

1 \mathcal{R}_0 for small pox

(a)

Denote susceptible state by S , incubation state by E , recovered state by R and infectious stages by I_1, I_2, I_3, I_4 . For simplicity, we consider pustules & scabs stage and resolving scabs stage as one stage due to common infectiousness. Note that all states are represented by proportions.

Let σ be percapita rate at which an infected individual develops symptom and γ_i be the per capita rate at which an infected individual in stage i progresses to next stage. Note that γ_4 corresponds to per capita recovery rate. Finally, let β_i be infectiousness (per contact transmission rate) of an infected individual in stage i and μ be per capita natural birth/death rate. Then, we can write an ODE model for this system as follows:

$$\begin{aligned}\frac{dS}{dt} &= \mu(1 - S) - (\beta_1 I_1 + \beta_2 I_2 + \beta_3 I_3 + \beta_4 I_4)S \\ \frac{dE}{dt} &= (\beta_1 I_1 + \beta_2 I_2 + \beta_3 I_3 + \beta_4 I_4)S - (\sigma + \mu)E \\ \frac{dI_1}{dt} &= \sigma E - (\gamma_1 + \mu)I_1 \\ \frac{dI_2}{dt} &= \gamma_1 I_1 - (\gamma_2 + \mu)I_2 \\ \frac{dI_3}{dt} &= \gamma_2 I_2 - (\gamma_3 + \mu)I_3 \\ \frac{dI_4}{dt} &= \gamma_3 I_3 - (\gamma_4 + \mu)I_4 \\ \frac{dR}{dt} &= \gamma_4 I_4 - \mu R\end{aligned}$$

(b)

In order for an infected individual to infect another susceptible individual, it must survive through incubation period and become infectious. Then, we can think of infection occurring in each infectious stage contributing to \mathcal{R}_0 . For example, contribution of infection from first stage would be equivalent to \mathcal{R}_0 of an SEIR model:

$$\beta_1 \times \frac{\sigma}{\sigma + \mu} \times \frac{1}{\gamma_1 + \mu}$$

where $\beta_1/(\gamma_1 + \mu)$ represent average number of infections that occur in stage 1 and $\sigma/(\sigma + \mu)$ is the probability that an infected individual does not die before incubation period is over. In order for infection to occur in stage $i > 1$, an infected individual must not die from natural mortality before reaching stage i . Then, contribution of infection during the second stage to \mathcal{R}_0 is

$$\beta_2 \times \frac{\sigma}{\sigma + \mu} \times \frac{\gamma_1}{\gamma_1 + \mu} \times \frac{1}{\gamma_2 + \mu}$$

Note that we now have $\gamma_1/(\gamma_1 + \mu)$ to account for probability of progressing to stage 2 without dying from natural mortality while in stage 1. Likewise, we can do a similar computation for all other stages. Then, we have

$$\begin{aligned}\mathcal{R}_0 &= \beta_1 \times \frac{\sigma}{\sigma + \mu} \times \frac{1}{\gamma_1 + \mu} \\ &+ \beta_2 \times \frac{\sigma}{\sigma + \mu} \times \frac{\gamma_1}{\gamma_1 + \mu} \times \frac{1}{\gamma_2 + \mu} \\ &+ \beta_3 \times \frac{\sigma}{\sigma + \mu} \times \frac{\gamma_1}{\gamma_1 + \mu} \times \frac{\gamma_2}{\gamma_2 + \mu} \times \frac{1}{\gamma_3 + \mu} \\ &+ \beta_4 \times \frac{\sigma}{\sigma + \mu} \times \frac{\gamma_1}{\gamma_1 + \mu} \times \frac{\gamma_2}{\gamma_2 + \mu} \times \frac{\gamma_3}{\gamma_3 + \mu} \times \frac{1}{\gamma_4 + \mu}\end{aligned}$$

For this particular system, we have

Linearizing at the disease free equilibrium, we have

[illegible]

