Intentional infection as a method of population-level disease control I. Intentional infection of newborns (Draft)

Roger Zhang

June 16th 2018

Abstract

In this paper, we study the possible advantages of intentional infection, as a method of population-level disease control. Intentional infection is a generalization of variolation, which was invented in 15th century, and widely used around the world in 17th and 18th century. People believed that by variolation, a mild but protective infection would result, which give them a higher chance of survival compared to being naturally infected. This paper aims to provide a mathematical model which describes the dynamics of infected classes, when intentional infection is introduced on a population level, and perform predictions based on the model.

Contents

1 Introduction

In history, before vaccination became a developed technology, humanity has limited power when facing viral infection. Intentional infection however, act as a precursor of vaccination, was introduced long ago. Although people did not fully understand the detailed mechanism of intentional infections before modern centuries, this method was used extensively to battle some deadly disease, smallpox as a famous representative.
There are different strategies in vaccination. Some vaccinations are applied to younglings, for example, polio. Other vaccination may be applied to adults, such as flu vaccination. In fact, same strategies may be translated to intentional infection usage as well.

In this paper, we developed and analyzed a compartmental model, which coupled direct intentional infection and transmission of intentionally infected cases.

2 Model: Modification to SIR model

2.1 System of differential equations

We begin our analysis by modifying SIR model. Our first strategy is to intentionally infect newborn individuals, with a certain proportion. The following assumptions are made to simplify the model to start with:

- No difference between intentionally infected and naturally infected individuals.
- No disease induced mortality(Addition of disease induced mortality will be).
- Birth and natural death rate are the same(total population N remains constant).
- The latent period(time from infection to becoming infectious) is short enough to be ignored.
- All susceptible individuals are equally likely to be infected, and all infected individuals are equally infectious.

Equipped with the assumptions above, we now setup our system of differential equations.

Just like in SIR model, S, I and R represent the proportion of susceptible, infected and recovered with respect to total population.

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= \mu(1-p) - \beta SI - \mu S\,, \\ \frac{\mathrm{d}I}{\mathrm{d}t} &= \beta SI + \mu p - \gamma I - \mu I\,, \\ \frac{\mathrm{d}R}{\mathrm{d}t} &= \gamma I - \mu R\,. \end{aligned} \tag{1}$$

Here, β is the transmission rate, γ is the recovery rate, μ is the *per capita* rate of birth and death, p is the proportion of newborns that are intentionally infected.

We non-dimensionalize Equation 1 by scaling time, by

$$\tau = (\gamma + \mu)t\,, \tag{2}$$

so the time unit now is "mean time infected".

The dimensionless system is:

$$\frac{\mathrm{d}S}{\mathrm{d}\tau} = \epsilon(1-p) - \mathcal{R}_0 SI - \epsilon S\,, \tag{3a}$$

$$\frac{\mathrm{d}I}{\mathrm{d}\tau} = \mathcal{R}_0 SI + \epsilon p - I\,, \tag{3b}$$

where $\epsilon = \frac{\mu}{\gamma+\mu}$, $\mathcal{R}_0 = \frac{\beta}{\gamma+\mu}$.

We are not considering $\frac{\mathrm{d}R}{\mathrm{d}\tau}$ since it does not impact the dynamics of S and I, and we do not need to track the proportion of recovered individuals in this model.

2.2 Equilibria

By letting Equation 3 equal to 0, we solve for equilibria. The only equilibrium for this model is,

$$\hat{S} = \frac{1}{\mathcal{R}_0} - \frac{2p}{(\mathcal{R}_0-1) + \sqrt{(\mathcal{R}_0-1)^2 + 4\mathcal{R}_0 p}}\,, \tag{4a}$$

$$\hat{I} = \frac{\epsilon(\mathcal{R}_0-1) + \epsilon\sqrt{(\mathcal{R}_0-1)^2 + 4\mathcal{R}_0 p}}{2\mathcal{R}_0}\,. \tag{4b}$$

Notice, Equation 4b does not return 0 for any p value between 0 and 1, meaning there is always infected individuals present in the population. Therefore, we can claim that this is not a disease free equilibrium. It follows that the equilibrium above is an endemic equilibrium (EE).

We would like to know if the EE is stable, therefore we need the Jacobian matrix of Equation 3. The Jacobian is,

$$\mathcal{J} = \begin{bmatrix} -\mathcal{R}_0 I - \epsilon & -\mathcal{R}_0 S \\ \mathcal{R}_0 I & \mathcal{R}_0 S - 1 \end{bmatrix}\,. \tag{5}$$

Now for simplicity, let

$$K = (\mathcal{R}_0 - 1) + \sqrt{(\mathcal{R}_0-1)^2 + 4\mathcal{R}_0 p}\,. \tag{6}$$

For the purpose of our discussion, we are interested in disease that transmits fast enough to result in an epidemic. Therefore, the $\mathcal{R}_0$ value for the disease has to be greater than 1.

Notice, $K > 0$ if $p \neq 0$.

Thus, the Jacobian evaluated at endemic equilibrium is,

$$\mathcal{J}|_{EE} = \begin{bmatrix} -\frac{\epsilon K}{2} - \epsilon & -1 + \frac{2p\mathcal{R}_0}{K} \\ \frac{\epsilon K}{2} & -\frac{2p\mathcal{R}_0}{K} \end{bmatrix}, \tag{7}$$

The eigenvalues of Equation 7 are,

$$\lambda_{1,2} = \frac{-(\epsilon K^2 + 2\epsilon K + 4p\mathcal{R}_0) \pm \sqrt{(\epsilon K^2 + 2\epsilon K + 4p\mathcal{R}_0)^2 - 4(2\epsilon K^3 + 8\epsilon K p\mathcal{R}_0)}}{4K} \tag{8}$$

Since $(2\epsilon K^3 + 8\epsilon K p\mathcal{R}_0) > 0$, if the discriminant is positive, we have

$$\sqrt{(\epsilon K^2 + 2\epsilon K + 4p\mathcal{R}_0)^2 - 4(2\epsilon K^3 + 8\epsilon K p\mathcal{R}_0)} \leq |\epsilon K^2 + 2\epsilon K + 4p\mathcal{R}_0|\,, \tag{9}$$

thus, $\Re(\lambda_{1,2}) < 0$.

But if the discriminant is negative, we have

$$\Re(\lambda_1) = \Re(\lambda_2) = -(\epsilon K^2 + 2\epsilon K + 4p\mathcal{R}_0) < 0\,, \tag{10}$$

As a result, we can conclude that EE is stable.

To fully investigate the dynamics of the system, we're also interested in whether the eigenvalues could be complex, which will lead to damped oscillation.

Although it is hard to determine the sign of discriminant analytically, we can plot the value of discriminant as a function of other parameter, i.e. p or $\mathcal{R}_0$.

We will start our analysis with specific values of each parameter. Given the variolation history of smallpox, it is reasonable to adopt its parameter values as an example. The values are listed in Table 1.

Table 1: Model parameters and smallpox values.

Symbol	**Meaning**	**Value**
μ	Natural *per capita* death rate	$\frac{1}{50*365}$ per day
γ	Recovery rate	$\frac{1}{22}$ per day
$\mathcal{R}_0$	Basic reproductive number	4.5

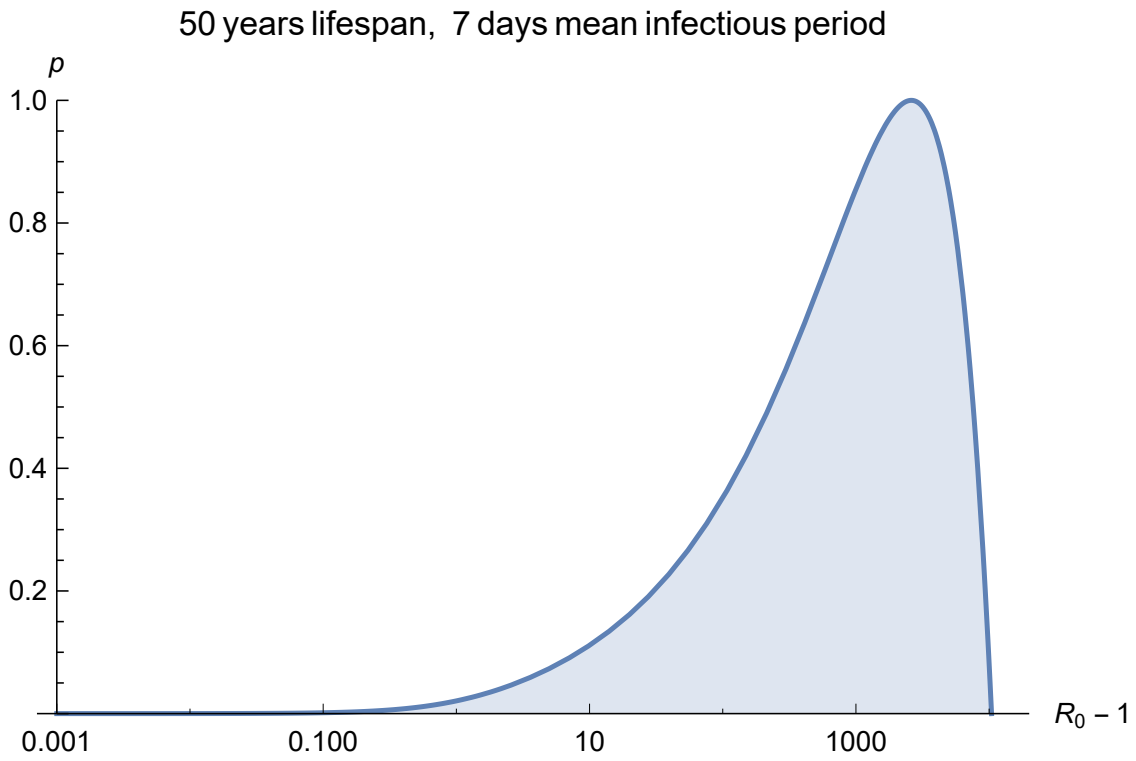
2.3 Region of $(\mathcal{R}_0, p)$ plane where there are damped oscillations (fixed ϵ)

p is the proportion of intentional infection and $\mathcal{R}_0$ is the basic reproduction number.

In the following graphs, the shaded area represent the region where the system has damped oscillation.

