# SIR Models

# Disease Modeling

- Creating **models** for **disease dynamics**
- Why?

# Lecture Outline

- Consider models for directly transmitted, micro parasitic infectious diseases:
  - Simple deterministic models
  - Focus is on providing a feel for relevant models, terminology and methodology

# Learning Outcome

- Increase understanding of disease modelling
- Build your own disease models
- Formulate questions in your work that can be answered through modelling

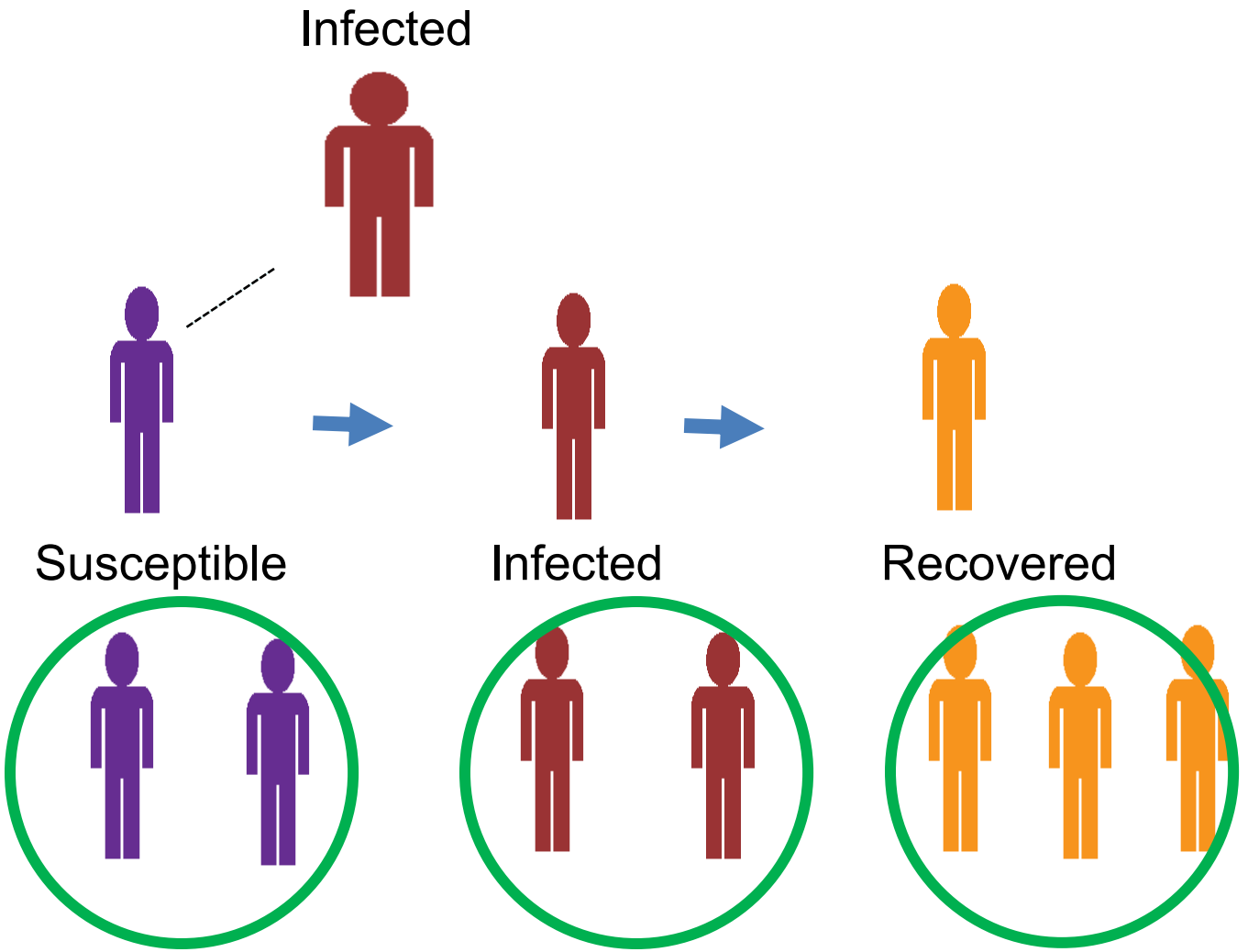
# Natural Definitions

- Incubation period ($t_{inc}$) = time between infection and the appearance of visible symptoms
- Latent period ($t_{lat}$) = time between infection and the ability to infect someone else
- $t_{inc} > t_{lat}$

# Infection Mechanism

- What are the ways different infections get transmitted?

