A Demand Model of Influenza Vaccine in a Heterogeneous Population

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ABSTRACT

In this paper, we develop a demand model for influenza vaccine. When the vaccination is not compulsory, exploration of demand mechanism and total demand anticipation, help the governments better organize their efforts and adopt more effective measures to contain influenza outbreak in advance of influenza season. In this research, the population is divided into two classes. Pre 65 years old class and over 65-year-old class. Current influenza vaccines have different effectiveness on each age class. We build a game theoretic demand model for each age class based on utilities of individuals. Utilities of individuals is a function of the vaccine effectiveness, price, chance of getting infected, estimated cost of infection and a random element specific to each individual. Since getting vaccinated for an individual exerts positive externalities on the others, the decision of individuals is not independent of each other.

KEYWORDS: Demand Model, Influenza Vaccine, Heterogeneous Population.

1. INTRODUCTION

Severe infectious diseases have always been a threat to human society from both economic and non economic perspectives. Influenza is one of these diseases capable of causing pandemic. Worldwide, annual influenza epidemics result in about three to five million cases of severe illness, and about 250,000 to 500,000 deaths. Most deaths associated with influenza in industrialized countries occur among people age 65 or older (Who, 2009). Influenza virus has a property which distinguishes it from most other infectious diseases. Its virus might change (technically mutates) from year to year. Due to this, vaccine formulations should be changed each year to include probable strains of influenza viruses which circulate in the upcoming influenza season. Governments in most countries use a national vaccination program to prevent influenza epidemics or at least mitigate its consequences. The influenza vaccine production cycle is about 7 to 8 month long. This imposes the need for advance anticipation of influenza demand well before influenza season. There is little literature on influenza demand models. Hence, we outline literature which developed demand models for vaccines generally.

The papers are categorized into econometric (or empirical) models and game-theoretic (or theoretical). Before game theory could play a rule, we should make an assumption about individuals being aware of herd immunity¹. The herd immunity assumption is the fundamental assumption in all papers which develop demand models using game theory.

Brito et al. (1991) is the seminal work on developing a game-theoretic model for equilibrium fraction of vaccination within a population with homogeneous income but heterogeneous on their cost of vaccination². Boulier et al. (2007) used different utility function to quantify marginal social benefit of vaccination and magnitude of vaccination externalities. They also assumed a totally homogeneous population. Bauch and Earn (2004) used game theory to model decision making of parents on whether or not vaccinate their newborns against childhood vaccine-preventable diseases. Bauch (2005) assumed there is a perceived risk of adverse vaccination effect (death, secondary infections...). They found a convergently stable Nash equilibrium (CSNE) for their model. Bauch (2005) used different approach than (Bauch and Earn, 2004) using differential games. He assumed non-vaccinator parents with a time varying rate relatively imitate the vaccination behaviour of parents who vaccinated their children. Montano (1986) and Mullahy (1999) are the only papers we are aware of which conducted an extensive empirical survey on individual behaviour on vaccination against influenza and its determinants.

Montano (1986) used a random sample of 439 patients among high risk patients for flu complications, registered at the Seattle VA Medical Center’s Medical Comprehensive Care Unit (MCCU) clinic. Mullahy (1999) is especially unique due to its national coverage. In his work, it is shown that immunization propensity follows expected patterns by age, health status, race, household structure, income and insurance. Geoffard and

¹ herd immunity means the immunity conferred to an unvaccinated individual through vaccination of others. The higher the proportion of individuals who are vaccinated, the lower the likelihood that a susceptible person will come into contact with an infectious individual thereby the higher the immunity
² we mean by homogeneous income population, a population comprised of individuals with same marginal utility of income

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Philipson (1997) developed a prevalence-price dependent demand and investigated its implication for disease eradication.

d’Onofrio and Manfredi (2010) investigated the situation where the driving force of the vaccine demand is given by the time changes in the perceived risk of suffering a vaccine side effect on the contrary to demand driven by the disease incidence or probability of infection. They especially presented their model for the time when the perceived risk of serious disease is steadily low.

