# Modelling Epidemics

## Lecture 5: Deterministic compartmental epidemiological models in homogeneous populations

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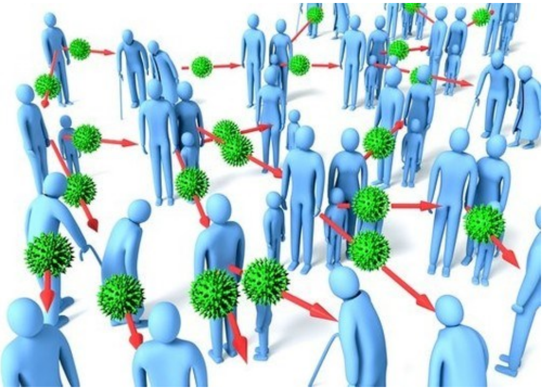
# Overview

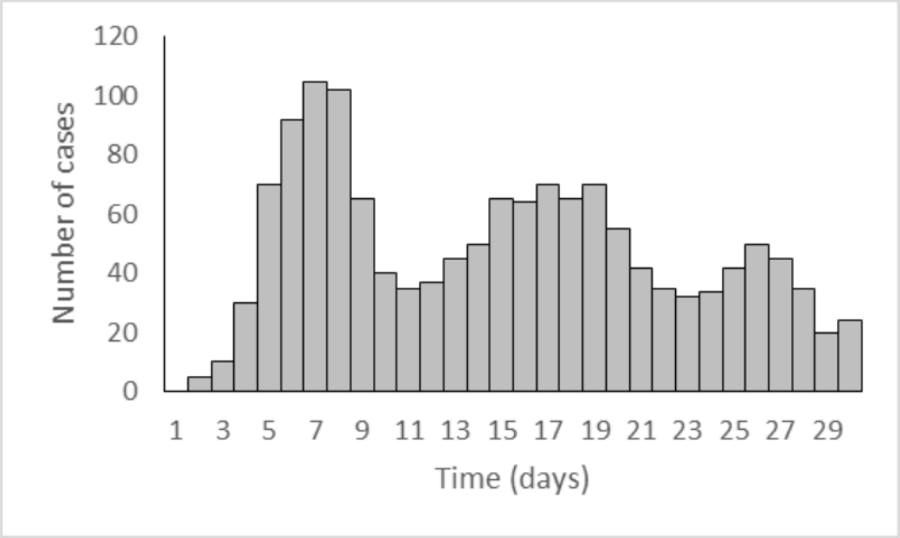
- Key characteristics of epidemics
  - What is an epidemic and what do we need to know about them?
  - The basic reproductive number $R_0$
- Modelling epidemics: basic compartmental models
  - Deterministic model formulation
  - SIR model without demography
  - SIR model with demography
- Adding complexity
  - Loss of immunity
  - Inclusion of chronic carriers

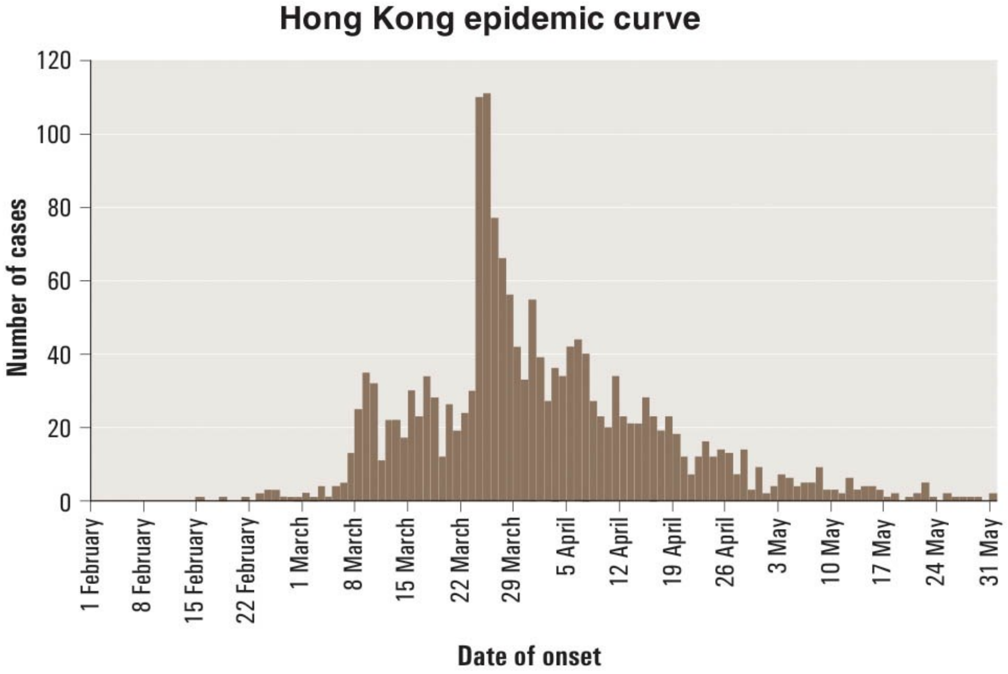
# What is an epidemic?

*Definition: <u>Epidemic</u>*

*A **widespread** occurrence of an **infectious disease in a community at a particular time***





# Questions for modelling epidemics

- **What is the risk** of an epidemic to occur?
- **How severe** is the epidemic?
  - What proportion of the population will become infected?
  - What proportion will die?
- **How long** will it last?
- Are **all individuals** at risk of becoming infected?
- How far will it spread?
- What **impact** does a particular **intervention** have on the risk, severity and duration of the epidemic?

