Imperial College London – Zambart

Workshop on *Analysing and modelling epidemic data*

Practical: Expanding the SIR model.

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Adapted using materials from Prof Nim Arinaminpathy

The aims of the practical are:

- To introduce yourselves to the rationale for expanding a mathematical model.
- To explore the concepts of constant vs varying hazards in a dynamic transmission model.

In this hand-out, generally:

▶ Indicates an instruction.

▶ Indicates a useful tip or note.

▶ Indicates a question.

Example 1: open SIR model

► *Navigate to the odin interface* https://shiny.dide.ic.ac.uk/infectiousdiseasemodels-lusaka-2022/ *in Chrome or Safari.*

► *In the Thursday section, "Expanding the SIR model", click on "Example 1".*

Thus far, we have been working with a simple SIR model where the populations is 'closed'. This means we assume the total number of people in the model *N* remains constant throughout the simulations albeit 'flowing' between three compartments

$$\frac{dS}{dt} = -\beta \frac{SI}{N}$$

$$\frac{dI}{dt} = \beta \frac{SI}{N} - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

In this sense, the 'hazards' of transitioning across model states are unchanged (albeit the force of infection is dynamic, given change in model states over time!). However simple, the SIR model has been very useful to explore some key concepts of dynamic disease transmission. Here, we will expand it to explore concepts of varying hazards.

► *In groups of four, can you discuss what discuss what sort of varying hazards you would incorporate in a transmission model to make it useful for analysing an outbreak? How would you adapt the model to account for these varying hazards? (5 min)*

The list can be quite long, but generally we would like to consider

- Age-stratification: expand model compartments
- Changing contact-rates (e.g. NPIs): change the value of β over time
- Waning of immunity: flow from *R* back to *S*
- Different infectivity (i.e. onward transmission) of infectious classes (e.g. vaccinated vs unvaccinated): expand model compartments
- Pathogen mutations: change the value of β over time given changes in transmissibility, or change IFR given changes in severity
- Vaccination: expand model compartments, add rate of transition to vaccinated classes (age-eligibility?)

Before moving on to more complex adaptations, let's first 'open up' the model population. By this we mean we need to account for births and background (i.e. all-cause) mortality. Note that, in order to do so, we are assuming all new individuals are born into the *Susceptible* compartment, yet **all** compartments are subject to background mortality.

$$\frac{dS}{dt} = bN - \beta\frac{SI}{N} - \mu S$$

$$\frac{dI}{dt} = \beta\frac{SI}{N} - \gamma I - \mu I$$

$$\frac{dR}{dt} = \gamma I - \mu R$$

► *Code in the above ODEs into the* **Editor tab** *and compile your code with the parameters and initial conditions provided.*

► *Once you are happy with your code, go to the* **Visualise tab** *and run the model for 1,825 days (5 years).*

► **Question 1:** what do you observe towards the end of the simulations that differs from what you have seen thus far by modelling closed populations? Now, rerun the model for 15,000 days (~41 years). What do you observe?

```
# Your code should look like this
deriv(S) <- b * N - beta * (I / N) * S - mu * S
deriv(I) <- beta * (I / N) * S - (mu + gamma) * I
deriv(R) <- gamma * I - mu * R
```

Note that for the case of *I* we are adding up (mu + gamma), as these are both transition rates moving individuals our of *I*. At the end of the first simulation, it can be seen the number of susceptible individuals is gradually increasing. Despite our assumption of permanent immunity (i.e. people don't go back from *R* to *S*), the model is increasing its pool of susceptible given births. You can further corroborate this is you plot *Rt* on a secondary Y axis.

For the second model run, at approximately 35 years there is a second outbreak. That is, the pool of susceptible individuals increased enough to increase the value of *Rt* above the epidemic threshold. It should be noted, though, Rt increased above 1 well before the second outbreak. This is an intrinsic limitation of our model! It is not actually tracking individuals but rates of transition between compartments, so the value of *I* never got to 0 but rather very low decimal values. We will revisit this during week 2, when we talk about stochasticity.

► *Go back to the* **Editor tab** *and modify your ODEs to allow immunity to wane over time* σ.

► Remember this is a new parameter we need to declare. Firstly, declare the parameter by typing in the code below at the end of your script **exactly as follows**

```
waning_t <- user(1) # average number of years natural immunity lasts for
sigma <- 1 / (waning_t * 365) # natural immunity waning rate (match time frame of the model)
```

► *Once you are happy with your code, compile it and run the model for 500 days. Plot Rt on a secondary Y axis again.*

► You might find it useful to consider where individuals are flowing out from (-) and where are they flowing to (+).

► **Question 2:** How is the R_t changing over the course of the outbreak? How does this relate with the model compartments? What does this tell you about changes in the underlying force of infection? What happens if you increase/decrease the average duration of immunity (plot I only) by 10%? Does varying the mean birth rate have the same effect over the model duration (500 days)? Lastly, if you run the model for 2000 days with baseline parameters, what do you observe (plot only I)?

Your ODEs should now look like this

```
deriv(S) <- b * N - mu * S - beta * (I / N) * S + sigma * R
deriv(I) <- beta * (I / N) * S - (mu + gamma) * I
deriv(R) <- gamma * I - mu * R - sigma * R
```

It can be seen that the epidemic peaks (max number in I) at roughly the same time as the value of R_t is equal to 1. From this point onward, the epidemic starts to decline. Interestingly, the pool of susceptible individuals was matched by the number of individuals who had recovered (and therefore were immune) shortly after this point.

