Chapter 4 (Solutions)

What do models tell us about the dynamics of infections?

4.1 a) Figure S4.1a plots the observed data for Gothenburg. This shows that two pandemic waves occurred, with the first occurring in July 1918 and the second occurring in September-October 1918. The cumulative numbers of cases for these waves are shown in Figure S4.1b. The natural log of the cumulative numbers of cases for these two waves are shown in Figure S4.1c.

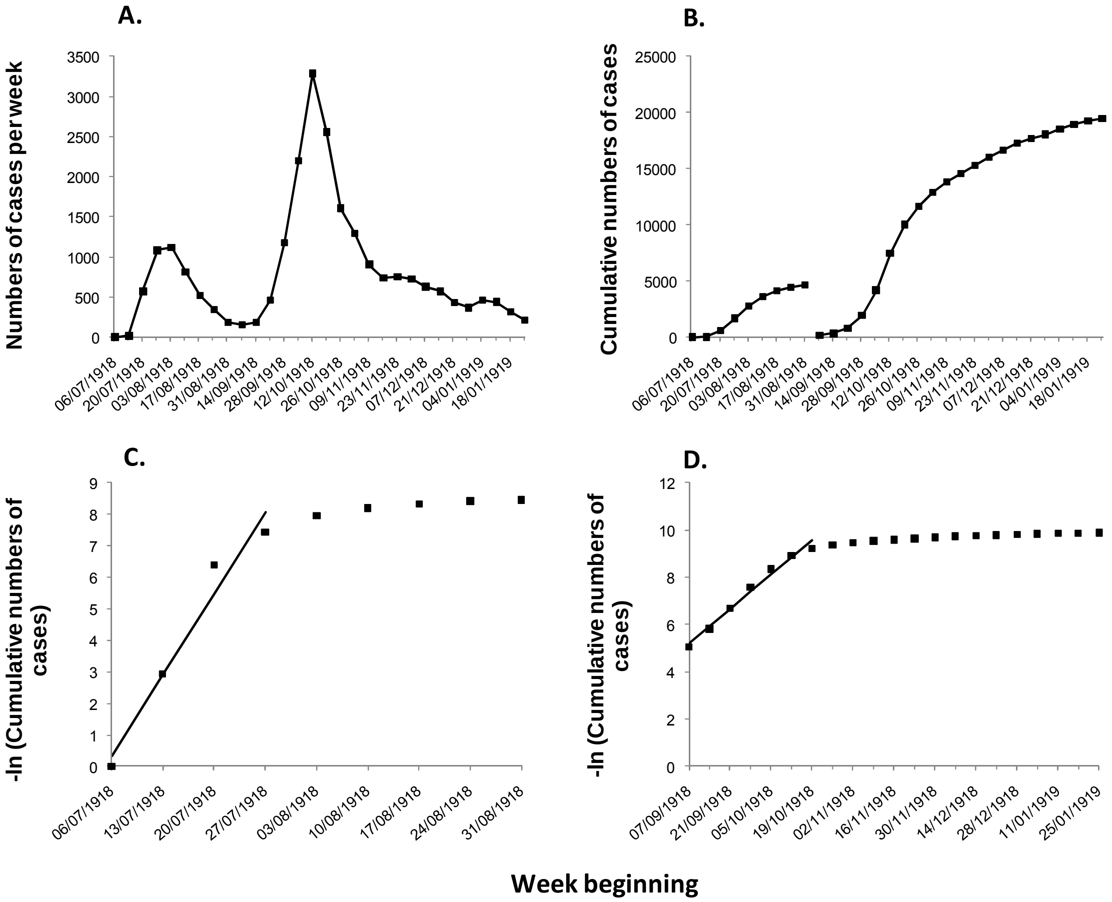

Figure S4.1: Summary of A. The numbers of cases reported each week, B. The cumulative numbers of reported cases and C. and D. the natural log of the cumulative numbers of cases observed during the first and second waves (C. and D. respectively) of the influenza pandemic in Gothenberg, Sweden in 1918.

A straight line can be drawn through the first 4 points of the natural log of the cumulative numbers of cases for the first wave (corresponding to the period 6/7/1918-27/7/1918); this line (drawn either by eye or formally by regression) has a slope of 0.367 per day.

A straight line can be drawn through the first 7 points of the natural log of the cumulative numbers of cases for the second wave (corresponding to the period 7/9/1918-19/10/1918). This line has a slope of 0.104 per day.

The following summarizes the estimates for the net and basic reproduction numbers obtained using the different formulae in Table 4.1, with R_0 estimated to be about 4 for the first wave and just under 3 for the second wave of the pandemic. These estimates are slightly higher than the values that have typically been estimated for the 1918 (Spanish) influenza pandemic (see references in the book for details). Notice that estimates obtained using the formula $(1+\Lambda D)(1+\Lambda D')$ and $\dfrac{\Lambda D\left(\frac{\Lambda D'}{m}+1\right)^{m}}{\left(1-\left(\frac{\Lambda D}{n}+1\right)^{-n}\right)}$ are very similar.

