

Game theory and epidemiology

Biomathematics Seminar Fall 2016

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Why apply game theory in vaccination?

- Theory and examples
- Application in vaccination
- References

Vaccination games in homogeneous mixing population

- Case of perfect vaccine
- Case of imperfect vaccine
- Uniqueness of NEs (Nash Equilibria)
- Proof of uniqueness
- Extension to more complicated epidemic
- References

What will happen if population has 2 or more sub-groups

- Two vaccination games
- Some partial results
- References

Some open problems

Game theory

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4. The theory of "Game theory and vaccination" is identical with evolutionary game theory. These two both deal with problems on population-levels.

Example

We consider a population with two types.

Example		
	Type A	Type B
Type A	a	b
Type B	c	d

This payoff matrix is used to describe interactions of two types: If A interacts with another A , the payoff is a ; and so on. We have

$$x = x_1 = 1 - x_2,$$

where x_1 is the fraction of type A and x_2 is the fraction of type B . The payoffs are

$$\pi_A = ax + b(1 - x),$$

$$\pi_B = cx + d(1 - x).$$

The dynamics of this type of game is described by replicator equation (General formula):

$$\dot{x}_i = x_i(\pi_i - \langle \pi \rangle).$$

$\langle \pi \rangle$ represents the average payoff of the whole population. In this game, the replicator equation is

$$\dot{x} = x(1-x)[(a-b-c+d)x + b-d].$$

There are three fixed points, two trivial ones are $x = 0$ and $x = 1$. The third one is

$$x^* = \frac{d-b}{a-b-c+d},$$

for $a > c$ and $d > b$ or for $a < c$ and $d < b$.

1. *Dominance*. If $a > c$ and $b > d$, type A dominates type B . In this case, the fixed point at $x = 1$ is stable and the fixed point at $x = 0$ is unstable. If $a < c$ and $b < d$, type B dominates type A . In this case, the fixed point at $x = 0$ is stable and the fixed point at $x = 1$ is unstable.
2. *Bistability*. If $a > c$ and $d > b$, the fixed points at $x = 0$ and $x = 1$ are both stable and the fixed point at x^* is unstable.
3. *Coexistence*. If $a < c$ and $d < b$, the fixed points at $x = 0$ and $x = 1$ are both unstable and the fixed point at x^* is stable. The population eventually becomes a stable mixture of type A and type B . This is the case we will meet in the vaccination games.
4. *Neutrality*. For $a = c$ and $b = d$.

The formal game and its payoff matrix

Vaccination offers protection, but also cost and risk. Before the outbreak of epidemic, people need to evaluate the costs of infection and vaccination. Eventually, a certain percentage of people goes into the vaccinated class, while others stay in the susceptible class.

The formal vaccination game can be described as:

Vaccination Game as general		
	Vaccinated individual j	Susceptible individual j
Vaccinated individual i	$-\hat{C}_v$	$-\hat{C}_v$
Susceptible individual i	0	$-\pi_p \hat{C}_i$

All elements can be translated easily. By using game theory, the expected vaccine coverage level is expressed in terms of the attack ratio. We need to use mathematical models to find another relation between attack ratio and vaccine coverage level, to make the prediction more accurate.

