

Using simulation to establish appropriate vaccination rates and copayment policies from a cost perspective

Sang-Man Kim · Arben Asllani

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Abstract Making the best decisions on vaccination policy during influenza seasons can be critical in minimizing overall costs for an insurance company. Using administrative data, company records, and published reports for the flu season during 2007–2008, a simulation model is developed to mimic the spread of influenza in children, to calculate the cost of vaccination, and the cost of treatment for infected children. The model is designed to allow for sensitivity analysis with different scenarios of vaccination rates and is implemented in a healthcare insurance company located in Southeast region of the USA. The experimental results show several advantages of simulation methodology, including its ability to mimic the complex behavior of a spreading influenza in a selected population group, while testing a range of alternative solutions for different disease scenarios. Based on the historical data, the proposed simulation suggests a vaccination policy that could significantly reduce the overall cost of the vaccination program.

Keywords Simulation · Vaccination policy · Health insurance planning · Influenza modeling

1 Introduction

Influenza (i.e., flu) is a highly contagious respiratory infection that is caused by a variety of influenza viruses. Even in recent years, high levels of influenza activity

S.-M. Kim
School of Management & Management Research Institute, Kyung Hee University,
Seoul 130-170, Korea
e-mail: smkim@khu.ac.kr

A. Asllani (✉)
University of Tennessee-Chattanooga, Chattanooga, TN 37403-2598, USA
e-mail: beni-asllani@utc.edu

sustained statewide. The pandemic 2009 influenza virus accounted for $\sim 50\%$ of cases of influenza-like illness and over 92% of influenza viruses (Dawood et al. 2009). The illness produced by the influenza virus can be mild to severe and can even lead to death. It is estimated that between 5 and 20% of the population in the US is infected each year (Kapustin 2008) by this disease. Observations have suggested that most infections occur in younger individuals: 40% between 10 and 18 years and 95% for those younger than 50 years. Especially high rates (147 per $100,000$) occur in children aged 5 – 14 years (Louie et al. 2009). Considering the severity of the disease, Prosser et al. (2008) suggests an increase in vaccination rates which currently remain far below national goals in the US.

The World Health Organization raised the worldwide pandemic influenza alert to its highest level in response to the global spread of a novel influenza virus (Black et al. 2009). In the today's modern society, government involvement in the provision of public services, including high-quality health services, is expected (Armistead and Pettigrew 2008). Also, policy makers focus on improving the health care service quality while providing lower costs to meet high expectations of quality health care. Most healthcare organizations and practitioners tend to focus on input costs and other aspects of costs have relatively received less attention (Rayna and Striukova 2009; Chung et al. 2010).

The overall insurance costs of flu during any given season consist of two major components: the cost of vaccination (prevention) and cost of patient treatment (if the disease is not averted). The cost of vaccination is computed by multiplying the average cost of a vaccine (minus any copayment) times the number of people who receive the vaccine. For practical purposes, the cost of vaccination can be assumed to be a linear function of the number of individuals who receive the vaccine. The cost of treatment is computed by multiplying the number of people who contract the disease times the average cost of disease treatment (minus any deductible and/or copayment). Components of the cost of treatment include the average for the use of physicians, hospitals, or emergency rooms (ERs). The treatment cost is inversely related to the number of people who receive the vaccine. That is, for a given target population, the number of people requiring treatment decreases as the vaccination rate increases. It is assumed that treatment costs are inversely and nonlinearly related to the vaccination rate. As shown in Fig. 1, the sum of the two cost components is the total cost curve, which is U-shaped. Thus, there exists a mathematically optimal rate of vaccination, which will minimize the overall insurance costs of the disease.

From a societal perspective, increasing vaccination rates has mixed results with respect to cost-effectiveness. For example, Prosser et al. (2008) suggest that non-traditional settings (pharmacies, workplaces) could be used to deliver routine influenza vaccinations, resulting in cost savings for healthy adults aged 50 – 64 and which is relatively cost effective for healthy adults aged 18 – 49 . Opportunities exist for healthcare practitioners to exercise and use judgment on vaccination strategies. To aid the selection process from a cost perspective, decision-making tools can be used to evaluate the proper degree of vaccination for different population segments.

Establishing an optimal vaccination policy is a complex task. It involves a high degree of uncertainty and a large number of input factors, most of which are random. This paper seeks to demonstrate how a simulation model can be used to

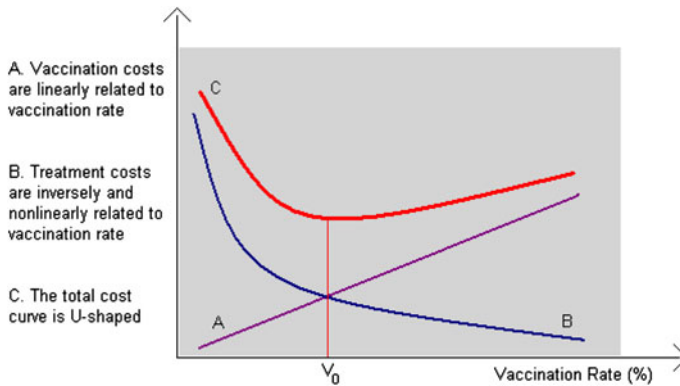


Fig. 1 Relationships between costs and vaccination rate

find an appropriate vaccination rate, which reduces the total cost of vaccination and treatment. Nichol et al. (1994) found that immunization in the elderly saved \$117 per person in medical costs. While vaccination is generally considered to be cost effective from a societal perspective, and can be beneficial for children or the elderly, there is no universal tool that can be used to investigate the effectiveness of a vaccination program, such as proposed in this paper.