Equation used to calculate the reproduction number:		R_n		R_0*	
		1st wave	**2nd wave**	**1st wave** (s=0.7)	**2nd wave** (s=0.5)
$1+\Lambda D$		1.73	1.21	2.48	2.42
$(1+\Lambda D)(1+\Lambda D')$		3.01	1.46	4.30	2.92
$\dfrac{\Lambda D\left(\frac{\Lambda D'}{m}+1\right)^{m}}{\left(1-\left(\frac{\Lambda D}{n}+1\right)^{-n}\right)}$	m=n=10	2.94	1.37	4.20	2.75
	m=n=100	2.94	1.36	4.20	2.73

* Calculated using the expression R_n/(proportion susceptible (s) at the start of the wave)

b) It would be sensible to apply the epidemic size formula to data from the two waves separately.

Considering the first wave of the pandemic (taken to be during the period 6/7/1918-31/8/1918), 4,657 individuals were reported to have experienced disease. If 70% of individuals were susceptible at the start of the first wave (s_0=0.7), the proportion that were susceptible at the end of the first wave is given by the difference between 0.7 and the proportion of the population who experienced disease during the first wave. This calculation assumes that all of those who were reported as cases became immune (see below). We therefore obtain the following result:

$$s_f = 0.7 - 4{,}657/196{,}943 \approx 0.676$$

Substituting for s_0 and s_f into the equation $R_0 = \frac{\ln(s_f) - \ln(s_0)}{s_f - s_0}$ implies that R_0 equals the following:

$$R_0 = \frac{\ln(0.676) - \ln(0.7)}{0.676 - 0.7} = 1.45$$

Considering the second wave of the pandemic (the period after 7/9/1918), 19,484 individuals were reported to have experienced disease. Assuming that 50% of individuals were susceptible at the start of this wave (s_0=0.5), then applying a similar reasoning to that used to calculate s_f for the first wave, we obtain the following for the proportion of the population that was susceptible at the end of the second wave:

$$s_f = 0.5 - 19{,}484/196{,}943 \approx 0.401$$

Substituting for s_0 and s_f into the equation $R_0 = \frac{\ln(s_f) - \ln(s_0)}{s_f - s_0}$ implies that R_0 equals the following:

$$R_0 = \frac{\ln(0.401) - \ln(0.5)}{0.401 - 0.5} = 2.23$$

c) The estimates of R_0 that are based on the growth rate are likely to be more reliable than are those based on the final epidemic size, since they are independent of the proportion of cases that are reported (unless this changes over time). It is unlikely that all cases were reported during the pandemic, and therefore R_0 based on the epidemic size is likely to have been underestimated. However, estimates based on both methods need to make assumptions about the proportion of individuals that are susceptible at the start of the first and second waves. Whilst the values assumed (70% and 50% for the start of the first and second waves respectively) are plausible, it is unclear as to whether they are correct.

d) The lower estimate of R_0 for the second wave (calculated using the epidemic growth rate), as compared with that for the first wave suggests that in Gothenberg, the transmissibility decreased between the first and second waves. However, the value for R_0 during the first wave seems somewhat high in contrast with estimates obtained elsewhere (see references cited in the main text) and it seems plausible that the proportion of cases that were reported changed during the early stages of the first wave of the pandemic. Such changes in the proportion of cases that were reported would have led to an overestimate in R_0.

4.2 a) According to equation 4.31, the inter-epidemic period is given by the following:

$$T = 2\pi\sqrt{\frac{L(D + D')}{R_0 - 1}}$$

We can rearrange this equation to obtain the following equation for R_0:

$$R_0 = 1 + \frac{4\pi^2 L(D + D')}{T^2}$$

Substituting for L=70×365 days, T=2×365 days, D'=8 days and D=7 days into this equation leads to the following:

$$R_0 = 1 + \frac{4\pi^2 \times 70 \times 365 \times (7+8)}{(2 \times 365)^2} \approx 29$$

b) According to equation 4.32, the inter-epidemic period (T) is given by the equation:

$$T = 2\pi\sqrt{A(D+D')}$$

This equation can be rearranged to give the following for the average age at infection:

$$A = \frac{T^2}{4\pi^2(D+D')} \qquad \text{S4.1}$$

Substituting for T=3×365 days, D'=8 days and D=7 days into this equation implies that

$$A = \frac{(3 \times 365)^2}{4\pi^2(7+8)} \approx 2{,}025 \text{ days} = 2{,}025/365 \approx 5.5 \text{ years.}$$

The limitations of this estimate are as follows:

i) The equation on which it is based assumes that individuals mix randomly, which is unrealistic (see chapter 7).

ii) The measles vaccination coverage increased after vaccination was introduced in 1968, and therefore the inter-epidemic period would have changed over time. This equation does not account for changes in the inter-epidemic period over time.