

## **DH301: Basic Epidemiology**

# Mathematical Epidemiology

(Lecture 3)

Sandip Mandal

Email: [mandal.iitb@gmail.com](mailto:mandal.iitb@gmail.com)

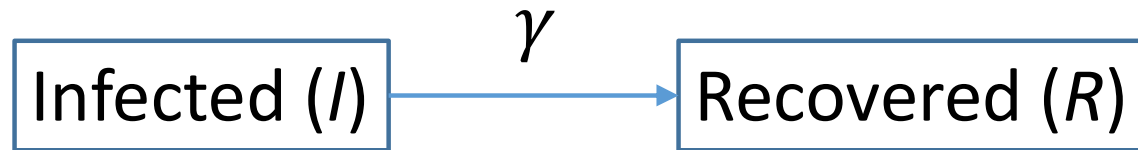
Indian Institute of Technology - Bombay

28 August 2024

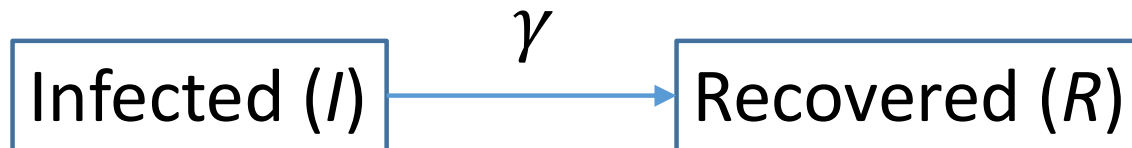
# Concepts we'll cover with additional examples

- **Boxes and arrows**
  - Building a simple compartmental model
  - Relation between a model diagram and its equations
- **Competing hazards**
  - Modelling different possible outcomes
- **Force of infection**
  - What makes an infectious disease model
  - The basic reproduction number ( $R_0$ )
- **More complex models**

## Recap: Modelling an infected cohort



## Practical 1: Modelling an infected cohort



We are looking at a cohort of 1000 currently infected people, and no one has recovered so far. The average duration of infection is 10 days. The question we want to answer is how many people will recover from the infection over a 4-week period.

- **Question:** Based on the output, how many people have recovered after 4 weeks? What proportion of the total population does this correspond to?
- **Question:** Based on the plot, at what time point were infected and recovered individuals equal in number?
- try varying *gamma* to see how it affects the output. For example, change *gamma* to correspond to an average infectious period of 2 days and 20 days. What is the recovery rate in these 2 cases?
- **Question:** What changes do you observe in the transition to the recovered compartment if *gamma* is higher or lower? For example, how long does it take for everyone to recover in both cases?

## Modelling an infected cohort

How long it takes for a cohort of infected people to recover?

You need to keep track of 2 populations:

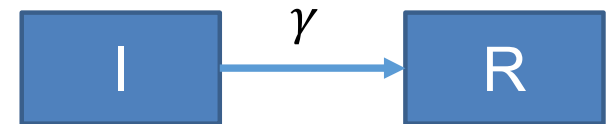
1. those that are infected (compartment I),
2. those that have recovered (compartment R).

Infected people recover at a rate  $\gamma$ .

The differential equations describing this are:

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

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



We are looking at a cohort of 1000 currently infected people, and no one has recovered so far. The average duration of infection is 10 days. The question we want to answer is how many people will recover from the infection over a 4-week period.

# Two approaches

Analytical  
Numerical

## Model

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

If there is no death,  $I + R = N$  (Constant), we can concentrate only on single equation.

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

$$I = I_0 e^{-\gamma t}$$

At  $t = 0$ ,  $I = I_0$  (initial value of  $I$ )

As per the problem,  $I_0 = 1000$

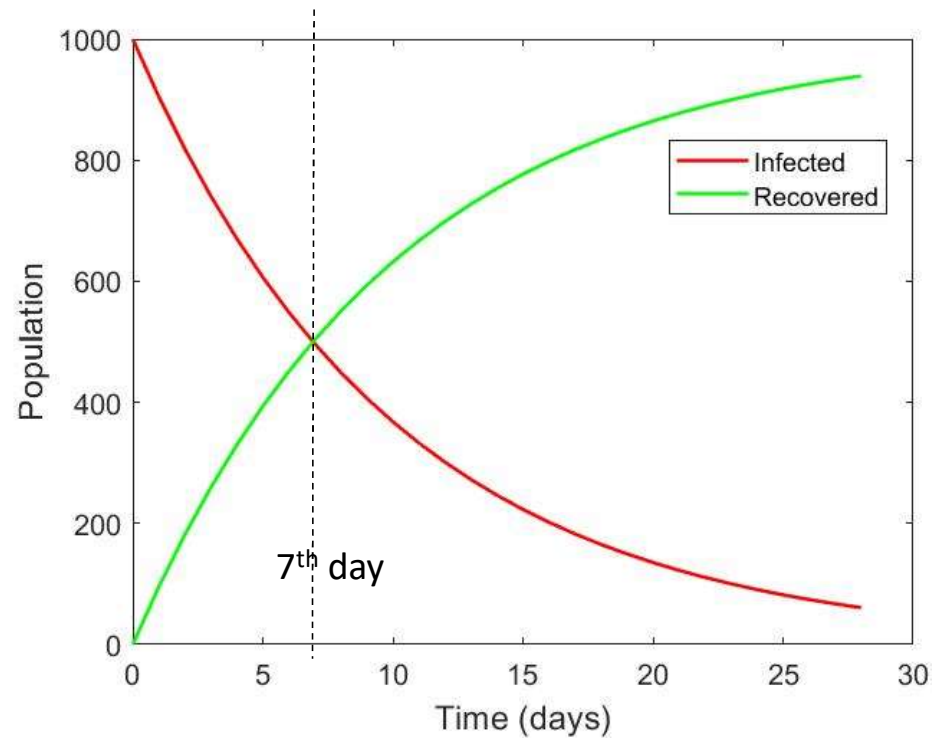
$t = 28$  days (4 weeks)

