SWEN90004
Modelling Complex Software Systems

Lectures Cx.04
ODE Models II: Epidemics

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Recap

- building a mathematical model
  - starting with a simple model
  - extending models to include additional aspects of real world
- models:
  - populaton growth
  - species interaction (predator-prey)
- representing behaviour of dynamic systems
  - time series plots (how system state changes over time)
  - phase portraits (how state variables change with respect to each other)
- exploring behaviour
  - numerically (using matlab or R to evaluate system)
  - analytically (working directly with equations)

Objectives

- explore the SIR model of infectious disease transmission
- use this model to ask and answer questions
- understand the difference between stochastic and deterministic models

Questions

- What level of vaccine coverage do we need to maintain to prevent measles spreading?
- Given a limited supply of antiviral drugs, who should we prioritise in the next flu pandemic?
- When might socially and economically disruptive interventions, such as closing schools or airports, make sense?
- How can we prevent future outbreaks of a disease like Ebola?

Recap – model terminology

Infectious disease models are **dynamic** models—they describe how an infection spreads through a population over time.

A model has a **state**, which describes all relevant aspects of the system at a particular point in time (eg, which people are currently healthy/sick).

A model has **update rules**, which describe how the state of a model changes over time (eg, how healthy people become sick).

These rules often involve **parameters**, which can be varied to calibrate the rules to a real world scenario (eg, how long it takes a typical person to recover from measles or influenza).

The basic SIR model

The Susceptible, Infectious, Recovered (SIR) model is one of the simplest disease models, proposed almost 100 years ago and still the basis of ID modelling today.

The SIR model sorts people into three categories based on their disease state:

Susceptible – can be infected

Infectious – can infect others

Recovered – cannot be infected nor infect others

The basic SIR model

If we think about a single person in our population, there are two possible events that can occur to them:

1. If they are susceptible, and they encounter an infectious person, they may be infected

2. If they are infectious, they may recover

A simple implementation of the basic SIR model

State: A population of $N = 10$ people, each with a state S, I or R.

Initial condition: On day zero, 9 people are susceptible (S) and 1 is infectious (I)

$$t = 0: \quad [\mathtt{S},\ \mathtt{S},\ \mathtt{S},\ \mathtt{S},\ \mathtt{S},\ \mathtt{S},\ \mathtt{I},\ \mathtt{S},\ \mathtt{S},\ \mathtt{S}]$$

Rules: As this is a small group of people, we'll assume that everybody meets everybody else each day

- *Infection*: each time a susceptible person meets an infectious person, they have a probability q of becoming infectious on the next day

Recovery: an infectious person will recover (R) on the next day with probability γ

Parameters: q and γ

Working out whether an event happens?

What does it mean for infection to happen with probability $q = 0.2$?

If a susceptible person meets an infectious person, they have a 20% chance of becoming sick.

Alternatively, for every five such contacts that occur, on average one of them will result in disease transmission occurring.

We can simulate this process in a computer by generating a random number x between 0 and 1

eg, 0.3465, 0.1989, 0.8796, ...

If x is less than q, we will say that transmission has occurred.

Running our model

Do the following steps for each day:

1. *Infection*: Check each susceptible person X:
   - Check each contact between X and each infectious person Y:
     - pick a random number n
     - if $n < q$, then X is infected by Y
2. *Recovery*: Check each infectious person Y:
   - pick a random number n
   - if $n < \gamma$, Y will recover
3. If there are no more infectious people, stop. Otherwise, continue to the next day (return to step 1).

Running our model – output

Population size: $N = 10$, with one infectious at $t = 0$

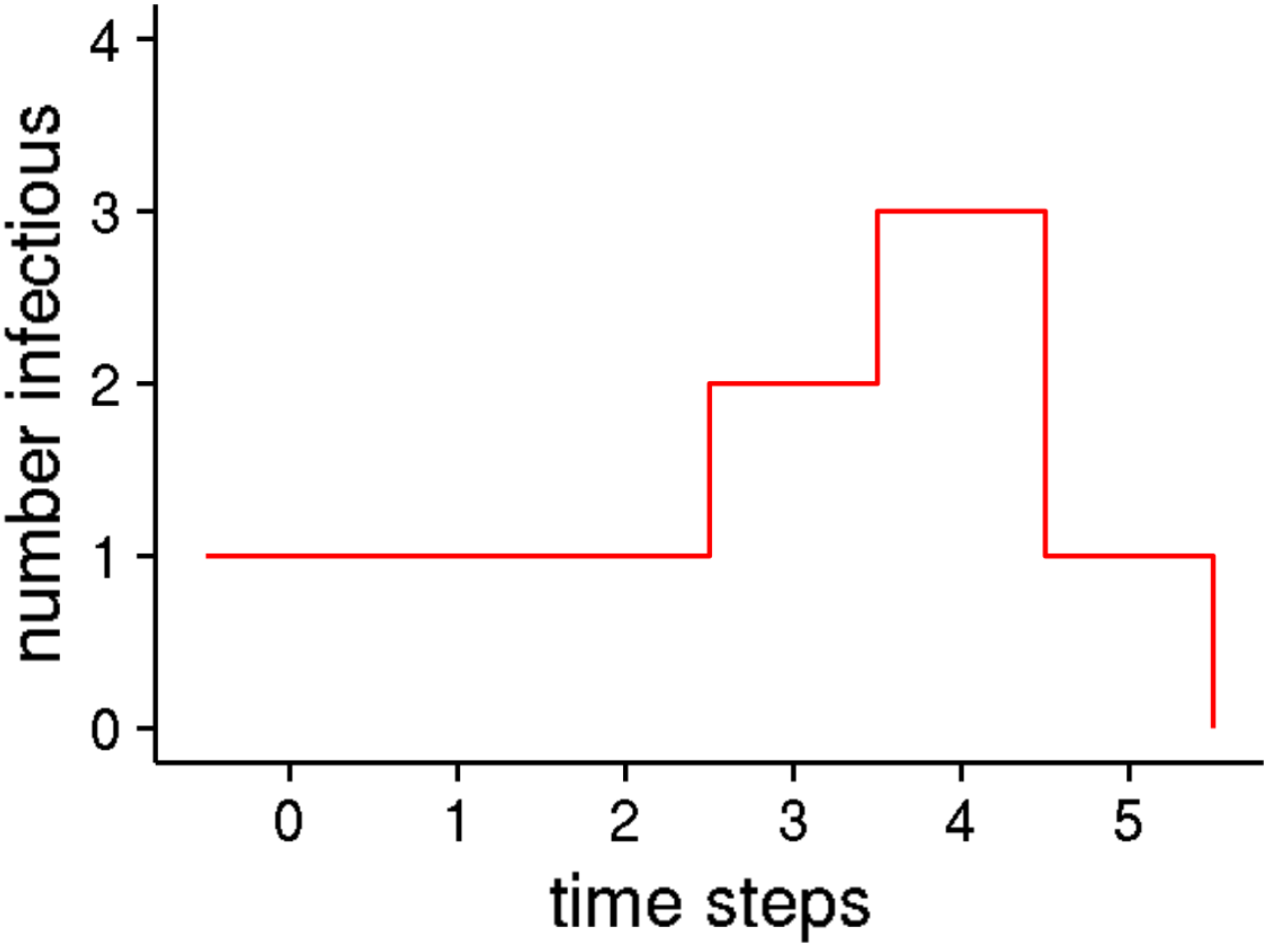
Probability of infection (per contact): $q = 0.2$

Probability of recovery (per day): $\gamma = 1.0$ (ie, every infectious person recovered after being infectious for exactly one day)

$t = 0$: [S, S, S, S, S, S, I, S, S, S]; $|I| = 1$
$t = 1$: [S, S, I, S, S, S, R, S, S, S]; $|I| = 1$
$t = 2$: [S, I, R, S, S, S, R, S, S, S]; $|I| = 1$
$t = 3$: [S, R, R, I, S, S, R, I, S, S]; $|I| = 2$
$t = 4$: [S, R, R, R, I, I, R, R, S, I]; $|I| = 3$
$t = 5$: [I, R, R, R, R, R, R, R, S, R]; $|I| = 1$
$t = 6$: [R, R, R, R, R, R, R, R, S, R]; $|I| = 0$

Running our model – output

Parameters: $N = 10; q = 0.2; \gamma = 1$



Running our model – output

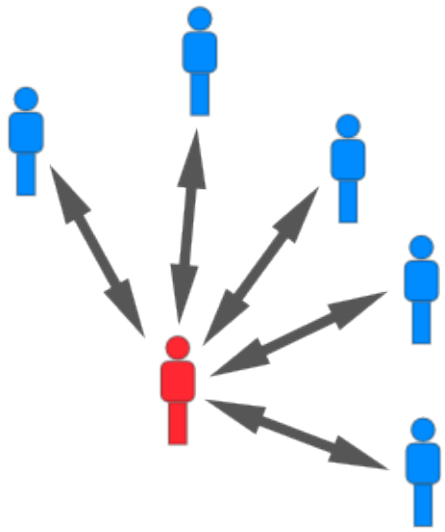
What will happen if q is very low and γ is very high?

What will happen if q is very high and γ is very low?

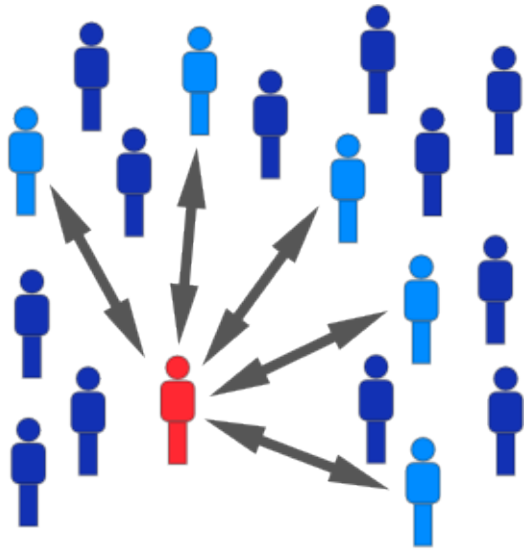
Can you see any problems with this approach?

How does contact scale with population size?

We typically assume that even if the size of the population increases, any one person still encounters roughly the same number of people on a given day (we will call this number c).



small population



large population

A different way of calculating the risk of infection

If a susceptible person comes into contact with an infectious person, they still have a probability q of being infected.

Therefore, each susceptible person has a probability

$$\lambda = c \times q \times \frac{I}{N}$$

of being infected on a given day.

ie, the number of contacts $\times$ the probability of transmission (if a contact is infectious) $\times$ the probability that a contact is infectious.

Note: $\frac{c \times q}{N}$ is often written as β, which is the per capita rate at which two individuals come into effective contact (ie, sufficient to allow disease transmission to occur). In this case, $\lambda = \beta I$

A revised SIR model

State: The number of people with each disease state: [S, I, R]. Note that S+I+R=N.

