Analyzing Rotavirus Vaccinations using Game Theory

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Purpose and Motivation

- We analyze rotavirus using a mathematical model and game theory to determine the optimal vaccination strategy.
- Kenya has the highest number of child rotavirus deaths, accounting for about 2% of all rotavirus deaths [5].

Source:https://www.lonelyplanet.com/maps/africa/kenya/

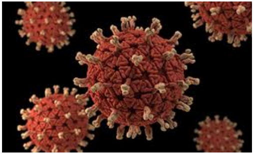
Background: Rotavirus

Rotavirus

- Discovered in 1973.
- Causes gastroenteritis (most commonly in young children) [2].
- Causes 2 million hospitalizations and 500,000 deaths in children < 5 years of age [8].
- Transmitted through feces, contaminated food, water, surfaces, and objects.

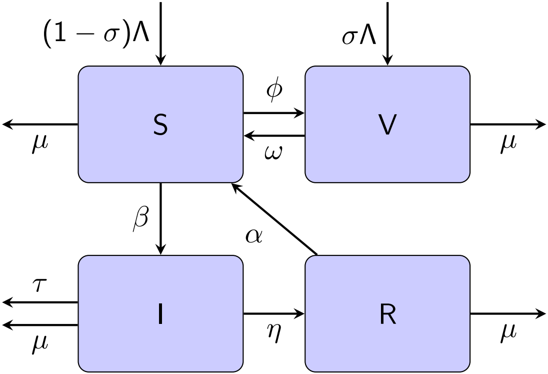
Rotavirus Vaccine

- Rotarix (RV1) 2008 (2 and 4 months)
- Neonatal Vaccine (RV3-BB) [4] (0, 8, and 14 weeks)



Source: https://ecdc.europa.eu/en/rotavirus-infection

SVIR Model


$(1-\sigma)\Lambda$
$\sigma\Lambda$
S
V
I
R
ϕ
ω
μ
μ
β
α
τ
μ
η
μ

Parameters

Symbol	Description	Values(per day)	Ref
Λ	Birth Rate	3117.85	[3] (Estimated)
μ	Natural Mortality Rate	1.8×10^{-5}	[3] (Estimated)
τ	Infectious Mortality Rate	3.42×10^{-7}	[7] (Estimated)
β	Infection Rate	5.57×10^{-7}	[6] (Estimated)
η	Recovery Rate	1.43×10^{-1}	[1] (Assumed)
ω	Vaccine Waning Rate	1.37×10^{-3}	[2] (Estimated)
α	Recovered Immunity Waning Rate	2.74×10^{-3}	[1] (Estimated)
ϕ	Vaccination Rate	Variable	
σ	Proportion of Newborns Vaccinated	Variable	

Differential Equations

From our model diagram, we get our differential equations:

$$\frac{dS}{dt} = (1-\sigma)\Lambda + \omega V + \alpha R - \beta SI - (\phi + \mu)S$$
$$\frac{dV}{dt} = \phi S + \sigma\Lambda - (\omega + \mu)V$$
$$\frac{dI}{dt} = \beta SI - (\eta + \tau + \mu)I$$
$$\frac{dR}{dt} = \eta I - (\alpha + \mu)R$$
$$N(t) = S(t) + V(t) + I(t) + R(t)$$

Disease Free Equilibrium (E^0)

Finding the Disease Free Equilibrium (E^0)

$$S^0 = \frac{\Lambda[\mu(1-\sigma)+\omega]}{\mu(\mu+\omega+\phi)}$$

$$V^0 = \frac{\Lambda(\mu\sigma+\phi)}{\mu(\mu+\omega+\phi)}$$

$$I^0 = 0$$

$$R^0 = 0$$

Our Disease Free Equilibrium is

$$E^0 = (S^0, V^0, I^0, R^0) = \left(\frac{\Lambda[\mu(1-\sigma)+\omega]}{\mu(\omega+\phi+\mu)}, \frac{\Lambda(\mu\sigma+\phi)}{\mu(\omega+\phi+\mu)}, 0, 0\right).$$

Endemic Equilibrium (E^*)

