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The Economic Value of a Quadrivalent versus Trivalent Influenza Vaccine

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Abstract

The recently licensed quadrivalent seasonal influenza vaccine (QIV) may provide better protection than the traditional trivalent influenza vaccine (TIV) as it includes one more influenza B strain. We developed a Monte Carlo simulation model to determine the economic value of a QIV compared to the TIV for ten influenza seasons (1999–2009). The addition of the influenza B strain to convert the TIV into a QIV could result in substantial cost savings to society (median of $3.1 billion) and third party payers (median of $292 million), even when the cost of QIV is significantly higher

Keywords

Influenza; Quadrivalent Vaccine; Trivalent Vaccine; Economics

INTRODUCTION

By including one more influenza B strain than the traditional trivalent influenza vaccine (TIV), the recently licensed quadrivalent seasonal influenza vaccine (QIV; MedImmune FluMist Quadrivalent for persons aged 2 to 49 years[1]) may provide better protection for the population [2–3]. Each year, the TIV contains three influenza strains, A/H1N1, A/H3N2, and one of two B strains, selected at least 6 months prior to the start of the influenza season [3–4]. The QIV may be an important advantage since predicting which of the two influenza B strain lineages, Yamagata and Victoria, will circulate in the following influenza season has been a continuing challenge and a vaccine with just one B strain may offer little protection against the other B strain [2–4]. Reed et al. estimated the additional influenza cases that a QIV may have averted over TIV during the past decade [3]. In this study, we utilize the results from the Reed et al. study to determine the potential cost-savings the QIV may provide, which can in turn help guide pricing, adoption, and reimbursement of the QIV.

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MATERIALS AND METHODS

We developed a Monte Carlo simulation model in Microsoft Excel (Microsoft, Redmond, WA) using a Crystal Ball (Oracle, Redwood City, CA) add-in to determine the economic value of a QIV compared to the TIV for ten influenza seasons (1999–2009) from the third party payer and societal perspectives. The third party payer perspective included only the direct costs of illness (i.e., cost of outpatient visits and hospitalization), while the societal perspective included direct and indirect costs of illness (i.e., productivity losses due to missed work and mortality). Table 1 shows our model inputs. All costs were age-stratified where applicable and in 2012 $US, converted using a 3% discount rate[5].

The age-stratified population (using the following groups: <1, 1–17, 18–44, 45–64, 65–84, and ≥85 years) for each influenza season came from the US Census Bureau (e.g., the 2008–2009 influenza season assumed the 2008 US population estimate) [6].

The study by Reed et al. provided the number of all influenza cases, hospitalizations, and deaths averted each year by vaccinating with a QIV compared to the TIV[3]. The first step was to separate these numbers into three mutually exclusive categories by age (using the age distributions from Table 1):

- *Persons who were infected without requiring hospitalization:* A symptomatic person drew from the distribution of days of school or work missed (depending on age), which would then result in costs of lost patient (or caregiver in the case of a child) productivity to society (based on wage data from the Bureau of Labor Statistics assuming an 8-hour work day). A symptomatic person also had a probability of an outpatient clinic visit, which would result in the cost of a clinic visit (both perspectives) and four hours of lost productivity (just from the societal perspective).
- *Those who required hospitalization and survived:* A hospitalized person incurred the cost of an outpatient visit (both perspectives), the cost of a hospitalization drawn from a distribution in Table 1 (both perspectives), and the lost productivity during the days of hospitalization (just the societal perspective).
- *Those who were hospitalized and died:* A hospitalized person who did not survive who accrue the additional cost of death and lost lifetime productivity (just societal perspective), calculated from the expected life expectancy of that person [7] and the discounted expected value of the person's remaining lifetime earnings [8].

