Coupling an individual adaptive-decision model with a SIRV model of influenza vaccination reveals new insights for epidemic control

Qinling Yan[1], Robert A. Cheke[2], Sanyi Tang*[3]

[1]School of Science, Chang'an University, Xi'an, 710064, P.R. China
[2]Natural Resources Institute, University of Greenwich at Medway, Chatham Maritime, Kent, ME4 4TB, UK
[3]School of Mathematics and Statistics, Shaanxi Normal University, Xi'an, 710062, P.R. China

Correspondence
*Sanyi Tang, School of Mathematics and Statistics, Shaanxi Normal University, Xi'an, 710062, P.R. China.

Email: sytang@snnu.edu.cn & sanyitang219@hotmail.com

Summary
Past seasonal influenza epidemics and vaccination experience may affect individuals' decisions on whether to be vaccinated or not, decisions that may be constantly reassessed in relation to recent influenza related experience. To understand the potentially complex interaction between experience and decisions and whether the vaccination rate is likely to reach a critical coverage level or not, we construct an adaptive-decision model. This model is then coupled with an influenza vaccination dynamics (SIRV) model to explore the interaction between individuals' decision making and an influenza epidemic. Nonlinear least squares estimation (NLSE) is used to obtain the best-fit parameter values in the SIRV model based on data on new influenza-like illness (ILI) cases in Texas. Uncertainty and sensitivity analyses are then carried out to determine the impact of key parameters of the adaptive decision-making model on the ILI epidemic. The results showed that the necessary critical coverage rate of ILI vaccination could not be reached by voluntary vaccination. However, it could be reached in the fourth year if mass media reports improved individuals' memory of past vaccination experience. Individuals' memory of past vaccination experience, the proportion with histories of past vaccinations and the perceived cost of vaccination are important factors determining whether an ILI epidemic can be effectively controlled or not. Therefore, health authorities should guide people to improve their memory of past vaccination experience through media reports, publish timely data on annual vaccination proportions and adjust relevant measures to appropriately reduce vaccination perceived cost, in order to effectively control an ILI epidemic.

KEYWORDS:
Influenza-like illness (ILI), Vaccination, Adaptive-decision model, SIRV, Critical coverage rate

ABBREVIATIONS: ILI, influenza-like illness; NLSE, nonlinear least squares estimation; SIRV, susceptible-infective-recovery-vaccination.

INTRODUCTION

Influenza, an acute respiratory infectious disease caused by the influenza virus, brings serious harm to human health. Its antigenicity changes readily and the virus spreads rapidly, so there are seasonal epidemics every year.[1,2] According to the World Health Organization (WHO) estimates, about 3 000 000 to 5 000 000 cases of severe illness and 290 000 to 650 000 deaths result from these annual seasonal influenza outbreaks.[3] More than 60 years of vaccination practice and many studies from around the world have proved that the influenza vaccine is the safest and most effective means of reducing the risk of transmission, thereby preventing influenza and its complications.[1-4]

To determine what proportion of the population would need to be vaccinated, so as to prevent an influenza epidemic, researchers have established both complex and simple models at the population level.[5-11] However, the transmission characteristics of infectious diseases in a population are affected significantly by individual decision-making. Understanding the danger of infectious diseases and the risks involved with vaccination are drivers of vaccination choices and so has an impact on vaccination coverage at the population level. Individuals who choose to be vaccinated protect themselves and their contacts, thus preventing the further spread of the influenza epidemic. When a large number of individuals are vaccinated, the disease can no longer spread, thus protecting the whole population (ie, herd immunity).[5] Generally, individuals' knowledge of herd immunity may affect their vaccination behavior. If individuals act in their own self-interests, they may rely on the immunity of others for protection rather than vaccinate themselves, resulting in a "free-rider problem."[12]

In recent years, infectious disease models, embedding individual vaccination decision-making that is affected by both individual risk perception and others' perception of whether to vaccinate, have attracted much attention.[6] First, researchers have considered a homogeneous group with rational and self-interested characteristics, who opt to obtain vaccination through deductive reasoning. Based on game theory, individuals choose to be vaccinated with a given probability to maximize their benefits and achieve a Nash equilibrium solution. The probability of vaccination is obtained by assuming that all individuals in the population rely on the same information and perception (based on SIR or SEIR epidemiology models) and make the same rational decision. For example, the policy of voluntary vaccination of smallpox vaccine may lead to "free-riders" according to game theory, that is, the vaccination coverage rate is far lower than the optimal level.[13] Similarly, voluntary vaccination itself cannot eradicate children's diseases such as measles, since some parents still decide not to vaccinate their children.[14,15]

These models could predict the stable vaccination coverage of the population. However, for heterogeneous populations, since they have different views on infection costs, vaccination costs, or other behavioral mechanisms, vaccination coverage may fluctuate.[16] For example, childhood diseases occur when parents imitate other parents' vaccination choices or make decisions based on past epidemic information.[17-19] Ghaffarzadegan et al showed that the endogenous representation of human behavior in interactions with an evolving epidemic are the most important factors determining the long-term predictive power of epidemic models based on a study of behavioral response feedbacks.[20] Besides, vaccination cannot necessarily provide permanent immunity against the pathogen, which may also fluctuate, so individuals may make decisions on vaccination many times in their lives, which is the case with seasonal influenza. Due to the high mutation rate of the influenza virus, it is necessary to decide whether to vaccinate every year or not. In addition, as vaccinations do not inhibit the

transmission of all influenza virus strains within a year individuals may decide whether or not to be vaccinated each year, based on their past influenza epidemic and vaccination experience.

