Intentional infection as a method of population level disease control

Newborn infection

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June 18th 2018

Motivation

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- What are the historical examples?
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- This method is out of date, banned in some places, why do we care?
  - In history, the mechanisms and benefits of intentional infection on a population level was not quite understood.
  - New application to immunology, i.e. Transmissible vaccine.

Method

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

Where S, I and R represent susceptible, infected and recovered.

- μ is birth/death rate
- β is the transmission rate
- γ is recovery rate

Method

The following assumptions are made to simplify the model to start with:

- There is no difference between intentionally infected and normally infected individuals.
- There is no disease induced mortality.
- Birth and natural death rate are the same, so the total population remains constant.
- The latent period is short enough to be ignored.
- All susceptible individuals are equally likely to be infected, and all infected individuals are equally infectious.

Method

With intentional infection on newborn, we have,

$$\begin{aligned}
\frac{\mathrm{d}S}{\mathrm{d}t} &= \mu(1-p) - \beta SI - \mu S\,, \\
\frac{\mathrm{d}I}{\mathrm{d}t} &= \beta SI + \mu p - \gamma I - \mu I\,, \\
\frac{\mathrm{d}R}{\mathrm{d}t} &= \gamma I - \mu R\,.
\end{aligned} \tag{2}$$

In addition to the parameters above,
p is the proportion of newborn intentionally infected.

We non-dimensionalize the above system by scaling time, by

$$\tau = (\gamma + \mu)t\,, \tag{3}$$

which yields

$$\frac{\mathrm{d}S}{\mathrm{d}\tau} = \epsilon(1-p) - \mathcal{R}_0 SI - \epsilon S\,, \tag{4a}$$

$$\frac{\mathrm{d}I}{\mathrm{d}\tau} = \mathcal{R}_0 SI + \epsilon p - I\,, \tag{4b}$$

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

Equilibria

Solving equations above to find equilibria, we obtain,

$$\hat{S} = \frac{1}{\mathcal{R}_0} - \frac{2p}{(\mathcal{R}_0 - 1) + \sqrt{(\mathcal{R}_0 - 1)^2 + 4\mathcal{R}_0 p}}, \tag{5a}$$

$$\hat{I} = \frac{\epsilon(\mathcal{R}_0 - 1) + \epsilon\sqrt{(\mathcal{R}_0 - 1)^2 + 4\mathcal{R}_0 p}}{2\mathcal{R}_0}. \tag{5b}$$

Notice, $\hat{I} \neq 0$ for all p between 0 and 1. Meaning there is always infected cases in the population. Therefore, the equilibrium is an Endemic Equilibrium (EE).

Stability of Equilibria

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$$\mathcal{J} = \begin{bmatrix} -\mathcal{R}_0 I - \epsilon & -\mathcal{R}_0 S \\ \mathcal{R}_0 I & \mathcal{R}_0 S - 1 \end{bmatrix}. \tag{6}$$

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- If intentional infected cases have the same case fatality proportion as normally infected cases, then we will end up killing more people.
  - Therefore, we need to have separate case fatality proportion for each of them.
- We need to divide I into two separate infective classes. V for intentionally infected class, I for naturally infected class.

Model with disease induced mortality rate

Therefore, our model becomes,

$$\frac{\mathrm{d}S}{\mathrm{d}\tau} = \epsilon(1-p) - \mathcal{R}_0 S(V+I) - \epsilon S\,, \tag{7a}$$

$$\frac{\mathrm{d}V}{\mathrm{d}\tau} = \mathcal{R}_0 SV + \epsilon p - V\,, \tag{7b}$$

$$\frac{\mathrm{d}I}{\mathrm{d}\tau} = \mathcal{R}_0 SI - I\,, \tag{7c}$$

$$\frac{\mathrm{d}M}{\mathrm{d}\tau} = p_V(1-\epsilon)V + p_I(1-\epsilon)I\,, \tag{7d}$$

$$\frac{\mathrm{d}R}{\mathrm{d}\tau} = (1-p_V)(1-\epsilon)V + (1-p_I)(1-\epsilon)I - \epsilon R\,, \tag{7e}$$

Where p_V and p_I represent the case fatality proportion for intentionally infected and naturally infected cases, respectively.

Equilibria

If $p \neq 0$, the equilibrium is,

$$\hat{S} = \frac{1}{\mathcal{R}_0} - \frac{2p}{(\mathcal{R}_0 - 1) + \sqrt{(\mathcal{R}_0 - 1)^2 + 4\mathcal{R}_0 p}}\,, \tag{8a}$$

$$\hat{V} = \frac{\epsilon(\mathcal{R}_0 - 1) + \epsilon\sqrt{(\mathcal{R}_0 - 1)^2 + 4\mathcal{R}_0 p}}{2\mathcal{R}_0}\,, \tag{8b}$$

$$\hat{I} = 0\,. \tag{8c}$$

It is interesting that, at equilibrium, naturally infected cases cease to exist. This may be helpful for eradication of disease.