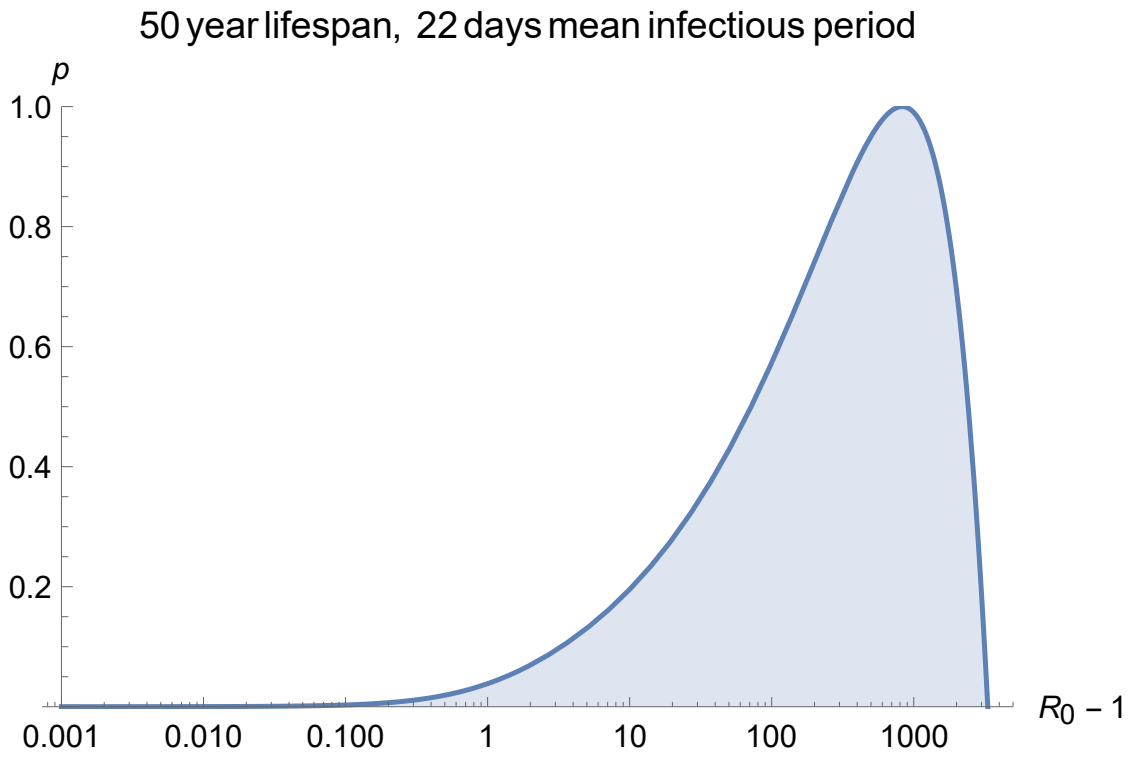
2.3.1 $\epsilon = \frac{7}{18257}$

Figure 1:



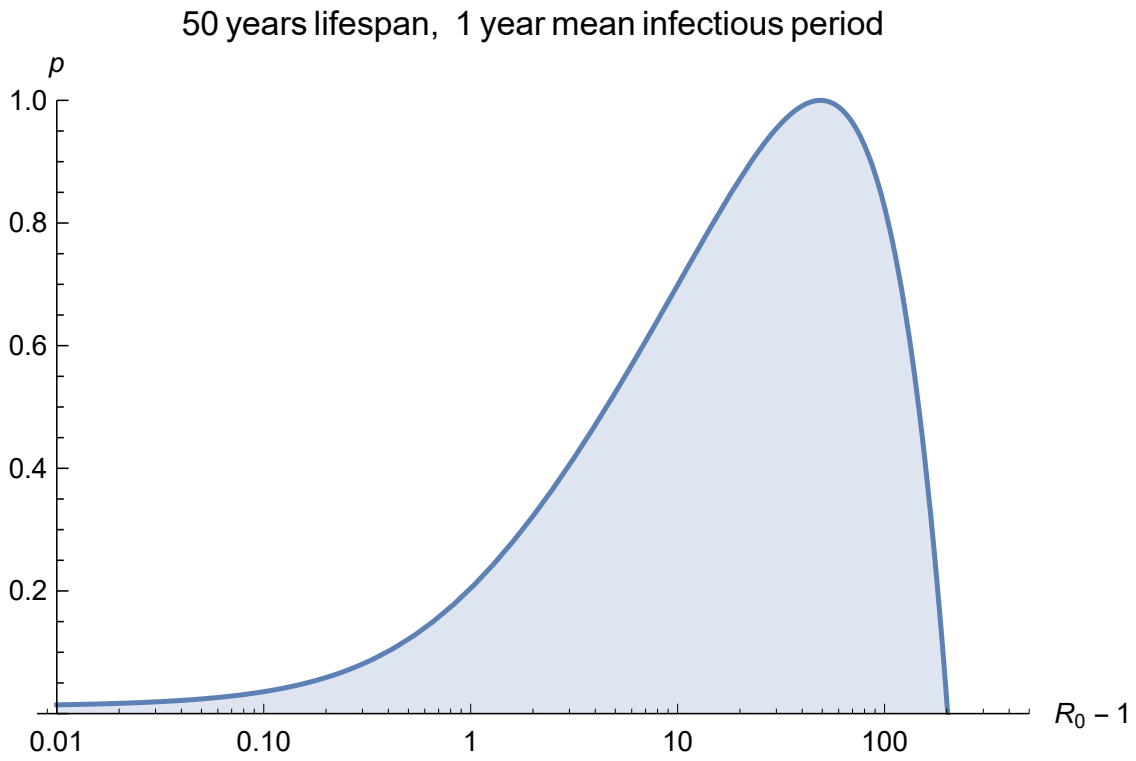
2.3.2 $\epsilon = \frac{11}{9136}$

Figure 2:



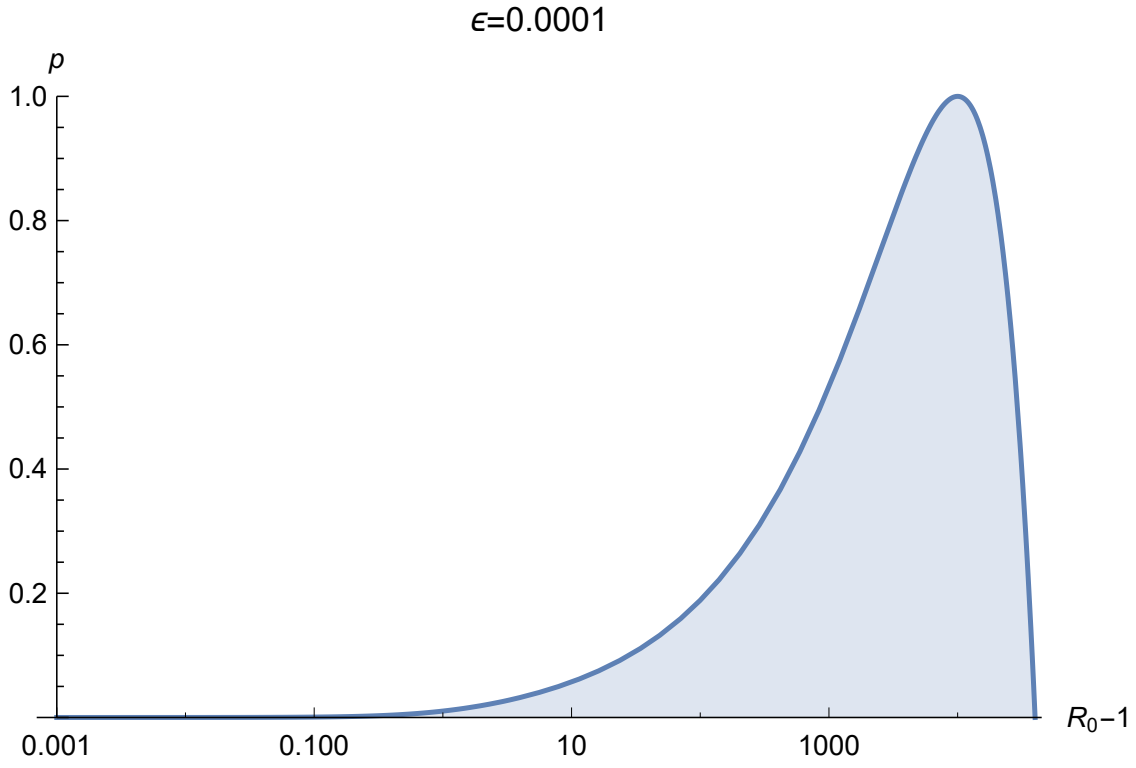
2.3.3 $\epsilon = \frac{1}{51}$

Figure 3:



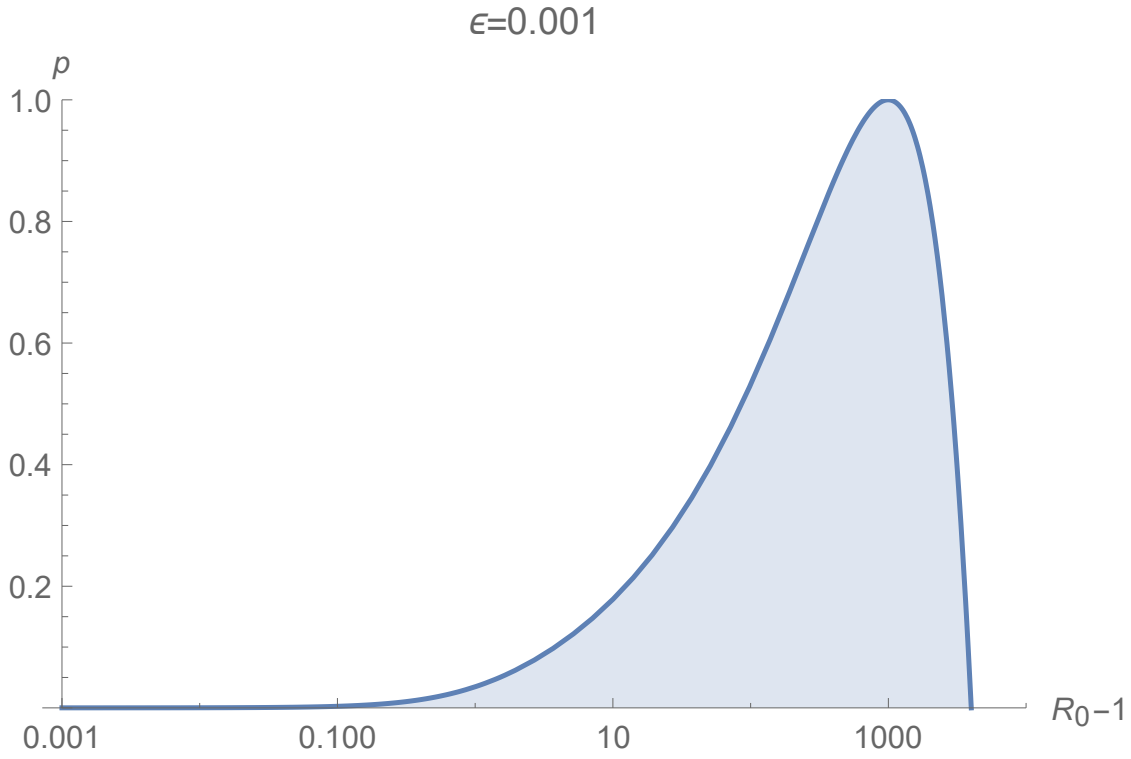
2.3.4 $\epsilon = \frac{1}{10000}$

Figure 4:



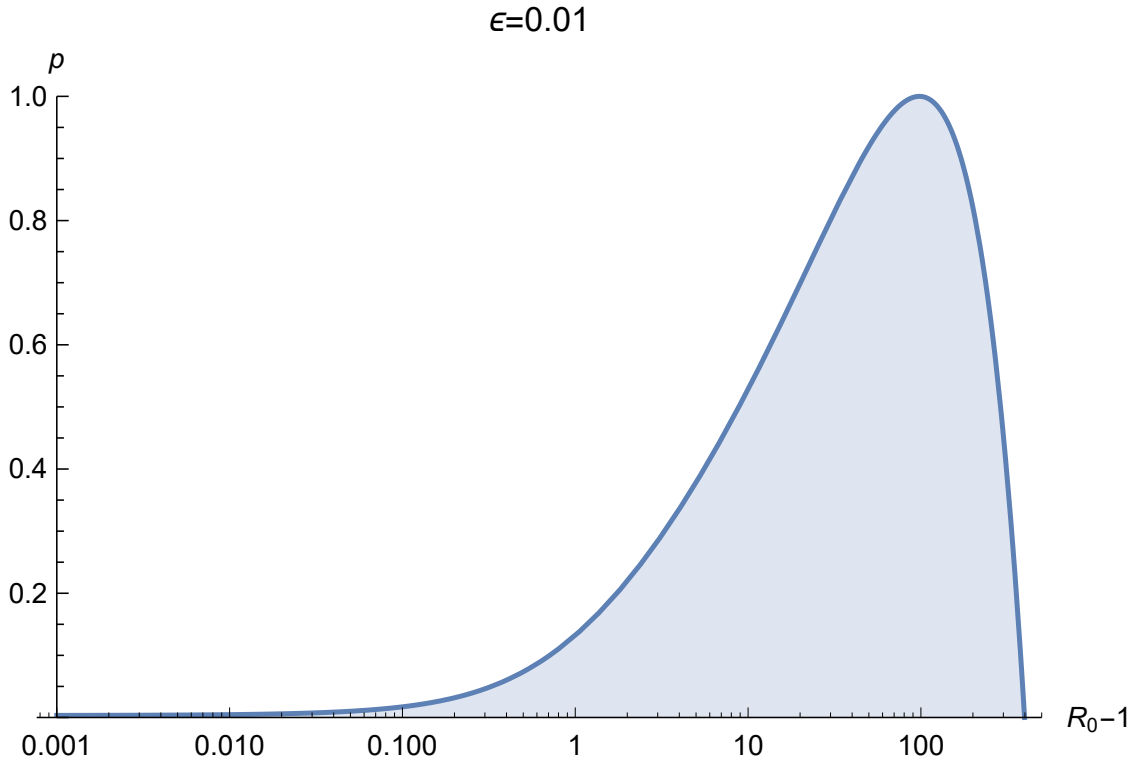
2.3.5 $\epsilon = \frac{1}{1000}$

Figure 5:



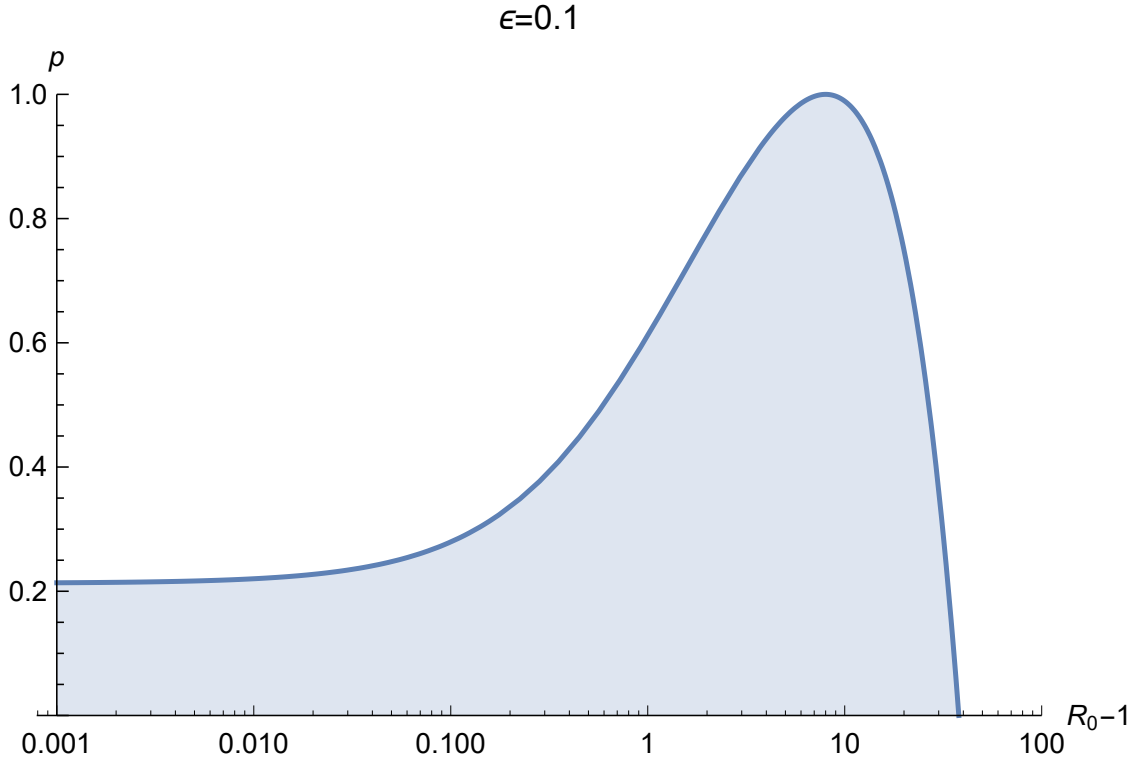
2.3.6 $\epsilon = \frac{1}{100}$

Figure 6:



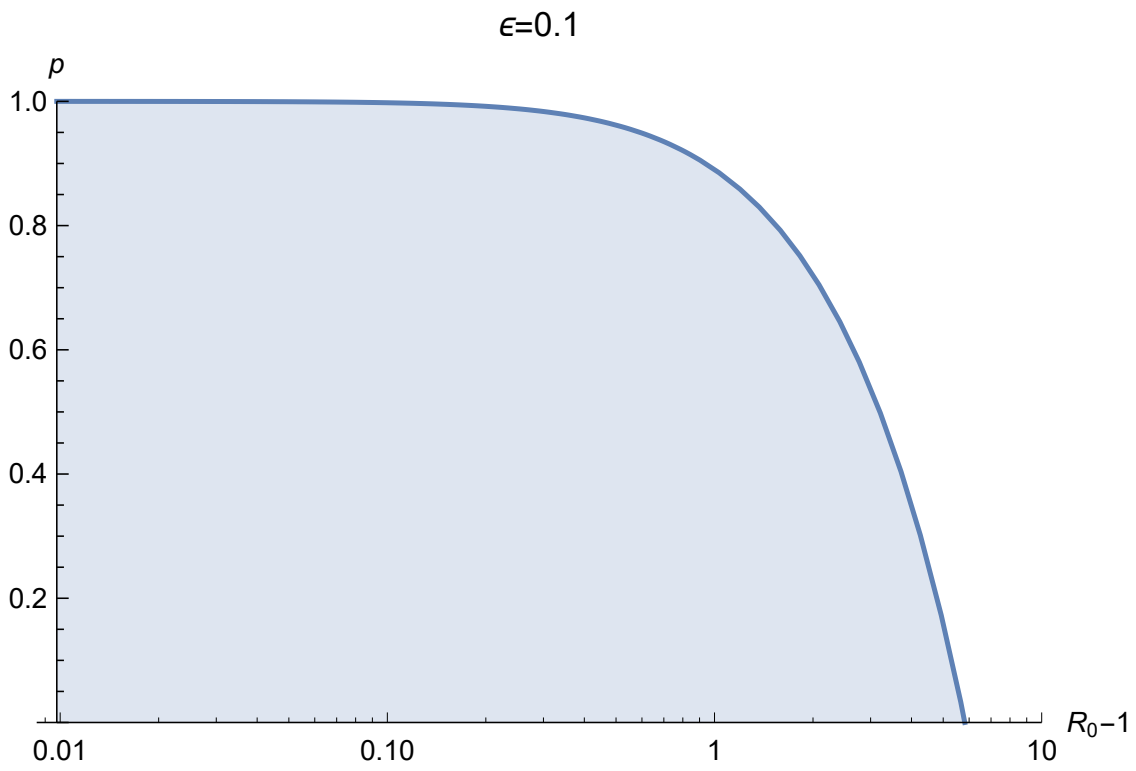
2.3.7 $\epsilon = \frac{1}{10}$

Figure 7:



2.3.8 $\epsilon = 0.5$

Figure 8:

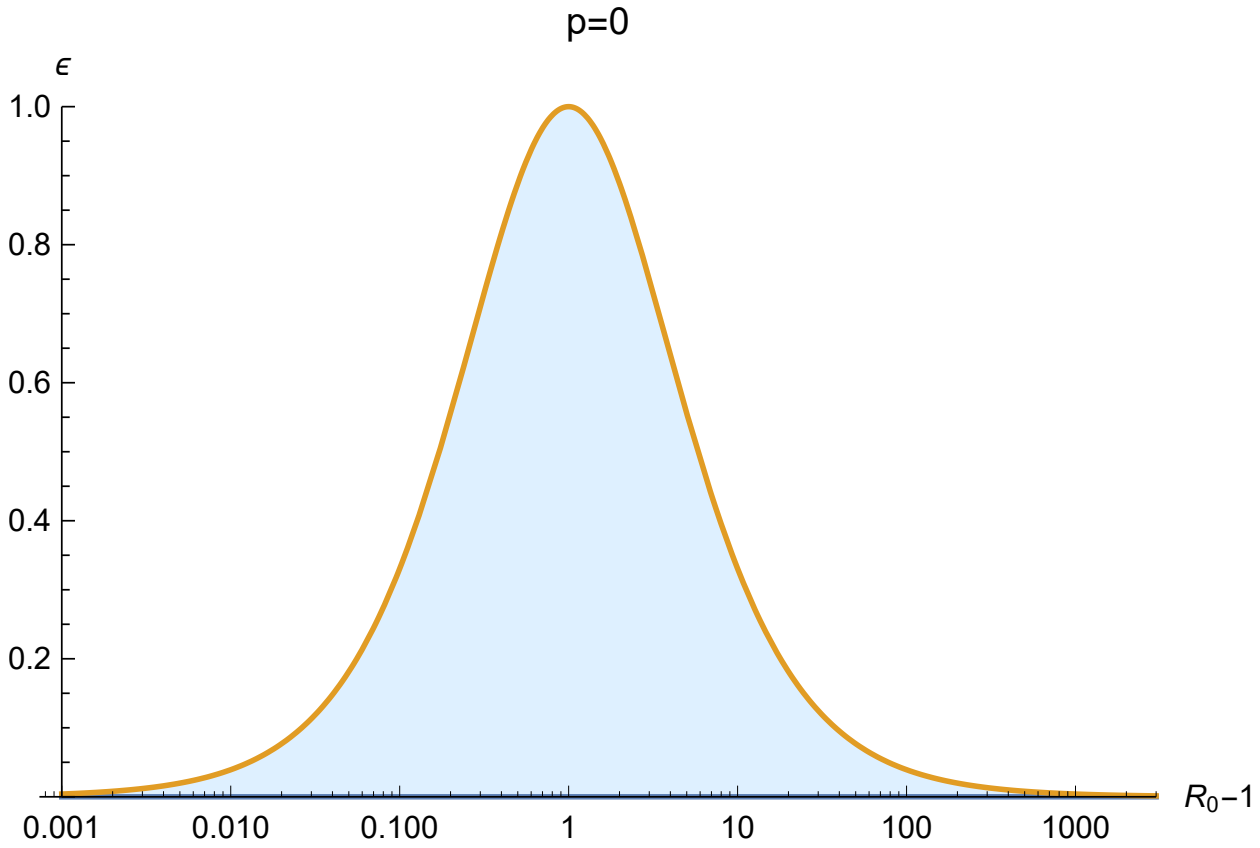


2.4 Region of $(\mathcal{R}_0, \epsilon)$ plane where there are damped oscillations (fixed p)

Again, I made plots with different p in increasing order, the shade area between the blue curve and the orange curve represent the region where the system has damped oscillation.

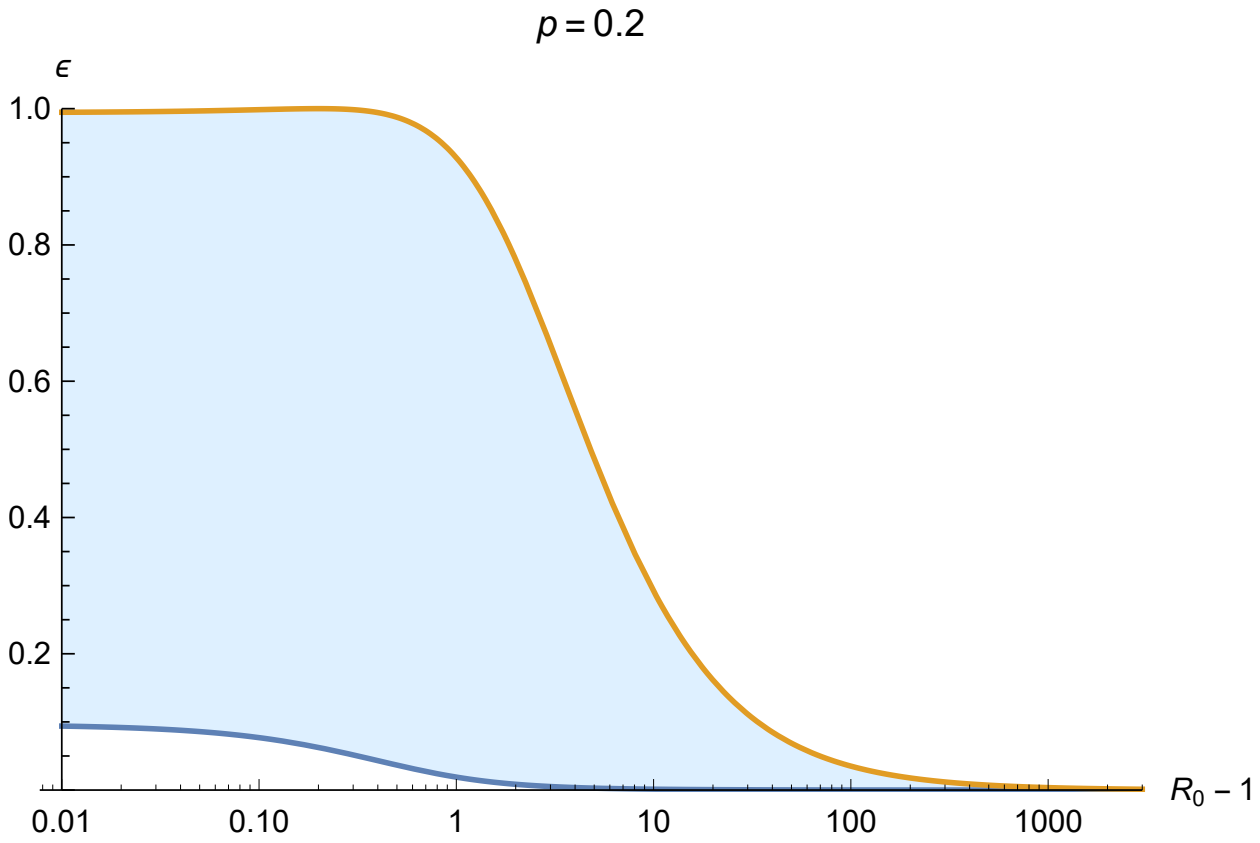
2.4.1 $p = 0$

Figure 9:



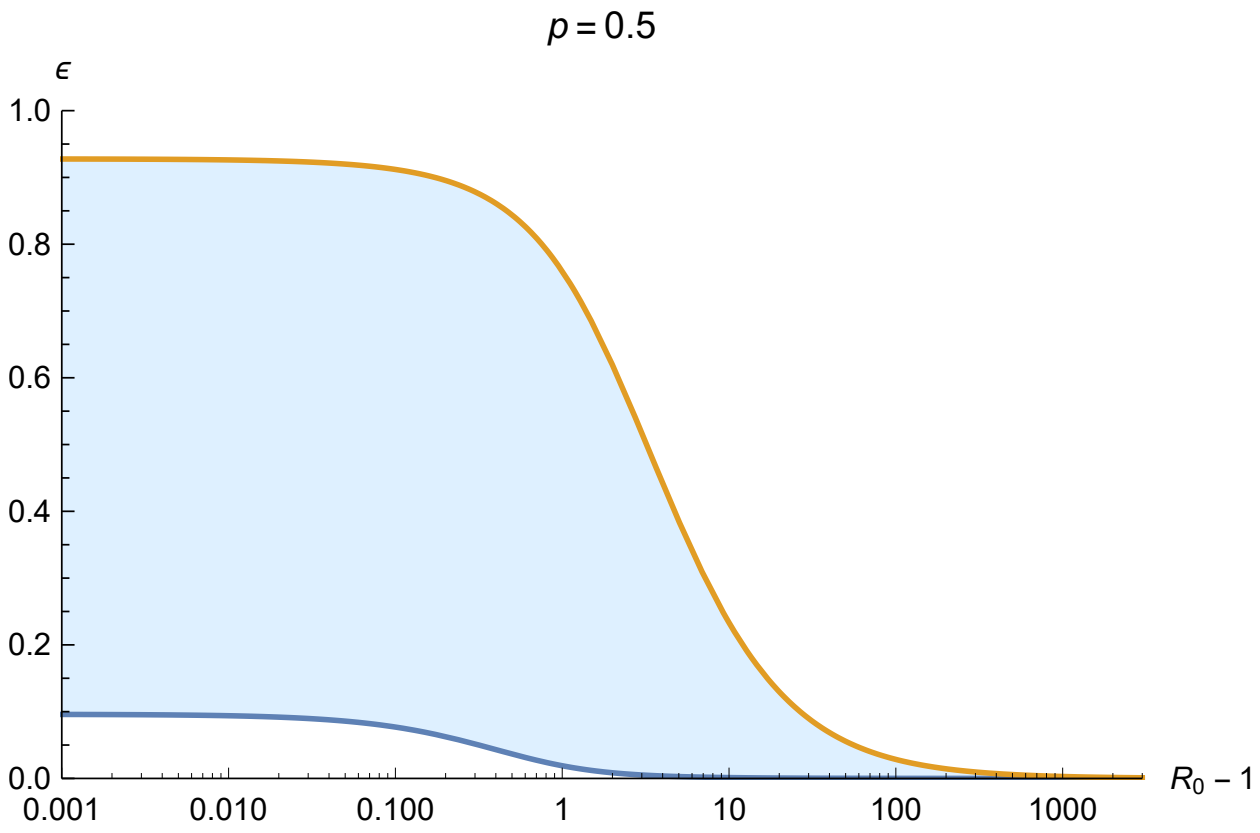
2.4.2 $p = 0.2$

Figure 10:



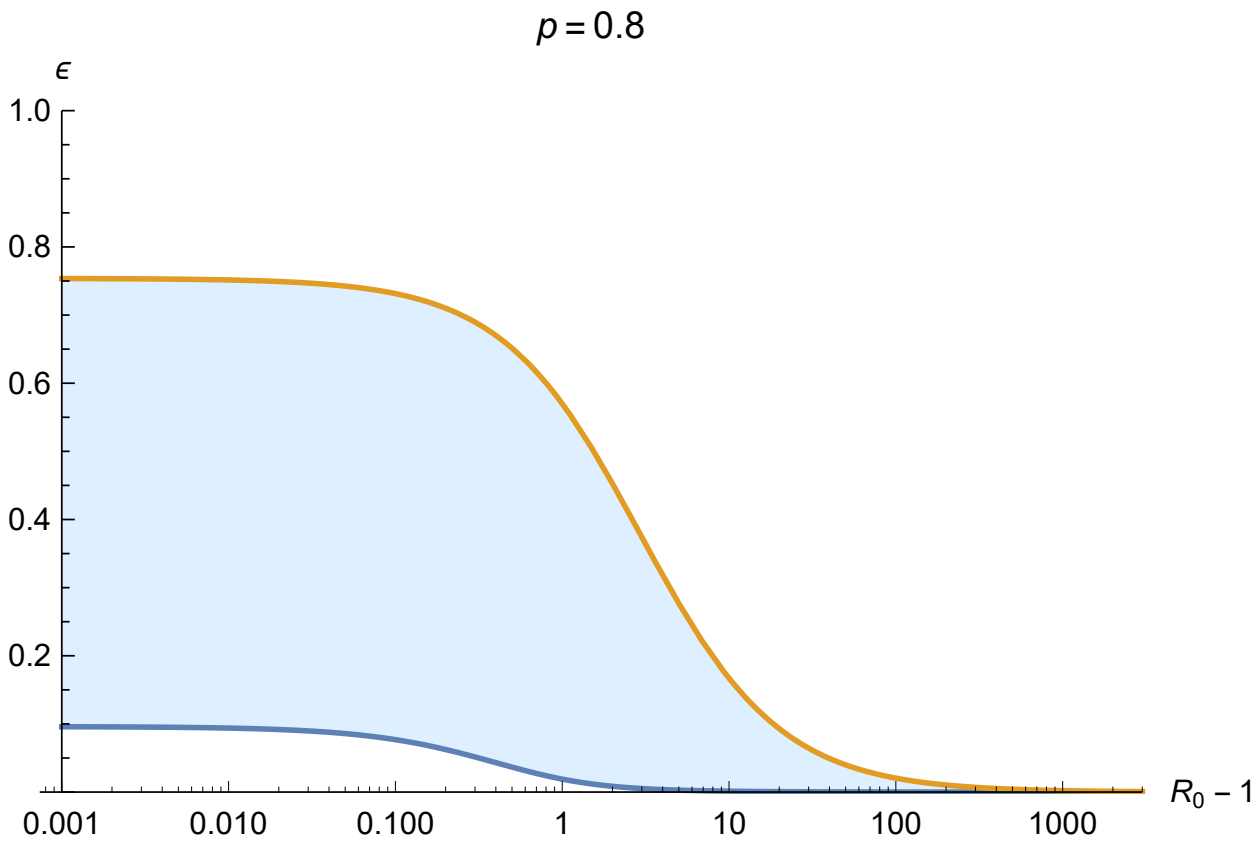
2.4.3 $p = 0.5$

Figure 11:



2.4.4 $p = 0.8$

Figure 12:



2.5 Comments and discussion on this model

This is the initial model of intentional infection on newborns, compare to vaccination model, the main difference is the direction of flow of the individuals being treated with intentional infection or vaccination. Intentionally infected individuals are capable of transmitting the disease to susceptible individuals, whereas the vaccinated individuals will enter R directly, therefore not able to impact the dynamics of the system anymore.

In ideal cases, once an individual is intentionally infected, either directly or infected by others of the same kind, this individual will not be naturally infected anymore. Therefore, we should divide infected compartment into 2 new groups, namely, intentionally infected cases and naturally infected cases.

In the past, people believed that individuals that are intentionally infected die less often, in comparison with naturally infected cases. Here we define "advantageous" by fewer total death. More specifically, we would be comparing total disease induced mortality. Therefore, we need to involve a new parameter, namely, case fatality proportion.

3 Model: Addition of disease induced mortality

3.1 System of differential equations

Historic application of variolation have shown a lower case fatality proportion, compared to being naturally infected. Therefore, we need to assign different case fatality proportion to each classes. This also requires us to divide I from our previous model into two distinct infective classes. Here, we call them "Intentionally infected" (V) and "Naturally infected" (I).

In this model, we still assume no latent period, and similar to the last assumption in our previous model, we assume that all individuals in the same infective class are equally

infectious.

Therefore, our model becomes,

$$\begin{aligned}
\frac{\mathrm{d}S}{\mathrm{d}t} &= \mu(1-p) - \beta S(V+I) - \mu S\,, \\
\frac{\mathrm{d}V}{\mathrm{d}t} &= \beta SV + \mu p - \gamma V - \mu V\,, \\
\frac{\mathrm{d}I}{\mathrm{d}t} &= \beta SI - \gamma I - \mu I\,, \\
\frac{\mathrm{d}M}{\mathrm{d}t} &= p_V \gamma V + p_I \gamma I\,, \\
\frac{\mathrm{d}R}{\mathrm{d}t} &= (1-p_V)\gamma V + (1-p_I)\gamma I - \mu R\,.
\end{aligned} \tag{11}$$

In addition to the previous model, p_V and p_I represent the case fatality proportion for intentionally infected and naturally infected cases, respectively.

Again, we non-dimensionalize Equation 11 by time, by

$$\tau = (\gamma + \mu)t\,, \tag{12}$$

which yields,

$$\frac{\mathrm{d}S}{\mathrm{d}\tau} = \epsilon(1-p) - \mathcal{R}_0 S(V+I) - \epsilon S\,, \tag{13a}$$

$$\frac{\mathrm{d}V}{\mathrm{d}\tau} = \mathcal{R}_0 SV + \epsilon p - V\,, \tag{13b}$$

$$\frac{\mathrm{d}I}{\mathrm{d}\tau} = \mathcal{R}_0 SI - I\,, \tag{13c}$$

$$\frac{\mathrm{d}M}{\mathrm{d}\tau} = p_V(1-\epsilon)V + p_I(1-\epsilon)I\,, \tag{13d}$$

$$\frac{\mathrm{d}R}{\mathrm{d}\tau} = (1-p_V)(1-\epsilon)V + (1-p_I)(1-\epsilon)I - \epsilon R\,, \tag{13e}$$

3.2 Equilibria

By letting Equation 13a, Equation 13b and Equation 13c equal to 0, we solve for solutions.

If $p = 0$, meaning there is no intentional infection, our system reduces to the standard SIR model.

There are two equilibriums for the standard SIR model, an Endemic equilibrium,

$$\hat{S} = \frac{1}{\mathcal{R}_0}\,, \tag{14a}$$

$$\hat{V} = 0\,, \tag{14b}$$

$$\hat{I} = \epsilon(1 - \frac{1}{\mathcal{R}_0})\,. \tag{14c}$$

And a disease free equilibrium(since both $\hat{V}$ and $\hat{I}$ are 0),

$$\hat{S} = 1\,, \tag{15a}$$

$$\hat{V} = 0\,, \tag{15b}$$

$$\hat{I} = 0\,. \tag{15c}$$

However, if $p \neq 0$, the equilibrium is,

$$\hat{S} = \frac{1}{\mathcal{R}_0} - \frac{2p}{(\mathcal{R}_0 - 1) + \sqrt{(\mathcal{R}_0 - 1)^2 + 4\mathcal{R}_0 p}}\,, \tag{16a}$$

$$\hat{V} = \frac{\epsilon(\mathcal{R}_0 - 1) + \epsilon\sqrt{(\mathcal{R}_0 - 1)^2 + 4\mathcal{R}_0 p}}{2\mathcal{R}_0}\,, \tag{16b}$$

$$\hat{I} = 0\,. \tag{16c}$$

Since $\hat{V} \neq 0$, for any p between 0 and 1, this equilibrium is not disease free. It follows that this equilibrium is the endemic equilibrium.

Stability analysis relies on Jacobian matrix, which is,

$$\mathcal{J} = \begin{bmatrix} -\mathcal{R}_0(V + I) - \epsilon & -\mathcal{R}_0 S & -\mathcal{R}_0 S \\ \mathcal{R}_0 V & \mathcal{R}_0 S - 1 & 0 \\ \mathcal{R}_0 I & 0 & \mathcal{R}_0 S - 1 \end{bmatrix}. \tag{17}$$

Eigenvalues of Jacobian are given as follow,

$$\lambda_1 = -1 + \mathcal{R}_0 S \tag{18a}$$

$$\lambda_2 = \frac{-1 + \mathcal{R}_0 S - \epsilon - \mathcal{R}_0 V - \sqrt{(-1 + \mathcal{R}_0 S - \epsilon - \mathcal{R}_0 V)^2 - 4(\mathcal{R}_0 + \epsilon - \mathcal{R}_0 S\epsilon)}}{2} \tag{18b}$$

$$\lambda_3 = \frac{-1 + \mathcal{R}_0 S - \epsilon - \mathcal{R}_0 V + \sqrt{(-1 + \mathcal{R}_0 S - \epsilon - \mathcal{R}_0 V)^2 - 4(\mathcal{R}_0 + \epsilon - \mathcal{R}_0 S\epsilon)}}{2} \tag{18c}$$

By using Equation 16a and Equation 18a, we obtain

$$-1+\mathcal{R}_0 S=-\frac{2p\mathcal{R}_0}{(\mathcal{R}_0-1)+\sqrt{(\mathcal{R}_0-1)^2+4\mathcal{R}_0 p}}<0 \tag{19}$$

Therefore,

$$\Re(\lambda_1)=-1+\mathcal{R}_0 S<0\,, \tag{20}$$

To determine the real part of λ_2 and λ_3, we need to determine the sign of the quantity under the square root.

By using Equation 16a again, we have

$$\mathcal{R}_0 S\epsilon<\epsilon\,, \tag{21}$$

Therefore,

$$(\mathcal{R}_0+\epsilon-\mathcal{R}_0 S\epsilon)>\mathcal{R}_0>0\,, \tag{22}$$

which means, if the sign of the quantity under the square root is positive, we will have

$$\sqrt{(-1+\mathcal{R}_0 S-\epsilon-\mathcal{R}_0 V)^2-4(\mathcal{R}_0+\epsilon-\mathcal{R}_0 S\epsilon)}<|(-1+\mathcal{R}_0 S-\epsilon-\mathcal{R}_0 V)| \tag{23}$$

Therefore, $\Re(\lambda_2)<\Re(\lambda_3)<0$.

Certainly, if the sign of the quantity under the square root is negative,

$$\Re(\lambda_2)=\Re(\lambda_3)=-1+\mathcal{R}_0 S-\epsilon-\mathcal{R}_0 V<0 \tag{24}$$

We are able to conclude that EE is stable.

3.3 Effect of intentional infection on total mortality

In epidemic analysis, one way of measuring whether a certain method is more advantageous than another is to compare the total disease induced mortality.

We first take a look at the mortality rate at EE,

$$\frac{\mathrm{d}M}{\mathrm{d}\tau}|_{EE}=p_V(1-\epsilon)V=\frac{p_V(1-\epsilon)\epsilon(\mathcal{R}_0-1)+p_V(1-\epsilon)\epsilon\sqrt{(\mathcal{R}_0-1)^2+4\mathcal{R}_0 p}}{2\mathcal{R}_0}\,, \tag{25}$$

An important observation is, at EE, mortality rate increases as p increases. This tells us, in the long run, having a larger proportion of intentional infection is unwise, since it leads extra deaths.