2 Notations

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
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<tbody>
<tr>
<td>$P_a$</td>
<td>Administration cost</td>
</tr>
<tr>
<td>$v_y$</td>
<td>Fraction of age group of the young (&lt;65) vaccinated</td>
</tr>
<tr>
<td>$v_e$</td>
<td>Fraction of age group of the elderly(≥65) vaccinated</td>
</tr>
<tr>
<td>$\lambda_r$</td>
<td>Fraction of the young in the population</td>
</tr>
<tr>
<td>$\lambda_e$</td>
<td>Fraction of the elderly in the population</td>
</tr>
<tr>
<td>$m_y$</td>
<td>Vaccine efficacy for young individuals(0% to 100%)</td>
</tr>
<tr>
<td>$m_e$</td>
<td>Vaccine efficacy for elderly individuals</td>
</tr>
<tr>
<td>$k_y$</td>
<td>Mean cost of infection for a young person</td>
</tr>
<tr>
<td>$k_e$</td>
<td>Mean cost of infection for an elderly person</td>
</tr>
<tr>
<td>$\theta_y$</td>
<td>A young person’s type in terms of time, searching cost, pain being incurred due to vaccination</td>
</tr>
<tr>
<td>$\theta_e$</td>
<td>An elderly person’s type in terms of time, searching cost, pain being incurred due to vaccination</td>
</tr>
<tr>
<td>$S(t)$</td>
<td>The number of susceptible population</td>
</tr>
<tr>
<td>$I(t)$</td>
<td>The number of infected population at time t</td>
</tr>
<tr>
<td>$R(t)$</td>
<td>The number of infected population at time t</td>
</tr>
<tr>
<td>$C$</td>
<td>The variable cost of a influenza vaccine dose(whether contaminated or approved)</td>
</tr>
<tr>
<td>$P$</td>
<td>Price of one dose of influenza vaccine</td>
</tr>
<tr>
<td>$Y_i$</td>
<td>Random yield of vaccine production at factory i</td>
</tr>
<tr>
<td>$Q$</td>
<td>Total realized production quantity ($Q = \sum_{i \in \mathbb{I}} q_i$)</td>
</tr>
<tr>
<td>$F_p(\cdot)$</td>
<td>Cumulative distribution function of $\theta_p$</td>
</tr>
<tr>
<td>$F_{\theta}(\cdot)$</td>
<td>Cumulative distribution function of $\theta_y$</td>
</tr>
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</table>

Decision Variables

<table>
<thead>
<tr>
<th>$q_i$</th>
<th>Target production quantity of factory i</th>
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</thead>
<tbody>
<tr>
<td>$\bar{q}_i$</td>
<td>The realized production quantity of factory i ($\bar{q}_i = y_i q_i$)</td>
</tr>
<tr>
<td>$x_i$</td>
<td>The quantity which government purchases from manufacturer i before the target production quantity is set</td>
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</table>

3 Demand model

In this section first, we first outline Boulier et al. (2007) model and afterwards will present our extensions. In their paper Boulier et al. (2007) assumed

1. Individuals are identical and risk neutral.
2. Individuals are rational.
3. The side effects of vaccination are very rare and negligible.
4. All information is common

Upon using SIR model to model the dynamics of influenza disease, the probability of an individual being ever infected is given by $P(v)$.

$$P(v) = \frac{r_0 - i_0}{s_0} = \frac{r_0 - i_0}{1 - m_v - i_0}$$

$v$ is the fraction vaccinated i.e. $V/N$. The numerator shows the final number of infections excluding who got flu before completion of vaccination program (it means before time $t=0$). The denominator denote the initial susceptible individuals (the number of susceptibles at time $t=0$) every rational decision maker purchases the vaccine if the mean cost of inoculation is less than the mean cost of no inoculation. The cost of inoculation is $P+(1-m)vP(v)$ and the mean cost of no inoculation is $P(v)k$ given vaccination coverage is $v$ percent at the time of decision making.

Therefore, if the benefit of vaccination, $P(v)-(P+(1-m)vP(v))=mP(v)k-p$, is greater than zero, an individual vaccinates. Boulier et al. (2007) call $mP(v)k-p$ the marginal private benefit of a vaccination. The marginal vaccinator is someone who is indifferent between vaccination and no vaccination. It means $mP(v)k-p=0$. it is

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3 refer to appendix A for a short introduction
easily proved that at this level of coverage people are in equilibrium and no one is willing to change his decision. It is also the Nash level of vaccination.

