DH301: Basic Epidemiology

Mathematical Epidemiology

(Lecture 2)

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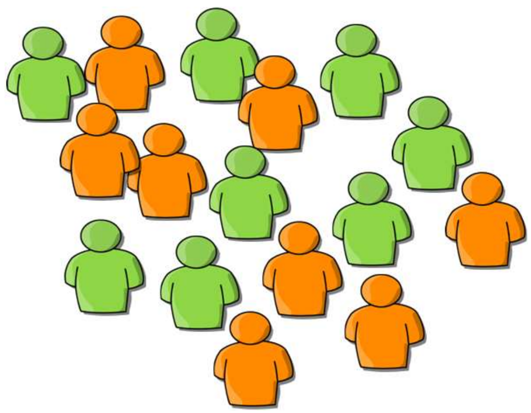
Lecture 2

Introduction to Ordinary Differential Equation and Basic principles of compartmental models

Imagine a population of size *N*

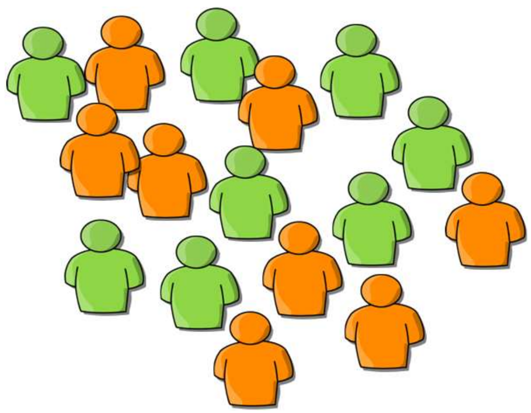


$\frac{dN}{dt}$ is the **rate of change** of this population over time

If $\frac{dN}{dt}$ is **large and positive**, the population is *growing quickly*

If $\frac{dN}{dt}$ is **small and negative**, the population is *declining slowly*

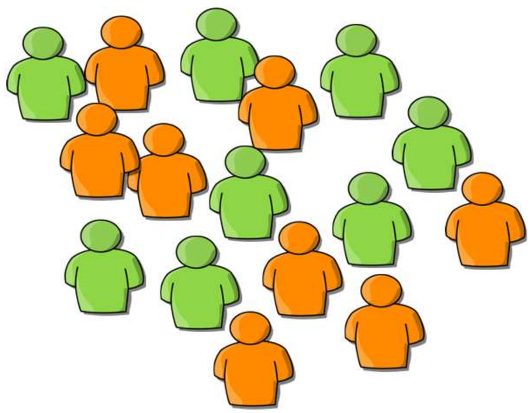
Example 1: The population is constant



The rate of change of *N* is zero, meaning:

$$\frac{dN}{dt} = 0$$

Example 2: The population is growing at a constant rate



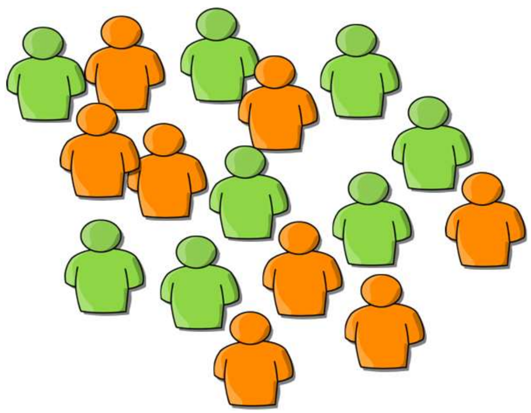
The rate of change of *N* is constant and positive, meaning:

$$\frac{dN}{dt} = c$$

for some positive number *c*

Simple example of an *ordinary differential equation* (as opposed to partial differential equations)