The Reed et al. study made several key assumptions that also hold in our study: (1) QIV would have efficacy against each included strain comparable to the strain included in the TIV (47–68%), assuming that the added B strain in the QIV would have the same efficacy as the B strain that was included (2) efficacy would not differ as substantially over different age strata and influenza strain/lineage; and (3) fewer does of QIV would be produced and its introduction would be in stages rather than wholesale replacement of TIV. Reed et al. also used population averages, and therefore did not account for potential differences in age, influenza strain/lineage, and health impact. Additionally, as the Reed study used vaccine coverage rates (18–30%) based on prior vaccination target population recommendations for each particular year, our study does as well.

Probabilistic sensitivity analyses simultaneously varied each parameter throughout their ranges listed in Table 1. Additional sensitivity analyses varied the price premium of the QIV vaccine over the TIV vaccine (range: $0–$120). Each simulation involved 5,000 iterations or trials.

RESULTS

Table 2 shows expected median cost-savings across the entire United States for the third party payers and society if the QIV instead of the TIV were used at different price premiums for the QIV vaccine (i.e., if the QIV cost $5, $15, $30, and $120 more than the TIV). This would translate to a median of $3.1 billion societal cost-savings (mean: $3.1 billion; 95% range: $2.8–3.5 billion) and a median of $292 million third party payer costs savings (mean: $294 million; 95% range: $251–342 million) during the decade if the QIV were used instead of the TIV and priced equally to the TIV. Raising the price of the QIV over the TIV decreased the median cost-savings. A higher costing vaccine would still be beneficial in some seasons, as cost-savings were seen for the QIV up to premiums of $120 for society and $105 for third party payers. Utilization of QIV becomes less cost-saving as QIV price premiums surpass $105 for third party payers.

Over the entire decade, 2,684,145 total cases were averted. From the third party payer perspective, a $120 premium would have saved $11 per case and a $0 premium would have saved $109 per case across the entire decade (from 1999–2009). Cost-savings per case across the entire decade from the societal perspective ranged from $1,163 ($0 premium) to $1,041 ($120 premium). The cost per case tended to increase as premiums decreased, resulting in less cost-savings.

As there were no cases averted for the 1999–2000 and 2000–2001 influenza seasons, there was no cost advantage of the QIV. From the third party payer perspective, the 2007–2008 season yielded the highest median cost-savings per case and death averted, even saving costs with a premium as high as $120 ($2 per case averted and $3,831 per death averted). Whereas the highest cost-savings per hospitalization averted were found for the 2001–2002 influenza season for all premiums up to $105 (from both perspectives). At higher premiums it would cost third party payers up to $23–$38 to averted one case, $4,450–$7,332 to averted one hospitalization, and $45,865–$75,570 to averted one death, for premiums of $105 and $120 respectively.

DISCUSSION

Adding an additional B strain to the seasonal influenza vaccine could reap substantial cost-savings for society and third party payers, even if the QIV enjoyed a significant price premium over TIV. It is not common for a new medical technology, especially one that is a variation of an existing technology, to immediately generate cost-savings[9]. (Most technologies require additional costs to result in health benefits.) Such savings may reassure third party payers of the value of covering a more expensive QIV as they would be likely to recoup this investment through averting healthcare costs. This in turn could facilitate adoption and also motivate additional scientists, developers, and manufacturers to enter the QIV market and investigate the possibility of adding even more strains to the vaccine. Moreover, the cost-savings could be greater in the coming decade as the Advisory Committee on Immunization Practices (ACIP) has increased the scope of whom they recommend should be vaccinated[10], which could in turn increase coverage of the overall population.

These findings also highlight the difficulty in accurately predicting the circulating influenza strains for the upcoming influenza season and the cost of inaccurate predictions. For example, missing on the B strain for the 2007–2008 influenza season seems to have cost third party payers well over $100 million and society well over $1 billion. This year 29% of all influenza were influenza B viruses, of which 98% were from the Yamagata lineage, while the TIV vaccine was manufactured with the Victoria lineage[3]. Although there are

continuing efforts to improve the accuracy of strain predictions, adding more strains to the seasonal vaccine could be a promising route.