Evolutionary game theory based on individual level models provides a method to describe the coupling of the dynamics of an influenza epidemic with vaccination decision-making. Vardavas et al assumed that there is a uniformly mixed population in the model, in which individuals evaluate their decision to be vaccinated based on their own past infection experience and take the vaccination critical coverage rate as an indicator of influenza severity.[21,22] In this model, different individuals have different perception of infection risk due to their different experiences of influenza epidemics and influenza vaccination. Therefore, individuals do not consider others and do not depend on them to decide on vaccination for themselves, and this heterogeneity of vaccination behavior is also embedded in the dynamics model. However, the above results do not show whether this critical coverage rate can be really achieved, nor do they explore how the vaccination decision-making behavior at the individual level affects the transmission trend of the disease based on the actual observed data.

Therefore, we construct an adaptive decision-making model with human cognition and behavior at the individual level, and explore whether the critical coverage rate can be achieved through voluntary vaccination by simulating the individuals' vaccination decision-making. Then, the adaptive-decision model is coupled with an influenza Susceptible-Infected-Recovered-Vaccinated (SIRV) model with vaccination dynamics. Based on the weekly number of new influenza-like illness (ILI) cases in Texas from the 36thweek of 2016 to the 35thweek of 2019 (as shown in Figure 1),[23] we applied nonlinear least squares estimation to identify the best-fit parameter values in the SIRV model. To determine the impact of key parameters of the adaptive decision-making model on the epidemic trend of ILI, uncertainty and sensitivity analyses were carried out.

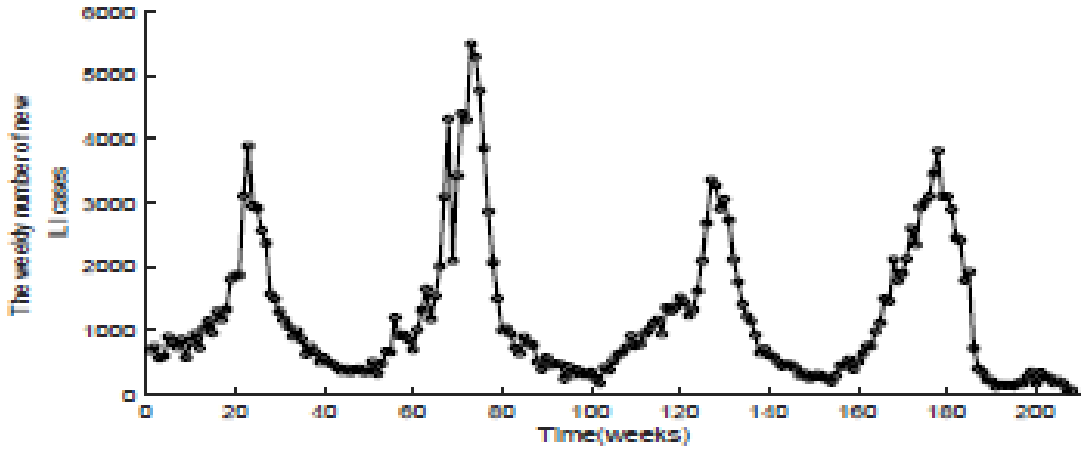

FIGURE 1 The weekly number of new ILI cases in Texas from the 36th week of 2016 to the 35th week of 2020

2 ILI VACCINATION ADAPTIVE-DECISION MODEL WITH PERCEIVED COST

2.1 The adaptive-decision model

Deterministic epidemiological mathematical models based on ordinary differential equations show that there is a threshold for vaccination coverage, below which an epidemic will break out, but if it is exceeded, an epidemic will be controlled.[16,22,24] Let Pn represent the vaccination coverage in the nth year, πc the coverage threshold and $q(Pn)$ the probability of infection in the nth year. Since unvaccinated individuals may be protected from infection due to herd immunity, we assume that $q(Pn)$ decreases linearly with Pn if $Pn < \pi c$, otherwise $q(Pn) = 0$. Individuals who decide to obtain vaccine will evaluate their choices based on whether the ILI is prevalent or not. If the current year's vaccination coverage Pn is equal to or greater than the critical coverage rate πc (ie, $Pn \geq \pi c$), individuals think it is not necessary to be vaccinated next year to avoid infection. Otherwise, if the coverage is lower than the critical coverage rate (ie, $Pn < \pi c$), individuals believe that vaccination is helpful to avoid infection. Individuals who do not get vaccinated evaluate their choices based on whether he/she is infected or not. If infected, he/she thinks that the decision that he/she does not get vaccinated next year is harmful, and vaccination is necessary to avoid infection. In contrast, if uninfected, he/she thinks it is unnecessary to be vaccinated next year. Therefore, we have the following assumptions for the model:

(i) The total number of people changes over time according to birth and death processes.
(ii) Each individual has to make a decision on whether to be vaccinated or not every year, bearing in mind their past vaccination results and experience to decide whether to obtain vaccine each time. These individuals are self-contained and do not discuss their decisions with others. Their main goal is not to become infected without vaccination.
(iii) Individuals obtain vaccine once a year only during a specific period (such as September to October) at the beginning of the influenza epidemic, and the vaccinations are effective for a year.
(iv) The parameter s is used to represent the individual's memory of the vaccination results of the previous year ($0 \leq s < 1$). $s = 0$ indicates that the individual completely ignores the vaccination results of the previous years; and the more the individual clearly remembers the previous vaccination results the larger the value of s.
(v) Let $\chi(I)n(t)$ indicate whether the individual i obtains vaccine at the tth week of the nth year, then $\chi(i)n(t)$ follows a Bernoulli distribution with parameter $w(i)n(t)$ (ie, $\chi(i)n(t) = 1$ indicates vaccination, otherwise $\chi(i)\,n(t) = 0$). $w(i)\,n(t)$ is the probability that individual i obtains vaccine at the tth week of the nth year; $E(i)n(t)$ is individual i's experience with previous vaccination, and $w(i)n(t)$ is determined by $E(i)n(t)$.
(vi) Let $\eta(i)n(t)$ indicate whether the individual i becomes infected at the tth week of the nth year, then $\eta(i)n(t)$ follows a Bernoulli distribution with parameter $q(Pn)$ (ie, $\eta(i)n(t) = 1$ if infection, otherwise $\eta(i)n(t) = 0$).
(vii) $E(i)n(t)$ is updated in the following four cases (as shown in Figure 2):
(a1) If individual i obtains vaccine at the tth week of the nth year and an influenza epidemic did not occur, then the individual believes that it is not necessary to be vaccinated in the next year; that is, if $\chi(i)n(t) = 1$ and $Pn \geq \pi c$, then $E(i)\,n{+}1(t) = sE(i)n(t)$;