$\gamma = 0.1$  day<sup>-1</sup>

$I = 61$  (infected),

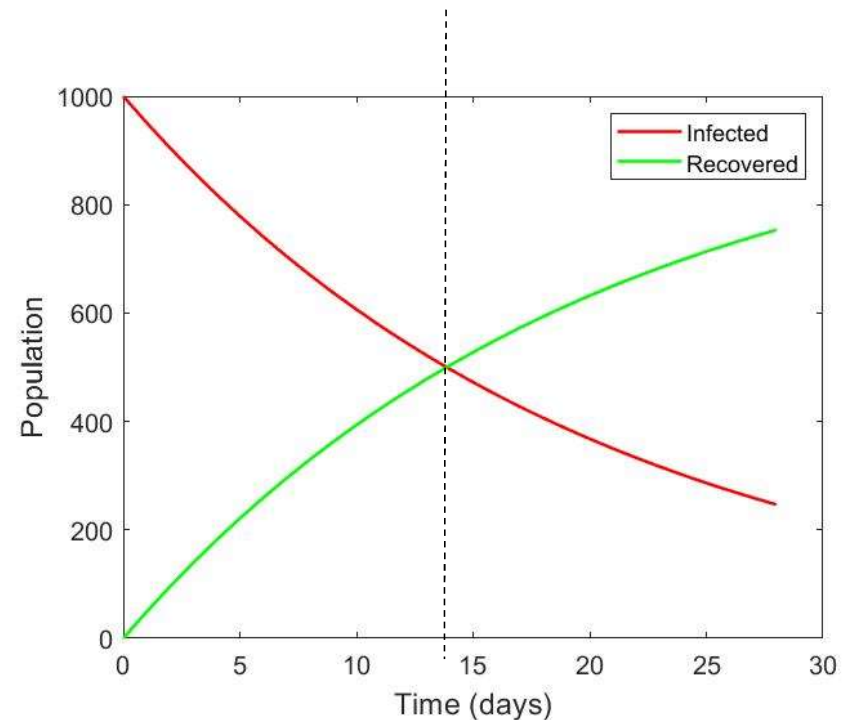
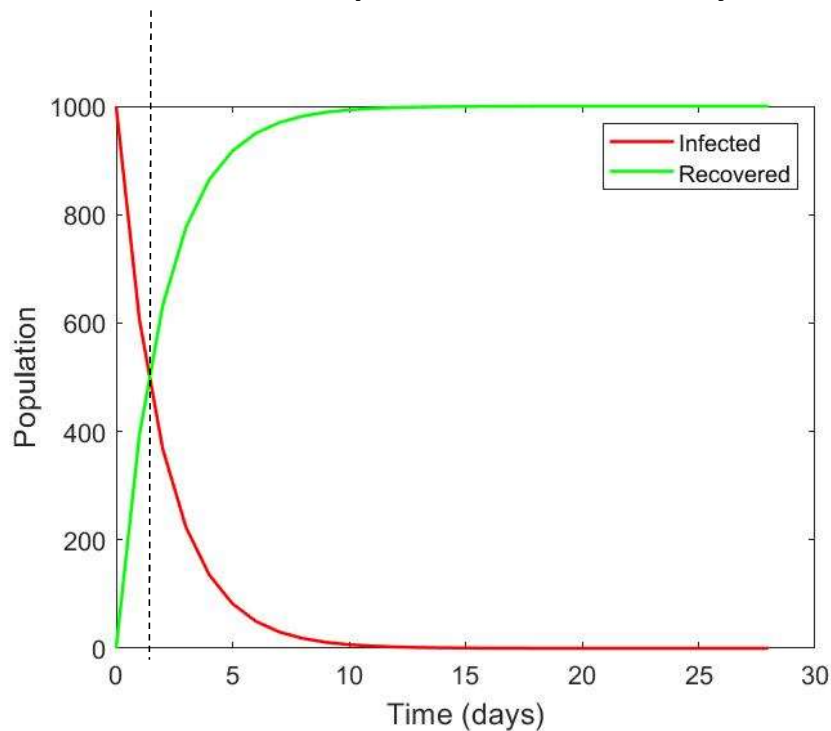
$R = 939$  (recovered) i.e. 94% of total population of the cohort

**Question: Based on the plot, at what time point were infected and recovered individuals equal in number?**



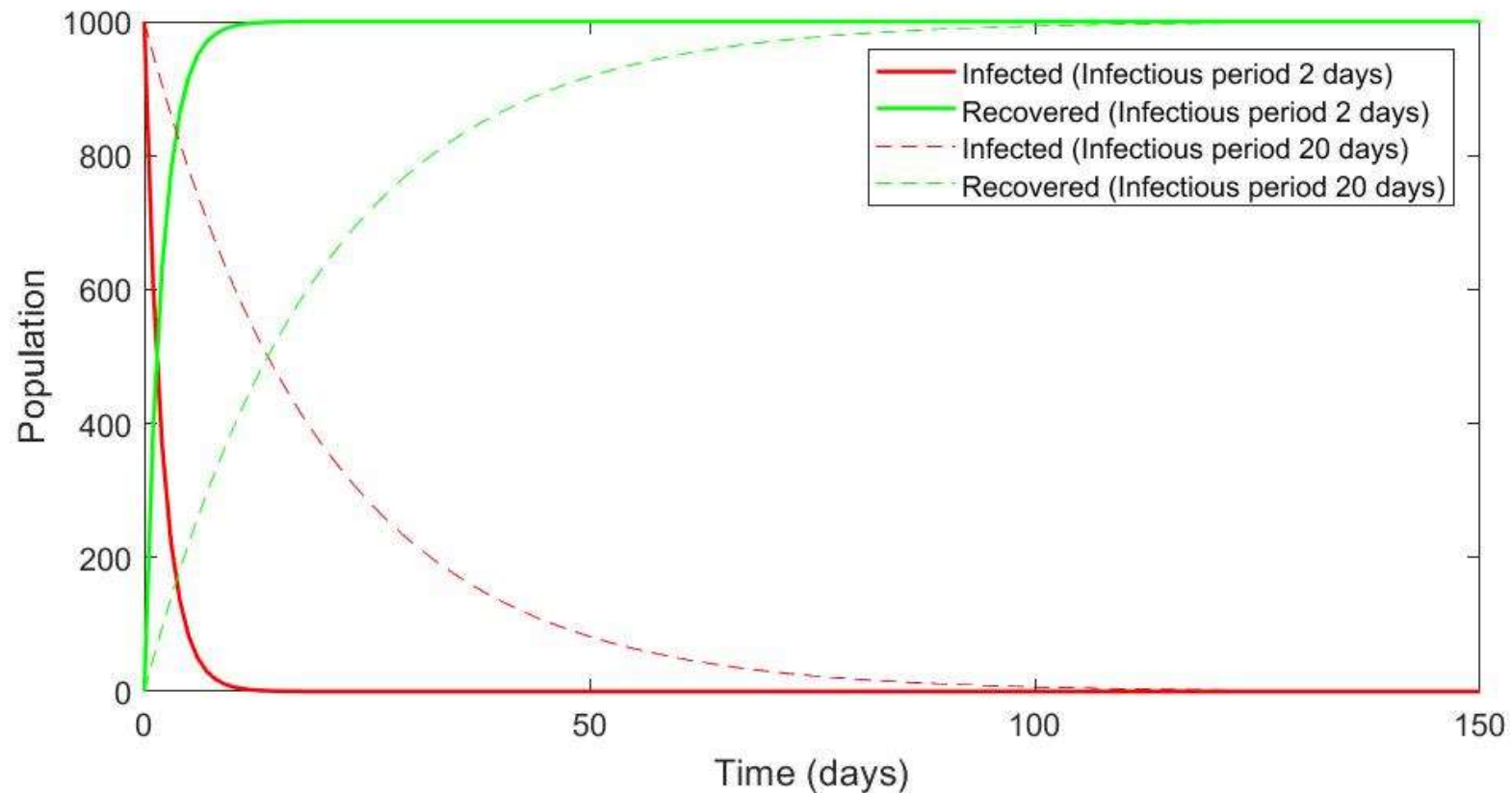
Try varying *gamma* to see how it affects the output. For example, change *gamma* to correspond to an average infectious period of 2 days and 20 days. What is the recovery rate in these 2 cases?