Currently, only MedImmune's QIV has FDA approval , but GlaxoSmithKline, Sanofi Pasteur, and Novartis Vaccines are in various stages of QIV development; their QIV formulations are expected to reach the market for the 2013–14 influenza season [11]. MedImmune plans to discontinue the current TIV FluMist and offer only the FluMist Quadrivalent vaccine for the 2013–14 influenza season, where as GlaxoSmithKline and Sanofi Pasteur plan to introduce their QIV formulations in conjunction with their current TIV vaccines[11].

Every model is a simplification of real life and cannot account for every possible factor and outcome[12]. Our results assume that QIV vaccine production could have been high enough to cover the number of TIV doses administered each year, which should eventually be possible, but could require an expansion in production capacity to accommodate the additional strain[2]. Therefore, the realization of cost-savings would depend on the timing of replacement of TIV with QIV: more slowly for gradual replacement and more near term if companies such as MedImmune do rapid en masse replacement[11]. Expansion of vaccine manufacturing capacity since the 2005–06 season and the inception production methods (e.g., cell culture) could further foster industry's ability to replace TIV[11]. On the other hand, additional limitations may make our estimates of the cost-savings conservative. Our study used the adjusted vaccine production numbers from Reed et al.; using less conservative numbers would increase QIV's cost-savings by averting more influenza outcomes. Current and future broader target population recommendations may further enhance the economic value of the QIV. It also did not account for over-the-counter self-treatment and all additional costs from medical problems (e.g., congestive heart failure or pulmonary disease exacerbations) that may be precipitated by influenza. Our model did not include any potential adverse events since reported ones are infrequent and relatively minor (e.g., runny nose, nasal congestion, sore throat)[1] and evidence does not suggest a higher rate than TIV. Our study draws from the Reed et al. study and therefore is subject to its limitations and assumptions.

In conclusion, the addition of the influenza B strain to convert the TIV into a QIV could result in substantial cost-savings to society and third party payers, even when the cost of QIV is significantly higher, information which could be useful to insurers (e.g., coverage decisions), manufacturers (e.g., production and pricing), developers (e.g., prioritizing research), and policy makers (e.g., adoption).

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Highlights

- We model the economic value of a QIV compared to the TIV for ten influenza seasons
- QIV provided cost savings during the decade if used instead of the TIV
- A higher costing (up to $120) vaccine would still be beneficial in some seasons
- Adding an additional B strain could reap substantial savings

Table 1

Model Input Parameters

Parameter	Mean or Median	Standard Deviation or Range	Source
Median Hourly Wage	17.26		[8]
Missed Work Days	3.2	1.5 – 4.9	[13]
Missed School Days	2.54		[14]
Probability of Outpatient Visit			
<1 year old	45.5	26 – 65	[15]
1 – 17 years old	31.8	20 – 44	[15]
18 to 64 years old	31.3	29 – 34	[15]
65 years and older	62	57 – 67	[15]
Cost of Outpatient Visit			
<1 year old	76.17		[16]
1 – 17 years old	81.47		[16]
18 – 64 years old	102.51		[16]
65 – 84 years old	93.46		[17]
85 years and older	90.04		[17]
Duration of Outpatient Visit (hours)	4		Assumption
Cost of Hospitalization			
<1 year old	4,221.24	385.29	[18]
1 – 17 years old	6,119.74	751.64	[18]
18 – 44 years old	10,517.29	444.16	[18]
44 – 64 years old	11,372.51	403.39	[18]
65 – 84 years old	9,502.05	387.78	[18]
85 years and older	8,545.11	407.72	[18]
Productivity Loss due to Mortality			
<1 year old	1,461,022		[7–8]
1 – 17 years old	1,413,302		[7–8]
18 – 44 years old	1,226,143		[7–8]
44 – 64 years old	889,374		[7–8]
65 – 84 years old	516,093		[7–8]
85 years and older	222,244		[7–8]