Example 3: The population is growing at a rate proportional to *N*

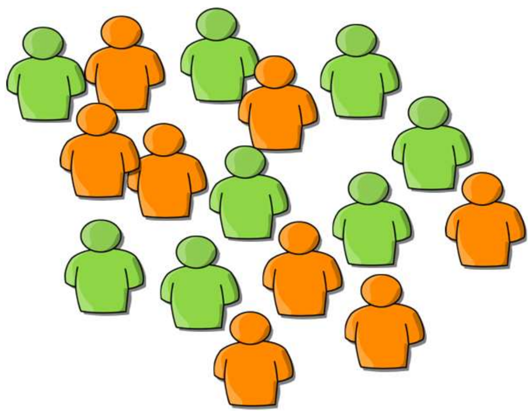


The rate of change of *N* is proportional to *N*, meaning:

$$\frac{dN}{dt} = bN$$

for some positive number *b*

Example 4: Birth and death rates

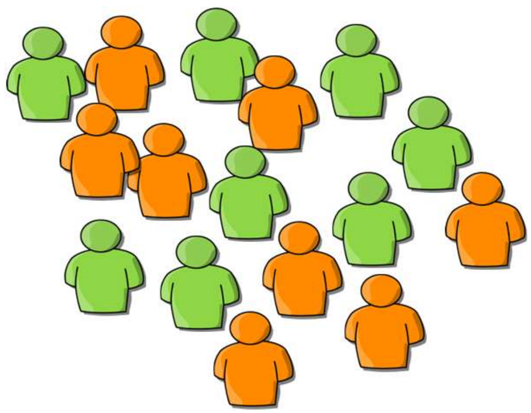


Birth rate (new members of population) is proportional to N

Death rate (exit from population) is proportional to N

What is an ODE equation for this process?

Example 4: Birth and death rates



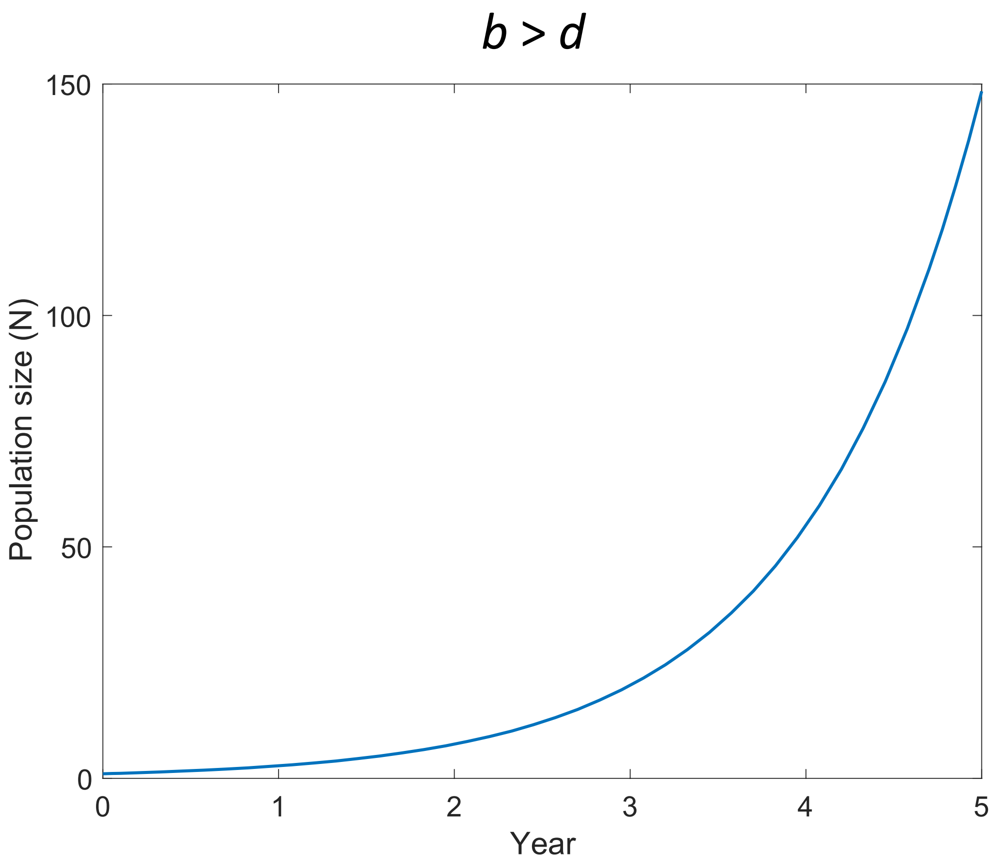
Birth rate (new members of population) is proportional to *N*