- Infectious period = 2 days  $\rightarrow$  Recovery rate  $\gamma = 0.5 \text{ day}^{-1}$
- Infectious period = 20 days  $\rightarrow$  Recovery rate  $\gamma = 0.05 \text{ day}^{-1}$





**Question: What changes do you observe in the transition to the recovered compartment if  $\gamma$  is higher or lower? For example, how long does it take for everyone to recover in both cases?**



## Numerical approach (Computer simulation)



```
library(deSolve)
library(graphics)

initial_number_infected <- 1000
initial_number_recovered <- 0

recovery_rate <- 1/10
follow_up_duration <- 4*7

initial_state_values <- c(I = initial_number_infected, R =
initial_number_recovered)

parameters <- c(gamma = recovery_rate)

times <- seq(from = 0, to = follow_up_duration, by =1)

cohort_model <- function(time, state, prameters){
  with(as.list(c(state,parameters)),{
    dI <- -gamma*I
    dR <- gamma*I
    return(list(c(dI, dR))))}
}
```

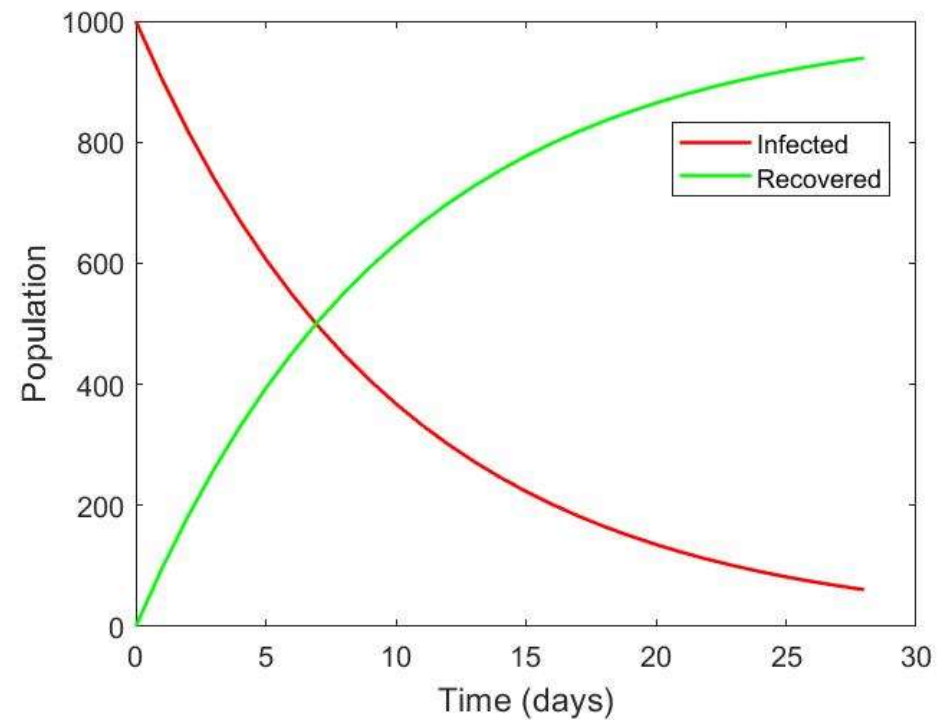
```
output <- as.data.frame(ode(y = initial_state_values,
                           times = times,
                           func = cohort_model,
                           parms = prameters))

output
```

## output

Time	Infected	Recovered
0	1000	0
1	904.8	95.2
2	818.7	181.3
3	740.8	259.2
4	670.3	329.7
5	606.5	393.5
6	548.8	451.2
7	496.6	503.4
8	449.3	550.7
9	406.6	593.4
10	367.9	632.1
11	332.9	667.1
12	301.2	698.8
13	272.5	727.5
14	246.6	753.4
15	223.1	776.9
16	201.9	798.1
17	182.7	817.3
18	165.3	834.7
19	149.6	850.4
20	135.3	864.7
21	122.5	877.5
22	110.8	889.2
23	100.3	899.7
24	90.7	909.3
25	82.1	917.9
26	74.3	925.7
27	67.2	932.8
28	60.8	939.2

## Plotting the output



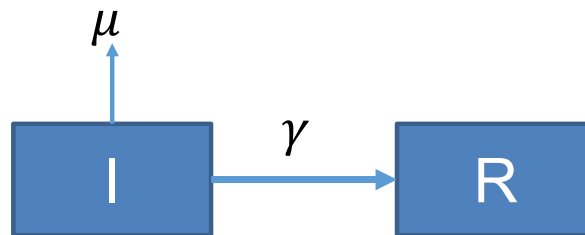
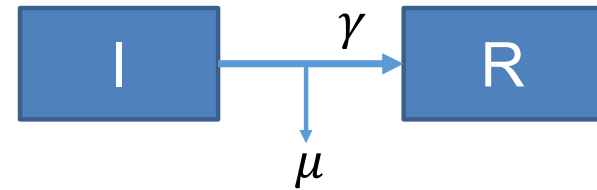
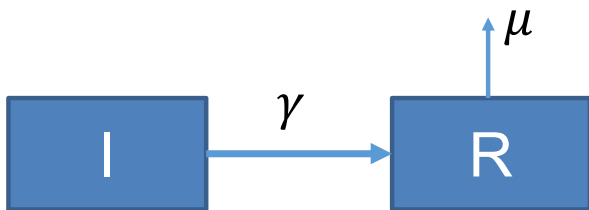
## Practical 2: Simulating competing hazards

In the previous practical 1 you modelled an infected cohort in R. In this practical, the focus is on adding disease-induced mortality to this model, to explore the concept of competing hazards introduced in the last lecture and calculate the case fatality ratio.

