IISE Transactions on Healthcare Systems Engineering

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/uhse21

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To cite this article: Ting-Yu Ho, Zelda B. Zabinsky, Paul A. Fishman & Shan Liu (2022): Prevention of seasonal influenza outbreak via healthcare insurance, IISE Transactions on Healthcare Systems Engineering, DOI: 10.1080/24725579.2022.2145393

To link to this article: https://doi.org/10.1080/24725579.2022.2145393

Published online: 25 Nov 2022.

IISE TRANSACTIONS ON HEALTHCARE SYSTEMS ENGINEERING
https://doi.org/10.1080/24725579.2022.2145393

Prevention of seasonal influenza outbreak via healthcare insurance

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ABSTRACT

The outbreak of seasonal flu costs billions of dollars in health care utilization and lost productivity. Despite the effectiveness of vaccination and antiviral medications to prevent serious flu-related complications and slow down the spread of an influenza epidemic, only 52% of the U.S. population aged 6 months and older received flu vaccines in the 2019-20 flu season. In addition, a costly out-of-pocket expense results in fewer patients seeking treatment, leading to potential hospitalizations and even flu-related deaths. In this study, we develop an integrated healthcare insurance mechanism that optimizes two incentive policies, vaccination reward and cost-sharing, to alleviate the medical cost and disease burden while preventing the outbreak of seasonal influenza. We model the dynamic interaction between a single insurer and multiple insureds as a Stackelberg vaccination game; we then embed the game into an agent-based simulation to model the spread of flu in a population under different policies. Finally, we apply machine learning and simulation optimization to optimize healthcare incentive policies in a large-scale flu transmission simulation. Simulation results indicate that the proposed methodology efficiently identifies a set of good incentive policies under different scenarios of flu vaccine efficacy and reproduction numbers.

KEYWORDS

influenza vaccination; healthcare management; incentive mechanism; Stackelberg game; agent-based simulation

1. Introduction

Flu is a contagious respiratory illness caused by the influenza virus that infects about 3%-11% of the U.S. population in each flu season (CDC, 2019c). The Centers for Disease Control and Prevention (CDC) estimated that, in the 2019–2020 (2018–2019) flu season, approximately 35 million (29 million) people contracted the flu, resulting in 16 million (13 million) people visiting a health care provider, 380, 000 (380, 000) hospitalizations, and 20, 000 (28, 000) deaths (CDC, 2019a, 2020a). The CDC recommends an annual flu vaccine, offering protection against the influenza virus, as the first and most effective step in preventing the seasonal flu (CDC, 2020c; Grohskopf et al., 2018). Getting a yearly vaccine is especially important for vulnerable populations such as infants and the elderly. Each vaccinated individual also protects others in the community who cannot be vaccinated since susceptible individuals are now less likely to catch the flu. If more individuals become vaccinated, community immunity, also called "herd immunity," protects the unvaccinated masses by decreasing the circulation of the influenza virus. Vaccination also reduces the risk of flu-associated hospitalization and death. To promote vaccination in the U.S., flu shots are often widely available and covered at no out-of-pocket expense for individuals with health insurance. Nevertheless, in the 2019-2020 flu season, the CDC estimates that only 48.4% of adults (an increase of 3.1 percentage points from the prior flu season) and 63.8% of children (an increase of 1.2 percentage points from the prior flu season) in America received flu vaccines (CDC, 2019b, 2020 b). Many individuals fail to vaccinate due to personal, religious, and philosophical beliefs, as well as access barriers including complexity in scheduling, inconvenience, and lack of knowledge and perceived benefit. Value-based insurance models routinely offer a variety of incentives to encourage more efficient health-seeking behavior. Pharmacies and other healthcare providers often offer financial rewards to all individuals seeking flu shots, in the form of a $5-25 store coupon or direct cash reward.

Once having symptoms of the flu, the CDC recommends that individuals at high risk, e.g., young children, the elderly, or those with chronic respiratory diseases, visit healthcare providers. Medical treatments such as antiviral drugs can be used to treat the flu and further prevent serious flu-related complications (Atkins et al., 2011; CDC, 2021; Spagnuolo et al., 2016). However, many studies have shown that patient's out-of-pocket expenses, known as "cost-sharing charge" in health insurance terminology, reduce the healthcare resource utilization in preventive care, drug treatment, and adherence (Eaddy et al., 2012; Goldman et al., 2007; Huskamp et al., 2003; Mann et al., 2014). Specifically, high cost-sharing discourages infected insureds from seeking treatment, resulting in potential hospital stays or even flu-related deaths. On the other hand, insureds with flu-like symptoms are more likely to visit healthcare providers if the cost-sharing charge is low, potentially leading to excessive medical costs for the insurer. To improve vaccination

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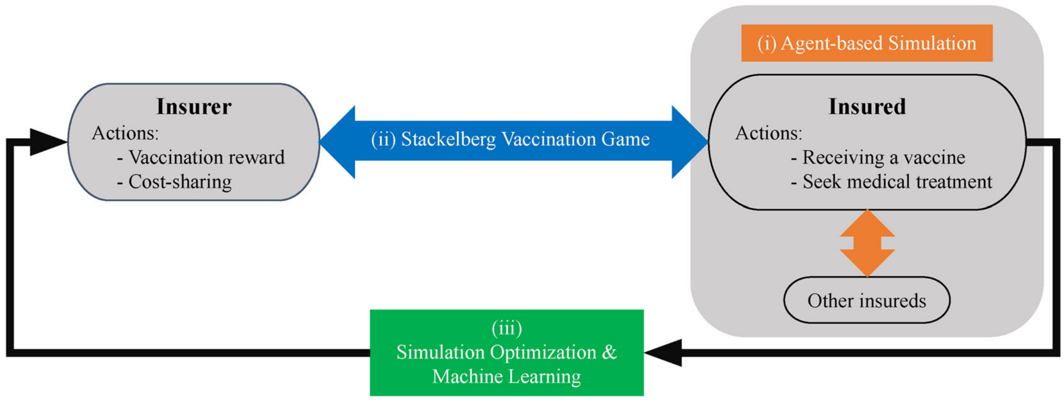


Figure 1. Interactions between a single insurer and insureds and mechanism design.

coverage while lowering the medical cost and the loss of productivity, it is thus necessary to consider the impact of vaccination reward and cost-sharing on individuals' vaccination and treatment-seeking behaviors, as well as the population health outcome.

We are interested in the following questions from an insurer's perspective: What are near-optimal policy ranges on vaccination reward and cost-sharing and their impact on the percentage of the population vaccinated, infected, and overall medical cost? Moreover, how sensitive are these health outcomes to limited information before the flu season starts, e.g., uncertain vaccine efficacy and unclear flu basic reproduction numbers?

We propose an incentive mechanism design approach to address these questions. As illustrated in Figure 1, our approach considers two main players, an insurer, and insureds. The insurer could be a health plan or purchaser (for example, Kaiser, Geisinger or HealthPartners) that combines insurance and health care, or a government agency that manages socialized medicine (for example, the National Health Service in the UK, or Medicare in Canada). The insurer takes a risk of paying a high medical cost incurred by antiviral treatment, hospitalization, and death. To minimize the insurer's expected medical cost while considering the population health, the insurer adopts two incentive-based healthcare policies: the first is to provide a monetary incentive to encourage vaccination uptake among susceptible insureds, and the second is to adjust the cost-sharing to ensure appropriate medical care-seeking behavior among infected insureds. We assume that pharmacy chains and other healthcare providers have enough supply to offer flu vaccines to all insureds (i.e., with no vaccine shortages or delays). Susceptible insureds determine whether or not to receive a vaccine by considering their convenience cost of vaccination, the incentive offered by the insurer, cost-sharing, risk of infection, and direct (e.g., healthcare expenses) and indirect costs (e.g., lost productivity). At each time period during the flu season, a susceptible insured decides to receive the flu vaccine only if their expected cost of vaccination is lower than their expected cost of not getting vaccinated. Similarly, an infected insured determines whether to seek medical treatment by comparing their respective expected costs of treatment vs. not taking treatment.

The flu vaccine cost is not factored into the insureds and insurer's objectives. Flu vaccinations are covered at no out-of-pocket cost for insureds under the Affordable Care Act since insurers are required to cover the cost of immunizations and preventive care. We consider the manufacturing and distribution cost of the vaccine, as discussed in Chick et al. (2008) and Mamani et al. (2013), a fixed cost. In this research, we focus on costs impacted by the actions of the insureds.

Our proposed incentive mechanism design approach includes three components:

(i) **Agent-based simulation**: Although a wide variety of research has been conducted for controlling and preventing infectious disease using vaccination promotion, they either adopt *mandatory vaccinations* or model a *population-level response* toward incentives instead of considering individuals' response toward incentives. We first present an *agent-based simulation model* to simulate the spread of influenza virus considering individual decision-making.

(ii) **Stackelberg vaccination game model**: We build a *Stackelberg vaccination game* that incorporates insureds' vaccination and treatment-seeking behaviors and the dynamic interaction between the insurer and insureds, and integrate it into the agent-based simulation. The integrated model allows us to take the behavior and decision-making process of individuals with different characteristics into consideration. The integration is implemented by extending an open-source validated flu simulation model, FluTE (Chao et al., 2010).

(iii) **Simulation optimization and machine learning approaches**: The integrated model involving complex interactions among individuals in a large-scale setting is computationally challenging to optimize. We, therefore, apply *simulation optimization and machine learning* to efficiently solve for near-optimal incentive policies and analyze the sensitivity of these policies to model parameters.

Previous research has shown that an effective vaccine incentive should be carried out at the individual and interpersonal levels (Kolff et al., 2018). Significant research efforts have concentrated on either modeling realistic disease spread in a population under various levels of vaccination coverage or investigating the theoretical aspects of long-term infectious disease equilibrium under different vaccination behaviors. There is a gap in creating computational models that can handle the complexity of disease spread while solving for near-optimal vaccination incentives at the individual decision-making level. Our study provides insights into the impact of incentives on vaccination uptake and disease outcomes.