Initial condition: On day zero, 9 people are susceptible (S) and 1 is infectious (I).

$$t = 0\text{: [S=9, I=1, R=0]}$$

Rules: Each time step—

- the probability of a susceptible person becoming infected is $\lambda = \beta I$.
- the probability of an infectious person recovering is γ

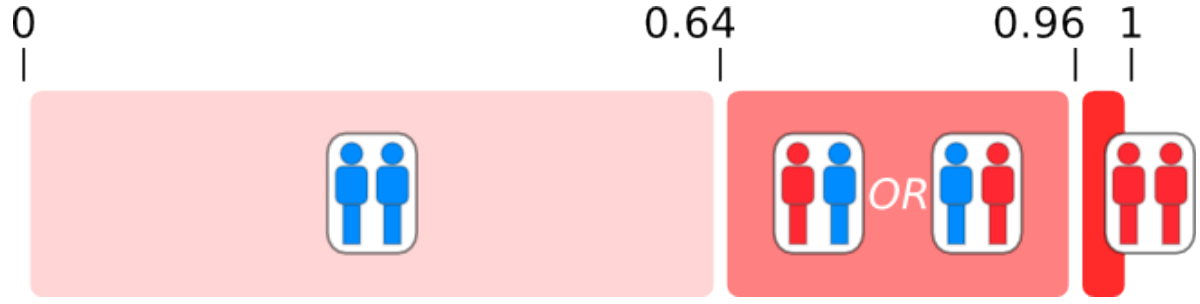
Parameters: β $(= \frac{c \times q}{N})$ and γ

Sampling from a distribution

Say there are two susceptible people at risk of infection (with probability λ). There are three possible outcomes:

outcome	**probability**	**eg,** $\lambda = 0.2$
neither person gets infected	$(1-\lambda) \times (1-\lambda)$	0.64
one person gets infected	$[(1-\lambda) \times \lambda] \times 2$	0.32
both people get infected	$\lambda \times \lambda$	0.04

Now, rather than using our random number x to determine whether a single contact event results in infection, we use it to work out how many successful infections occurred.



Running our revised model

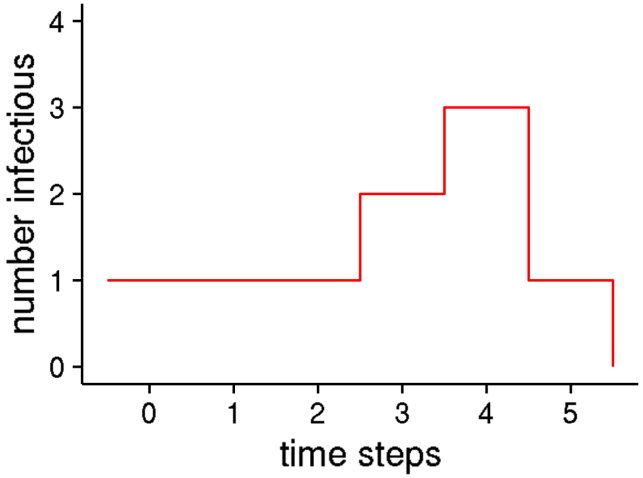
For each time interval (eg, each day):

1. *Infection*:
   - Calculate the probability λ that a susceptible person is infected, as described on the previous slide.
   - Calculate the *distribution* of the number of susceptible people who will be infected during the current day.
   - *Sample* from this distribution to determine how many susceptible people will be infectious on the next day.
2. *Recovery*:
   - Calculate the distribution of the number of infectious people who will recover during the current day.
   - *Sample* from this distribution to determine how many infectious people will be recovered on the next day.
3. If the number of infectious people is 0, stop.

Running our revised model – output

Equivalent output to before:

$$
\begin{aligned}
t = 0 &: [9, 1, 0] \\
t = 1 &: [8, 1, 1] \\
t = 2 &: [7, 1, 2] \\
t = 3 &: [5, 2, 3] \\
t = 4 &: [2, 3, 5] \\
t = 5 &: [1, 1, 8] \\
t = 6 &: [1, 0, 9]
\end{aligned}
$$



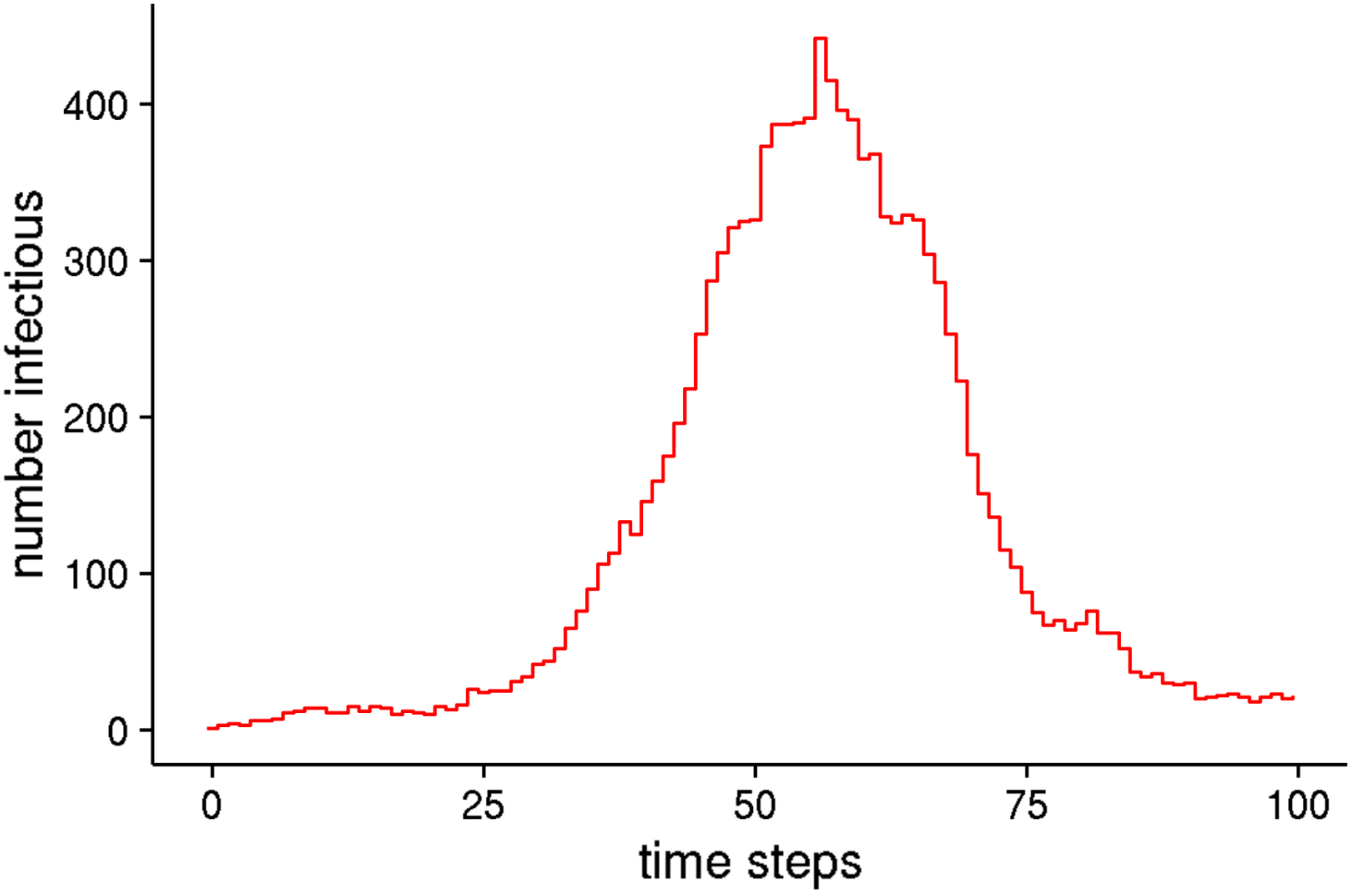
Note that we no longer need to keep track of every single person or to simulate every single contact event, we simply need to know how many people are currently susceptible and infectious. Much faster to run models with large populations:

$N = 10$: 12 vs 40 random numbers required.

$N = 1000$: 60 vs 165,000 random numbers required!!!

An outbreak in a larger population

Parameters: $N = 10,000; \beta = 5 \times 10^{-5}; \gamma = 0.4$



Stochastic models

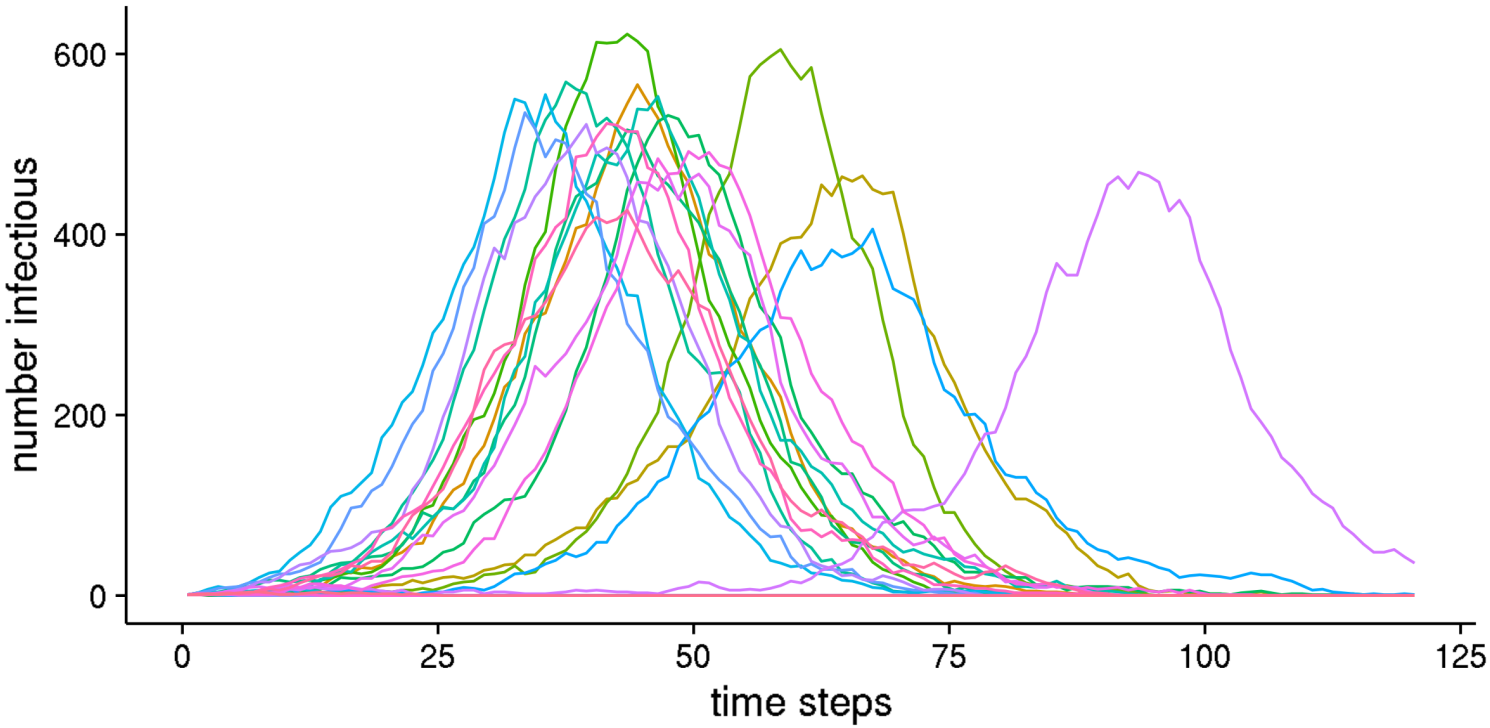
These models we have just described are *stochastic models*: they incorporate the effects of chance.

Stochastic processes are non-deterministic in that a state does not fully determine the next state.

Each time we run a stochastic model in a computer, we observe a different outcome. Sometimes an outbreak occurs, other times it doesn't. If an outbreak does occur, sometimes it may be small, other times it may be large.

Stochastic models

Parameters: $N = 10,000; \beta = 5.6 \times 10^{-5}; \gamma = 0.4$



Obviously, in the real world, only **ONE** possible future will come to pass. Stochastic models can help us to estimate what the *most likely* sequence of future events might be.