Flowchart

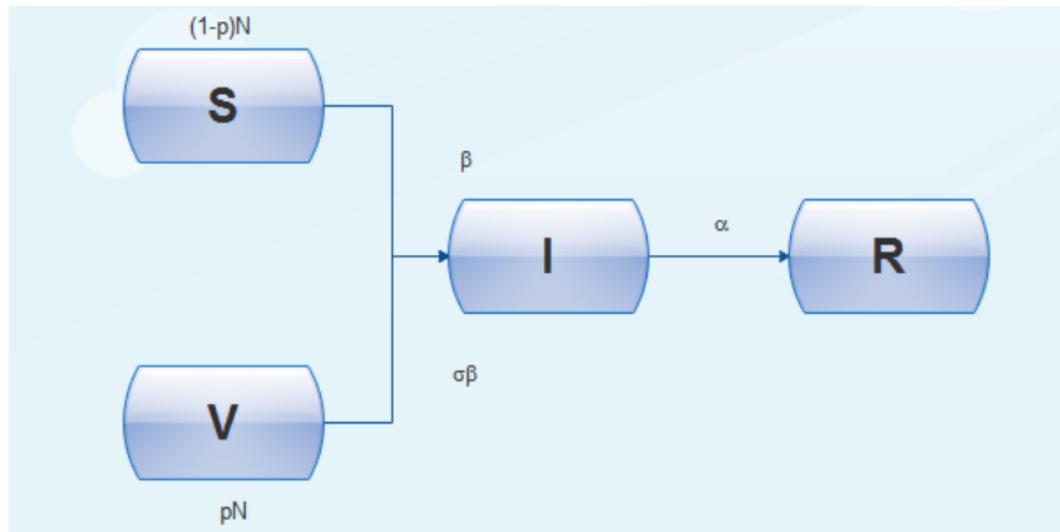


Figure: Vaccination model

The major goal of "Vaccination games" is to predict the expected vaccine coverage levels. Two weapons are: Game theory and mathematical models.

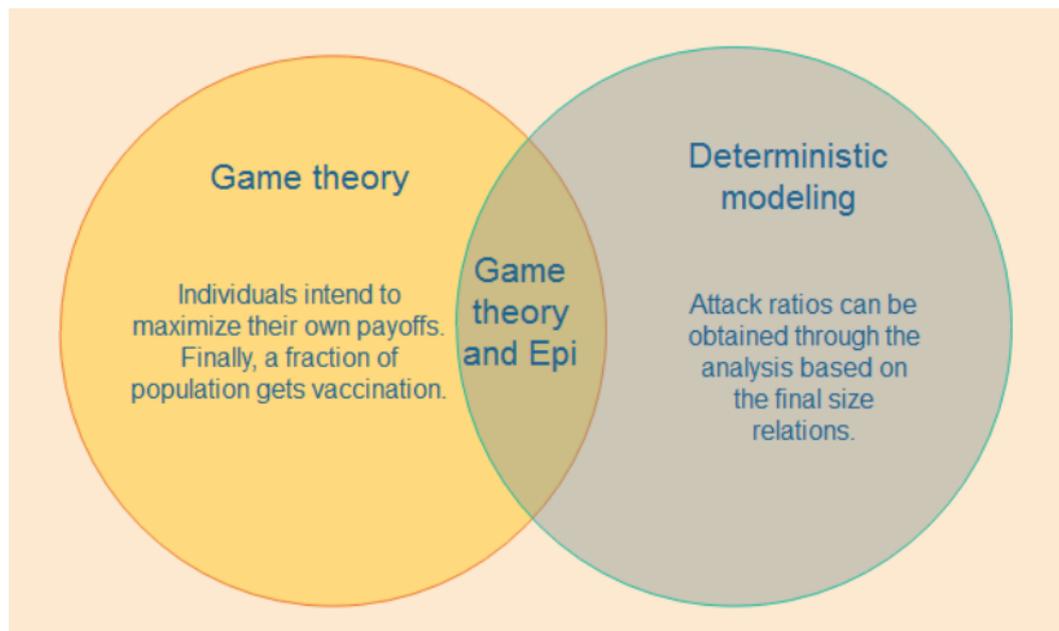


Figure: Vaccination game theory

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Vaccination game with perfect vaccine

Fully-effective Vaccination Game		
	Vaccinated individual j	Susceptible individual j
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2. All elements are negative.
3. We assume that $C_i > C_V$.

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5. Question is: How to find p ?

Assume the final fraction of people who take vaccination is p ; the fraction of people to be vaccinated is x_v and the fraction of people not to be vaccinated is x_s , $\{x_v, x_s\} = \{p, 1 - p\}$.