By using the same method as the previous model, we again showed that the equilibrium is stable.

Effect of intentional infection on total mortality

Smallpox

Table: Model parameters and smallpox values.

Symbol	Meaning	Value
$\frac{1}{\mu}$	Average lifespan	50 years
$\frac{1}{\gamma}$	Mean infectious period	22 days
$\mathcal{R}_0$	Basic reproduction number	4.5
p_V	Intentionally infected cases fatality proportion	0.01
p_I	Naturally infected cases fatality proportion	0.3

Effect of intentional infection on total mortality

Mortality rate at EE

$$\left.\frac{\mathrm{d}M}{\mathrm{d}\tau}\right|_{\mathrm{EE}} = \frac{p_V(1-\epsilon)\epsilon(\mathcal{R}_0-1) + p_V(1-\epsilon)\epsilon\sqrt{(\mathcal{R}_0-1)^2+4\mathcal{R}_0 p}}{2\mathcal{R}_0}, \tag{9}$$

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- Mortality rate increases as p increases.

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- Mortality rate increases as p increases.
- In the long run, a larger proportion of intentional infection will lead to more deaths.

Initial state being at equilibrium

In history, intentional infect is introduced when the population is at equilibrium, which is the equilibrium for $p = 0$.

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$$\hat{S} = \frac{1}{\mathcal{R}_0}\,, \tag{10a}$$

$$\hat{V} = 0\,, \tag{10b}$$

$$\hat{I} = \epsilon(1 - \frac{1}{\mathcal{R}_0}) \tag{10c}$$

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We are interested in the time it takes to reach the new EE. We need to define a threshold for reaching equilibrium.

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We are interested in the time it takes to reach the new EE. We need to define a threshold for reaching equilibrium.
Since the new equilibrium has $\hat{I} = 0$, we define reaching equilibrium by $I \leq 10^{-6}$ (one in a million).