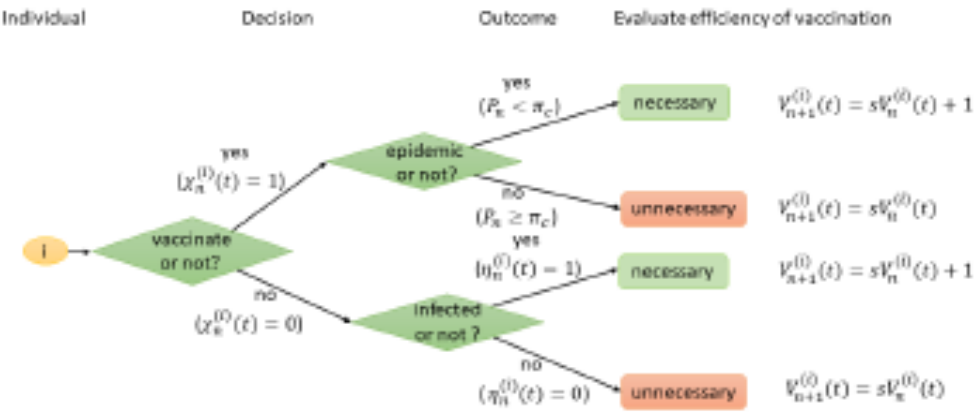

FIGURE 2 A schematic diagram illustrating the decision process of the adaptive-decision model.

(a2) If individual *i* obtains vaccine at the *t*th week of the *n*th year and an influenza epidemic occurred, then the individual believes that it is necessary to be vaccinated in the next year; that is, if $\chi(i)n\ (t) = 1$ and $Pn < \pi c$, then $E(i)n+1(t) = sE(i)n\ (t) + 1$;
(b1) If individual *i* does not obtain vaccine at the *t*th week of the *n*th year and is infected, then the individual believes that it is necessary to be vaccinated in the next year; that is, if $\chi(i)n\ (t) = 0$ and $\eta(i)n\ (t) = 1$, then $E(i)n+1(t) = sE(i)n\ (t) + 1$;
(b2) If individual *i* does not obtain vaccine at the *t*th week of the *n*th year and is not infected, then the individual believes that it is not necessary to be vaccinated in the next year; that is, if $\chi(i)n\ (t) = 0$ and $\eta(i)n\ (t) = 0$, then $E(i)n+1(t) = sE(i)n\ (t)$.
(viii) It is assumed that individuals have adaptability when deciding whether to be vaccinated or not, and the parameter ε is used to describe the adaptability of individuals based on their past vaccination experience ($0 \leq \varepsilon \leq 1$). Therefore, the probability of individuals choosing to be vaccinated in the next year is updated as follows:

$$w_{n+1}^{(i)}(t) = (1-\varepsilon)w_n^{(i)}(t) + \varepsilon V_{n+1}^{(i)}(t)(1-s)/(1-s^{n+1})$$

That is, the probability of vaccination in the next year is given by the updated cumulative vaccination experience. $E(i)\ n+1(t)$ is normalized by division by $1 - sn+1/(1 - s)$ (where $1 - sn+1/(1 - s)$ is the maximum value of $E(i)\ n+1(t)$ in the case that individual *i* benefited in the previous *n* years).

2.2 The adaptive-decision model with vaccination perceived cost

Each individual will consider the perceived cost before vaccination,[25,26] which is related to the actual vaccine cost, and the risks of vaccination side-effects and death caused by vaccination. Therefore, it is assumed that the perceived cost for individual *i* in the *n*th year $r(i)\ n$ caused by vaccination in the *n*th year increases year by year:

$$r_n^{(i)} = a + b * (n-1),$$

where a, b are non-negative constants. The higher the perceived cost, the more reluctant people are to choose vaccination. Therefore, it is assumed that individual i is vaccinated at the tth week of the nth year satisfies

$$\chi_n^{(i)}(t) \sim Bernoulli(w_n^{(i)}(t) * \frac{1}{r_n^{(i)}}).$$

The vaccination coverage at the tth week of the nth year is

$$P_n(t) = \sum_{i=1}^{N} \chi_n^{(i)}(t)/N_n(t),$$

where $Nn(t)$ is the total population at the tth week of the nth year.

The probability of individual i being infected in the nth year is

$$q(P_n) = \begin{cases} q_0[1 - P_n/\pi_c], & if \quad P_n < \pi_c, \\ 0, & if \quad P_n \geq \pi_c. \end{cases}$$

where $P_n = \sum_{t=1}^{T} P_n(t)$, q_0 is the maximum infection probability.