In history, smallpox was present in human population long before variolation was invented. When variolation was introduced, the population was already near equilibrium, with no intentional infection($p = 0$). We are interested in the scenario where intentional infection is introduced after the population is in equilibrium, with no intentional infection.

One of the questions we want to answer is how long does it take for our system to reach the new EE. In fact the system will only infinitely approach the equilibrium instead of reaching it, therefore we need to define a threshold, which mean, how close does it need to be away from the equilibrium, do we consider it being at the equilibrium.

Since the new equilibrium has $\hat{I} = 0$, we define reaching equilibrium by $I \leq 1 \times 10^{-6}$ (one in a million).

In fact, if the case fatality proportion for intentionally infected cases is 1%, we can hardly observe any difference between different proportion of intentional infection. To help us observe the dynamics better, we assume intentional infection has a 20% case fatality proportion.

by plotting, we obtain Figure 13, we can see that it takes shorter time to reach the new EE for a larger proportion of intentional infection.

We are also interested in the time it takes for intentional infection to be more advantageous than non-intentional infection, by comparing total mortality.

From previous analysis, we learned that $\frac{\mathrm{d}M}{\mathrm{d}\tau}$ decreases over time, and stabilizes at a constant rate when reaching the new EE. But at the new EE, $\frac{\mathrm{d}M}{\mathrm{d}\tau}$ is higher when p is higher.

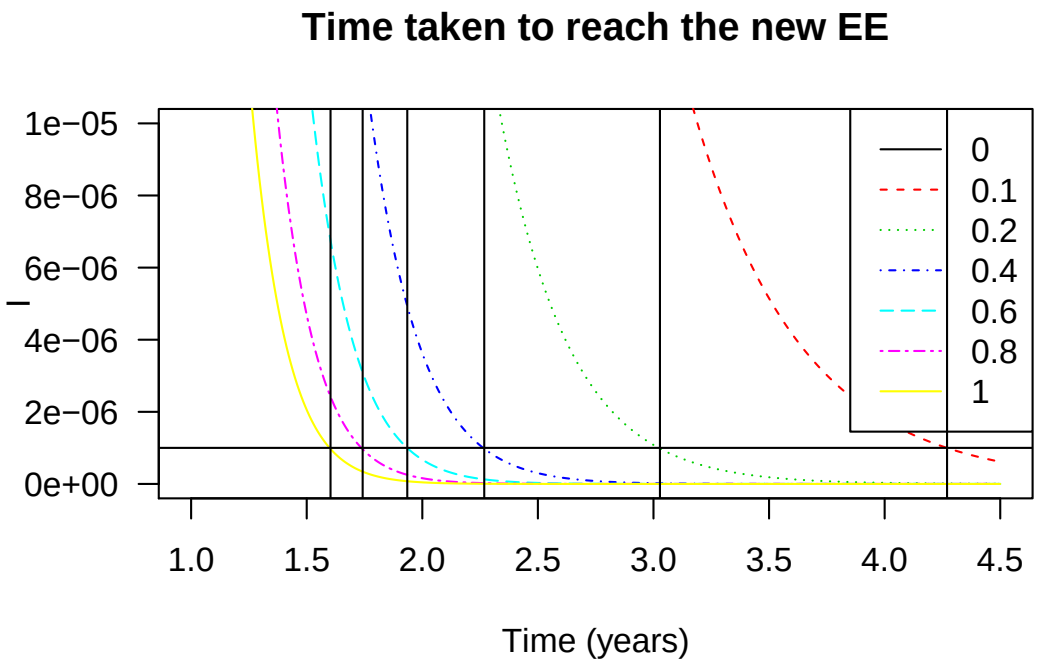


Figure 13: Determination of time taken to reach equilibrium

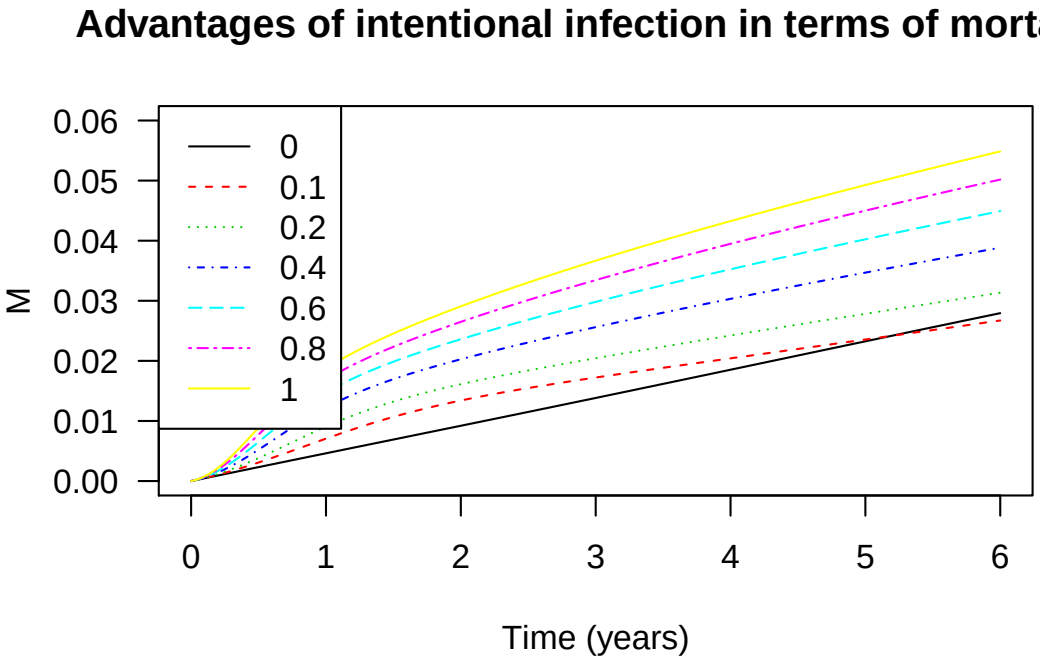


Figure 14: An illustration of intentional infection have advantages over non-intentional infection

Figure 14 shows, at earlier times, intentional infections have steeper slopes than the black line, which is non-intentional infection. The slopes for intentional infection decreases over time, and eventually intentional infection with any proportion will have fewer total death than non-intentional infection.

Table 2 summarize the times required to reach the new EE and time required to have advantages over non-intentional infection.

Table 2: Time required to reach equilibrium and have advantages over non-intentional infection

p	**Time to EE**	**Time to have advantages**
0.1	4.27 yrs	5.20 yrs
0.2	3.03 yrs	8.81 yrs
0.4	2.27 yrs	17.45 yrs
0.6	1.94 yrs	28.37 yrs
0.8	1.74 yrs	42.43 yrs
1.0	1.60 yrs	61.46 yrs

The table showed that as p increases, the system reaches the new EE faster, but the time required to have advantages over non-intentional infection increase.

In fact, if $p_V = 0.01$, then the time required to have advantages over non-intentional infection is minimal, and the difference between different p is also insignificant on a scale of years.

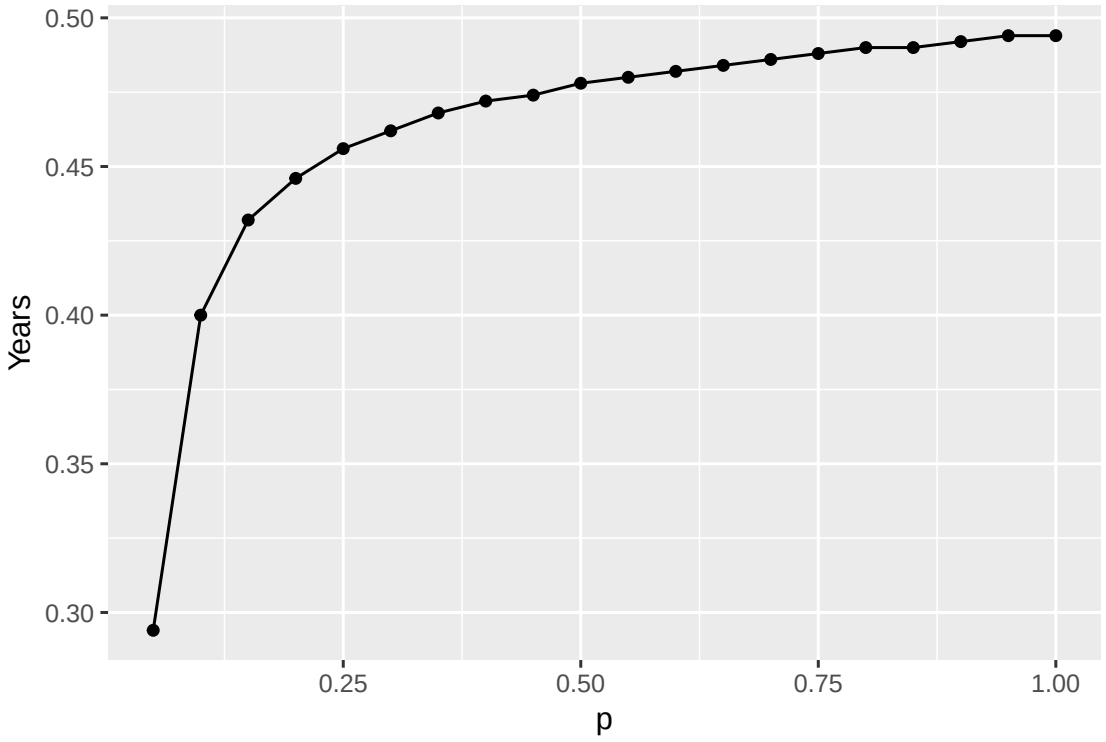


Figure 15: Time to advantage, as a function of p

Figure 15 shows us a relationship between time to advantage and p.

Here it shows, with a lower proportion of intentional infection, we gain advantage relatively faster. This conclusion is misleading, because it is suggesting that, with a minimal proportion of intentional infection, we can minimize the time it takes to gain advantage.

We found that, if p is small, though it gains advantage faster, the number of deaths actually stays very close to non-intentional infection. In another word, the advantage is very insignificant.

Therefore, we want to suggest that, we can define a method being "More advantageous" than another to be: mortality by intentional infection is at least 10% lower than mortality with no intentional infection.