Histograms – distribution of possible outcomes

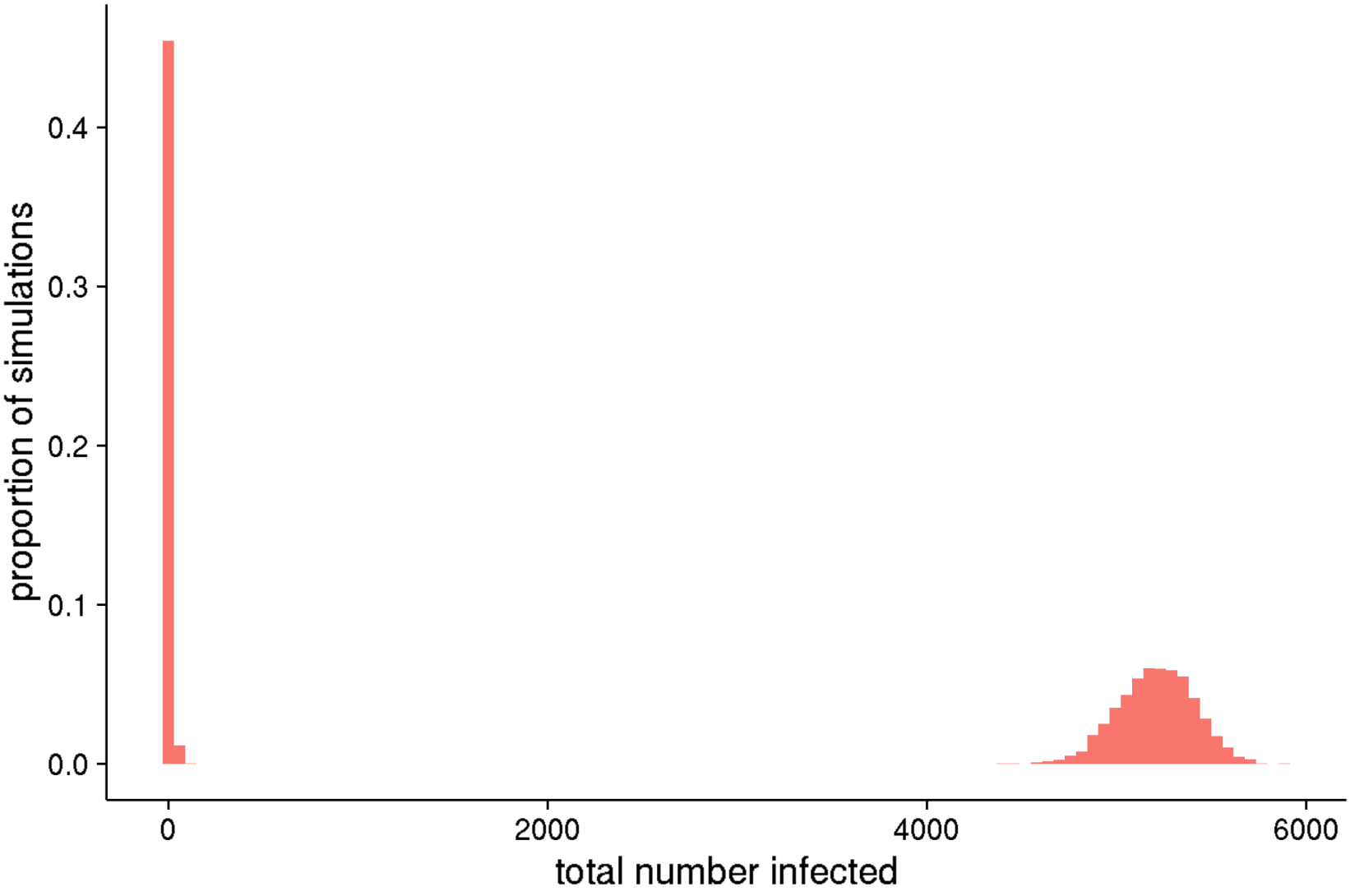
Which outcomes are more or less likely?

Having run a model multiple times, we can measure various properties of the outbreak (or otherwise) and use a histogram to show the distribution of probabilities that each outcome will eventuate.

Common properties of interest include:

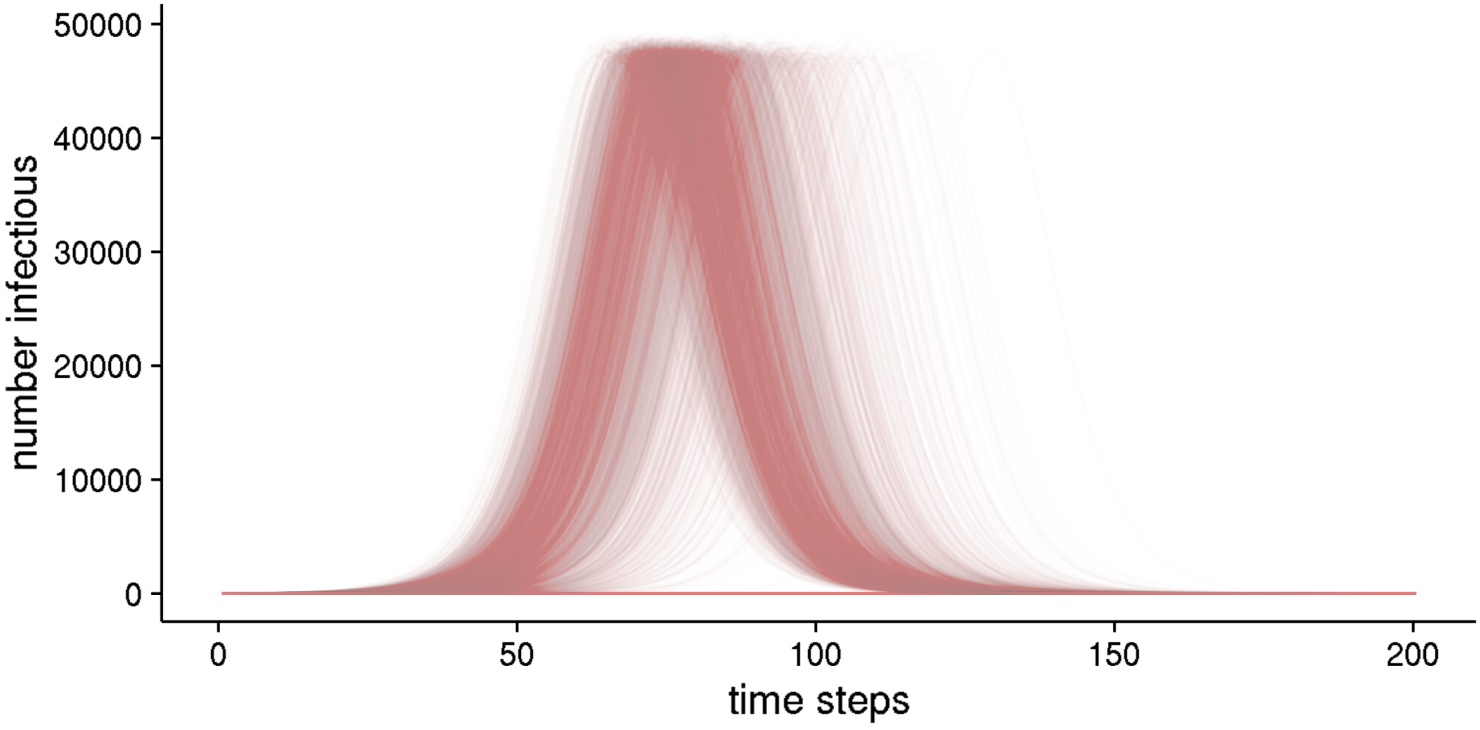
- the final size of the outbreak
- the size of the outbreak at its peak
- the time that the outbreak peak is reached

Final size of the outbreak



Increasing the size of our population

10,000 simulations with N=1,000,000:



What is predictable across each of these outbreaks? What remains variable? Why is this?

The basic reproduction number

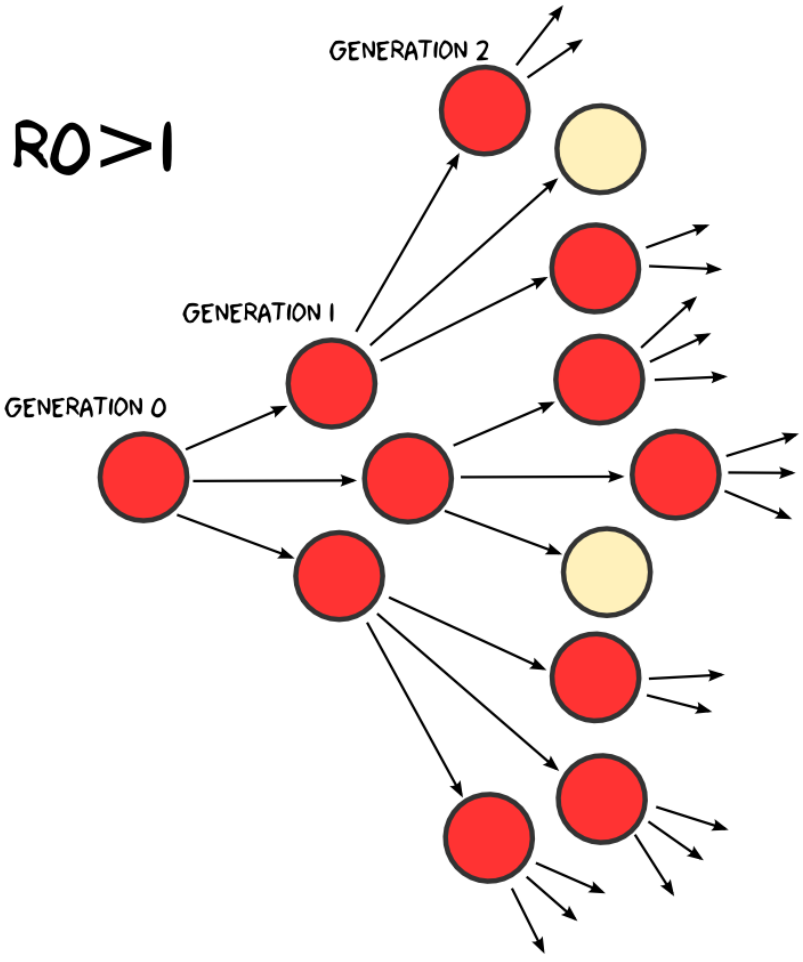
A key concept in infectious disease epidemiology is the **reproduction number** R, often defined as the average number of secondary cases infected by a typical primary case.

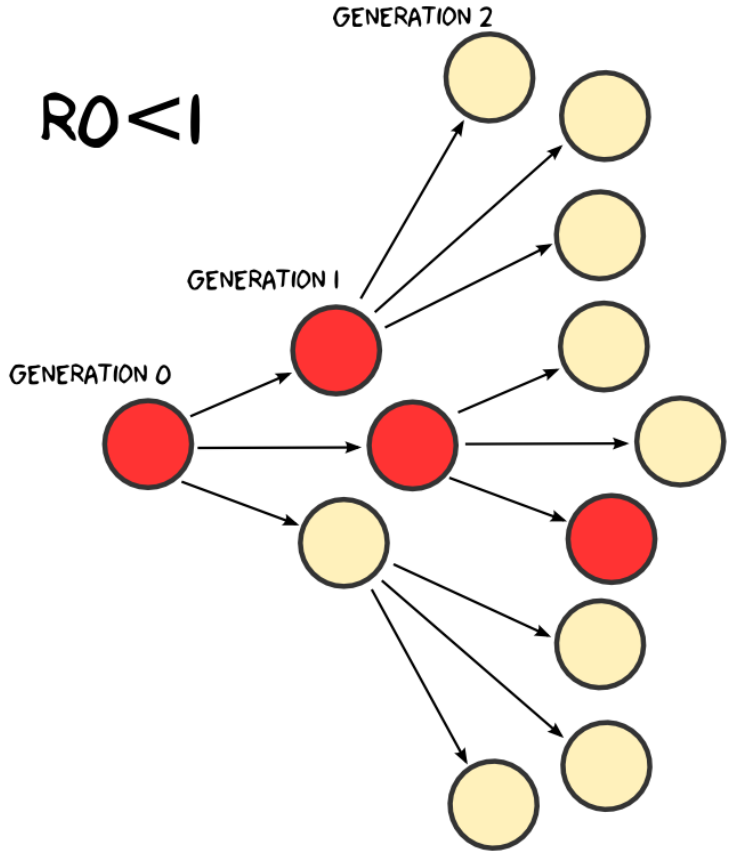
The **basic** reproduction number R_0 is the average number of secondary cases infected by a typical primary case in a *totally susceptible* population.