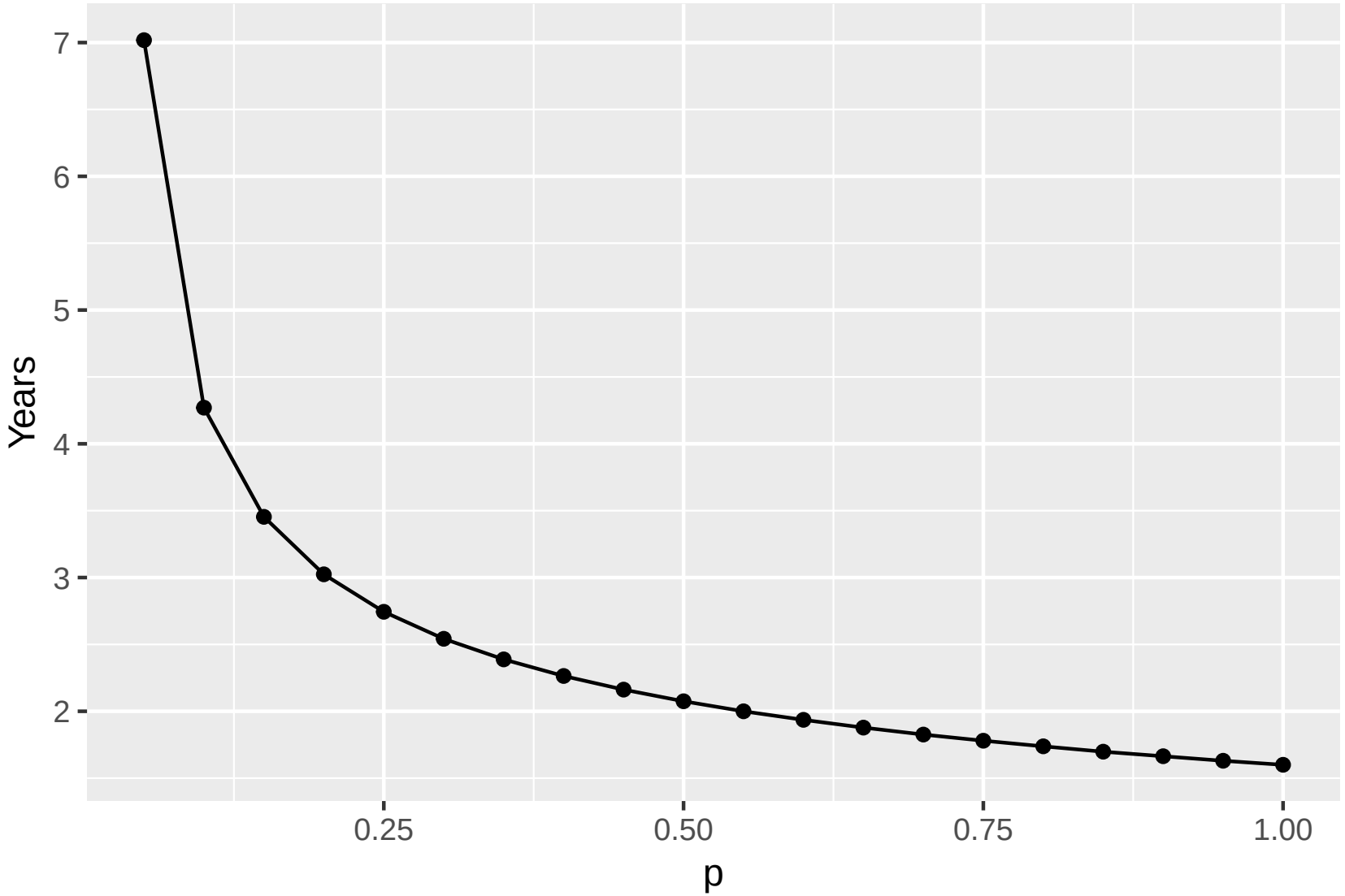

Figure: Determination of time taken to reach equilibrium

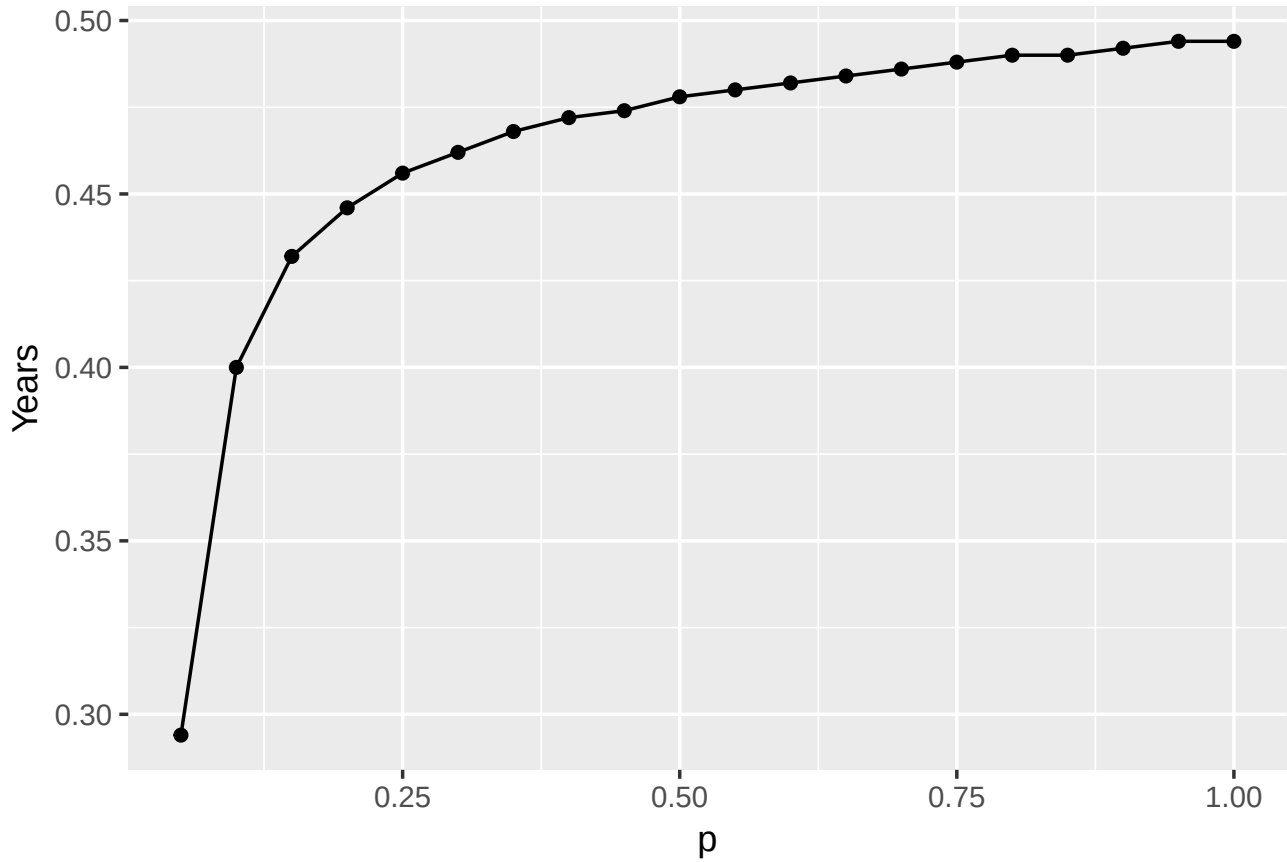

Figure: Time to advantage, as a function of p

With a lower proportion of intentional infection, we can gain advantages relative faster.

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How about intentionally infected cases? Can they burn out?