- What drives how many people get infected with:
  - Influenza?
  - HIV?
  - Dengue?
  - Measles?


Infected
Susceptible
Infected
Recovered

# Basics: Classifying Individuals

- **Susceptible:** individual/host is susceptible to infection: no pathogen is present; just a low-level nonspecific immunity within the host.
- **Exposed:** individual/host may or may not exhibit obvious signs of infection and abundance of pathogen may be too low to allow further transmission.
- **Infectious:** Individual/host becomes infected with a microparasite; abundance of the parasite grows with time.
- **Recovered** individual/host is either no longer infectious or ‘removed’ (dead).

# Compartmental Modeling

- The technique is an extremely natural and valuable means with which to formulate processes.
- Many processes may be considered as compartmental models:
  - The process has inputs to and outputs from a "compartment" over time
- Based on the **balance law**

# SIR compartmental diagram


Depicting:

- The number of people in each group/compartment
- And then how they change
  - People becoming infected
  - People recovering

# Model Assumptions

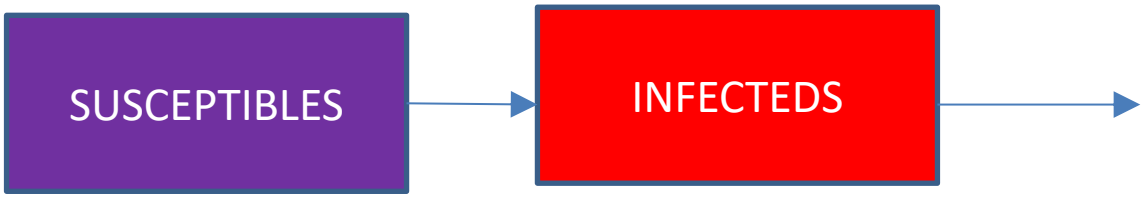
- Large populations – ignore random differences
  - Homogeneous population (well-mixed)

Scenario: flu epidemic at a boarding school over 30 days

- Ignore birth and death
- Disease spread by contact
- Neglect latent period
- Within time period = those recovered are immune

# Compartmental diagram

Scenario: flu epidemic at a boarding school over 30 days



# From diagram to word equations

- {Rate of change in susceptibles} = 0 – {rate of susceptibles become infected}

- {rate of change in infected} = {rate susceptibles become infected} – {rate infected become recovered}

# From word to mathematics

- {rate susceptible become infected}
- Consider susceptibles, *S*, infected by a single infected: more *S* then *I* increase
- Rate of susceptible become infected by one infected is directly proportional to number of susceptibles

{rate susceptible become infected} = $bSI$

- *b* = constant of proportionality = transmission rate = infection rate

# From word to mathematics

- {rate infected become recovered}
- Should not depend on susceptibles

- Assume infected recovered is directly proportional to number of infected

{rate infected become recovered} = $rI$

# Transform word to mathematics

- {Rate of change in susceptibles} = 0 – {rate of susceptibles become infected}

$$\frac{dS}{dt} = -bSI$$

- {rate of change in infected} = {rate susceptibles become infected} – {rate infected become recovered}

$$\frac{dI}{dt} = bSI - rI$$

# Interpretation of Parameters

- Large $b$ = disease easily spread
- => degree of population interact
- Estimating $b$
- $b = \frac{\lambda}{N}$
- $\lambda$ = per capita contact rate = force of infection
- $N$ = constant total population

# Force of infection (FOI)

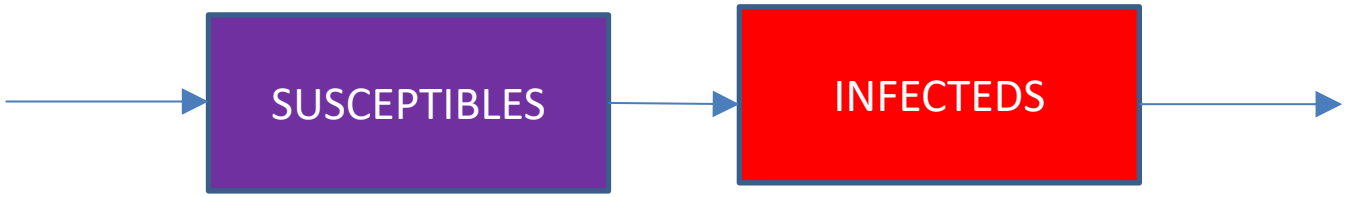
- FOI quantifies how much transmission there is.
- FOI tells us about the rate at which individuals get infected in the population
- The higher the FOI the earlier an individual is likely to get infected.
- Dirty hands…