The reproduction number can tell us whether an outbreak can occur:

- if $R < 1$, then the outbreak will die out.
- if $R > 1$, then the outbreak may take off.

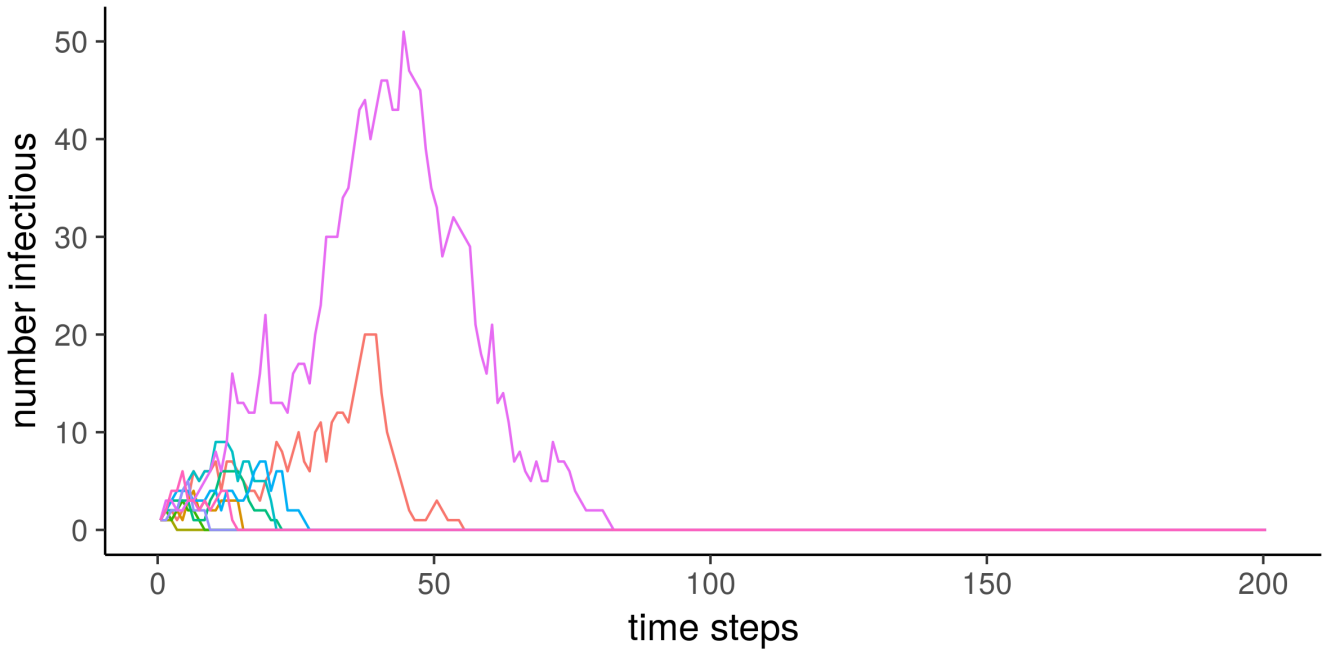
The basic reproduction number





Outbreak dynamics when R_0 is near 1

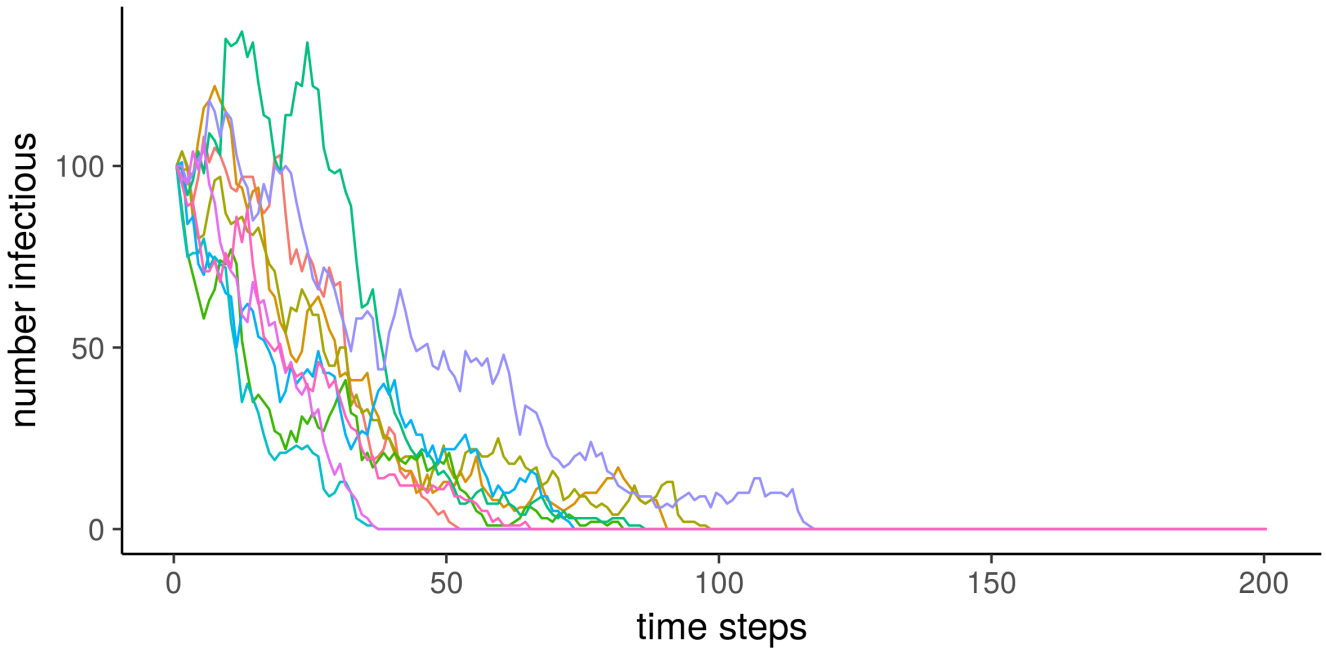
Parameters: $N = 10,000$; $\beta = 4 \times 10^{-5}$; $\gamma = 0.4$ (1 initial infectious person; 25 simulations)



Even with plenty of susceptible people to infect, a disease with $R_0 = 1$ will struggle to persist.

Outbreak dynamics when R_0 is near 1

Parameters: $N = 10,000; \beta = 4 \times 10^{-5}; \gamma = 0.4$ (100 initial infectious person; 25 simulations)



Outbreaks can fade out even when the initial number of infectious people is relatively large (100 people). For example, H5N1 can spread from birds to humans, but is not usually human transmissible.

Stochastic models summary

As our population size increases, the influence of chance diminishes. Perhaps we can ignore stochasticity altogether if our population is large enough?

When does stochasticity matter?

Deterministic models

An alternative to stochastic models, which generate distributions of *potential* outcomes, is deterministic models, which generate *unique* outcomes based on a given set of parameters and initial condition.

Unlike stochastic models, for each state of a deterministic model, there is only *one* possible future state.

If we are happy to ignore the variability in potential epidemic outcomes, we can set up a model that efficiently simulates the *average* behaviour of a system.

A deterministic version of the SIR model

State: S_t, I_t and R_t are the number of susceptible, infectious and recovered people at time t.

Rules: We use mathematical functions to specify how the state of the system at time t changes at time $t + \delta t$. By convention, we often say $\delta t = 1$ timestep, the length of which we then choose (eg, 1 day, 1 week, 6 hours, etc)

$$S_{t+1} = S_t - \beta S_t I_t$$
$$I_{t+1} = I_t + \beta S_t I_t - \gamma I_t$$
$$R_{t+1} = R_t + \gamma I_t$$

Parameters:

β and γ are now the *rates* of effective contact (per capita) and recovery.

Recovery rate and duration of infection

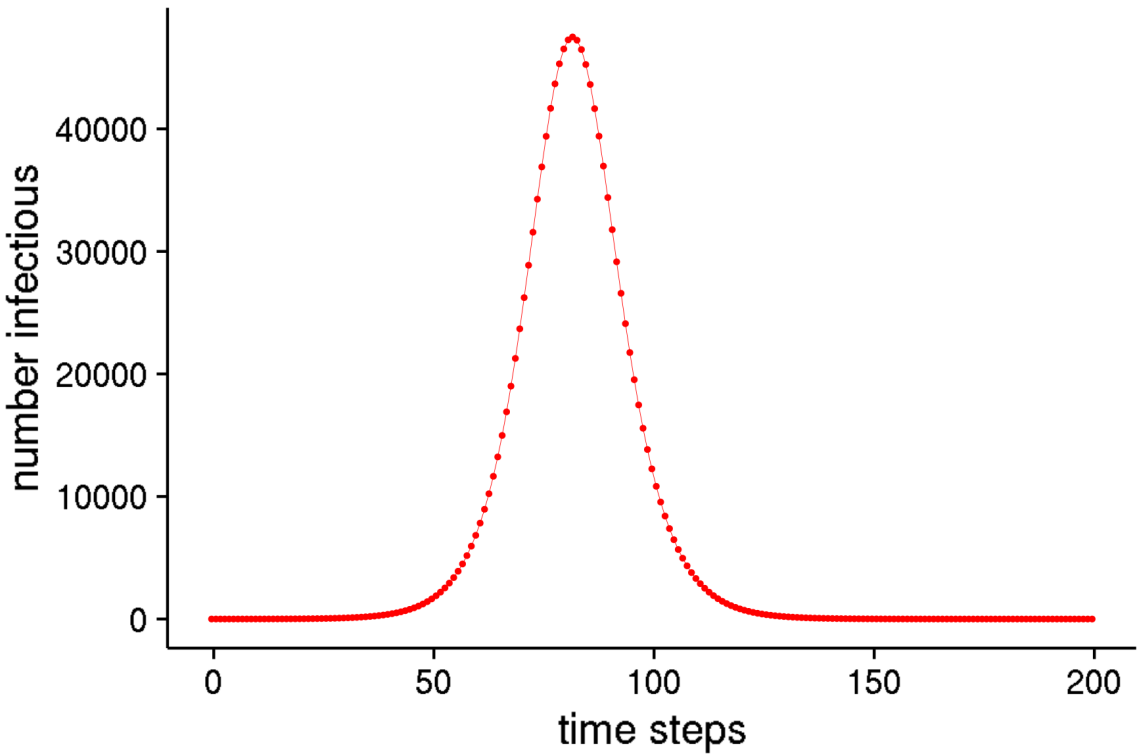
The inverse of a rate is the average time until something occurs – so $D = 1/\gamma$ is the average length of time that someone is infectious.

For example if the rate of recovery is $1/4$ days then we would expect an infected person to experience one recovery every four days.

Alternatively, on any given day, we would expect $1/4$ of the infected population to recover.

Running the deterministic SIR model – output

The mathematical equations on the previous slide can be set up very simply in a spreadsheet, or a package such as R or Matlab.



Note that, unlike the stochastic model, each time we run the deterministic model we get exactly the same result.

