Intentional infection as a method of population-level disease control

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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 would give them a higher chance of survival than by being naturally infected. This paper aims to provide mathematical models which describes the dynamics of infected classes, when intentional infection is introduced on a population level, and perform predictions based on the models.

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1 Introduction

Disease control has drawn people's attention since the early age of human civilization. Other than curing diseases by medication, people have also discovered and attempted a vast range of method for disease prevention. Nowadays, people have vaccination as a primary method to protect the population [1]. However, before vaccination became a developed technology, people had limited power when encountering fatal diseases such as smallpox.

A practice called variolation was invented as an attempt to contain smallpox [2]. The earliest record of such method can be found in 15th century's ancient Chinese documentation [3]. It is a method used to immunize individuals against smallpox, with materials taken from other smallpox patient or recently variolated individuals. People have found that, by variolation, a mild, but protective infection will likely occur [3]. Instead of having a considerable chance of becoming gravely ill, a vast majority of variolated cases will survive after an infection. As a result, variolated individuals die much less often.

More generally speaking, a similar method may be applied to other diseases for disease control as well. Fundamentally speaking, variolation is an example of intentional infection, since individuals are deliberately exposed living virus. Although an individual benefits from intentional infection when there is threat of being transmitted with fatal disease, people did not understand whether intentional infection can also bring positive effects when applied on a population level.

Similar to vaccination, there are different strategies for variolation. One example of strategies is to intentional infect newborn individuals. In fact, newborn infection does not mean instant infection when people are born, but rather after their maternal immunity wanes. Another strategy we consider in this paper is to intentionally infect susceptible individuals in the population, at a certain rate.

2 Models: Intentional infect proportion of Newborn

2.1 Model: Modification to SIR model

2.1.1 System of differential equations

We begin our analysis by modifying the 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 (Disease induced mortality will be introduced in the later models).
- 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.

2.1.2 Equilibria

By setting 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 the discriminant analytically, we can plot the value of the 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

2.1.3 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.

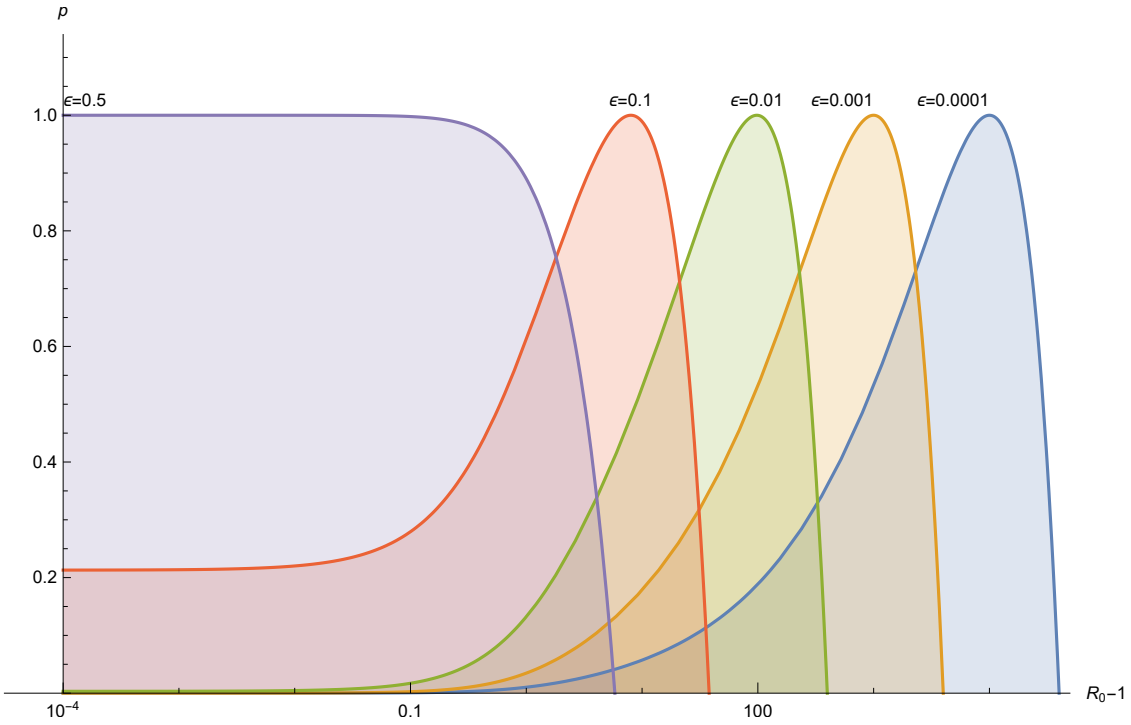

Figure 1: The areas under each curves, which are shaded in different color, represent the region of damped oscillations, with respect to different ϵ values.

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

The plots below were made 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.

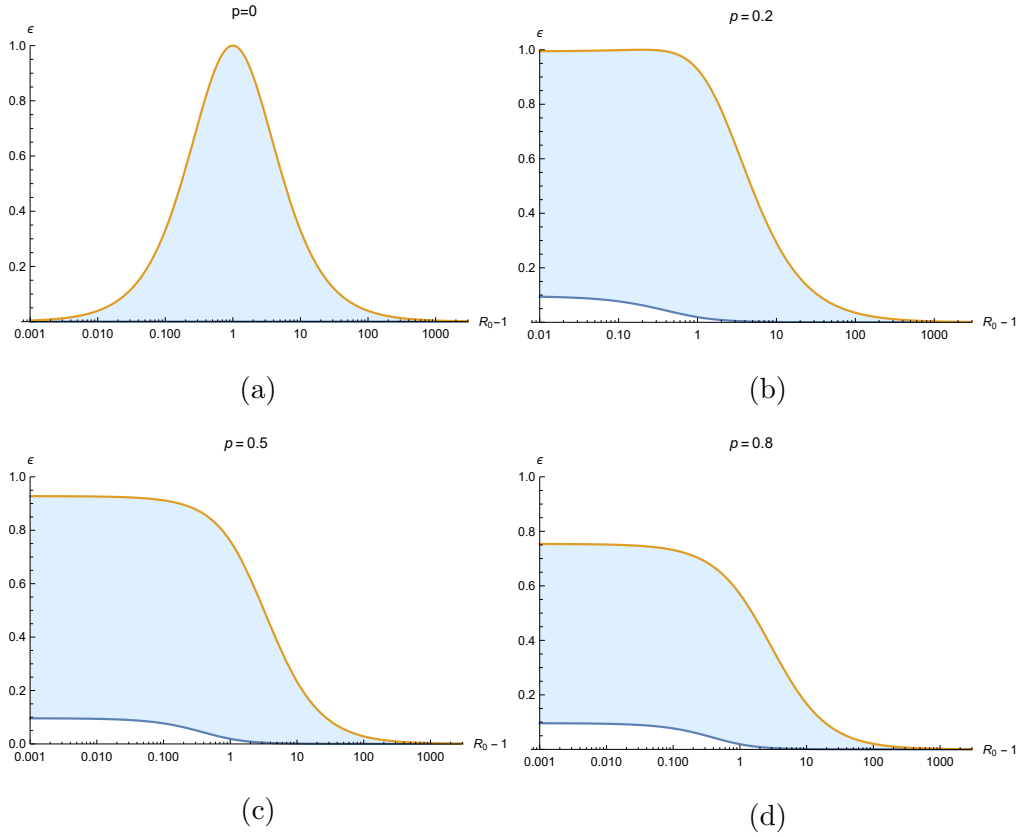

Figure 2: Panel (a)-(d) illustrate $(\mathcal{R}_0, \epsilon)$ planes with different p values. The shaded regions represent the range of conditions for damped oscillation to occur.
a) $p = 0$, b) $p = 0.2$,c) $p = 0.5$, d) $p = 0.8$

2.1.5 Comments and discussion on this model

This is the initial model of intentional infection on newborns, which we obtained by directly modifying standard SIR model. Notice, the main difference between the intentional infection model and the vaccination model is the direction of flow of the individuals being treated with intentional infection/vaccination. Intentionally infected individuals are capable of transmitting the disease to susceptible individuals, whereas the vaccinated individuals will enter R(recovered) directly, therefore not being 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 the infected compartment into two separate infective classes, namely, intentionally infected and naturally infected.

In the past, for the case of smallpox, people believed that individuals that are variolated die much less often, compared 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.

2.2 Model: Addition of disease induced mortality

2.2.1 System of differential equations

Disease induced mortality is created by deaths of infected population, with a certain ratio. The ratio is also known as case fatality proportion.

Historic application of variolation have shown a lower case fatality proportion to those being variolated, 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 infected individuals(including V and I) 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,

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

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

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

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

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

Notice here that $\mathcal{R}_0$, which is equal to $\frac{\beta}{\gamma+\mu}$, is again the basic reproduction number of the naturally infected cases. Since we assume that the transmission rate of naturally infected and intentionally infected cases are identical, $\mathcal{R}_0$ also plays a role as the basic reproduction number of intentionally infected cases as well.

2.2.2 Equilibria

By setting Equation 13a, Equation 13b and Equation 13c equal to 0, we solve for equilibria.

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

There are two equilibria 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(with 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 $p \neq 0$, there is only one equilibrium,

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

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

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

It is worthwhile mentioning that, 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. Here in our derivations, we are considering $S = \hat{S}$, $V = \hat{V}$.

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

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

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

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 in equation Equation 18b and Equation 18c.

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 locally asymptotically stable.