# The basic reproductive ratio $R_0$

- $R_0$ is a key epidemiological measure for how "infectious" a disease is

***Definition: <u>Basic reproductive ratio $R_0$</u>***
***The average number of people an infectious person will infect, assuming that the rest of the population is susceptible***

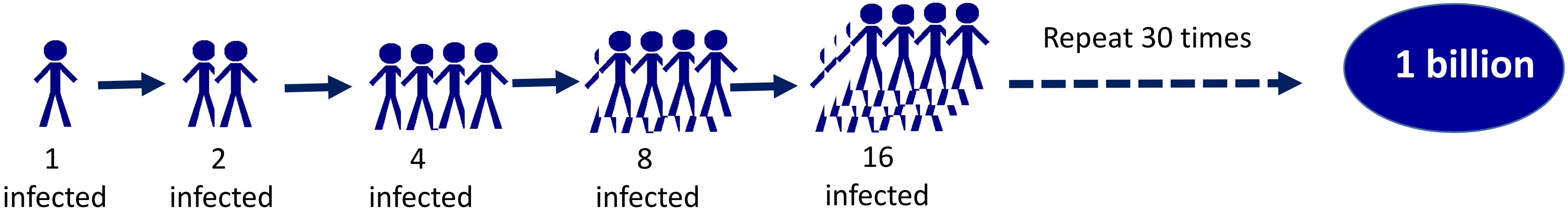
- $R_0 = 1$ is a threshold between epidemic / no epidemic
- $R_0 > 1$: Disease can invade
- $R_0 < 1$: Disease will die out

# The basic reproductive ratio $R_0$

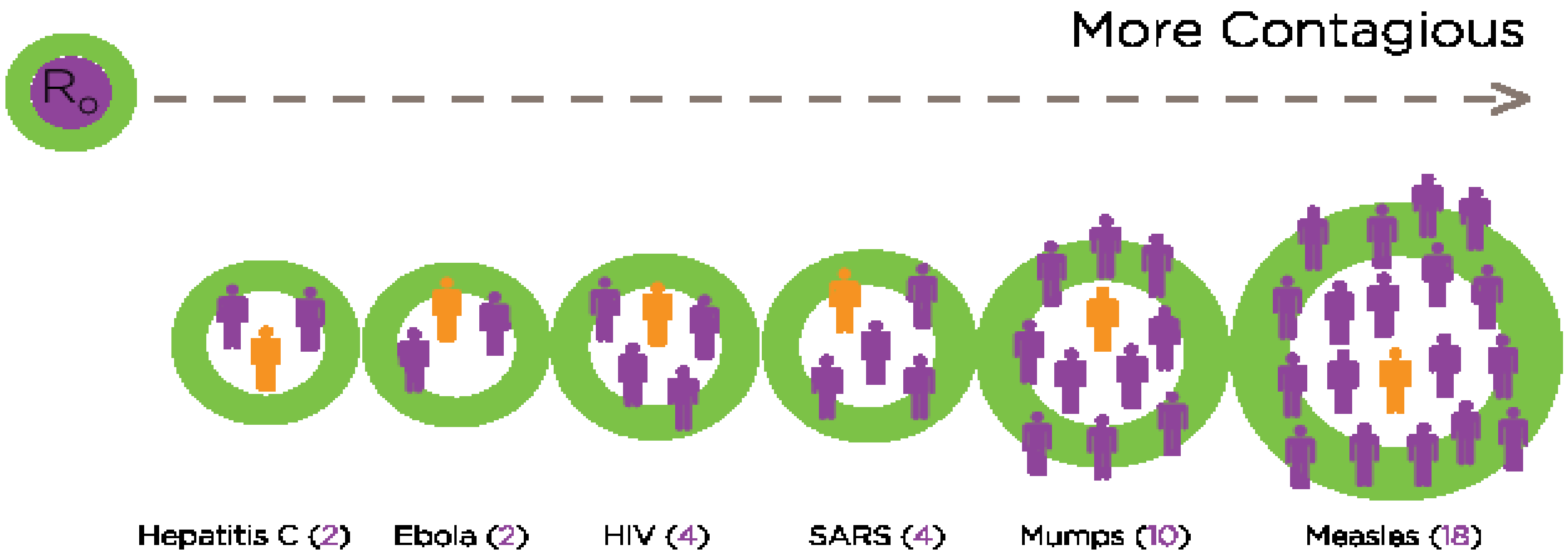
- $R_0$ is a key epidemiological measure for how "infectious" a disease is

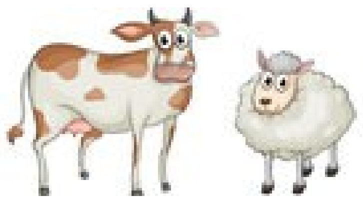

In Contagion, Dr. Erin Mears (Kate Winslet) explains R0

- E.g. $R_0$ = 2 (Contagion)