The approach is illustrated with data from an insurance company located in the Southeast region of the USA. The model “mimics” the spread of flu in school-aged children and calculates the cost of vaccination, as well as the cost of treatment of the infected children. Parameters of the simulation model are estimated from administrative data and company records during the 2007–2008 season of influenza. The conceptual and logical design of the proposed simulation model is based on the existing theory of vaccination models as described in the following section.

2 Literature review

Mathematical models, which depict the impact of vaccination on the spread of disease, have existed for over 100 years. In 1880, a Swiss physician, Theophil Lotz, rigorously analyzed available statistical data and developed a basic mathematical model to clarify the impact of a vaccination program (Lotz 1880). He foresaw two of the most important theoretical concepts in modern infectious disease epidemiology: basic reproduction number and herd immunity. The basic reproduction number, R_0 , is the average number of secondary cases arising from the introduction of an initial case (Anderson and May 1991; Diekmann and Heesterbeek 2000). Dietz (1993) provides a survey of the various estimation methods available for R_0 .

To further describe the dynamics in the generation of new cases, Lotz (1880) also suggested an average time of 15 days for what now would be called the “generation interval” or the “serial interval”, which is the mean time interval between onset of initial case and onset of secondary cases (Bailey 1975; Diekmann and Heesterbeek 2000; Fine 2003). The number of people, which can be infected by a single case

during one generation, is known as reproduction number. When the reproduction number is two, starting with a single case, $1 \times 2^6 = 64$ cases in the sixth generation and $1 \times 2^8 = 256$ cases in the eighth generation are infected.

The discussions following the above theory regarding reproduction number come very close to determining the required vaccination coverage for eradication in a randomly mixed population (Anderson and May 1982; Diekmann and Heesterbeek 2000). Threshold vaccination coverage for eradication is based on several factors: non-homogenous distribution of population and contacts, contact tracing, and ring vaccination (Fine 1993). In addition, evidence of herd immunity was finally suggested after smallpox eradication, based on surveillance data on vaccination coverage and population density (Arita et al. 1986). Herd immunity not only decreases the disease frequency in the non-immunized, but also affects those who are vaccinated, if the vaccine is not 100 % effective (Mühlemann and Weiss 1997).

Based on this research, many models that predict the impact of vaccination programs have been introduced. These models can be grouped into two main categories: dynamic and static. A major difference between them is that dynamic models capture the indirect protection resulting from immunization (i.e., herd immunity effect). Herd immunity is the population-level consequence of acquired immunity among some individuals, which will reduce the risk of acquiring infection among susceptible individuals. Immunity can be acquired either through natural infection or through artificial inoculation with a vaccine (Garnett 2005).

Currently, most economic evaluations of vaccination programs use static models (Brisson and Edmunds 2003). In recent decades, several new methodologies have been introduced (Hill and Longini 2003). Examples of methodological choices are type of analysis (cost-benefit, cost-effectiveness, or cost-utility), the perspective (societal or payer), valuation technique (willingness to pay, standard gamble, multi-attribute utility scores), and discount rates (Briggs 2000; Briggs and McGray 1999). Further, recent literature shows many models with parameter uncertainties (Brisson and Edmunds 2006). Uncertainties include parameters, such as biological, demographic, epidemiological, medical, and economic.

The objective functions in other proposed models vary from the willingness-to-pay method to cost-benefit analysis (Birch et al. 1999). However, the literature suggests that in spite of the measure, it is very important that proposed models are consistent with a coherent theory of health condition (Weinstein et al. 2003). In lieu of such requirements, many disease and population-specific studies are conducted to investigate the impact of vaccination rate on the cost of a vaccination (Jacobson et al. 1999; Jacobson and Sewell 2002; Sewell and Jacobson 2003; Griffiths et al. 2005; Jackson et al. 1995).

Most recently, Sander et al. (2009) provide an economic evaluation of influenza pandemic mitigation strategies based on a dynamic influenza micro-simulation transmission model. The authors use simulation to evaluate sixteen mitigation strategies, pre-vaccination being one of them. While these single and mixed strategies are formulated from a societal perspective, the paper is focused on different vaccination strategies from a health insurance perspective. Similar to this paper, Weycker et al. (2005) use a stochastic simulation model to illustrate the

benefits of vaccinating children. However, they investigate the scenario from a societal perspective.

The proposed simulation model is dynamic, because it considers the herd immunity effect. It is also stochastic, because many input variables, such as reproduction number, transmission period, event outcomes, and treatment costs, are random variables generated using well-defined statistical distribution functions.

3 Mathematics of vaccination model

In this paper homogeneous mixing of the population is assumed. The individuals in the population under scrutiny make contact at random and do not mix solely in a smaller subgroup. Homogeneous mixing is a reasonable assumption to simplify the mathematics of the model. Hill and Longini (2003) describe a mathematical model to optimally allocate vaccines to several subpopulations with potentially heterogeneously mixing of individuals.

