UNIT 7: Infectious disease

1 Introduction

Infectious disease

- Extremely common
- Huge impacts on ecological interactions
- A form of exploitation, but doesn't fit well into our previous modeling framework
  - How many people are there?
  - How many influenza viruses are there?
  - How do they find each other?

Disease agents

- Can you name an infectious agent that causes disease in humans?
- Disease agents vary tremendously:
  - Most **viruses** have just a handful of genes that allow them to hijack a cell and get it to make virus copies
    - **Answer:** influenza virus, Ebola virus, HIV, measles
  - **Bacteria** are independent, free-living cells with hundreds or thousands of chemical pathways
    - **Answer:** Tuberculosis, anthrax, pertussis
  - **Eukaryotic** pathogens are nucleated cells who are more closely related to you than they are to bacteria
    - **Answer:** Malaria, various worms

Microparasites

- For infections with small pathogens (viruses and bacteria), we don't attempt to count pathogens, but instead divide disease into stages
  - Latently infected
  - Productively infected
  - Recovered

Microparasite models

- We model microparasites by counting the number of hosts in various **states**:
  - **Susceptible** individuals can become infected
  - **Infectious** individuals are infected and can infect others
  - **Resistant** individuals are not infected and cannot become infected
- More complicated models might included other states, such as latently infected hosts who are infected with the pathogen but cannot yet infect others

Models as tools

- Models are the tools that we use to connect scales:
  - individuals to populations
  - single actions to trends through time

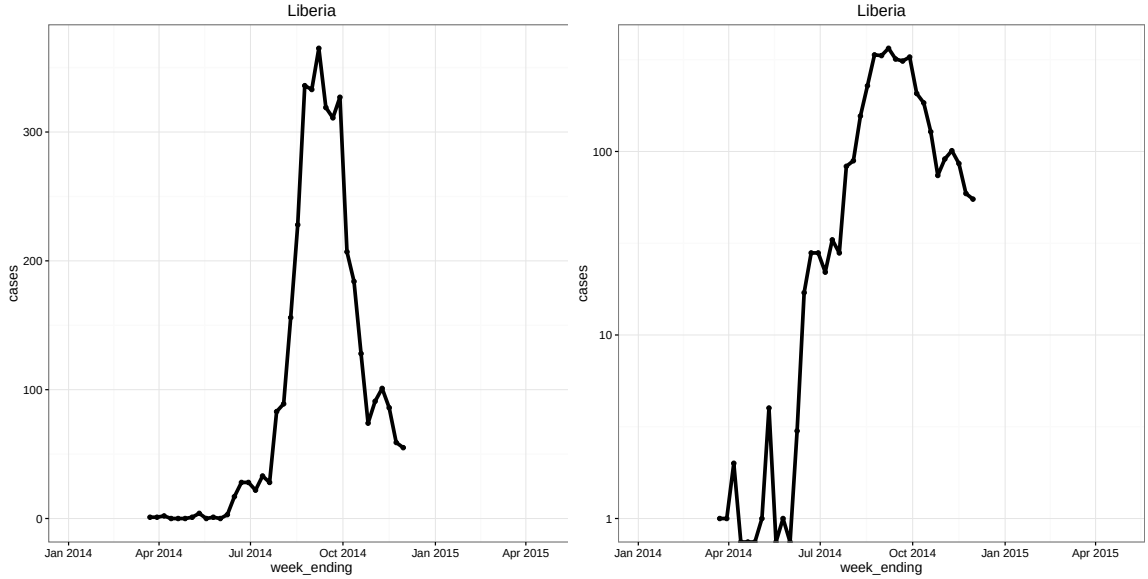
2 Rate of spread

- For many diseases, especially new diseases, we can *observe* and *estimate* r
  - **Answer:** the exponential rate of spread
- Want to know what factors contribute to that, and how it relates to $\mathcal{R}$
  - **Answer:** number of new cases per case

Basic reproductive number

- People in the disease field love to talk specifically about $\mathcal{R}_0$
- But they don't always mean the same thing:
  - Maximum value of $\mathcal{R}$ in a population
  - Theoretical value in a naive population without control efforts
  - Actual value before an epidemic

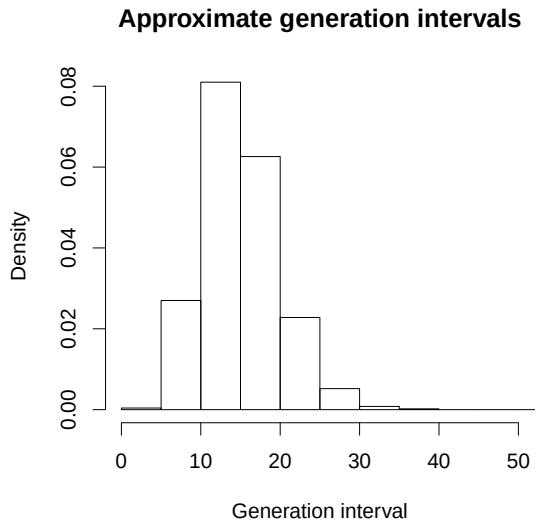
Example: the West African Ebola epidemic