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$$S = \frac{1}{\mathcal{R}_0}$$

If S stays below this threshold until V goes extinct, then we can achieve complete eradication of this disease.

Possibility of disease eradication

For example, if our initial intentional infection has a proportion $p = 1$, then

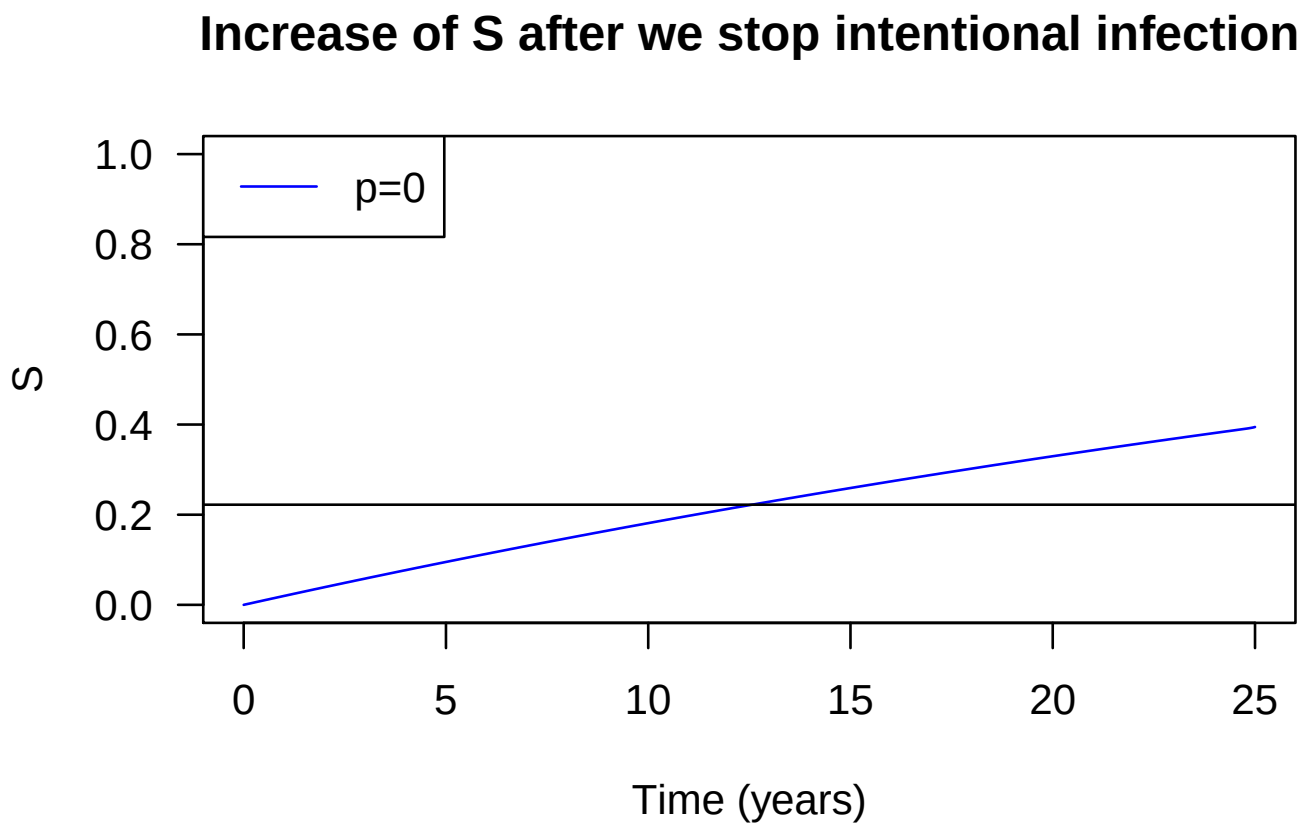

Figure: For more than 10 years after we stop intentional infection, $S < \frac{1}{\mathcal{R}_0}$