You can see how the reduction in the pool of susceptible brings about a decrease in the force of infection, despite the proportion of infected in the population continued to increase for a few more days. This can be better visualised by setting the y axis to the log scale. At the point in which the *S* and *R* trajectory lines cross, there is a deceleration in the growth trajectory of the *I* line, which was previously increasing exponentially.

Similarly, as the pool of susceptible individuals is “replenished” by both births but also those who have transitioned from the recovered compartment, the force of infection increases again and a second outbreak is triggered.

With a shorter duration of natural immunity (i.e. smaller value of waning_t) not only is the size of the secondary outbreak larger, but it’s faster to take off as individuals are losing their natural immunity at a faster rate. Given the average life-span of individuals in the model, changing the average birth-rate has no impact at all on the timing and size of the secondary outbreak.

After a series of outbreaks (~3) of progressively lower magnitude, the disease reaches an endemic equilibrium (i.e. number of individuals in I remains stable at a value greater than 0 as Rt remains stable at around 1).

Example 2: age-stratified SIR model

Well done! Between yesterday and today, you have been learning about modifications to your SIR model to model time-varying hazards. We are now going to account for age, which is a key driver of varying hazards in infectious disease transmission.

We know populations don't mix equally. For example, younger individuals in the population tend to interact much more with other young age groups, and older individuals with older age groups. This has important implications in the control of infectious diseases, as vaccination campaigns would usually account for this to decide who to target in the population.

► *Navigate to the odin interface* https://shiny.dide.ic.ac.uk/infectiousdiseasemodels-lusaka-2022/ *in Chrome or Safari.*

► *In the Thursday section, "Expanding the SIR model", click on "Example 2".*

This is an example of an age-stratified SIR model, with only three age compartments. Note that all compartments in the population are now multiplied by 3! This is because we are explicitly accounting for the fact these are heterogeneous populations of individuals. Furthermore, in lines 65-76 we are defining their age-specific force of infection.

► ***DO NOT RUN THE MODEL YET! Answer Question 3 without running the model.***

► **Question 3:** What does the age-specific forces of infection, $\lambda_1, \lambda_2, \lambda_3$ are telling you about how the population interacts? Assume age groups are 1 kids, 2 adults, and 3 elderly.

Firstly, without even looking at the specific values for the parameters used to calculate $\lambda_1, \lambda_2, \lambda_3$, we can see we are assuming they all have the same probability of becoming infected should they come into contact with an infectious individual, an assumption that is quite common in dynamic infectious disease models. This is being defined as *b*, the per contact probability of transmission.

However, what really varies across age groups is their contact patterns. For each age-group pair linking a potential infectee-infector encounter (e.g. children-children, children-adult, etc.), we are calculating a value for β, that is the contact rate at which they mix multiplied by the per contact probability of transmission, and the age-specific prevalence of infection in the population. The age-specific value for lambda, thus correspons to the addition of all three age-specific β values pertaining to an age-compartment.

► *Now you can run the model!*

► *First, it would be useful if you hide the pop_n and lambda_n variables in the* **Editor tab**.

► *Next, go to the* **Visualise tab** *and run the model for 200 days.*

► Visualise either one age group at a time (e.g. S_1, I_1 and R_1) or one disease stage at a time (e.g. I_1, I_2 and I_3).

► **Question 4:** As a proportion of the total population, what age group is mostly affected by the epidemic? How about as a proportion of the population in that age group? Why do you think that is? Which age group was most affected by this infectious disease?

At the peak of the outbreak, 22% (e.g. 220k / 1M) of the infected cases were adults, 7% were children and only 3% elderly. However, compared to the population in each age group, 36% (e.g. 71k / 200k) of children were infected at the peak of the outbreak, compared to 34% of adults and 24% of elderly.

Most notably, the number of infected cases in each group peaked at slightly different times in the outbreak. Both these trends (e.g. proportion affected and timing of the peak) are driven by the relation between the heterogenous mixing in the population (i.e. contact rates across and within age groups) and the dynamics of disease prevalence for each age group.

In this outbreak, we can see that children were the most affected age group, followed by adults and then the elderly.

You can begin to see how accounting for varying hazards is of paramount importance in infectious disease modelling. For example, the above disease dynamics would have important implications for a vaccination campaign. Consider which age group would you target with a vaccine that prevents infection? What if the vaccine was no good at preventing infection, but decreases the risk of severe disease and death?

As we have said in this workshop thus far, the choice of model and building in its complexity should be driven by the research/policy questions we are aiming to answer. A key question is, how fast is the disease spreading; that is, what is its reproduction number and growth rate. A simple parametric calculation of R_o even with just three age compartments would be almost impossible to derive by hand.

► *In your own time, navigate to the odin interface* https://shiny.dide.ic.ac.uk/infectiousdiseasemodels-lusaka-2022/ *in Chrome or Safari.*

► *In the Thursday section, "Expanding the SIR model", download the script "Example 3" and explore the code to derive this disease'* R_o using *the next generation matrix.* You will need to run this in your own computer in an R-Studio session.

This is the end of the practical!