To reach the equilibrium characterized by the former demand model, it is not required, each individual know the exact parameters’ values (the exact marginal profit of vaccination). It only suffices to know the marginal profit of vaccination is positive or negative at the moment of making decision to vaccinate or not.

In our first extension in section 3.1 we will relax identity assumption and in the second extension in section 3.2 the other assumptions will be partly relaxed.

3.1 Simple Demand Model

In this section we relax the assumption of homogeneous population and divide the population into two groups. The young group includes individuals less than 65 years old and the elderly group includes the 65 years old and above. It seems realistic to think two groups have different characteristics. We still assume as the base assumption in simple SIR model, individuals have the same effect on prevalence of disease. In other words, the contact number of two groups is equal within and between them again. This assumption could also be readily relaxed but we leave it to the future researches. In that case the probability of infection would change for two groups.

The probability of infection given the uptake levels of the young \( v_y \) and the elderly \( v_e \), is

\[
p(v_y, v_e) = \frac{r - i_0}{1 - m_e d_y v_y - m_e d_e v_e - i_0}
\]

Here, the marginal benefit of vaccination for an elderly individual and a young individual are

\[
m_e d_y (v_y, v_e) k_e - p \quad \text{and} \quad m_e d_y (v_y, v_e) k_y - p \quad \text{respectively.}
\]

Without loss of generality, it is assumed

\[ m_e k_e > m_e k_y \]

Assumption 1

If it holds, it tells us that the marginal benefit of vaccination for an unvaccinated elderly individual, i.e. \( m_e d_y (v_y, v_e) k_e - p \), is greater than the marginal benefit of vaccination for an unvaccinated young individual, i.e. \( m_e d_y (v_y, v_e) k_y - p \), at the current level of vaccine uptake taken by population. This assumption simplifies our analysis, but it could simply be relaxed by interchanging the indices. Let \( \Pi_y = \frac{p}{m_y k_y} \) and \( \Pi_e = \frac{p}{m_e k_e} \).

Assumption 2

\[ P_e \leq P(0,0) \]

If this assumption does not hold in the equilibrium, no one is vaccinated. Because the marginal benefit of vaccination would be negative for all.

Theorem 1

Let \( v_y^* \) and \( v_e^* \) denote equilibrium fractions of young and elderly population who are vaccinated,

1) if \( P(0,1) \geq \Pi_y \) then \( v_e^* = 1 \) and \( v_y^* = 0 \) and \( v_e^* \) is the unique root of equation \( P(v_y^*, v_e^*) = \Pi_e \)

2) else if \( \Pi_e \leq P(0,1) \leq \Pi_y \) then \( v_y^* = 0 \) and \( v_e^* = 1 \) is the unique root of equation \( P(v_y^*, v_e^*) = \Pi_e \)

3) otherwise \( v_y^* = 0 \) and \( v_e^* = 1 \)

proof Case 1: in the indicated point \( (v_y^*, v_e^*) \) the marginal benefit of vaccination for an un- vaccinated young individual is \( m_y k_y (P(v_y^*, v_e^*) - \Pi_y) \) which is zero. The marginal benefit of no vaccination for a vaccinated young individual is \( m_y k_y (P_e - P(v_y^*, v_e^*)) \) which is zero. The marginal benefit of no vaccination for a vaccinated elderly individual is \( m_e k_e (\Pi_e - P(v_y^*, v_e^*)) \) which is negative. The marginal benefit of vaccination for an unvaccinated elderly individual is \( m_e k_e (P(v_y^*, v_e^*) - \Pi_e) \) which is positive, but there is no unvaccinated elderly individual left(Because \( v_e^* = 1 \) ) Therefore, \( (v_y^*, v_e^*) \) is equilibrium. Therefore, no one can simply improve its utility simply by changing his decision. Moreover, it is unique. Proof of uniqueness is straightforward, it is sufficient to pick another point(denote it by \( (v_y^*, v_e^*) \) and show that at least, one individual in one of four groups(the unvaccinated young, the vaccinated elderly, the unvaccinated young, the vaccinated young) will be better off if changes his decision. The proof of uniqueness for case 1 and proof of other cases are simple and likewise, we leave it to the interested reader.