Assuming each case carries the contagion to only two others, the number of cases will grow from generation to generation, starting with one case and growing to 2, 4, 8, 16, 32, 64, etc. When the initial number of cases is denoted by a , the reproduction number by R_0 , and the generation number by n , the number of cases increases according to the series $a, aR_0, aR_0^2, aR_0^3, \dots, aR_0^n$. Starting with a single initial case, the number of cases in the n th generation is equal to the reproduction number (R_0) to the power of n . This exponential growth assumes that the infection ratio is the same as the reproduction number. However, as the disease progresses from one generation to the next, infected people are no longer susceptible to the disease. Since vaccines can reduce the risk of infection to exposed individuals susceptible to infection and can reduce the probability of transmission from a vaccinated individual infected with influenza (Longini et al. 1978), the infection ratio or the number of people infected in the next generation from a single case, changes and can be calculated as:

$$I = R_0 \frac{S}{P}, \quad (1)$$

where I is the number of people infected from a single case, R_0 is the reproduction number for a given disease and population group, S is the number of susceptible individuals in the population group, and P is the size of population group.

When $I = 1$, an infectious disease is said to be endemic. In such a case, it can be sustained in a population without the need for external inputs. This means that, on average, each infected person is infecting *exactly* one other person. For a disease to be in the endemic steady state, the higher the basic reproduction number, the lower the proportion of the population must be susceptible and vice versa. If $I > 1$, the disease is considered to be in an epidemic state, and the number of people infected will grow exponentially. If $I < 1$, then the disease will die out. From a medical perspective, the number of people infected from a single case must be either less than or equal to 1. As such:

$$I = R_0 \frac{S}{P} \leq 1. \quad (2)$$

Formula (2) indicates that in order to eliminate a disease or keep it in an endemic state, the number of susceptible individuals must be kept lower than or equal to the ratio between population size and the reproduction number, as follows:

$$S \leq \frac{P}{R_0}. \quad (3)$$

Formula (3) indicates the rationale of a vaccination program from a medical perspective. In order for any vaccination program to work, it must immunize as many people as possible so that the number of susceptible (S) is kept below the threshold. Hill and Longini (2003) suggest a method for determining minimal vaccine allocations to prevent an epidemic by setting the reproduction number to 1. Their proposed framework can be sufficiently applied to several epidemic situations. If V represents the number of people to be vaccinated before the first infection occurs, then $S = P - V$. Replacing S in (3), the lower boundary for V , named V_m is calculated:

$$V \geq V_m = \frac{P(R_0 - 1)}{R_0} \quad (4)$$

While (4) establishes values of V_m for the disease to be in the endemic state, it is suggested that the optimal value of V_m must be calculated from a cost perspective. Because the reproduction number, cost of the vaccine, physician cost, loss of productivity, and other variables in the model are stochastic, these variables can better be represented with a range of values, very often described with a statistical distribution. As such, a cost-based vaccination program can be better modeled as stochastic and can be solved via simulation.

4 Conceptual model of the vaccination

When an infection arrives in a susceptible population, the disease is spread based on the reproduction number and immunization rate. Figure 2 shows that people who are infected can either self-recover, seek physician help, or go to the ER. The physician or the ER doctor will provide the necessary treatment. In more serious cases, the physicians may admit a patient to the hospital. After hospital treatment, patients recover but in rare cases the model assumes that some patients die.

Longini et al. (1978) provide a formula which calculates the number of people being infected at a given time. Formula (1) suggests that in the first generation, when there are V_m vaccinated (immunized) people, the number of people infected (I_1) will be:

$$I_1 = R_0 \left(\frac{P - V_m}{P} \right) \quad (5)$$

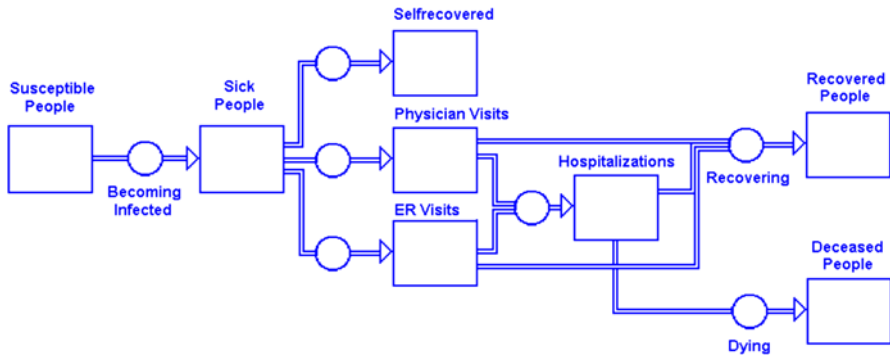


Fig. 2 Basic scenario for simulation model

In the second generation, there will be $(I_1 - H_1)$ new sources of infection, where H_1 patients are healed (or recover) during the reproduction period. The number of people infected in the second generation (I_2) will be:

$$I_2 = (I_1 - H_1) \times R_0 \left(\frac{P - V_m - I_1}{P} \right). \tag{6}$$

The number of people infected in the n th generation is calculated as:

$$I_n = \sum_{g=1}^{n-1} (I_g - H_g) \times R_0 \left(\frac{P - V_m - \sum_{g=1}^{n-1} I_g}{P} \right) \tag{7}$$

The model formulas (6) and (7) consider three groups of patients: susceptible, infectious, and removed individuals (Chick et al. 2008). The number of individuals in each group varies as a function of time t according to a deterministic differential equation (Chick et al. 2008).