# Examples for $R_0$



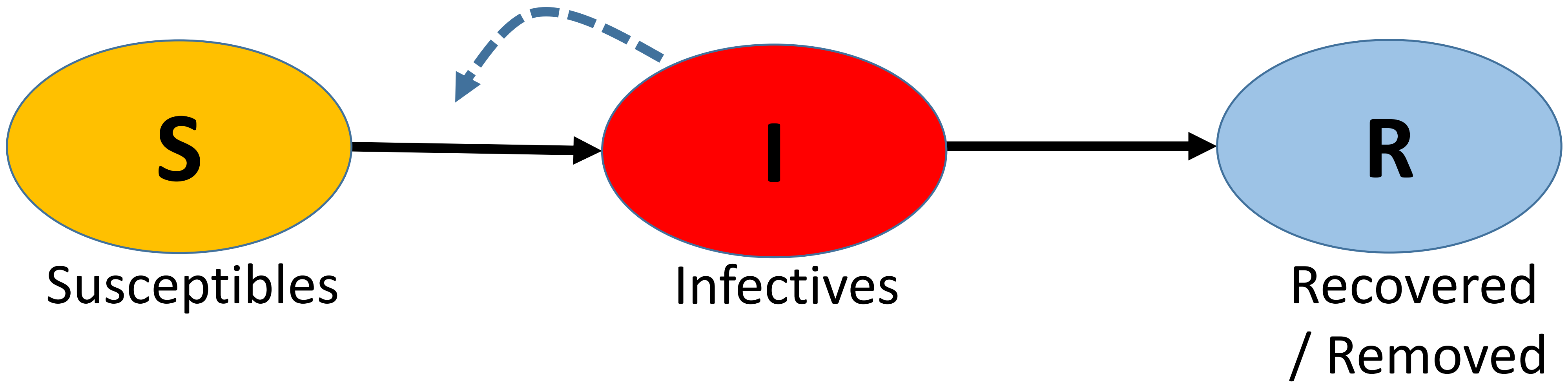



BSE $0 \leq R_0 \leq 14$

Scrapie $1.6 \leq R_0 \leq 3.9$

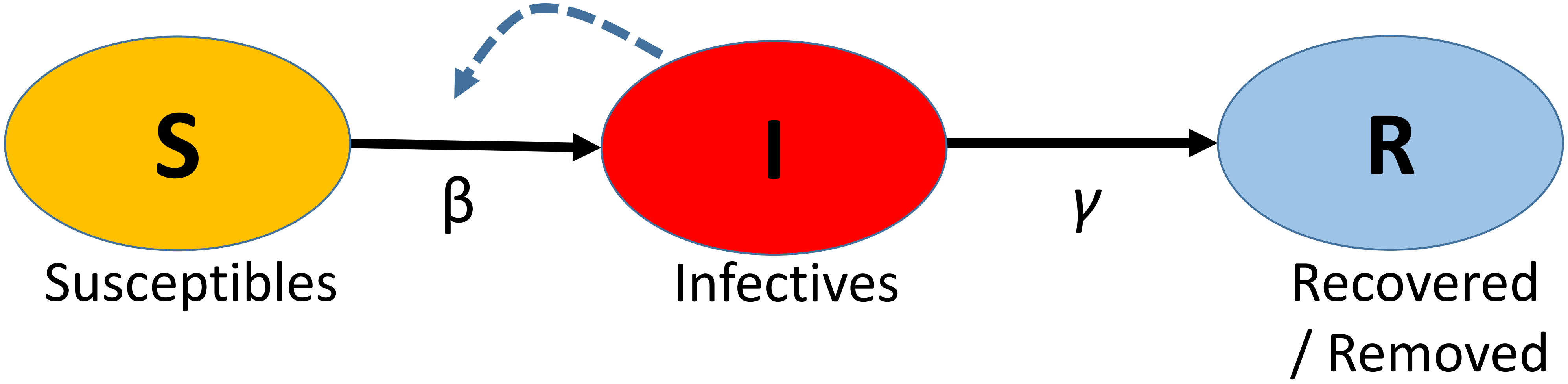
Foot & Mouth Disease $1.6 \leq R_0 \leq 4.6$

# Modelling Epidemics: The SIR model




- X = nr of susceptibles, Y = nr of infectives, Z = nr of recovered
- Describes acute infections transmitted by infected individuals;
- Pathogen causes illness for a period of time followed by death or life-long immunity

# Modelling Epidemics: The SIR model




We must determine:

- The rate at which susceptible individuals get infected (S→I)
- The rate at which infected individuals recover (or die) (I→R)

This gives rise to 2 model parameters:

- The transmission term β
- The recovery rate γ

# Transmission rate S→I

- Depends on the prevalence of infectives, the contact rate and the probability of transmission given contact

*Definition: Transmission coefficient β = contact rate x transmission probability*

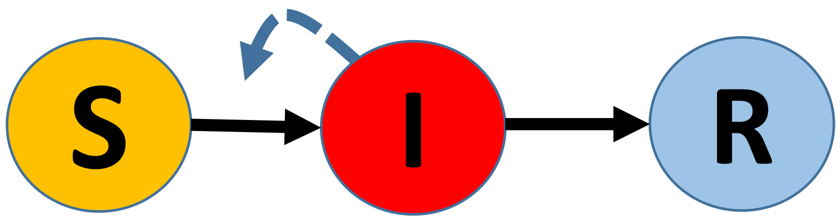
*Definition Force of infection λ:*
*Per capita rate at which susceptible individuals contract the infection*

- New infectives are produced at a rate λ x X, where X = nr of susceptibles

# Frequency versus density dependent transmission

- Force of infection λ depends on the number of infectious individuals (Y(t))
- Frequency dependent transmission: $\lambda(t) = \beta \times Y(t)/N(t)$
  - Force of infection depends on frequency of infectives
  - Assumption holds for most human diseases where contact is determined by social constraints rather than population size
- Density dependent transmission: $\lambda(t) = \beta \times Y(t)$
  - Force of infection increases with population size (e.g. individuals crowded in a small space)
  - Assumption appropriate for plant and animal diseases
- The distinction only matters if the population size varies.
  - Otherwise 1/N can be absorbed into the parameter β