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$$\dot{x}_V = x_V (f_V - \bar{f}),$$

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with

$$\bar{f} = x_V f_V + x_S f_S.$$

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3. The fraction $x_V = 1 - \frac{C_V}{\pi_p C_i}$. If we define the relative cost $r = \frac{C_V}{C_i}$, the expected vaccine coverage level is:

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4. π_p can be estimated by epidemic models.

Game theory and epidemiology

- └ Vaccination games in homogeneous mixing population

- └ Case of perfect vaccine

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$$\frac{dS}{dt} = -\beta SI$$

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$$\ln \frac{S_0}{S_\infty} = \frac{\beta}{\alpha} [S_0 - S_\infty].$$

3. The attack ratio can be expressed in terms of p ,

$$\ln \frac{1}{1 - \pi_p} = \frac{\beta}{\alpha} (1 - p) N \pi_p.$$

Vaccination with imperfect vaccine

Partial-effective Vaccination Game			
	Vaccinated individual		Susceptible individual
Vaccinated individual	$-\hat{C}_V$	—	$-\hat{C}_V$
	$\sigma \pi_V \hat{C}_i$		$\sigma \pi_P \hat{C}_i$
Susceptible individual	$-\pi_V \hat{C}_i$		$-\pi_P \hat{C}_i$

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2. Cost of infection is $-C_i$ and cost of vaccination is $-C_V$, π_V and π_P are attack ratios.
3. The expected vaccine coverage level p and attack ratios π_P and π_V satisfy

$$\frac{r}{1 - \sigma} = p\pi_V + (1 - p)\pi_P,$$

with r relative cost to measure the vaccine. π_P and π_V can be expressed by SVIR model.

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4. p is smaller than the threshold value p_C (Herd immunity threshold).

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2. Construct the SVIR model,

$$\frac{dS}{dt} = -\beta SI,$$

$$\frac{dV}{dt} = -\sigma\beta VI,$$

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3. The final size relation can be derived from the model,

$$\ln \frac{S_\infty}{S_0} = \frac{\beta}{\alpha} [S_\infty + V_\infty - S_0 - V_0],$$

$$\ln \frac{V_\infty}{V_0} = \frac{\sigma\beta}{\alpha} [S_\infty + V_\infty - S_0 - V_0].$$

Epi-game theory has been applied to different types of epidemic:

- ▶ Influenza
- ▶ Smallpox
- ▶ Chickenpox
- ▶ Measles
- ▶ Rubella

Uniqueness

$$\pi_p(1 - p) = r,$$

$$p\pi_v + (1 - p)\pi_p = \frac{r}{1 - \sigma}.$$

For uniqueness:

1. From the equations of vaccine coverage level in vaccination game with perfect vaccine, to differentiate the left side of the equation,

$$\pi'_p(1 - p) - \pi_p,$$

2. From the equations of vaccine coverage level in vaccination game with imperfect vaccine, to differentiate the left side of the equation,

$$\begin{aligned} & \pi_v + p\pi'_v - \pi_p + (1 - p)\pi'_p \\ = & (\pi_v - \pi_p) + p\pi'_v + (1 - p)\pi'_p. \end{aligned}$$

Uniqueness

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3. Both right sides of two equations are constants. $\pi'_p < 0$ and $\pi'_v < 0$ are important for uniqueness of Nash equilibria.

Perfect vaccine

$$\ln \frac{S_0}{S_\infty} = \frac{\beta}{\alpha} S_0 \left[1 - \frac{S_\infty}{S_0} \right],$$

$$\frac{dS_\infty}{dp} = - \frac{\frac{1}{S_0} - \frac{\beta}{\alpha}}{\frac{1}{S_\infty} - \frac{\beta}{\alpha}} > 0,$$

$$\frac{d\pi_p}{dp} < 0.$$

Theorem

In the SIR compartmental model, when vaccine coverage level p increases from 0 to the herd immunity threshold p_c , the final size S_∞ of susceptible class will increase, the attack ratio will decrease. If $p \geq p_c$, the whole population is protected completely by the vaccine.