3.1 The construct of the SIRV model

We now incorporate ILI vaccination adaptive-decision with cost into the classical SIR (susceptible-infective-recovery) type epidemiological model.21 We stratify the susceptible ($Sn(t)$), infected ($In(t)$) and recovered ($Rn(t)$) compartments (at the tth week of the nth year) in the classical SIR model, to include the number of ILI vaccinations at the tth week of the nth year as a new variable, denoted by $Vn(t)$. Then $Nn(t) = Sn(t) + In(t) + Rn(t) + Vn(t)$ is the total population at the tth week of the nth year. We assume that the susceptible individuals are infected by infectious individuals at a rate β, and become infectious; recovered individuals are removed at a rate γ from the possibility of infection through immunity; the birth rate of susceptible individuals is Λ; the natural mortality of individuals is μ; the disease-related mortality is negligible.27,28
This leads to the following SIRV model:

$$\begin{cases} \frac{dS_n(t)}{dt} = \Lambda - \beta S_n(t) I_n(t)/N_n(t) - \mu S_n(t) - \delta_n(t) P_n(t) S_n(t), \\ \frac{dI_n(t)}{dt} = \beta S_n(t) I_n(t)/N_n(t) - \gamma I_n(t) - \mu I_n(t), \\ \frac{dR_n(t)}{dt} = \gamma I_n(t) - \mu R_n(t), \\ \frac{dVa_n(t)}{dt} = \delta_n(t) P_n(t) S_n(t) - \mu V a_n(t), \end{cases}$$

$$\delta_n(t) = \begin{cases} 1, & t \in [T_1, T_2] \\ 0, & t \in [T_2 + 1, T_{end}], \end{cases}$$

Here $T1$ and $T2$ are the week of the beginning and the end of ILI vaccination, respectively. For Texas, $T1$, $T2$, Tend are the 36th week, 43rd week at the nth year and the 35th week of the n + 1th year, respectively (as shown in Figure 1).29

3.2 Parameter estimation, model fitting and prediction

Since the models (2-3) combined with the adaptive-decision model in the previous part is a multi-scale system, it is difficult to estimate all unknown parameters of the individual-level model and the population-level model at the same time. Therefore, based on the Reference 21, we fix the unknown parameters as follows: $\pi c = 0.6$, $s = 0.7$, $q0 = 0.8$, $\varepsilon = 1$, $a = 10$, $b = 2$, and then perform uncertainty and sensitivity analyses on the unknown parameters in the next section. Let the initial value of the total population in the nth year be $Nn(0) = 100\,000$ ($n = 1, 2, 3$), and the initial values of infected are $I1(0) = 487$, $I2(0) = 525$, $I3(0) = 451$ (obtained directly from the data), and the initial values of the number of recovered are $Rn(0) = 0$ ($n = 1, 2, 3$), and the initial values of the vaccinated population are $Vn(0) = 0$ ($n = 1, 2, 3$), so the initial value of susceptibles is $Sn(0) = Nn(0) - In(0) - Rn(0) - Vn(0)$ ($n = 1, 2, 3$).

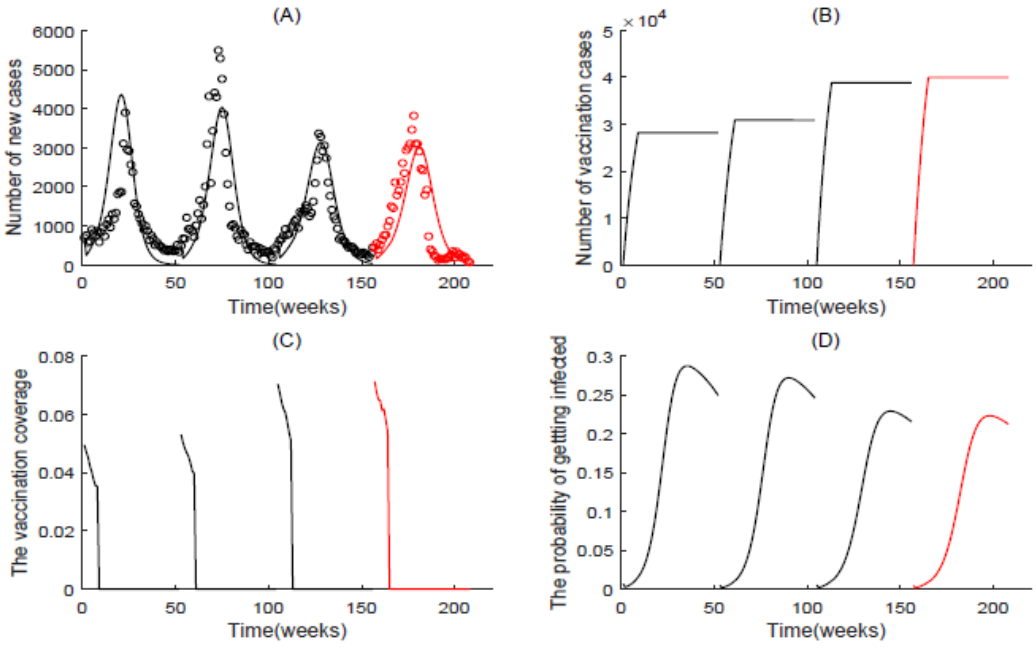

FIGURE 3 Model fitting, simulation, and prediction. (A) Number of new ILI cases; (B) cumulative number of vaccinations; (C) and (D) vaccination coverage and the proportion of infections (the proportion of new infections in the susceptible population). The black circles and curve represent the observed data and simulation for Texas from the 36th week of 2016 to the 35th week of 2019, respectively. The red circles and curve represent the observed data and prediction for Texas from the 36th week of 2019 to the 35th week of 2020, respectively.