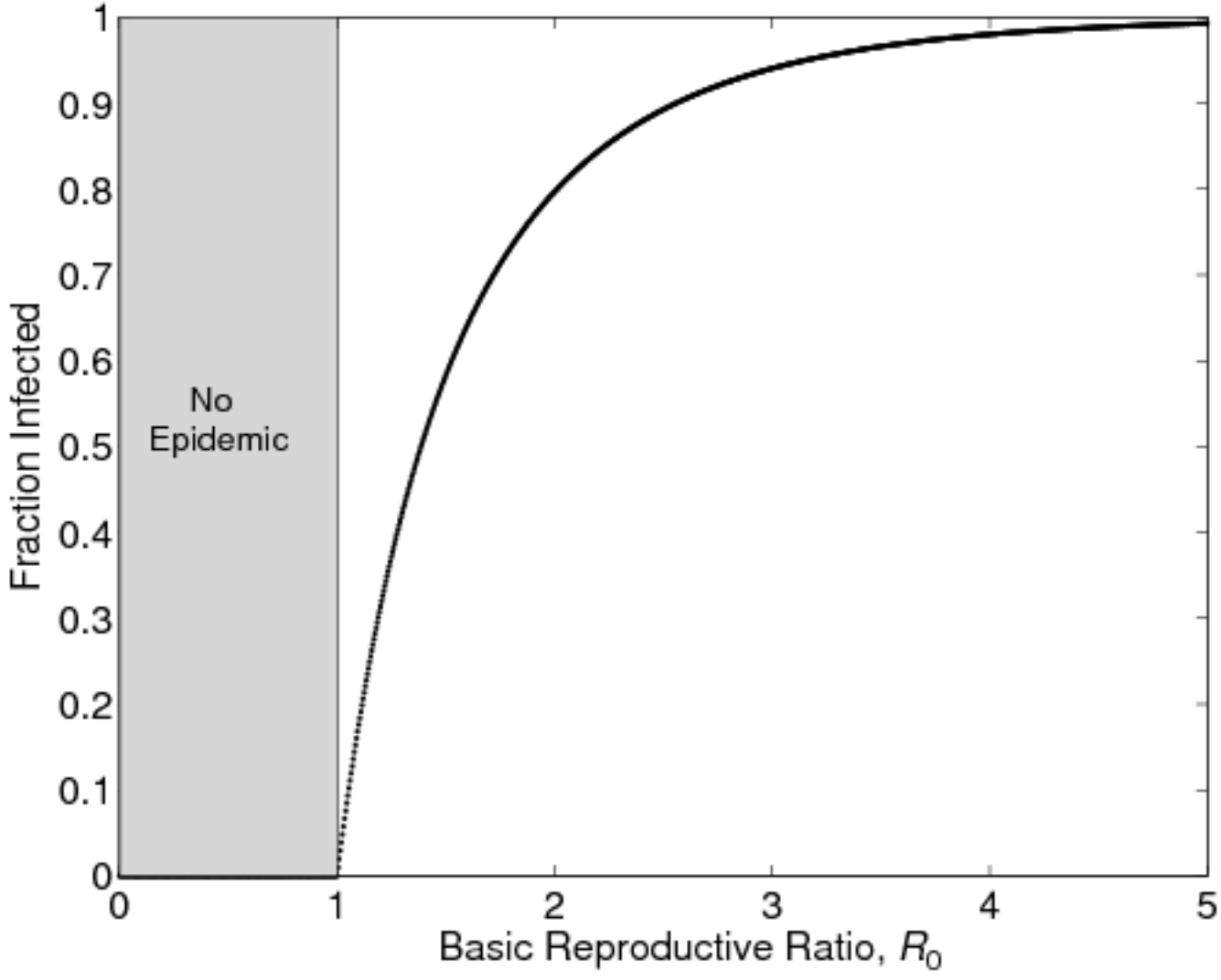
Difference equations and differential equations

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

Note: Models often describe the *fraction* of the population in each compartment; ie, $S + I + R = 1$

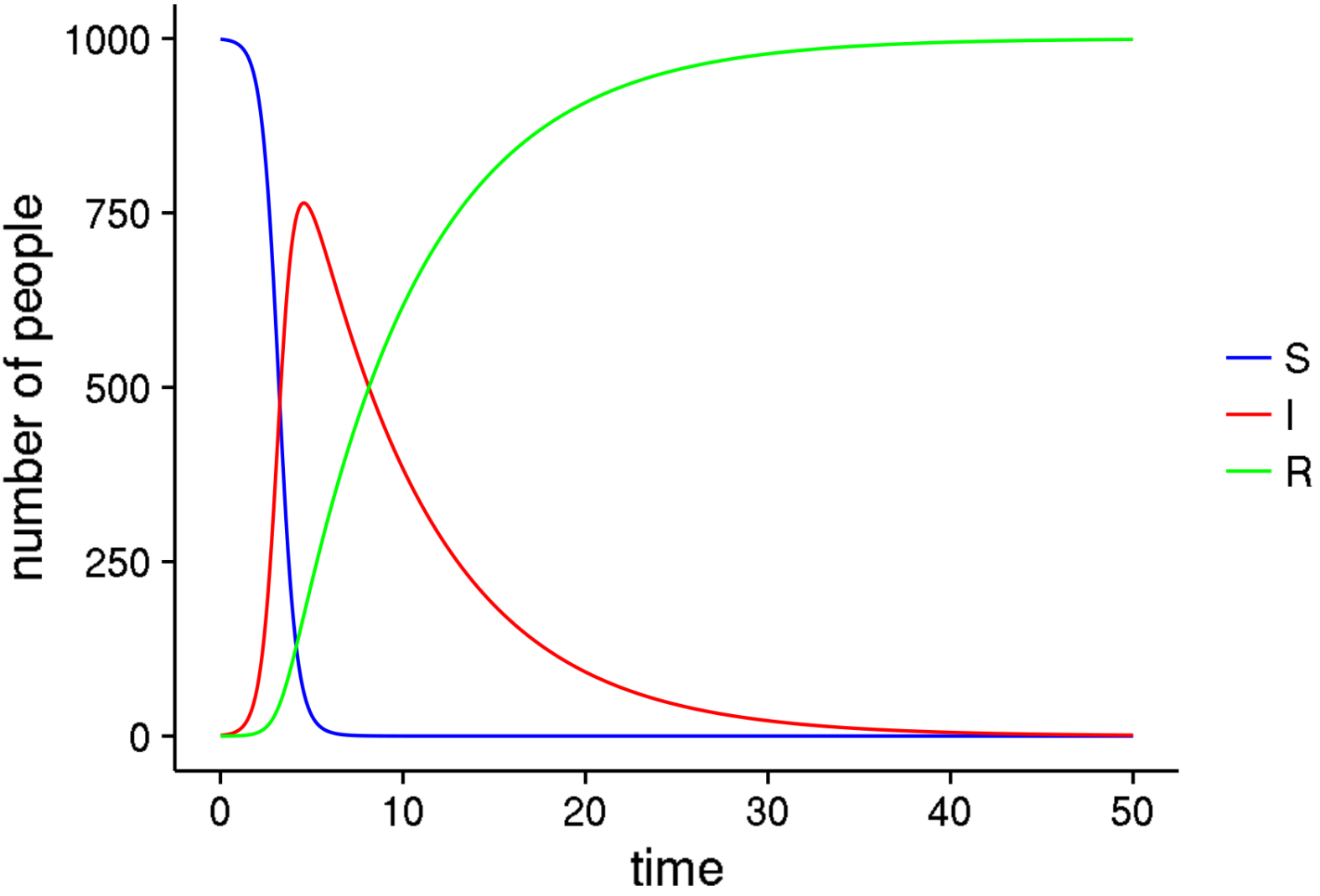
The basic reproduction number and outbreak size

R can also let us estimate what proportion of a population will have been infected by the end of an outbreak – the final attack rate.



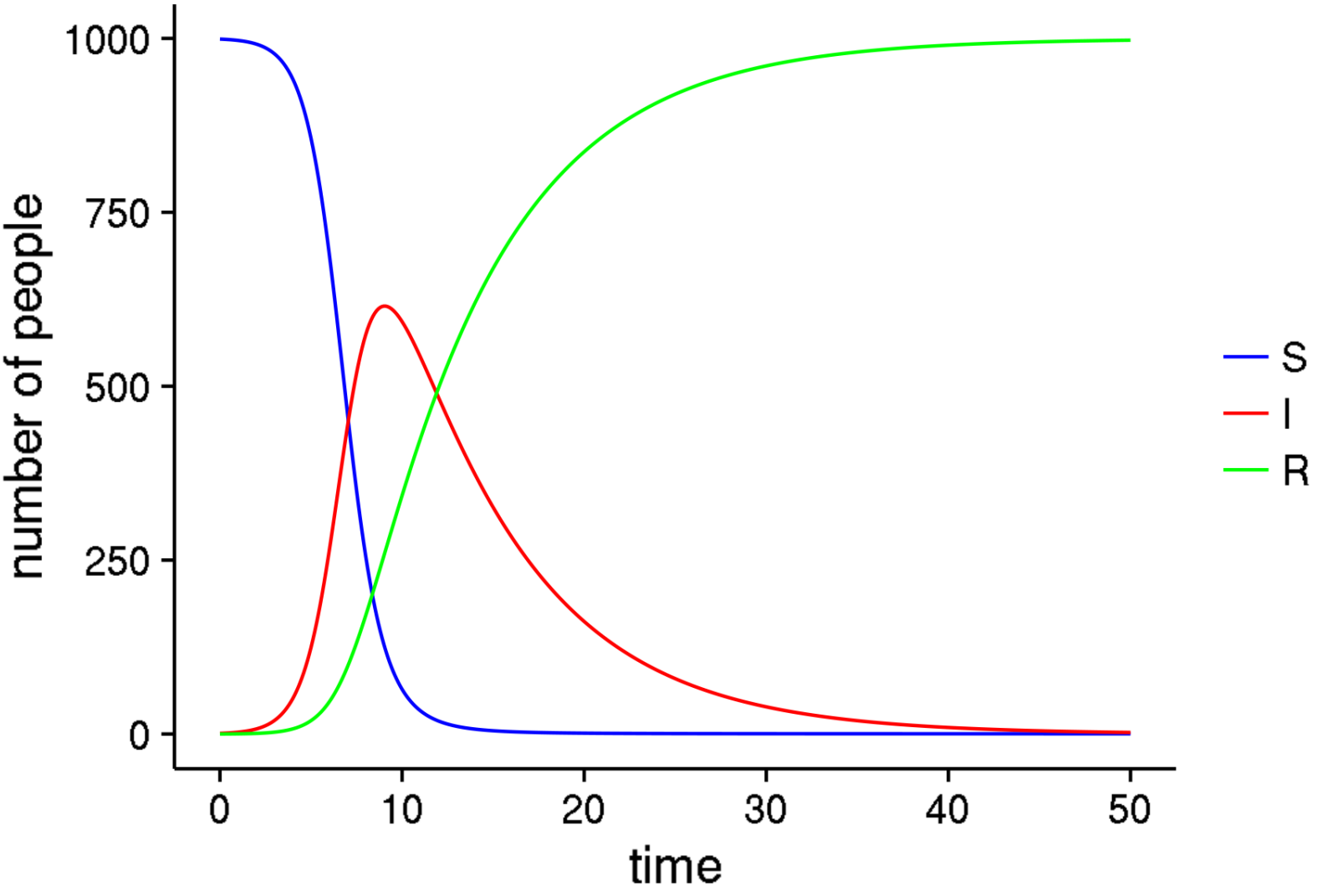
Examples: a measles-like illness

$R_0 = 16; \gamma = 0.14$ ($1/\gamma = 7$ days)