Imperfect vaccine

Lemma

In the SVIR model with infection factor σ , there exists a threshold value σ_c , which is defined as

$$\left(\frac{S_0}{S_\infty}\right)^{\sigma_c} = \mathcal{R}_c = \frac{\beta}{\alpha} N.$$

If the infection factor σ is smaller than σ_c , $\frac{V_0}{V_\infty} < \mathcal{R}_c < \frac{S_0}{S_\infty}$ holds when the vaccine coverage level is low, and by increasing the vaccine coverage level p , $\mathcal{R}_c < \frac{V_0}{V_\infty} < \frac{S_0}{S_\infty}$. If the infection factor σ is bigger than σ_c , the inequality $\mathcal{R}_c < \frac{V_0}{V_\infty} < \frac{S_0}{S_\infty}$ holds.

Theorem

If σ is smaller than σ_c , there exists a critical value p_0 , as vaccine coverage level p increasing from 0 to p_0 , S_∞ will decrease and V_∞ will still increase; while p increasing from p_0 to 1, S_∞ and V_∞ both increase, where p_0 is the critical value we described in previous lemma. If σ is bigger than σ_c , when the vaccine coverage level p increases, S_∞ will decrease and V_∞ will increase. If the vaccine coverage level p increases between 0 and the herd immunity threshold, for vaccinated group, for non-vaccinated group and for the whole population, the attack ratios decrease. The infection factor σ and the attack ratios are independent.

application of age-of-infection models

1. If in previous two vaccination games, the diseases have more compartments such as exposed stage, whether the results on attack ratios still hold? Whether these two games have unique Nash equilibria?

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2. All compartmental epidemic models can be describe by age-of-infection model, such as:

$$S' = -\frac{a}{N_0} S\phi$$

$$\begin{aligned}\phi(t) &= \phi_0(t) + \int_0^t \frac{a}{N_0} S(t-\tau)\phi(t-\tau)A(\tau)d\tau \\ &= \phi_0(t) + \int_0^t [-S'(t-\tau)]A(\tau)d\tau.\end{aligned}$$

We are able to prove the final size relation to this general age-of-infection model is similar comparing with SIR/SVIR models.

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We are able to prove the final size relation to this general age-of-infection model is similar comparing with SIR/SVIR models.

3. One example: influenza has exposed stage. We analyze the vaccination game of influenza, this game has one unique Nash equilibrium.

Game theory and epidemiology

- └ Vaccination games in homogeneous mixing population
 - └ Extension to more complicated epidemic

1. If the epidemic is described by SEIR model,

$$S' = -\beta S(I + \epsilon E)$$

$$E' = \beta S(I + \epsilon E) - \kappa E$$

$$I' = \kappa E - \alpha I$$

$$R' = \alpha I.$$

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2. This SEIR can be expressed by age-of-infection model with distribution function

$$A(\tau) = \epsilon e^{-\kappa\tau} + \frac{\kappa}{\kappa - \alpha} [e^{-\alpha\tau} - e^{-\kappa\tau}].$$

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2. This SEIR can be expressed by age-of-infection model with distribution function

$$A(\tau) = \epsilon e^{-\kappa\tau} + \frac{\kappa}{\kappa - \alpha} [e^{-\alpha\tau} - e^{-\kappa\tau}].$$

3. The final size relation of age-of-infection model shows that the attack ratios are decreasing functions, vaccination games with SEIR-structure epidemics have unique NEs.



Bauch C.T., Earn D.J.D., 2004, *Vaccination and the theory of games*, *Proc. Natl Acad. Sci. USA* 101: 13391-13394.



Bai F., 2016, *Uniqueness of Nash equilibrium in vaccination games*, *Journal of Biological Dynamics* 10: 395-415.

formal games

Some basic setup:

- 1, The sizes of two sub-groups are N_1 and N_2 , respectively. N_1 and N_2 are constants.
- 2, Group i members make a_i contacts in unit time and the fraction of contacts made by a member of group i is with a member of group j is p_{ij} , ($i, j = 1, 2$).
- 3, Costs of vaccination for members in sub-group 1 is C_{v1} and for members in sub-group 2 is C_{v2} .
- 4, Probabilities of being infected for two groups are π_{p1} and π_{q2} associated with the vaccine coverage level p and q in each subgroup.