We would also like to investigate the global stability of the EE. A Lyapunov function is usually required to conclude on the global stability of an equilibrium. However, such function may not always be easily found. Therefore, instead of searching for a Lyapunov function, we would like to show global stability by simulating the system with random initial conditions. If the EE is globally asymptotically stable (GAS), the dynamics of the system should eventually converge to the EE, regardless of the selection of the initial condition.

Here, we define a function, which describes the distance between any point in the system to the EE. Knowing that the EE is $(\hat{S}, \hat{V}, \hat{I})$, the distance between any point (S, V, I) to the EE is given by:

$$d((S, V, I)) = ((\hat{S} - S)^2 + (\hat{V} - V)^2 + (\hat{I} - I)^2)^{\frac{1}{3}} \tag{25}$$

If EE is GAS, the output of the distance function with any initial condition will eventually approach 0. If not, we will see the distance function unable to approach 0, for some initial conditions.

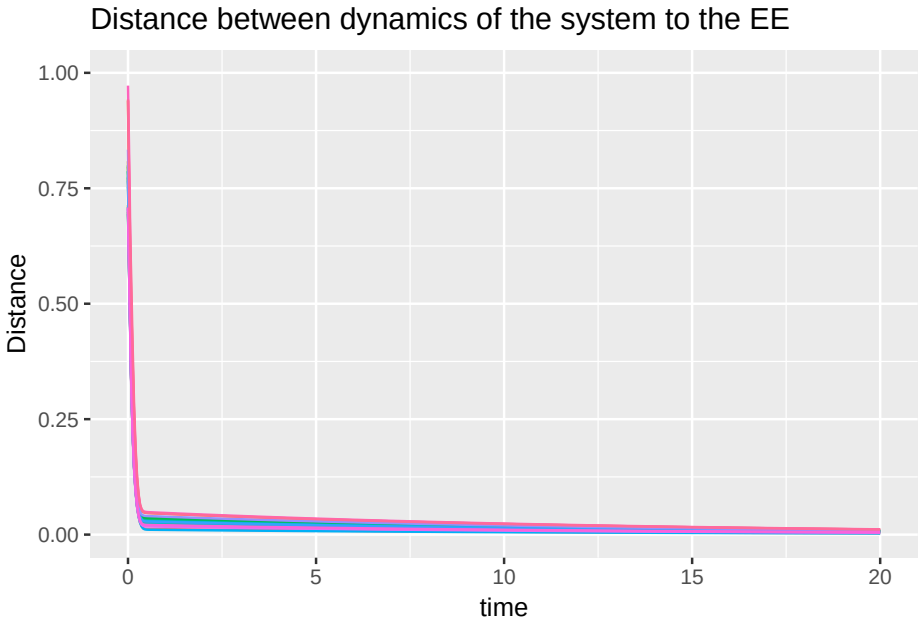

Figure 3: Distance between the dynamics of the system to the EE, as a function of time. If EE is GAS, distance function should approach 0, no matter which initial condition is chosen. This figure shows the distance function of 50 different initial conditions. We have enough confidence to conclude that EE is GAS.

2.2.3 Effect of intentional infection on total mortality

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

We first take a look at the mortality rate at EE, and insert $\hat{V}$ [Equation 16b] and $\hat{I}$ $(= 0)$ in Equation 13d to obtain

$$\left.\frac{\mathrm{d}M}{\mathrm{d}\tau}\right|_{\mathrm{EE}} = p_V(1-\epsilon)V = \frac{p_V(1-\epsilon)\epsilon(\mathcal{R}_0-1) + p_V(1-\epsilon)\epsilon\sqrt{(\mathcal{R}_0-1)^2+4\mathcal{R}_0 p}}{2\mathcal{R}_0}, \tag{26}$$

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 to extra deaths.

In history, smallpox was present in the 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 reach the equilibrium only after infinite time. Therefore, we need to define a threshold distance from the equilibrium that we will consider to be "at 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 differences between different proportion of intentional infection. To help us observe the dynamics better, we assume intentional infection has a 20% case fatality proportion.

Figure 4 shows 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 advanta-

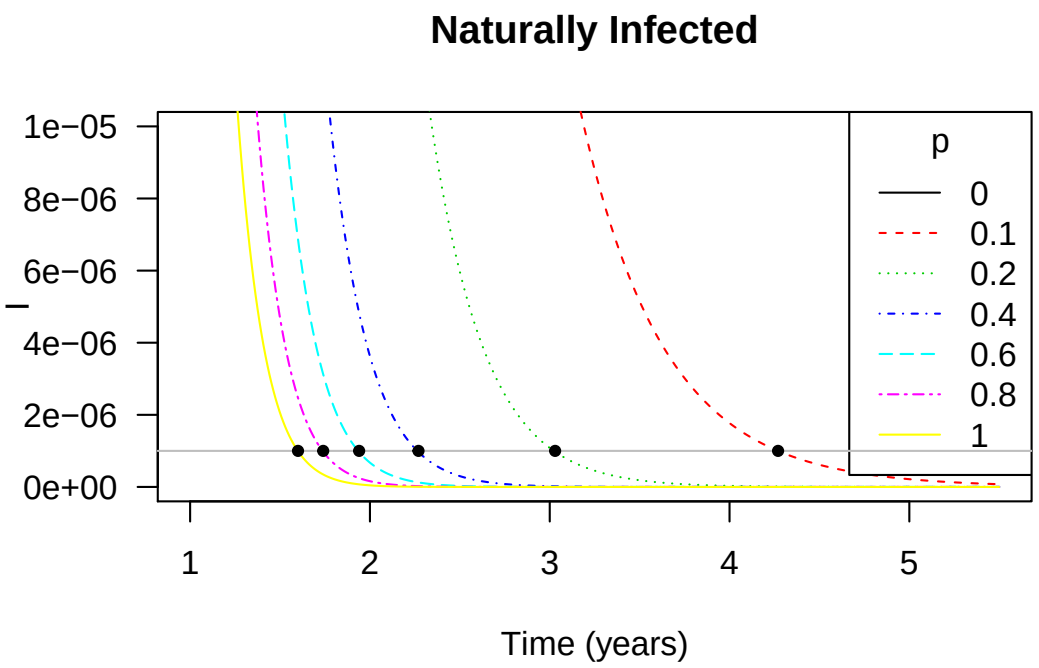

Figure 4: Determination of time taken to reach equilibrium. The horizontal line at $I = 10^{-6}$ is the threshold we define to be "at equilibrium". The figure shows, with a larger proportion of intentional infection on newborn, the system reaches the equilibrium more quickly.

geous than non-intentional infection, by comparing total mortality.

From previous analysis, we have 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, the magnitude of $\frac{\mathrm{d}M}{\mathrm{d}\tau}$ is larger when p is larger.

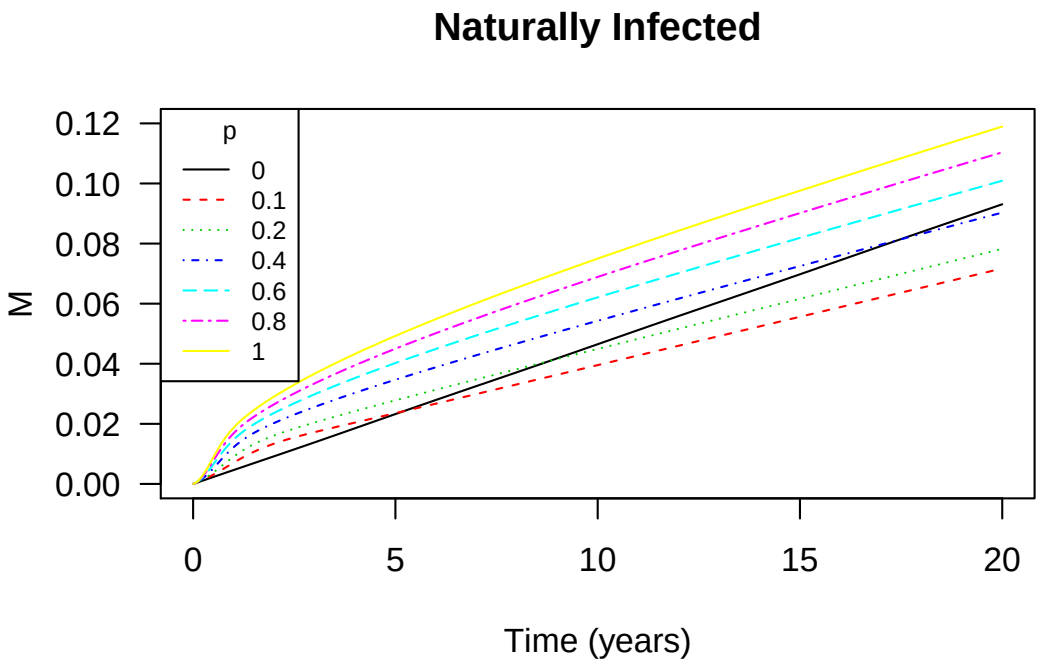

Figure 5: An illustration of intentional infection have advantages over non-intentional infection, with a case fatality proportion from intentional infection of $p_V = 0.2$. Cumulative mortality (M) increases linearly with time without intentional infection ($p = 0$, black line). For any $p > 0$, cumulative mortality is initially greater than for $p = 0$, but eventually crosses the black line so is eventually lower (i.e., fewer deaths).

Figure 5 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 get close to the equilibrium ($\hat{I} < 10^{-6}$) and time to have advantages over non-intentional infection (i.e., lower cumulative mortality M).

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 increases.

If we were to make the equivalent of Figure 5 with the CFP for intentional infection $p_V = 0.01$, then the time required to have advantages over non-intentional infection is minimal for any p (the difference in time to advantage is less than a year regardless of the value of p). Figure 6 shows the general relationship between time to advantage and p.