- **Question: what do *gamma* and *mu* represent? Draw the model diagram corresponding to these equations.**
- **Question: after 4 weeks, do you expect more people to have recovered or more people to have died, and why? Proceed with the next steps to check if you are right.**
- **Question: based on the model output, what proportion of the initially infected cohort died before recovering over the 4 week period?**
- **Question: now use the competing hazards formula given in the lecture to calculate the case fatality rate. Does this agree with your answer to the previous question?**
- **Question: Which value of *mu* do you need to get a case fatality rate of 50% assuming *gamma* stays fixed? You can calculate this on paper.**

# Modelling an infected cohort (considering mortality)

adding disease-induced mortality to this model



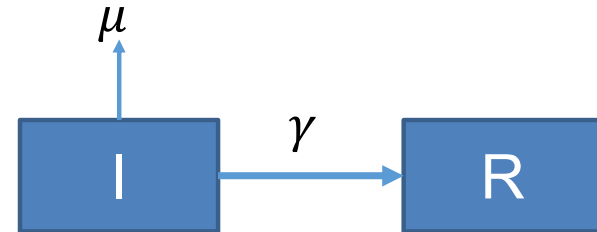
# Modelling an infected cohort (considering mortality)

The differential equations for the model look like this:

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

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

$$\frac{dM}{dt} = \mu I$$



At the start, there are 1000000 infected people. No one has recovered or died yet. The recovery rate  $\gamma$  is 0.1 day<sup>-1</sup> and the mortality rate  $\mu$  is 0.2 day<sup>-1</sup>. Again we want to model the course of the infection over 4 weeks.

**Question: after 4 weeks, do you expect more people to have recovered or more people to have died, and why? Proceed with the next steps to check if you are right.**

time	I	R	M
0	1000000.0000	0.00	0.0
1	740818.2240	86393.93	172787.9
2	548811.6238	150396.13	300792.3
3	406569.6441	197810.12	395620.2
4	301194.1295	232935.29	465870.6
5	223130.0332	258956.66	517913.3
6	165298.7445	278233.75	556467.5
7	122456.2989	292514.57	585029.1
8	90717.8284	303094.06	606188.1
9	67205.4086	310931.53	621863.1
10	49786.9751	316737.67	633475.3
11	36883.0919	321038.97	642077.9
12	27323.6579	324225.45	648450.9
13	20241.8599	326586.05	653172.1
14	14995.5341	328334.82	656669.6
15	11108.9626	329630.35	659260.7
16	8229.7197	330590.09	661180.2
17	6096.7248	331301.09	662602.2
18	4516.5637	331827.81	663655.6
19	3345.9518	332218.02	664436.0
20	2478.7415	332507.09	665014.2
21	1836.2963	332721.23	665442.5
22	1360.3615	332879.88	665759.8
23	1007.7803	332997.41	665994.8
24	746.5819	333084.47	666168.9
25	553.0813	333148.97	666297.9
26	409.7326	333196.76	666393.5
27	303.5373	333232.15	666464.3
28	224.8659	333258.38	666516.8

**Question: based on the model output, what proportion of the initially infected cohort died before recovering over the 4 week period?**

Ans: 0.6665

**Question: now use the competing hazards formula given in the lecture to calculate the case fatality rate. Does this agree with your answer to the previous question?**

$$CFR = \frac{\mu}{\mu + \gamma} = 0.666$$

**Question: Which value of  $\mu$  do you need to get a case fatality rate of 50% assuming  $\gamma$  stays fixed? You can calculate this on paper.**

**Which value of  $\mu$  do you need to get a case fatality rate of 50% assuming  $\gamma$  stays fixed?**

Switching around the CFR equation above to solve for  $\mu$  gives:

$$\begin{aligned}CFR &= \frac{\mu}{\mu + \gamma} \\ \mu &= CFR(\mu + \gamma) \\ \mu &= \mu CFR + \gamma CFR \\ \mu - \mu CFR &= \gamma CFR \\ \mu(1 - CFR) &= \gamma CFR \\ \mu &= \frac{\gamma CFR}{1 - CFR}\end{aligned}$$

Calculating  $\mu$  with CFR = 0.50 and  $\gamma$  = 0.1:

$$\begin{aligned}\mu &= \frac{0.1 * 0.50}{1 - 0.50} \\ \mu &= 0.1\end{aligned}$$

This makes sense! If  $\mu$  and  $\gamma$  are equal, half of people die and half recover, so the case fatality rate is 50%.

Double-check this by modifying the code to simulate the model using these parameters:

---



Now including infection...



*Governing equations:*

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

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

Now including infection...



*Governing equations:*

$$\frac{dS}{dt} = -\lambda S$$

$$\frac{dI}{dt} = \lambda S - \gamma I$$

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

## SIR model with a constant force of infection



Depending on how many people in the population are infectious, susceptible people experience a force of infection  $\lambda$ , **which is the transition rate at which they become infected.**

$$\frac{dS}{dt} = -\lambda S$$

$$\frac{dI}{dt} = \lambda S - \gamma I$$

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

An example of this situation is the COVID-19 virus epidemic in China in 2020: since the corona virus had not spread there before, there was a large pool of susceptible hosts when the first source of infection arrived.