By fitting data on the number of new ILI cases from the 36th week of 2016 to the 35th week of 2019, we obtain other unknown parameter values in the population model (2). To do so, we utilized the nonlinear least-square (NLES) method inMATLAB to fit the aforementioned real data sets, which correspond to themodel solution time series $\beta Sn(t)In(t)/Nn(t)$. The results are shown in Figure 3A (the black curve). Estimated values of unknown parameters are $\beta = 0.3505$, $\gamma = 0.0066$, $\Lambda = 0.9997$, $\mu = 1.0562 * 10-5$. Simulation results of the cumulated number of vaccinated, vaccination coverage and infection proportion (proportion of newly infected people in the susceptible population), are shown in Figure 3B-D (the black curve). From Figure 3 it can be obtained that from 2016 to 2019, with the increase of vaccination coverage, the number of vaccinations increased, but the probability of infection and the number of infected individuals decreased. In addition, by adding up the simulated vaccination coverage for the first 8 weeks, the simulated accumulated vaccination coverage in the first three years of the study period is 33.25%, 36.74%, 48.66%, that is, the coverage rate could not reach the critical coverage rate of ILI vaccination through voluntary vaccination ($\pi c = 0.6$).

At the same time, we also predict the number of new ILI cases, the cumulated number of vaccinated, vaccination coverage, and infection probability in Texas from the 36thweek of 2019 to the 35thweek of 2020, as shown in Figure 3 (the red curve). Error bars are used to describe the relative error between the simulated value/predicted value and the observed data ((simulated value - observed data)/observed data). We repeat the prediction 1000 times at each time point, calculate the mean value and 95% confidence interval of relative error at each time point, as shown in Figure A1A. Combined with the observed data on the number of new ILI cases (the red circles), we found that the model predicted the number of new ILI cases well, but the cumulated vaccination coverage was 51.06%, which still could not reach the critical coverage rate for ILI vaccination.

3.3 Uncertainty and sensitivity analyses for parameters of the adaptive-decision model

To study the effect of vaccination parameters on the number of new ILI cases, we used sensitivity analysis to explore the impact of memory of previous year's vaccination results s, the critical coverage rate πc, the maximum infection probability $q0$, the perceived cost of vaccination a (ie, $r(i)$ n), individual adaptability based on their past vaccination experience ε on ILI transmission and vaccination coverage from the 36th week of 2019 to the 35th week of 2020. Therefore, for different vaccination parameters, we used a wide range of parameter values (ie, $s \in [0, 1)$, $\pi c \in [0.4, 0.8]$, $q0 \in [0, 1]$, $a \in [6, 14]$, $\varepsilon \in [0, 1]$).

The effects of individual's memory s of the vaccination results of the previous year on the simulated number of new ILI cases, accumulated number of vaccinations, vaccination coverage and the proportion of infections are shown in Figure 4. From the figure we can see that the greater the individual's memory of the vaccination results of the previous year, the greater the simulated vaccination coverage, the more vaccinated people, the lower the proportion of infection and the smaller the number of new ILI cases. In particular, if it is almost fully remembered (ie, $s = 0.99$), the number of simulated new ILI cases will reach the maximum by the 27th week of 2020, reduced by 19.30%. The accumulated vaccination coverage simulated in the fourth year was 63.45%, reaching the critical coverage rate of ILI

vaccination ($\pi c = 0.6$). If completely forgotten (ie, $s = 0$), the number of simulated new ILI cases will reach the maximum by week 22 of 2020, increased by 75.33%. Thus, if an individual has no memory of past vaccination experience, he/she will only consider his own interests. The main goal of an individual is not to be infected without vaccination, so he/she is likely to choose not to be vaccinated, resulting in an increase in the number infected.

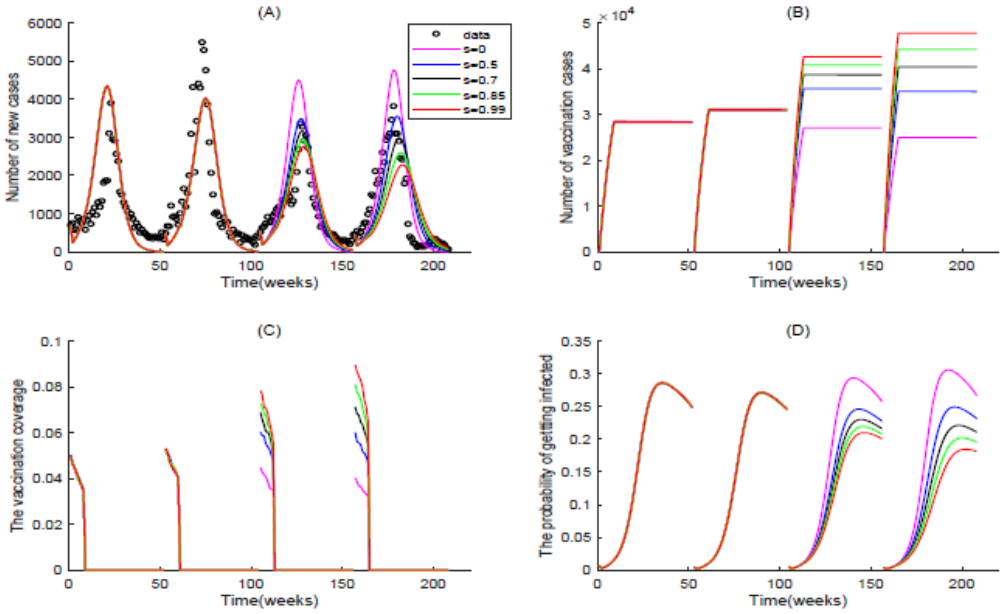

FIGURE 4 Sensitivity analysis for parameter *s*. (A) Number of new ILI cases; (B) cumulative number of vaccinations; (C) and (D) vaccination coverage and the proportion of infections. Magenta ( ), blue ( ), black ( ), green ( ), and red ( ) represent the simulation and prediction of number of new ILI cases, the cumulative number of vaccinations, vaccination coverage and the proportion of infections for (A-D) when the parameter *s* takes 0, 0.5, 0.7, 0.85, and 0.99 (the baseline $s = 0.7$), respectively.