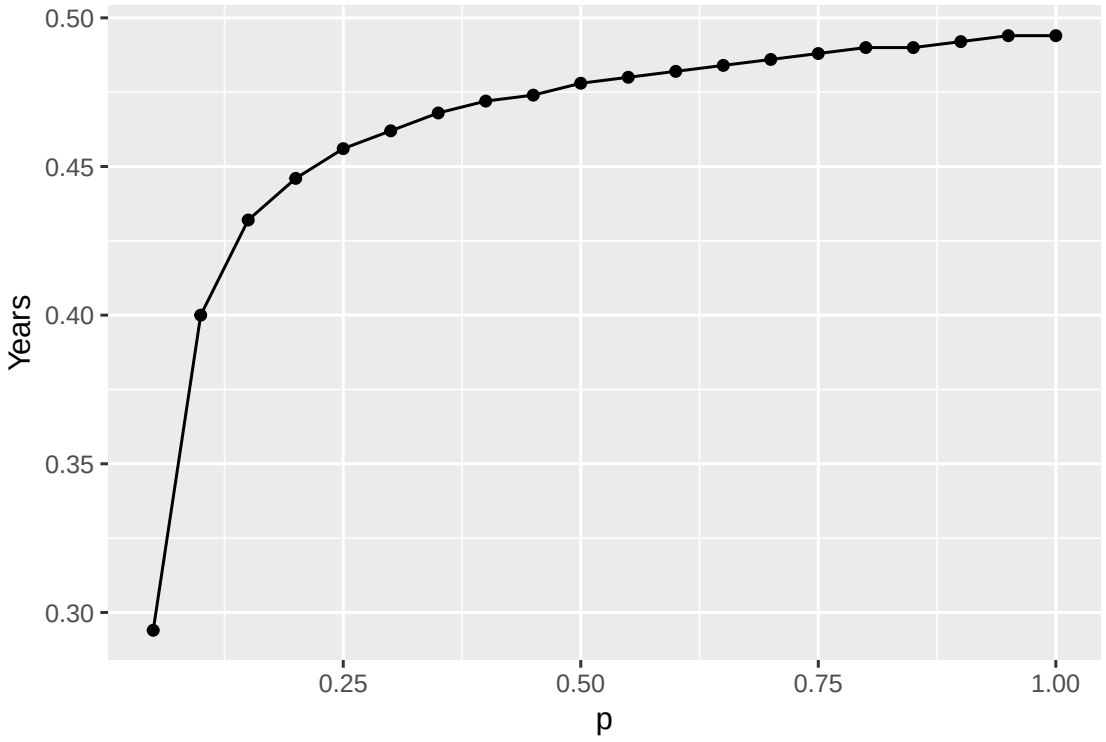

Figure 6: Time to advantage, as a function of p. The time required for intentional infection to be more advantageous than non-intentional infection increases as the proportion of intentional infection on newborn increases.

Figure 6 shows that with a lower proportion of intentional infection p, we gain advantage 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 other words, although the advantage is obtained quickly, its magnitude is too small to be significant. With this in mind, we will consider one intentional infection strategy (p value) to be "More advantageous" than another if mortality with the strategic value of p is at least 10% lower than mortality with no intentional infection ($p = 0$)

Figure 7: Time required for cumulative mortality of intentional infection becomes at least 10% lower than of non-intentional infection. Under our new definition, with a larger proportion of intentional infection on newborn, intentional infections can have fewer death than non-intentional infection in shorter time.

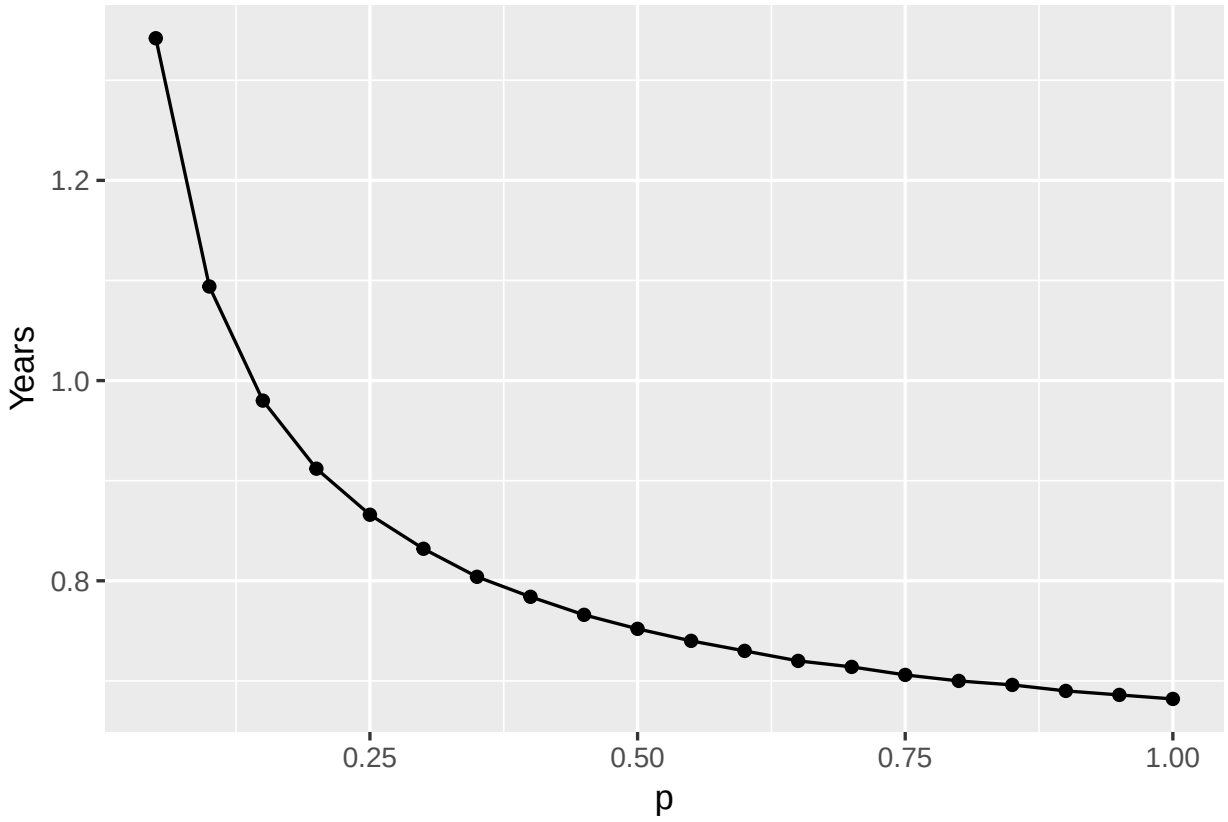

Figure 7 indicates that under our new definition of "more advantageous", the situation is reversed: a larger proportion of intentional infection yields an advantage more quickly.

2.2.4 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. Which suggests, in history, the introduction of this practice does have positive effects on disease control, intuitively by reducing the number of deaths. However, as we have discussed in the beginning of subsubsection 2.2.3, a larger

proportion of intentional infection on newborn will have a larger mortality rate once the equilibrium is reached. Though it can reduce total death and become more advantageous than non-intentional infection faster, it is unwise to keep infecting such a large proportion of newborns simply because it will lead to more death.

To summarize the above argument, if our strategy of intentional infection remains the same at all time, then in the long run, with a minimal proportion of intentional infection, total mortality could be minimized. However, in a 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 the possibilities of improving on the strategies of intentional infection, 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 rates. Therefore, our next model could consider various possibilities of these parameters, and draw conclusions to its behavior.

2.2.5 Possibility of eradication

If we define the disease as 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 can 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,