Formula (7) is used to simulate arrivals of infected people in the “susceptible people” section in Fig. 2. This is a stochastic feed. R_0 is generated as a stochastic variable, and the value of the rest of the variables in (7) is uncertain at the time new infections are introduced in the model. Also, the time between arrivals of the new set of infections is a random variable. In the model, the number of infections are assumed to increase exponentially with a mean R_p , where reproduction period R_p represents the expected time to transmit the disease from one person to another.

Once people are infected and move to the “sick people” section of the simulation model, there are three potential outcomes: self-recovered, physician visit, or ER. The model assigns probabilities for each of the above three options. Such probability values depend on the type of disease and population profile, such as age, insurance coverage, income level, and so on. Further, the above three events are collectively exhaustive and mutually exclusive. The collectively exhaustive property requires that when a person is infected, at least one of the events must occur: the person must either self-recover, or see a physician, or visit the ER. The

mutually exclusive property requires that the occurrence of any of the three events automatically implies the non-occurrence of the remaining two events: the infected person cannot self recover and see a physician for the same infection, or cannot see a physician and visit the ER at the same simulation scenario.

Once a patient has received medical assistance through a physician or through the ER, he or she will have two possible outcomes: recovered or hospitalized. These two events are also collectively exhaustive and mutually exclusive. Probabilities for each of these two options are assigned based on the historical data of the disease under investigation. Once hospitalized, the patient will either recover or will die, again based on “assigned” probabilities. Once a patient is deceased, the population size is reduced, accordingly. Once patients recover or self-recover, they cannot become infected again. As such, the number of susceptible people is also reduced, accordingly.

5 Experimental design

To examine the efficacy of the proposed simulation model a similar experimental approach to Deng et al. (2008) is utilized. The simulation model is implemented using ProModel[®], simulation software provided by ProModel[®] Corporation. The goal of such a demonstration is to investigate whether a health insurance provider can reduce the overall cost by using the simulation model to generate optimal vaccination policies. Appendix shows the code for the base scenario of the simulation model. As mentioned earlier, data from this scenario are generated from the 2007–2008 season of influenza as recorded by a Health Insurance Company (HIC) headquartered in a Southeast City of the USA. HIC is an independent, not-for-profit, locally governed health plan company. It has been centered on the health and well being of its members for more than 60 years. The company has more than 15,000 customer companies and more than 2.3 million members.

The focus of the investigation is a small segment of HIC’s customer base: school-aged children. The company has provided data about ~9,200 children who are insured with the company through their parents’ policies. During the 2007–2008 flu season, there were no specific vaccination policies for this population group. HIC wants to know if the use of the simulation model could provide any significant savings. If such savings are realized, the company may use the model for the upcoming flu seasons for school-aged children, as well as other segments of its members, such as selected companies, the elderly, teachers, at risk patients, etc. HIC believes that the vaccination rate can be controlled by manipulating copayments on the vaccine.

Table 1 shows the vaccination rate and the copayment level based on the records from the last few years. The average base cost for the vaccination of \$10.90, based on the recent CDC data (www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm). The first row in the table represents the base scenario: company offers no incentives (patient copayment is 100 %). In this scenario, the company estimates that 0–10 % of the children will be vaccinated on a voluntary basis. Since the copayment for this scenario is 100 %, HIC’s cost for vaccination is \$0. As one progresses through scenarios, the cost to a patient decreases proportionally with the copayment level and cost to the insurance company increases also proportionally.

Table 1 Vaccination rate and copayment policy

Scenarios	Patient's copayment (%)	Vaccination rate	Cost of vaccine to HIC
Base scenario	100	0–10	\$0.00
Scenario 1	80	10–20	\$2.18
Scenario 2	60	20–40	\$4.36
Scenario 3	40	40–50	\$6.54
Scenario 4	20	50–60	\$8.72
Scenario 5	0	60–80	\$10.90

Actual values, as well as statistical distributions, used in the model are shown in the last column of Table 2. These data are estimated based on transaction records of HIC, as well as general information found in the website of the Center for Disease Control (<http://www.cdc.gov>). Using Stat:Fit[®], a component of ProModel[®], several statistical distributions are generated using a series of observed data.

As shown, variables used in the model are grouped into three classifications: controlled variables, decision variables, and the objective function. The first set, controlled variables are used to design a simulation scenario. The other two sets, decision variables and the objective function, are used to optimize a simulation scenario. The table shows that 9,200 children records are investigated. It also shows that reproduction ratio for the disease follows a uniform distribution with a mean of 2.3 and range of 0.6.

Obviously, the higher the vaccination rate, the more people are vaccinated, and the less people are infected. However, the answer to this question becomes more difficult when considering the “herd immunity” effect. As such, the simulation model is used to calculate the level of vaccination rate, which will trigger “herd immunity”. While the answer to this question is mathematically provided for deterministic models, the simulation investigates “herd immunity” in a stochastic environment, which is more realistic for disease scenarios (Table 3).

Upon starting the simulation of each scenario, the decision maker is prompted with the following questions:

- What is the expected size of the population?
- What is the expected reproduction number?
- What is the copayment policy or vaccination rate?
- What is the expected time to transmit the disease from one person to another?
- What is the cost of the vaccine?

Each answer set is based on the information from the flu season and allows the decision maker to identify a given scenario. After each scenario is created, the simulation is run using an appropriate number of replications allowing statistically significant results. Harrell et al. (1995) provide an approach to computing the number of replications required to ascertain a selected degree of accuracy. In the example, each scenario is replicated one hundred times to ensure data reliability. The data generated by the model can be further analyzed to fine tune the model and the resulting decisions.