3.1.1 Demand dynamics

To contrary to the model of Boulier et al. (2007) here the equilibrium is not globally stable in general. To show this, consider when case 3 of theorem 1 is equilibrium. At the beginning no one is vaccinated. Consider a
young individual; the marginal benefit of vaccination for him is \( m_{y}k_{y}P(0, \theta) - P_{y} \) which is clearly positive regarding assumptions 1 and 2 hold. Hence, if some of young individuals make decision before the others and get vaccinated, the equilibrium will never be reached. The only way to revive the equilibrium point is to assume who have higher marginal benefit of vaccination get vaccinated sooner. In this case, it is clear that, the level of vaccination will reach the Nash equilibrium eventually. For other cases also, this assumption guarantee reaching Nash equilibrium with the same argument made before.

3.2 Extended Demand Model

The demand model of section 3.1 was too simplistic although insightful. In real world there are a lot more criteria affecting the final vaccination decision. Among them, the most important are lost time(time cut from other activities due to vaccination like leisure time, work time), pain, facilitating items(familiar procedure, closeness to a healthcare center, social influences, family physician’s recommendation, perceived side effects, level of disease prevalence in the previous season, risk attitudes. Moreover, there are always biases in measuring the correct value of quantifiable criteria by individuals. Moreover, each criterion is differently valued for different individuals. Hence, it is plausible to assume the value of each criterion is random. We model the aggregate effect of these measures with a random variable. We assume, the aforementioned measures, have additive effect on overall utility of vaccinating over not vaccinating(marginal benefit of vaccination). The aggregate effect is denoted by \( \theta_{y} \) for the young individuals and \( \theta_{e} \) for the elderly individuals. Central limit theorem is the justification to consider \( \theta_{y} \) and \( \theta_{e} \) are normally distributed. In this model the probability of a susceptible individual being ever-infected is shown by

\[
p(v_{y}, v_{e}) = \frac{r - i_{0}}{s_{0}} = \frac{r - i_{0}}{1 - m_{y}\lambda_{y}v_{y} - m_{e}\lambda_{e}v_{e} - i_{0}}
\]

**Assumption 2** Cumulative density functions \( F_{y}(\cdot) \) and \( F_{e}(\cdot) \) are both differentiable in \( R \)

**Theorem 2** In the equilibrium, if a young individual with \( \theta_{y} = \theta_{y}^{1} \) chooses to be vaccinated(i.e. his marginal benefit of vaccination is positive) then it is not possible, another young individual with \( \theta_{y} = \theta_{y}^{2} \) and \( \theta_{y}^{2} < \theta_{y}^{1} \) chooses not to be vaccinated. Likewise, this is true for every type \( \theta_{y} \) and \( \theta_{y}^{1} \) elderly individuals.

**Proof** Assume this would happen. Because type \( \theta_{y}^{1} \) individual chooses to be vaccinated, then \( m_{y}P(v_{y}, v_{e}^{*})k_{y} - \theta_{y}^{1} > p \) otherwise one could improves his utility by changing decision to not being vaccinated. Therefore from \( \theta_{y}^{2} < \theta_{y}^{1} \), we have

\[
m_{y}P(v_{y}^{*}, v_{e}^{*})k_{y} - \theta_{y}^{2} > m_{y}P(v_{y}^{*}, v_{e}^{*})k_{y} - \theta_{y}^{1} > p
\]

Therefore, type \( \theta_{y}^{2} \) individual also should have chosen to be vaccinated otherwise this is a contradiction to being in equilibrium. \( \Box \)

