

# Modeling to Inform Infectious Disease Control

by Niels G. Becker, <https://www.crcpress.com/product/isbn/9781498731065>

## Solutions to Even-Numbered Exercises

June 2015

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### Chapter 2

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2. (a) Taking the natural logarithm of both sides and solving for  $R$  gives  $R = \frac{\ln(\pi)}{\pi-1}$ .
- (b) From the transmission threshold result,  $\pi = 1$  when  $R < 1$ . For  $\pi < 1$ , insert the values 0.01, 0.02, 0.03, ..., 0.99 for  $\pi$  into one column of a spreadsheet and use  $R = \frac{\ln(\pi)}{\pi-1}$  to compute the corresponding values of  $R$  in a second column. Then the graphics of the spreadsheet can be used to plot values of  $\pi$  against values of  $R$ .
4. As the selection for vaccination in the two campaigns is independent, the fraction of individuals susceptible following the second campaign is  $(1 - v)^2$ . Therefore, after the second campaign the mean number infected by an early infective is  $R^* = (1 - v)^2 R$ . This is less than 1 when  $v > 1 - 1/\sqrt{R} = 1 - 1/\sqrt{5} = 0.5528$ . Therefore, the smallest value of  $v$  that prevents epidemics with this two-dose strategy is 0.553.
6.  $R' > 1$  may be used in the statement of the transmission threshold property, because
- (i)  $R' > 1$  implies  $R > 1$ , and (ii)  $R' < 1$  implies  $R < 1$ .
8. (a) When  $R = 5$  and  $R^* = 0.8$  we find
- (i)  $\nu_1 = \frac{1}{1-R^*} = \frac{1}{1-0.8} = 5$ .
- (ii) Suppose the primary infective infects  $X$  individuals, each initiating a minor outbreak of mean size  $1/(1 - R^*)$ . Since the mean of  $X$  is 5, we obtain  $\nu_2 = 1 + \frac{5}{1-0.8} = 26$ .
- (ii) Arguing similarly we find  $\nu_4 = 1 + 5 + 25 + \frac{125}{1-0.8} = 656$ .
- (b) Delay has a dramatic effect on the mean size of the outbreak. This stems from the fact that reproduction is a multiplicative process.
10. By analogy with the first equation on Book Page 18, we find  $\pi' = \frac{1}{1+2f-2f\pi}$  where, by Book Equation (2.11),  $\pi = 1/R = \frac{1}{2}$ . This gives  $\pi' = \frac{1}{1+f}$ . Its graph is shown in Figure 1.

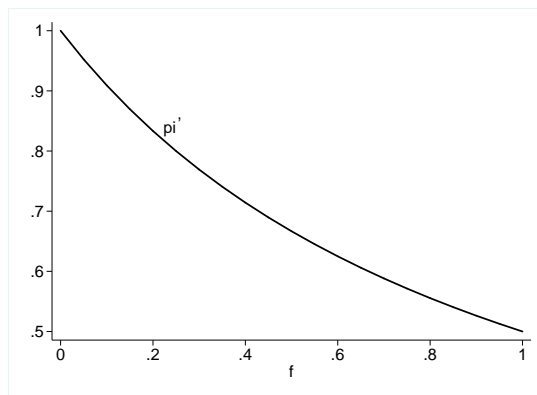


Figure 1: Graph of  $\pi'$  against  $f$ .

Let's spell this solution out in greater detail:

$\pi'$ , the probability of a minor outbreak, is given by

$$\pi' = p'_0 + p'_1\pi + p'_2\pi^2 + p'_3\pi^3 + \dots, \quad (1)$$

where  $\pi$  is the probability of a minor outbreak when the primary infective spends all of his infectious period back in his community. That is,

$$\pi = p_0 + p_1\pi + p_2\pi^2 + p_3\pi^3 + \dots. \quad (2)$$

Here  $p_0, p_1, p_2, \dots$  are the probabilities of a Geometric distribution with mean 2, while  $p'_0, p'_1, p'_2, \dots$  are the probabilities of a Geometric distribution with mean  $2f$ . That is,

$$p_j = \frac{1}{1+R} \left( \frac{R}{1+R} \right)^j = \frac{1}{3} \left( \frac{2}{3} \right)^j \quad \text{and} \quad p'_j = \frac{1}{1+2f} \left( \frac{2f}{1+2f} \right)^j$$

We need the geometric series equation  $1 + x + x^2 + x^3 + \dots = \frac{1}{1-x}$ , which holds when  $0 < x < 1$ .

With  $x = \frac{2}{3}\pi$  in Equation (2) the geometric series equation gives  $\pi = \frac{1}{3-2\pi}$ . Solve this to get  $\pi = \frac{1}{2}$ .

With  $x = \frac{2f\pi}{1+2f} = \frac{f}{1+2f}$  in Equation (1) the geometric series equation gives  $\pi' = \frac{1}{1+f}$ .

12. Assume that  $R < 1$  and let

$X'$  = the number of offspring resulting from direct contacts with the primary infective,

$Y'$  = the total outbreak size, and

$Y$  = total outbreak size when the primary infective spends his entire infectious period in the community.

Conditionally, given  $X' = x$ , the size of the outbreak  $Y'$  may be written

$$Y' = \begin{cases} 1, & \text{if } x = 0, \\ 1 + Y_1 + \dots + Y_x, & \text{if } x > 0, \end{cases} \quad (1)$$

where  $Y_1, Y_2, \dots, Y_x$  are independent random variables with the same distribution as  $Y$ .

$$\begin{aligned} \text{Using (1) we find } E(Y' | X' = x) &= \begin{cases} 1, & \text{if } x = 0, \\ 1 + E(Y_1) + E(Y_2) + \dots + E(Y_x), & \text{if } x > 0, \end{cases} \\ &= 1 + xE(Y). \end{aligned}$$

Therefore, provided  $R < 1$ ,  $E(Y') = E[E(Y' | X')] = E[1 + X'E(Y)] = 1 + E(X')E(Y)$ , where  $E(Y) = 1/(1 - R)$  and  $E(X') = R'$ , because the primary infective spends only part of his infectious period in the community.