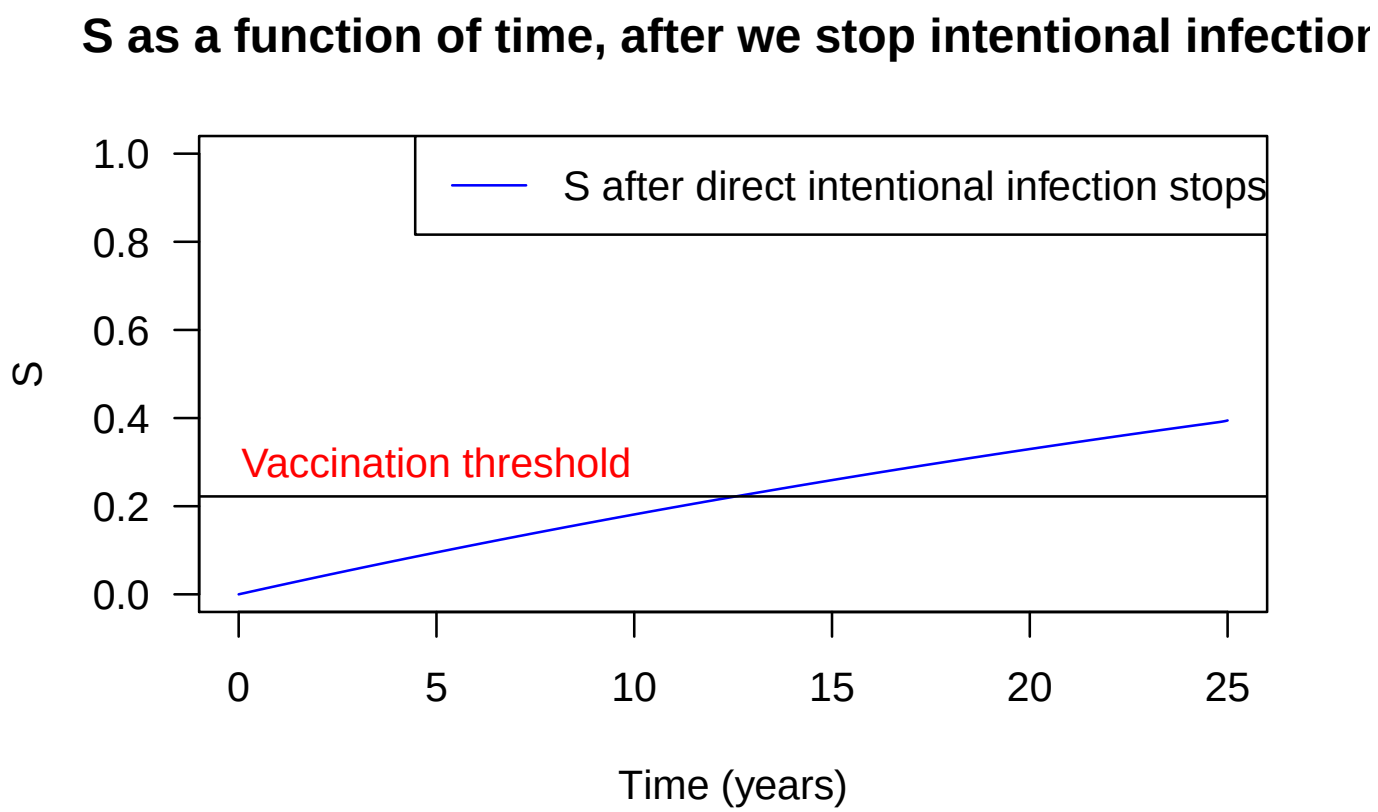

Figure 8: The black line is the vaccination threshold, for a disease with $\mathcal{R}_0 = 4.5$. The blue curve represent the dynamics of susceptible, after we stop intentional infection. The figure shows, for more than 10 years after we stop intentional infection, the amount of susceptible stays below the vaccination threshold.

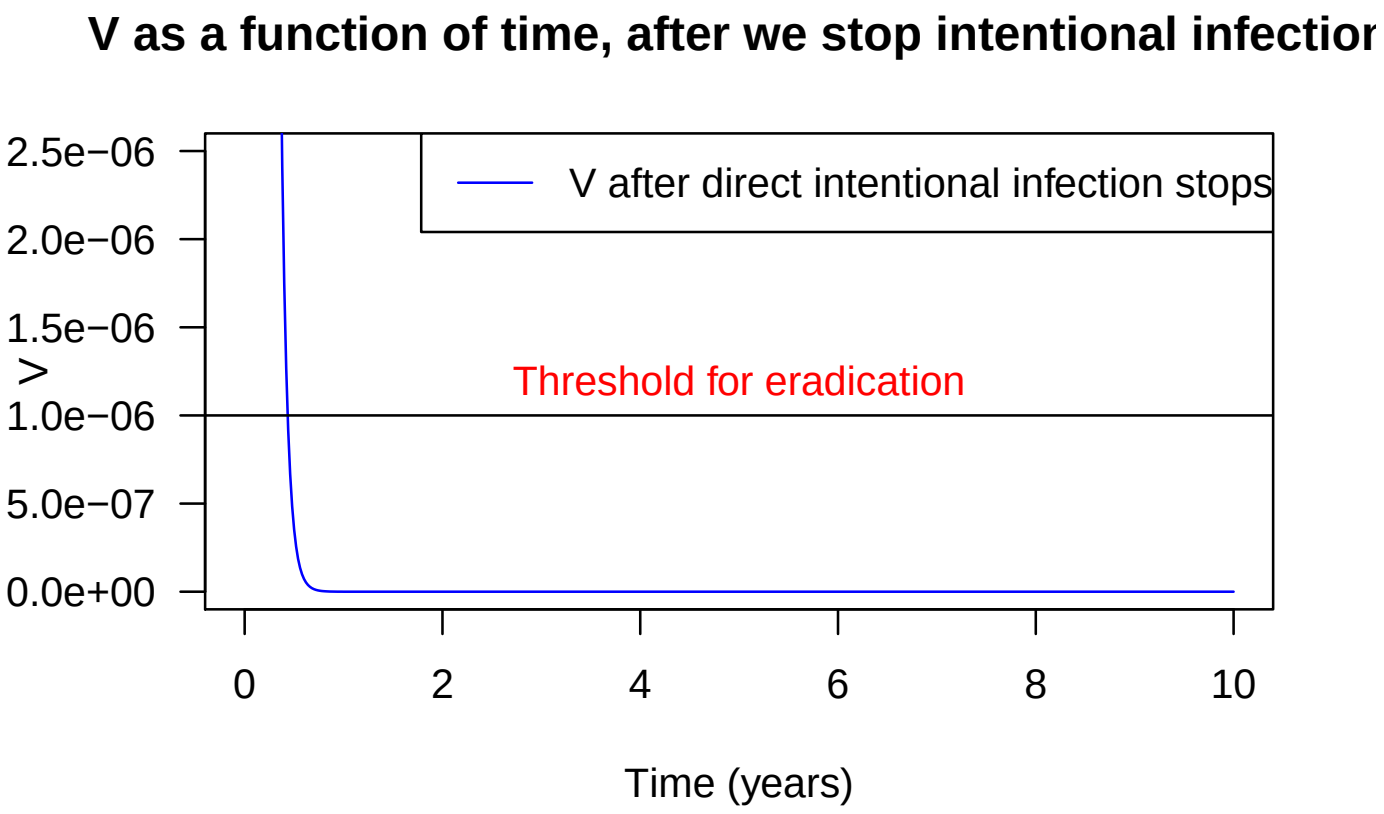

Figure 9: The black line is the eradication threshold we defined, which is $V = 10^{-6}$. The blue curve represent the dynamics of V, after we stop intentional infection. The figure shows, it takes less than 1 year for V to fall below the eradication threshold.

Figure 8 and Figure 9 have shown an example of disease eradication, by our definition. In our example, we assumed $p = 1$, however, Other values of p will still need to be investigated.

2.3 Model: Different transmission rate and recovery rate

2.3.1 System of differential equations

As we mentioned above, we need to involve new parameters for different transmission and recovery rates. 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,

$$\begin{aligned}
\frac{\mathrm{d}S}{\mathrm{d}t} &= \mu(1-p) - \beta_V SV - \beta_I SI - \mu S\,, \\
\frac{\mathrm{d}V}{\mathrm{d}t} &= \beta_V SV + \mu p - \gamma_V V - \mu V\,, \\
\frac{\mathrm{d}I}{\mathrm{d}t} &= \beta_I SI - \gamma_I I - \mu I\,, \\
\frac{\mathrm{d}M}{\mathrm{d}t} &= p_V \gamma_V V + p_I \gamma_I I\,, \\
\frac{\mathrm{d}R}{\mathrm{d}t} &= (1-p_V)\gamma_V V + (1-p_I)\gamma_I I - \mu R\,,
\end{aligned} \tag{27}$$

We non-dimensionalize Equation 27 by scaling time, by

$$\tau = (\gamma_I + \mu)t\,, \tag{28}$$

As the result, we obtain,

$$\frac{\mathrm{d}S}{\mathrm{d}\tau} = \epsilon(1-p) - \mathcal{R}_{0,V} SV - \mathcal{R}_{0,I} SI - \epsilon S\,, \tag{29a}$$

$$\frac{\mathrm{d}V}{\mathrm{d}\tau} = \mathcal{R}_{0,V} SV + \epsilon p - \tilde{\gamma} V\,, \tag{29b}$$

$$\frac{\mathrm{d}I}{\mathrm{d}\tau} = \mathcal{R}_{0,I} SI - I\,, \tag{29c}$$

$$\frac{\mathrm{d}M}{\mathrm{d}\tau} = p_V(\tilde{\gamma} - \epsilon)V + p_I(1-\epsilon)I\,, \tag{29d}$$

$$\frac{\mathrm{d}R}{\mathrm{d}\tau} = (1-p_V)(\tilde{\gamma} - \epsilon)V + (1-p_I)(1-\epsilon)I - \epsilon R\,, \tag{29e}$$

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

2.3.2 Equilibria

To solve for all equilibria, we set equations Equation 29a, Equation 29b and Equation 29c equal to 0, and solve for equilibria.

