Imperial College London – Zambart

Workshop on *Analysing and modelling epidemic data*

Practical 2 Part 2: Competing risks model using transition rates - SOLUTIONS.

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Background

In Part 1 of Practical 2, we estimated the average time to recovery and death among patients infected with a novel disease. We will now be incorporating this into our cohort model that we began developing yesterday.

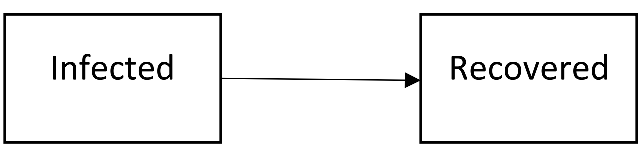
Objectives

- Expand cohort model to include recovery and deaths compartment.
- Parameterise model using estimates from Practical 2 Part 1.
- Calculate the CFR under different parameter estimates.

Example 1: Expanding our cohort model to a competing risks model (written)

Because not all patients of a disease will recover, we want to expand our cohort model to incorporate the competing risks of recovery or death.

Recall from yesterday's practical:



This basic cohort model has only two compartments, I and R , and is written:

$$\frac{\partial I}{\partial t} = -\gamma I$$

$$\frac{\partial R}{\partial t} = \gamma I$$

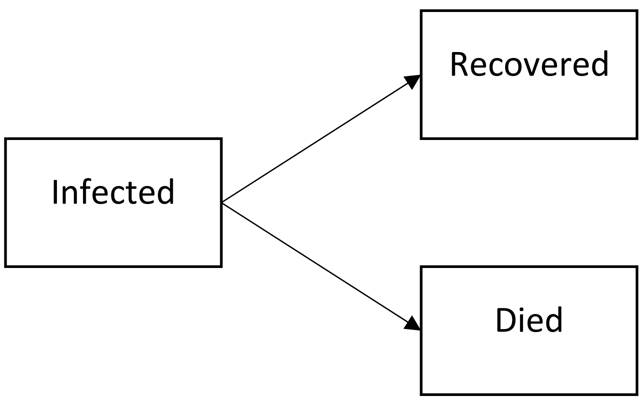
Recall that:

- Mean duration of infectiousness = $\frac{1}{\gamma}$
- So, the inverse will be the recovery rate

$$\gamma = \frac{1}{mean\ duration\ of\ infectiousness}$$

1. Draw and write out the equations (on paper, no code!) for an extended version of the model above which also includes deaths.

Solution:



We now have three compartments, I , R and D . We write this as follows:

$$\frac{\partial I}{\partial t} = -\gamma I - \mu I$$

$$\frac{\partial R}{\partial t} = \gamma I$$

$$\frac{\partial D}{\partial t} = \mu I$$

γ continues to correspond to the rate of recovery, while μ represents the rate of death.

Example 2: Expanding the cohort model code to a competing risks model (code)

Now that you have finalised your model design, we want to think about how we adapt the cohort model code to incorporate our new compartment.

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

Recall that the SIR model code is as follows:

```
# state variables
deriv(I) <- -gamma * I
deriv(R) <- gamma * I
# initial conditions of the variables
initial(I) <- 1000
initial(R) <- 0
# input parameters
recovery_time <-    # mean number of days to recovery
# calculated parameters
gamma <- 1 / recovery_time    # recovery rate
```

We are going to look at each of the sections in the model in turn.

1. Update the state variables to reflect the inclusion of the Deaths compartment. Note that it is not just the deaths compartment that changes, we also have to update the Infected compartment to reflect that people can exit this in two ways (e.g., the competing risks).

Solution:

```
# state variables
  deriv(I) <- -gamma * I - mu * I
  deriv(R) <- gamma * I
  deriv(D) <- mu * I
```

2. Update the initial conditions.

Solution:

```
# initial conditions of the variables

initial(I) <- 1e6

initial(R) <- 0

initial(D) <- 0
```

3. Update the input parameters.

Solution:

```
# input parameters

recovery_time <- user()

death_time <- user()
```

4. Update the calculated parameters.

Solution:

```
# calculated parameters

gamma <- 1 / recovery_time # recovery rate

mu <- 1 / death_time      # death rate
```

Once you have reached this stage, please ask one of the demonstrators to check your code before proceeding to the next sections.