That is  $E(Y') = 1 + R'/(1 - R)$ , as in Book Equation (2.12).

## Chapter 3

2. (a) (i) The immunization campaign changes the mean number an early infective infects outside his household from  $\mu$  to  $\mu^* = \frac{2}{3}\mu$ .
- (ii) Using the Binomial distribution, the  $H$  households with 2 susceptibles prior to the campaign become  $\frac{1}{9}H$  households with no susceptibles,  $\frac{4}{9}H$  households with 1 susceptible and  $\frac{4}{9}H$  households with 2 susceptibles.

The  $H$  households with 1 susceptible prior to the campaign become  $\frac{1}{3}H$  households with no susceptibles and  $\frac{2}{3}H$  households with 1 susceptible.

As a consequence, post-campaign there are  $\frac{10}{9}H$  households with one susceptible and  $\frac{4}{9}H$  households with 2 susceptibles.

$$\text{Using Book Equation (3.3), on page 40, we find } \nu_H^* = \frac{\frac{10}{9}H + 2 \times \frac{4}{9}H\nu_2}{\frac{10}{9}H + 2 \times \frac{4}{9}H} = (5+4\nu_2)/9.$$

(iii)  $R_H^* = \mu^*\nu_H^* = \frac{2}{3}\mu \times [(5 + 4\nu_2)/9] = 2\mu(5 + 4\nu_2)/27$

(b) The solid curve in Figure 2 shows the graph of the ratio

$$\frac{R_H^*}{R_H} = \frac{2\mu(5 + 4\nu_2)/27}{\mu(1 + 2\nu_2)/3} = \frac{2}{9} \frac{5 + 4\nu_2}{1 + 2\nu_2} = \frac{2}{9} \left( 2 + \frac{3}{1 + 2\nu_2} \right)$$

against  $\nu_2$ .

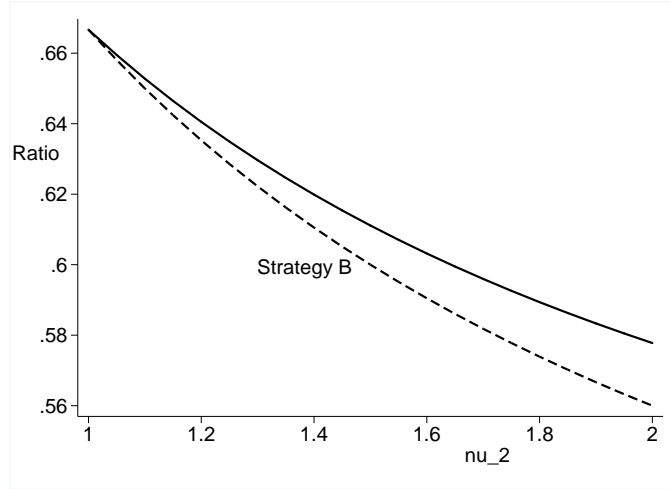


Figure 2. Solid curve: Graph of the ratio  $R_H^*/R_H$  against  $\nu_2$ .

Dashed curve: Corresponding graph for Strategy B, as in Book Figure 3.2.

By comparing this graph with the graphs of Book Figure 3.2 we see that randomly selecting individuals for vaccination reduces  $R_H$  more than Strategy A, almost as much as Strategy B, but substantially less than Strategy C.

4. For a community in which individuals mix uniformly, Book Equation (2.5) gives  $\nu = 1/(1 - R)$ . In Section 2.7.2 we substituted  $\nu$  by  $\bar{y}$ , the mean of observed outbreak sizes, and used the equation to obtain an estimate of  $R$ .

With a household outbreak as the unit that transmits the infection the corresponding estimating equation is  $\bar{m}_H = 1/(1 - R_H)$ , where  $\bar{m}_H$  is the mean of the number of infected household in observed outbreaks. Solving this equation for  $R_H$  gives the estimate of Book Equation (3.6).

## Chapter 4

2. (a)  $\Pr(\text{Type 1 primary infective infects at least one Type 2 individual}) = 0.2 + 0.1 + 0.1 = 0.4$ .

(b)  $\mu_{12} = 0 \times 0.6 + 1 \times 0.3 + 2 \times 0.1 = 0.5$ .

(c) Compute  $\mu_{11}$ ,  $\mu_{21}$  and  $\mu_{22}$  similarly, to get mean matrix  $\begin{pmatrix} \mu_{11} & \mu_{12} \\ \mu_{21} & \mu_{22} \end{pmatrix} = \begin{pmatrix} 0.3 & 0.5 \\ 0 & 1.3 \end{pmatrix}$ .

Therefore

$$\begin{aligned} R_T &= \frac{1}{2} \left( \mu_{11} + \mu_{22} + \sqrt{(\mu_{11} - \mu_{22})^2 + 4\mu_{12}\mu_{21}} \right) \\ &= \frac{1}{2} \left( 0.3 + 1.3 + \sqrt{(0.3 - 1.3)^2 + 0} \right) = 1.3. \end{aligned}$$

- (d) The equation  $x_2 = \sum_i \sum_j p_2(i, j) x_1^i x_2^j = 0.2 + 0.3x_2 + 0.5x_2^2$  can be written  $x_2^2 - 1.4x_2 + 0.4 = (x_2 - 1)(x_2 - 0.4) = 0$ .