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,

$$\hat{S} = \frac{\mathcal{R}_{0,V} + \tilde{\gamma} - \sqrt{\mathcal{R}_{0,V}^2 - 2\mathcal{R}_{0,V}\tilde{\gamma} + \tilde{\gamma}^2 + 4p\mathcal{R}_{0,V}\tilde{\gamma}}}{2\mathcal{R}_{0,V}}\,, \tag{30a}$$

$$\hat{V} = \frac{\epsilon - \frac{\tilde{\gamma}\epsilon}{\mathcal{R}_{0,V}} + \frac{\epsilon\sqrt{\mathcal{R}_{0,V}^2 - 2\mathcal{R}_{0,V}\tilde{\gamma} + \tilde{\gamma}^2 + 4p\mathcal{R}_{0,V}\tilde{\gamma}}}{\mathcal{R}_{0,V}}}{2\tilde{\gamma}}\,, \tag{30b}$$

$$\hat{I} = 0\,, \tag{30c}$$

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,

$$\mathcal{J} = \begin{bmatrix} -\mathcal{R}_{0,V}V - \mathcal{R}_{0,I}I - \epsilon & -\mathcal{R}_{0,V}S & -\mathcal{R}_{0,I}S \\ \mathcal{R}_{0,V}V & \mathcal{R}_{0,V}S - \gamma & 0 \\ \mathcal{R}_{0,I}I & 0 & \mathcal{R}_{0,I}S - 1 \end{bmatrix}. \tag{31}$$

Eigenvalues of Jacobian are given as follow,

$$\lambda_1 = -1 + \mathcal{R}_{0,I}S \tag{32a}$$

$$\lambda_2 = \frac{-\tilde{\gamma} + \mathcal{R}_{0,V}S - \epsilon - \mathcal{R}_{0,V}V - \sqrt{(-\tilde{\gamma} + \mathcal{R}_{0,V}S - \epsilon - \mathcal{R}_{0,V}V)^2 - 4(\mathcal{R}_{0,V}\tilde{\gamma} + \epsilon\tilde{\gamma} - \mathcal{R}_{0,V}S\epsilon)}}{2} \tag{32b}$$

$$\lambda_3 = \frac{-\tilde{\gamma} + \mathcal{R}_{0,V}S - \epsilon - \mathcal{R}_{0,V}V + \sqrt{(-\tilde{\gamma} + \mathcal{R}_{0,V}S - \epsilon - \mathcal{R}_{0,V}V)^2 - 4(\mathcal{R}_{0,V}\tilde{\gamma} + \epsilon\tilde{\gamma} - \mathcal{R}_{0,V}S\epsilon)}}{2} \tag{32c}$$

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

By using Equation 30a, we have

$$-\tilde{\gamma} + \mathcal{R}_{0,V}S - \epsilon - \mathcal{R}_{0,V}V < 0\,, \tag{33}$$

Therefore,

$$\Re(\lambda_2) < -\tilde{\gamma} + \mathcal{R}_{0,V} S - \epsilon - \mathcal{R}_{0,V} V < 0\,, \tag{34}$$

Next, notice

$$\mathcal{R}_{0,V}\tilde{\gamma} + \epsilon\tilde{\gamma} - \mathcal{R}_{0,V} S\epsilon > 0\,. \tag{35}$$

It follows that

$$\sqrt{(-\tilde{\gamma} + \mathcal{R}_{0,V} S - \epsilon - \mathcal{R}_{0,V} V)^2 - 4(\mathcal{R}_{0,V}\tilde{\gamma} + \epsilon\tilde{\gamma} - \mathcal{R}_{0,V} S\epsilon)} < |-\tilde{\gamma} + \mathcal{R}_{0,V} S - \epsilon - \mathcal{R}_{0,V} V| \tag{36}$$

As the result, $\Re(\lambda_3) < 0$.

Lastly, we look at λ_1. Here we noticed that $\Re(\lambda_1)$ is not necessarily negative, it depends on all other parameters. For the purpose of our interest, we would like to use specific value of smallpox to simulate the result.

We set $\mathcal{R}_{0,I} = 4.5$, for $\mathcal{R}_{0,V}$, we are aware that logically it should be less than $\mathcal{R}_{0,I}$, so here we set $\mathcal{R}_{0,V} = 2.5$, and plotted the (γ, p) plane.

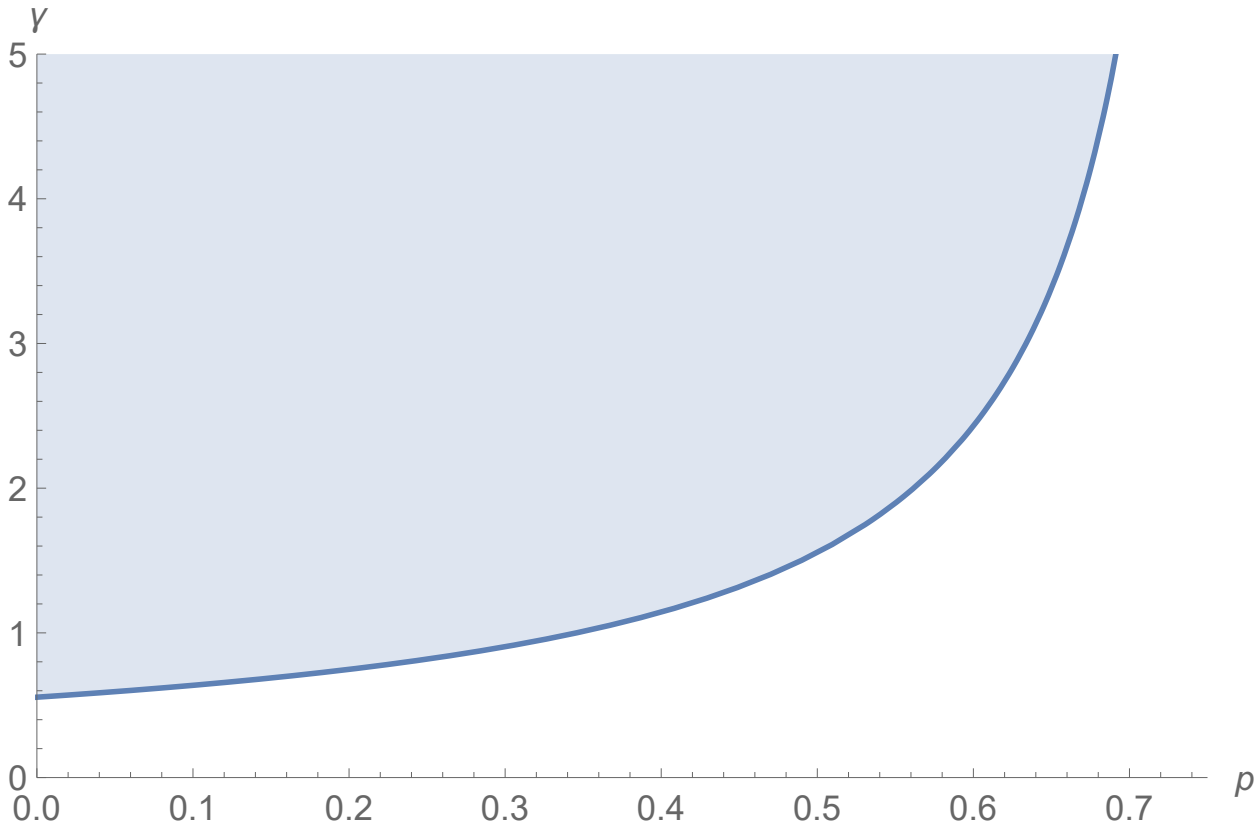

Figure 10: (γ, p) plane when $\mathcal{R}_{0,V} = 2.5, \mathcal{R}_{0,I} = 4.5$. The shaded area is the region where $\Re(\lambda_1) < 0$, which means the system is locally asymptotically stable.

2.3.3 Comments and discussion on this model

Parameters of this model such as $\mathcal{R}_{0,V}$ and γ_V can be immensely different depending on the design of the pathogen used for intentional infection.

Previous studies have shown that, for a similar model which does not consider death, a significant decrease in final size is expected [4], for a transmissible vaccine, even when $\mathcal{R}_{0,V}$ is less than 1, for instance, $\mathcal{R}_{0,V} = 0.5$, 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.

3 Model: Intentionally infect susceptible with a certain rate

3.1 Model: Modification to SIR model

3.1.1 System of differential equations

Our second strategy is to intentionally infect susceptible individuals with a certain rate. Again, we start our analysis by modifying the standard SIR model.

The following assumptions are made:

- No disease induced mortality.
- Birth and natural death rate are the same, the total population remains constant.
- Latent period is short enough to be ignored.
- All susceptible individuals are equally likely to be infected, and all infected individuals are equally infectious.

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= \mu - \beta SI - rS - \mu S\,, \\ \frac{\mathrm{d}I}{\mathrm{d}t} &= rS + \beta SI - \gamma I - \mu I\,, \\ \frac{\mathrm{d}R}{\mathrm{d}t} &= \gamma I - \mu R\,. \end{aligned} \tag{37}$$

Here, β is transmission rate, γ is recovery rate, μ is the *per capita* rate of birth and death, r is the rate of intensional infection on susceptible individuals. We will discuss the reasonable value of r in later sections.

We convert our system into dimensionless form, by scaling time, by

$$\tau = (\gamma + \mu)t\,. \tag{38}$$

Therefore, the dimensionless system is:

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}\tau} &= \epsilon - \mathcal{R}_0 SI - \eta S - \epsilon S\,, \\ \frac{\mathrm{d}I}{\mathrm{d}\tau} &= \eta S + \mathcal{R}_0 SI - I\,, \\ \frac{\mathrm{d}R}{\mathrm{d}\tau} &= (1-\epsilon)I - \epsilon R\,, \end{aligned} \tag{39}$$

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

3.1.2 Equilibrium

We obtain only one solution by solving the system:

$$\hat{S} = \frac{1}{\mathcal{R}_0} - \frac{2\eta}{\mathcal{R}_0(-(\eta+\epsilon-\epsilon\mathcal{R}_0) + \sqrt{(\eta+\epsilon-\epsilon\mathcal{R}_0)^2 + 4\mathcal{R}_0\epsilon\eta} + 2\eta)} \tag{40a}$$

$$\hat{I} = \frac{-(\eta+\epsilon-\epsilon\mathcal{R}_0) + \sqrt{(\eta+\epsilon-\epsilon\mathcal{R}_0)^2 + 4\mathcal{R}_0\epsilon\eta}}{2\mathcal{R}_0} \tag{40b}$$

Notice, for any non-zero η, $\hat{I} \neq 0$, it follows that this equilibrium is also an endemic equilibrium, since there is always proportion of population that are infected.