# Interpretation of Parameters

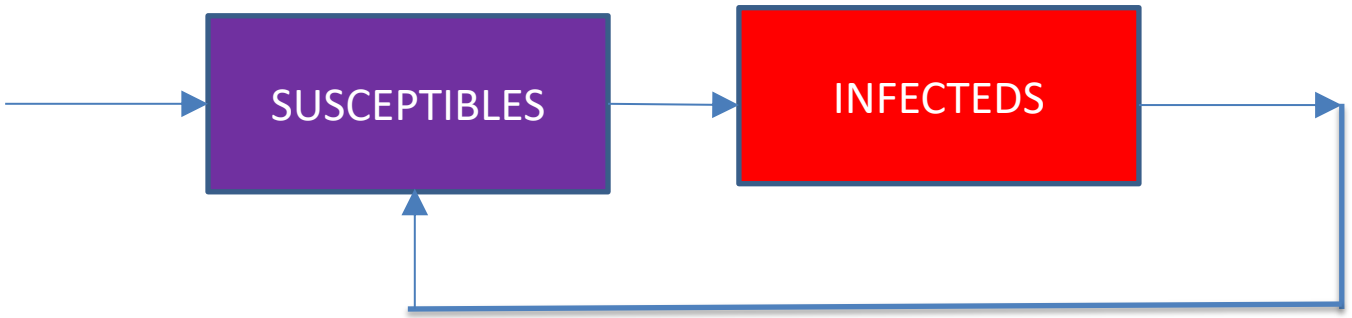
- Estimating $r$
- 1/{average period of being infectious}
- $r = \frac{1}{t_{inc}}$
- If $t_{lat}$ is considered then
- $r = \frac{1}{t_{inc} - t_{lat}}$

# Model Variants

- Effect of births




- Disease without immunity



# Questions to ask

- When a rapid increase in *I* is always followed by a decrease?
- If parameters are adjusted, can we limit the increase? Or prevent it?
- Must the transmission coefficient be constant? Or can it vary? – vary with population size?

# Questions to ask

- Consider at initial stage, $I_0$ introduced into a population of $S_0$
  - Will an epidemic occur? Or will it die out?

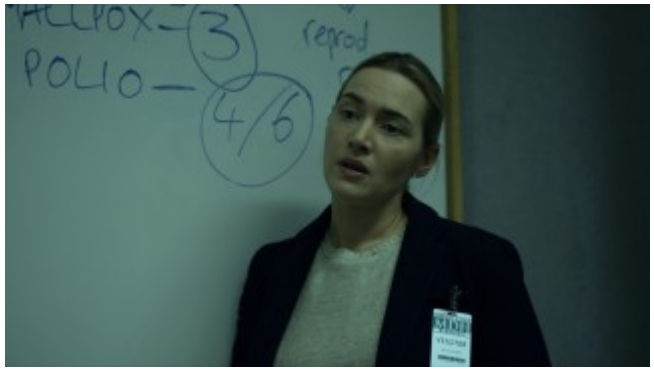
$$\frac{dI}{dt} = bSI - rI = I(bS - r)$$

  - If $S_0 < \frac{r}{b}$ then $\frac{dI}{dt} < 0$ implying infection dies out
  - **Threshold phenomenon**
  - If $S_0 > \frac{r}{b}$ then $\frac{dI}{dt} > 0$ implying epidemic occur

# $R_0$ (Basic reproduction number)

The average number of people infected by one infected person in a fully susceptible population.