$\pi_2$  is the smaller root of this equation. Therefore  $\pi_2 = 0.4$ .

- (e) Substitute  $\pi_2 = 0.4$  into equation

$$\pi_1 = \sum_i \sum_j p_1(i, j) \pi_1^i \pi_2^j = 0.4 + 0.2\pi_1 + 0.2\pi_2 + 0.1\pi_1\pi_2 + 0.1\pi_2^2$$

to get  $\pi_1 = 0.496 + 0.24\pi_1$ . Therefore  $\pi_1 = 0.6526$ .

- (f) When a fraction  $v_2$  of the initial Type 2 susceptibles is vaccinated, with a vaccine that provides full protection, the mean matrix becomes

$$\begin{pmatrix} \mu_{11}^* & \mu_{12}^* \\ \mu_{21}^* & \mu_{22}^* \end{pmatrix} = \begin{pmatrix} 0.3 & 0.5(1 - v_2) \\ 0 & 1.3(1 - v_2) \end{pmatrix}.$$

The post-campaign reproduction number is

$$\begin{aligned} R_T^* &= \frac{1}{2} \left( \mu_{11}^* + \mu_{22}^* + \sqrt{(\mu_{11}^* - \mu_{22}^*)^2 + 4\mu_{12}^*\mu_{21}^*} \right) \\ &= \frac{1}{2} \left( 0.3 + 1.3(1 - v_2) + \sqrt{[0.3 - 1.3(1 - v_2)]^2 + 0} \right) \quad (\text{A graph of this helps!}) \\ &= \begin{cases} 0.3, & \text{when } v_2 \geq \frac{10}{13}, \\ 1.3(1 - v_2), & \text{when } v_2 < \frac{10}{13}. \end{cases} \end{aligned}$$

We deduce that  $R_T^*$  is below 1 when the fraction of Type 2 susceptibles immunized is greater than  $3/13$ .

4. (a) Substituting  $\mu_{11} = \mu_{21} = \mu_1$  and  $\mu_{12} = \mu_{22} = \mu_2$  gives

$$R_T = \frac{1}{2} \left( \mu_1 + \mu_2 + \sqrt{(\mu_1 - \mu_2)^2 + 4\mu_2\mu_1} \right) = \mu_1 + \mu_2.$$

- (b) As  $\mu_{11} + \mu_{12} = \mu_1 + \mu_2$  and  $\mu_{21} + \mu_{22} = \mu_1 + \mu_2$ , the mean of the total number infected by an infective is the same for the two types. Therefore infectives are ‘homogeneous’, in the sense assumed in Chapter 2, and the reproduction number is  $\mu_1 + \mu_2$ , the common mean number infected.

Note, however, that Type 1 and Type 2 individuals may differ in other disease characteristics. For example, Type 1 infectives might be more infectious, but for a shorter period of time.

## Chapter 5

2. (a)  $\Pr(\text{B and C avoid being infected by A})$

$$\begin{aligned} &= \Pr(\text{B avoids infection by A}) \times \Pr(\text{C avoids infection by A}) \\ &= \exp(-1.5) \times \exp(-1.5/4) = 0.223 \times 0.687 = 0.153. \end{aligned}$$

- (b)  $\Pr(\text{C is infected by A, but B is not})$

$$\begin{aligned} &= \Pr(\text{C is infected by A}) \times \Pr(\text{B avoids infection by A}) \\ &= (1 - 0.687) \times 0.223 = 0.07. \end{aligned}$$

4. (a) Equating the total area under the graph of  $\omega(u)$  to 1 gives  $c = 0.25$ .

- (b) The probability that a primary household infective infects his susceptible household partner is  $1 - \exp[-\text{total area under the graph of } \omega(u)] = 1 - e^{-1} = 0.632$ .

- (c)  $R_H = \mu\nu_H$ , where  $\mu = \text{total area under the graph of } 2\omega(u)$  and  $\nu_H = 1 + \Pr(\text{primary household infective infects his household partner})$ .

$$\text{Therefore } R_H = \mu\nu_H = 2 \times (1 + 0.632) = 3.26.$$

- (d) When  $1 < u^* < 5$ , isolating each infective  $u^*$  time units after their infection changes  $\mu$  to  $\mu^* = \frac{1}{2}(u^* - 1)$  and  $\nu_H$  to  $\nu_H^* = 2 - \exp[-(u^* - 1)/4]$ .

Therefore we want  $u^*$  such that

$$\frac{u^* - 1}{2} \left[ 2 - \exp\left(-\frac{u^* - 1}{4}\right) \right] = 1$$

Numerical solution, e.g. using a spreadsheet, gives  $u^* = 2.52$  days.

6. (a) The initial mean matrix is  $\begin{pmatrix} \mu_{AA} & \mu_{AC} \\ \mu_{CA} & \mu_{CC} \end{pmatrix} = \begin{pmatrix} 0.8 \times 1 & 0.2 \times 1.5 \\ 0.8 \times 2 & 0.2 \times 3.0 \end{pmatrix} = \begin{pmatrix} 0.8 & 0.3 \\ 1.6 & 0.6 \end{pmatrix}$ .

