Episouth Training Module, Madrid (June 2008)

Modelling the dynamics of immunizing infections using Excel

Practical Solutions

Part I: setting up models using difference equations

Step 2, page 3: The expressions set up in parts a and b should be:

a) =D43+C43*dis_rate-D43*rec_rate
b) =E43+D43*rec_rate

Q1.1 You should notice that the number of cases increases to a peak at about 40 days and then decreases. No further cases arise in the population after a certain time as there are no more susceptible individuals -- all have been infected, have developed disease and are immune to further infection. According to the graph, no further cases occur after about 80 days. According to the values in column D, there is less than 1 case present in the population after day 120.

Q1.2 To make the measles epidemic finish sooner, you could decrease the latent period, infectious periods and R_0. To make the measles epidemic finish later, you could increase the latent period, infectious periods and R_0.
Note that for the model to reflect the transmission dynamics of measles, the latent and infectious periods have to lie within a given interval (corresponding to a latent period of 6-9 days and an infectious period of 6--7 days).

Q1.3 To describe the infection process in a **town/country** you might increase the population size. You might also consider incorporating more diversity eg in transmission between individuals (eg incorporate age-dependent transmission).
To model the infection process over a period of years in both settings you would need to incorporate individuals being born and dying in the population.
In a town, you may need to incorporate imported infections (e.g. migrants) entering the population from other towns; this assumption may be less important for modelling the infection process in a country.

Q1.4 The daily mortality rate is 3.914×10^{-5} /day. The birth rate is the same as the mortality rate and therefore the population size should remain unchanged over time.

Q1.5 The daily number of births is given by Total population size $\times$ birth rate.

Q1.6 It is not **realistic**, since infants have some immunity derived from maternal antibodies. However, it is a **reasonable** assumption to make, since infants comprise a relatively small proportion of the total population, and so will not contribute much to the overall transmission dynamics considered. To make the model more realistic, you could add another "compartment" reflecting infants with maternally-derived immunity and have these individuals become susceptible to infection at a constant rate.

Q1.7 Individuals are not born infected, infectious or immune and therefore equations 2-4 do not need to be altered.

Q1.8

$$E_{t+1} = E_t + ßS_t I_t – fE_t - m\_rate \times E_t \quad (2)$$
$$I_{t+1} = I_t + f E_t – r I_t - m\_rate \times I_t \quad (3)$$
$$R_{t+1} = R_t + r I_t - m\_rate \times R_t \quad (4)$$

Q1.9 If you are just looking at the graph, your answer should be identical to that for Q1.6 (ie 80 days). Looking at the numbers in column D, this should be about 136 days. If you model the infection process over a long time period, then you might expect the number of new cases to oscillate over time.

Q1.10 You should now see a few peaks in the number of susceptible and immune individuals occuring roughly every 3 years about 30 years after the start of the simulations. Note also that when the number of susceptibles peaks, you see a dip in the number of immune individuals.

PART II: The relationship between the basic and net reproduction numbers and the herd immunity threshold

Q2.1 The R_n cycles over time, and on average, it is 1. When the disease incidence reaches a peak or a trough, R_n=1.

Q2.2 When R_n<1, the disease incidence is declining; when R_n>1, the disease incidence is increasing. When R_n=1, the disease incidence is neither increasing nor decreasing. ie it starts to increase when R_n is just slightly above 1. This is intuitively reasonable (at least for measles in the absence of control): if R_n>1, then each case is leading to more than one other case and so you'd expect the disease incidence to be increasing.

You might wonder if this is true for all infections. If the R_n is above 1 at a given time, should the disease incidence also be increasing at the same time if eg the latent period is very long (months? decades?)

Q2.3 The fact that the disease incidence has reached a peak suggests that R_n=1. Given estimates of the proportion of individuals who are susceptible in the population, you could calculate R_0 as 1/(proportion susceptible).

Q2.4 The proportion susceptible is about 0.078 when the disease incidence peaks or troughs. Given that R_n=1 at a peak/trough, this implies that R_0= 1/0.078 = 13 (approximately)

Q2.5 HIT=1-1/13 = 0.92 = 92%

Q2.6 The proportion immune is about 0.92 when the disease incidence peaks or troughs. It is above 0.92 when the disease incidence is decreasing and below 0.92 when the disease incidence is increasing.

The increases/decreases in incidence correlate with whether the proportion of individuals who are immune in the population is below/above the herd immunity threshold. Therefore, for the disease to die out in the population, the proportion immune would have to be maintained above the herd immunity threshold.

Supplementary questions – analyses of factors influencing the cycles in disease incidence

Q3.1 NB your answer will depend on the scale you use for the y-axis. The following shows what you would have seen if you hadn't changed the settings at all, with the y-axis scale going up to 100 cases (in 3 days).

	Number of cycles in disease incidence/decade in a population with an R_0 of:		
Time period	5	13	18
0-10 yrs	1	1	1
11-20 yrs	0	1	1
21-30 yrs	0	2	2
31-40 yrs	1	2	2.5
41-50 yrs	0	3	3
51-60 yrs	0	3	4
61-70 yrs	1	3	4
71-80 yrs	1	3	4
81-90 yrs	0	3	4
91-100 yrs	1	3	--
101-110 yrs	1	--	--
121-130 yrs	2	--	--
141-150 yrs	2	--	--
Inter-epidemic period (yrs)	5	3.3	2.5

The inter-epidemic period is calculated as Time period/(number of cycles in that period), eg 10/(number of cycles in a 10 year period). You might argue that in the population for which R_0=18, the epidemics die out after about 90 years, though you would still see fluctuations in the disease incidence if you refine the y axis scale (using e.g. a linear scale, going from 30 to 40).

Note: You should notice that though the incidence of infectious cases oscillates over time, these oscillations become less marked, and ultimately they seem to disappear entirely. This pattern is inconsistent with what happens in reality --- in many populations in which measles vaccination has not been introduced, measles incidence exhibits regular biennial cycles. This inconsistency has led modellers to suggest that other factors must help to sustain the epidemic cycles eg immigration, seasonality in transmission; mixing patterns (eg age-dependent transmission). (See also section 6.5 in Anderson and May (1991) for a detailed discussion of these factors).

Q3.2 Measles is transmitted more “efficiently” (ie each case leads to more secondary infectious cases) in populations with an R_0 of 18 as compared with one in which the R_0 is 5. Thus the time elapsed before the prevalence of susceptibles in the second population *decreased sufficiently to lead to decreases* in disease incidence is longer than in populations in which the R_0 is 5.

Q3.3 Using the equation you should get 5.3 (R_0=5); 3.1 years (R_0=13); 2.6 years (R_0=18).
Note that D'+D in the formula given is the "serial interval" or generation time (the time interval between sucessive cases in a chain of transmission.

Q3.4 The values you should get are:

Infection	**R_0**	Latent period (days)	Infectious period (days)	Inter-epidemic period (yrs)
Measles	13	8	7	3.1
Mumps	8	15	6	4.8
Rubella	7	10	11	5.0
Chickenpox	7	10	10	5.0

Note that the inter-epidemic period is very similar for mumps, rubella and chickenpox, as the average serial intervals are identical.

You would expect the inter-epidemic period for measles to be shorter than for the other infections as the time interval between successive generations (or the serial interval!) is also shorter. In addition, measles is more "infectious" than these infections, as its R_0 is higher. This suggests that it might pass through a population (and thus cycle through epidemics) more quickly than the other infections.