Figure 16: Time for mortality of intentional infection is at least 10% lower than non-intentional infection

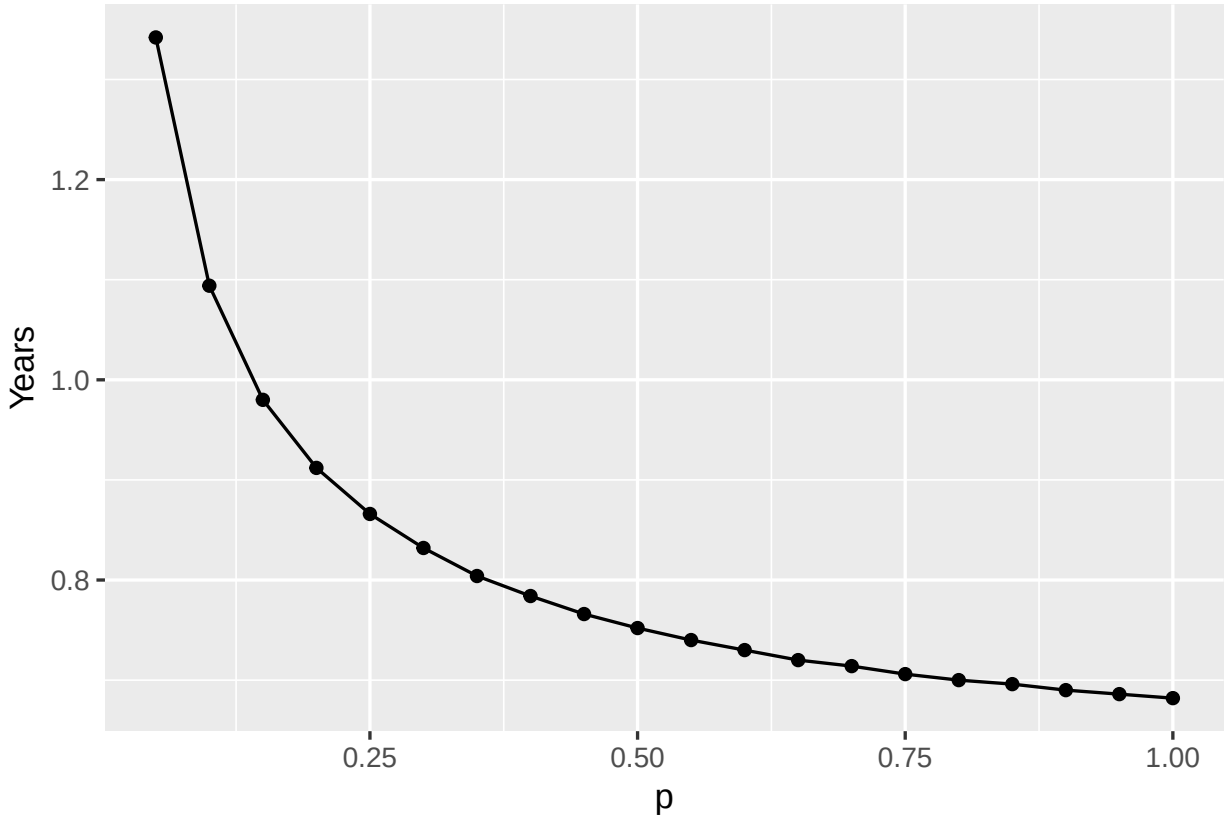


Figure 16 suggests, under our new definition of "Have advantage", the situation is reversed and larger proportion of intentional infection can be more advantageous relatively faster.

3.4 Comments and discussion on this model

In this model, we have shown that intentional infection has advantages over non-intentional infection in terms of total mortality. However, interestingly, since a larger p will lead to more death in the long run. Though a larger proportion of intentional infection can reduce total death and become more advantageous than non-intentional infection faster, it is unwise to keep infecting such a larger proportion of newborns.

To summarize the above argument, if our strategy of intentional infection remain the same at all time, then in the long run, with a minimal proportion of intentional infection, total mortality could be minimized. However, in real life scenario, strategy does not need to be constant, it may be possible to intentionally infect at a relatively higher proportion initially, and decrease the proportion, or even stop intentional infection, with a combination of strategies like that, we could possibly minimize the total mortality. Or even eradicate the disease.

Other than strategic evolvement, there could still be some development to the model itself to make it more suitable to a realistic scenario. Since Intentional infection has a lower death rate, we could assume a milder symptom for intentionally infected cases. As a result, since aggressive symptoms are typical routes of disease transmission, lack of such pathways will lead to a decrease of transmission rate. Besides, intentionally and naturally infected cases could have different recovery rate. Therefore, our next model could consider various possibilities of these parameters, and draw conclusions to its behavior.

3.5 Possibility of eradication

If we define the disease been eradicated if the proportion of infected is less than one in a million. Then, our model is able to predict possible eradication of the disease.

At EE, $I = 0$, although I is going to approach 0 asymptotically, it will never completely cease to exist. However, we know that there is a point in forward time where $I < 1 \times 10^{-6}$. Therefore, we can claim that naturally infected cases could be eradicated(we will show an example in the next section).

The next question would be whether it is possible for intentionally infected cases to burn out. After I being wiped out, we could stop intentional infecting any other newborns. From then on if $S < \frac{1}{\mathcal{R}_0}$ for a long enough period of time, which means the effective $\mathcal{R}_0$ is less than 1, we could possibly observe $V < 1 \times 10^{-6}$, which in return, represent the eradication of intentionally infected cases as well.

We use one example to illustrate the occurrence of such scenario. Assume we have $p = 1$ until we reach EE. We could calculate $\hat{S}$ and $\hat{I}$. Now if we set the initial condition being the $\hat{S}$ and $\hat{I}$ we just calculated, and let $p = 0$, we run the simulation and obtain the following,

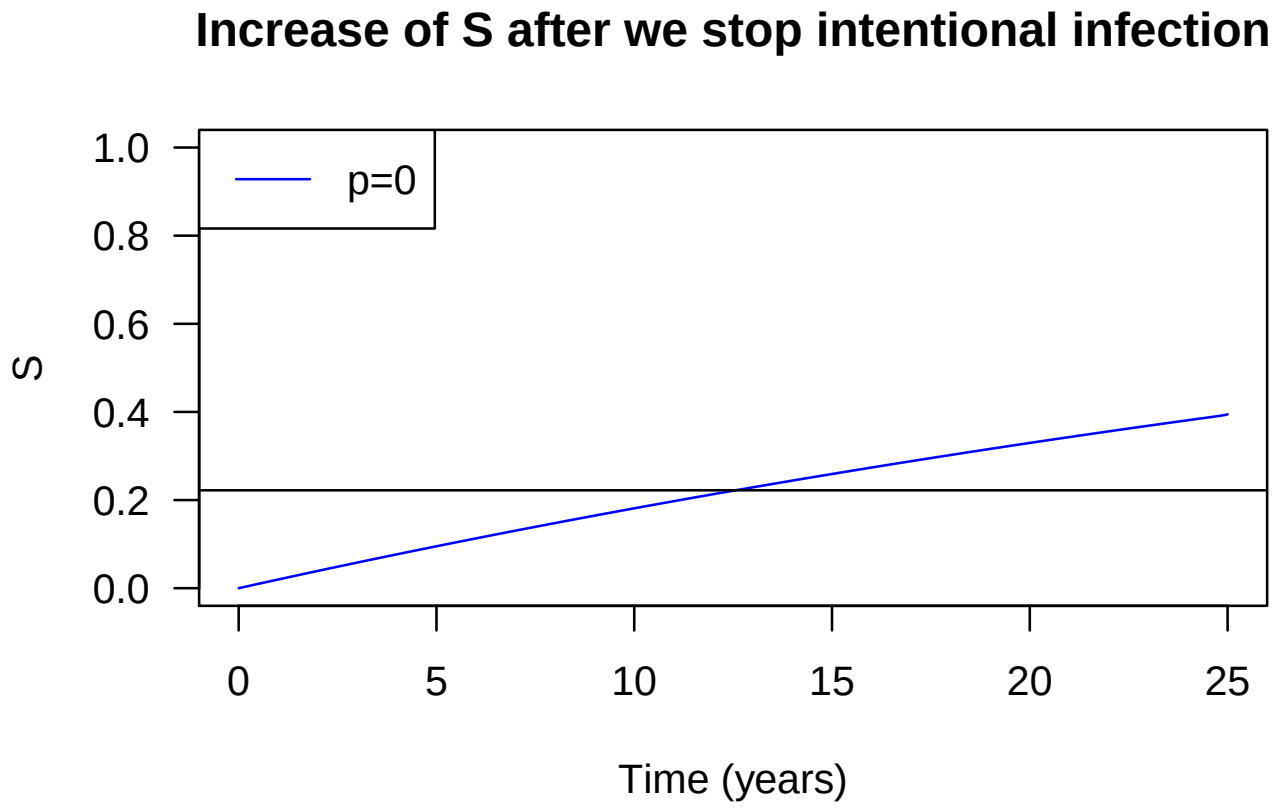


Figure 17: For more than 10 years after we stop intentional infection, $S < \frac{1}{\mathcal{R}_0}$

