Imperial College London – Zambart

Workshop on *Analysing and modelling epidemic data*

Practical 1: Designing an SEIR model of SARS-CoV-2.

Dr Pablo N Perez-Guzman

With contribution from materials from Prof Peter White & Dr Isobel Blake

The aims of the practical are:

- To introduce you to the conceptualisation of a compartmental model of disease transmission.
- To understand the concepts of designing a model diagram, thinking of its parameters and differential equations.

In this hand-out:

► Indicates an instruction.

► Indicates useful tips or notes.

In this practical we will see how a flow diagram is developed to reflect the natural history of an infection, Covid-19 in this case, and how this is used to write the equations for a compartmental model.

For simplicity, we will not consider modelling treatment or vaccination, only the natural history of disease. We will consider only acute Covid-19 infection (i.e. not long-Covid or other secondary effects of disease). We will start by writing a 'simple' SEIR model, and then look at how we can make it more realistic (i.e. complicated!). We strongly recommend working in pencil so you can easily make changes as you reflect on your answers and receive feedback from the demonstrators.

At the end of today's session, you will be able to see a completed version of this practical if you:
► *Navigate to the workshop interface* https://shiny.dide.ic.ac.uk/infectiousdiseasemodels-lusaka-2022/ *in Chrome or Safari.*
► *Click on "Practicals (Week 1), then "Practical 1 solutions".*

Feel free to compare your answers with solutions provided but do make your best effort to complete all sections of the practical before!

Model 1: Simple SEIR model of disease transmission

► Important features of acute Covid-19 that we would want to capture in a model are:
1. When an individual becomes *exposed*, they initially develop latent infection (i.e. they do not have symptoms) before progressing to disease.
2. After this initial period, individuals progress to an infection episode.

► Draw a flow diagram to represent these features of Covid-19 using **as few compartments as possible**.

► For simplicity in this initial model, we will make the following assumptions:
a. Only those with an infection episode are infectious (i.e. those exposed will not be infectious).
b. All individuals with Infection episodes flow into *Recovered* and remain there for the rest of the model duration
c. Keep the model population closed (i.e. no births or '*background*' deaths).

We know these assumptions are not true! People experience different levels of disease severity and asymptomatic transmission is a hallmark of Covid-19. We will incorporate these features later.

- The task is to simply draw the compartments of an SEIR model.
- However simple, this is a powerful analytical tool that can be applied to the study of many different infectious diseases.
- One of its key features (i.e. as opposed to the SIR model) is that it explicitly incorporate a latent (*Exposed*) phase. N.B. despite the naming of compartments, '*new transmission'* events (i.e. *new infections*) are only occurring between *S* and *E*

Please let the class demonstrator know you are finished.

► Now write the **model equations in words**.

► You may find the following steps helpful:
1. Identify what differential equations are required
2. Assign flows to them (e.g. rates of change in the model compartments). Think of these as forces moving individuals in (+) or out (-) of the compartments.

- Four compartments require four equations
- Equations specify rates of change in the numbers in each compartment

$$\frac{dS}{dt} = -Infections$$

$$\frac{dE}{dt} = Infections - Progressions\ to\ Disease$$

$$\frac{dI}{dt} = Progressions\ to\ Disease - Recoveries$$

$$\frac{dR}{dt} = Recoveries$$

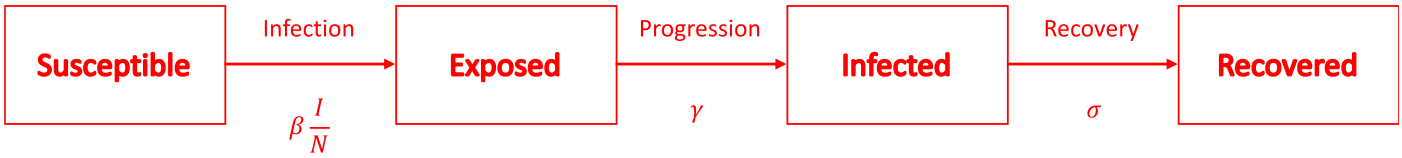
Please let the class demonstrator know you are finished.