(b) The initial reproduction number is

$$R_T = \frac{1}{2} \left( 0.8 + 0.6 + \sqrt{(0.8 - 0.6)^2 + 4 \times 0.3 \times 1.6} \right) = 1.4.$$

(c) Suppose onset of symptoms occurs in a child  $s$  time units after its infection. Then, isolating infected children at onset of symptoms changes the initial mean matrix to

$$\begin{pmatrix} \mu_{AA}^* & \mu_{AC}^* \\ \mu_{CA}^* & \mu_{CC}^* \end{pmatrix} = \begin{pmatrix} 0.8 & 0.3 \\ 1.6 \Omega_C(s) & 0.6 \Omega_C(s) \end{pmatrix},$$

where  $\Omega_C(s)$  is the area under infectivity profile  $\omega_C(u)$  from  $u = 0$  to  $u = s$ . Under this control measure the reproduction number  $R_T^*$  becomes

$$\begin{aligned} & \frac{1}{2} (\mu_{AA}^* + \mu_{CC}^* + \sqrt{(\mu_{AA}^* - \mu_{CC}^*)^2 + 4\mu_{AC}^*\mu_{CA}^*}) \\ &= \frac{1}{2} \left( 0.8 + 0.6 \Omega_C(s) + \sqrt{[0.8 - 0.6 \Omega_C(s)]^2 + 4 \times 0.3 \times 1.6 \Omega_C(s)} \right) = 0.8 + 0.6 \Omega_C(s). \end{aligned}$$

As  $R_T^* = 1$  implies  $\Omega_C(s) = \frac{1}{3}$ , we need  $s =$  ‘duration from infection until onset of symptoms’ small enough so that  $\Omega_C(s) \leq \frac{1}{3}$  is satisfied.

(d) Adults cannot infect anyone if all infected adults are isolated prior to becoming infectious. The mean matrix corresponding to this scenario is  $\begin{pmatrix} 0 & 0 \\ 1.6 & 0.6 \end{pmatrix}$ , which leads to reproduction number

$$R_T^* = \frac{1}{2} \left( 0 + 0.6 + \sqrt{(0 - 0.6)^2 + 4 \times 0 \times 1.6} \right) = 0.6.$$

As this is less than 1, it is indeed possible to prevent epidemics by very early isolation of most infected adults.

8. (a) The solution to Book Equation (5.8) is  $x(u) = x(0) \exp \left[ \lambda u - \int_0^u \varphi(w) dw \right]$ .

With  $\varphi(u) = \begin{cases} 0, & \text{for } 0 \leq u \leq \tau, \\ \alpha(u - \tau)^\gamma, & \text{for } u > \tau, \end{cases}$  this becomes

$$x(u) = \begin{cases} x(0) \exp(\lambda u), & \text{for } 0 \leq u \leq \tau, \\ x(0) \exp \left[ \lambda u - \frac{\alpha}{\gamma+1} (u - \tau)^{\gamma+1} \right], & \text{for } u > \tau. \end{cases}$$

(b) Figure 3 shows two curves from this family.

(i) Solid curve:  $\tau = 2, \lambda = 2, \alpha = 2.0$  and  $\gamma = 0.3$ ,

(ii) Dashed curve:  $\tau = 2, \lambda = 2, \alpha = 0.2$  and  $\gamma = 2.0$ .

The curves are scaled so that the area under the curve is 1.

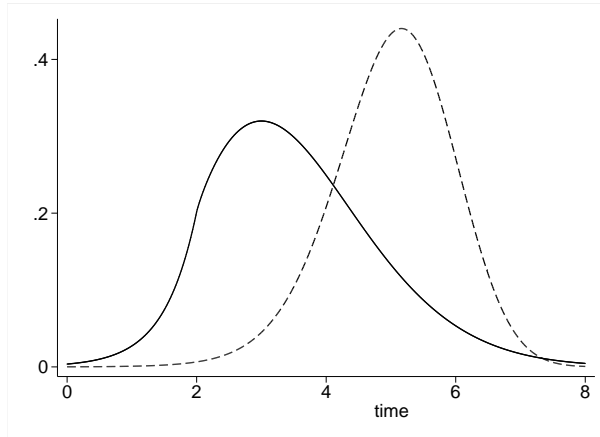


Figure 3: Infectivity profiles based on a model for the pathogen population size.

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## Chapter 6

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2. (a) With full vaccination coverage, Vaccines 1, 2 and 3 achieve post-campaign effective reproduction numbers of 0.5, 0.42 and 0.18, respectively (using  $R_1 = abR_0$ ). In this case Vaccine 3 achieves the lowest post-campaign effective reproduction number.
- (b) With achievable coverage  $v$  the post-campaign effective reproduction number becomes  $R_v = [1 - (1 - ab)v]R_0$ . With  $v$  values of 0.7, 0.5 and 0.3 for Vaccines 1, 2 and 3, respectively, the post-campaign effective reproduction numbers are 0.95, 1.21 and 1.454.
- Vaccine 1 should be adopted for an immunization campaign.

4. Let fully susceptibles be Type 1 individuals and successfully vaccinated individuals be Type 2. Type 1 individuals include vaccinees whose vaccination failed. With vaccination coverage  $v$ , the fraction of community members that are Type 1 is  $1 - (1 - f)v$  and a fraction  $(1 - f)v$  are Type 2.

- (a) Post-campaign, the type-specific mean number of offspring for the two types is

$$\begin{pmatrix} \mu_{11} & \mu_{12} \\ \mu_{21} & \mu_{22} \end{pmatrix} = \begin{pmatrix} [1 - (1 - f)v]R_0 & a(1 - f)vR_0 \\ b[1 - (1 - f)v]R_0 & ab(1 - f)vR_0 \end{pmatrix}.$$

This gives the post-campaign reproduction number as  $R_T^* = [1 - (1 - ab)(1 - f)v]R_0$ .