Death rate (exit from population) is proportional to *N*

$$\frac{dN}{dt} = bN - dN$$

for positive constants *b, d*

Simple population growth



Solution to the equation:

$$\frac{dN}{dt} = bN - dN$$

Compartmental models

Concepts we'll cover

- **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)

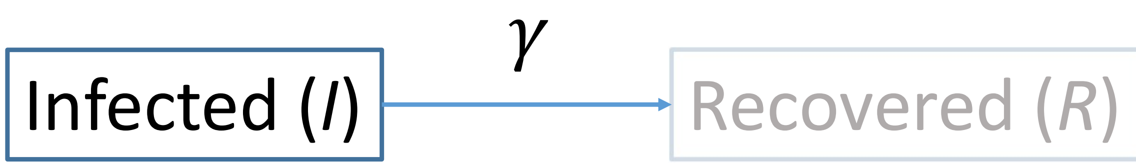
Boxes and arrows

- A cohort of 100 people with an infection, being observed over time

$$\boxed{\text{Infected } (I)} \xrightarrow{\gamma} \boxed{\text{Recovered } (R)}$$

Boxes and arrows

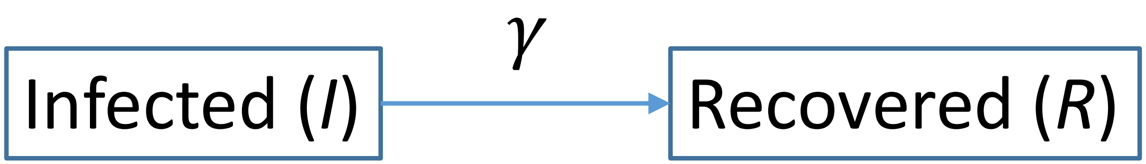
- A cohort of 100 people with an infection, being observed over time



1. Whenever there is a rate ***exiting*** a compartment, the relevant term in the equation is the negative product of the two (see $-\gamma I$)

Boxes and arrows

- A cohort of 100 people with an infection, being observed over time



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Boxes and arrows

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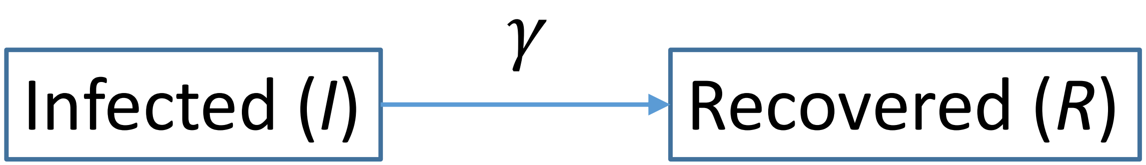


1. Whenever there is a rate ***exiting*** a compartment, the relevant term in the equation is the negative product of the two (see $-\gamma I$)

2. Every negative term should be balanced by a positive term in the receiving compartment (see γI)

Statistical perspective: assumptions

- Everyone in the same compartment faces the same hazards of transition
  - Variation in the population? Can introduce further compartments
  - Also note: once people arrive in a compartment, they have no 'memory' of how they got there

- Hazard rate is uniform over time
  - Residence in any compartment is an *exponentially distributed* survival process
  - Simplest type of survival process

- **Average** residence time is the inverse of the sum of hazard rates

Non-statistical perspective

- γ is known as a 'per-capita transition rate'
  - Note: this is not the same as 'rates' in traditional epidemiology usage!
- γ has units of inverse time
  - E.g. day^{-1}, year^{-1}, etc
- The average duration of transition from *I* to *R* is given by $1/\gamma$
  - E.g. if $\gamma = 1/3\ \mathrm{day}^{-1}$, then the average treatment duration is 3 days
  - *What is the average duration if* $\gamma = 52\ year^{-1}$?