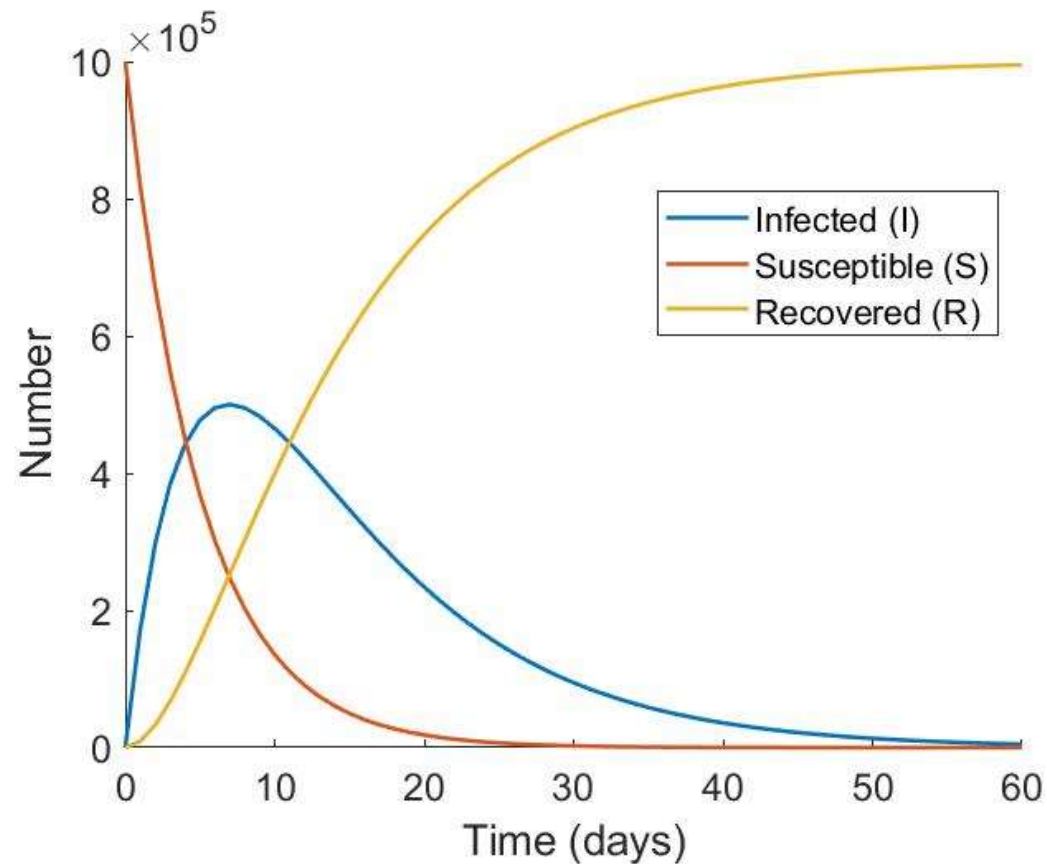
In terms of the initial conditions for our model, we can define:

**S = 999999, I = 1 and R = 0.**

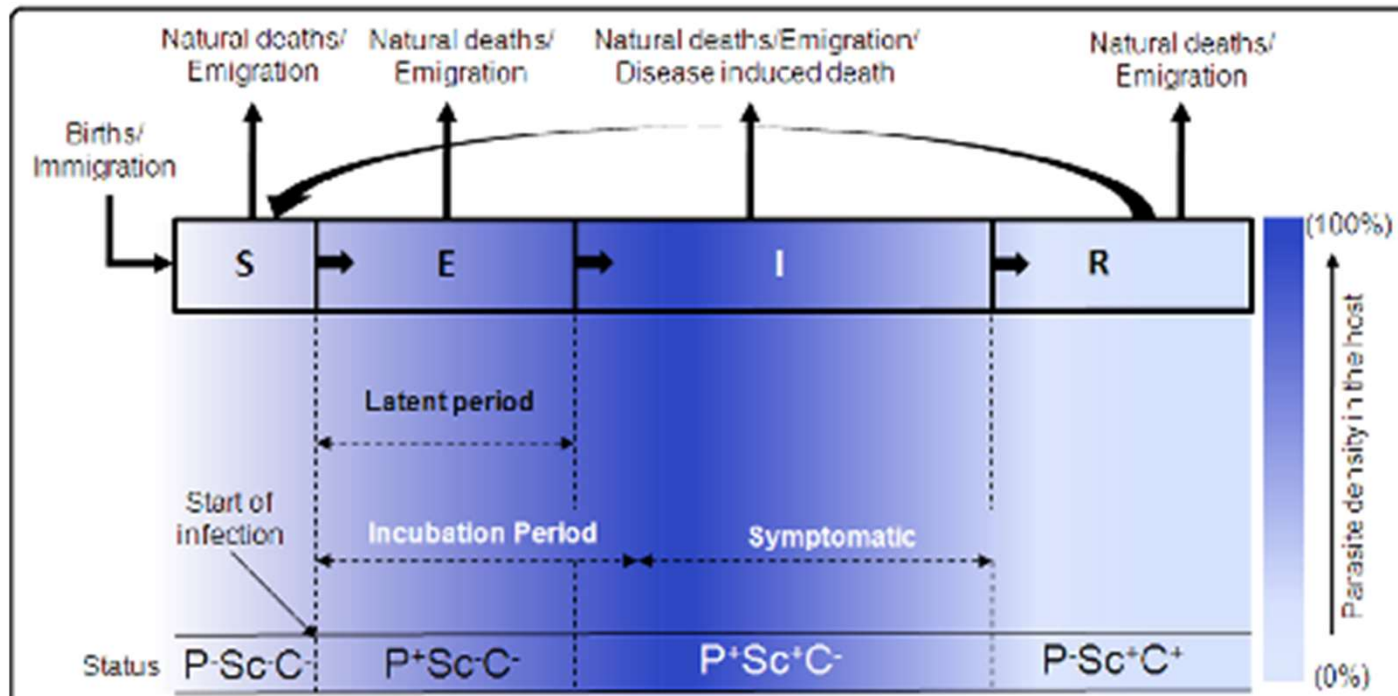
Assume a constant force of infection of 0.2 days<sup>-1</sup>

The infection has an average duration of 10 days

**Question: based on the plot, describe the pattern of the epidemic over the 2 month period. How does the number of people in the susceptible, infected and recovered compartment change over time? After how many days does the epidemic reach its peak? When does it end?**



## Epidemiological compartment and time line for infection



**S, E, I, R -** Susceptible, Exposed, Infected and Recovered fraction of the population

**Thick black Arrows on the top** - different ways of population loss and transfer from one compartment to another.

**Dotted black arrows** - Different periods (Latent, Incubation, Symptomatic) characteristic infection

**Bottom panel** - status of clinical markers for each compartment –

PCR (P), Seroconversion (Sc) and Cellular immunity (C) (positive or negative).