Finding our Endemic Equilibrium:
By letting our differential equations equal to 0, we can obtain:

$$S^* = \frac{\eta + \tau + \mu}{\beta}$$

$$V^* = \frac{\phi(\eta + \tau + \mu) + \sigma\Lambda\beta}{\beta(\omega + \mu)}$$

$$I^* = \frac{(\alpha + \mu)[\Lambda\beta(\omega + \mu - \sigma\mu) - \mu(\omega + \phi + \mu)(\eta + \tau + \mu)]}{\beta(\omega + \mu)[(\alpha + \mu)(\tau + \mu) + \eta\mu]}$$

$$R^* = \frac{\eta I^*}{\alpha + \mu}$$

Basic Reproduction Number (R_0)

Definition

The **Basic Reproduction Number**, R_0, is defined as the average number of secondary infections an infectious individual would cause over his infectious period in an entirely susceptible population.

Next Generation Matrix Method

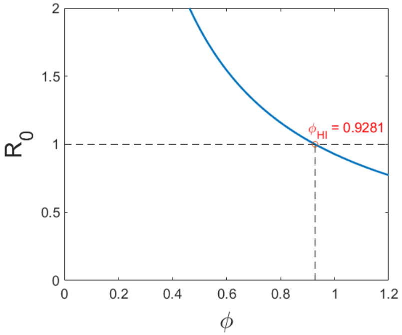
$\mathcal{F}_i$ - rate at which new infections enter compartment i
$\mathcal{V}_i$ - rate of transfer of infected individuals in and out of other compartments

Basic Reproduction Number (R_0)

Using the results from the Disease Free Equilibrium we obtain the following basic reproduction number.

$$R_0 = \frac{\beta S^0}{\eta + \tau + \mu} = \frac{\beta \Lambda[\mu(1 - \textcircled{\sigma}) + \omega]}{\mu(\omega + \textcircled{\phi} + \mu)(\eta + \tau + \mu)}.$$

Graph of R_0 in terms of ϕ

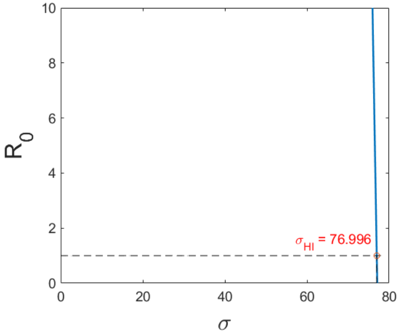


We can determine the herd immunity for ϕ by letting $R_0 = 1$ and $\sigma = 0$.

$$\phi_{HI} = \frac{\beta\Lambda(\mu+\omega)-\mu(\mu+\omega)(\eta+\tau+\mu)}{\mu(\eta+\tau+\mu)}$$

$$\phi_{HI} = 0.9281$$

Graph of R_0 in terms of σ



Similarly, the herd immunity for σ can be determined by letting $R_0 = 1$ and $\phi = 0$.

$$\sigma_{HI} = \frac{\beta\Lambda(\mu+\omega) - \mu(\mu+\omega)(\eta+\tau+\mu)}{\mu\beta\Lambda}$$

$$\sigma_{HI} = 76.996$$

Game Theory

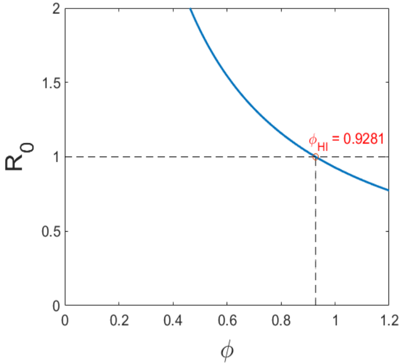
Game Theory

Game Theory is the science of strategy. It attempts to determine mathematically and logically the actions that "players" should take to secure the best outcomes for themselves in a wide array of "games."

Goal

Our goal is to apply Game Theory to our mathematical model to determine what the best strategy is for an individual. We consider the Rotarix and RV3-BB vaccines independently and together.