Competing hazards – key points

- The proportion of people who **die** before **recovering** is:

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

- This is just the same as the case fatality rate
- You can use similar logic for the cure rate: $\frac{\gamma}{\mu+\gamma}$

Questions

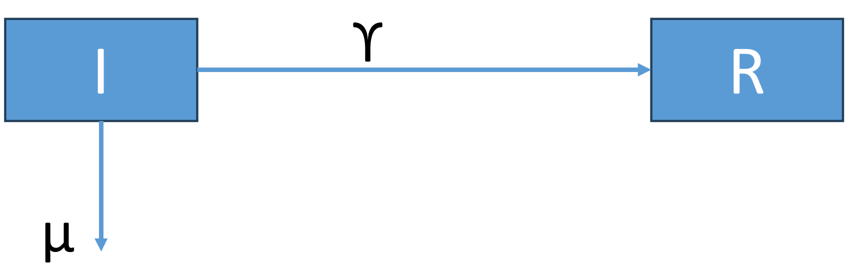
Construct the model and indicate the parameter values

- You have 1,000 people who are infected with a disease. All of them recover, on average, in within 7 days.

Questions

Construct the model and indicate the parameter values

- You have 1,000 people who are infected with a disease.
  - Some of them recover, but unfortunately 40% die.
  - The average duration of disease is 5 days.

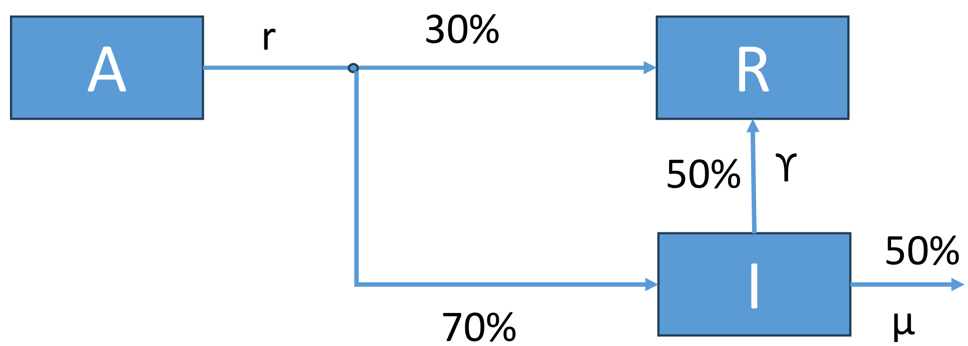


Questions

Construct the model and indicate the parameter values

You have 1,000 people having an asymptomatic infection.

- On average, the duration of asymptomatic infection is 3 days.
- 30% of them recover, while others go on to develop symptoms.
- Of those, 50% recover, while the remainder die.
- The average duration of symptomatic disease is 7 days.



Practical 1: Modelling an infected cohort

$$\text{Infected } (I) \xrightarrow{\gamma} \text{Recovered } (R)$$

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?**

Practical 2: Simulating competing hazards

In the previous practical 1 you modelled an infected cohort in *R code (or your preferred language)*. 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.**

End of first part of lecture 2

Concepts we'll cover

- **Boxes and arrows**
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  - 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)

Now including infection…

Susceptible (*S*) $\xrightarrow{\lambda}$ Infected (*I*) $\xrightarrow{\gamma}$ Recovered (*R*)

Governing equations:

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

Now including infection…

$$\boxed{\text{Susceptible } (S)} \xrightarrow{\lambda} \boxed{\text{Infected } (I)} \xrightarrow{\gamma} \boxed{\text{Recovered } (R)}$$

Governing equations:

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

Now including infection…

$$\text{Susceptible } (S) \xrightarrow{\lambda} \text{Infected } (I) \xrightarrow{\gamma} \text{Recovered } (R)$$

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

Governing equations:

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

What is β (‘beta’)?