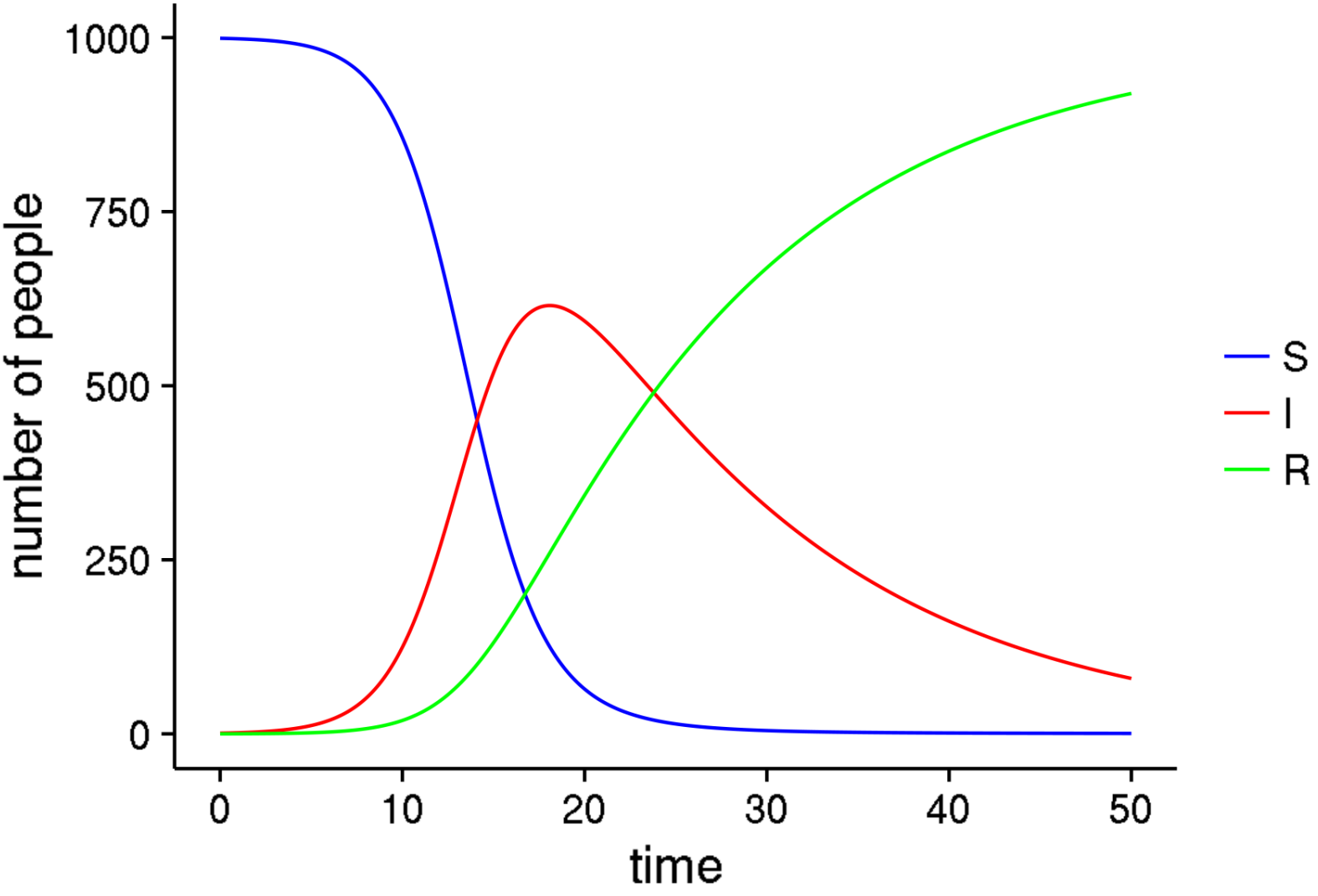
Examples: a chicken pox-like illness

$R_0 = 8; \gamma = 0.14$ ($1/\gamma = 7$ days);



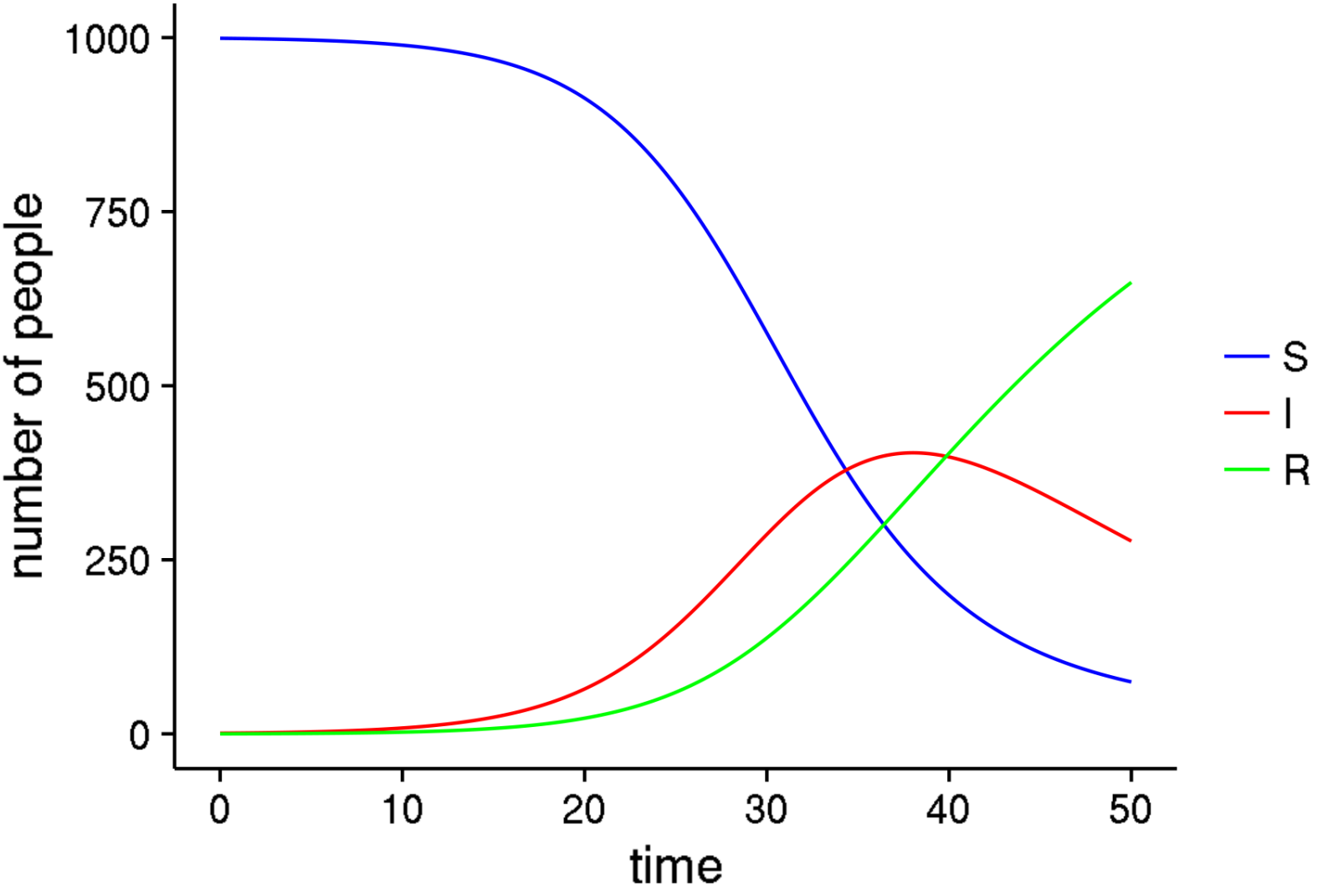
Examples: a mumps-like illness

$R_0 = 8; \gamma = 0.07$ ($1/\gamma = 14$ days);

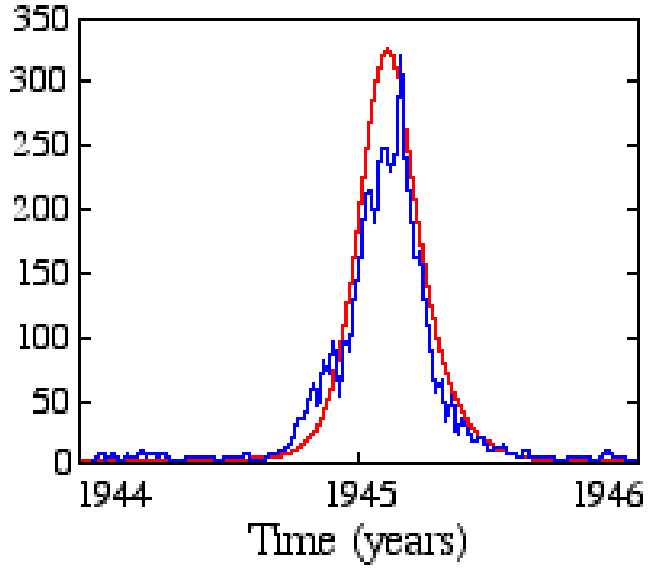


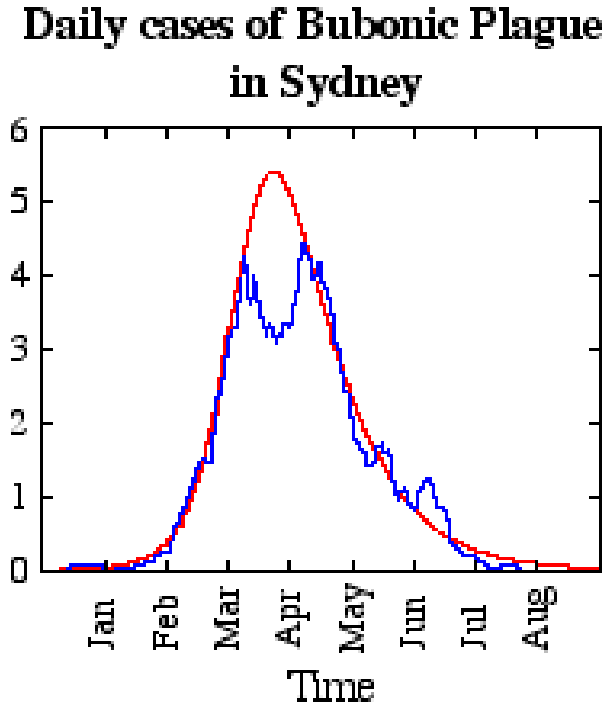
Examples: a smallpox-like illness

$R_0 = 4; \gamma = 0.07$ $(1/\gamma = 14$ days);