Scenario 1: $\phi > \phi_{HI}$



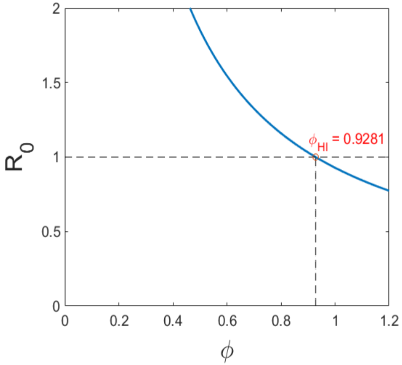
Conditions

- $\phi > \phi_{HI}$
- $R_0 < 1$
- Disease Free

Strategy:

- Individual Does Not Vaccinate

Scenario 2: $\phi < \phi_{HI}$



Conditions

- $\phi < \phi_{HI}$
- $R_0 > 1$
- Endemic

Strategy:

- Consider Expected Pay-off Value

Game Theory: Expected Pay-off

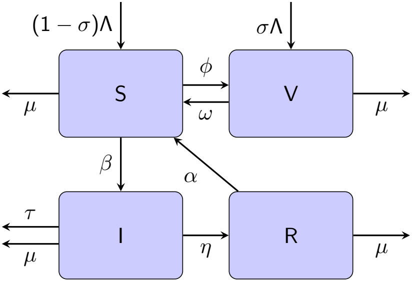
Expected Payoffs for ϕ:

$$E_{V1} = E(1, \phi) = -C_\phi - C_I(\pi_{V \to I})$$
$$E_{NV} = E(0, \phi) = -C_I(\pi_{S \to I})$$

We scale the cost by letting $C_1 = \frac{C_\phi}{C_I}$.

$$E_{V1} = -C_1 - \pi_{V \to I}$$
$$E_{NV} = -\pi_{S \to I}$$

Game Theory: Expected Pay-off



We calculate the probabilities using our SVIR model.

$$\pi_{S \to I} = \frac{\beta \boldsymbol{I}^*}{\beta \boldsymbol{I}^* + \mu}$$

$$\pi_{V \to S} = \frac{\omega}{\omega + \mu}$$

$$\pi_{V \to I} = (\pi_{V \to S})(\pi_{S \to I}) = \frac{\omega \beta \boldsymbol{I}^*}{(\beta \boldsymbol{I}^* + \mu)(\omega + \mu)}$$

Game Theory: Expected Pay-off

Expected Payoffs for σ:

$$E_{V2} = E(1,\sigma) = -C_\sigma - C_I(\pi_{V\to I})$$
$$E_{NV} = E(0,\sigma) = -C_I(\pi_{S\to I})$$

We scale the cost by letting $C_2 = \frac{C_\sigma}{C_I}$.

$$E_{V2} = -C_2 - \pi_{V\to I}$$
$$E_{NV} = -\pi_{S\to I}$$

Game Theory: Expected Pay-off

Conditions

- $\phi < \phi_{HI}$
- $R_0 > 1$
- Endemic

Strategy:

(a) Individual should take the vaccine.
(b) Individual should not take the vaccine.
(c) Consider Nash Equilibrium.

Cases

(a) $E(1, \phi) > E(0, \phi)$

(b) $E(1, \phi) < E(0, \phi)$

(c) $E(1, \phi) = E(0, \phi)$

Game Theory: Nash Equilibrium

Definition

Nash Equilibrium is a solution concept of a non-cooperative game involving two or more players in which each player is assumed to know the equilibrium strategies of the other players, and no player has anything to gain by changing only their own strategy.

Letting $E_{V1} = E_{NV}$:

$$
\begin{aligned}
-C_1 - \pi_{V \to I} &= -\pi_{S \to I} \\
C_1 &= \pi_{S \to I} - \pi_{V \to I} \\
C_1 &= \frac{\beta I^*}{\beta I^* + \mu}\left(1 - \frac{\omega}{\omega + \mu}\right) \\
I^* &= \frac{(\alpha + \mu)[\Lambda\beta(\omega + \mu) - \mu(\omega + \phi + \mu)(\eta + \tau + \mu)]}{\beta(\omega + \mu)[(\alpha + \mu)(\tau + \mu) + \eta\mu]}
\end{aligned}
$$