**Colour Bar** - density of parasites in host in different compartments (0-100%).

# Construct a TB-model and indicate the rate parameters as per given information



Uninfected



Latent TB

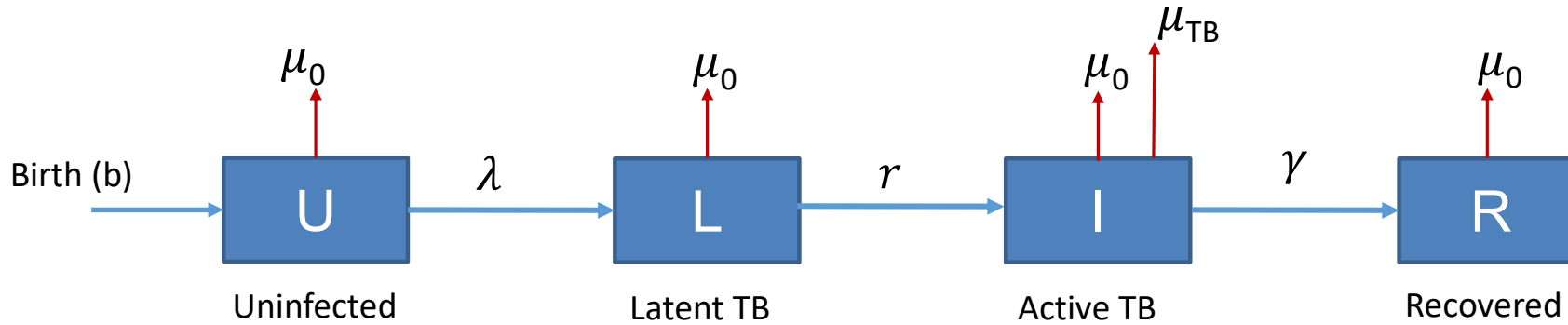


Active TB



Recovered

- Average infectious period: 3 years
- Case Fatality Rate (CFR): 50%
- Latent TB: 10% life time risk of getting active TB
- Average lifetime without TB: 70 years



- Average infectious period: 3 years
- Case Fatality Rate (CFR): 50%
- Latent TB: 10% life time risk of getting active TB
- Average lifetime without TB: 70 years

Force of infection



Now including dynamic force of infection...



Governing equations:

$$\frac{dS}{dt} = -\lambda S$$

$$\lambda = \beta \frac{I}{N}$$

$$\frac{dI}{dt} = \lambda S - \gamma I$$

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

In reality  $\lambda$  changes over time,  
depending on the number of  
infected people in the population.

# What is $\beta$ ('beta')?

$$\lambda = \beta \frac{I}{N}$$

- The rate-of-infection: it reflects how quickly infection spreads, from a single infectious person
  - Effectively, the number of infections per day when everyone else is susceptible
- Shaped by contact rates, and infectiousness per contact
  - Usually, cannot be measured directly
  - Needs to be *estimated* in order to match the available data

Now including infection...

SIR model



$\beta, \gamma$  are **parameters**: their values need to be specified in order to simulate the model

*Governing equations:*

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

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

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

## SIR model with a dynamic force of infection



$$N = S + I + R$$

In reality  $\lambda$  changes over time, depending on the number of infected people in the population.

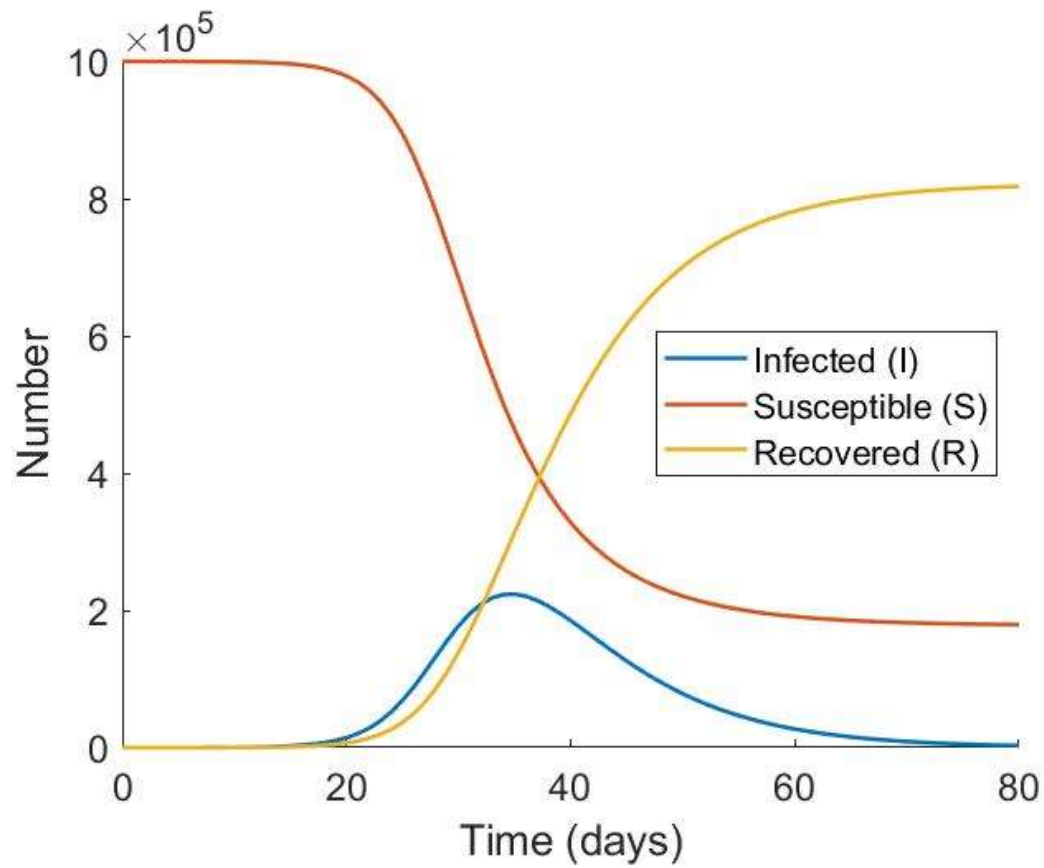
$\lambda$  is a function of the infection rate,  $\beta$ ,  
and the proportion of the population that is infectious,  $I/N$

$$\lambda = \beta \frac{I}{N}$$

$$\begin{aligned}\frac{dS}{dt} &= -\beta \frac{I}{N} S \\ \frac{dI}{dt} &= \beta \frac{I}{N} S - \gamma I \\ \frac{dR}{dt} &= \gamma I\end{aligned}$$