$$R_0 = \frac{b}{r} S_0$$




http://www.dvdizzy.com/images/c/contagion-02.jpg

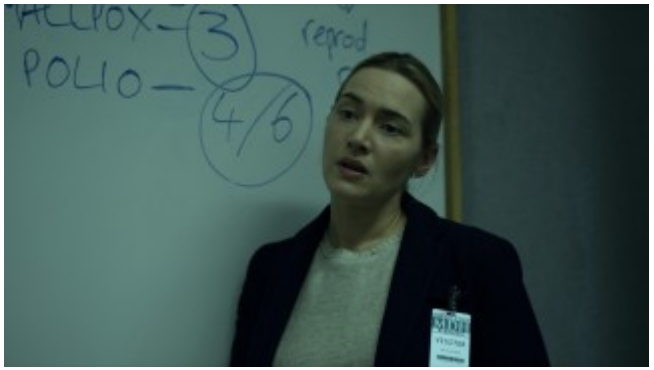
# $R_0$ (Basic reproduction number)

| Disease | Transmission | $R_0$ |
|---|---|---|
| Measles | Airborne | 12–18 |
| Diphtheria | Saliva | 6–7 |
| Smallpox | Airborne droplet | 5–7 |
| Polio | Fecal-oral route | 5–7 |
| Rubella | Airborne droplet | 5–7 |
| Mumps | Airborne droplet | 4–7 |
| HIV | Sexual contact | 2–5 |
| Pertussis | Airborne droplet | 5.5 |
| SARS | Airborne droplet | 2–5 |
| Influenza (1918 pandemic strain) | Airborne droplet | 2–3 |
| Ebola (2014 Ebola outbreak) | Bodily fluids | 1.5-2.5 |

- Contact rate and probability of transmission.
- Must remember these are also context specific.

# $R_0$ (Basic reproduction number)

- Can also be viewed as a threshold
- If each person infects more than one person then the infection takes off
- If not, then the infection will die out…
- Transmission rate and length of transmission




http://www.dvdizzy.com/images/c/contagion-02.jpg

# The importance of $R_o$

For an infectious disease with average infectious period $1/\gamma$ and transmission rate $\beta$, $R_o = \beta/\gamma$:

- For a closed population, an infectious disease can only invade if there is a threshold fraction of susceptibles greater than $1/R_o$.
- Vaccination policy: if proportion of susceptibles is reduced to below $1/R_o$, can eradicate the disease.

# Effects of Parameters


- Parameters :
  - How quickly do people move from one compartment to another?
  - What drives this?

# Constructing a mechanistic model


- "Fitting" to data
  - Do we have counts for the components of the model?
  - How well does the model match these?
    - Can we recreate the patterns of the data?
    - Are we "close" to the actual values of our outcome?
    - Data: cases (over time), serology= past infections
- Sometimes we estimate the parameters using this data

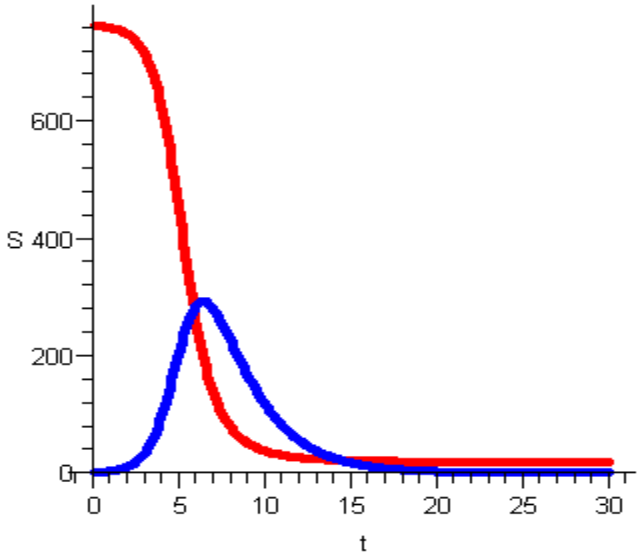
# Numerical solution

- Number of infectives starts small and increases substantially over 6 days then decreasing gradually

$\beta = 0.00218$

$\gamma = 0.44$

Susceptible (Red)
Infectives (Blue)



# SIR model with demography

More general formulation of SIR model:

- Assume rate at which individuals in any class suffer natural mortality = $\mu$. Historically, $\mu$ is also crude birth rate (to keep total population constant: $\frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0$.

$$\begin{aligned}
\frac{dS}{dt} &= \mu - \beta SI - \mu S \\
\frac{dI}{dt} &= \beta SI - \gamma I - \mu I \\
\frac{dR}{dt} &= \gamma I - \mu R.
\end{aligned}$$

- If we assume entire population is susceptible,

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

($R_0$= transmission rate* infectious period)

# SIR model with demography: equilibrium

- Inclusion of host demographic dynamics may permit a disease to persist in a population in the long term.
- *Disease-free equilibrium*: pathogen has suffered extinction and everyone in the population is susceptible.
  $(S^*, I^*, R^*)$=(1,0,0). How likely is this? Consider $\frac{dI}{dt}$:

$$\beta SI - (\gamma + \mu)I = 0.$$

  After factoring for $I$, $I(\beta S - (\gamma + \mu)) = 0$.
- Above is satisfied when $I^* = 0$ or $S^* = \frac{\gamma+\mu}{\beta}$.
- $I^* = 0$ is disease-free equilibrium.