# The SIR model without demography



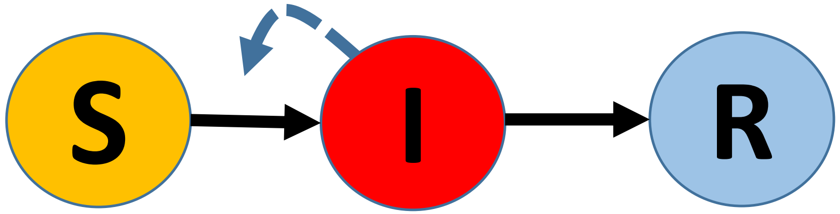

- Consider a closed population of constant size N
- Model Variables

  S(t) = proportion of susceptibles (X(t)/N)

  I(t) = proportion of infectives (Y(t)/N)

  R(t) = proportion of recovered (Z(t)/N)
- Model Parameters
  - β: transmission coefficient
  - γ: recovery rate ( the inverse of average infectious period)

# The SIR model without demography




- Model equations

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

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

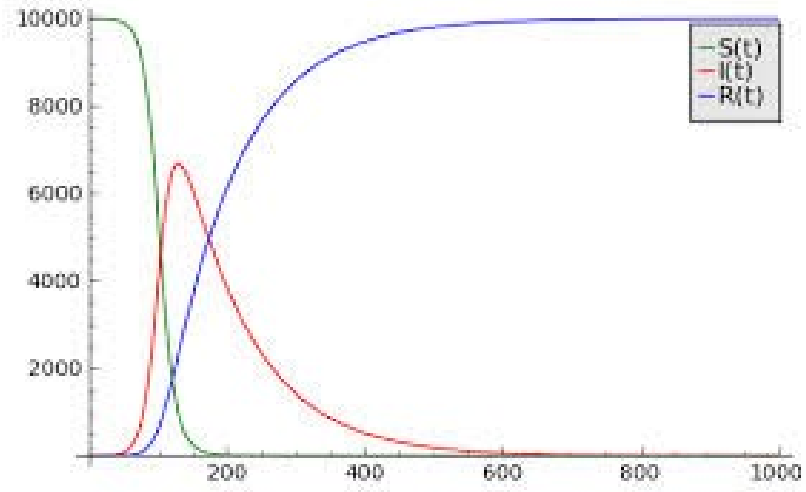
$$\frac{dR}{dt} = \gamma I$$

With initial conditions

*S(t=0) = S(0)*

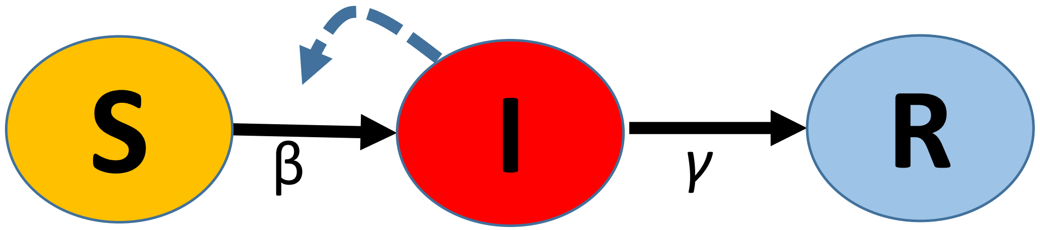
*I(t=0) = I(0)*

*R(t=0) = R(0)*




- Equations describe the rate at which the proportions of susceptible, infectious and recovered individuals change over time
- The model cannot be solved explicitly, i.e. no analytical expression for S(t), I(t), R(t)!
  - Need computer programme
- Constant population size implies S(t) + I(t) + R(t) = 1 for all times t

# The Threshold Phenomenon




Imagine a scenario where $I_0$ infectives are introduced into a susceptible population.

**Will there be an epidemic?**

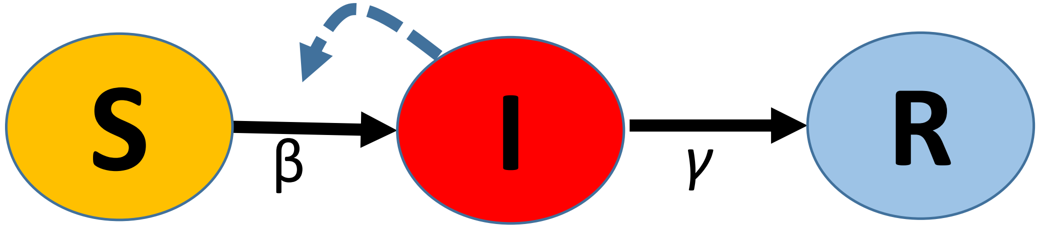
- Epidemic will occur if the proportion of infectives increases with time: $\frac{dI}{dt} > 0$
- From the 2nd equation of the SIR model:

$$\frac{dI}{dt} = \beta SI - \gamma I = I\,(\beta S - \gamma) > 0 \quad \text{only if } S > \gamma/\beta$$

- Thus, the infection will only invade if the initial proportion of susceptibles $S_0 > \gamma/\beta$

*What does this result imply for vaccination or other prevention strategies?*

# The Threshold Phenomenon & $R_0$




Imagine a scenario where $I_0$ infectives are introduced into a susceptible population.

