Intentional infection as a method of population level disease control

Newborn infection

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  - In history, the mechanisms and benefits of intentional infection on a population level was not quite understood.
  - New application to disease control: transmissible vaccines

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 (total population size N is constant)
- β is transmission rate
- γ is recovery rate

Method

Assumptions:

- No difference between intentionally infected and naturally infected individuals.
- No disease induced mortality (in first version of model)
- 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.

Method

With intentional infection of newborns,

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

where

$$p = \text{proportion of newborns intentionally infected}$$

Non-dimensionalize the above system by scaling time, by

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

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Dimensionless system is:

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

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

where

$$\epsilon = \frac{\mu}{\gamma+\mu} \qquad \text{(infectious period as proportion of lifetime)}\,, \tag{5a}$$

$$\mathcal{R}_0 = \frac{\beta}{\gamma+\mu} \qquad \text{(basic reproduction number)}\,. \tag{5b}$$

Equilibria

Solving equations above to find equilibria, we obtain only one solution,

$$\hat{S} = \frac{1}{\mathcal{R}_0} - \frac{2p}{(\mathcal{R}_0 - 1) + \sqrt{(\mathcal{R}_0 - 1)^2 + 4\mathcal{R}_0 p}}, \tag{6a}$$

$$\hat{I} = \frac{\epsilon(\mathcal{R}_0 - 1) + \epsilon\sqrt{(\mathcal{R}_0 - 1)^2 + 4\mathcal{R}_0 p}}{2\mathcal{R}_0}. \tag{6b}$$

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- $\hat{I} \neq 0$ for all p between 0 and 1.
- This equilibrium is an **Endemic Equilibrium (EE)**.
- Without intentional infection ($p = 0$) EE reduces to

$$\hat{S} = \frac{1}{\mathcal{R}_0}, \qquad \hat{I} = \epsilon\left(1 - \frac{1}{\mathcal{R}_0}\right). \tag{7}$$

Stability of Equilibria

Jacobian Matrix,

$$\mathcal{J} = \begin{bmatrix} -\mathcal{R}_0 I - \epsilon & -\mathcal{R}_0 S \\ \mathcal{R}_0 I & \mathcal{R}_0 S - 1 \end{bmatrix}. \tag{8}$$

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  - But variolation had lower CFP $\implies$ revise model to include different CFP for intentional infections.
- 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,

$$\frac{\mathrm{d}S}{\mathrm{d}\tau} = \epsilon(1-p) - \mathcal{R}_0 S(V+I) - \epsilon S\,, \tag{9a}$$

$$\frac{\mathrm{d}V}{\mathrm{d}\tau} = \mathcal{R}_0 SV + \epsilon p - V\,, \tag{9b}$$

$$\frac{\mathrm{d}I}{\mathrm{d}\tau} = \mathcal{R}_0 SI - I\,, \tag{9c}$$

$$\frac{\mathrm{d}M}{\mathrm{d}\tau} = p_V(1-\epsilon)V + p_I(1-\epsilon)I\,, \tag{9d}$$

$$\frac{\mathrm{d}R}{\mathrm{d}\tau} = (1-p_V)(1-\epsilon)V + (1-p_I)(1-\epsilon)I - \epsilon R\,, \tag{9e}$$

where p_V and p_I represent the case fatality proportion (CFP) for intentionally infected and naturally infected cases, respectively.

Equilibria

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

$$\hat{S} = \frac{1}{\mathcal{R}_0} - \frac{2p}{(\mathcal{R}_0 - 1) + \sqrt{(\mathcal{R}_0 - 1)^2 + 4\mathcal{R}_0 p}}\,, \tag{10a}$$

$$\hat{V} = \frac{\epsilon(\mathcal{R}_0 - 1) + \epsilon\sqrt{(\mathcal{R}_0 - 1)^2 + 4\mathcal{R}_0 p}}{2\mathcal{R}_0}\,, \tag{10b}$$

$$\hat{I} = 0\,. \tag{10c}$$

- No naturally infected cases at endemic equilibrium (EE).
  - Helpful for disease eradication.

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 CFP	0.01
p_I	Naturally infected CFP	0.3

Effect of intentional infection on total mortality

Mortality rate at EE

$$\left.\frac{\mathrm{d}M}{\mathrm{d}\tau}\right|_{\mathrm{EE}} = \frac{p_V(1-\epsilon)\epsilon(\mathcal{R}_0-1)+p_V(1-\epsilon)\epsilon\sqrt{(\mathcal{R}_0-1)^2+4\mathcal{R}_0 p}}{2\mathcal{R}_0}, \tag{11}$$

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- Mortality rate at EE increases as proportion intentionally infected (p) increases.
- In the long run, a larger p will lead to more deaths.

Initial state near equilibrium

In history, intentional infection was introduced when the population was endemic, so near the equilibrium for $p = 0$.

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$$\hat{S} = \frac{1}{\mathcal{R}_0}\,, \tag{12a}$$

$$\hat{V} = 0\,, \tag{12b}$$

$$\hat{I} = \epsilon(1 - \frac{1}{\mathcal{R}_0}) \tag{12c}$$

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- What is the time it takes to reach the new EE?
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- What is the time it takes to reach the new EE?
  - Need to define a threshold.
  - Since the new equilibrium has $\hat{I} = 0$, define reaching equilibrium by $I \leq 10^{-6}$.