Possibility of disease eradication

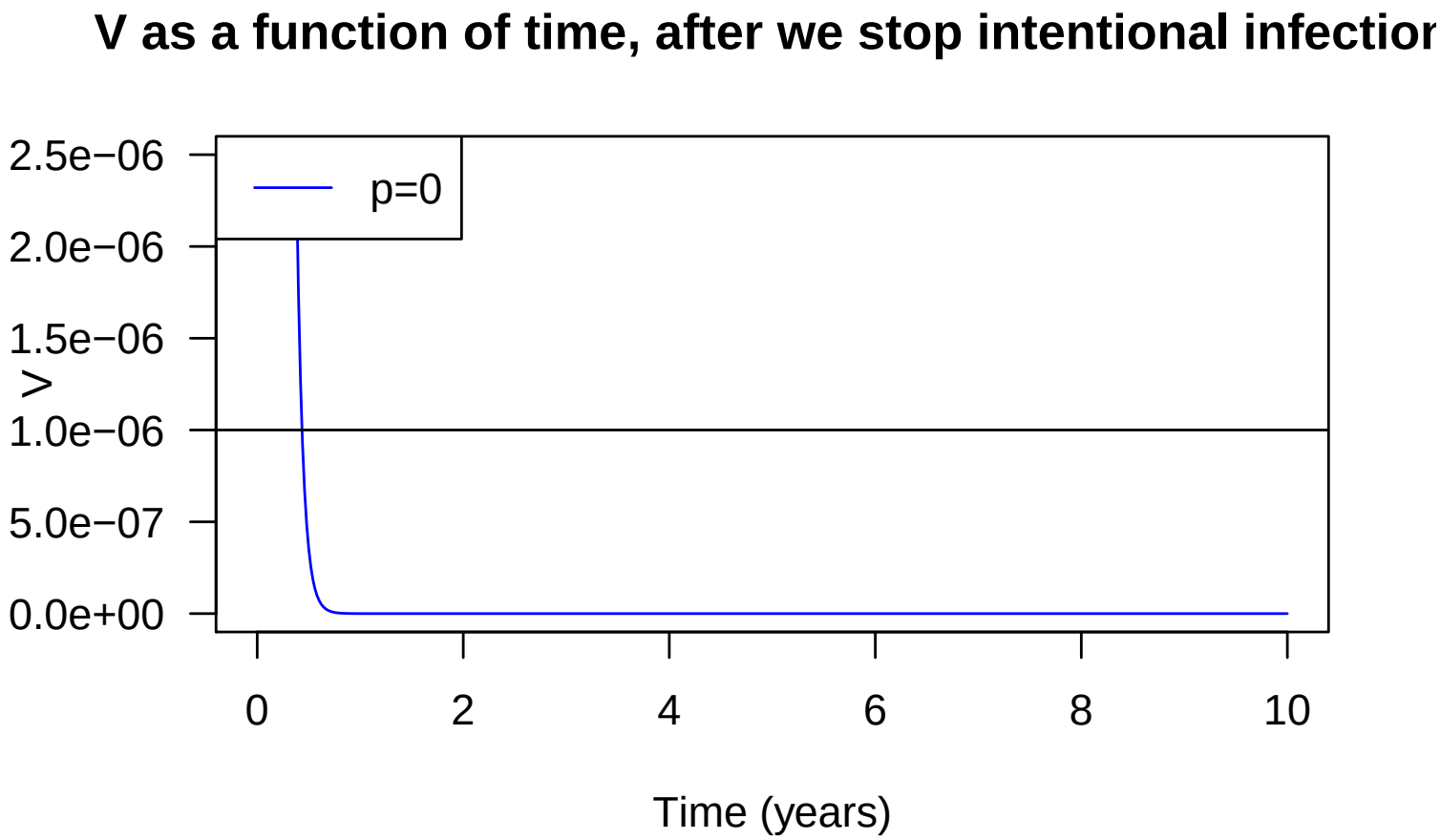

Figure: It takes less than 1 year for V to fall below 1×10^{-6}

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- Other strategies for intentional infection

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\frac{\mathrm{d}R}{\mathrm{d}t} &= \gamma I - \mu R\,,
\end{aligned} \tag{11}$$

Challenges to this method

- Identify susceptible individuals

References

Paulinevan den Driessche *Reproduction numbers of infectious disease models*, Infectious Disease Modelling, Volume 2, Issue 3, August 2017, Pages 288-303.

R.M. Anderson, R.M. May *Infectious diseases of humans: Dynamics and control*, Oxford University Press, Oxford, UK (1991)