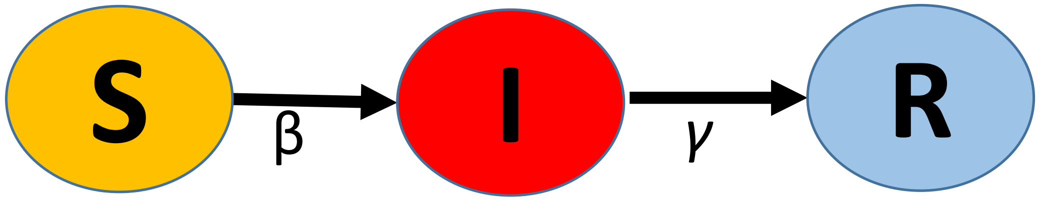
*Will there be an epidemic?*

- The infection will only invade if the initial proportion of susceptibles $S_0 > {}^{\gamma}/_{\beta}$
- An average infected individual
  - is infectious for a period of 1/γ days
  - infects β susceptible individuals per day
  - will thus generate β x 1/γ new infections over its lifetime

➢ $R_0 = \frac{\beta}{\gamma}$

- Infection can only invade if $S_0 > {}^{1}/_{R_0}$

# Epidemic burnout




Imagine a scenario where $I_0$ infectives are introduced into a susceptible population with $S_0 > {}^{\gamma}/_{\beta}$

***What happens in the long-term?***

***What proportion of the population will contract the infection?***

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

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

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

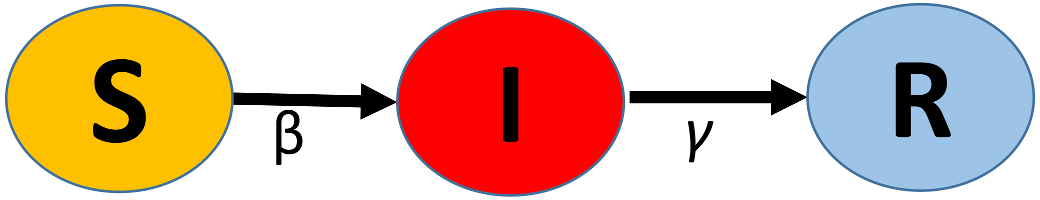
$$\frac{dS}{dR} = -\frac{\beta S}{\gamma} = -\, R_0 S$$

Solve: $$S(t) = S(0)e^{-R(t)R_0}$$

Given R(t) ≤1, this implies that the proportion of susceptibles remains always positive with $S(t) > e^{-R_0}$ for any time t

- ➢ *What will stop the epidemic?*

# Epidemic burnout




***What happens in the long-term?***

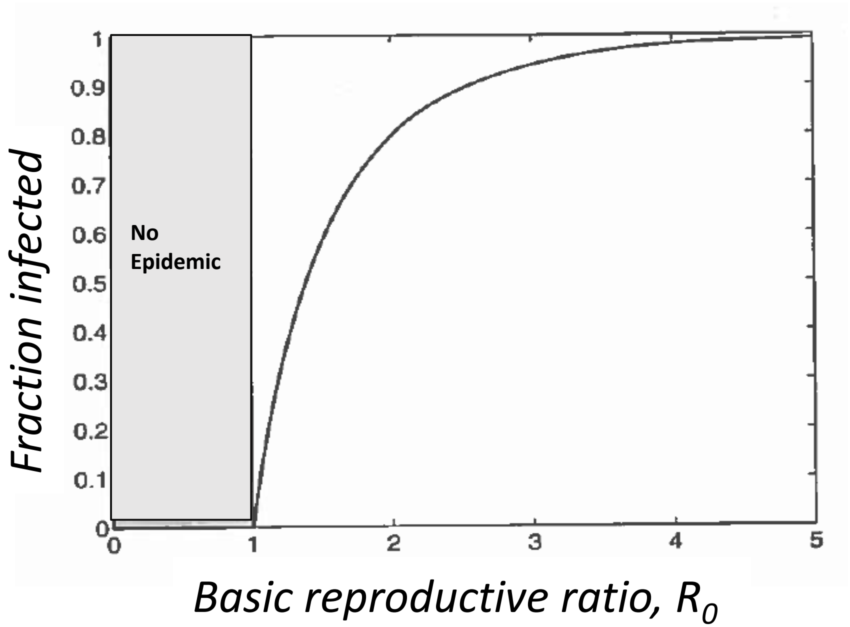
***What proportion of the population will contract the infection?***

From above: $$S(t) = S(0)e^{-R(t)R_0}$$

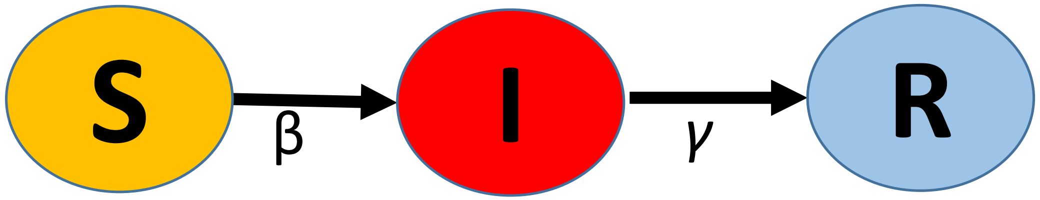
At end of epidemic: I = 0.
Given S+I+R=1, we can use this equation to calculate the **final size** $\boldsymbol{S(\infty)}$ of the epidemic ($R(\infty) = 1 - S(\infty)$):

$$S(\infty) = S(0)e^{(S(\infty)-1)R_0}$$

- The above equation can only be solved numerically for $S(\infty)$. It produces the graph on the right.
- This equation if often used to estimate $R_0$.