Payoff matrices

Fully-effective vaccination game with two-subgroups				
	Vaccinated individual 1	Susceptible individual 1	Vaccinated individual 2	Susceptible individual 2
Vaccinated individual 1	$-C_{v1}$	$-C_{v1}$	$-C_{v1}$	$-C_{v1}$
Susceptible individual 1	0	$-\pi_{p1} C_{i1}$	0	$-\pi_{q2} C_{i1}$
Vaccinated individual 2	$-C_{v2}$	$-C_{v2}$	$-C_{v2}$	$-C_{v2}$
Susceptible individual 2	0	$-\pi_{p1} C_{i2}$	0	$-\pi_{q2} C_{i2}$

The NE can be expressed as:

$$p = 1 - \frac{C_{r1}p_{22} - C_{r2}p_{21}}{p_{11}p_{22} - p_{12}p_{21}} \frac{1}{\pi_{p1}}, \quad q = 1 - \frac{C_{r2}p_{11} - C_{r1}p_{12}}{p_{11}p_{22} - p_{12}p_{21}} \frac{1}{\pi_{q2}}$$

Partial-effective Vaccination Game with two-subgroups				
	Vaccinated individual 1	Susceptible individual 1	Vaccinated individual 2	Susceptible individual 2
Vaccinated individual 1	$-C_{v1} - \sigma_1 \pi_{pv1} C_{i1}$	$-C_{v1} - \sigma_1 \pi_{pv1} C_{i1}$	$-C_{v1} - \sigma_1 \pi_{qv2} C_{i1}$	$-C_{v1} - \sigma_1 \pi_{qi2} C_{i1}$
Susceptible individual 1	$-\pi_{pv1} C_{i1}$	$-\pi_{pi1} C_{i1}$	$-\pi_{qv2} C_{i1}$	$-\pi_{qi2} C_{i1}$
Vaccinated individual 2	$-C_{v2} - \sigma_2 \pi_{pv1} C_{i2}$	$-C_{v2} - \sigma_2 \pi_{pi1} C_{i2}$	$-C_{v2} - \sigma_2 \pi_{qv2} C_{i2}$	$-C_{v2} - \sigma_2 \pi_{qi2} C_{i2}$
Susceptible individual 2	$-\pi_{pv1} C_{i2}$	$-\pi_{pi1} C_{i2}$	$-\pi_{qv2} C_{i2}$	$-\pi_{qi2} C_{i2}$

The NE is:

$$p = \frac{\frac{C_{r1}(p_{11}p_{22} + p_{12}p_{21})}{1 - \sigma_1} - \frac{C_{r2}(p_{12}p_{21} + p_{11}p_{22})}{1 - \sigma_2} - \pi_{pi1}(p_{11}p_{22} - p_{12}p_{21})}{(\pi_{pv1} - \pi_{pi1})(p_{11}p_{22} - p_{12}p_{21})},$$

$$q = \frac{\frac{C_{r1}(p_{11}p_{21} + p_{12}p_{21})}{1 - \sigma_1} - \frac{C_{r2}(p_{11}p_{21} + p_{11}p_{22})}{1 - \sigma_2} - \pi_{qi2}(p_{12}p_{21} - p_{11}p_{22})}{(\pi_{qv2} - \pi_{qi2})(p_{12}p_{21} - p_{11}p_{22})},$$

Results on uniqueness

It is quite difficult to prove the uniqueness of vaccine coverage levels p and q , the idea is to focus on the properties of several attack ratio functions. This problem is still open.

References



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Some interesting and open problems:

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1. Long time scale. Involve human birth and human death (Malaria for example).
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3. Analysis of uniqueness of NE in vaccination games in population with two or more sub-groups.

Thank you for attending!