This paper makes several contributions to the healthcare literature:

- We consider a novel incentive combination of vaccination reward and cost-sharing charge to reduce the spread of seasonal flu in a health insurance setting, which includes the self-interest behavior of each individual insured and the cost-minimizing objective of the insurer. We develop a Stackelberg vaccination game to characterize the individual-level model of the insured by his/her own attributes (i.e., age and risk type) when making the vaccination and treatment decisions. The hierarchical and two-stage decision-making processes provide healthcare payers an understanding of how incentive policies may impact individuals throughout the entire flu season.
- We integrate the agent-based simulation with a game theoretic approach to simulate the dynamic spread of influenza in a heterogeneous population while providing a realistic outlook of economic and health outcomes. Using the integrated simulation model, we can observe the response of a particular age and risk group to various policies, and estimate the population outcome such as vaccination rate, the number of influenza illnesses, medical visits, flu-associated hospitalizations and deaths, and corresponding medical cost.
- The proposed simulation optimization and machine learning approaches allow an insurer to efficiently identify a *set of incentive policies* that minimize total flu-related medical cost while considering the population health outcome under different scenarios (e.g., different vaccine efficacy and basic reproduction number) in a flu simulation model. In other words, instead of finding one unique Stackelberg equilibrium, the proposed approach efficiently discovers multiple Stackelberg equilibria that provide near-optimal performance. Providing a set of good incentive policies gives the insurer *flexibility* in policy implementation.
- Furthermore, using the combination of simulation optimization and machine learning, the quality and sensitivity of the solutions can be explored in practical computation time with realistic large population networks. The approach provides insights into the sensitivity of cost, percent of the population vaccinated, and percent of the infected under uncertain or limited information.

In summary, the proposed mechanism not only estimates the burden of influenza in the population and the impact of influenza vaccination reward and treatment cost-sharing, but it also provides an incentive-optimization solution for effective and efficient healthcare management. Our research, therefore, highlights the potential societal benefit gained from improving the policy-setting process in healthcare organizations. Going beyond seasonal flu, our proposed approach may impact millions of individuals by providing policy makers with a tool to design vaccination incentives for other seasonal vaccines and the emerging COVID epidemic with annual or biannual booster vaccine scenarios.

The rest of the paper is structured as follows. Section 2 briefly reviews related work. In Section 3, we propose the insurance-based incentive mechanism design framework for preventing the spread of seasonal flu. Section 4 presents the details of the experimental setting of the simulation considering flu transmission in Seattle, and Section 5 presents the experimental results and the sensitivity analyses. Section 6 summarizes our findings and closes with a discussion.

2. Literature review

Financial incentive reward is a practical and common approach to encourage vaccination behavior (Briss et al., 2000; Tan, 2018). The United States Preventive Services Task Force demonstrated that even small monetary interventions are effective and successful in improving adult immunization coverage (United States Preventive Services Task Force, 2015). For example, Bronchetti et al. (2015) showed that college students were more willing to get a flu vaccine when offered a $20 reward (19% vs. 9%). Francis (2004) explored the conditions under which the free-rider problem can be overcome through the use of taxes and subsidies. Furthermore, convincing evidence has suggested that reducing out-of-pocket costs and adding incentives are effective interventions for improving vaccination coverage and overcoming vaccination hesitancy (Betsch et al., 2015). Vardavas et al. (2007) found that offering vaccination incentives are necessary to prevent severe epidemics. Nowalk et al. (2010) found that a $5 financial incentive increased flu vaccination rates in the workplace. Also, recent COVID-19 vaccine promotion events have demonstrated that financial incentives, such as store coupons, or small amount of cash rewards, can effectively boost vaccination rate (American Association of Retired Persons (2021), Campos-Mercade et al. (2021)).

Antiviral treatments for influenza symptoms can be a second-line of defense against the spread of seasonal flu. Treatments are able to prevent serious flu complications and shorten recovery time. In some cases, they may be used to prevent the flu. However, a high cost-sharing charge in healthcare insurance may reduce the chance of individuals making a doctor visit. Cost-sharing is used to change the utilization of services or prescription drugs for the enrollees of health insurance. The RAND Health Insurance Experiment has demonstrated that the amount of copayment affects a patient's usage of medical care and service (Gruber, 2006). The introduction of a cost-sharing charge will decrease the utilization of most types of medical services (Andersen & Newman, 2005; Wong et al., 2001). Goldman et al. (2007) showed that increased cost-sharing in healthcare insurance is associated with lower rates of drug treatment, poorer adherence among existing patients, and more interruption of continuation of therapy. Fishman et al. (2012) showed that unmet deductibles lower the likelihood for an individual to make an initial therapy visit for treatment of depression. Cherkin et al. (1989) found that a $5 copay significantly modified utilization of outpatient doctor visits.

Several approaches have been applied to model a flu epidemic at a population level. One approach is to apply a deterministic compartmental model commonly used in epidemiology, such as the Susceptible-Infectious-Recovered (SIR) model based on ordinary differential equations (Chick et al., 2008, 2017; Kermack & McKendrick, 1927; Sun et al., 2009; Yamin & Gavious, 2013). Although compartment differential equation modeling is less computationally intensive than agent-based simulation models, the model itself assumes homogeneity in each compartment and adding additional compartments and equations into the model is required if any additional characteristic is considered, e.g., age, risk type, economic status, and vaccination status, making the model more complicated to solve. Agent-based modeling, on the other hand, captures heterogeneity across individuals and interactions among them in the network. Each individual agent in the network can have his/her own characteristics, which affect his/her own decision making and thus influence the likelihood of changing status. Many simulation programs are available in an open-source format, including FluTE, EpiFire, GEM and GSAM (Dunham, 2005; Grefenstette et al., 2013).

Game-theoretical analyses of epidemics are widely used to explore the population response to disease dynamics or interventions. For example, Bauch et al. (2003) focused on smallpox and studied the conflict between self-interest and group interest; Bauch and Earn (2004) further developed a game-theoretical interpretation based on an epidemic model of the rational exemption phenomenon. However, it is suggested that pure voluntary contributions make eradicating a vaccine-preventable infectious disease nearly impossible due to free-riding (Barrett, 2007; Galvani et al., 2007; Vardavas et al., 2007). On the other hand, Schimit and Monteiro (2011) studied the effect of a mandatory vaccination program promoted by the government against the propagation of a contagious infection. These previous models study *mandatory vaccination or voluntary participation* at a *population-level response*. However, there is a strong public health and scientific rationale for studying the interaction of disease dynamics and individual behavior (Wang et al., 2017).

Research interested in incorporating the effects of individual vaccination choices into flu epidemic modeling has been growing in recent years. For example, Fu et al. (2011) studied the roles of individual imitation behavior and population structure in vaccination uptake. Perisic and Bauch (2009) simulated the transmission of a vaccine-preventable disease using a Susceptible-Exposed-Infectious-Recovered model through a random, static contact network and examined individual vaccination behavior based on neighborhood. Nevertheless, an individual's motive to vaccinate is not only influenced by disease factors such as infectious neighbors or vaccination costs but also by *incentives* provided by policy makers, e.g., insurance companies. Incentives designed for controlling and preventing flu should also be factored into a rational self-interested decision-making process.

3. Methodology: Incentive mechanism design

In this section, we describe our approach to incentive mechanism design in an insurance-based setting. The goal is to design incentive policies that minimize the insurer's overall flu-related medical cost and population health burden. Section 3.1 builds an agent-based simulation to model flu transmission. It captures the dynamic population health evolution and the effect of insurance policies during the spread of seasonal flu. Section 3.2 formulates the insurer and the insureds' decision-making problems in the agent-based simulation. Section 3.3 demonstrates how to address the computational issue of optimizing the healthcare policy in a simulated population network by applying machine learning and simulation optimization techniques.

3.1. Flu transmission agent-based simulation

The agent-based simulation model simulates the spread of seasonal influenza with a modified SIR structure (Kermack & McKendrick, 1927), incorporating vaccination and corresponding rules that govern the transmission of flu, as depicted in the flow diagram in Figure 2. Each individual insured is represented as an agent in the model. Agents are grouped into eight health state compartments, three of which are absorbing compartments. The first compartment consists of susceptible (S) agents, who may become infected. The second compartment consists of vaccinated agents (V), who receive flu vaccines. The third compartment consists of infectious agents (F), who are contagious. The fourth compartment consists of untreated agents (U), who are infected with the flu and decide not to receive outpatient healthcare services. The fifth compartment consists of treated agents (T), who receive outpatient healthcare services after becoming infected. After the infection period, the treated and untreated agents may recover from the flu and enter the recovery compartment (R). The seventh compartment consists of hospitalized agents (H), who are being hospitalized. The eighth compartment consists of agents that die (D) due to flu-related illness.