► Now rewrite the equations and label your model diagram using **algebraic expressions.** Use the model parameter letters that will be projected in class.

► You may find the following steps helpful:

1. Write down again your 'word equations' from above, in as few words as possible (e.g. *Infection*, *Progression*, *Recovery*), then write the algebraic expressions that describe each equation below.
2. Assign the letters for the model parameters to:
    a. The per capita flow rate (arrow in your diagram)
    b. The per population rate in your model equations.

- By convention, flow rates are *per* capita rates, so only the Greek letter (or expression, as in the case of *infection* rate) representing them is noted in the model diagram
- When adding the compartment state variable letter (capital letter) to the per capita rate, this is now a *per population* rate. Don't forget to have the full mathematical expression in your model equations!



Infections

$$\frac{dS}{dt} = -\beta \frac{I}{N} S$$

Infections – Progressions

$$\frac{dE}{dt} = \beta \frac{I}{N} S - \gamma E$$

Progressions - Recoveries

$$\frac{dI}{dt} = \gamma E - \sigma I$$

Recoveries

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

Please let the class demonstrator know you are finished.

Model 2: Heterogeneous *Infection* compartments

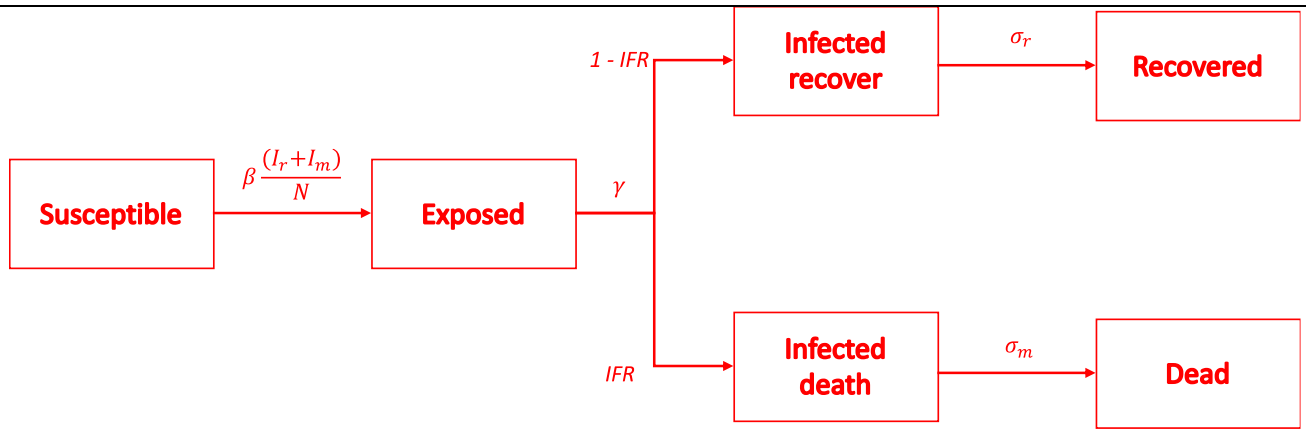
To capture heterogeneity in compartmental models, we can have 'classes' in model compartments which can be 'arranged in parallel'. Important features of Covid-19 we must capture are that:

1. Individuals who develop an infection episode can have mild or severe disease.
2. Depending on the severity of disease, individuals will either recover or die.

► Modify your initial model by adding a 'fork' in the flow from the *Exposed* compartment into the *Infection* compartments: one that will recover and another that will die. Assume both *Infection* classes contribute equally to transmission and that the flow out of *Exposed* to *Diseased* is the same for both.

► You may find the following steps helpful:

1. Think about the flow out of each new *Infection* compartment (i.e. one flows into *Recovered* and the other to *Death*).
2. Think of the additional model parameters you will need for: a) the probability of severe disease leading to death, and b) the flows in and out of the *Infection* compartments.