Game Theory: Nash Equilibrium

Similarly letting $E_{V2} = E_{NV}$:

$$-C_2 - \pi_{V \to I} = -\pi_{S \to I}$$
$$C_2 = \pi_{S \to I} - \pi_{V \to I}$$
$$C_2 = \frac{\beta I^*}{\beta I^* + \mu}\left(1 - \frac{\omega}{\omega + \mu}\right)$$
$$I^* = \frac{(\alpha + \mu)[\Lambda\beta(\omega + \mu - \sigma\mu) - \mu(\omega + \mu)(\eta + \tau + \mu)]}{\beta(\omega + \mu)[(\alpha + \mu)(\tau + \mu) + \eta\mu]}$$

Game Theory: Nash Equilibrium

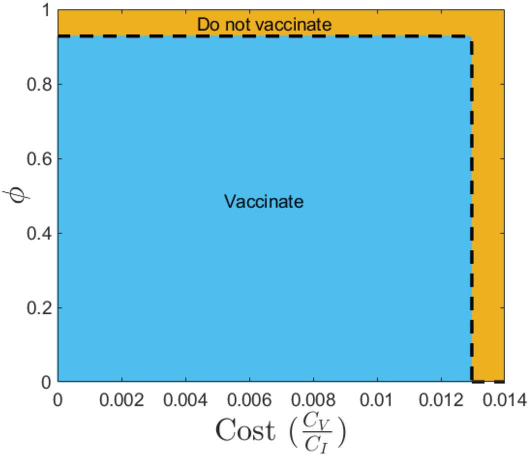
Nash Equilibrium for ϕ:

$$\phi_{NE}(C_1) = \frac{C_1(\omega+\mu)^2[(\alpha+\mu)(\tau+\mu)+\eta\mu]}{(\alpha+\mu)(\eta+\tau+\mu)[(\omega+\mu)(C_1-1)+\omega]} + \frac{\Lambda\beta(\omega+\mu)}{\mu(\eta+\tau+\mu)} - \omega - \mu$$

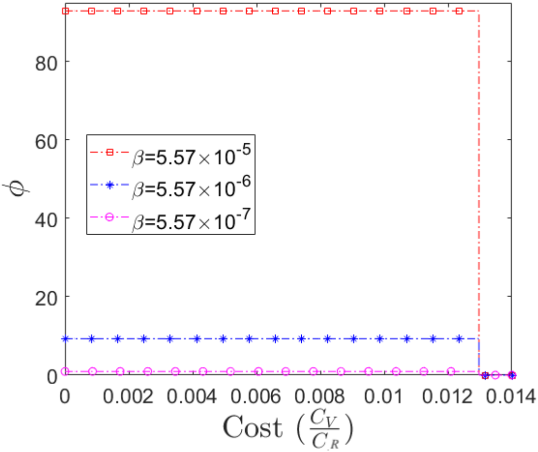
Nash Equilibrium for σ:

$$\sigma_{NE}(C_2) = \frac{C_2(\omega+\mu)^2[(\alpha+\mu)(\tau+\mu)+\eta\mu]}{\Lambda\beta(\alpha+\mu)[(\omega+\mu)(C_2-1)+\omega]} - \frac{(\eta+\tau+\mu)(\omega+\mu)}{\Lambda\beta} + \frac{\omega+\mu}{\mu}$$