Solution:

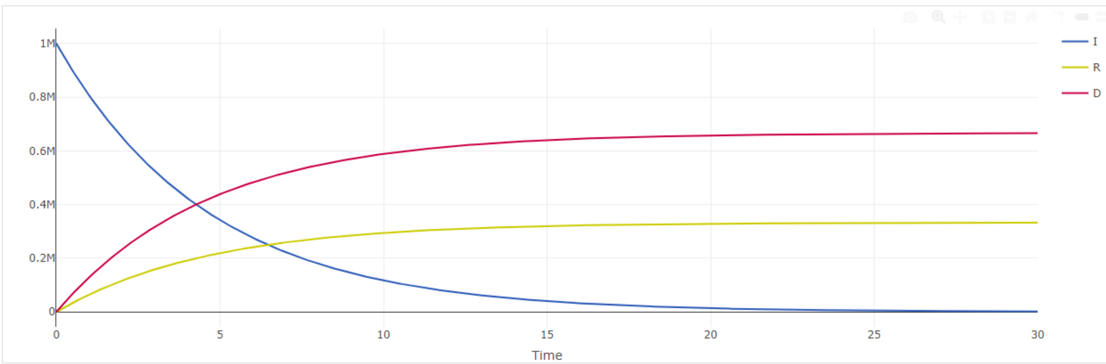
```
# state variables

deriv(I) <- -gamma * I - mu * I

deriv(R) <- gamma * I

deriv(D) <- mu * I

# initial conditions of the variables

initial(I) <- 1e6

initial(R) <- 0

initial(D) <- 0

# input parameters (insert the values you derived from data in the previous practical)

recovery_time <- user()

death_time <- user()

# calculated parameters

gamma <- 1 / recovery_time # recovery rate

mu <- 1 / death_time       # death rate
```

Example 3: Running the model

We are now ready to assess the model output.

1. Navigate to the 'Visualise' tab of the online editor. To run the model, specify the parameters estimated in Part 1 of today's practical (average time to recovery 14 days; average time to death 7 days). An end time of 28 days (4 weeks) is sufficient, but you can try different values if you have time.
2. Press run and look at the resulting plot.

Solution:



Example 4: Interpreting the model output

We can now evaluate the results of our model to answer the following questions. Recall that the values at each point can be obtained by hovering over the image in the editor.

1. Based on the output, what proportion of the initially infected cohort died before recovering over the 4-week period?

Solution: At day 28, '665.0142k' people had died, which equates to 665,014.2 people. Given that we began with 1,000,000 people, this means that 665,014.2/1,000,000 = 0.665 of people initially infected had died by the end of the period.

2. Using the model parameters, can you calculate the case fatality rate? What do you notice about the result?

Solution: Recall that:

$$\gamma = \frac{1}{14}$$

$$\mu = \frac{1}{7}$$

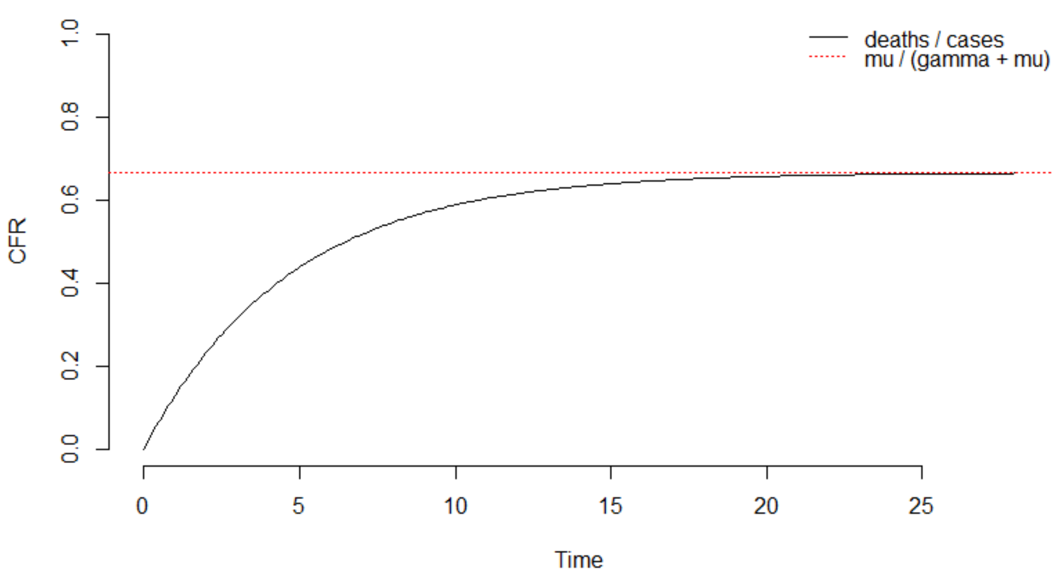
The CFR can be estimated as:

$$CFR = \frac{\mu}{\gamma + \mu}$$

In this instance, we have that CFR = 0.667.

3. Calculate the naïve CFR estimated by the model by considering the ratio of cumulative deaths over time to the total number of people initially infected. You can do this by downloading the model output using the 'Download' button on the bottom right of the editor and then working in Excel. What do you notice about the results?

Solution: As time increases, the naïve CFR approaches that we estimated in the previous question.



Example 5: Impact of varying parameters

Now we want to consider what would happen when we vary the parameters.