- (b) The campaign is able to prevent epidemics provided the reproduction number  $R_T^*$  is below 1 when vaccination coverage is 100%. That is, provided  $(1 - ab)(1 - f) > 1 - 1/R_0$ . When the values of  $a$ ,  $b$  and  $f$  satisfy this condition, we solve the equation  $R_T^* = 1$  for  $v$  to obtain the critical vaccination coverage

$$v^\dagger = \frac{1 - 1/R_0}{(1 - ab)(1 - f)}.$$

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## Chapter 7

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2. (a) Let non-responders and responders be Type 1 and Type 2, respectively. Using Book Equation (7.1), the post-intervention mean matrix is

$$\begin{pmatrix} \mu_{11}^* & \mu_{12}^* \\ \mu_{21}^* & \mu_{22}^* \end{pmatrix} = \begin{pmatrix} 0.6 \times R_0 & 0.5 \times 0.4 \times R_0 \\ 0.5 \times 0.6 \times R_0 & 0.5^2 \times 0.4 \times R_0 \end{pmatrix} = \begin{pmatrix} 0.6R_0 & 0.2R_0 \\ 0.3R_0 & 0.1R_0 \end{pmatrix}.$$

For this mean matrix, Book Equation (4.2) gives the reproduction number  $0.7R_0$ . This is less than 1 provided  $R_0 < 1/0.7 = 1.43$ .

- (b) Let Type 1 be individuals who adjust their mixing by a small amount and Type 2 be those who reduce their mixing substantially. Post-intervention the mean matrix is

$$\begin{pmatrix} 0.8^2 \times 0.7 \times R_0 & 0.8 \times 0.2 \times 0.3 \times R_0 \\ 0.8 \times 0.2 \times 0.7 \times R_0 & 0.2^2 \times 0.3 \times R_0 \end{pmatrix} = \begin{pmatrix} 0.448R_0 & 0.048R_0 \\ 0.112R_0 & 0.012R_0 \end{pmatrix}.$$

For this mean matrix, Book Equation (4.2) gives the reproduction number  $0.46R_0$ . This is less than 1 provided  $R_0 < 1/0.46 = 2.17$ .

4. When a fraction of community members change their mixing rate we have two types of individual, non-responder (Type 1) and responder (Type 2).

- (a) The type-specific mean number of primary household cases generated by the two types of infective is described by

$$\begin{pmatrix} \mu_{11}^* & \mu_{12}^* \\ \mu_{21}^* & \mu_{22}^* \end{pmatrix} = \begin{pmatrix} 0.5\mu & 0.5a\mu \\ 0.5a\mu & 0.5a^2\mu \end{pmatrix}.$$

The mixing by non-responders and responders within households is identical. As both members of each household are of the same type we have  $\begin{pmatrix} \nu_{11}^* & \nu_{12}^* \\ \nu_{21}^* & \nu_{22}^* \end{pmatrix} = \begin{pmatrix} \nu_H & 0 \\ 0 & \nu_H \end{pmatrix}$ .

Therefore  $\begin{pmatrix} m_{11}^* & m_{12}^* \\ m_{21}^* & m_{22}^* \end{pmatrix} = \begin{pmatrix} 0.5\mu\nu_H & 0.5a\mu\nu_H \\ 0.5a\mu\nu_H & 0.5a^2\mu\nu_H \end{pmatrix}$  and  $R_{HA}^* = \frac{1}{2}(1+a^2)R_{H0}$ .

When  $R_{H0} = 1.6$ , an epidemic is prevented when  $\frac{1}{2}(1+a^2) \times 1.6 < 1$ , i.e.  $a < 0.5$ .

- (b) The type-specific mean number of primary household cases generated is again

$$\begin{pmatrix} \mu_{11}^* & \mu_{12}^* \\ \mu_{21}^* & \mu_{22}^* \end{pmatrix} = \begin{pmatrix} 0.5\mu & 0.5a\mu \\ 0.5a\mu & 0.5a^2\mu \end{pmatrix}.$$

However, when every household has one individual of each type, we have

$$\begin{pmatrix} \nu_{11}^* & \nu_{12}^* \\ \nu_{21}^* & \nu_{22}^* \end{pmatrix} = \begin{pmatrix} 1 & \nu_H - 1 \\ \nu_H - 1 & 1 \end{pmatrix}, \text{ giving } \begin{pmatrix} m_{11}^* & m_{12}^* \\ m_{21}^* & m_{22}^* \end{pmatrix} = \frac{1}{2}\mu \begin{pmatrix} \tilde{a} + a\nu_H & \nu_H - \tilde{a} \\ a\tilde{a} + a^2\nu_H & a\nu_H - a\tilde{a} \end{pmatrix}.$$

Therefore  $R_{HB}^* = \frac{1}{2}\tilde{a}^2\mu + a\mu\nu_H$ .

- (c) With  $a = 0.6$  and  $\nu_H = 1.9$  we find

$$R_{HA}^* = \frac{1}{2}(1+a^2)\mu\nu_H = 1.292\mu \quad \text{and} \quad R_{HB}^* = \frac{1}{2}\tilde{a}^2\mu + a\mu\nu_H = 1.22\mu.$$

Hence  $R_{HA}^* > R_{HB}^*$  when  $a = 0.6$  and  $\nu_H = 1.9$ .

- (d)  $R_{HA}^* \geq R_{HB}^*$  when  $\frac{1}{2}(1+a^2)\mu\nu_H \geq \frac{1}{2}\tilde{a}^2\mu + a\mu\nu_H$ . This requires

$$(1+a^2)\nu_H - (1-a)^2 - 2a\nu_H = (1-a)^2(\nu_H - 1) \geq 0.$$

This is always true and hence  $R_{HA}^* > R_{HB}^*$  is always true.