In the flow diagram in Figure 2, agents in the susceptible compartment S may acquire the infection with a given infection probability and move into the infected compartment F. Agents in F may infect their neighbors with a given probability. Agents in the treatment compartment T will recover (move into R) after the infected period. Catching the flu twice in one flu season is possible due to different strains of the virus; however, this is unlikely (Sonoguchi et al., 1986). In this research, we assume that recovered agents are resistant to the seasonal flu during a single season (as also assumed in other flu studies (Chao et al., 2010; Francis,

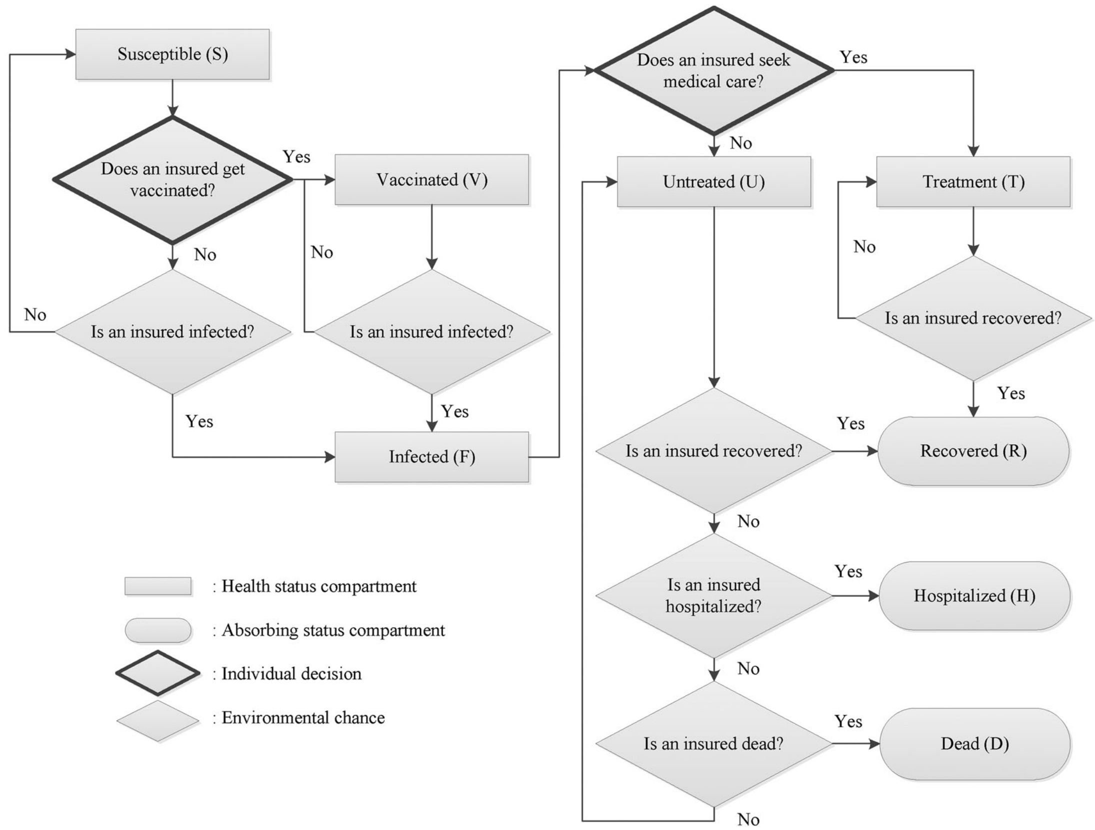


Figure 2. Flow diagram for the agent-based simulation involving individual decision making.

2004)), and will not return to the susceptible compartment *S*. Therefore we treat the recovered compartment as an absorbing state. The hospitalized (*H*) and dead (*D*) compartments are also absorbing states since there is no follow-up decision-making from the insureds' side. Agents in the untreated compartment *U* may recover (move into *R*), be hospitalized (move into *H*), or die from flu-related illness (move into *D*) based on given recovery, hospitalization, and death probabilities.

Although we adopt a stochastic approach to traverse agents' health states using infection, recovery, hospitalization, and death probabilities, two health state transitions are determined by the insureds themselves: the vaccination decision "Does the insured get vaccinated?" (traverse from the compartment *S* to the compartment *V*); and the outpatient visit decision "Does the insured seek medical care?" (traverse from the compartment *F* to the compartment *T*). We assume the insureds make the vaccination decision in every time period (i.e., if the insured does not get vaccinated this time period, s/he faces the same decision in the next time period). Each infected insured makes the treatment decision only once. The susceptible and infected agents calculate their expected costs associated with the insurance policies and decide whether to get a vaccination and/or treatment based on their expected costs.

3.2. Stackelberg vaccination game model

In this section, we derive the expected cost for insureds by modeling the dynamic interaction between the insurer and insureds as a Stackelberg vaccination game played by a single insurer and multiple insureds. It is assumed that the insurer and insureds are risk-neutral, as is commonly assumed in game theory. The insurer and insureds are modeled as a leader and followers, respectively. The insurer moves first by announcing the incentive policies before the flu season, i.e., vaccination reward and coinsurance rate to insureds. We adopt a coinsurance rate, where the insureds pay a percentage of the cost for a health care service, as a form of cost-sharing policy in health insurance. Each individual insured responds to the insurer's policies by calculating two expected costs. The expected cost of vaccination is used to determine whether to get a vaccine each day given the seasonal policy announcement. If a non-vaccinated insured is infected, the expected cost of an outpatient visit is used to determine whether or not to seek treatment, i.e., visiting with a doctor or other health care professional. Incorporating the game-theoretic approach into the agent-based simulation model allows individual agents to act in their own self-interest in response to the influenza evolution and neighboring environment.

3.2.1. Vaccination and treatment seeking problem for the insured

The expected cost of the insured depends on whether s/he eventually gets vaccinated or infected. Table 1 presents the notation used in the Stackelberg vaccination game. Note that the medical cost for an outpatient visit, $c^{a,r}_{med,T}$, includes not only an office visit fee but other treatment-associated

Table 1. Notation for Stackelberg vaccination game modeling.

Indices	
a	index of insured's age, $a \in \{0-4, 5-17, 18-49, 50-64, 65+\}$
r	index of insured's risk type, $r \in \{\text{normal, high risk of severe complications from influenza}\}$
Input parameters	
$c^{a}_{med,U}$	medical cost in the case of no medical attendance for an untreated insured with age a
$c^{a,r}_{med,T}$	medical cost of an outpatient visit for a treated insured with age a and risk type r
$c^{a,r}_{med,H}$	medical cost of hospitalization for a hospitalized insured with age a and risk type r
$c^{a,r}_{med,D}$	medical cost of death for a dead insured with age a and risk type r
$c^{a}_{ind,U}$	indirect cost, i.e., lost productivity, not medically attended for an untreated insured with age a
$c^{a,r}_{ind,T}$	indirect cost, i.e., lost productivity, for a treated insured with age a and risk type r
$c^{a,r}_{ind,H}$	indirect cost, i.e., lost productivity, for a hospitalized insured with age a and risk type r
$c_{ind,V}$	indirect vaccination cost, e.g., the value of work loss time for vaccination
f_H	coinsurance rate of medical expense for a hospitalized insured
f_D	coinsurance rate of medical expense for a dead insured
$p^{a}_{F\|S}$	probability that an unvaccinated insured with age a will be infected in a given time period
$p^{a}_{F\|V}$	probability that a vaccinated insured with age a will be infected in a given time period
$p^{a}_{H\|F}$	probability that an infected insured with age a is hospitalized
$p^{a}_{D\|F}$	probability that an infected insured with age a dies due to flu-related illness
w	weight of health outcomes
Decision variables	
x_{reward}	monetary vaccination reward in healthcare insurance given to vaccinated insured (unit: dollar)
$x_{sharing}$	coinsurance rate in healthcare insurance (unit: percentage)
Intermediate variables	
$E^{a,r}_{U}$	expected cost of insured with age a and risk type r when not receiving treatment
$E^{a,r}_{T}$	expected cost of insured with age a and risk type r when receiving treatment
$E^{a,r}_{S}$	expected cost of insured with age a and risk type r when not vaccinated
$E^{a,r}_{V}$	expected cost of insured with age a and risk type r when vaccinated
Output	
ϕ_V	proportion of vaccinated insureds
$\phi^{a,r}_{F}$	proportion of infected insureds with age a and risk type r
$\phi^{a,r}_{T\|F}$	proportion of the infected insureds with age a and risk type r that receive treatment
$\phi^{a,r}_{H\|F}$	proportion of the infected insureds with age a and risk type r that are hospitalized
$\phi^{a,r}_{D\|F}$	proportion of the infected insureds with age a and risk type r that die

fees such as laboratory tests and prescription medications. Antiviral treatment and drugs that are recommended to be taken as early as possible for the higher risk patient to avoid influenza complications are included in $c^{a,r}_{med,T}$. Even though an individual insured makes a vaccination decision before the treatment-seeking decision, we first discuss treatment-seeking since the expected cost from the treatment decision should be factored into the vaccination decision. Insureds choose whether or not to seek treatment based on their respective expected costs with and without medical care. This is a one-time decision. The expected cost of an untreated insured with age a and risk type r is

$$E^{a,r}_{U} = (1 - p^{a}_{H|F} - p^{a}_{D|F})(c^{a}_{med,U} + c^{a}_{ind,U}) + p^{a}_{H|F}(f_H c^{a,r}_{med,H} + c^{a,r}_{ind,H}) + p^{a}_{D|F}(f_D c^{a,r}_{med,D}) \tag{1}$$

where $c^{a}_{med,U} + c^{a}_{ind,U}$, $f_H c^{a,r}_{med,H} + c^{a,r}_{ind,H}$, and $f_D c^{a,r}_{med,D}$ are an untreated insured's cost for no medical care, hospitalization, and death, respectively.

The expected cost of a treated insured is

$$E^{a,r}_{T} = x_{sharing} c^{a,r}_{med,T} + c^{a,r}_{ind,T}. \tag{2}$$

If $E^{a,r}_{T} < E^{a,r}_{U}$, then the insured decides to seek medical care.

Insureds choose whether or not to vaccinate based on their respective expected costs with and without vaccination. If the insured does not get vaccinated today, s/he can still receive a vaccination in the following days. The expected cost of an unvaccinated insured with age a and risk type r staying in compartment S is

$$E^{a,r}_{S} = p^{a}_{F|S} \min\{E^{a,r}_{U}, E^{a,r}_{T}\} \tag{3}$$

where $p^{a}_{F|S}$ is the infection probability for a susceptible insured that is continually updated in the implementation every time period, and $\min\{E^{a,r}_{U}, E^{a,r}_{T}\}$ is an infected insured's minimum expected cost involving treatment-seeking behavior. At each time period, the infection probability $p^{a}_{F|S}$ changes according to the health state of an insured's neighbors.