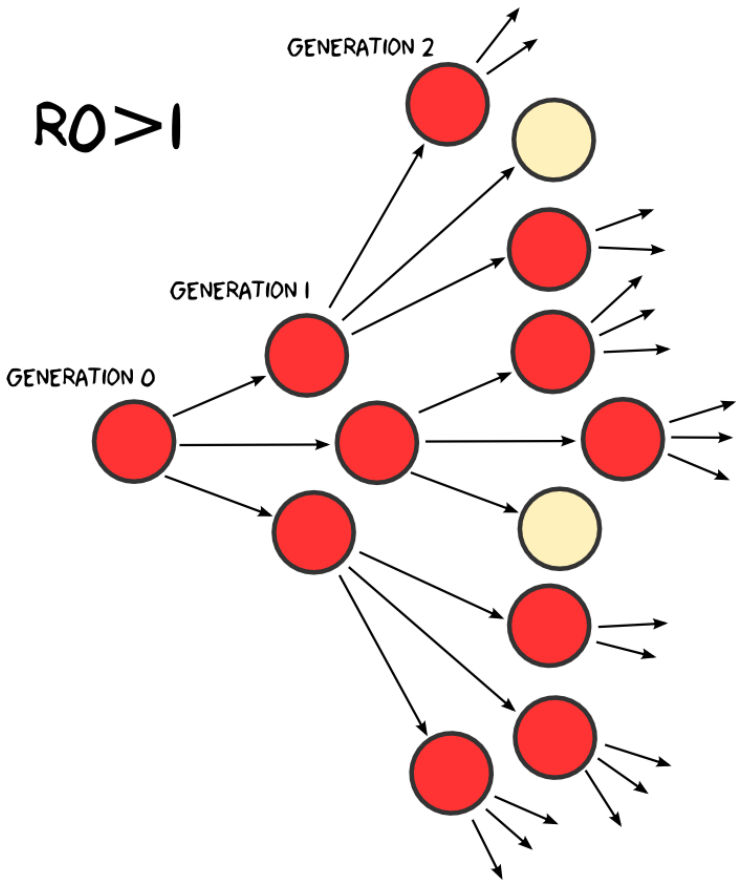
Fitting the SIR model to data

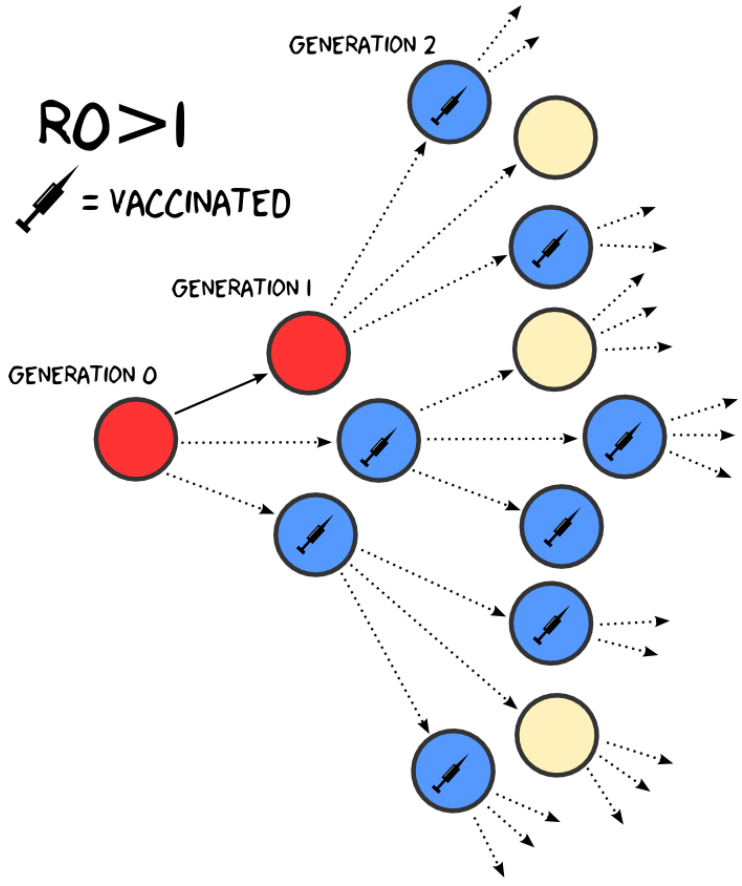




Preventing outbreaks with vaccination

One way that vaccinations can protect people is by preventing them from becoming infected; this is equivalent to moving them from the S into the R compartment.





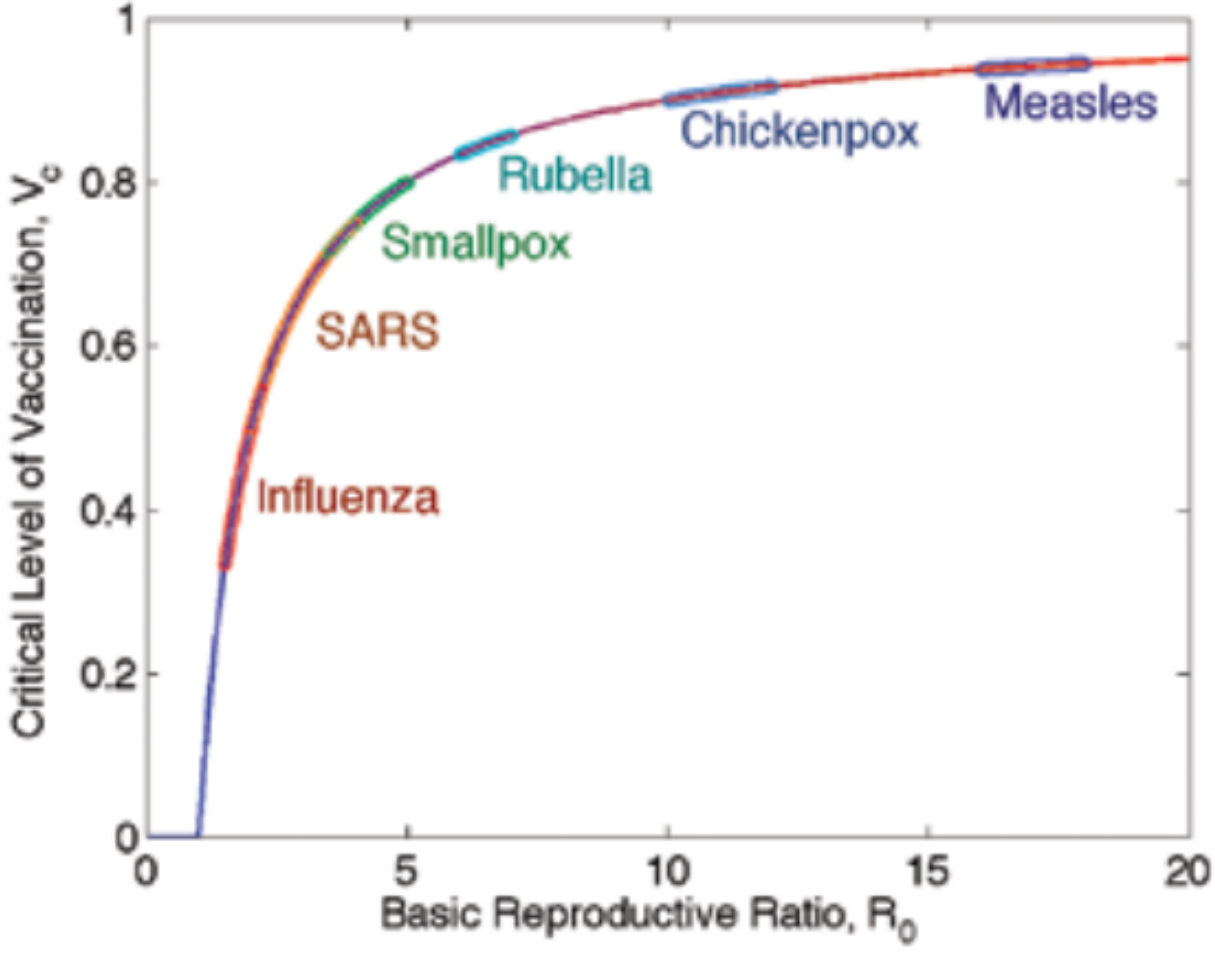
The basic reproduction number and vaccination

A further important property of the reproduction number is that it allows us to estimate the fraction v of the population that need to be vaccinated in order to prevent an outbreak from occurring:

$$v >= 1 - \frac{1}{R_0}$$

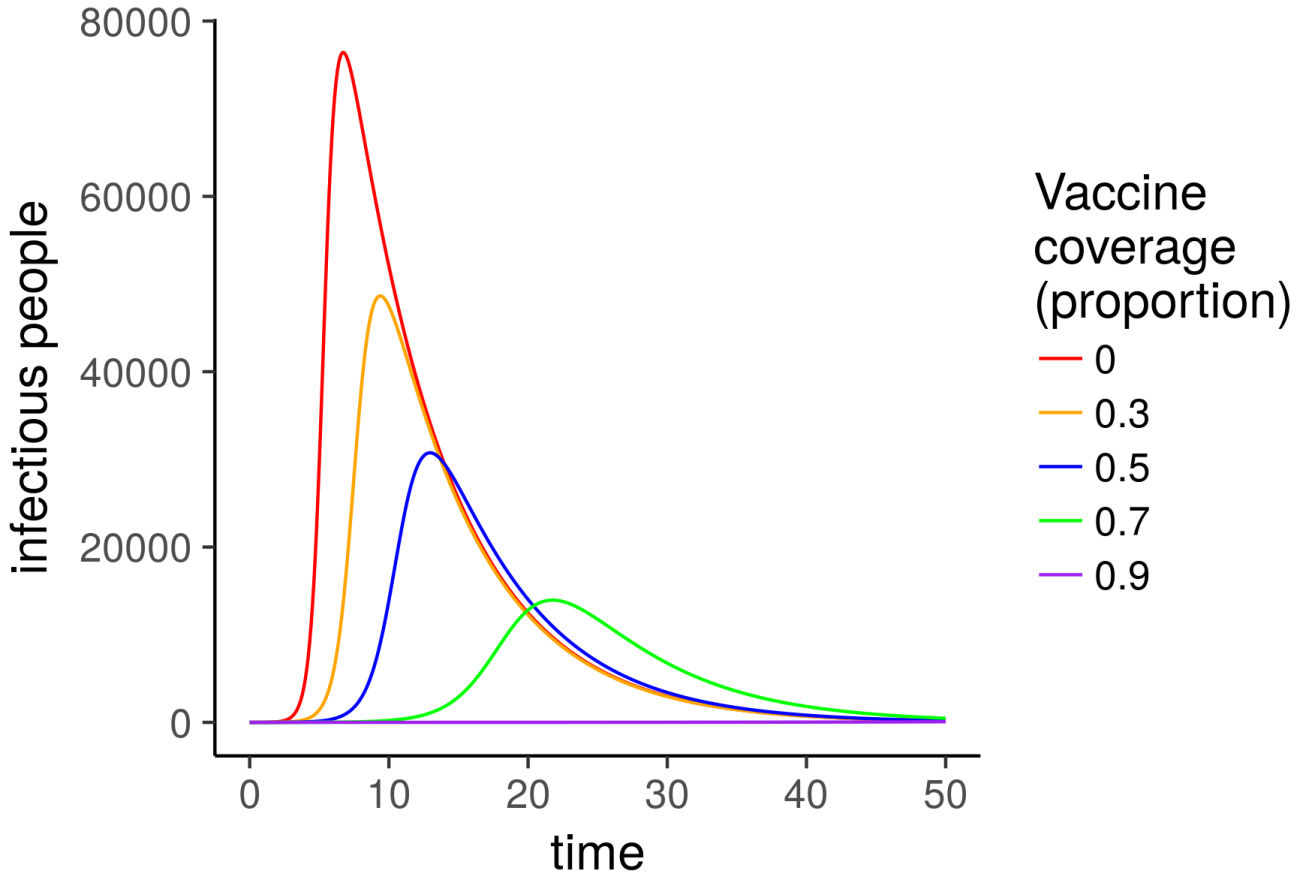
The basic reproduction number and vaccination

The coverage needed to prevent an outbreak increases with R_0.



vaccination

Parameters: $N = 100000; R0 = 16$; varying proportion of population vaccinated at t_0.

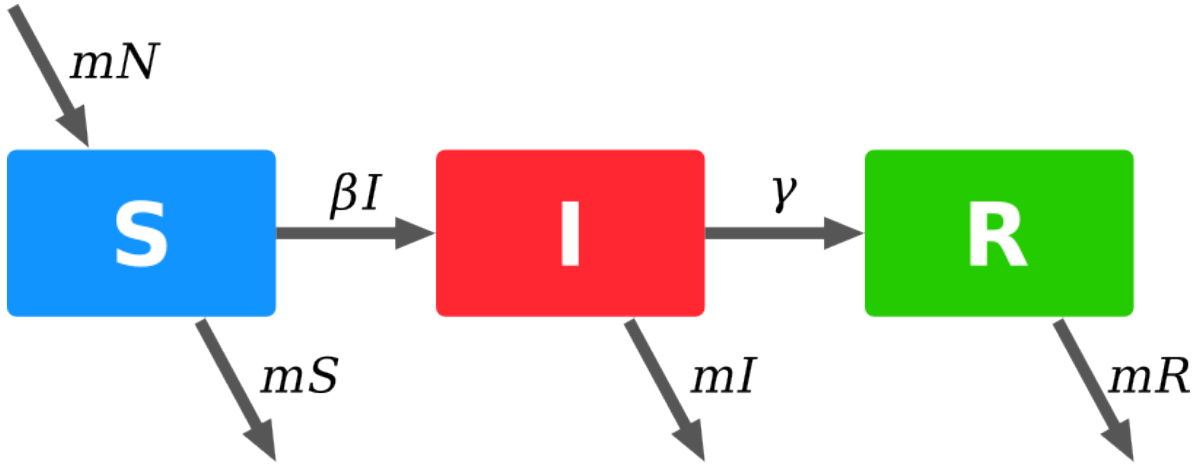


Extending the basic SIR model—adding demography

The SIR model makes the assumption that the size and composition of the population is fixed over time: no one enters or leaves.