Table 2 Major input variables of vaccination model

Variable name	Description	Notation in the model	Random	Value in the model
Population size	Number of children subjected to a vaccination program	Pop_Size	No	9,200
Reproduction ratio	Average number of children infected by another infected child	R_0	Yes	Uniform U(2.3, .6)
Reproduction period	Expected time to transmit the disease from one person to another	R_period	Yes	Exponential E(2.6) days
Wait until doctor	Average time people wait while sick until they decide to see a doctor in hope of self-recovery	W_until_dr	Yes	E(3.5) days
Wait until recovered	Average time people have to wait until they are considered recovered	W_until_recovered	Yes	E(5.5) days
Cost of vaccine	The cost to buy and administer a single vaccine	Vaccine_C	No	\$10.90
Physician cost	Average cost HIC pays to a physician for a single visit	Physician_C	Yes	Uniform U(155, 54)
Hospital cost	Average cost HIC pays for a single hospitalization case	Hospital_C	Yes	Triangular T(7030, 13159, 39792)
ER cost	Average cost HIC pays for a single visit to the ER	ER_C	Yes	Uniform U(4740, 1250)

Table 3 Major decision and derived variables of simulation model

Variable	Description	Notation in the model	Type
Vaccination rate	Percentage of population vaccinated before the simulation starts. Several values are used to illustrate different scenarios, as well as “herd immunity” effect	V_rate	Decision variable
Number of infections	Number of people who are infected	Infected	Derived value
Immunized	Number of people vaccinated before the simulation starts	Immunized	Derived value
Recovered	Number of people infected and recovered or self-recovered	Recovered	Derived value
Total vaccination cost	Total cost of vaccination program, calculated as a product of number of people vaccinated times the portion of cost covered by HIC	Vaccination_C	Derived value
Total treatment cost	Total cost of treatment, calculated as a sum of physician cost, hospitalization cost, and ER cost	Treatment_C	Derived value
Total cost	Total cost of the disease, calculated as a sum of total vaccination cost and total treatment cost. Goal is to minimize this	Total_C	Derived value

6 Results and analysis

6.1 Model validity

It is expected that a valid simulation model should mimic the actual data, given the same basic input parameters. In this validity exercise the proposed model and its parameters should represent the behavior of the disease (flu) during the target year under investigation (2007–2008).

Table 4 represents a comparison between the simulation model parameters and characteristics of the flu season during 2007–2008. As shown in this table, the model produced very close behavior. Three main characteristics (attack rate, reproductive number, and hospitalization per 10,000) fell within the expected range with a 95 % level of confidence. Specifically, while the attack rate for the season is reported between 20 and 50 % (last column), the simulation produced an average attack rate of 20.48 % with a confidence interval between 20.05 and 21.91 %. Similarly, while the reproductive number for the season is reported between 1.5 and 3, the simulation produced an average reproductive number of 2.34 with a confidence interval between 2.27 and 2.41. Similar results are shown for the hospitalization rate among children between 0 and 23 months. The fourth parameter, mortality rate, 9.1 %, fell outside the confidence interval of 10.2–11.69 %. The model is still considered as valid, since mortality is not included in the overall cost.

The impact of “herd immunity” in the number of people infected can provide insights about the model’s construct and its validity. Two alternatives are compared: scenario model with “herd immunity” and scenario model, where “herd immunity” is purposefully suppressed.

As shown in Fig. 3a, in a given scenario where the vaccination rate is selected at 20 %, the infection of the population increases to 40 %. After that point, herd immunity will not allow the spread of further infections. In Fig. 3b, where the “herd immunity” effect is removed, and the same vaccination rate of 20 % is applied, infection will continue to spread until 80 % are infected.

Table 4 Comparison of model results with reports for 2007–2008 flu

Parameter	Simulation results			CDC and other sources
	Mean	Confidence interval (95 %)		
		From	To	
Attack rate	20.48 %	20.05 %	21.91 %	20–50 % ^a
Reproductive number	2.34	2.27	2.41	1.5–3 ^a
Pediatric hospitalization per 10,000	38.61	37.08	40.15	41.6 per 10,000 ^b
Mortality rate	10.95 %	10.2 %	11.69 %	9.1 % ^a

^a <http://www.cdc.gov/flu/weekly/weeklyarchives2007-2008/07-08summary.htm>

^b http://www.upenn.edu/ldi/issuebrief12_3.pdf

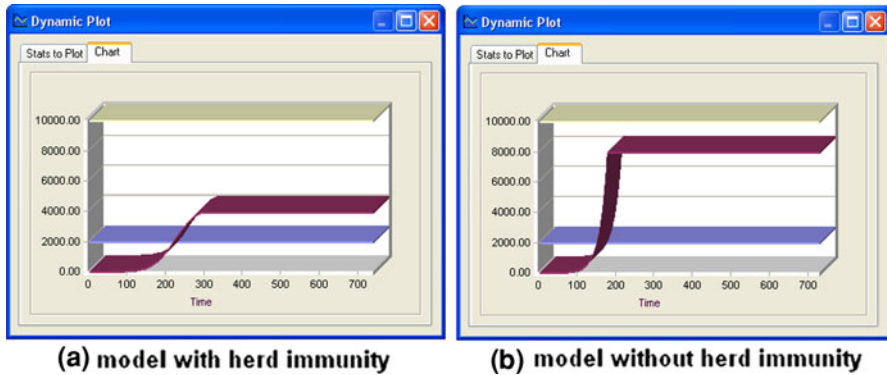


Fig. 3 Impact of herd immunity on the number of infections

Table 5 Simulation results

Scenarios	Patient's copayment (%)	Vaccination rate	Cost of vaccine to HIC	Sample mean for total cost
Base scenario	100	0–10	\$0.00	\$383,713.42
Scenario 1	80	10–20	\$2.18	\$187,821.07
Scenario 2	60	20–40	\$4.36	\$18,402.76
Scenario 3	40	40–50	\$6.54	\$16,604.08
Scenario 4	20	50–60	\$8.72	\$23,284.99
Scenario 5	0	60–80	\$10.90	\$32,380.37