The expected cost of a vaccinated insured is,

$$\begin{aligned} E^{a,r}_{V} &= (1 - p^{a}_{F|V})(c_{ind,V} - x_{reward}) \\ &\quad + p^{a}_{F|V}(c_{ind,V} - x_{reward} + \min\{E^{a,r}_{U}, E^{a,r}_{T}\}) \\ &= c_{ind,V} - x_{reward} + p^{a}_{F|V} \min\{E^{a,r}_{U}, E^{a,r}_{T}\} \end{aligned} \tag{4}$$

where $p^{a}_{F|V}$ is the infection probability for a vaccinated insured that is continually updated in the implementation every time period, $c_{ind,V}$ is an indirect vaccination cost, and x_{reward} is the monetary incentive given to the vaccinated insured. Since an insured's immune response to the flu vaccine is not perfect, the following infection cost, $\min\{E^{a,r}_{U}, E^{a,r}_{T}\}$, is added.

Comparing the expected cost to remain unvaccinated, $E_S^{a,r}$ in (3), with the expected cost to get vaccinated, $E_V^{a,r}$ in (4), we can see the influence of the infection probability, $p_{F|S}^a$ versus $p_{F|V}^a$. If the flu vaccine is effective, we expect $p_{F|V}^a$ to be much smaller than $p_{F|S}^a$. In addition, $E_V^{a,r}$ in (4) contains the incentive reward for vaccination x_{reward} and an indirect cost for vaccination $c_{ind,V}$, assuming the direct cost is free. If $E_V^{a,r} < E_S^{a,r}$, the insured decides to receive a flu vaccine; otherwise, s/he may still receive a flu vaccine in the future using the same decision rule.

3.2.2. Incentive policy setting problem for the insurer

The insurer's goal is to minimize the total expected cost from both vaccination and flu infection while considering other hidden economic costs. Let ϕ_V and $\phi_F^{a,r}$ be the proportion of the population that is vaccinated and infected (by age and risk), respectively. Let $\phi_{T|F}^{a,r}$, $\phi_{H|F}^{a,r}$, and $\phi_{D|F}^{a,r}$ be the proportion of influenza-attributable cases that lead to outpatient visits, hospitalization, and death, respectively. We express the insurer's objective as

$$\min_{x_{reward}, x_{sharing}} \quad E_{Insurer} \tag{5}$$

where

$$\begin{aligned} E_{Insurer} = {} & \phi_V x_{reward} \\ & + \sum_{a,r} [\phi_F^{a,r} \phi_{T|F}^{a,r} (1 - x_{sharing}) c_{med,T}^{a,r} \\ & \quad + \phi_F^{a,r} \phi_{H|F}^{a,r} (1 - f_H) c_{med,H}^{a,r} \\ & \quad + \phi_F^{a,r} \phi_{D|F}^{a,r} (1 - f_D) c_{med,D}^{a,r}] \\ & + w \sum_{a,r} \phi_F^{a,r}. \end{aligned} \tag{5}$$

The first term is the total reward cost for vaccination and the second term is the total medical cost paid by the insurer for outpatient visits, hospitalization, and death. The insurer's medical cost includes the product of each population proportion and the associated cost of the insurer's responsibility. The last term reflects the hidden economic cost of flu on the insurer, for example, the productivity loss of insureds or other possible medical service utilization after getting the flu. We use the parameter w as a weight of health outcomes to capture the hidden costs of infection from the insurer's point of view.

It is worth noting that x_{reward} and $x_{sharing}$ in Equation (5) are time-independent and determined before the start of the flu season but the proportions ϕ_V, $\phi_F^{a,r}$, $\phi_{T|F}^{a,r}$, $\phi_{H|F}^{a,r}$, and $\phi_{D|F}^{a,r}$ are outputs of the simulation model. Even though the relationship between induced total outpatient/hospitalization/death cost and the corresponding proportion is linear, these proportions are non-linear functions of the decision variables x_{reward} and $x_{sharing}$, e.g., $\phi_F^{a,r}(x_{reward}, x_{sharing})$. Therefore, the relationship between induced total medical cost and the amount of incentive is also non-linear.

A coupling relationship exists between x_{reward} and $x_{sharing}$. A high x_{reward} will increase the total vaccination reward cost, while a low x_{reward} may cause a lower vaccination rate, leading to a higher infection rate. On the other hand, increasing $x_{sharing}$ will discourage the infected insureds from seeking treatment, leading to higher hospitalization and mortality cases while decreasing $x_{sharing}$ increases the insurer's medical payment.

The Stackelberg vaccination game is incorporated into the agent-based simulation logic as follows. The simulation proceeds over iterations and one iteration can be seen as one decision-making period (e.g., daily). The insurer's incentive policy, x_{reward} and $x_{sharing}$, is determined at the beginning of the flu season simulation. The behavior of insureds is modeled with two decisions, i.e., vaccination uptake and treatment seeking. In the first decision, each insured decides whether or not to vaccinate based on Equations (3) and (4) every decision period. Once an insured is infected, the second decision is made whether or not to receive medical treatment based on Equations (1) and (2). An insured's decision is determined via comparing expected costs based on direct and indirect costs, the incentive policy, and the probability of being infected. The probability of an agent becoming infected is updated every time period based on the health status of its contact agents in the same group, i.e., family, neighborhood, workplace, playgroup, daycare, and school. At the end of each iteration, the health status of all insureds is updated to simulate the spread of flu. The process continues until the end of the flu season.

3.3. Simulation optimization and machine learning to analyze healthcare incentive policies

The agent-based simulation with the Stackelberg game provides a model of a population during the flu season. It is used to predict the population's behavior under different insurance policies and guide policy decisions. However, fully exploring the simulation for policy optimization is impractical since a single simulation run requires significant computation time. In order to efficiently identify good incentive policies within a reasonable computation time, we combine the advantages of a simulation optimization algorithm and a machine learning approach.

From the insurer's perspective, the proposed agent-based simulation with embedded Stackelberg vaccination game described in Sections 3.1 and 3.2 can be seen as a black-box function evaluation, with vaccination reward x_{reward} and coinsurance $x_{sharing}$ as the input, and the observed cost $E_{insurer}$ as the output. We develop a low-fidelity model, similar to surrogate modeling or meta-modeling approaches, to use in the optimization that allows us to generate high quality solutions using computer resources efficiently. In this paper, we apply random forest regression to construct a statistically valid low-fidelity model. Further, we couple the random forest regression model with a simulation optimization method, Probabilistic Branch-and-Bound (PBnB) algorithm (Huang & Zabinsky, 2013; Zabinsky & Huang, 2020), to analyze the incentive policies and corresponding population behavior. The proposed methodology is presented in Figure 3 and consists of four main steps.

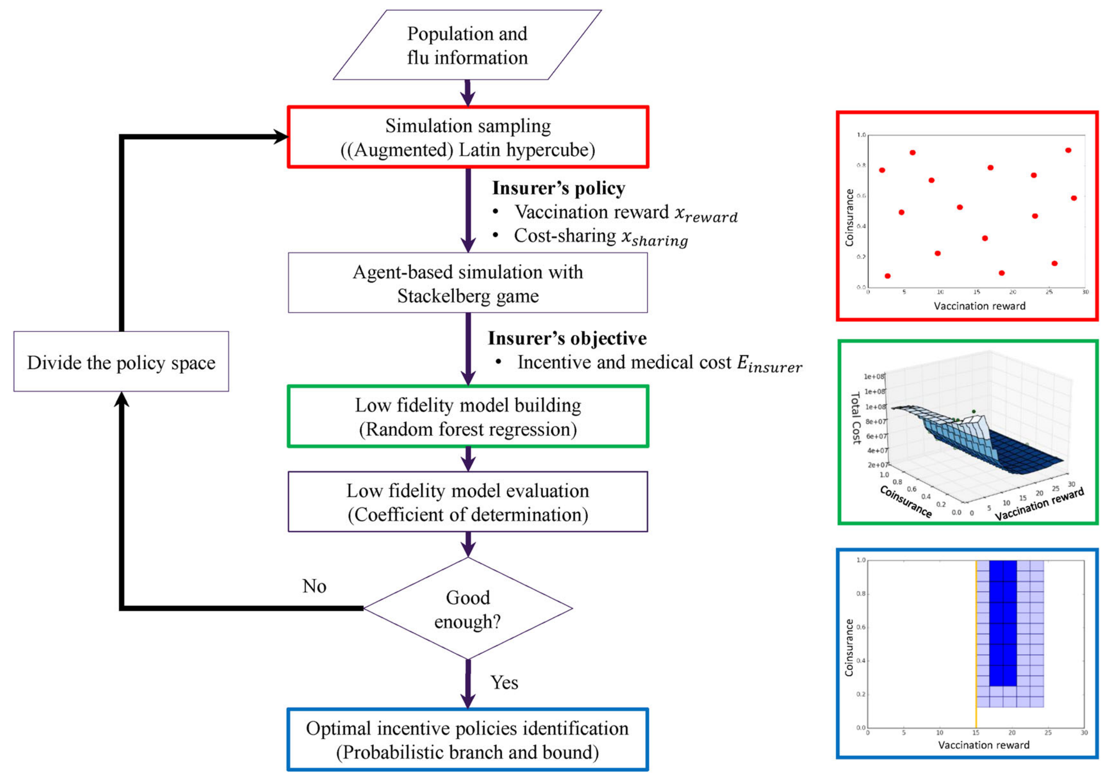


Figure 3. Simulation optimization and machine learning framework in the agent-based simulation and Stackelberg game.

3.3.1. Simulation sampling using Latin hypercube design

First, we use a space-filling Latin hypercube sampling design (Stein, 1987) to determine the sample points (i.e., values of x_{reward} and $x_{sharing}$) as the initial input to the agent-based simulation. As illustrated in Figure 3's upper-right corner, a Latin hypercube sampling design ensures that the sampling space is evenly sampled.