*For $R_0$=2, what proportion of the population will eventually get infected if everybody is initially susceptible?*




# Dynamic behaviour

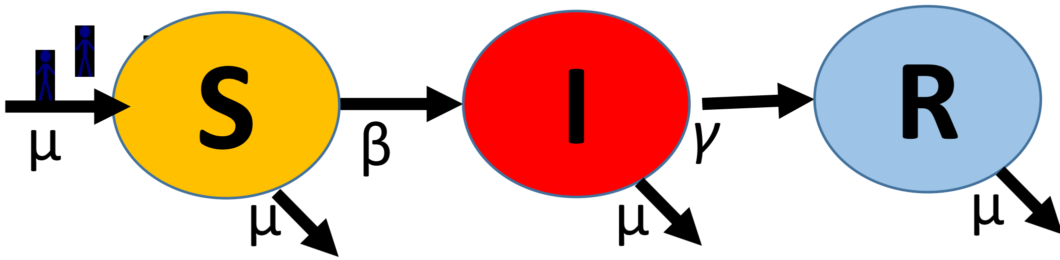
$$\frac{dS}{dt} = -\beta\, S\, I$$

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

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

- The exact time profiles depend on the model parameters and on the initial conditions S(0), I(0), R(0)
- See Tutorial 1 for investigating the impact of these on prevalence profiles

# The SIR model with demography




- Assume the epidemic progresses at a slower time scale so that the assumption of a closed population is no longer valid
- Assume a natural host lifespan of 1/μ years and that the birth rate is similar to the mortality rate μ (i.e. population size is constant)

Generalized SIR model equations:

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

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

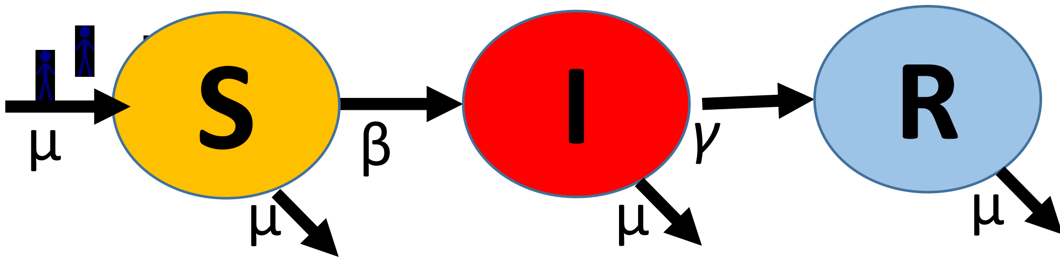
$$\frac{dR}{dt} = \gamma I - \mu R$$

With initial conditions:

*S(t=0) = S(0)*
*I(t=0) = I(0)*
*R(t=0) = R(0)*

$$\frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0$$

# The SIR model with demography




- Transmission rate per infective is β
- Each infective individual spends on average $\frac{1}{\gamma+\mu}$ time units in class I

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

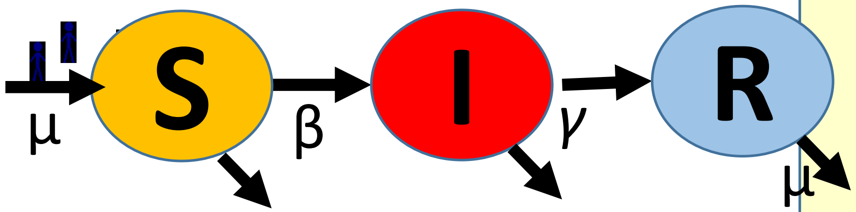
- $R_0$ is always smaller than for a closed population

$$\frac{dS}{dt} = \mu - \beta\, S\, I \; - \; \mu S$$

$$\frac{dI}{dt} = \beta\, S\, I - \; \gamma I \; - \; \mu I$$

$$\frac{dR}{dt} = \gamma I - \mu R$$

# Equilibrium state




$$\frac{dS}{dt} = \mu - \beta\, S\, I \; - \; \mu S$$

$$\frac{dI}{dt} = \beta\, S\, I - \; \gamma I \; - \; \mu I$$

$$\frac{dR}{dt} = \gamma I - \mu R$$

***What is the final outcome of the infection?***

- The disease will eventually settle into an equilibrium state ( S*, I*, R*) where

$$\frac{dS}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0$$

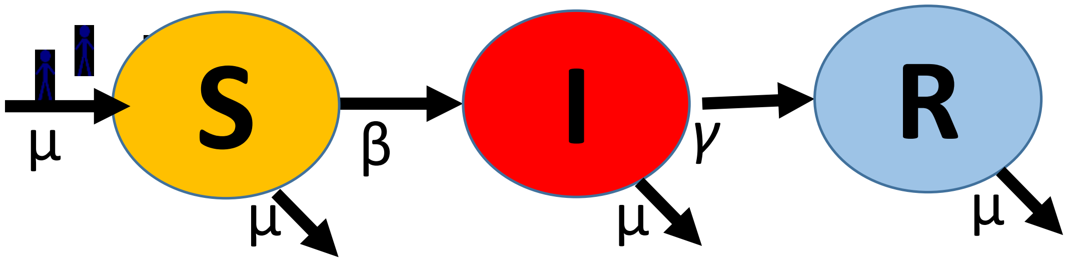
- Setting the SIR model equations to zero leads to 2 equilibria (outcomes):

( S*, I*, R*) = (1, 0, 0) *Disease free equilibirum*

( S*, I*, R*) = $\left( \frac{1}{R_0}, \frac{\mu}{\beta}(R_0 - 1), 1 \; - \frac{1}{R_0} - \; \frac{\mu}{\beta}(R_0 - 1) \right)$ *Endemic equilibrium*