Figure 5A,B show the variation in the simulated number of new ILI cases and vaccination coverage with the critical coverage rate πc. It follows from Figure 5A,B that the critical coverage rate πc has little effect on the number of new ILI cases and vaccination coverage. The effects of the parameter $q0$ on the ILI infection and vaccination coverage are shown in Figure 5C,D. It implies that, with the increasing of the maximum infection probability $q0$, the vaccination coverage increased, and the simulated number of new ILI cases decreased significantly in the second, third and fourth years, while the simulated vaccination coverage and the simulated number of new ILI cases in the first year did not change. As the maximum infection probability increases, individuals may make decisions through the adaptive-decision model and think that vaccination is conducive to avoiding infection and take vaccination measures when vaccinating takes place in the next year. Therefore, the vaccination coverage increases and the simulated number of new ILI cases decreases significantly in the second, third and fourth years. In particular, when $q0$ is reduced to 0.1, and the simulated number of new ILI cases will increase to 6952 by the 20th week of 2020; and when $q0$ is increased to 1, the simulated number of new ILI cases is reduced to 1925.

As mentioned before, we chose a wide range of parameter values for a (and of course for $r(i)n$) to show the significance of the perceived cost incurred by vaccination on the simulated number of new ILI cases and vaccination coverage, as shown in Figure 6A,B. Obviously, as the perceived cost a increases, the annual simulated vaccination coverage decreases, the number of new ILI cases increases significantly, and the level of the impact decreases year by year. That is because with the increasing of vaccination perceived cost, individuals will only consider their own interests as their main goal is not to be infected without vaccination. Therefore, they are likely to choose not to be vaccinated, so the number of infected will increase.

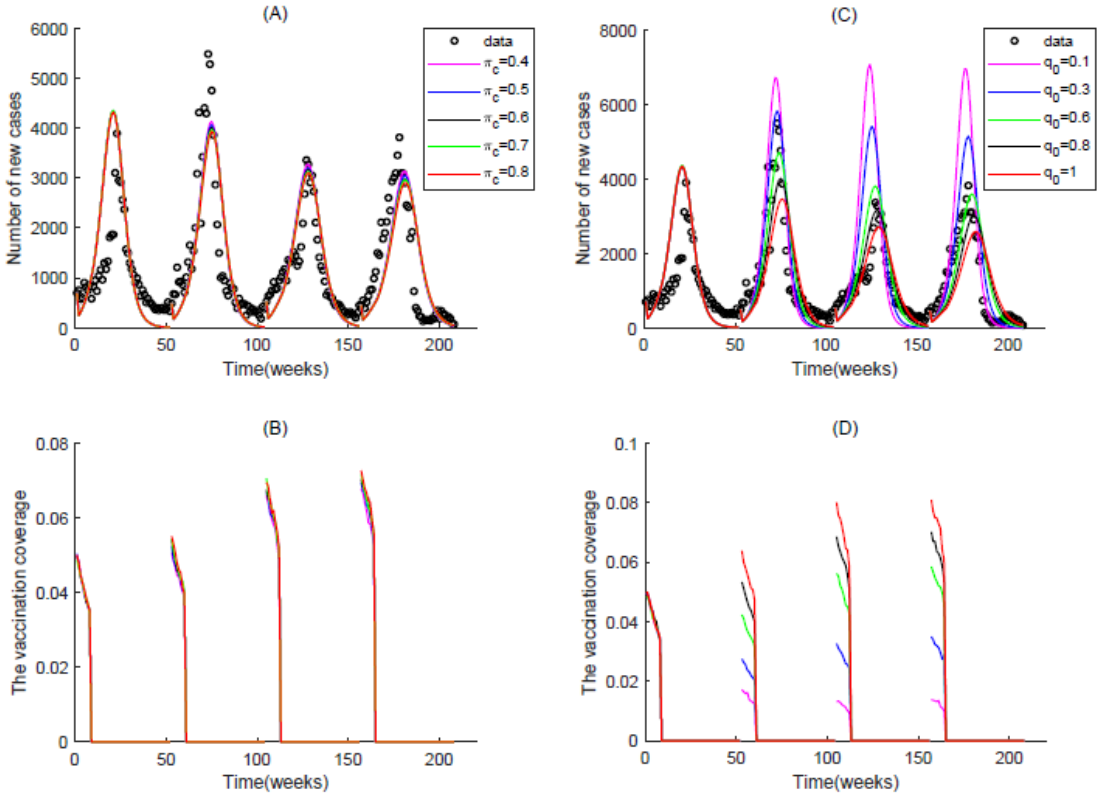

FIGURE 5 Sensitivity analysis for parameters π_c and q_0. (A) The predicted number of new ILI cases and (B) vaccination coverage when the parameter π_c takes values of 0.4, 0.5, 0.6, 0.7, 0.8 (the baseline $\pi_c = 0.6$), (magenta(—), blue(—), black(—), green(—) and red(—), respectively); (C) The predicted of number of new ILI cases and (D) the vaccination coverage for when the parameter q_0 takes values of 0.1, 0.3, 0.6, 0.8, 1 (the baseline $q_0 = 0.8$), (magenta(—), blue(—), green(—), black(—) and red(—), respectively).

The impact of individual adaptability based on their past vaccination experience ε on the ILI epidemic is shown in Figure 6C,D. It indicates that the greater the value of the parameter ε, the greater the simulated vaccine coverage is, and the less the simulated number of new ILI cases. In particular, the simulated number of new ILI cases will reach the maximum at 2980 by the 25th week of 2020 if individuals' decisions were entirely based on the past vaccination situation (ie, $\varepsilon = 1$); the maximum number of simulated new cases will be 5429 by week 22 of 2020 if individuals rely entirely on experience (ie, $\varepsilon = 0$). Since greater adaptability depends on past vaccination experience, an individual will make a rational

decision based on the past vaccination situation, and then choose to be vaccinated, so as to reduce the number infected. Noting that error bars for the results in Figures 4–6 can be found in Figure A1B-F.