3.3.2. Low-fidelity model design using random Forest regression

After running the agent-based simulation at each sample point, we acquire a data set consisting of policies (inputs) and corresponding total costs (outputs). We use machine learning (specifically, random forest regression) to capture the input-output relationships in the simulation. An example of the low-fidelity model is illustrated in Figure 3's center-right position. Random forests are one of the widely-used ensemble machine learning techniques (Ho, 1995). A random forest is useful for the regression task due to its simplicity and quality of fitting even without hyperparameter tuning. To understand infectious disease models, other techniques such as the active-learning approach can be used to build surrogate models (Willem et al., 2014). While these approaches give a good approximation of the response variable when all the model parameters are given; the learning process is not able to be traced if the model involves a large number of parameters.

3.3.3. Low-fidelity model evaluation using the coefficient of determination

The model fit is measured by the coefficient of determination (R^2). The R^2 value is calculated by the proportion of the variance in the overall cost that is predictable from the given incentive policies. An R^2 value close to 1 indicates that the random forest regression can replicate the observed response well.

If the R^2 measurement is above the specified threshold, the methodology can continue to PBnB to identify near-optimal policies. If the R^2 is smaller than the threshold, we can divide the policy space into two subsets, and use an augmented Latin hypercube sampling design to sample more points and build a random forest regression in each sub-region. An augmented Latin hypercube sampling design adds more points to the original Latin hypercube sampling design while maintaining the space-filling properties (Stein, 1987).

3.3.4. Optimal incentive policies identification using probabilistic branch-and-bound

We apply PBnB (Huang & Zabinsky, 2013; Zabinsky & Huang, 2020) to the random forest regression model to determine a set of near-optimal reward and cost-sharing policies.

PBnB approximates a target level set of good solutions by partitioning the solution space into subregions and updating its estimate of a good subregion (Huang & Zabinsky, 2013; Zabinsky & Huang, 2020). The target level set is specified by a desired quantile level δ. For examaple, setting $\delta = 0.1$ can be interpreted as seeking the solutions with the best 10% objective function values.

The lower-right corner of Figure 3 illustrates PBnB outputs to visualize the partitioning and target level set approximation. The deep blue (dark gray) regions are "maintained" regions representing the approximate set of top 10 percent quantile solutions, the white regions are "pruned" regions (i.e., with statistical confidence there is no overlap with the target 10% quantile set), and the light blue (light gray) are undecided regions. In this manner, we approximate the set of solutions with near-optimal performance.

By providing a *set* of solutions, as opposed to a single solution, policy makers can explore a range of decisions that provide similar good performance. Since the implementation and execution of a desired solution will not align exactly with model predictions, having multiple solutions allows decision makers to see how large the range may be and still provide top quality performance.

4. Numerical experiment

In this research, we demonstrate our mechanism design approach with a stochastic influenza epidemic simulation model, FluTE (Chao et al., 2010), which has been used in many policy-making studies to compare the effectiveness of interventions (Kasaie & Kelton, 2013; Longini et al., 2005). The FluTE software is written in C++ and simulates the stochastic spread of influenza across age- and risk- structured population of individuals interacting in known population groups (FluTE, 2010). The Stackelberg game with realistic incentive policies is incorporated into FluTE with a natural history of influenza infection.

We extend the FluTE model by: (i) adding two more health states, i.e., flu-associated hospitalizations and flu-associated death, which CDC uses to estimate influenza disease burden in the United States each year; and (ii) replacing the policy makers or government-led compulsory interventions, i.e., vaccination intervention and outpatient treatment, with individual decision-making governed by self-interested behavior (Equations (1)-(4) in Section 3.2).

We incorporate hospitalization and death absorbing-state compartments (H and D) into FluTE based on the flow diagram illustrated in Figure 2 and described in Section 3.1. The population sizes of these compartments contribute to the expected cost for the insurer.

We also add the insureds' vaccination and treatment decision-making processes (Equations (1)-(4)) and the insurer's total cost calculation ($E_{Insurer}$ in Equation (5)) into FluTE. The costs and infection probabilities in the agent-based simulation model are associated with age and risk type. Table A1 in Appendix A lists the data that are used as simulation inputs to obtain the near-optimal solutions. To account for variation in costs by age and risk, the cost is estimated for five age groups: <5, $5-17$, $18-49$, $50-64$, and ≥ 65 years. In addition, the cost is varied for high-risk and non-high-risk groups. The probability of influenza-attributable hospitalizations and deaths, the corresponding medical cost, and the value of the lost productive day (indirect cost) are from Molinari et al. (2007), which estimated the annual economic burden of influenza epidemics. The age 65+ group has higher hospitalization and death probability than other groups. Healthcare costs and productivity losses are greater in high-risk groups than in non-high-risk groups.

We simulate a flu epidemic in Seattle with a population of 563, 441 agents. The agents are randomly generated using the U.S.-wide family-size distribution from the 2000 Census. The FluTE model has been calibrated to past influenza pandemics, Asian A (H2N2) and 2009 novel influenza A (H1N1) influenza (Chao et al., 2010), so that outcomes are consistent with these influenza viruses. The infection probability of an individual agent is updated daily based on the vaccination status of the agent, the agent's age, and the infection status of his/her connected agents in family, neighborhood, workgroup, or school transmissions. The infection probability of a group (e.g., family, neighborhood, work, and school) is updated in FluTE based on the number of infected in the group and the basic reproduction number R_0 of influenza. We adopt the default values of the flu and Seattle population parameters in the model but further extend it for more comprehensive infection phases in our Stackelberg vaccination game.

In the configuration file, the number of agents initially infected at the beginning of the simulation is set to 100. No healthcare intervention, e.g., compulsory pre-vaccination, is implemented before the epidemic. Fractions of individuals in each of the five age groups who are at high risk of complications from influenza are set to 0.089, 0.089, 0.212, 0.212, and 0.9, respectively (Chao et al., 2010). The time horizon in the simulation is 365 days, which corresponds to an insurer making annual adjustments to policies and covers a flu season. Each time period corresponds to a day.

We simulate 100 sample points, resulting in 100 simulation runs. The interval for vaccine reward x_{reward} is \$0-\$30, to reflect the current practice of giving store coupons to flu vaccine seekers. The range of values for coinsurance rate $x_{sharing}$ is the interval $[0, 1]$.

We use the Python package available in scikit-learn, a free software machine learning library for the Python programming language, to build random forest models (Pedregosa et al., 2011; Van Rossum & Drake, 2009). The incentive policies (x_{reward} and $x_{sharing}$) and overall cost ($E_{Insurer}$) are used as the independent and dependent variables, respectively. In the parameter setting, the number of trees in the forest is set to 100 and the maximum depth of the tree is set to eight. We used 70 simulation runs as a training set for the random forest regression, and used the remaining 30 simulation runs to evaluate the goodness of fit. We set the threshold of R^2 to 0.8 since a value of R^2 larger than 0.7 is typically considered good (Moore & Kirkland, 2007) We then set $\delta = 0.1$ in PBnB to identify a set of top 10% solutions.

5. Experiment results

5.1. Base case

In the base case, we set vaccine efficacy to 60%, the basic reproduction number is $R_0 = 1.6$, and the weight of health outcomes is $w = \$200$. The base value of 60% for vaccine efficacy is from CDC (2020c), and the basic reproduction

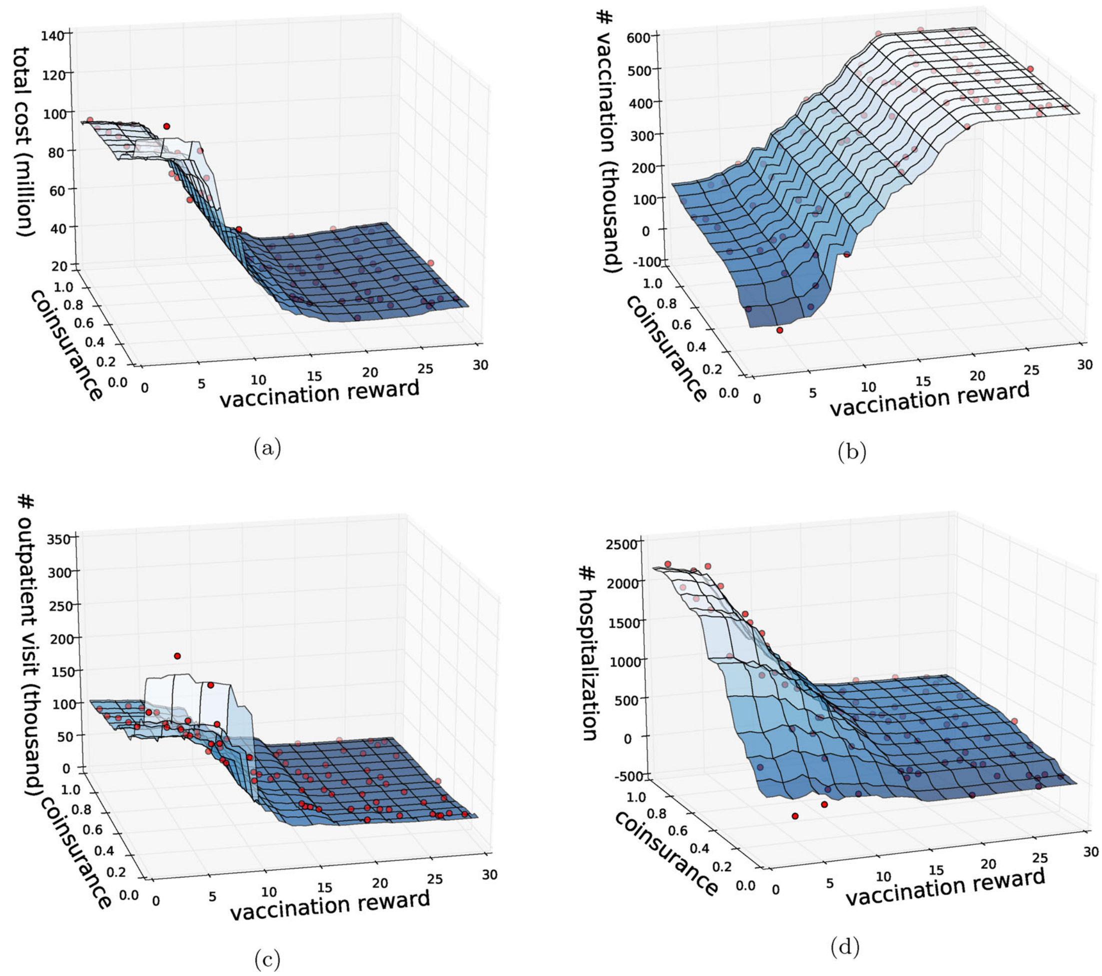


Figure 4. Random forest regression surfaces and simulated outputs (red dots) for the base case: (a) total cost (b) vaccinated population size (c) treated population size (d) hospitalized population size with respect to vaccination reward and coinsurance rate.