***Which outcome will be achieved?***

# Equilibrium state

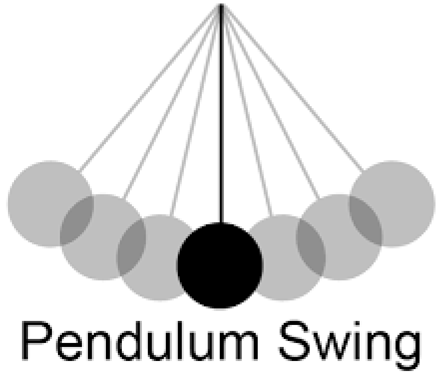



***Which outcome will be achieved?***

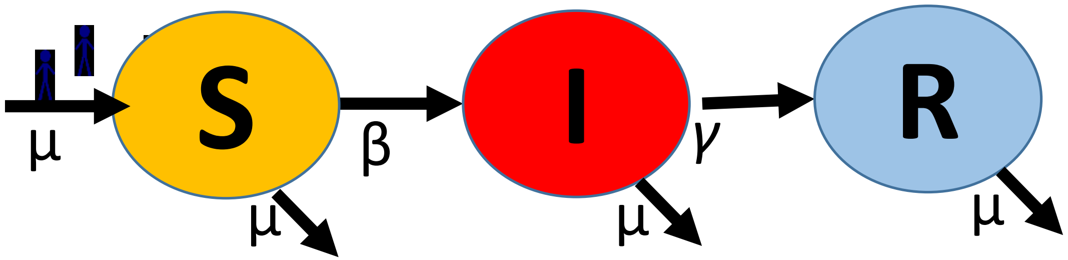
Disease free or endemic equilibrium?

This can be answered with *mathematical stability analysis:*

- Determines for which parameter values a specific equilibrium is stable to small perturbations
- It can be shown that
  - The disease free equilibrium is stable if $R_0 < 1$
  - The endemic equilibrium is stable if $R_0 > 1$

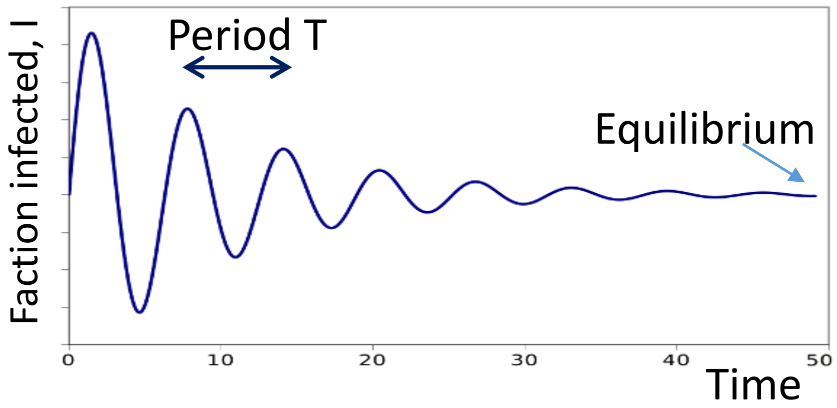



***If an infection can invade (i.e. if $R_0 > 1$) , then the topping up of the susceptible pool causes the disease to persist***




# Dynamic behaviour

- The SIR model with demography generates *damped oscillations:*

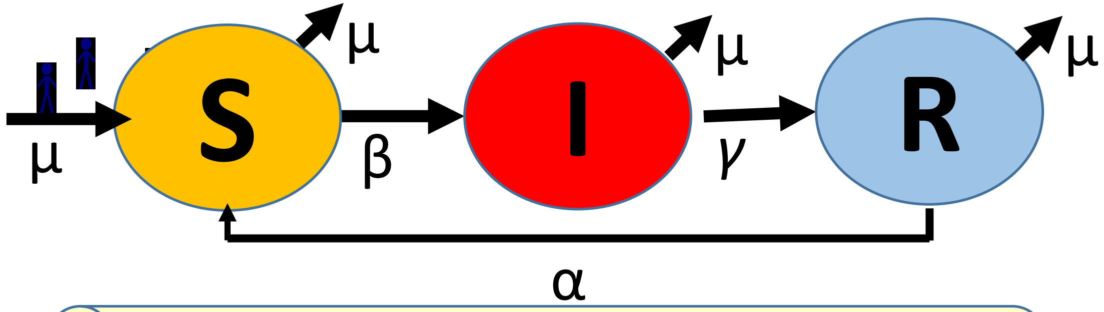



- With some algebra* it can be shown that:
  - The period T $\sim\sqrt{mean\ age\ of\ infection\ * mean\ duration\ of\ infectious\ period}$
  - Mean age of infection $A \approx \frac{L}{R_0 - 1}$ where *L = 1/μ* is the average life expectancy
- Measures of *A* and *L* lead to estimates for $R_0$