This analysis, not only re-enforces the validity of the model, but also shows the power of computer simulation as a decision-making tool. The decision maker is able to evaluate IF-THEN scenarios, which would be difficult, if not impossible, to generate in the real environment.

6.2 Experimental results and analysis

Six scenarios are simulated and tested, as shown earlier in Table 1. The first four columns in Table 5 are similar to those in Table 1. The fifth column shows the results of the simulation model for the average total costs for each scenario. The results indicated that the estimated total cost of each scenario varies from \$16,604.08 to \$383,713.42. Those results indicate that scenario 3, with a 40 % patient copayment policy, provides the lowest overall cost (\$16,604.08).

Further, analysis of variance (ANOVA) in conjunction with multiple comparison tests is used for comparing six scenarios. Each scenario corresponds to a different copayment policy. Base scenario (100 % patient copayment policy) along with scenarios 1–5 represents a single factor (copayment policy) treatment with $K = 6$ levels. The null hypothesis is that the mean total costs due to copayment policies do

Table 6 Analysis of variance

Source of variation	Degrees of freedom	Sum of squares	Mean square	F_{CALC}
Total (corrected)	$N - 1 = 599$	SSTC = 12,452,735,830,964.40		
Treatment (copayment policies)	$K - 1 = 5$	SST = 11,163,149,581,281.60	MST = 2,232,629, 916,256.33	1,028.38
Errors	$N - K = 594$	SSE = 1,289,586,249,682.77	MSE = 2,171,020, 622.36	

not differ. The alternate hypothesis states that the mean total costs due to the copayment policies differ among at least one pair of scenarios.

This is a balanced design, since the number of observations for each scenario is the same ($n = 100$). Parameters for this design are:

- Number of factor levels = number of alternative scenarios = $K = 6$
- Total number of observations = $N = nK = 100 * 6 = 600$

Using the fixed-effect model, the hypotheses are written as:

$$H_0 : \tau_0 = \tau_1 = \tau_2 = \tau_3 = \tau_4 = \tau_5 = 0$$

$$H_1 : \tau_i \neq 0 \text{ for at least one } i, \text{ for } i = 0, 1, 2, 3, 4, 5,$$

where τ_i is the effect of the i th treatment (i th scenario in case) as a deviation from the overall population mean (μ) and random variations (ε_{ij}) of the response variable (overall cost) that occurred during the j th replication of the i th scenario.

Table 6 presents an ANOVA table for this simulation model. Since $F_{CALC} = 1028.38$ is greater than $F_{CRITICAL} = F_{(5,594, 0.05)} \approx 2.23$, the null hypothesis H_0 is rejected, and one can conclude that the copayment policy significantly affects the mean total cost. A multiple comparison test is now conducted to determine which copayment policy causes the significance. Specifically, a protected least significant difference (LSD) will be utilized.

LSD requires that a 15 pair-wise comparisons of sample means be performed. LSD value is calculated as follows:

$$LSD(\alpha) = t_{(df(error), \alpha/2)} \sqrt{2(MSE)/n} = 1.96 * \sqrt{2 * 2,171,020,622.36/100} = 6,589 \quad (8)$$

As shown in Table 7, the following pairs of means are different concluded to be different:

$\mu_0 \neq \mu_1, \mu_0 \neq \mu_2, \mu_0 \neq \mu_3, \mu_0 \neq \mu_4, \mu_0 \neq \mu_5$ (cells in column 2, comparison to Base Scenario) $\mu_1 \neq \mu_2, \mu_1 \neq \mu_3, \mu_1 \neq \mu_4, \mu_1 \neq \mu_5$ (cells in column 3, comparison to Scenario 1), $\mu_2 \neq \mu_5$ (last cell in column 4, comparison to Scenario 2), $\mu_3 \neq \mu_4, \mu_3 \neq \mu_5$ (cells in column 5, comparison to Scenario 3), and $\mu_4 \neq \mu_5$ (last cell in column 6, comparison to Scenario 4). The null hypothesis cannot be rejected for $\mu_2 = \mu_3$ and $\mu_2 = \mu_4$ (cells in column 4, comparison to Scenario 2). One may be inclined to believe that the best copayment policy is scenario 3 (40 % patient, 60 % HIC), followed non-significantly by scenario 2 (60 % patient, 40 % HIC).

Table 7 LSD analysis

	Base scenario	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
Base scenario	–					
Scenario 1	195,892 > 6,589*	–				
Scenario 2	365,311 > 6,589*	169,418 > 6,589*	–			
Scenario 3	367,109 > 6,589*	171,217 > 6,589*	1,799 < 6,589	–		
Scenario 4	360,428 > 6,589*	164,536 > 6,589*	4,882 < 6,589	6,681 > 6,589*	–	
Scenario 5	351,333 > 6,589*	155,441 > 6,589*	13,978 > 6,589*	15,776 > 6,589*	9,095 > 6,589*	–

When comparing the best policy, Scenario 3, with the Base Scenario presently used by HIC, a savings of approximately of \$367,000 (95 % confidence interval: 357,000–377,000) is calculated. This analysis indicates that HIC will benefit significantly when using the proposed simulation model in future flu seasons. The savings can be even greater if HIC decides to expand the model to other member segments.