## Chapter 8

2. (a) The community attack rate  $y$  satisfies  $0.4 - y = 0.4 \exp(-6.4y)$ . Numerically, its solution is found to be  $y = 0.360$ .
- (b) The initial reproduction number is  $R = s_0 R_0 = 0.4 \times 6.4 = 2.56$ .
- (i) Need community coverage  $v$  such that  $(1-v)R = 1$ , giving  $v = 1 - \frac{1}{2.56} = 0.609$ .
- (ii) When we target susceptibles, the fraction of community members we need to vaccinate to prevent epidemics is  $v_s$ , given by  $(s_0 - v_s)R_0 = 1$ . This leads to  $v_s = s_0 - 1/R_0 = 0.4 - 1/6.4 = 0.244$ .
- (c) (i) Cost incurred by an epidemic is  $100 \times 0.360 \times 825,000 \simeq \$30\text{m}$ .
- (ii) Indiscriminate vaccination: Cost =  $100 \times 0.609 \times 625,000 \simeq \$38\text{m}$ .
- (iii) Vaccinating susceptibles: Cost =  $6,750,000 + 100 \times 0.244 \times 625,000 \simeq \$22\text{m}$ .
- (d) It depends on the risk of an epidemic. If an epidemic is likely, the cheapest option is to determine who is susceptible and vaccinating only susceptibles.
4. (a) The proportion of cases among unvaccinated individuals equals the proportion of cases among individuals vaccinated with an inactive vaccine.
- Therefore  $\frac{0.8 \times 0.12}{0.15} = \frac{0.2 \times 0.12}{0.85f}$ , which gives estimate  $\hat{f} = \frac{0.2 \times 0.15}{0.8 \times 0.85} = 0.044$ .
- That is, 4.4% of vaccinations are estimated to fail.

- (b) The initial fraction of individuals that are susceptible is  $s_0 = 0.15 + 0.85f = 0.1875$ . With this value of  $s_0$  the final-size equation becomes  $0.1875 - 0.12 = 0.1875 \exp(-0.12R_0)$  and we obtain the estimate  $\widehat{R}_0 = 8.51$ .
- (c) Initial  $R$  is estimated by  $\widehat{s}_0 \widehat{R}_0 = 0.1875 \times 8.51 = 1.60$ .
- (d) Final  $R$  is estimated by  $(\widehat{s}_0 - 0.12) \widehat{R}_0 = (0.1875 - 0.12) \times 8.51 = 0.57$ .
6. (a) With parameter values  $\alpha = 1$ ,  $\beta = 4$ ,  $s_{01} = 0.8$  and  $s_{02} = 0.2$ , Book Equations (8.3) become

$$1 - y_{S_1} = \exp(-0.8y_{S_1} - 0.2y_{S_2}) \quad \text{and} \quad 1 - y_{S_2} = \exp(-0.8y_{S_1} - y_{S_2}).$$

The first equation gives  $y_{S_2} = -\frac{0.8y_{S_1} + \ln(1 - y_{S_1})}{0.2}$ . In a spreadsheet, we can use this equation to find the values of  $y_{S_2}$  corresponding to a column of  $y_{S_1}$  values.

Substituting the pairs of  $(y_{S_1}, y_{S_2})$  values from this spreadsheet into the second equation allows us to find its solution.

This numerical solution gives  $y_{S_1} = 0.283$ ,  $y_{S_2} = 0.531$  and  $y = 0.8y_{S_1} + 0.2y_{S_2} = 0.333$ .

The type-specific reproduction number is obtained from the type-specific mean number of offspring, given by

$$\begin{pmatrix} \mu_{11} & \mu_{12} \\ \mu_{21} & \mu_{22} \end{pmatrix} = \begin{pmatrix} 0.8 & 0.2 \\ 0.8 & 1 \end{pmatrix}.$$

With these means, Equation (4.2) gives

$$R_T = \frac{1}{2} \left( 0.8 + 1 + \sqrt{(0.8 - 1)^2 + 4 \times 0.2 \times 0.8} \right) = 1.312.$$

- (b) For parameter values  $\alpha = 1$  and  $\beta = 0$  equations for the type-specific attack rates become  $1 - y_{S_1} = \exp(-0.8y_{S_1} - 0.2y_{S_2})$  and  $1 - y_{S_2} = \exp(-0.8y_{S_1} - 0.2y_{S_2})$ . We deduce that  $y_{S_1} = y_{S_2}$  and the common value satisfies  $1 - x = \exp(-x)$ . The only value satisfying this equation is  $x = 0$ . Hence  $y_{S_1} = y_{S_2} = y = 0$ . In other words, there is no epidemic. The type-specific reproduction number is obtained from the type-specific mean number of offspring, given by

$$\begin{pmatrix} \mu_{11} & \mu_{12} \\ \mu_{21} & \mu_{22} \end{pmatrix} = \begin{pmatrix} 0.8 & 0.2 \\ 0.8 & 0.2 \end{pmatrix}.$$

With these means, Book Equation (4.2) gives  $R_T = 1$ .

Comment: For these parameter values, a total ban on mass-gathering events is able to prevent an epidemic. Of course, in practice there would be considerable resistance to a total ban from those with vested interest in mass-gathering events.

## Chapter 9

2. (a) (i) From Book Equation (8.1), in the form  $1 - y = \exp(-1.6y)$ , we find the final attack rate  $y = 0.642$ . We predict that about 642 individuals will be infected.
- (ii) Compute an epidemic curve in generation time, as in Section 9.1.2, using a generation time of 2.5 days. A peak generation incidence of 82.23 is found. Therefore, we predict that the peak daily incidence attained is about  $82.23/2.5 \simeq 33$ .
- (iii) Let Generation 1 consist of the initial infective and calendar time  $t = 0$  correspond to his 'mid-infectious period'. The computed epidemic curve shows a peak for Generation 13, which corresponds to calendar time  $t = 12 \times 2.5 = 30$ . We predict that peak incidence occurs about 30 days after the mid-infectious period of the initial infective.
- (iv) Expect the daily incidence to be above 10 when the generation size is above 25. This occurs for 9 generations, which corresponds to about 22 to 23 days.
- (b) Now the initial number of susceptibles is 800.