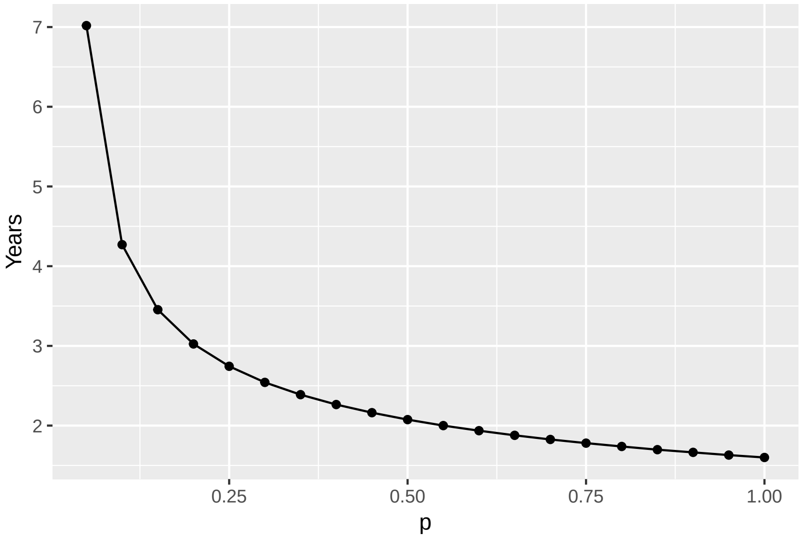

Figure: Determination of time taken to reach equilibrium

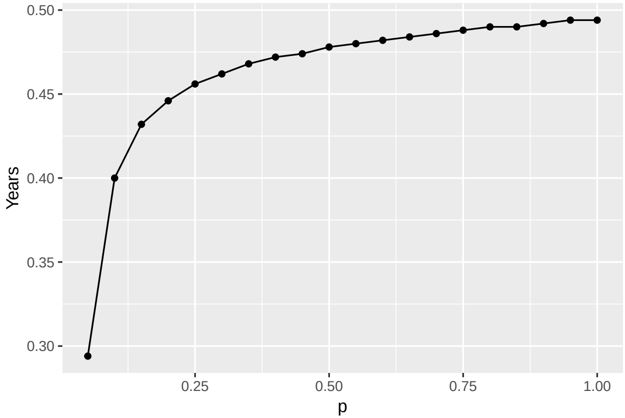

Figure: Time to advantage, as a function of p

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

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    - Not enough susceptible present in population for disease to effectively transmit.
    - Size of infected decreases.

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Threshold for susceptible: $S = \frac{1}{\mathcal{R}_0}$

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

Possibility of disease eradication

Example: $p = 1$ initially, stop intentional infection after reaching EE,

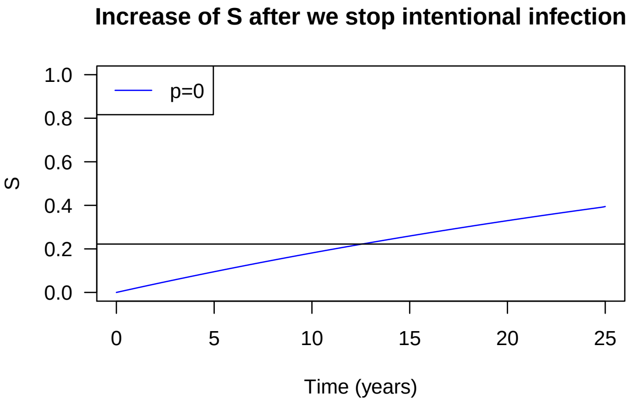

Figure: For more than 10 years after we stop intentional infection, $S < \frac{1}{\mathcal{R}_0}$

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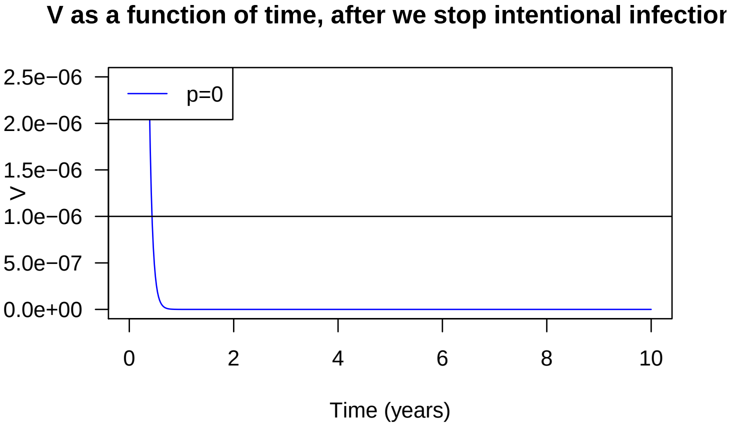

Figure: It takes less than 1 year for V to fall below 1×10^{-6}

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- Other approaches for intentional infection

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Challenges to this method

- Identify susceptible individuals

Conclusion

- Intentional infection has positive effects on population level disease control.
- Further study is required for determining intentional infection strategies to optimize this method.

References

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