7 Managerial insights

The simulation model should be of interest to managers of health insurance organizations to establish appropriate vaccination copayment policies for a given influenza season. In addition, the model is applicable to employers who may consider vaccination of their workforce in order to prevent absence from work or underperformance for an upcoming flu season. Although this uses influenza scenarios for school-aged children to cover the more typical vaccination program, this model can be easily extended to any type of disease and any subpopulations: adults, elderly, high-risk patients, or selected workforce of any given employer. For example, insurance companies or employers should utilize the model as a foundation to build a decision support system to generate vaccination policies for their members or employees. Specifically, the proposed model can help healthcare practitioners who want to design a vaccination program to:

- (i) Establish an optimal vaccination rate or an appropriate copayment policy, which will result in the best possible vaccination rate. The goal here is to minimize the overall cost of a vaccination program, including vaccination and treatment costs. For any given disease where vaccination is suggested, and any given population segment, the decision maker can consider several random input variables, such as reproduction rate, transmission time, vaccine efficacy, and costs of hospitalization, physicians, and ER.
- (ii) Calculate an acceptable cost of a single dose of vaccination, which makes a given vaccination program economically feasible. Such value can be defined via sensitivity analysis of a given vaccination program scenario, and can help establish a price for a vaccine when negotiating with a vaccine manufacturer. In summary, insurance company practitioners can use the model to determine optimal vaccination rates, given acceptable costs and economic targets.

8 Conclusion and implications for future research

This paper proposes a simulation model, which can be applied by health insurance organizations as a decision-making tool in flu vaccination programs. The model can be used by practitioners to identify an appropriate vaccination rate based on cost considerations. The proposed model is illustrated with an example from the perspective of an insurance provider interested in establishing a cost effective copayment policy. It is shown that using the proposed model can lead to significant savings when establishing copayment policies for vaccinations against influenza or other diseases.

Simulation has several advantages over mathematical or other decision-making methods when applied to this healthcare situation. Simulation allows the decision maker to “mimic” the behavior of the disease as it arrives in a given population target. Once the simulation model is validated, the decision maker can test alternative solutions for different disease scenarios. In addition, the robustness of the alternative solutions can be tested by “tweaking” the model to reflect changes in the parameters of the system. Another advantage of the proposed model is its flexibility. The decision maker is able to recreate scenarios for a certain disease, a given population target, or different vaccination rates.

This is the first research to provide a simulation model to investigate the cost-effectiveness of vaccination policies from a health insurance perspective. However, there are some potential limitations of the proposed method, especially when trying to investigate scenarios from an employer’s or even societal perspectives. Some of the limitations are listed in Table 8. An exploration of these limitations within the

Table 8 Limitations of current model and adjustment for future studies

Limitation	Description	Health insurance perspective	Other scenarios
Vaccine quantity discount	As shown in Fig. 1, it is assumed that the vaccination cost is linear and proportional to the number of people vaccinated	This assumption is correct, because health insurance companies pay the same (copayment) amount for each vaccine	A societal or employer’s perspective in the model might consider quantity discount, since pharmaceutical companies may be willing to provide lower cost vaccine for larger quantities
Vaccine efficacy	The model assumes that the vaccine is 100 percent effective, that is, everyone who is vaccinated is immune from the flu	This assumption is reasonable in the case of the flu, especially from an insurance perspective. The number of people who are vaccinated and still need to see a doctor is very small, so no additional treatment costs occur	As other research indicates (Hill and Longini 2003), future studies need to consider vaccine efficacy, especially when investigating other diseases
Mortality cost	Mortality cost is not included in our study. It is calculated the number of children who die for model validation purposes	There is a lack of data and lack of interest from the insurance perspective to calculate such a cost	It is necessary to include mortality cost when the model is designed from a societal perspective. Other published studies consider cost of death (Prosser et al. 2008)
Parents’ work absence or productivity	Any cost-effectiveness study about children becoming sick should include the cost of missing work or underperforming at work because parents are fatigued	There is a lack of data and lack of interest from the insurance perspective to calculate such a cost	It is necessary to include parents’ work related costs when the model is designed from a societal or employer’s perspective

context of the simulation approach is suggested for future research. Future extensions of this simulation paper might also include the incorporation other costs, such as parental time lost, expected costs of missing school, and for some healthcare situations, long-term care associated with permanent disabilities. Finally, simulations show what could happen under various scenarios—they do not show what will happen. Even with a very good simulation model, there are potentially many factors not included in the model that can determine the real world outcome. Therefore, far reaching decisions should not be based solely on the outcomes of simulations.