- (i) From Book Equation (8.1), in the form  $0.8 - y = 0.8 \exp(-1.6y)$ , we find final attack rate  $y = 0.322$  and so predict that about 322 individuals will be infected.
  - (ii) Peak daily incidence attained is about  $21.66/2.5 \simeq 9$ .
  - (iii) Peak incidence predicted to be on day 42 or 43.
  - (iv) Expect the daily incidence to be above 10 when the generation size is above 25. It is predicted that this will not happen.
- (c)
- Immunizing only 20% of susceptibles roughly halves the total number of cases.
  - The number of cases prevented exceeds the number of individuals immunized.
  - The reduction of the peak of daily incidence, from 33 to 9, lowers the burden on resources at the peak time substantially.
  - This immunization delays the time of the peak of the epidemic substantially, which helps by providing more time to prepare for the period when demand on medical facilities will be highest. However, it does mean that the epidemic may linger longer.
  - The immunization reduces the period of high demand on resources substantially, e.g. the time period during which there are more than 10 cases per day.
4. (a) The probability distribution of a sample mean is approximately Normal when the sample size is moderate to large, which we assume. This Normal approximation gives the 95% confidence interval

$$(6.9 - 1.96 \times 0.2, 6.9 + 1.96 \times 0.2) = (6.508, 7.292)$$

for the population mean age at infection.

Using this in Book Figure 9.9, as shown in Figure 4, leads to the 95% confidence interval (8.71, 9.57) for  $R_0$ .

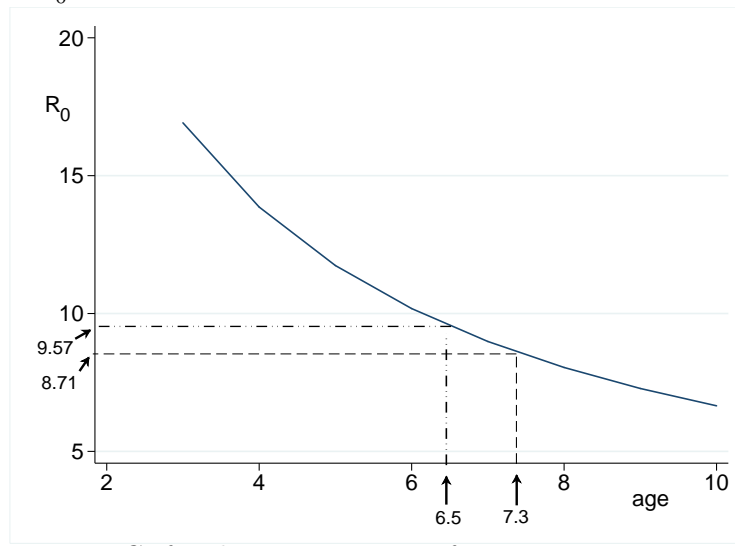


Figure 4: Using a CI for the mean age at infection to construct a CI for  $R_0$ .

- (b) With a mean age at infection of 16.9, a similar approach leads to 95% confidence interval
- $$(16.9 - 1.96 \times 0.2, 16.9 + 1.96 \times 0.2) = (16.508, 17.292)$$
- for the mean age at infection parameter. The graph of  $R_0$  versus ‘mean age at infection’ now leads to the 95% confidence interval (4.14, 4.31) for  $R_0$ .
- (c) The two confidence intervals differ in two obvious ways. First, a larger ‘mean age at infection’ leads to a smaller estimate of  $R_0$ , as expected by inspecting Book Figure 9.9. Second, the larger ‘mean age at infection’ led to a narrower confidence interval. This might also be expected from Book Figure 9.9. [Note, however, that the width of the confidence intervals differ, in part, because the standard error of the sample mean in (a) and (b) was the same. It is far from clear that this happens in practice.]
6. (a) Suppose in Generation  $r$  there are  $I_r$  infectives of Type 1 and  $J_r$  infectives of Type 2. The number of susceptibles exposed to these Generation  $r$  infectives is  $S_r$  for Type 1 and  $W_r$  for Type 2.

From the given data  $I_1 = 0$ ,  $J_1 = 1$ ,  $S_1 = 1200$ ,  $W_1 = 800$  and

	Mean number of susceptibles infected	
	Type 1	Type 2
Type 1 Infective	$\frac{1200}{2000}\beta_{11} = 0.6$	$\frac{800}{2000}\beta_{12} = 0.8$
Type 2 Infective	$\frac{1200}{2000}\beta_{21} = 1.2$	$\frac{800}{2000}\beta_{22} = 2.0$

This gives  $\beta_{11} = 1$ ,  $\beta_{12} = 2$ ,  $\beta_{21} = 2$  and  $\beta_{22} = 5$ .

Generation sizes are computed iteratively using

$$I_{r+1} = S_r [1 - \exp(-I_r/2000 - 2J_r/2000)] \quad \text{and} \quad S_{r+1} = S_r - I_{r+1} \quad \text{for Type 1,}$$

$$J_{r+1} = W_r [1 - \exp(-2I_r/2000 - 5J_r/2000)] \quad \text{and} \quad W_{r+1} = W_r - J_{r+1} \quad \text{for Type 2.}$$

These computations lead to the three epidemic curves in Figure 5, where ‘day’ is the number of days following the median of the primary infective’s infectivity profile. (A generation is taken as 4 days.)