number $R_0 = 1.6$ is from Chao et al. (2010). The weight \$200 is approximated by the hidden annual economic burden divided by an estimated number of symptomatic illness (CDC, 2017; Ozawa et al., 2016). Figure 4 presents the total cost and numbers of vaccination, treatment, and hospitalization cases as functions of vaccination reward and coinsurance. The 100 dots indicate the observed values from the agent-based simulation, and the surface is derived from the random forest regression. Each simulation run takes about 30 minutes on a personal computer. No further division of the policy space was necessary since the performance of built random forest regression meet the performance threshold, i.e., $R^2 = 0.8$.

From the total cost output for the base case illustrated in Figure 4, it is observed that the effect of vaccination reward dominates the effect of coinsurance, indicating that the policy makers should prioritize prevention over treatment. However, the coinsurance rate has a significant influence on the number of individuals vaccinated, treated, and hospitalized when the vaccine reward is low. A high coinsurance rate may be seen as a penalty for infected insureds, so it will encourage more vaccination behavior (see Figure 4(b)). However, it also discourages treatment-seeking behavior due to significant medical care cost (see Figure 4(c)), resulting in high hospitalization rate (see Figure 4(d)).

Figure 5 presents the PBnB output using the random forest regression model for the base case. More than half of the policy region is pruned by PBnB (pruned region is white), indicating it is unnecessary to evaluate more points for good policy exploration. The policies with too high and too low vaccine rewards are pruned. This is because a low vaccination reward region will result in a high total cost from high numbers of infected, hospitalized, and dead. Setting the reward too high also causes a high total cost since almost all the population is vaccinated and thus the marginal reduction of medical costs cannot catch up with an increasing reward cost. The low total cost region (maintained region is deep blue color/dark gray) appears in the medium vaccination reward and coinsurance rate region. To give more specific policy recommendations, the result of PBnB in Figure 5 approximates the best 10% incentive policies with the base case setting. The coinsurance rate in the maintained region is between $25\% - 100\%$ and the vaccination reward ranges from \$17–\$21. This provides insight on the sensitivity of the policy decision to the policy maker.

5.2. Comparison to a case without vaccination reward

To demonstrate how a vaccination reward and co-insurance incentive can reduce the total cost and affect flu transmission, we compare three good policies selected from the maintained region of the base case (see Figure 5) with a case that has no vaccination reward. In this case, there is no vaccination reward offered and the vaccination decision is replaced with a fixed vaccination probability of 30% for all age and risk-type populations. The treatment-seeking decision is replaced with the treatment-receiving probability $p^{a,r}_{T|F}$ (as in Table A1). We use a standard coinsurance rate of 15% to calculate the medical cost. The other parameters are set at the base case values (vaccine efficacy is 60%, the basic reproduction number is $R_0 = 1.6$, and the weight of health outcomes is $w = \$200$).

Table 2 shows the potential benefit of offering policy interventions with a vaccination reward and adjusted co-insurance rates. The total cost of the base case with no vaccination reward is approximately three times the cost of any of the three intervention policies selected from the maintained region for the base case. Notice that less than one-third of the population gets vaccinated in the base case with no vaccination reward.

5.3. Sensitivity analysis on three parameters

In this section, we conduct three one-way sensitivity analyses, varying vaccine efficacy, basic reproduction number R_0, and weight of health outcomes w as in Table 3.

5.3.1. Vaccine efficacy

The first sensitivity analysis studies how different values of vaccine efficacy affect the near-optimal incentives. Figures A, 5, and A illustrate good policies in the maintained regions for values of vaccine efficacy of 30%, 60%, 90%, respectively, with fixed base values for $R_0 = 1.6$ and weight of health outcomes $w = 200$. It is observed that the maintained region gradually shifts as vaccine efficacy improves. The reason is that higher vaccine efficacy leads to lower infection probability ($p^a_{F|V}$). The threshold value of x_{reward} which makes $E^{a,r}_S > E^{a,r}_V$ for each individual agent is therefore lower.

It is also observed that Figures 5, A, & A demonstrate the value of a set of near-optimal solutions, which provides policy makers the flexibility to implement a healthcare policy even with uncertainty or limited information about vaccine efficacy. Comparing the overlapping maintained regions between Figures 5, A, & A provides the sensitivity of near-optimal incentive policies. If the vaccine efficacy is lower than 60%, as in Figure A, the reward increases to encourage uptake however the co-insurance also increases, whereas an increase in vaccine efficacy, as in Figure A, can result in a reduced reward with reduced co-insurance.

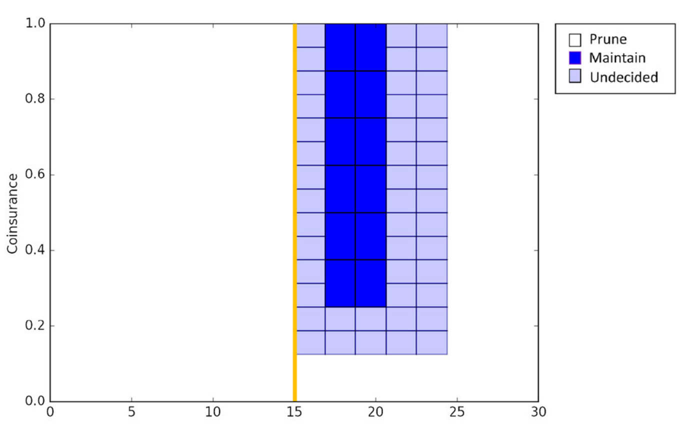


Figure 5. PBnB output for the base case (vaccine efficacy = 60%, R_0 = 1.6, and w = $200).

5.3.2. Reproduction number

In the second sensitivity analysis, we study the basic reproduction number for seasonal flu that captures how infectious the flu is. A high R_0 indicates that a high number of new cases occurred in the population during a specified period. Tuning the value of R_0, we can simulate different numbers of new infections from a single infected individual in a susceptible population. It is observed from Figures 5 and 6(c) and (d) that more vaccination reward should be offered to encourage vaccination behaviors as R_0 increases. It is also observed in the base case and high R_0 cases, that the subregions with low reward are pruned due to relatively high hospitalization and death cost.

5.3.3. Weight of health outcomes

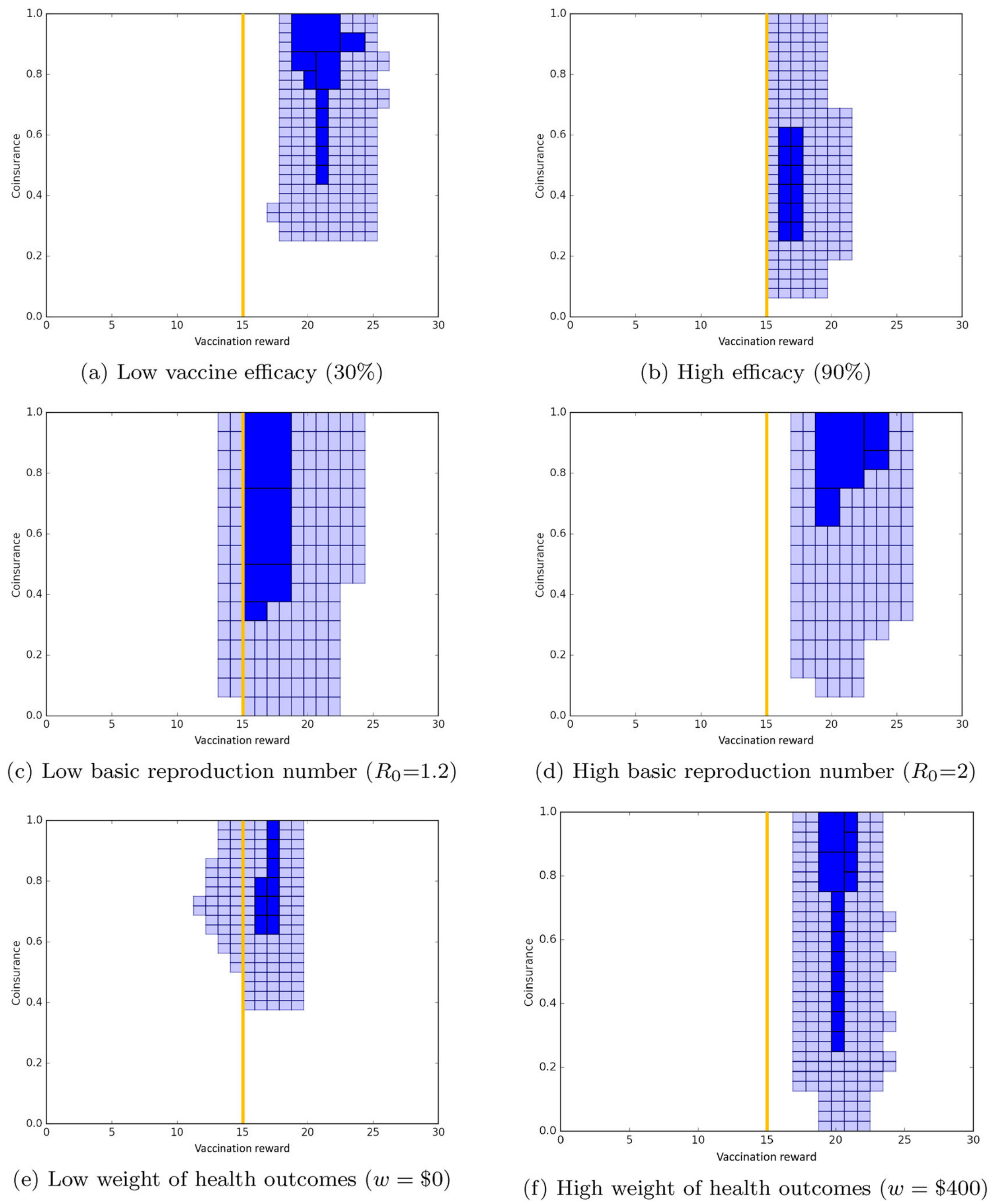
In the third sensitivity analysis, we vary the value of the weight of health outcomes ($0, $200, and $400) to see the effect of how a policy maker values the population health outcome. Comparing a scenario with a high value for the weight of health outcomes with a scenario with a low value, the results in Figure 6(f) suggest that a health insurance agency with a high weight of health outcomes would tend to raise the vaccination reward to encourage vaccination behavior and avoid outbreaks, whereas the scenario with a low weight of health outcomes has a smaller range of