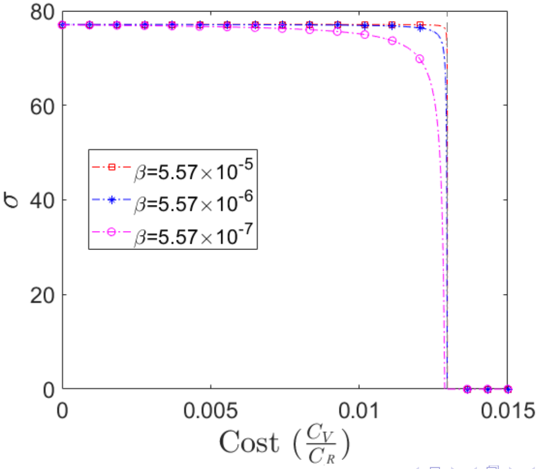
ϕ_{NE} in terms of Cost



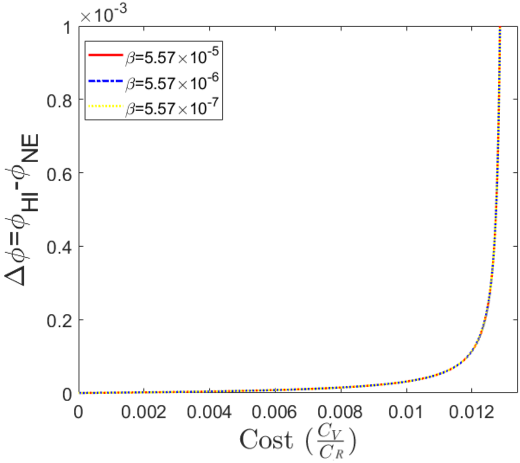
ϕ_{NE} in terms of Cost



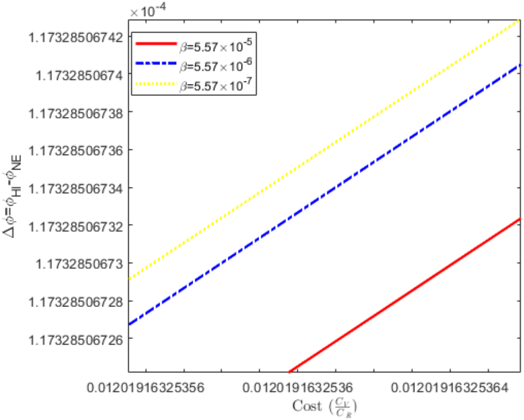
σ_{NE} in terms of Cost



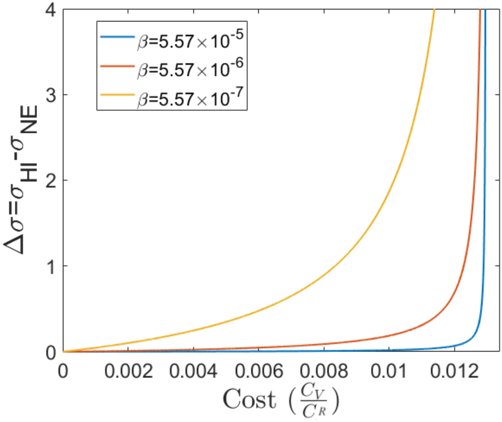
$\Delta\phi$ in terms of Cost



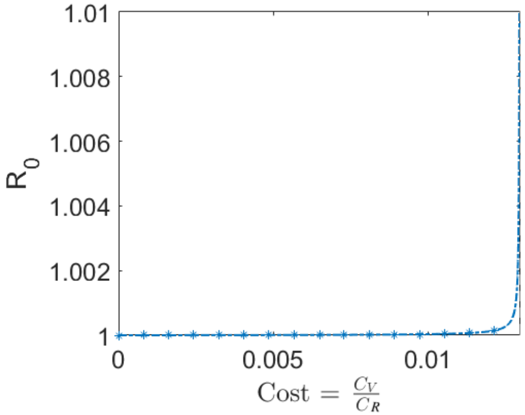
$\Delta\phi$ in terms of Cost



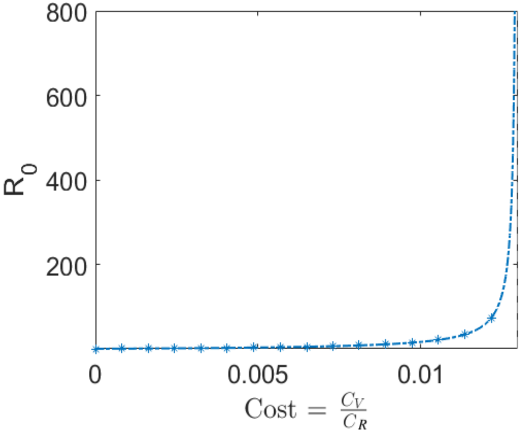
$\Delta\sigma$ in terms of Cost



R_0 in terms of cost for ϕ



R_0 in terms of cost for σ



Conclusion and Future Works

From our data, we can conclude:

- The neonatal vaccine RV3-BB σ is more sensitive to the infection rate β than the Rotarix vaccination ϕ.
- We determined that the Rotarix vaccine is the optimal strategy for an individual given the population of vaccinated individuals.

For future works, we recommend a closer analysis on the relative cost of vaccination to determine the conditions for the dominant and mixed strategies for the Rotarix and RV3-BB vaccines.

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Questions