*See e.g. Keeling & Rohani 2008

# Adding complexity: The SIRS model

- The SIR model assumes lifelong immunity
- What if this is not the case, i.e. assume immunity is lost at a rate α




$$\frac{dS}{dt} = \mu + \alpha R - \beta S I - \mu S$$

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

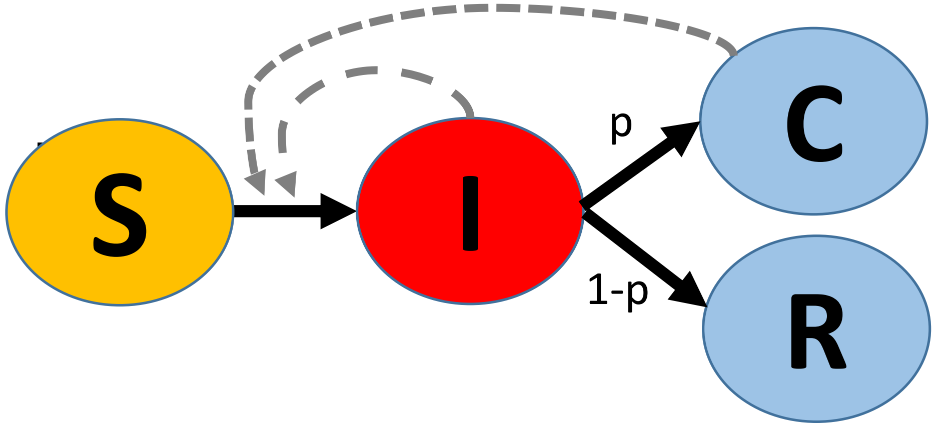
$$\frac{dR}{dt} = \gamma I - \alpha R - \mu R$$

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

- Loss of immunity does not affect the onset of the disease (same $R_0$!)
- What effect does loss of immunity have on the disease dynamics & equilibrium?
  - ➢ See tutorial

# Adding complexity: Infections with a carrier state

- Assume a proportion *p* of infected individuals become chronic carriers
- These carriers transmit the infection at a reduced rate $\varepsilon\beta$, with ε<1




$$R_0 = \frac{\beta}{\gamma + \mu} + \frac{p\gamma}{\mu}\frac{\varepsilon\beta}{(\gamma + \mu)}$$

Acutely infecteds

Chronic Carriers

$$\frac{dS}{dt} = \mu - (\beta I + \varepsilon\beta C)S - \mu S$$

$$\frac{dI}{dt} = (\beta I + \varepsilon\beta C)S - \gamma I - \mu I$$

$$\frac{dC}{dt} = \gamma q I - \mu C$$

$$\frac{dR}{dt} = \gamma(1 - q)I - \mu R$$

# Adding complexity: Infections with a carrier state

- Assume a proportion *p* of infected individuals become chronic carriers
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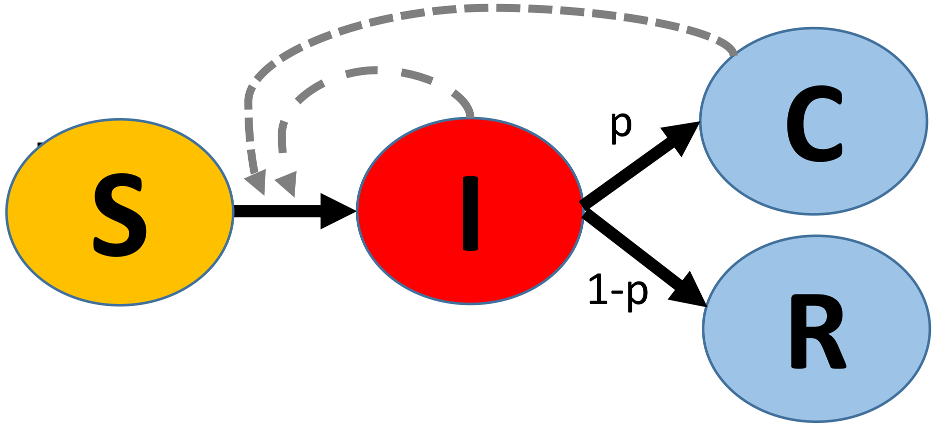


$$R_0 = \frac{\beta}{\gamma + \mu} + \frac{p\gamma}{\mu}\frac{\varepsilon\beta}{(\gamma + \mu)}$$

Acutely infecteds

Chronic Carriers

- Asymptomatic chronic carriers can cause underestimation of $R_0$
- What effect does the presence of chronic carriers have on the disease dynamics & equilibrium?
  - ➢ See tutorial

# Summary

- Epidemics can be represented by compartmental ODE models
- Even the simplest epidemiological models require computer algorithms to estimate prevalence profiles
  - But criteria for invasion and for equilibrium conditions can be derived analytically
- The basic reproductive ratio $R_0$ is a key epidemiological measure affecting criteria for invasion extinction and size of the epidemic
- An infection experiences deterministic extinction if $R_0<1$
- In the absence of demography, strongly immunizing infections will always go extinct eventually and not all individuals will have become infected
- In the SIR model with demography, the endemic equilibrium is feasible if R0>1. Prevalence curves approach this equilibrium through damped oscillations.

# References


- Keeling, Matt J., and Pejman Rohani. Modeling infectious diseases in humans and animals. Princeton University Press, 2008.
- Anderson, Roy M., Robert M. May, and B. Anderson. Infectious diseases of humans: dynamics and control. Vol. 28. Oxford: Oxford university press, 1992.
- Heesterbeek, J. A.  Mathematical epidemiology of infectious diseases: model building, analysis and interpretation. Vol. 5. John Wiley & Sons, 2000.
- Roberts, M., & Heesterbeek, H. (1993). Bluff your way in epidemic models.*Trends in microbiology*, *1*(9), 343-348.
- Hesterbeek J.A., A brief history of R0 and a recipe for its calculation. Acta Biotheor. 2002, 50(4):375-6.
- Heffernan, J. M., R. J. Smith, and L. M. Wahl. Perspectives on the basic reproductive ratio. Journal of the Royal Society Interface 2.4 (2005): 281-293.