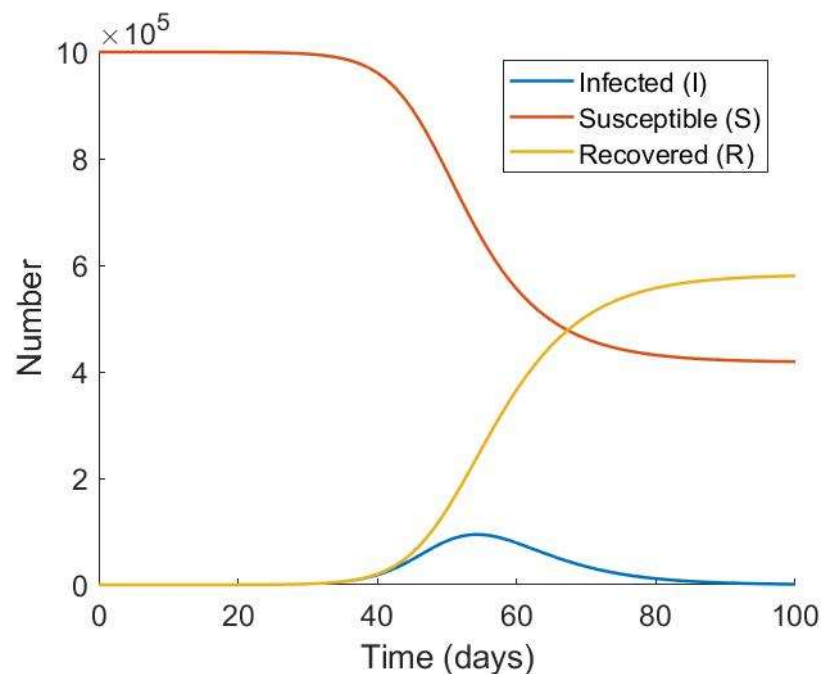
### Assumptions

- A homogeneous population – everyone in the same compartment is subject to the same hazards
- A well-mixed population – all susceptible people have the same risk as getting infected, dependent on the number of infected people
- A closed population-there are no birth or deaths, so the population size stays constant



Population = 1 million  
Initially infected population = 10  
Infection rate (beta) = 0.2 day<sup>-1</sup>  
Average infectious period = 10 days

What do you observe when  $\beta = 0.5$  and  $\gamma = 0.25$ ? (Population size: 1 million)



- An epidemic occurs, reaching a peak 56 days after introduction of the first infectious case,
- At peak 15% of the population are infected.
- By the end of the epidemic, about 80% of the population have been infected and recovered.

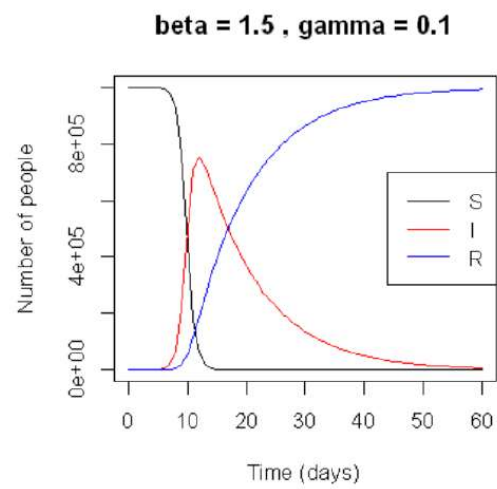
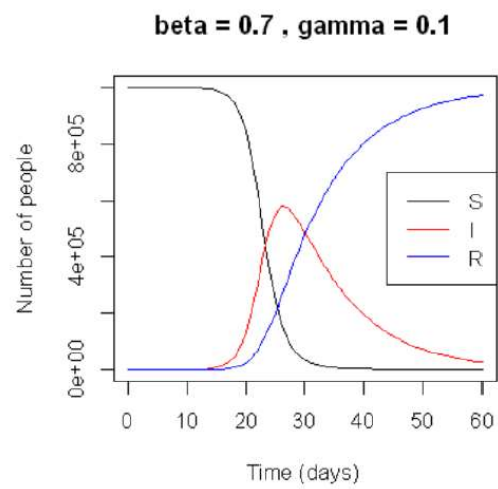
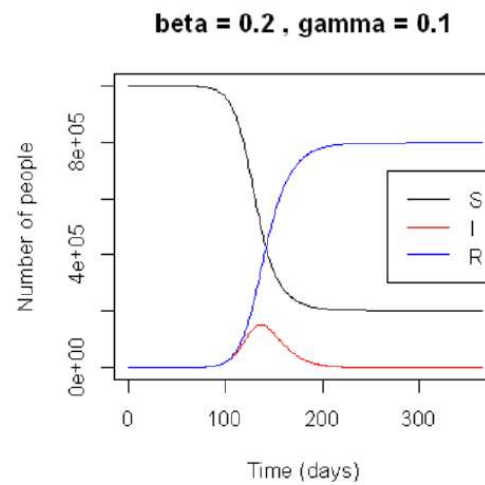
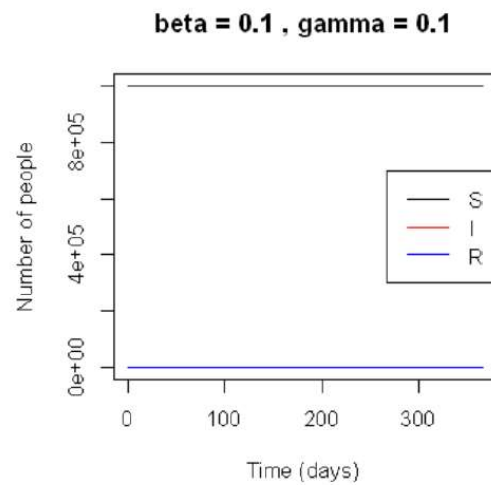
**Question: How does the pattern of the epidemic change under the following scenarios:**

- a) holding  $\gamma$  constant at  $0.1 \text{ day}^{-1}$ , vary  $\beta$  between 0.1 to 1.5  
(e.g. try *beta* = 0.1, 0.2, 0.7, 1.5 or similar)**
- a) holding *beta* constant at 1, vary  $\gamma$  between 0.01 to 1**

**Question: How do these different parameter combinations affect when the peak of the epidemic happens, how many people are infected at the peak, when the epidemic ends?**

**Question: Imagine a disease where every person infects 1 person on average, every 2 days, and is infectious for 4 days. What are the values for *beta* and *gamma*?**

**Question: Assuming *beta* equals  $0.1 \text{ days}^{-1}$ , what value of *gamma* do you need in order to get an epidemic? In real life, what could give rise to such a change in *gamma*?**