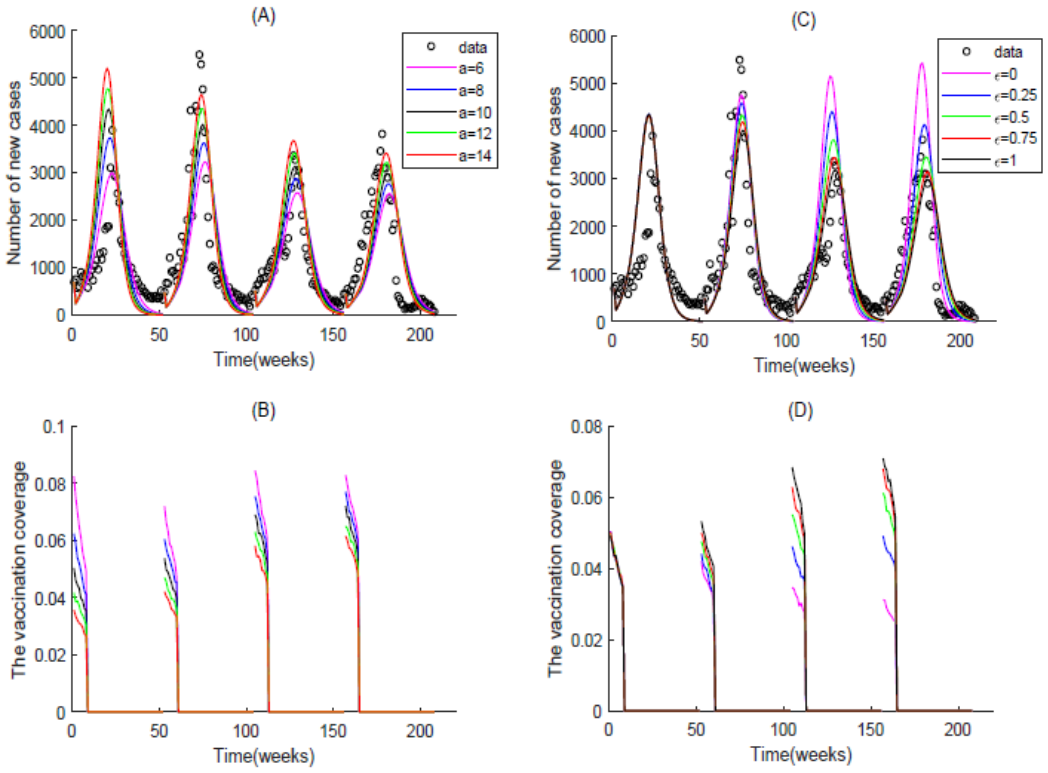

FIGURE 6 Sensitivity analysis for parameters a and ε. (A) The predicted number of new ILI cases and (B) the vaccination coverage when the parameter a takes values of 6, 8, 10, 12, 14 (the baseline $a = 10$) (magenta(—), blue(—), black(—), green(—) and red(—) respectively); (C) The predicted number of new ILI cases and (D) the vaccination coverage when the parameter ε takes values of 0, 0.25, 0.5, 0.75, 1 (the baseline $\varepsilon = 1$)(magenta(—), blue(—), green(—), red(—) and black(—), for (C-D) respectively).

4 DISCUSSION

The decision of an individual to be vaccinated or not is affected by the perceived risk of ILI infection and the perceived cost and risks of vaccination. In addition, due to herd immunity and the probability of individual infection depending on the number of vaccinations, there are also interactive strategies between individuals when individuals decide about vaccination. Therefore, when the annual ILI vaccination coverage is not ideal, we need to better understand the interaction between vaccination coverage, individual vaccination behavior and the development of ILI dynamics. This information will help to improve influenza vaccination coverage through intervention measures and provide qualitative and quantitative decision-making as a basis for better predictions and evaluations of the impact of vaccination strategies on ILI epidemics. To understand this potentially complex interaction and whether vaccination coverage is likely to reach the critical coverage rate, we constructed an adaptive decision-making model embedded with human cognition and behavior at the individual level and simulated individual vaccination decisions. The adaptive-decision model was coupled with an SIRV model (including ILI vaccination dynamics) at the

population level, and the interaction between individual-level decisions and an ILI epidemic was explored.

First, considering ILI vaccination willingness and perceived cost, we established an adaptive-decision model at the individual level, and simulated the interaction between ILI vaccination decision and an ILI epidemic by inductive reasoning. The adaptive-decision model introduces the idea that the tendency of individuals to obtain vaccination depends on their past vaccination experience, infection experience and whether there is an ILI epidemic or not. Overall vaccination coverage affects whether unvaccinated individuals are infected and the conditions that determine the ILI prevalence. The total vaccination coverage in a particular year will change the probability of individuals seeking vaccination in the next year, which in turn determines the total vaccination coverage in the next year.

Second, to explore the interaction between individual-level decisions and an ILI epidemic, the ILI vaccination adaptive-decision with cost was incorporated into the classical SIR type epidemiological model and the number of ILI vaccinations was included as a new variable in this study. By uncertainty and sensitivity analyses, Figures 4–6 indicate that, if vaccination is voluntary, but the epidemic prevention and control authority takes measures such as guiding people to improve their memory of past vaccination experience (s), publishing the annual vaccination situation to the public (ε), adjusting relevant measures and appropriately reducing the perceived cost of vaccination (α), the vaccination coverage will increase in the second, third and fourth year, so that the ILI epidemic can be effectively controlled. In particular, if individuals almost fully remembered their past vaccination experience (ie, s = 0.99), the simulated accumulated vaccination coverage is 63.45% in the fourth year, reaching the critical coverage rate of ILI vaccination ($\pi c = 0.6$), which is inconsistent with the results of Vardavas et al.[21,22] The main reasons are as follows: first, according to the actual situation, our model divides the annual influenza period into vaccination season (36th-43rd weeks) and non-vaccination season (44th-35th weeks in the next year). During the vaccination season, individuals can decide whether to be vaccinated or not every week, which is closer to the actual situation and could more accurately describe the dynamic changes of vaccination rates. Besides, our model has greater biological complexity than previous models, since it is necessary to consider individuals' vaccination perceived cost when modeling annual ILI vaccination decisions, and vaccination perceived cost may also have an impact on vaccination rates.