Appendix: The code for the base scenario simulation model

```

vacc_rate_cost_KAS - Notepad
File Edit Format View Help
*****
*
*          APPENDIX A:
*          SIMULATION CODE:  VACCINATION RATE AND COSTS
*
*****

#This model simulates a vaccination program and is designed to assist you
in the process of deciding the best vaccination rate in order to keep a
disease under control and minimize the overall the cost of a given disease.
The model also illustrates the impact of "herd immunity", endemic, and
epidemic states.
#
#This is a general template and can be customized for a specific disease,
population group, disease reproduction number, and reproduction period.
You will be able to test several scenarios with different vaccination
rate and see the impact on the disease control.
#
#
Initialization Logic:
                                animate 40
                                infected = 1
                                immunized = POP_size*v_rate
                                Vaccination_C = immunized*Vaccine_C

                                activate Sub_DP
                                activate Sub_setup

*****
*
*          Locations
*
*****

Name          Cap      Units Stats      Rules      Cost
-----
Susceptible_people POP_SIZE 1      Time Series oldest, ,
Sick_people      POP_SIZE 1      Time Series oldest, ,
Self_recovered   POP_SIZE 1      Time Series oldest, ,
Physician_visit  POP_SIZE 1      Time Series oldest, ,
ER_visit         POP_SIZE 1      Time Series oldest, ,
Hospitalization  POP_SIZE 1      Time Series oldest, ,
Recovered_people POP_SIZE 1      Time Series oldest, ,
Deceased_people  POP_SIZE 1      Time Series oldest, ,

*****
*
*          Entities
*
*****

Name ----- Patient
*****

```

```

vacc_rate_cost_KAS - Notepad
File Edit Format View Help
*****
*                               Processing                               *
*****
Entity  Location      Operation      Blk Output  Destination  Rule      Move Logic
-----
Patient  susceptible_people  wait E(w_until_dr) day
                             1 Patient Sick_people  FIRST 1
Patient  Sick_people         If (Pop_size-immunized-infected)>0 Then
Begin
newly_infected = U(2,0.6)*((Pop_size-immunized-recovered-infected)/Pop_size)
order newly_infected patient to susceptible_people
infected = infected + newly_infected
Route 1
else Route 2      1 Patient Self_recovered  0.620000 1 inc recovered
inc self_recovered_P
                             Patient Physician_visit  0.220000 inc seeing_dr_P
                             Patient ER_visit  0.160000 inc ER_P
                             Patient EXIT  FIRST 1
Patient  Self_recovered    wait E(w_until_recovered) day
                             2 Patient ER_visit  0.160000 inc ER_P
                             Patient EXIT  FIRST 1
Patient  Physician_visit    wait E(1) day
T_Physician_C = T_Physician_C+U(155,54)
                             1 Patient Recovered_people  0.950000 1 inc recovered_P
inc hospital_P
                             Patient Hospitalization  0.050000 inc hospital_P
Patient  ER_visit        wait E(1) day
T_ER_C = T_ER_C+U(740, 250)
                             1 Patient Recovered_people  0.950000 1 inc recovered_P
inc hospital_P
Patient  Hospitalization  wait E(3) day
T_Hospital_C = T_Hospital_C+U(2820, 550)
                             1 Patient Recovered_people  0.700000 1 inc recovered_P
inc hospital_P
                             Patient Deceased_people  0.300000 inc recovered_P
DEC POP_SIZE
inc dying_P
Patient  Recovered_people  wait E(w_until_recovered) day
inc recovered
Treatment_C = T_physician_C + T_ER_C + T_hospital_C
Total_C = Vaccination_C + Treatment_C
                             1 Patient EXIT  FIRST 1
Patient  Deceased_people  accum infected  1 Patient EXIT  FIRST 1
*****

```

```

vacc_rate_cost_KAS - Notepad
File Edit Format View Help
*****
*                               Arrivals                               *
*****
Entity  Location      Qty Each  First Time occurrences  Frequency  Logic
-----
Patient  susceptible_people  1         0         1
*****
*                               variables (global)                               *
*****
ID      Type      Initial value      Stats
-----
POP_SIZE  Integer  9200              Time Series
RO       Real     U(2,0.6)          Time Series
infected Integer  0                Time Series
recovered Integer  0                Time Series
immunized Integer  0                Time Series
v_rate   Real     U(0.06,0.04)     Time Series
R_period Real     2.6              Time Series
w_until_dr Integer  3.5             Time Series
hospital_time Integer  3                Time Series

```

```

w_until_recovered Integer 5.5 Time Series
newly_infected Integer 1 Time Series
self_recovered_P Integer 0 Time Series
recovered_P Integer 0 Time Series
seeing_dr_p Integer 0 Time Series
ER_P Integer 0 Time Series
hospital_P Integer 0 Time Series
dying_P Integer 0 Time Series
Susceptible_P Integer 0 Time Series
Vaccine_C Real 0 Time Series
Vaccination_C Integer 0 Time Series
Physician_C Integer U(155, 54) Time Series
ER_C Integer U(740, 250) Time Series
Hospital_C Integer U(2820, 550) Time Series
Treatment_C Integer 0 Time Series
Total_C Integer 0 Time Series
T_Physician_C Integer 0 Time Series
T_Hospital_C Integer 0 Time Series
T_ER_C Integer 0 Time Series

```

```

*****
*                               subroutines                               *
*****

```

ID	Type	Logic
Sub_DP	None	WAIT 4 HR DYNPLOT "Immunization Versus Infection Rate"
Sub_setup	None	PROMPT "Please enter the expected size of population:", POP_SIZE PROMPT "Please enter the expected reproduction number:", RO PROMPT "Please enter vaccination rate:", v_rate PROMPT "Please enter the expected time to transmit the disease from one person to another:", R_period PROMPT "Please enter the cost of the vaccine:", vaccine_C

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