# SIR model equilibrium [cont'd]

- $S^* = \frac{\gamma+\mu}{\beta} = \frac{1}{R_0}$. Hence, *endemic equilibrium* (where the disease is always present without any re-introduction) is characterized by the fraction of susceptibles in the population being the inverse of $R_o$. This equilibrium is only feasible when $R_0 > 1$ (otherwise positivity of variables not always satisfied.)
- Since $S^* = 1/R_0$, can solve for $\left(S^*, I^*, R^*\right) = (\frac{1}{R_0}, \frac{\mu}{\beta}(R_0 - 1), 1 - \frac{1}{R_0} - \frac{\mu}{\beta}(R_0 - 1)\Big)$.
- Endemic equilibrium is stable if $R_0 > 1$ otherwise disease-free equilibrium is stable.

# Another variant

- Model disease that does not confer long lasting immunity
  - Example: rotavirus, STD

# And another

- Immunity lasts for a limited period before waning such that individual is once again susceptible
  - Example?

# another

- Taking into account latent period
  - Pathogen in individual but not transmittable to other susceptible (not infectious)

# Estimating parameters in deterministic models

- Parameter estimation in deterministic models is often carried out using numerical techniques.
- Since learning about the influence of the parameters on the behavior of the model is of much interest, it is critical to carry out a sensitivity analysis.
- “Sensitivity analysis is often used to study how the variation in the output of a model can be apportioned, qualitatively or quantitatively, to different sources of variation, and of how the given model depends on the information fed into it.” (see Saltelli et al., 2000, 2008)
- Some likelihood-based approaches are available, but can be very expensive since a large number of missing parameters need to be integrated out.

# Summary

- Modeling disease dynamics is a very active and exciting research area with a huge number of interesting applications.
- Historically, disease modeling has been dominated by deterministic, differential equations-based models.
- While there are many researchers working on statistical methods, sound inferential techniques are still in their infancy relative to the forward models developed.
- Modeling dynamics in space is a particularly interesting and challenging area for research.

# Some topics not discussed

- Detailed discussions on Stochastic and Spatial & temporal models
- Approximate Bayesian Computation
- Likelihoods
- Filtering approaches
- Network models

# Terminology (Recollection)

Deterministic: same outcome every time you run the model with the same parameters

Stochastic: different outcome every time you run the model with the same parameters (randomness)

Differential equation model/compartmental model: Individuals in the population are grouped

Individual based/agent based model: Each individual in the population is modelled separately and behaves according to rules

# Modelling Interventions

Hannah Clapham, PhD
OUCRU

# Overview

- Criticial vaccination threshold and $R_0$
- SIR model with vaccination
- SIR vector model with vector control

# Modelling Interventions


- Once we have a model of how a system works we can add interventions.
- What does:
  - wearing masks do?
  - treating people so they are infected for a shorter length of time?
  - vaccination?