Let us consider a scenario in which the CFR decreased by 50% to 33%.

1. Assuming that the recovery rate remains stable, what would we need the death rate be in order to achieve this lower CFR? (Hint: recall how we calculated the CFR above).

Solution:

As

$CFR = \frac{\mu}{\mu+\gamma}$,

rearranging implies:

$$\mu = \frac{CFR \times \gamma}{1 - CFR}$$

Therefore, to achieve a CFR of 0.33 when the recovery rate remains at $\frac{1}{14}$, $\mu = 0.036.$

2. Validate your estimate of μ by calculating the CFR you get using this value and the recovery rate.

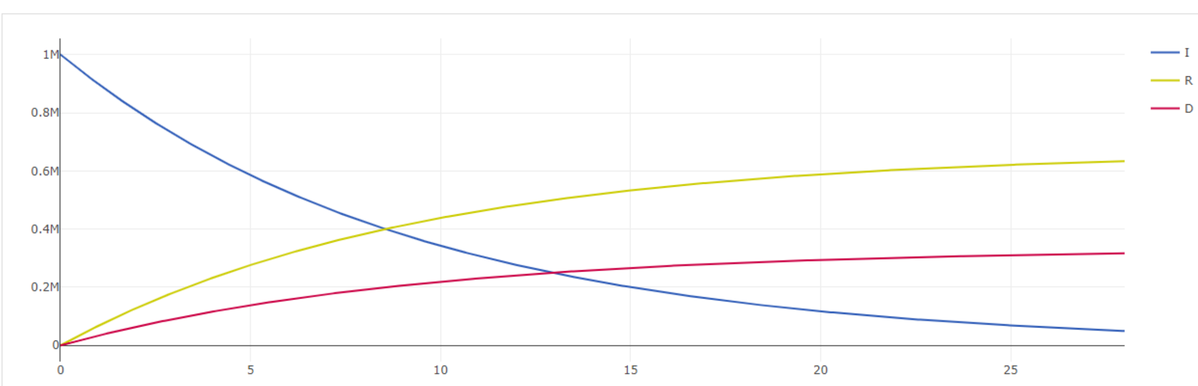
Solution: Putting in these values gives $CFR = 0.33$.

3. In order to have this lower CFR, does this mean that on average people are dying quicker or slower than the initial 7 days that we estimated?

Solution: The average time to die under this new death rate is 28 days, which is four times slower than the original 7 days.

4. Corroborate your findings by re-running your model with this new death rate.

Solution:



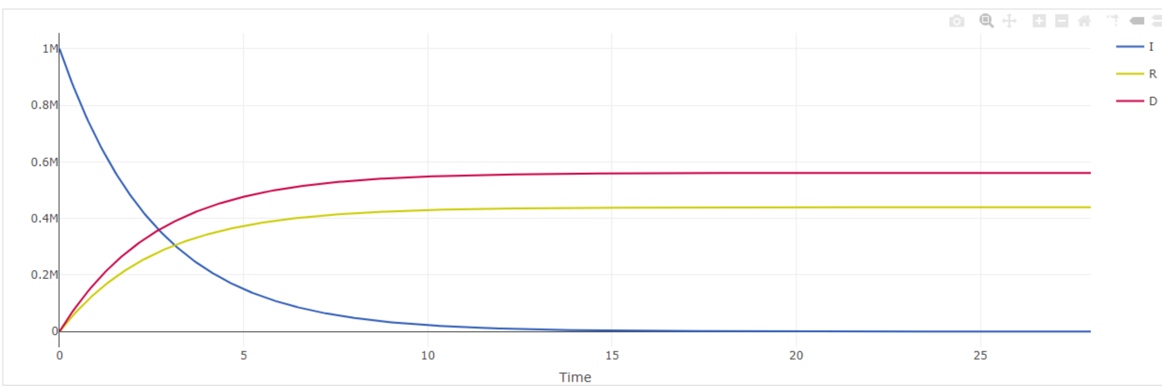
As we did above, at day 28 316,737.6 people have died. This results in a CFR of 0.317, which is close to the true value of 0.33. As we only run the model to 28 days, which is the average time to death, the model needs to run for slightly longer to reach this value. For example, if we run the model for 40 days, we get that the CFR is 0.329.

Extension: Running the model under the biased parameters from Part 1

If you have completed the rest of this practical, let us consider the following example. We now return to the original model parameters of 14 days to recovery and 7 days to death, on average. Recall that when we estimated these parameters with truncated data, we estimated 6 days to recovery and 4.7 days to death.

1. Run the model with truncated estimates.

Solution:



2. What is the CFR under these estimates? Calculate this value in both the ways that we have done above.

Solution: Both methods give CFR of 0.561.

3. Comment on the results. What happens to our understanding of the CFR when we work with biased parameter estimates?

Solution: We are underestimating the CFR.