Stability analysis rely on Jacobian matrix, which is,

$$\mathcal{J} = \begin{bmatrix} -\mathcal{R}_0 I - \eta - \epsilon & -\mathcal{R}_0 S \\ \eta + \mathcal{R}_0 I & \mathcal{R}_0 S - 1 \end{bmatrix}. \tag{41}$$

For simplicity. Let

$$G = -(\eta+\epsilon-\epsilon\mathcal{R}_0) + \sqrt{(\eta+\epsilon-\epsilon\mathcal{R}_0)^2 + 4\mathcal{R}_0\epsilon\eta}. \tag{42}$$

Notice, if $\epsilon, \eta \neq 0$, $G > 0$.

So Jacobian at EE becomes,

$$\mathcal{J}|_{E.E.} = \begin{bmatrix} \frac{G}{2} - \eta - \epsilon & -1 + \frac{2\eta}{G+2\eta} \\ \eta + \frac{G}{2} & -\frac{2\eta}{G+2\eta} \end{bmatrix}. \tag{43}$$

The eigenvalues of of Jacobian are:

$$\lambda_{1,2} = \frac{-(G^2 + 4\eta G + 2\epsilon G + 4\eta^2 + 4\epsilon\eta + 4\eta)}{4(G + 2\eta)} \tag{44}$$

$$\pm \frac{\sqrt{((G^2 + 4\eta G + 2\epsilon G + 4\eta^2 + 4\epsilon\eta + 4\eta)^2 - 4(2G^3 + 12\eta G^2 + 24\eta^2 G + 8\epsilon\eta G + 16\eta^3 + 16\epsilon\eta^2)}}{4(G + 2\eta)}$$

$$\tag{45}$$

We know that $G > 0$, and since the rate of intentional infection is non-zero, $\eta > 0$

Since we are only interested in the case where the rate of intentional infection is non-zero, we assume that $\eta > 0$. Together with the fact that $G > 0$, the discriminant(Δ) satisfies the following inequality,

$$\Delta < |(G^2 + 4\eta G + 2\epsilon G + 4\eta^2 + 4\epsilon\eta + 4\eta)| \tag{46}$$

Therefore, we can conclude that Re(λ)< 0, which means, EE is stable.

For global stability analysis, we applied the same method as in previous section, which is by using distance function.

The identical distance function was used to run the simulation, and the result is obtain in the following plot:

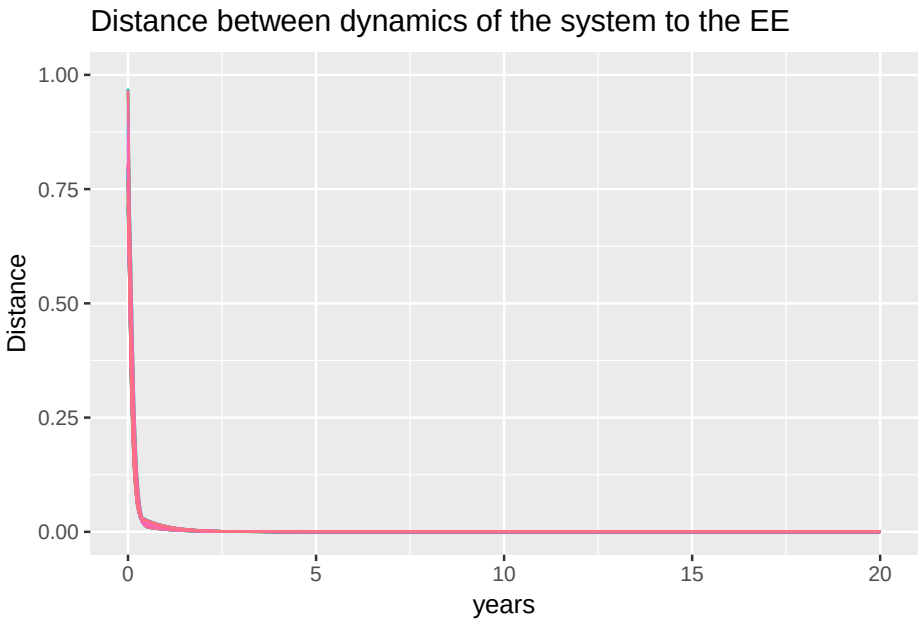

Figure 11: Distance between the dynamics of the system to the EE, as a function of time. If EE is GAS, distance function should approach 0, no matter which initial condition is chosen. This figure shows the distance function of 50 different initial conditions. We have enough confidence to conclude that EE is GAS.

To fully understand the dynamics of the system, we want to know whether or not there is a damped oscillation. This is done by determining the sign of the discriminant.

We will start our analysis with specific values of each parameter. Again, we will use parameters of smallpox. The values are listed in Table 1.

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

η is the rate of intentional infection, $\mathcal{R}_0$ is the basic reproduction number.

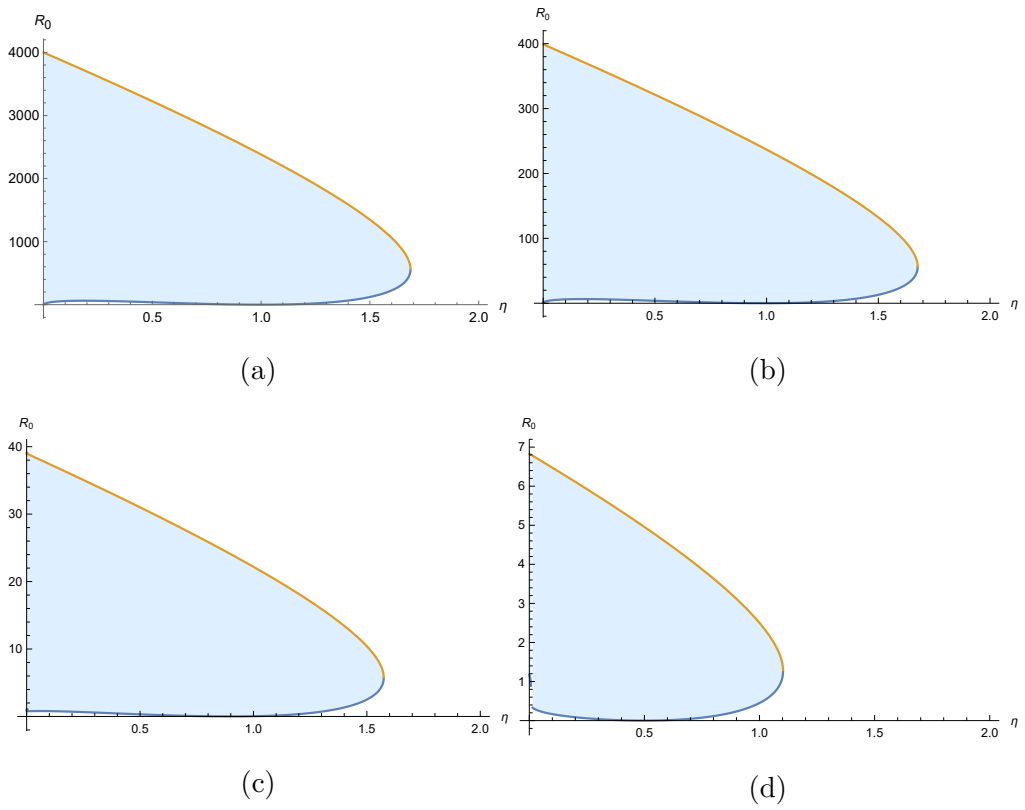

Figure 12: Panel (a)-(d) show $(\mathcal{R}_0, \eta)$ plane for different ϵ values. The shaded region represent the range of conditions where the system has damped oscillations. a) $\epsilon = 0.001$, b) $\epsilon = 0.01$, c) $\epsilon = 0.1$, d) $\epsilon = 0.5$

3.1.4 Comments and discussion on this model

Similar to our newborn infection model, the model obtained by modifying the standard SIR model is rather simple. We will still need to divide the infected compartment into intentionally and naturally infected classes.

Furthermore, to help us conclude whether or not there is any positive effect by intentionally infecting, we will need to involve disease induced mortality. This may also help us compare two different strategies of intentional infection.

3.2 Model: Addition of disease induced mortality

3.2.1 System of differential equations

The addition of disease induced mortality will require the involvement of case fatality proportion, again.

Here, we are doing exactly the same adjustment as we did in subsection 2.2. Our new system is,

$$\frac{\mathrm{d}S}{\mathrm{d}t} = \mu - \beta S(V + I) - rS - \mu S\,, \tag{47a}$$

$$\frac{\mathrm{d}V}{\mathrm{d}t} = \beta SV + rS - \gamma V - \mu V\,, \tag{47b}$$

$$\frac{\mathrm{d}I}{\mathrm{d}t} = \beta SI - \gamma I - \mu I\,, \tag{47c}$$

$$\frac{\mathrm{d}M}{\mathrm{d}t} = p_V\gamma V + p_I\gamma I\,, \tag{47d}$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = (1 - p_V)\gamma V + (1 - p_I)\gamma I - \mu R\,, \tag{47e}$$

where β is transmission rate, γ is recovery rate, μ is the *per capita* rate of birth and death, r is the rate of intensional infection on susceptible individuals.