This assumption is appropriate for a single outbreak (eg, of influenza). It is less appropriate for looking at long term behaviour of a disease over years or decades, when death and birth will lead to most or all of the population being replaced.

Extending the basic SIR model—adding demography

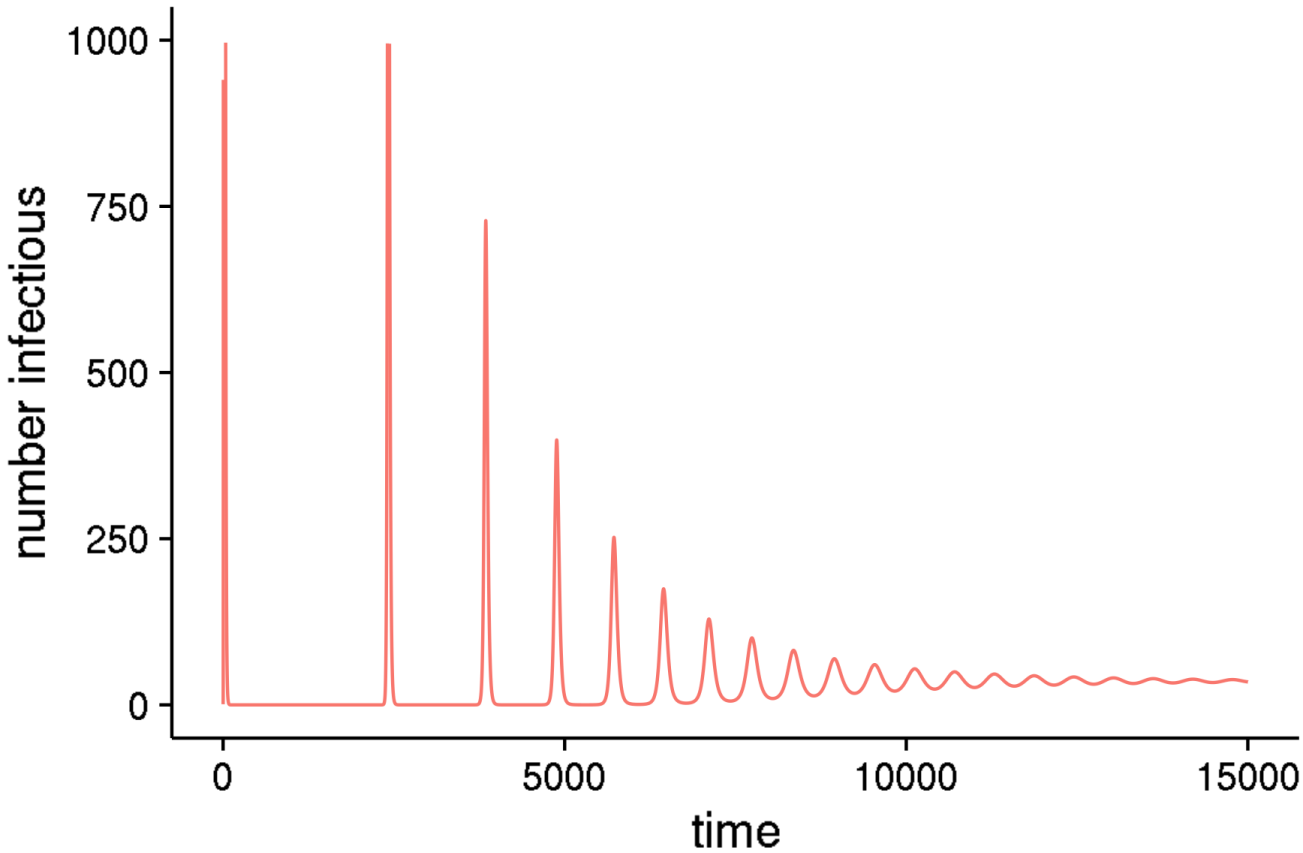


$$\frac{dS}{dt} = mN - \beta SI - mS$$
$$\frac{dI}{dt} = \beta SI - \gamma I - mI$$
$$\frac{dR}{dt} = \gamma I - mR$$

In this model, we assume that people are born susceptible at a rate m, and die at the same rate irrespective of their disease state, and that the size of the population will remain constant over time.

The SIR model with demography – output

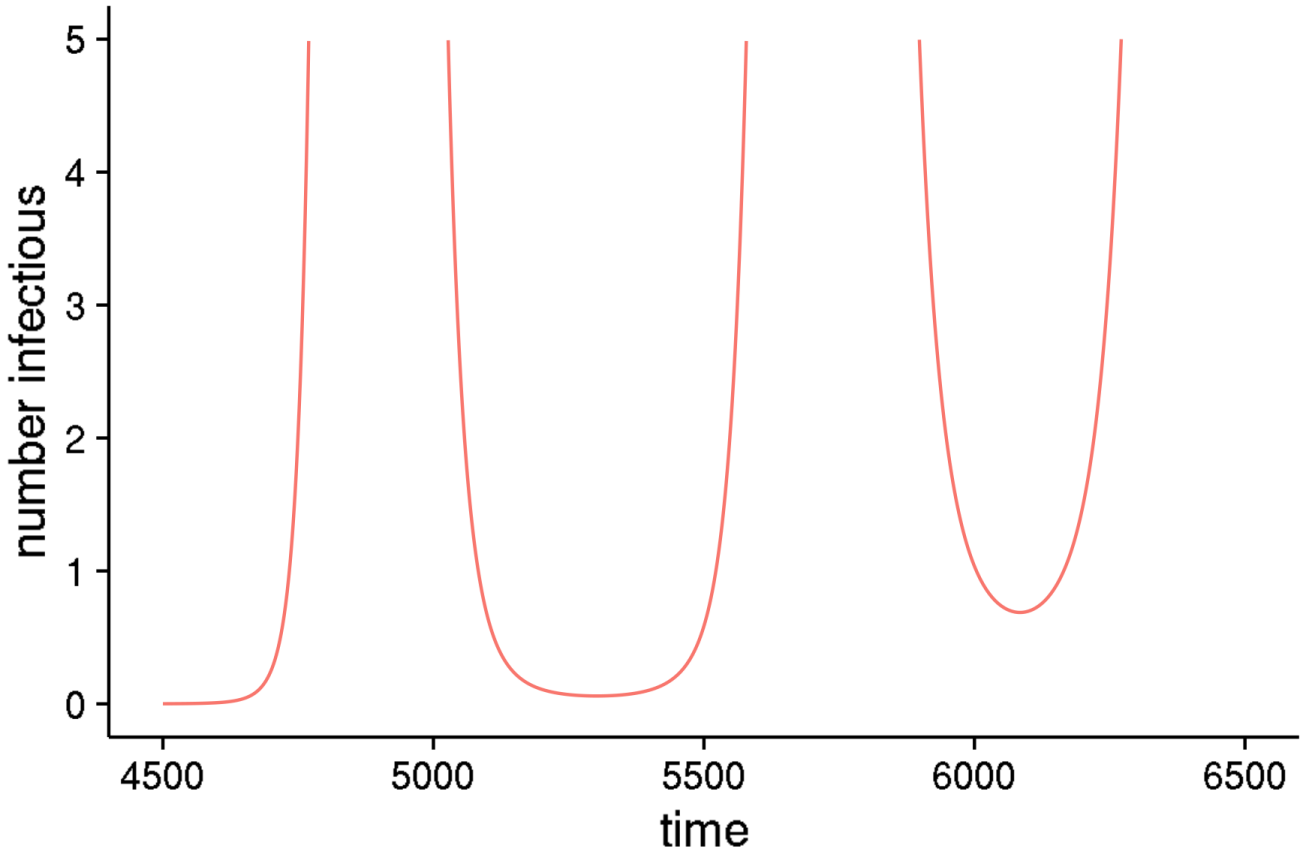
$N = 100,000; R_0 = 16; \gamma = 1/7; m = 5.5 \times 10^{-5}$ ($= 1/50$ years)



Note that the first y-axis has been truncated—the first outbreak peaks at ~76,000 infectious cases!

Caution!

Zooming in on the time period from day 4,500 to day 6,500:



Caution!

In this example, we saw that the number of infectious people dropped very low between each outbreak.

How big is our population?

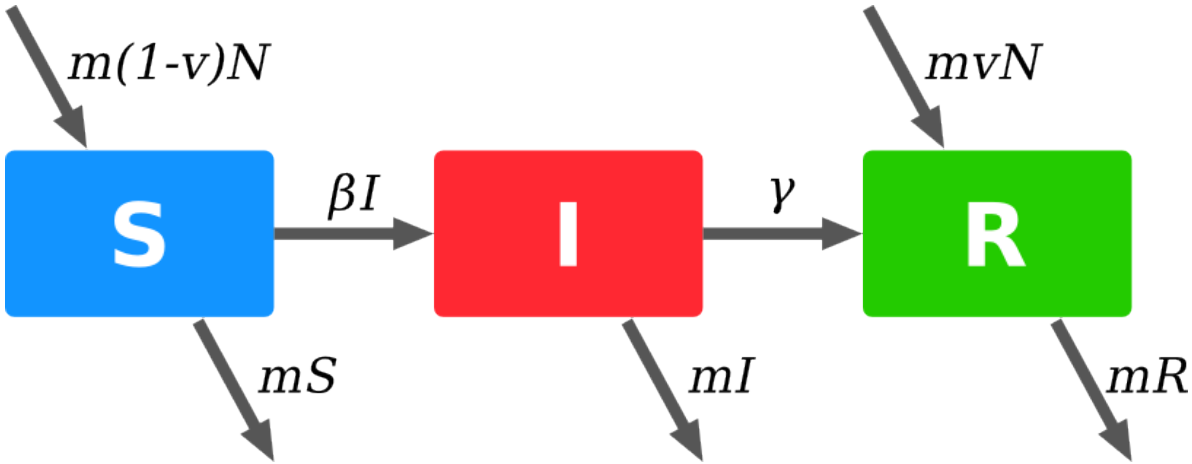
How many people were infectious in the trough between outbreaks?

If less than one person is infectious, the disease is eliminated.

But the model doesn't know this!

Demography and vaccination

A more elaborate model, in which a fraction v of newborns receive immunity from vaccination:



$$\frac{dS}{dt} = m(1-v)N - \beta SI - mS$$
$$\frac{dI}{dt} = \beta SI - \gamma I - mI$$
$$\frac{dR}{dt} = mvN + \gamma I - mR$$

Summary

The SIR model of infectious disease transmission

Assumptions of the SIR model:

- homogeneous population: everyone is the same
- homogeneous mixing: everyone has the same chance of contact

Stochastic models:

- more computation – more suited to small populations (or small number of infectious people)
- provides information on *distribution* of outcomes

Deterministic models:

- more efficient to run – can explore more parameters
- analysis can provide more general insights
- only applicable when certain conditions hold (larger population, larger number of infectious people)