Table 3. Parameter setting in sensitivity analysis.

		Low case	Base case	High case
Experiment 1	Vaccine efficacy	30%	60%	90%
Experiment 2	Basic reproduction number R_0	1.2	1.6	2.0
Experiment 3	Weight of health outcomes w	$0	$200	$400

Table 2. Comparison of the base case with no vaccination reward to three policy interventions selected from the maintained region for the base case (as in Figure 5).

	Total cost	# Vaccination	# Treatment	# Hospitalization
Base case with no vaccination reward $x_{reward} = \$0$, $x_{sharing} = 15\%$	$93,092,400	164,426	106,710	445
$x_{reward} = \$18$, $x_{sharing} = 25\%$	$30,498,100	508,417	33,604	224
$x_{reward} = \$18$, $x_{sharing} = 50\%$	$30,186,600	511,795	26,578	379
$x_{reward} = \$18$, $x_{sharing} = 75\%$	$29,749,500	513,767	23,071	451



(a) Low vaccine efficacy (30%)

(b) High efficacy (90%)

(c) Low basic reproduction number (R_0=1.2)

(d) High basic reproduction number (R_0=2)

(e) Low weight of health outcomes (w = \$0)

(f) High weight of health outcomes (w = \$400)

Figure 6. Sensitivity analysis.

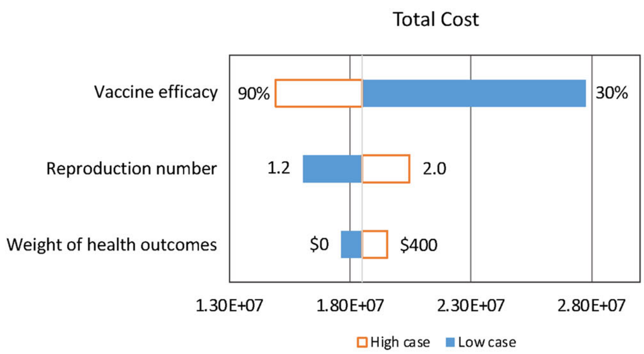
coinsurance in the maintained region. The reason is that the total cost in Equation (5) is more sensitive to the changes in the flu-infected population proportion due to the high weight of health outcomes.

5.3.4. Population outcome comparison

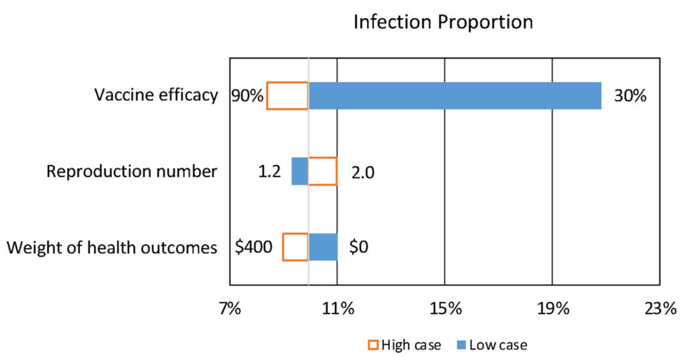
To better understand how uncertainties of the three parameters in our sensitivity analysis, i.e., vaccine efficacy, basic reproduction number, and weight of health outcomes, affect other population outcomes, we average the total cost, infection proportion and vaccination proportion for all simulated polices (reward and coinsurance) in the maintained region for the base case and six sensitivity scenarios.

The average total cost, average infection proportion, and average vaccination proportion in the base case is 18.5 million dollars, 9.93%, and 93.52%, respectively. Figure 7 compares the three outputs from the base case to the six sensitivity scenarios. As seen in Figure 7(a), low vaccine efficacy, high basic reproduction number, and high weight of health outcomes increase the total cost from the base case. Vaccine efficacy has the most significant impact on total cost, as well as on infection proportion (Figure 7(b)).

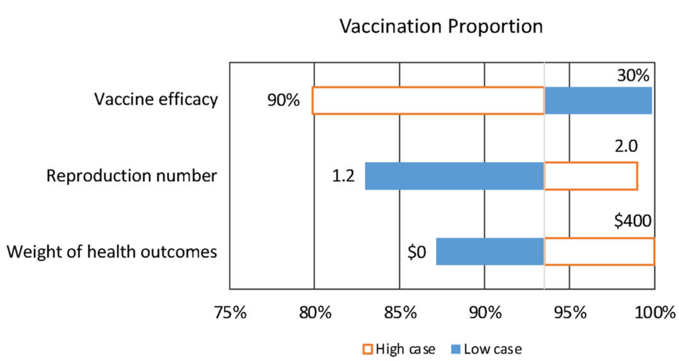
It is also observed that, even though the vaccination proportion decreases 10% in the low R_0 case, the infection proportion is still lower than its counterpart in the base case. In the high R_0 case, on the other hand, an additional 5%



(a) Total cost



(b) Infection proportion



(c) Vaccination proportion

Figure 7. Comparison of six sensitivity analysis scenarios and the base case.

population gets vaccinated to keep the infection proportion similar to its counterpart in the base case (only 1.06% higher).

Furthermore, a high weight of health outcomes results in a high total cost because a large incentive is given to improve vaccination behavior (results in sensitivity analysis 3). The vaccination proportion therefore increases 6.5% compared to the base case (Figure 7(c)), reaching 100% to reduce the infection proportion by 1% in Figure 7(b).

6. Conclusions

We considered a seasonal flu outbreak prevention problem where a policy maker's goal is to design insurance-based healthcare incentives to alleviate the medical cost and disease burden. We proposed a mechanism design approach to determine two effective healthcare incentive policies, vaccination reward and cost-sharing for seeking treatment to prevent the flu outbreak. We adopted a monetary reward for the susceptible population to incentivize vaccination behavior and selected a coinsurance rate to encourage appropriate treatment-seeking behavior and avoid overuse of health care services.

We made two modeling contributions to evaluate the effect of healthcare incentive policies on infectious disease outcomes. First, to represent a detailed model of the dynamic interaction between the insurer and the insured population, we embedded a Stackelberg vaccination game with the insurer as the leader and the population as followers, into an agent-based simulation. An advantage of this approach is to provide a mathematical description of the flu epidemic at the individual level while considering the interaction of multiple individuals. Second, we coupled random forest regression with PBnB to reduce the number of runs of the agent-based simulation while returning a set of statistically valid near-optimal incentive policies. The main disadvantage of agent-based simulation is its high computational cost, which may limit the number of reasonable runs and extent of sensitivity analysis. The methodology we propose in the paper conquers this computational limitation of agent-based simulation while keeping its advantage in order to provide health care policy makers more selection of interventions.

We incorporated the proposed game-theoretic model into the FluTE model to simulate the propagation of influenza in a Seattle population. We added two health states, hospitalization and death, and integrated the decision-making processes and corresponding population responses to FluTE. Moreover, we added medical care cost, loss of productivity, hospitalization, and death probability for all age-specific and risk groups as input parameters to the FluTE model, and generated overall medical care cost and population health outcome as the final output. We found that: (1) both vaccination reward and coinsurance are effective policies to encourage vaccination behavior and minimize the overall cost; and (2) the policy in the proposed mechanism keeps the infection rate low under different vaccine efficacy and basic reproduction number while taking the medical cost paid by the insurer and population health outcomes into consideration. We also demonstrated that vaccine efficacy has a strong influence on individuals' vaccination and treatment-seeking behaviors and, as a result, impacts long-term population health outcomes.

There are several limitations to our study. First, this paper assumes that both the insured and insureds are risk-neutral (as is common in the game theory approach in the literature), and make rational and fully-informed decisions. In reality, they may not be risk-neutral and have incomplete information. Adopting the concept of "bounded rationality" would reflect a more realistic decision-making process; however, our model is limited. We assume the insurer has information about the projected population outcomes (e.g., the proportion of vaccinated insureds and infected insureds during the season). And the insureds can fully observe all the probabilities, e.g., infection and hospitalization probabilities, and costs, e.g., medical cost and loss of productivity, when they make the expected cost comparison. We convert several factors to a common cost unit to use in the expected cost calculation. For example, the number of infected neighbors may factor into an individual insured's decision to vaccinate. In the agent-based simulation, each insured is aware of the status of its neighbors; however, to keep units consistent, we convert this to dollars in the calculation of the expected cost of an untreated insured. As a rational (risk-neutral) decision maker, each insured will make a decision that improves their expected cost.

