side effects	Point Estimate	0.03	-	[48]

Table 2

Cost, Effectiveness, and Incremental Cost-Effectiveness Ratio (ICER; Cost per QALY) of Switching from Annual to Universal Vaccine when Universal Vaccine Provides 5 years of Protection (50% Symptomatic Influenza Rate)

		Annual Vaccine Compliance	Vaccination Strategy	Cost	Effectiveness	ICER
Vaccine Cost $100	**Vaccine Efficacy 75%**	100%	Universal	1,580 – 2,120	25.52 – 28.29	Universal Dominates
			Annual	1,684 – 2,385	25.52 – 28.29	
		75%	Universal	1,579 – 2,118	25.53 – 28.29	Universal Dominates
			Annual	1,649 – 2,560	25.52 – 28.29	
		50%	Universal	1,579 – 2,120	25.52 – 28.29	Universal Dominates
			Annual	1,616 – 2,320	25.52 – 28.28	
		25%	Universal	1,577 – 2,118	25.53 – 28.29	Universal Dominates
			Annual	1,578 – 2,286	25.52 – 28.28	
	Vaccine Efficacy 50%	100%	Universal	1,775 – 2,473	25.52 – 28.29	Annual Dominates
			Annual	1,685 – 2,387	25.52 – 28.30	
		75%	Universal	1,777 – 2,474	25.53 – 28.29	**39,482** – 52,197
			Annual	1,650 – 2,351	25.53 – 28.29	
		50%	Universal	1,775 – 2,475	25.53 – 28.29	**31,544** – 74,353
			Annual	1,612 – 2,320	25.53 – 28.29	
		25%	Universal	1,775 – 2,474	25.53 – 28.29	**33,987 – 49,354**
			Annual	1,579 – 2,282	25.52 – 28.29	
Vaccine Cost $200	**Vaccine Efficacy 75%**	100%	Universal	2,019 – 2,718	25.52 – 28.30	77,108 – 124,575
			Annual	1,684 – 2,384	25.53 – 28.29	
		75%	Universal	2,214 – 2,893	25.52 – 28.29	171,099 – 319,601
			Annual	1,648 – 2,353	25.52 – 28.28	
		50%	Universal	2,020 – 2,717	25.53 – 28.29	79,422 – 81,349
			Annual	1,614 – 2,317	25.52 – 28.29	
		25%	Universal	2,018 – 2,718	25.53 – 28.30	**33,562 – 47,763**
			Annual	1,579 – 2,288	25.52 – 28.28	
	Vaccine Efficacy 50%	100%	Universal	2,411 – 3,072	25.53 – 28.29	Annual Dominates
			Annual	1,682 – 2,387	25.53 – 28.29	

Annual Vaccine Compliance	Vaccination Strategy	Cost	Effectiveness	ICER
75%	Universal	2,411 – 3,071	25.53 – 28.29	Annual Dominates – 495,957
	Annual	1,650 – 2,353	25.52 – 28.29	
50%	Universal	2,413 – 3,073	25.52 – 28.29	257,930 – 806,958
	Annual	1,614 – 2,560	25.52 – 28.29	
25%	Universal	2,412 – 2,284	25.53 – 28.29	144,542 – 172,231
	Annual	1,580 – 3,073	25.52 – 28.29	

Note: Bold ICER values are cost-effective.

Table 3

Cost, Effectiveness, and Incremental cost-effectiveness ratio (ICER) of Switching from Annual to Universal Vaccine when Universal Vaccine Provides 10 years of Protection (50% Symptomatic Influenza Rate)

		Annual Vaccine Compliance	Vaccination Strategy	Cost	Effectiveness	ICER
Vaccine Cost $100	**Vaccine Efficacy 75%**	100%	Universal	1,287 – 2,021	25.53 – 28.29	Universal Dominates
			Annual	1,685 – 2,385	25.52 – 28.29	
		75%	Universal	1,286 – 2,021	25.52 – 28.29	Universal Dominates
			Annual	1,648 – 2,353	25.52 – 28.29	
		50%	Universal	1,286 – 2,019	25.53 – 28.29	Universal Dominates
			Annual	1,613 – 2,319	25.52 – 28.29	
		25%	Universal	1,286 – 2,022	25.53 – 28.29	Universal Dominates
			Annual	1,581 – 2,283	25.52 – 28.29	
	Vaccine Efficacy 50%	100%	Universal	1,483 – 2,197	25.53 – 28.29	Universal Dominates
			Annual	1,685 – 2,386	25.52 – 28.29	
		75%	Universal	1,485 – 2,201	25.53 – 28.29	Universal Dominates
			Annual	1,649 – 2,351	25.53 – 28.29	
		50%	Universal	1,482 – 2,200	25.52 – 28.29	Universal Dominates
			Annual	1,615 – 2,316	25.52 – 28.29	
		25%	Universal	1,484 – 2,200	25.52 – 28.29	Universal Dominates
			Annual	1,579 – 2,282	25.52 – 28.29	
Vaccine Cost $200	**Vaccine Efficacy 75%**	100%	Universal	1,630 – 2,347	25.53 – 28.29	**9,180 – 45,456**
			Annual	1,683 – 2,386	25.53 – 28.29	
		75%	Universal	1,649 – 2,348	25.52 – 28.29	**1,285 – 31,956**
			Annual	1,629 – 2,354	25.53 – 28.29	
		50%	Universal	1,615 – 2,348	25.52 – 28.29	**4,222 – 4,755**
			Annual	1,616 – 2,378	25.52 – 28.29	
		25%	Universal	1,629 – 2,346	25.53 – 28.30	**5,194 – 5,970**
			Annual	1,580 – 2,285	25.52 – 28.29	
	Vaccine Efficacy 50%	100%	Universal	1,829 – 2,526	25.53 – 28.29	Annual Dominates
			Annual	1,684 – 2,384	25.53 – 28.29	

Annual Vaccine Compliance	Vaccination Strategy	Cost	Effectiveness	ICER
75%	Universal	1,827 – 2,530	25.52 – 28.29	Annual Dominates
	Annual	1,651 – 2,350	25.52 – 28.29	
50%	Universal	1,827 – 2,527	25.52 – 28.29	69,797 – 380,364
	Annual	1,613 – 2,322	25.52 – 28.29	
25%	Universal	1,827 – 2,527	25.53 – 28.29	59,443 – 74,421
	Annual	1,580 – 2,286	25.52 – 28.28	

Note: Bold ICER values are cost-effective.