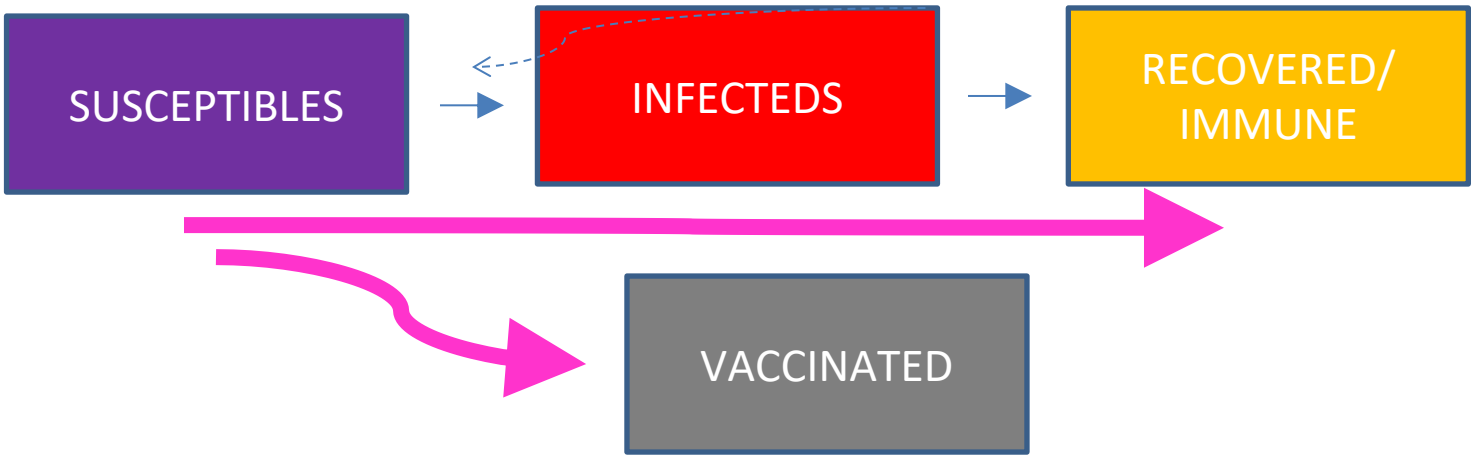
# Why?

- Can run a simulation of different scenarios or interventions and can help decide what to do more easily than running a huge trial
- Secondary effects can be incorporated, often hard to get in a trial
- Can also be useful in trial design

# Vaccination

- Vaccination- administration of antigenic material to stimulate the immune system to develop adaptive immunity to a pathogen
- Vaccine should reduce the risk of infection (or symptoms) with a certain pathogen

# SIR model with vaccination




- How can we include a vaccine in the model?
- Vaccinations moves individuals to the recovered class.

# SIR model with vaccination: Equations

$$\frac{dS}{dt} = -\beta SI - vS$$

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

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

- Vaccination moves individuals to the recovered class.

# SIR model with vaccination: Equations

$$\frac{dS}{dt} = -\beta SI - vS$$

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

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

$$\frac{dV}{dt} = vS$$

- Vaccination moves individuals to a different vaccinated group.

**Effective reproductive number**

$R_t = R_0\, s$

s: the fraction of the host population that is susceptible (s).

$R_t = R_0(1-v)$

# Critical vaccination threshold and $R_0$

- With vaccination we aim to bring R lower than 1.
- Assume a 100% efficacious vaccine
- After vaccination $R_t = R_0 \times (1-v)$, where v is the proportion vaccinated.
- So $R_t<1$ implies $v > 1-1/R_0$.
- So the larger $R_0$ the greater the proportion of the vaccination that needs to be vaccinated.
- Examples:

| Disease | $R_0$ | p |
|---|---|---|
| Measles | 14 | 0.92 |
| Rubella | 6 | 0.83 |
| Mumps | 5 | 0.8 |
| Influenza (1918) | 2.5 | 0.6 |