Second, we assume that the entire population is covered by a single health plan insurer, whereas in reality, a regional population includes individuals covered by many different insurers under many different plans, as well as a portion of uninsured individuals. Our model is immediately relevant to insurers that cover an entire population but also explains the behavior of insurers that may only be responsible for subsets of a defined population. Each insurer has the same incentive options and therefore we may assume that individual insurers behave identically concerning the cost-sharing arrangements they create. As a result, each individual with similar risk faces the same incentives with regard to health-seeking behavior. We also assume that individuals of similar risk share the same degree of susceptibility to monetary incentives.

Third, we assume that the insurer can set a co-insurance rate that would apply specifically to outpatient medical treatment of an infected individual. Traditional insurance models often use uniform cost-sharing arrangements for categories of services. For example, all outpatient visits, pharmacy fills, and lab tests would have the same copayment or co-insurance rates for each insurance product they offered. This traditional model has given way to value-based insurance products that routinely have different cost-sharing for otherwise similar services based on a variety of circumstances that include patient willingness to pursue specific therapeutic options. It is therefore increasingly likely that insurance companies tailor cost-sharing to micro-incent or disincent specific patient choices.

Fourth, we assume that the insurer is willing to financially reward individuals who choose to get vaccinated, which implementing rewards at a large scale would represent a huge financial cost, or seem to favor certain groups or interventions. Regarding to this feasibility issue, we believe value-based insurance models routinely offer a variety of incentives to encourage more efficient health-seeking behavior. While insurers are prohibited from using measures that might seem coercive, they often waive copayments or provide lower co-insurance rates if patients agree to submit biometric data or complete all of the recommended preventive services for their age and gender. Flu vaccines are a leading example of a preventive service for which insurers may offer such incentives. More importantly, the COVID-19 pandemic in 2020 has significantly increased the urgency of providing vaccination incentives to ensure sufficient coverage of the new COVID-19 vaccines due to the massive death tolls in the U.S. Starting in the fall of 2020, there were active discussions on providing direct financial payment to individual Americans as a measure to encourage COVID-19 vaccine uptakes in the hope of minimizing future loss-of-life and economic loss (Johns Hopkins University & Medicine, 2020).

There are also two exciting future research directions following this study. First, the current study is focused on the demand-side of vaccination. Incorporating the supply-side with the possibility of vaccine shortage and delay would increase the realism of our study. Second, the knowledge about vaccine effectiveness evolves during the flu season. Modeling the value of information on the vaccine effectiveness with population sampling, and how such knowledge will improve decision making during the season needs additional careful investigation.

In conclusion, we have proposed an incentive-based insurance mechanism to prevent the spread of seasonal influenza for a single health insurer and multiple insureds. Our model captures four critical sources of uncertainty from the insurer's perspective, such as uncertainty in population health status and behavior, the infectivity of flu, and vaccine effectiveness. We combined a Stackelberg vaccination game into an agent-based simulation and optimized the model to provide systematic insight as to how a insurer would incentivize self-interested insureds to uptake vaccine and seek treatment during the flu season.

Role of the funder

NSF had no direct role in the research.

Disclosure statement

No potential conflict of interest was reported by the authors.

Consent and approval

This study has been exempted from the requirement for approval by an institutional review board because there were no participants other than the authors in this study.

Funding

This work was supported by the National Science Foundation under Grant CMMI-1935403. Division of Civil, Mechanical and Manufacturing Innovation.

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Appendix A. Parameters used in the analysis of agent-based simulation

Table A1. Model parameter values.

Variable	Base Case (Range)/Distribution		Reference
Cost	Medical cost	Loss productivity	
No medical attendance	$c^{a}_{med,U}$	$c^{a}_{ind,U}$	Molinari et al. (2007)
All risk	log normal (mean, std)	Poisson (mean)	
Age 0–4	(2, 3)	145	
Age 5–17	(2, 3)	75	
Age 18–49	(2, 3)	75	
Age 50–64	(2, 3)	75	
Age 65+	(2, 3)	145	
Treatment	$c^{a,r}_{med,T}$		Molinari et al. (2007)
Normal	log normal (mean, std)		
Age 0–4	(167, 307)	145	
Age 5–17	(95, 258)	145	
Age 18–49	(125, 438)	145	
Age 50–64	(150, 766)	290	
Age 65+	(242, 1544)	435	
High risk	log normal (mean, std)		
Age 0–4	(574, 1266)	870	
Age 5–17	(649, 1492)	580	
Age 18–49	(725, 1717)	290	
Age 50–64	(733, 1307)	580	
Age 65+	(476, 1131)	1015	
Hospitalization	$c^{a,r}_{med,H}$	$c^{a,r}_{ind,H}$	Molinari et al. (2007)
Normal	log normal (mean, std)	Poisson (mean)	
Age 0–4	(10880, 36189)	1160	
Age 5–17	(15014, 86804)	1305	
Age 18–49	(19012, 44636)	1740	
Age 50–64	(22304, 95727)	1885	
Age 65+	(11451, 23128)	1885	
High risk	log normal (mean, std)	Poisson (mean)	
Age 0–4	(81596, 123626)	4495	
Age 5–17	(41918, 50393)	3335	
Age 18–49	(47722, 85644)	3045	
Age 50–64	(41309, 74798)	3480	
Age 65+	(16750, 32091)	2610	
Death	$c^{a,r}_{med,D}$		Molinari et al. (2007)
Normal	log normal (mean, std)		
Age 0–17	(28818, 24483)		
Age 18–49	(76336, 91654)		
Age 50–64	(118575, 333879)		
Age 65+	(41948, 96467)		
High risk	log normal (mean, std)		
Age 0–17	(267954, 221130)		
Age 18–49	(75890, 65267)		
Age 50–64	(118842, 345973)		
Age 65+	(33011, 61904)		

Note 1: Direct medical cost for the outpatient visit $c^{a,r}_{med,T}$ is the sum of outpatient and pharmaceutical claims, which included office visits, laboratory tests, imaging tests, professional consult fees, out-patient procedures, and prescription medications for each age and risk group. The antiviral treatment is included in the cost of an outpatient visit.

Note 2: Direct medical cost for hospitalized and death case, $c^{a,r}_{med,H}$ and $c^{a,r}_{med,D}$, are both calculated by summing of all inpatient, outpatient, and pharmaceutical claim for each age and risk group.

Table A1. Model parameter values (continued).

Variable	Base Case (Range)/Distribution	Reference
Indirect vaccination cost	90% population has (5, 20) uniform distribution	assume†
$c_{ind,V}$	10% population has 0 cost for voluntary vaccination	assume
Coinsurance rate		
f_H	30%	assume
f_D	30%	assume
Probability		FluTE (2010)
$p^a_{F\|S}$	intermediate parameter††	
$p^a_{F\|V}$	intermediate parameter††	
$p^a_{H\|F}$		Molinari et al. (2007)
All risk	log normal (mean, std)	
Age 0–4	(0.0141, 0.0047)	
Age 5–17	(0.0006, 0.0002)	
Age 18–49	(0.0042, 0.0014)	
Age 50–64	(0.0193, 0.0064)	
Age 65+	(0.0421, 0.014)	
$p^a_{D\|F}$		Molinari et al. (2007)
All risk	log normal (mean, std)	
Age 0–4	(0.00004, 0.00001)	
Age 5–17	(0.00001, 0)	
Age 18–49	(0.00009, 0.00003)	
Age 50–64	(0.00134, 0.00045)	
Age 65+	(0.0117, 0.0039)	
$p^{a,r}_{T\|F}$		Molinari et al. (2007)
Normal	log normal (mean, std)	
Age 0–4	(0.455, 0.098)	
Age 5–17	(0.318,0.061)	
Age 18–49	(0.313, 0.014)	
Age 50–64	(0.313, 0.014)	
Age 65+	(0.62, 0.027)	
High risk	log normal (mean, std)	
Age 0–4	(0.91, 0.25)	
Age 5–17	(0.635, 0.167)	
Age 18–49	(0.625, 0.118)	
Age 50–64	(0.625, 0.118)	
Age 65+	(0.82, 0.093)	
Population N	563,441	FluTE (2010)
Weight of health outcomes w	200 (0–400)†††	CDC (2017) Ozawa et al. (2016)

†The indirect vaccination cost $c_{ind,V}$ is based on the minimum wage in the USA of \$7.25 per hour (U.S. Bureau of Labor Statistics, 2020) and the median wage in 2019 of \$19.33 per hour (Gould, 2019), and an assumption that it takes 0.5 hours to get a vaccine. This results in a range of (5, 20) to represent the wage lost for 0.5 hours. We used a uniform distribution with support (5, 20).

††The intermediate parameters are updated daily based on the infection probability in family, neighborhood, workgroup, or school transmissions in FluTE, using $1 - \prod_{g \in G}(1 - \text{infection probability in each group } g \text{ for insured with age } a)$.

†††The weight 200 is approximated by the hidden annual economic burden \$5.8 billion divided by an estimated number of symptomatic illnesses, 29 million, in 2016-2017 flu season (CDC, 2017; Ozawa et al., 2016). The weights of the government-run health insurance agency and the private insurance company are assumed as 400 and 0, respectively.

Note 3: The probability distribution estimates reported by Molinari et al. (2007) have been converted into the daily probability by using the formula $p_d = 1 - (1 - p)^{(1/d)}$, where p_d is the daily probability we used in the agent-based simulation, p is the parameter in Molinari et al. (2007), and $d = 6$ days, indicating that if a susceptible individual is infected, he/she will be infectious for six days (FluTE, 2010). During the six days, infected individuals have a risk of hospitalization or death on each day.