Table 2

Cost-savings [median (95% range), $US in millions] of the additional benefits of QIV vs. TIV over ten influenza seasons to third party payers and society

Influenza Season	Price Premium of QIV over TIV			
	$5	**$15**	**$30**	**$120**
Cost-Savings to Third Party Payers [median (95% range)]				
1999–2000[a]	None	None	None	None
2000–2001[a]	None	None	None	None
2001–2002	21.1 (18.3–24.3)	18.4 (15.6–21.6)	14.2 (11.5–17.5)	**10.4 (7.0–13.0)**
2002–2003	0.2 (0.17–0.23)	0.17 (0.15–0.21)	0.14 (0.11–0.17)	**0.06 (0.03–0.09)**
2003–2004	2.2 (1.8–2.5)	1.9 (1.6–2.3)	1.6 (1.3–2.0)	**0.2** (0.19–**0.51**)
2004–2005	29 (24.9–33.6)	25.7 (21.6–30.4)	20.7 (16.7–25.4)	**8.9 (4.0–12.8)**
2005–2006	29.2 (25.2–33.8)	25.7 (21.7–30.4)	20.5 (16.5–25.1)	**11 (6.2–14.8)**
2006–2007	6.3 (5.3–7.4)	5.7 (4.7–6.8)	4.8 (3.9–5.9)	**0.42** (0.73–**1.3**)
2007–2008	155.8 (131.7–183.8)	142.3 (118.0–170.5)	122.1 (98.4–151.1)	2.5 (31.9–**20.7**)
2008–2009	35.8 (30.5–42.1)	32.5 (27.1–38.8)	27.5 (22.2–34.0)	**2.0** (4.6–**7.3**)
Decade Total	279.5 (238.1 – 327.8)	252.5 (210.5–301.1)	211.5 (170.7–261.4)	**30.4** (20.2–**70.4**)
Per Year	28 (23.8 – 32.8)	25.2 (21.0–30.1)	21.2 (17.1–26.1)	**3.0** (2.0–**7.0**)
Cost-Savings to Society [median (95% range)]				
1999–2000[a]	None	None	None	None
2000–2001[a]	None	None	None	None
2001–2002	307.2 (273.4–340.9)	304.5 (270.4–338.2)	300.3 (266.5–333.2)	275.2 (242.3–309.9)
2002–2003	2.4 (2.1–2.7)	2.4 (2.1–2.7)	2.4 (2.1–2.6)	2.1 (1.9–2.4)
2003–2004	23.2 (20.7–25.8)	23 (20.5–25.5)	22.7 (20.2–25.2)	20.8 (18.3–23.4)
2004–2005	371.2 (330.3–411.9)	367.9 (326.6–408.8)	363 (322.0–403.0)	332.7 (292.7–374.8)
2005–2006	392.3 (348.8–435.8)	388.9 (344.9–432.5)	383.5 (339.9–426.3)	351.5 (308.9–396.3)
2006–2007	66.7 (59.4–74.0)	66.2 (58.8–73.4)	65.3 (58.0–72.4)	59.9 (52.8–67.5)
2007–2008	1,536.8 (1,370–1,704)	1,524.30 (1,355–1,690)	1,503.7 (1,335–1,668)	1381.9 (1216.3–1554.4)
2008–2009	408.6 (367.1–450.0)	405.4 (363.5–446.6)	400.3 (358.9–440.9)	370.1 (329.5–412.9)
Decade Total	3,108.8 (2,771–3,446)	3,082.4 (2,742 –3,419)	3,040.9 (2,704–3,372)	2,793.9 (2,463.3–3,142.1)
Per Year	310.9 (277.1–344.6)	308.2 (274.2–341.9)	304.1 (270.4–337.2)	279.4 (246.3–314.2)

[a]The QIV did not provide any appreciable cost-savings as the influenza B strain for the TIV matched with the circulating strain[3]

Note: Bold values imply costs