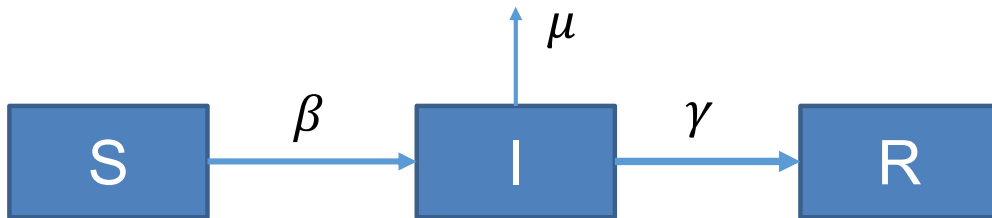


Reproduction number

Write expressions for  $R_0$

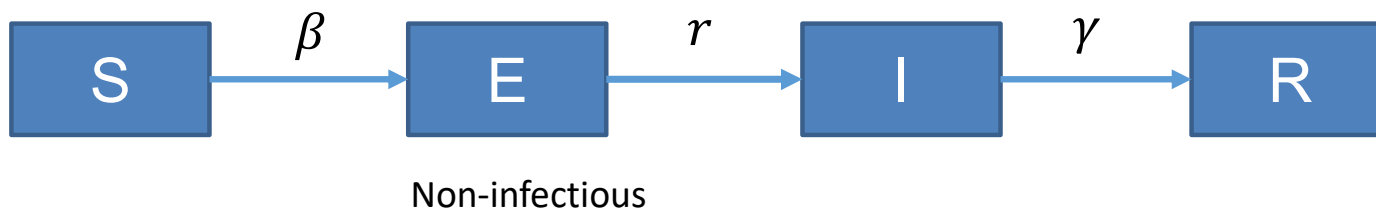


$$R_0 = \frac{\beta}{\gamma}$$

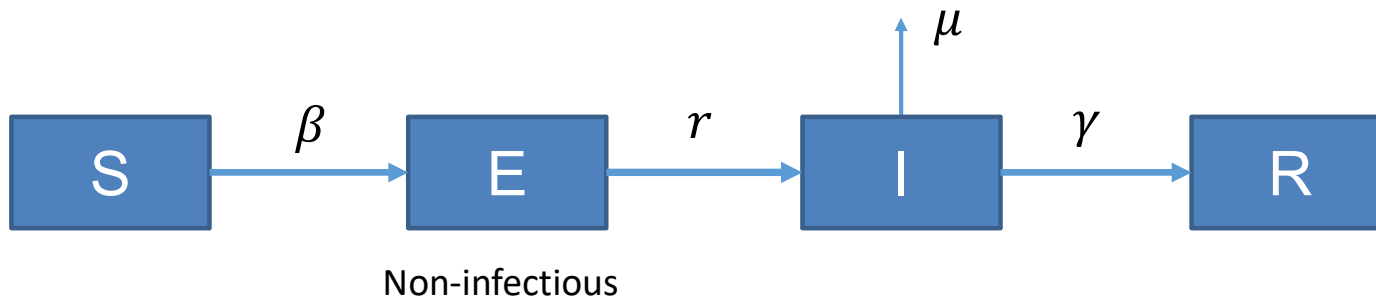


$$R_0 = \frac{\beta}{\mu + \gamma}$$

Write expressions for  $R_0$

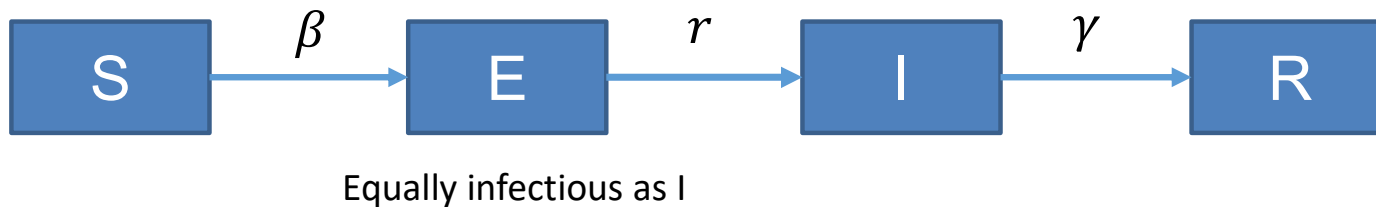


$$R_0 = \frac{\beta}{\gamma}$$



$$R_0 = \frac{\beta}{\mu + \gamma}$$

Write an expression for  $R_0$



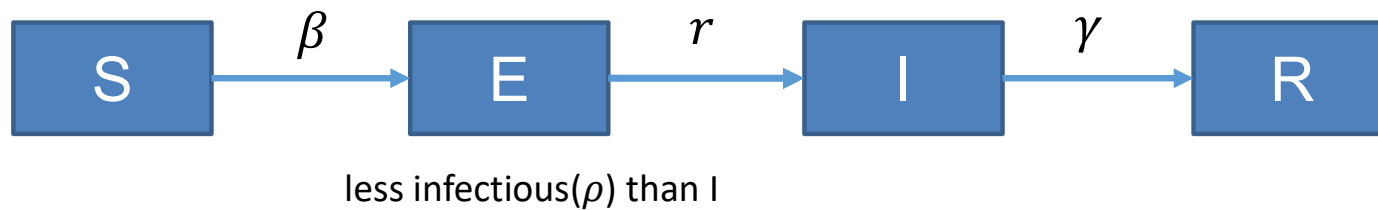
Average infectious period

$$\frac{1}{r} + \frac{1}{\gamma} = \frac{\gamma + r}{r\gamma}$$

$$R_0 = \frac{\beta}{\text{effective recovery rate}}$$

$$R_0 = \frac{\beta (r + \gamma)}{r\gamma}$$

Write an expression for  $R_0$



Average infectious period

$$\frac{\rho}{r} + \frac{1}{\gamma} = \frac{\rho\gamma + r}{r\gamma}$$

$$R_0 = \frac{\beta}{\text{effective recovery rate}}$$

$$R_0 = \frac{\beta (\rho\gamma + r)}{r\gamma}$$

**Question: How does  $R_{eff}$  vary over the course of the epidemic? What do you notice about the connection between the change in  $R_{eff}$  and the epidemic curve over time? In relation to  $R_{eff}$ , when does the epidemic peak and start to decline?**

# Questions – I

*Construct models with the following assumptions and look at the epidemic pattern*

*Assume a population of 100,000 people*

- **Perfectly immunizing infection**
  - No disease-induced mortality
  - Average duration of infection is 5 days
  - Basic reproduction number,  $R_0 = 3$
- **Perfectly immunizing infection**
  - 40% of infected individuals die, the rest recover
  - Average duration infection is 5 days
  - Basic reproduction number,  $R_0 = 3$

# Questions - II

- **Perfectly immunizing infection**

- Upon infection, there is an *incubation period* of 2 days on average (non-infectious)
- After the incubation period, 60% develop symptoms, the rest remain asymptomatic
- Asymptomatic infections are *half* as infectious as symptomatic infection
- No disease-induced mortality
- Average duration of symptomatic infection is 5 days
- Average duration of asymptomatic infection is 3 days
- Basic reproduction number,  $R_0 = 4$



*Thank you*

Questions?