N.B. we need to incorporate:

- *Two infectious compartments and two absorbing compartments (i.e. no flows out of them) with their respective flow rates; we will use the letter M (Latin 'mortis') for the dead compartment*
- *Two infectious classes when calculating the force of infection*
- *The infection fatality rate (IFR)*
- *We add subscripts where possible to avoid complicating the equations with too many different letters!*

$$\frac{dS}{dt} = -\beta \frac{I_r + I_m}{N} S$$

$$\frac{dE}{dt} = \beta \frac{I_r + I_m}{N} S - \gamma E$$

$$\frac{dI_m}{dt} = \gamma E \cdot IFR - \sigma_m I_m$$

$$\frac{dI_r}{dt} = \gamma E \cdot (1 - IFR) - \sigma_r I_r$$

$$\frac{dM}{dt} = \sigma_m I_m$$

$$\frac{dR}{dt} = \sigma_r I_r$$

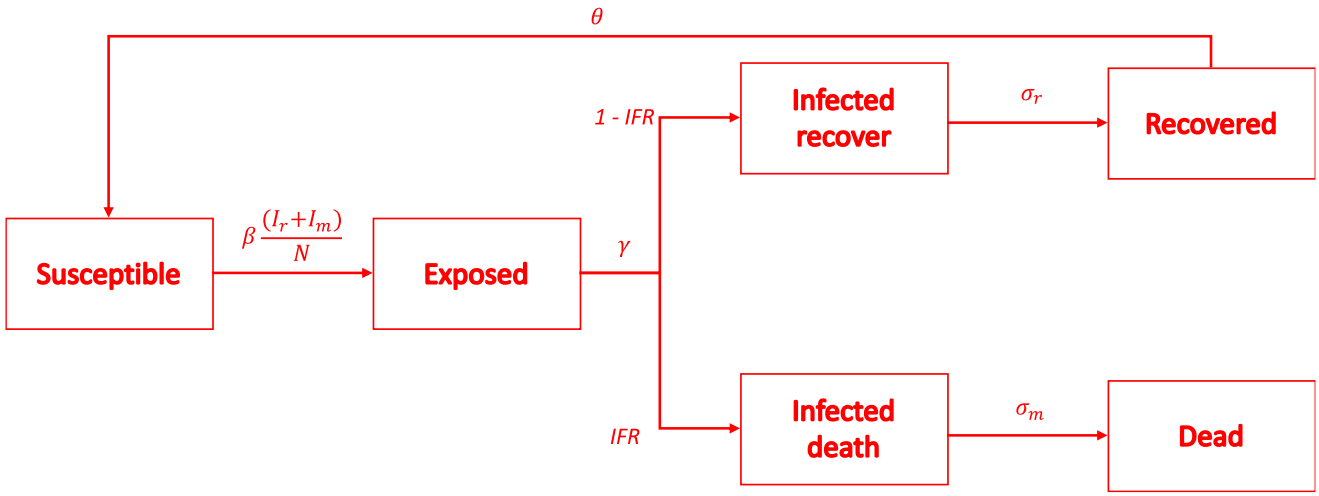
Please let the class demonstrator know you are finished.

Model 3: Waning of natural immunity and asymptomatic infection

Some final key features of Covid-19 we will consider in our model are that:

1. Natural immunity wanes off (i.e. individuals flow from *Recovered* back to *Susceptible*).
2. There is asymptomatic disease, and asymptomatic individuals also contribute to transmission. However, it is thought their contribution to the overall force of infection is smaller compared to that of symptomatic individuals.

► Firstly, add a flow and the mathematical expressions to represent the movement from *Recovered* back to *Susceptible*.



- Here, we use the *per capita* rate θ to express the rate of waning immunity
- This rate applies to those in the *Recovered* compartment as they flow back into the *Susceptible* population