**Theorem 3** In equilibrium, every young person with \( \theta_{y} \leq \theta_{y}^{*} \) and every elderly person with \( \theta_{e} \leq \theta_{e}^{*} \) is vaccinated. Where \( \theta_{y}^{*} \) and \( \theta_{e}^{*} \) and \( r^{*} \) constitute the unique solution of the following system

\[
m_{y}P(F(\theta_{y}^{*}), F(\theta_{e}^{*}))k_{y} = p + \theta_{y}^{*} \quad (1)
\]

\[
m_{e}P(F(\theta_{e}^{*}), F(\theta_{e}^{*}))k_{e} = p + \theta_{e}^{*} \quad (2)
\]

\[
1 - m_{y}\lambda_{y}F(\theta_{y}^{*}) - m_{e}\lambda_{e}F(\theta_{e}^{*}) - (1 - m_{y}\lambda_{y}F(\theta_{y}^{*}) - m_{e}\lambda_{e}F(\theta_{e}^{*}) - i_{0})e^{-r^{*}} - r^{*} = 0 \quad (3)
\]

\[
r^{*} \in [i_{0}, 1], \theta_{y}^{*} \geq 0, \theta_{e}^{*} \geq 0 \quad (4)
\]

**Proof** We rewrite 1 and 2 as below

\[
p(F(\theta_{y}^{*}), F(\theta_{e}^{*}), r^{*}) = \frac{p + \theta_{y}^{*}}{m_{y}k_{y}}
\]

\[
p(F(\theta_{e}^{*}), F(\theta_{e}^{*}), r^{*}) = \frac{p + \theta_{e}^{*}}{m_{e}k_{e}}
\]

Equating the right hand sides of the above equations gives

\[
\theta_{y}^{*} = \frac{m_{y}k_{y}}{m_{e}k_{e}}\theta_{e}^{*} + \frac{m_{y}k_{y}}{m_{e}k_{e}}p - p
\]

Let \( f(\theta_{y}) = 1 - m_{y}\lambda_{y}F(\theta_{y}) - m_{e}\lambda_{e}F(\theta_{e}) - i_{0} \). As it is clear, \( f(\theta_{y}^{*}) \) is the initial fraction of susceptibles at equilibrium. With rewriting 2 for \( r^{*} \) and substituting for \( \theta_{y}^{*} \), we have
Finally, if one substitute for \( r^* \) and \( \theta^*_e \) in (3) and simplifies it (with assuming \( f(\theta^*_e) > 0 \)), obtains
\[
H(\theta^*_e) = 1 - e^{-\frac{p + \theta^*_e}{m_e k_e}} f(\theta^*_e) + i_0 = 0, i_0 \leq r^* = \frac{p + \theta^*_e}{m_e k_e} f(\theta^*_e) + i_0 \leq 1
\]
If one proves uniqueness of roots of function \( H(\theta) \) under the above condition, the uniqueness of the main system is proved.

The derivative of \( H(\theta) \) is
\[
H'(\theta) = \frac{1}{\rho m_e k_e} ((f(\theta) + (p + \theta) f'(\theta)) e^{-\frac{p + \theta}{m_e k_e}} f(\theta^*_e) + i_0) - \frac{1}{m_e k_e}
\]
Which is strictly negative at \( \theta^*_e \). This follows from

1. \( f(\theta) e^{-\frac{p + \theta}{m_e k_e}} f(\theta^*_e) + i_0 = s_0 e^{-p r^*} = s_m < 1 / \rho (4 \text{ property } 1) \)
2. \( f'(\theta) = -m_e \lambda_e \frac{dF(e^{m_y k_e} f(\theta) + i_0)}{d\theta} - m_e \lambda_e dF(\theta) > 0 \)
3. \( f(\theta) > 0 \) this is always true if \( i_0 \) is small enough i.e. \( i_0 < 1 - m_y \lambda_y - m_e \lambda_e \)
4. \( \theta^*_e > -p \). This follows from \( r^* = \frac{p + \theta^*_e}{m_e k_e} f(\theta^*_e) + i_0 \geq i_0 \) and \( f(\theta^*_e) > 0 \)

Because, \( H'(\theta) \) is differentiable and negative in \( \theta^*_e \); it also is negative in a neighborhood of \( \theta^*_e \). In this case, if there is more than one equilibrium point, the above assertion is applicable for them too. Because, it is not possible, all roots of a function have negative derivative (if they are multiple). There is at most one root. Moreover, \( H(p) > 0 \) and \( H(\infty) < 0 \) and \( H(\theta) \) is continuous whereby it is proved the nonlinear system (1)-(3) has a unique solution. □

4. Conclusion

In this paper we developed two demand models for influenza vaccines which extend the previous non-dynamic game theoretic models. The second model either explicitly or implicitly captures the main factors affecting the decision making of people on vaccination. Both model give good insights about decision making of individuals. The second model also partially relaxes rationality assumption through incorporating individuals’ type variable into the model.