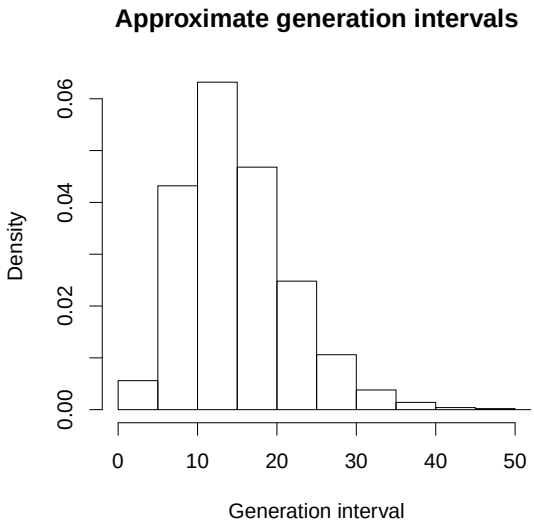


Generation intervals

- Researchers try to estimate the *proportion* of transmission that happens for different **ages of infection**
- How long from the time you are *infected* to the time you *infect someone else*?
- Analogous to a life table
- The effective generation time $\hat{G}$ has units of time

Generation intervals





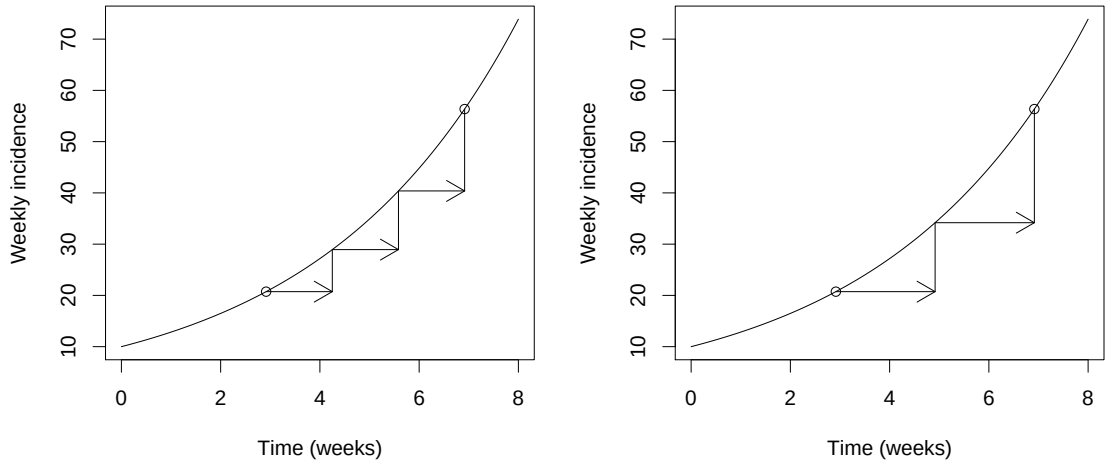
Speed and risk

- Which is more dangerous, a fast disease, or a slow disease?
  - How are we measuring speed?
  - How are we measuring danger?
  - *What do we already know?*

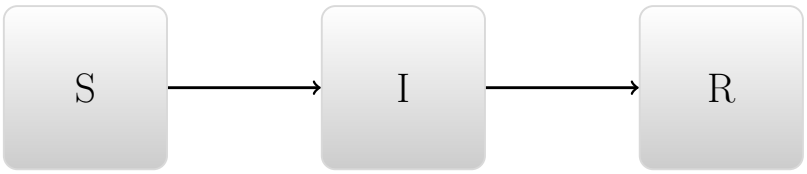
Generation time and risk

- If we know $\mathcal{R}$, what does the generation time tell us about r?
  - **Answer:** The faster the generations (small $\hat{G}$), the faster the exponential growth (large r)
- If we know r, what does the generation time tell us about $\mathcal{R}$?
  - **Answer:** The faster the generations (small $\hat{G}$), the the *smaller* the strength of the epidemic (small reproductive number $\mathcal{R}$)
- $\mathcal{R} = \exp(r\hat{G})$

Generation time and risk

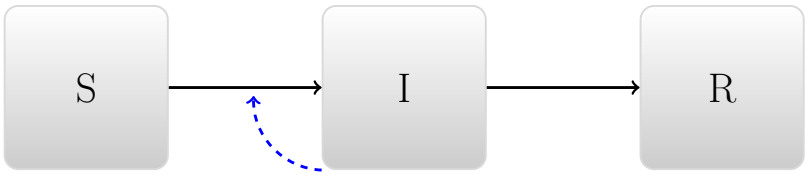


3 Single-epidemic model



- Susceptible → Infectious → Recovered
- We also use N to mean the total population

Transition rates



- What factors govern movement through the boxes?
  - People get better independently
  - People get infected by infectious people

Conceptual modeling

- What happens in the long term if we introduce an infectious individual?
  - **Answer:** The *may be* an **epidemic** – an outbreak of disease
  - **Answer:** Disease burns out
  - **Answer:** Everyone winds up either recovered or susceptible
  - **Answer:** Not everyone gets infected!