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

- 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…

Susceptible (*S*) $\xrightarrow{\lambda}$ Infected (*I*) $\xrightarrow{\gamma}$ Recovered (*R*)

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

Governing equations:

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

Now including infection…

SIR model

$$\text{Susceptible } (S) \xrightarrow{\lambda} \text{Infected } (I) \xrightarrow{\gamma} \text{Recovered } (R)$$

β, γ are ***parameters***: their values need to be specified in order to simulate the model

Governing equations:

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

When is an infection capable of causing a major epidemic?

- Basic reproduction number, R_0

- **Definition**: average number of secondary cases caused by a single infected case, in an otherwise susceptible population

- An epidemic is possible when $R_0 > 1$
- Otherwise, introductions of the infection go extinct without causing an epidemic

For an SIR model:
What is an expression for R_0 in terms of β and γ?

(A)

$$R_0 = \beta \times \gamma$$

(B)

$$R_0 = \beta + \gamma$$

(C)

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

$$S \xrightarrow{\lambda} I \xrightarrow{\gamma} R$$

$$\frac{dS}{dt} = -\beta \frac{I}{N} S \qquad \boldsymbol{\frac{dI}{dt} = \beta \frac{I}{N} S - \gamma I} \qquad \frac{dR}{dt} = \gamma I$$

β = infection rate
γ = removal rate

Infection progresses in population when

$$\boldsymbol{\beta \frac{I}{N} S > \gamma I} \Rightarrow \boldsymbol{\beta \frac{S}{N} > \gamma} \Rightarrow \boldsymbol{\frac{\beta}{\gamma} \frac{S}{N} > 1}$$

In completely susceptible population S = N

$$\Rightarrow \boldsymbol{\frac{\beta}{\gamma} > 1}$$

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

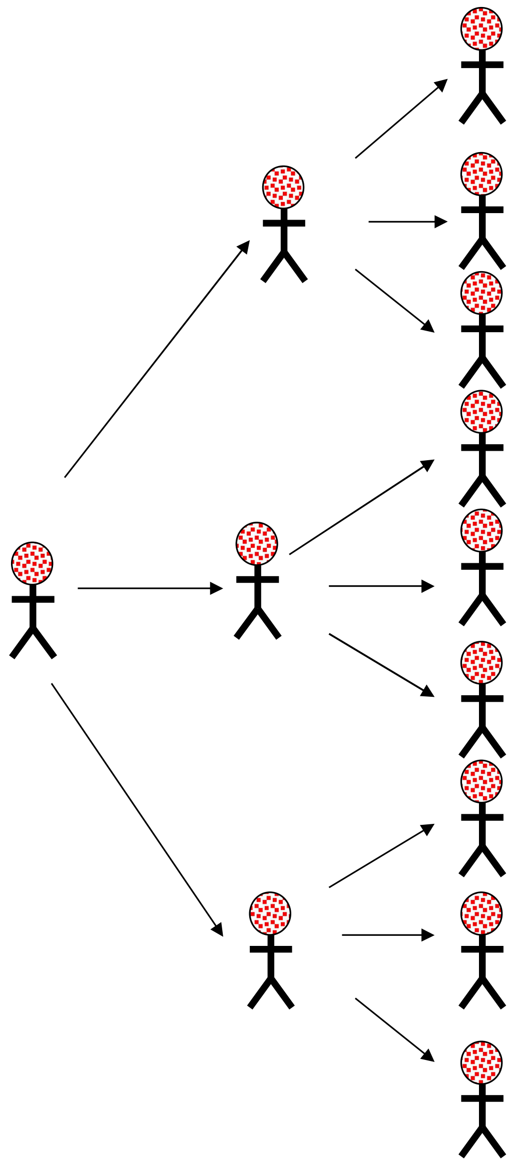
Basic Reproduction Number (R_0)