We non-dimensionalize Equation 47 by scaling time, by

$$\tau = (\gamma + \mu)t\,, \tag{48}$$

As the result, we obtain,

$$\frac{\mathrm{d}S}{\mathrm{d}\tau} = \epsilon - \eta S - \mathcal{R}_0 S(V + I) - \epsilon S\,, \tag{49a}$$

$$\frac{\mathrm{d}V}{\mathrm{d}\tau} = \mathcal{R}_0 SV + \eta S - V\,, \tag{49b}$$

$$\frac{\mathrm{d}I}{\mathrm{d}\tau} = \mathcal{R}_0 SI - I\,, \tag{49c}$$

$$\frac{\mathrm{d}M}{\mathrm{d}\tau} = p_V(1-\epsilon)V + p_I(1-\epsilon)I\,, \tag{49d}$$

$$\frac{\mathrm{d}R}{\mathrm{d}\tau} = (1-p_V)(1-\epsilon)V + (1-p_I)(1-\epsilon)I - \epsilon R\,, \tag{49e}$$

Where $\epsilon = \frac{\mu}{\gamma+\mu}$, $\mathcal{R}_0 = \frac{\beta}{\gamma+\mu}$, $\eta = \frac{r}{\gamma+\mu}$

3.2.2 Equilibria

If $\eta = 0$, the system will again be simplified to the standard SIR model, the equilibrium of that has been shown before. Here, we are only interested in the case where $\eta \neq 0$.

The only solution we obtain by solving the system is:

$$\hat{S} = \frac{1}{\mathcal{R}_0} - \frac{2\eta}{\mathcal{R}_0(-(\eta+\epsilon-\epsilon\mathcal{R}_0) + \sqrt{(\eta+\epsilon-\epsilon\mathcal{R}_0)^2 + 4\mathcal{R}_0\epsilon\eta} + 2\eta)}\,, \tag{50a}$$

$$\hat{V} = \frac{-(\eta+\epsilon-\epsilon\mathcal{R}_0) + \sqrt{(\eta+\epsilon-\epsilon\mathcal{R}_0)^2 + 4\mathcal{R}_0\epsilon\eta}}{2\mathcal{R}_0}\,, \tag{50b}$$

$$\hat{I} = 0\,, \tag{50c}$$

Notice, $\hat{V}$ is non-zero, therefore this equilibrium is not a disease free equilibrium. It follows that it is the endemic equilibrium.

3.2.3 Stability of Endemic Equilibrium

The Jacobian matrix of this system is,

$$\mathcal{J} = \begin{bmatrix} -\eta - \mathcal{R}_0(V+I) - \epsilon & -\mathcal{R}_0 S & -\mathcal{R}_0 S \\ \mathcal{R}_0 V + \eta & \mathcal{R}_0 S - 1 & 0 \\ \mathcal{R}_0 I & 0 & \mathcal{R}_0 S - 1 \end{bmatrix}. \tag{51}$$

Eigenvalues of Jacobian are ,

$$\lambda_1 = -1 + \mathcal{R}_0 S \tag{52a}$$

$$\lambda_2 = \frac{-1 + \mathcal{R}_0 S - \eta - \epsilon - \mathcal{R}_0 V + \sqrt{(-1 + \mathcal{R}_0 S - \eta - \epsilon - \mathcal{R}_0 V)^2 - 4(\eta + \mathcal{R}_0 V + \epsilon - \mathcal{R}_0 S\epsilon)}}{2} \tag{52b}$$

$$\lambda_3 = \frac{-1 + \mathcal{R}_0 S - \eta - \epsilon - \mathcal{R}_0 V - \sqrt{(-1 + \mathcal{R}_0 S - \eta - \epsilon - \mathcal{R}_0 V)^2 - 4(\eta + \mathcal{R}_0 V + \epsilon - \mathcal{R}_0 S\epsilon)}}{2} \tag{52c}$$

By using Equation 50a and Equation 52a, we get

$$\Re(\lambda_1) = -1 + \mathcal{R}_0 S = -\frac{2\eta}{(-(\eta + \epsilon - \epsilon\mathcal{R}_0) + \sqrt{(\eta + \epsilon - \epsilon\mathcal{R}_0)^2 + 4\mathcal{R}_0\epsilon\eta} + 2\eta)} < 0 \tag{53}$$

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

By using Equation 50a again, we have

$$\mathcal{R}_0 S\epsilon < \epsilon\,, \tag{54}$$

Therefore

$$(\eta + \mathcal{R}_0 V + \epsilon - \mathcal{R}_0 S\epsilon) > 0\,, \tag{55}$$

It follows that

$$\sqrt{(-1 + \mathcal{R}_0 S - \eta - \epsilon - \mathcal{R}_0 V)^2 - 4(\eta + \mathcal{R}_0 V + \epsilon - \mathcal{R}_0 S\epsilon)} < |(-1 + \mathcal{R}_0 S - \eta - \epsilon - \mathcal{R}_0 V)|\,. \tag{56}$$

It follows that we have two cases, if the quantity under square root is negative, then

$$\Re(\lambda_2) = \Re(\lambda_3) = -1 + \mathcal{R}_0 S - \eta - \epsilon - \mathcal{R}_0 V < 0\,, \tag{57}$$

Otherwise, we have

$$\Re(\lambda_3) < \Re(\lambda_2) < 0 \tag{58}$$

Thus, for any $\eta > 0$, we can conclude that the EE is locally asymptotically stable regardless of the values of other parameters.

3.2.4 The effect of intentional infection on mortality

We will again start by looking at the mortality rate at EE.

By inserting $\hat{V}$[Equation 50b] and $\hat{I}$ $(= 0)$ into Equation 49, we obtain the mortality rate at EE,

$$\frac{\mathrm{d}M}{\mathrm{d}\tau} = p_V(1-\epsilon)V = \frac{p_V(1-\epsilon)\epsilon(\mathcal{R}_0 - 1) + p_V(1-\epsilon)\epsilon\sqrt{(\mathcal{R}_0-1)^2 + 4\mathcal{R}_0 p}}{2\mathcal{R}_0}\,, \tag{59}$$

as shown the following graph,

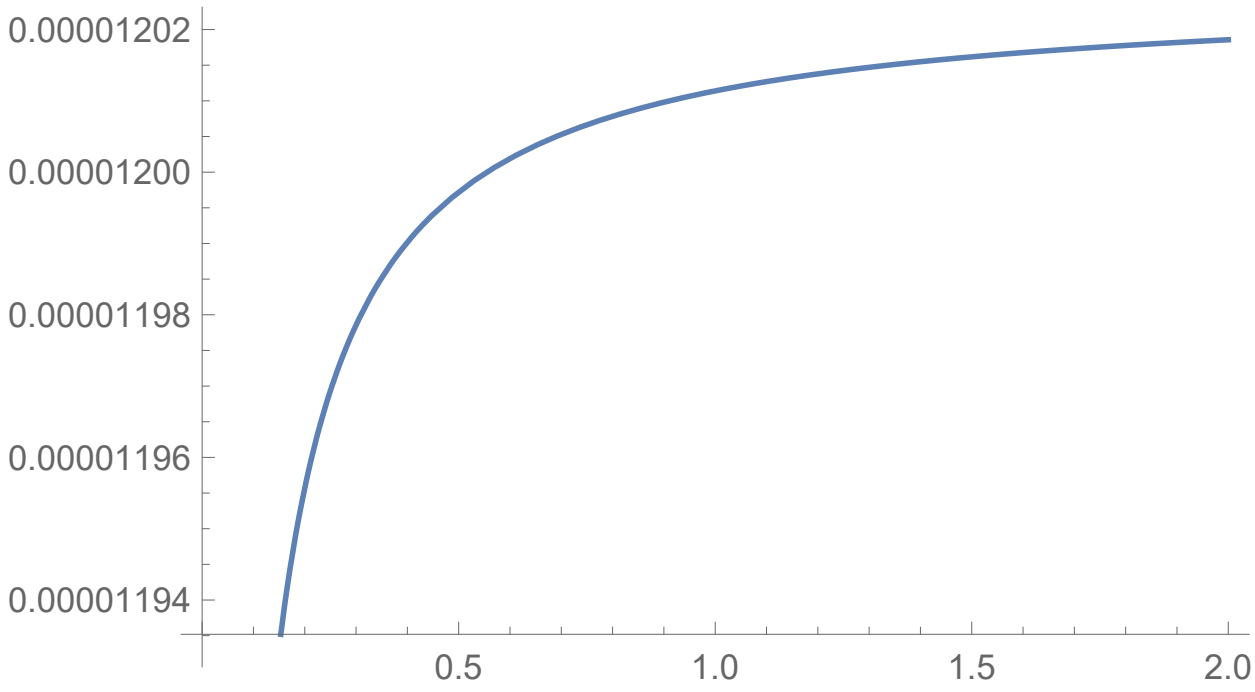

Figure 13: $\frac{\mathrm{d}M}{\mathrm{d}\tau}$ at EE as a function of η. $\frac{\mathrm{d}M}{\mathrm{d}\tau}$ increases as the rate of intentional infection on susceptible increase. The magnitude of $\frac{\mathrm{d}M}{\mathrm{d}\tau}$ eventually reaches an asymptote at $\frac{\mathrm{d}M}{\mathrm{d}\tau} = 0.00001202$.

It is worthwhile noticing that, as we increase the rate of intentional infection, the mortality rate eventually reaches an asymptote at around 1.2×10^{-5}, which is very close to the mortality rate when we intentionally infect newborn individuals with a highest proportion ($p = 1$). This suggests, in the long run, a high proportion of newborn infection would have similar results as intentionally infect susceptible at a high rate. A logical explanation to that is, when $p = 1$ for newborn infection model or when r is very high for susceptible model, at EE, there is almost nobody that is still susceptible ($\hat{S} = 0$). The only individuals entering the system are the newborns, but newborn model will intentionally infect 100% of them before they become susceptible. Similarly, susceptible model will intentionally infect almost all of them immediately after they become susceptible. As a result, the magnitude of $\hat{V}$ are essentially the same. Therefore, due to the fact that $\frac{\mathrm{d}M}{\mathrm{d}\tau}$ is directly proportional to $\hat{V}$, the magnitude of $\frac{\mathrm{d}M}{\mathrm{d}\tau}$ are similar.