$$\frac{dS}{dt} = -\beta \frac{I_r + I_m}{N} S + \theta R$$

$$\frac{dE}{dt} = \beta \frac{I_r + I_m}{N} S - \gamma E$$

$$\frac{dI_m}{dt} = \gamma E \cdot IFR - \sigma_m I_m$$

$$\frac{dI_r}{dt} = \gamma E \cdot (1 - IFR) - \sigma_r I_r$$

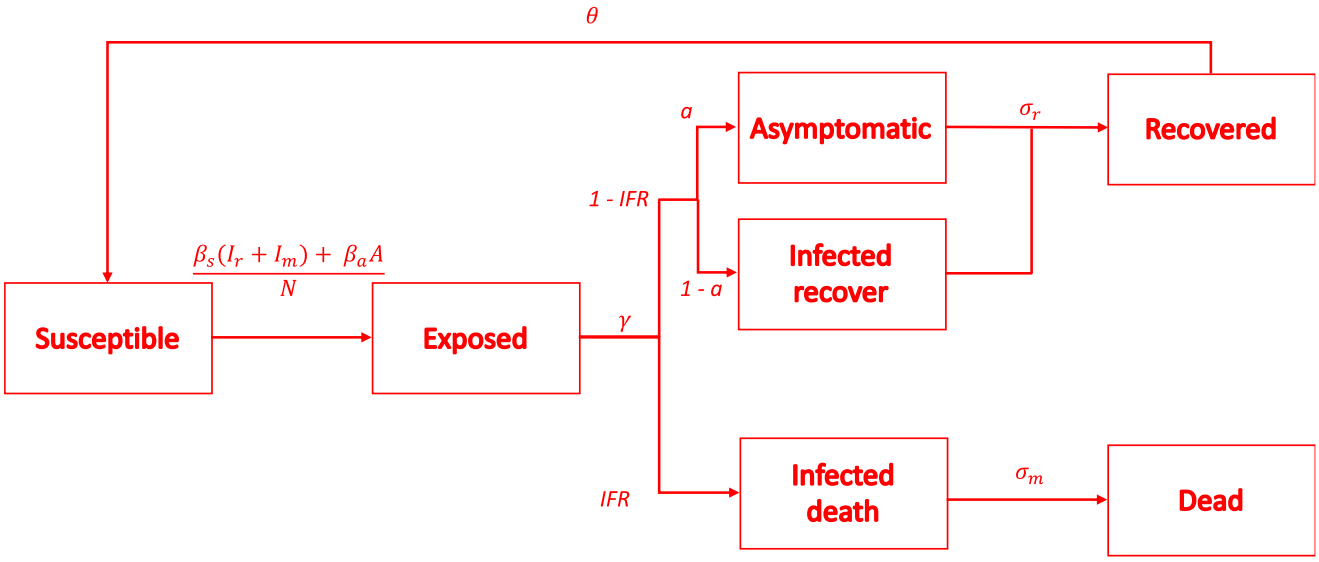
$$\frac{dM}{dt} = \sigma_m I_m$$

$$\frac{dR}{dt} = \sigma_r I_r - \theta R$$

Please let the class demonstrator know you are finished.

► Lastly, add a third 'diseased' compartment to account for the proportion that will be asymptomatic. Assume that:

1. A proportion of exposed will have asymptomatic infection.
2. The asymptomatic infection contributes less to the force of infection (i.e. give it a different value, β_a)
3. The flow rate from asymptomatic infection to recovery is the same as from *Diseased* to *Recovered*.



- Note we are now incorporating two β parameters, to reflect how those in the *Asymptomatic* compartment may have a different contribution to the overall force of infection
- Also note that, in doing so, we are still assuming that those in the *Infected recover* and *Infected death* compartments contribute equally to the force of infection
- Lastly, we are further assuming that the flow rates from *Exposed* to *Recovered* are the same for both the *Asymptomatic* and *Infected recover* are the same
- Can you think about the implications of these assumptions on the likely model outputs? What additional features of the natural history of disease would you incorporate and how would you go about it?

$$\frac{dS}{dt} = -\frac{\beta_s(I_r + I_m) + \beta_a A}{N} S + \theta R$$

$$\frac{dE}{dt} = \frac{\beta_s(I_r + I_m) + \beta_a A}{N} S - \gamma E$$

$$\frac{dI_m}{dt} = \gamma E \cdot IFR - \sigma_m I_m$$

$$\frac{dI_r}{dt} = \gamma E \cdot (1 - IFR) \cdot (1 - a) - \sigma_r I_r$$

$$\frac{dA}{dt} = \gamma E \cdot (1 - IFR) \cdot a - \sigma_r A$$

$$\frac{dM}{dt} = \sigma_m D_m$$

$$\frac{dR}{dt} = \sigma_r D_r + \sigma_r A - \theta R$$

This is the end of the practical!