Number of secondary infections that is produced by a single infected host during its entire infectious period, in a completely susceptible population

$R_0 > 1$ Epidemic **$R_0 = 1$ Endemic** **$R_0 < 1$ Eradication**

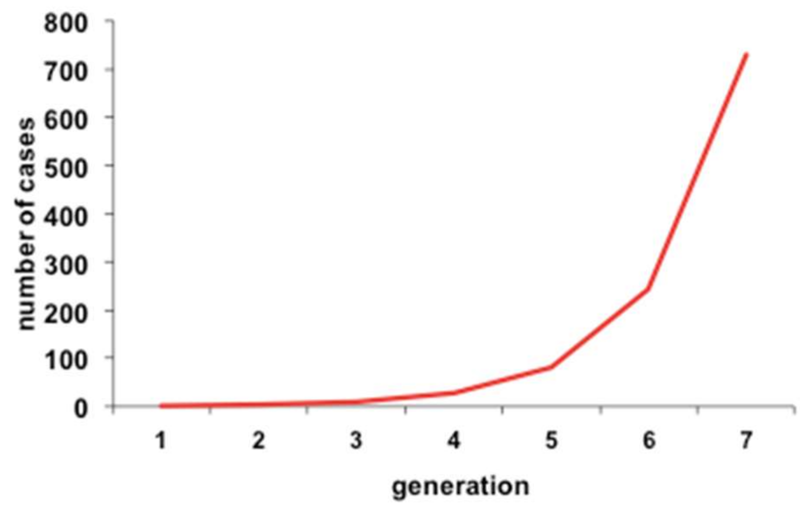
Effective reproduction number

$$\boxed{\boldsymbol{R_{eff} = R_0 \frac{S}{N}}}$$



Basic Reproductive Number

R_0



R_0 of childhood diseases

Infection/ infectious agent	R_0	Average age at infection*
Measles	11-18	4-5
Pertussis	16-18	4-5
Mumps	11-14	6-7
Rubella	6-12	6-10
Diphtheria	4-5	11-14
Polio	6-7	12-17

Source: Anderson & May, 2006

* In the absence of immunization

Vaccination

What proportion of the population would have to be vaccinated with to prevent an epidemic?

$\boldsymbol{R_0}$: Number of secondary infection if all are susceptible

If p proportion of people are vaccinated then
Effective Basic Reproduction number: $\boldsymbol{R_0} - p\,\boldsymbol{R_0}$

To prevent epidemic: $\boldsymbol{R_0} - p\,\boldsymbol{R_0} < 1$ $\quad\quad \boldsymbol{R_0}\,(1 - p\,) < 1$

$(1 - p\,) < \frac{1}{\boldsymbol{R_0}}$ $\quad\quad \boxed{p > \left(1 - \frac{1}{\boldsymbol{R_0}}\right)}$

Key points so far

- In compartmental models, rates of transition between compartments are closely linked with duration
  - E.g. a 'rate of recovery' $\gamma = \frac{1}{4}$ days^{-1} corresponds to an average infectious period of 4 days

- λ is the 'force of infection', which determines the rate at which susceptible people become infected.
- In a simple SIR model we write $\lambda = \beta I/N$, where β is a parameter representing the rate-of-infection from a single infected case
- β isn't usually measured directly, but estimated from available data

- The 'basic reproduction number' R_0 gives a measure of epidemic potential in a fully susceptible population
- In a simple SIR model, we have $R_0 = \beta/\gamma$

Questions – I

Construct a model and indicate the parameter values with the following information:

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?