Appendices

Appendix A: Influenza epidemiological model

The standard SIR model divide people into four groups at time \( t \): the susceptible \( S(t) \) (who can catch the disease), the infective \( I(t) \) (who are infected to disease and can transmit it), the removed \( R(t) \) (who either are recovered or died from the disease), the vaccinated \( V \) (who vaccinated before the prevalence of the disease i.e. before \( t = 0 \)). There are certain assumption about this classic model: 1) those who recovered from the disease will not be infected in the current season again 2) the population is uniformly mixed 3) the mean time between two consecutive contact of each individual is constant during an outbreak of disease (denote it by \( 1 / \rho \)). the above model is defined as follows.

\[
\frac{dS(t)}{dt} = -\beta \frac{I(t)}{N} S(t) \quad (5)
\]
\[
\frac{dI(t)}{dt} = \beta \frac{I(t)}{N} S(t) - \gamma I(t) = \gamma(\rho \frac{S(t)}{N} - 1) I(t) \quad (6)
\]
\[
\frac{dR(t)}{dt} = \gamma I(t) \quad (7)
\]
\[
S(0) = N - I(0) - mV > 0, I(0) > 0, R(0) = 0 \quad (8)
\]

\( N \) is the population size, \( m \) is the vaccine effectiveness, \( \beta \) is the product of contact rate \( (\phi) \) and probability of transmission of disease given the contact between a susceptible and an infective. Furthermore, \( I(t) / N \) also is the probability an occurred contact at time \( t \) is between a susceptible and an infective. Therefore, \( \frac{dI(t)}{dt} \) shows average number of individuals who are infected at time \( t \).

\[4 \text{ This is always true under assumption } i_0 < 1 - m_y \lambda_y - m_e \lambda_e \text{. It means the initial number of susceptibles is positive even if every individual vaccinates.} \]

912
\( \frac{1}{\gamma} \) is the duration of infective period and whereby \( \gamma \) is the removal rate from \( I(t) \) to \( R(t) \). \( \rho = \frac{\beta}{\gamma} \) is contact number. It shows the average number of susceptibles infected by an infective in a wholly susceptible population. It is clear from 6 if \( \frac{S(0)}{N} > \frac{1}{\rho} \), there will be an epidemic at time 0 (the population of the infective increases). This increase will continue until the fraction of susceptibles, \( \frac{S(0)}{N} \), fall at or below \( \frac{1}{\rho} \) again.

The above system of differential equations don’t have closed form solution. But, we only need the fraction ever-infected, \( \frac{R(\infty)}{N} \), which is the positive root of the transcendental equation

\[
\frac{S(\infty)}{N} = \frac{S(0)}{N} + \frac{I(0)}{N} - \frac{R(\infty)}{N} = \frac{S(0)}{N} - e^{-\rho s_0}
\]

With exploring the differential equation system 5-8, we find useful properties.

**Property A1:** \( s_0 = s_0 e^{\rho s_0} < \frac{1}{\rho} \)

If \( s_0 \) is less than \( \frac{1}{\rho} \), it remains so thereafter. Otherwise, i.e. \( s_0 \geq \frac{1}{\rho} \), \( I(t) \) increases because \( \frac{d I(t)}{d t} > 0 \) and \( S(t) \) decreases because \( S(t)I(t) > 0 \) until \( s(t) \) falls below \( \frac{1}{\rho} \) again. Thereafter, \( I(t) \) starts to decline until it reaches zero.

For more detailed account of the mathematical models of infectious diseases refer to [Murray (2002)] and recent articles on this subject are [Grassly, and Fraser (2008)].

**REFERENCES**