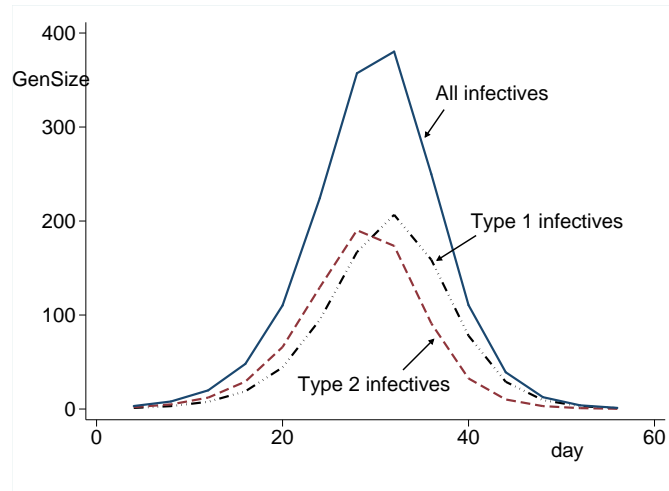


Figure 5. Epidemic curve for Type 1, Type 2 and ‘All’ infectives with no immunization. Vertical axis gives the number of infectives in generations 1, 2, 3, ..., 15. The horizontal axis has been stretched to reflect calendar time.

(b) Figure 6 shows the epidemic curves when there are 600 prior Type 1 vaccinations.

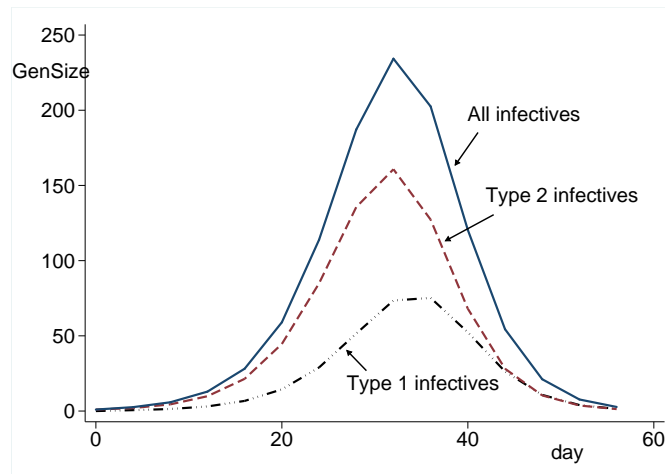


Figure 6: Corresponding epidemic curves with 600 prior Type 1 vaccinations.

Six hundred Type 1 vaccinations

- (i) reduce the maximum number of infections in a single generation from 380 to 234,
- (ii) change the time to reach peak incidence minimally.

- (c) Six hundred Type 2 vaccinations reduce  $R$ , the initial reproduction number, to 1.04. A deterministic model can only provide rough guidance when  $R$  is so close to 1, because chance plays a significant role in such outbreaks. A clear picture requires a simulation study.
- (i) The deterministic model predicts a maximum number of infectives in a single generation of about 2 or 3.
- (ii) The time of peak incidence is subject to considerable chance variation. Occasionally such outbreaks linger for a long time.
- (d) Targeting Type 2 individuals for vaccination is a far more effective way to mitigate the impact of an outbreak.

**Note:** To predict the *day* when the maximum incidence occurs requires more information on the form of the infectivity profile.

## Chapter 10

2. The chains and chain probabilities are as follows:

Chain	Binomial components	Chain-binomial probability
2	$q_2^3$	$q_2^3$
2 → 1	$3q_2^2(1 - q_2) \times q^2$	$3q^2 q_2^2 \tilde{q}_2$
2 → 1 → 1	$3q_2^2(1 - q_2) \times 2q(1 - q) \times q$	$6q^2 \tilde{q} q_2^2 \tilde{q}_2$
2 → 2	$3q_2(1 - q_2)^2 \times q_2$	$3q_2^2 \tilde{q}_2^2$
2 → 1 → 1 → 1	$3q_2^2(1 - q_2) \times 2q(1 - q) \times (1 - q)$	$6q \tilde{q}^2 q_2^2 \tilde{q}_2$
2 → 1 → 2	$3q_2^2(1 - q_2) \times (1 - q)^2$	$3\tilde{q}^2 q_2^2 \tilde{q}_2$
2 → 2 → 1	$3q_2(1 - q_2)^2 \times (1 - q_2)$	$3q_2 \tilde{q}_2^3$
2 → 3	$(1 - q_2)^3$	$\tilde{q}_2^3$

4. We test for the independence of two classifications of a contingency table. This is a large-sample test, so the expected frequency in each cell should be at least five. To ensure this we pool household outbreaks of size four and five, giving the frequencies shown below.

Outbreak size	Frequency			Total
	Overcrowded	Crowded	Uncrowded	
1	112 (115.3)	155 (153.5)	156 (154.2)	423
2	35 (35.7)	41 (47.5)	55 (47.7)	131
3	17 (16.4)	24 (21.8)	19 (21.9)	60
4 & 5	17 (13.6)	21 (18.1)	12 (18.2)	50
Total	181	241	242	664

The corresponding ‘expected’ frequencies, fitted under the assumption that the classifications ‘outbreak size’ and ‘level of crowding’ are independent, are shown in brackets. The fitted frequency corresponding to the observed frequency of a given cell is computed by

$$\frac{(\text{sum of observed frequencies for its row}) \times (\text{sum of observed frequencies for its column})}{664}$$

The value of the goodness-of-fit statistic is

$$\frac{(112 - 115.3)^2}{115.3} + \frac{(155 - 153.5)^2}{153.5} + \dots + \frac{(12 - 18.2)^2}{18.2} = 6.18.$$

This is less than 10.64, the 90<sup>th</sup> percentile of the  $\chi^2$ -distribution, with  $(4 - 1) \times (3 - 1) = 6$  degrees of freedom. Therefore we accept the independence of the two classifications. That is, we accept that the distribution of outbreak size is similar for the three levels of crowding.