As we did in the newborn model, we also want to know the time it takes for susceptible intentional infection to reach the new equilibrium, as well as the time it takes to be advantageous over non-intentional infection.

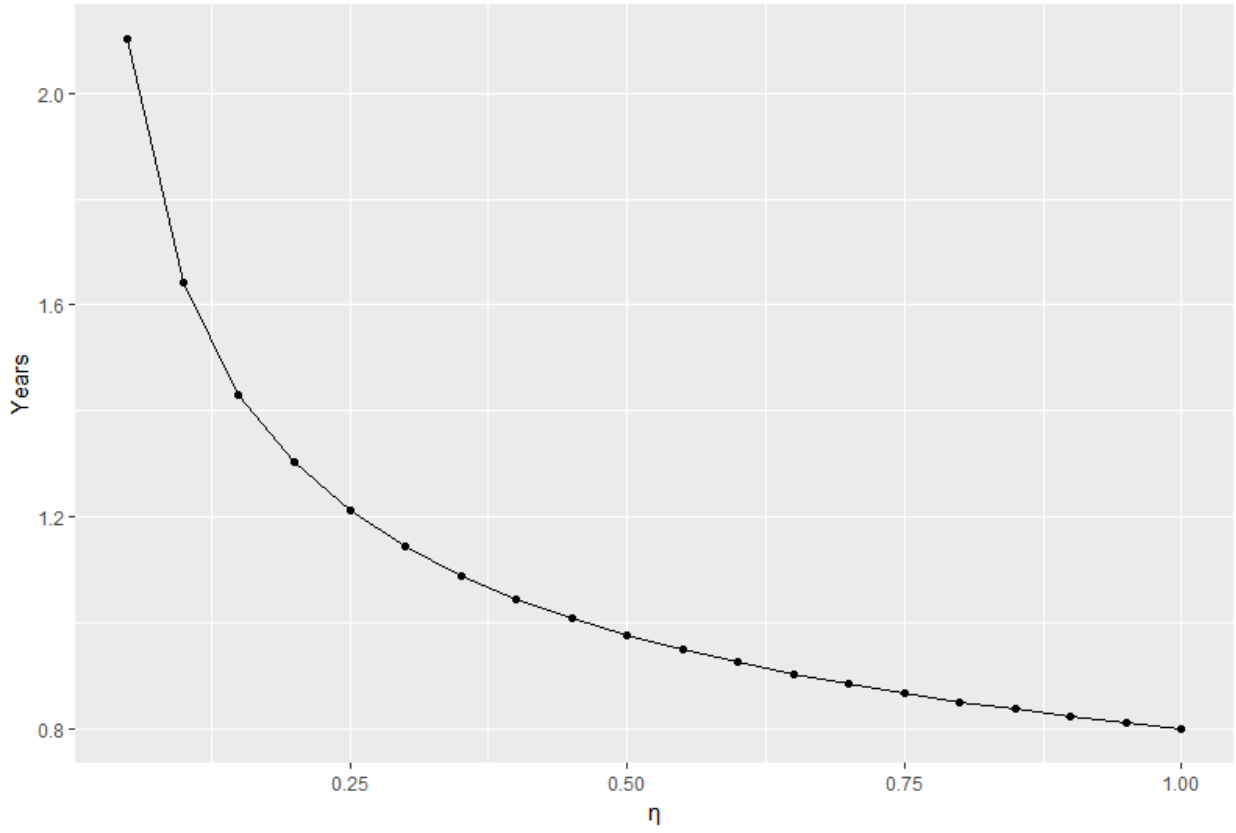

Figure 14: Time taken for susceptible intentional infection to reach the new equilibrium

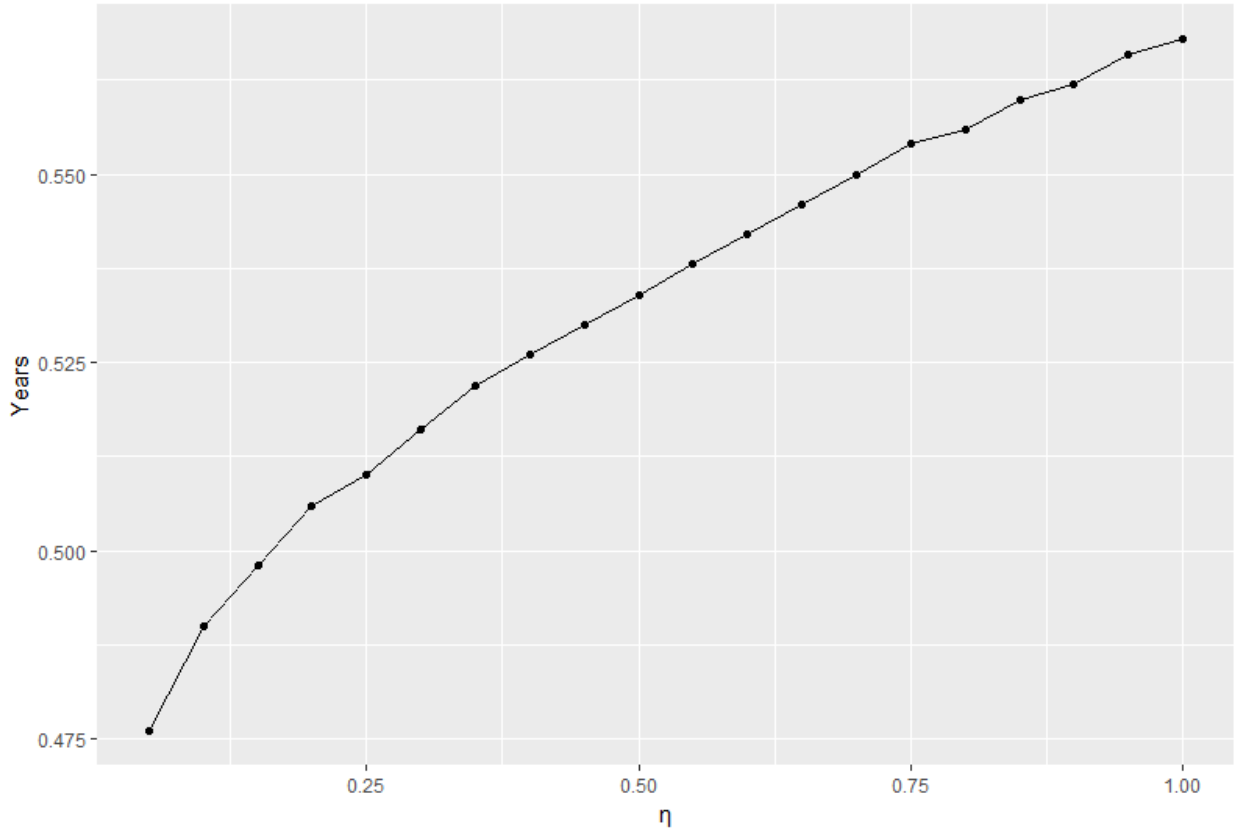

Figure 15: Time taken for susceptible intentional infection to have at least 10% fewer disease induced mortality, as a function of rate of intentional infection on susceptible.

Recall in subsubsection 2.2.3, we initially found that in the newborn infection model, with a larger proportion of newborn intentional infection, it becomes more advantageous over non-intentional infection more slowly. But after we change the definition of "more advantageous" to be: The cumulative mortality rate of the system with intentional infection is at least 10% less than of the system with no intentional infection, the situation was reversed. However, unlike the newborn infection model, in susceptible infection, the situation remain the same, even after the definition of "more advantageous" was changed. The time required for intentional infection to be more advantageous still increases as the rate of intentional infection increases. This means, with a very low rate of intentional infection on susceptible, not only can we ensure a lower cumulative mortality in the long run, but also able to be advantageous more quickly. This also means, we cannot conclude an optimal rate of intentional

infection on susceptible.

3.2.5 Comments and discussion to this model

This model has proven the benefit of intentional infection on susceptible individuals. We have shown that, with any positive rate of intentional infection on susceptible, we can always reduce the cumulative disease induced mortality. As we discussed in the previous section, we cannot conclude an optimal rate of intentional infection, since we have shown that the benefit is maximized, in every aspect, when the rate of intentional infection is at minimal. Further study is required to answer this question.

4 Conclusion

In our models, we have shown that both strategies can bring us benefit, in terms of having fewer deaths, in the long run. Though it may not be able to completely eradicate the disease, but both methods can greatly reduce disease induced mortalities, in the case of smallpox, death. This suggests, practices of smallpox variolation in history indeed saved many lives.

Due to the existence of special events or accidents in realistic scenario, which can alter the pattern of disease spread, we have many different factor not being considered in our models. For both strategies, the models can still be modified and developed to higher complexity. For example, in real life, smallpox variolation is done via skin. However, since the subject used to variolate is live smallpox virus, there could be some other pathways for live smallpox virus to enter respiratory system of the individual being variolated, or other people who has contacted this individual. An example of such a pathway could be touching the area of variolation followed by touching nose or mouth.

In such scenario, though the individual infected via skin might have symptoms much less severe than naturally infection, when the virus happens to enter respiratory system, a natural infection with much more serious symptoms could still occur. In our construction of

models, the result of that will be the individual entering naturally infected class.

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 can tell us if intentional infection can be a more effective method than vaccination in disease control. This may also lead us to the discussion of transmissible vaccine.
- We can use our model to see how well they fit the historical data for smallpox. This could help us much better understand the variolation history of smallpox.
- As described in discussion section, a more complicated model involving more parameter could be considered.

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