Then,

$$V^{-1} = \begin{pmatrix} \frac{1}{\sigma+\mu} & 0 & 0 & 0 & 0 \\ \frac{\sigma}{(\sigma+\mu)(\gamma_1+\mu)} & \frac{1}{\gamma_1+\mu} & 0 & 0 & 0 \\ \frac{\sigma\gamma_1}{(\sigma+\mu)(\gamma_1+\mu)(\gamma_2+\mu)} & \frac{\gamma_1}{(\gamma_1+\mu)(\gamma_2+\mu)} & \frac{1}{\gamma_2+\mu} & 0 & 0 \\ \frac{\sigma\gamma_1\gamma_2}{(\sigma+\mu)(\gamma_1+\mu)(\gamma_2+\mu)(\gamma_3+\mu)} & \frac{\gamma_1\gamma_2}{(\gamma_1+\mu)(\gamma_2+\mu)(\gamma_3+\mu)} & \frac{\gamma_2}{(\gamma_2+\mu)(\gamma_3+\mu)} & \frac{1}{\gamma_3+\mu} & 0 \\ \frac{\sigma\gamma_1\gamma_2\gamma_3}{(\sigma+\mu)(\gamma_1+\mu)(\gamma_2+\mu)(\gamma_3+\mu)(\gamma_4+\mu)} & \frac{\gamma_1\gamma_2\gamma_3}{(\gamma_1+\mu)(\gamma_2+\mu)(\gamma_3+\mu)(\gamma_4+\mu)} & \frac{\gamma_2\gamma_3}{(\gamma_2+\mu)(\gamma_3+\mu)(\gamma_4+\mu)} & \frac{\gamma_3}{(\gamma_3+\mu)(\gamma_4+\mu)} & \frac{1}{\gamma_4+\mu} \end{pmatrix}$$

Then, it is clear that matrix FV^{-1} consists of 0 entries except its first row. Hence, its eigenvalues are on its diagonal, four of which are zero. The only non-zero entry on the diagonal is the first column entry in first row, which is equal to previously derived \mathcal{R}_0 value:

$$\begin{aligned} & \beta_1 \times \frac{\sigma}{\sigma+\mu} \times \frac{1}{\gamma_1+\mu} \\ & + \beta_2 \times \frac{\sigma}{\sigma+\mu} \times \frac{\gamma_1}{\gamma_1+\mu} \times \frac{1}{\gamma_2+\mu} \\ & + \beta_3 \times \frac{\sigma}{\sigma+\mu} \times \frac{\gamma_1}{\gamma_1+\mu} \times \frac{\gamma_2}{\gamma_2+\mu} \times \frac{1}{\gamma_3+\mu} \\ & + \beta_4 \times \frac{\sigma}{\sigma+\mu} \times \frac{\gamma_1}{\gamma_1+\mu} \times \frac{\gamma_2}{\gamma_2+\mu} \times \frac{\gamma_3}{\gamma_3+\mu} \times \frac{1}{\gamma_4+\mu} \end{aligned}$$

Therefore, \mathcal{R}_0 derived using next generation method is consistent with \mathcal{R}_0 from a biological argument.

(d)

Note that for unaltered small pox, time scale of disease is much shorter than average life span of a person. Then, we can approximate \mathcal{R}_0 by assuming that $\mu \approx 0$. Then, the expression for \mathcal{R}_0 becomes

$$\mathcal{R}_0 \approx \frac{\beta_1}{\gamma_1} + \frac{\beta_2}{\gamma_2} + \frac{\beta_3}{\gamma_3} + \frac{\beta_4}{\gamma_4}$$

The alteration causes the early rash stage to be twice as long and so γ_2^{-1} changes from 4 days to 8 days. It is evident that increasing γ_2^{-1} will lead to increase in \mathcal{R}_0 .

Provided that infectiousness during the early rash stage is extreme, we can assume that at least half of the infection occurs during this stage. In the worst case scenario, all infections occur during the early rash stage. These assumptions are reasonable given that disease-induced death can occur in later stages (and so there would be little contribution to infection). Based on these assumptions, we have

$$2.5 < \frac{\beta_2}{\gamma_2} < 5$$

Since altering doubles γ_2 , we get

$$5 < \frac{\beta_2}{\gamma_{2,\text{altered}}} < 10$$

This translates to

$$7.5 < \mathcal{R}_{0,\text{altered}} < 10$$

(e)

We highly recommend CDC to start preparing for the smallpox terror immediately. Given that smallpox has been altered to have twice as long early rash stage, we expect \mathcal{R}_0 to increase by at least a factor of 1.5. In the worse case scenario, \mathcal{R}_0 of the altered smallpox will be twice as large as that of the unaltered smallpox, corresponding to the following range: $7.5 < \mathcal{R}_0 < 10$. This means that the final size of an epidemic will be almost 100% if the attack is successful.