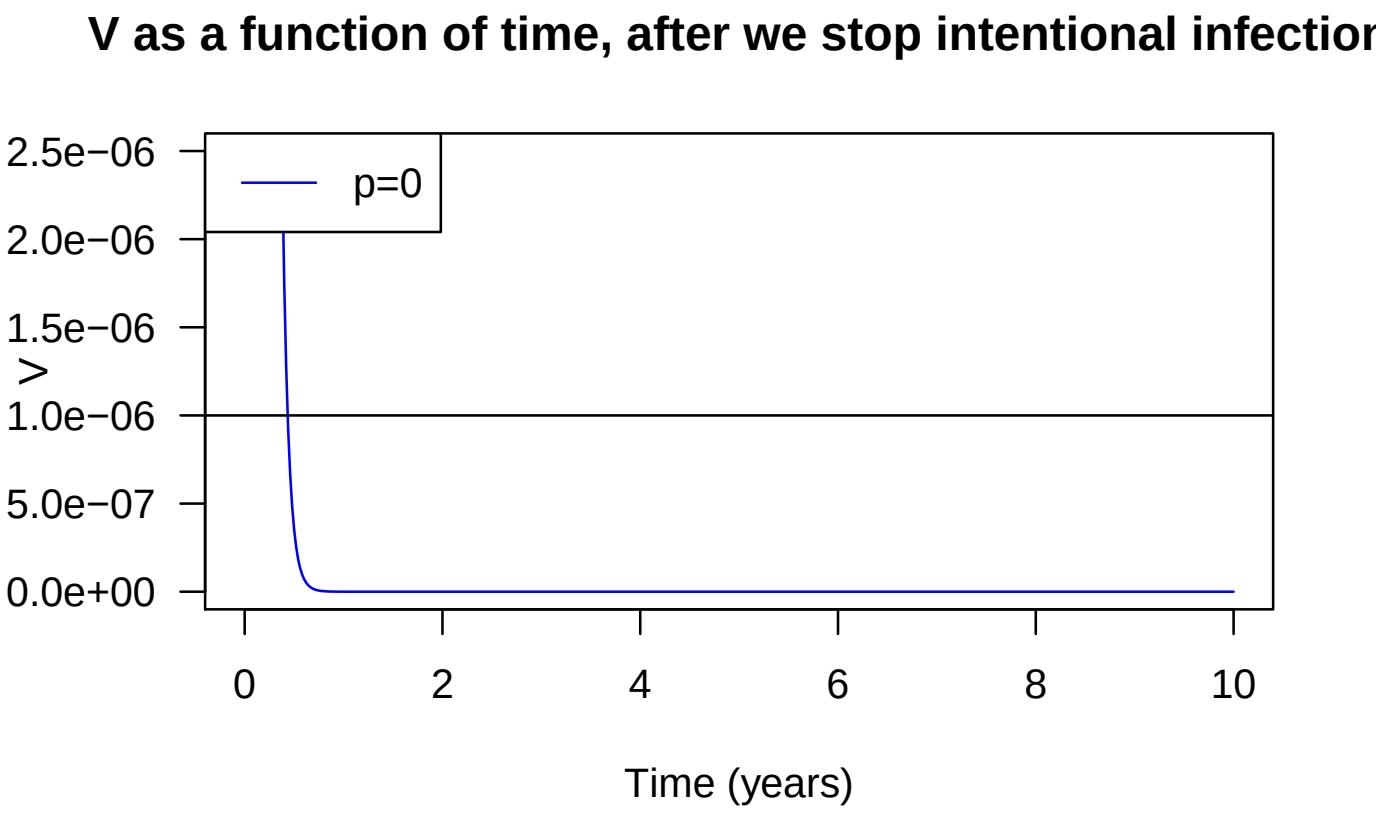


Figure 18: It takes less than 1 year for V to fall below 1×10^{-6}

Figure 17 and Figure 18 have shown an example of disease eradication, by our definition. Other values of p will still need to be investigated.

4 Model: Different transmission rate and recovery rate

4.1 System of differential equations

As we mentioned above, we need to involve new parameters for different transmission and recovery rate. Here, we let β_V and β_I represent the transmission rate of variolated cases and pathogen infected cases, respectively. γ_V and γ_I are the recovery rate of variolated cases and

pathogen infected cases, respectively.

With the new parameters in hand, we now setup our system of differential equation,

$$\begin{aligned}
\frac{\mathrm{d}S}{\mathrm{d}t} &= \mu(1-p) - \beta_V SV - \beta_I SI - \mu S\,, \\
\frac{\mathrm{d}V}{\mathrm{d}t} &= \beta_V SV + \mu p - \gamma_V V - \mu V\,, \\
\frac{\mathrm{d}I}{\mathrm{d}t} &= \beta_I SI - \gamma_I I - \mu I\,, \\
\frac{\mathrm{d}M}{\mathrm{d}t} &= p_V \gamma_V V + p_I \gamma_I I\,, \\
\frac{\mathrm{d}R}{\mathrm{d}t} &= (1-p_V)\gamma_V V + (1-p_I)\gamma_I I - \mu R\,,
\end{aligned} \tag{26}$$

We non-dimensionalize Equation 26 by scaling time, by

$$\tau = (\gamma_I + \mu)t\,, \tag{27}$$

As the result, we obtain,

$$\frac{\mathrm{d}S}{\mathrm{d}\tau} = \epsilon(1-p) - \mathcal{R}_{0,V} SV - \mathcal{R}_{0,I} SI - \epsilon S\,, \tag{28a}$$

$$\frac{\mathrm{d}V}{\mathrm{d}\tau} = \mathcal{R}_{0,V} SV + \epsilon p - \tilde{\gamma} V\,, \tag{28b}$$

$$\frac{\mathrm{d}I}{\mathrm{d}\tau} = \mathcal{R}_{0,I} SI - I\,, \tag{28c}$$

$$\frac{\mathrm{d}M}{\mathrm{d}\tau} = p_V(\tilde{\gamma} - \epsilon)V + p_I(1-\epsilon)I\,, \tag{28d}$$

$$\frac{\mathrm{d}R}{\mathrm{d}\tau} = (1-p_V)(\tilde{\gamma} - \epsilon)V + (1-p_I)(1-\epsilon)I - \epsilon R\,, \tag{28e}$$

Where $\mathcal{R}_{0,V} = \frac{\beta_V}{\gamma_I + \mu}$, $\mathcal{R}_{0,I} = \frac{\beta_I}{\gamma_I + \mu}$, $\tilde{\gamma} = \frac{\gamma_V + \mu}{\gamma_I + \mu}$, $\epsilon = \frac{\mu}{\gamma_I + \mu}$.

4.2 Equilibria

To solve for all equilibria, we let equations Equation 28a, Equation 28b and Equation 28c equal to 0, we solve for solutions.

We acquired three sets of solutions. However, given conditions that all $\hat{S}$, $\hat{V}$ and $\hat{I}$ have to be a non-negative number between 0 and 1, we can discard two of the solutions, and the

only set of solution left is,

$$\hat{S} = \frac{\mathcal{R}_{0,V} + \tilde{\gamma} - \sqrt{\mathcal{R}_{0,V}^2 - 2\mathcal{R}_{0,V}\tilde{\gamma} + \tilde{\gamma}^2 + 4p\mathcal{R}_{0,V}\tilde{\gamma}}}{2\mathcal{R}_{0,V}}\,, \tag{29a}$$

$$\hat{V} = \frac{\epsilon - \frac{\tilde{\gamma}\epsilon}{\mathcal{R}_{0,V}} + \frac{\epsilon\sqrt{\mathcal{R}_{0,V}^2 - 2\mathcal{R}_{0,V}\tilde{\gamma} + \tilde{\gamma}^2 + 4p\mathcal{R}_{0,V}\tilde{\gamma}}}{\mathcal{R}_{0,V}}}{2\tilde{\gamma}}\,, \tag{29b}$$

$$\hat{I} = 0\,, \tag{29c}$$

Similar to our previous models, since infected population at equilibrium is non-zero, this is not a disease free equilibrium but rather an endemic equilibrium.

Stability analysis rely on Jacobian Matrix,

$$\mathcal{J} = \begin{bmatrix} -\mathcal{R}_{0,V}V - \mathcal{R}_{0,I}I - \epsilon & -\mathcal{R}_{0,V}S & -\mathcal{R}_{0,I}S \\ \mathcal{R}_{0,V}V & \mathcal{R}_{0,V}S - \gamma & 0 \\ \mathcal{R}_{0,I}I & 0 & \mathcal{R}_{0,I}S - 1 \end{bmatrix}. \tag{30}$$

Eigenvalues of Jacobian are given as follow,

$$\lambda_1 = -1 + \mathcal{R}_{0,I}S \tag{31a}$$

$$\lambda_2 = \frac{-\tilde{\gamma} + \mathcal{R}_{0,V}S - \epsilon - \mathcal{R}_{0,V}V - \sqrt{(-\tilde{\gamma} + \mathcal{R}_{0,V}S - \epsilon - \mathcal{R}_{0,V}V)^2 - 4(\mathcal{R}_{0,V}\tilde{\gamma} + \epsilon\tilde{\gamma} - \mathcal{R}_{0,V}S\epsilon)}}{2} \tag{31b}$$

$$\lambda_3 = \frac{-\tilde{\gamma} + \mathcal{R}_{0,V}S - \epsilon - \mathcal{R}_{0,V}V + \sqrt{(-\tilde{\gamma} + \mathcal{R}_{0,V}S - \epsilon - \mathcal{R}_{0,V}V)^2 - 4(\mathcal{R}_{0,V}\tilde{\gamma} + \epsilon\tilde{\gamma} - \mathcal{R}_{0,V}S\epsilon)}}{2} \tag{31c}$$

By using Equation 29a, we know that

$$0 \leq S \leq \frac{\tilde{\gamma}}{\mathcal{R}_{0,V}}\,. \tag{32}$$

Therefore,

$$\Re(\lambda_1) < 0 \tag{33}$$

iff

$$\frac{\tilde{\gamma}}{\mathcal{R}_{0,V}} < \frac{1}{\mathcal{R}_{0,I}} \tag{34}$$

Or equivalently

$$\frac{\beta_V}{\beta_I} < \tilde{\gamma}^2 \tag{35}$$

Intuitively, if recovery rate are similar for variolated and normally infected cases, i.e. $\tilde{\gamma} \approx 1$, the endemic equilibrium is unstable if $\mathcal{R}_{0,V} < \mathcal{R}_{0,I}$

For the real part of λ_2 and λ_3, first we look at the terms before square root.

By using Equation 32, we have

$$-\tilde{\gamma} + \mathcal{R}_{0,V} S - \epsilon - \mathcal{R}_{0,V} V < 0\,, \tag{36}$$

Therefore,

$$\Re(\lambda_2) < -\tilde{\gamma} + \mathcal{R}_{0,V} S - \epsilon - \mathcal{R}_{0,V} V < 0\,, \tag{37}$$

Next, notice

$$\mathcal{R}_{0,V}\tilde{\gamma} + \epsilon\tilde{\gamma} - \mathcal{R}_{0,V} S\epsilon > 0\,. \tag{38}$$

It follows that

$$\sqrt{(-\tilde{\gamma} + \mathcal{R}_{0,V} S - \epsilon - \mathcal{R}_{0,V} V)^2 - 4(\mathcal{R}_{0,V}\tilde{\gamma} + \epsilon\tilde{\gamma} - \mathcal{R}_{0,V} S\epsilon)} < |-\tilde{\gamma} + \mathcal{R}_{0,V} S - \epsilon - \mathcal{R}_{0,V} V| \tag{39}$$

Therefore, $\Re(\lambda_3) < 0$.

As a result, we cannot directly conclude the stability of EE, but we have observed that stability depends on $\tilde{\gamma}$ and $\mathcal{R}_{0,I}$

4.3 Comments and discussion on this model

Parameters of this model such as $\mathcal{R}_{0,V}$ and γ_V are custom to the design of pathogen used for intentional infection.

Previous study have shown that, for a similar model which does not consider death, a significant decrease in final size is expected, for a transmissible vaccine, even when $\mathcal{R}_{0,V}$ is less than 1, e.g. $\mathcal{R}_{0,V} = 0.5$, we would expect similar results for our model, the difference

is, with the addition of birth and death rate, since our system have shown that the disease cannot be completely eradicated, there will always be newly infected cases, therefore, we do not have a final size estimation.

5 Future work

This section elaborates some ideas for future use and needs to be investigated later.

- Comparison between intentional infection and traditional vaccine, which does not transmit. This is for showing intentional infection as a more effective method to vaccinate.