# Critical vaccination threshold and $R_0$

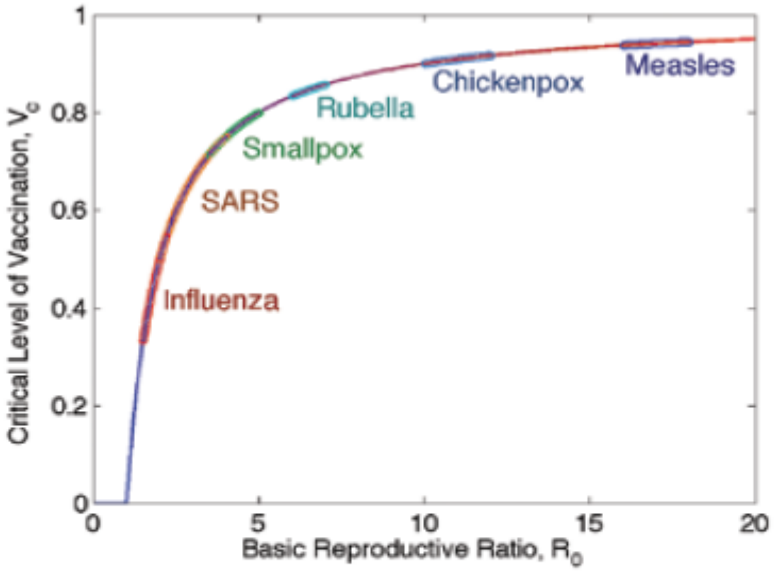
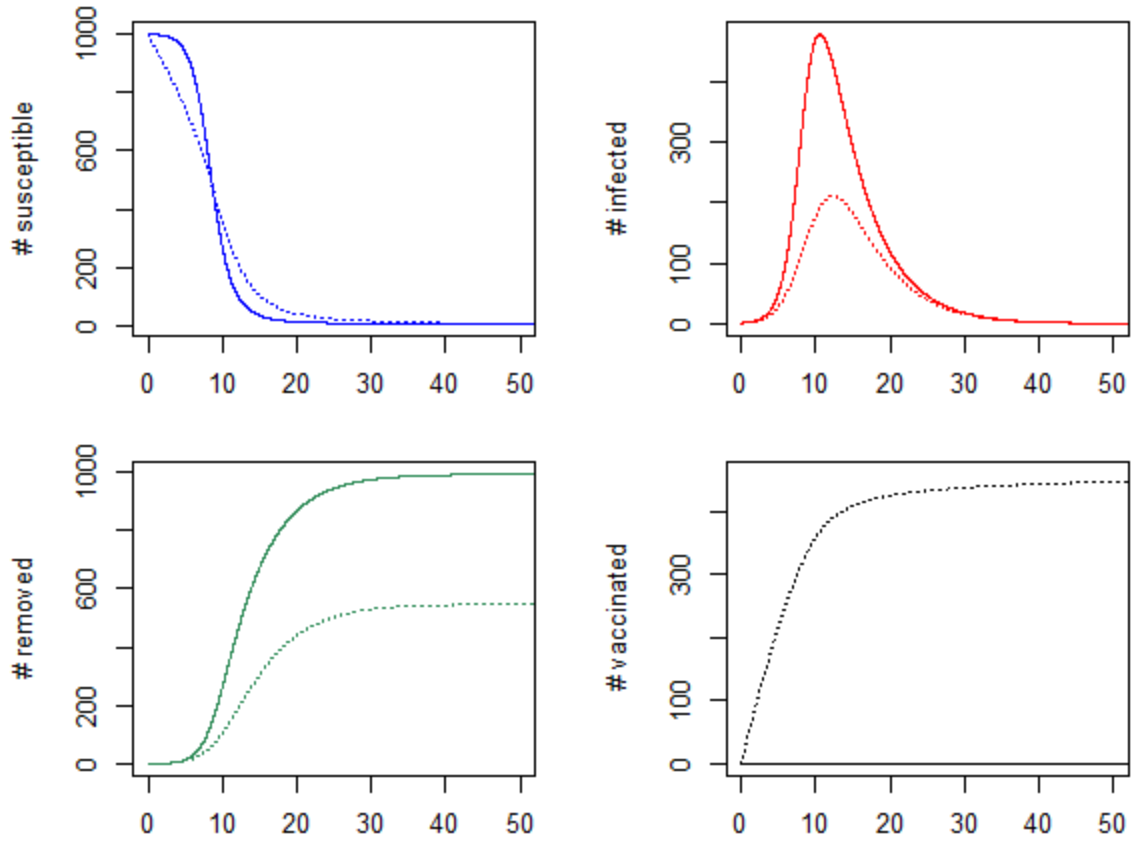



Figure 1: Theoretical impact of perfect vaccination. The graph shows the relationship between the critical level of vaccination needed to eradicate infection and the basic reproductive ratio, $R_0$. Superimposed on this curve are parameter estimates for six well-known infectious diseases, ranging from influenza (low $R_0$) to measles (high $R_0$).

Keeling et al The mathematics of vaccination, Mathematics Today 2013


# susceptible
0
200
600
1000
0
10
20
30
40
50
# infected
0
100
300
0
10
20
30
40
50
# removed
0
200
600
1000
0
10
20
30
40
50
# vaccinated
0
100
300
0
10
20
30
40
50

# Terminology (cont.)

Simulate: Running the model

Sensitivity analysis: Running the model with different parameters or different structure and assessing how different the outcome is

Fitting the model: Running the model with different parameters and comparing the outcome to some part of the model and then choosing the best parameters

# Acknowledgments


- Taken from Dr Hannah Clapham, OUCRU, lectures during DMo2018
- Also from online lecture notes by Murali Haran, Penn State University
- Main text referred, “Modeling Infectious Diseases in Humans and Animals”, Keeling & Rohani (2007), “Mathematical Modeling with Case Studies”, Barnes & Fulford (2010)