Our research results are almost consistent with those of Ghaffarzadegan et al, which were based upon a SEIRb model with behaviorally realistic representations of human decision-making create feedback mechanisms, have shown that endogenous behavioral responses to perceived risk points to a significant opportunity for enhancing predictive models and designing more effective policies/interventions during epidemics.[20] We further confirm that the importance of human decision-making create feedback mechanisms by combining an adaptive-decision model at the individual level with a SIRV model at the population level based on actual ILI data.

In addition, the number of ILI cases may be affected by the COVID-19 epidemic.[30,31] In accordance with the results of Ceccarelli et al, among 190 COVID-19 patients, 63.6% had a

recent ILI.30 Therefore, we collected COVID-19 data in Texas from the 1st week of 2020 to the 48th week of 2021 from the systems Science and Engineering (CSSE) at Johns Hopkins University,32 and then compared ILI data with COVID-19 data during this period, as shown in Figure A2. We also obtained the weekly number of new and cumulated ILI cases in Texas from the 1st week of 2011 to the 48th week of 2021, as shown in Figure A3. The data imply that the COVID-19 epidemic had an impact on the number of reported ILI cases. The possible reasons are as follows: (i) Medical resources are scarce. Since the COVID-19 epidemic appeared suddenly, the disease is highly infectious and with high mortality rates, most medical resources are used for the treatment of COVID-19 patients, which leads to medical resources for ILI patients becoming very scarce, and they could not go to the hospital; (ii) The implementation of strong policies, such as home quarantine, contacts being quarantined for 14 days and restrictions on population mobility. On the one hand, the ILI contact transmission rate is reduced; on the other hand, ILI patients have no chance to go to hospital; (iii) Concerns of ILI patients. Since the clinical symptoms of COVID-19 patients are very similar to those of ILI patients, such as fever, cough and muscle pain, some ILI patients are unwilling to go to the hospital due to worries that they could become infected with COVID-19; (iv) Individual responses to COVID-19 control measures, such as wearing masks, washing hands frequently, and avoiding going to public places, which reduce the ILI contact transmission rate and thus reduce the incidence rate.

Further, our models could not be directly applied to study the impact of COVID-19 vaccine on the epidemic. The possible reasons for this are as follows: (i) compared with influenza virus, the COVID-19 strain mutates faster and the duration of vaccine effectiveness is shorter; (ii) the assumptions of COVID-19 models are inconsistent with some of our model assumptions. For example, it is assumed that it is 100% effective within one year of ILI vaccination and will not be infected by influenza vaccination virus again, while the COVID-19 vaccine is only effective for about six months or less, and it is not 100% effective; influenza epidemics have been occurring for many years, and people have accumulated some experience on whether to vaccinate against influenza, and thus they can judge whether to vaccinate in that year by whether they were infected during epidemics in the past; but for the emerging infectious disease COVID-19, people almost know nothing about the vaccine. Therefore, we need to further improve our model to explore the complex interaction between individuals' decision-making and the COVID-19 epidemic, which will be discussed in our further work.

Our study has the following limitations. First, when constructing an adaptive decision-making model embedded with human cognition and behavior at the individual level, we assumed that individuals are self-interested and will not communicate their decisions with each other. If the assumptions are not met, the results may be different. Second, we took the roles of vaccination coverage, memory, adaptation, and vaccination perceived cost (vaccine cost, vaccine side effects, and deaths caused by vaccination) into account regarding vaccination decision-making, but there may be many other factors that will also affect individuals' vaccination decision-making, such as incentive measures.33 Besides, we assume that the efficiency of ILI vaccine is completely effective within one year.34 In fact, since the efficiency of ILI vaccine is relatively low, which will be embedded into our adaptive decision-making model as a proportion coefficient to better describe the actual problem in the near future.

5 CONCLUSION

This study presents a novel methodology by establishing an adaptive decision-making model embedded with human cognition and behavior at the individual level coupled with a dynamic SIRV model. We showed that combining an individual-level model with a population-level model is suitable for analyzing the interaction between vaccination decisions and an ILI epidemic. The results show that the ILI vaccination coverage could not reach the critical coverage rate through voluntary vaccination, based on observed data linked to media reports. However, the critical coverage rate of ILI vaccination could be reached in the fourth year of an epidemic by improving individuals' memory of past vaccination experience. All these results confirmed that individual memory of past vaccination experience, past vaccination proportions and vaccination perceived costs are important factors determining whether an ILI epidemic can be effectively controlled within three years. Therefore, for mitigating an ILI epidemic, health authorities should guide people to improve their memory of past vaccination experience through media publicity and reports, publish annual vaccination proportions and adjust relevant measures to appropriately reduce the perceived cost of vaccination, which are critical for the control of ILI epidemics.

AUTHOR CONTRIBUTIONS

Qinling Yan: Data curation; conceptualization; formal analysis; methodology; software; writing - original draft; review and editing. **Robert A. Cheke**: Writing - review and editing. **Sanyi Tang**: Conceptualization, writing - review and editing.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interests.

DATA AVAILABILITY STATEMENT

All data can be obtained from Texas Department of State Health Services website in this study.

ORCID

Qinling Yan https://orcid.org/0000-0002-0927-9197

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