Interpreting

- Why might there not be an epidemic?
  - **Answer:** Demographic stochasticity: if we only start with one individual, we expect an element of chance
- Why doesn't everyone get infected?
  - **Answer:**

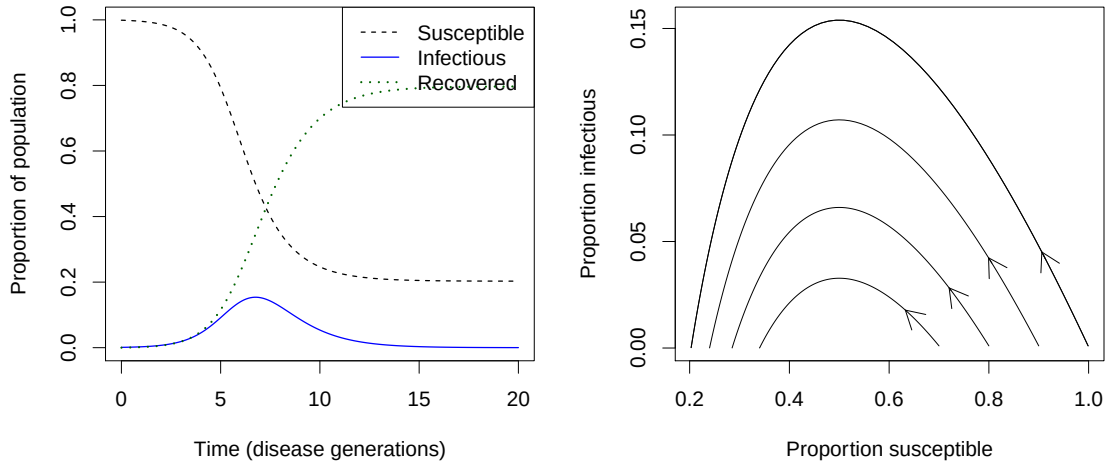
Implementing the model

- The simplest way to implement this conceptual model is with differential equations:
  - $$\frac{dS}{dt} = -\beta \frac{SI}{N}$$
  - $$\frac{dI}{dt} = \beta \frac{SI}{N} - \gamma I$$
  - $$\frac{dR}{dt} = \gamma I$$

Units

- S, I, R, N: [people] or [people/ha]
- β, γ: [1/time]

Simulating the model



Parameters

- Infectious people recover at *per capita* rate γ
  - Total recovery rate is γI
  - Mean time infectious is $D = 1/\gamma$
- Susceptible people have "potentially effective" contacts at rate β
  - These are contacts that would lead to infection if the person contacted is infectious
  - Total infection rate is $\beta I/N$, because I/N is the proportion of the population infectious

Basic reproductive number

- What *unitless* parameter can you make from the model above?
  - **Answer:** $\mathcal{R}_0 = \beta D = \beta/\gamma$ is the **basic reproductive number**
  - **Answer:** The *potential* number of infections caused by an average infectious individual
    - **Answer:** That is: the number they would cause on average if everyone else were susceptible

Basic reproductive number implications

- What happens early in the epidemic if $\mathcal{R}_0 > 1$?
  - **Answer:** Number of infected individuals grows exponentially
- What happens early in the epidemic if $\mathcal{R}_0 < 1$?
  - **Answer:** Number of infected individuals cannot grow (disease cannot invade)

Effective reproductive number

- The effective reproductive number gives the number of new infections per infectious individual in a partially susceptible population:
  - **Answer:** $\mathcal{R}_e = \mathcal{R}_0 S/N$
- What do we expect $\mathcal{R}_e$ to be at equilibrium?
  - **Answer:** 1. Each case causes on average one new case, at equilibrium.
  - **Answer:** At equilibrium, $S/N = 1/\mathcal{R}_0$
- Why doesn't everyone get infected?
  - **Answer:** Because when $\mathcal{R}_e < 1$, the disease dies out on its own (each case causes less than 1 new case)

3.1 Epidemic size

- In this model, the epidemic always burns out
  - No source of new susceptibles
- Epidemic size is determined by:
  - **Answer:** $\mathcal{R}_0$– larger $\mathcal{R}_0$ leads to a bigger epidemic
  - **Answer:** The number of susceptibles at the beginning of the epidemic
    - **Answer:** More susceptibles means a bigger epidemic – and therefore fewer susceptibles at the end

Ebola example

- In September, the US CDC predicted "as many as" 1.5 million Ebola cases in Liberia
- What happened?

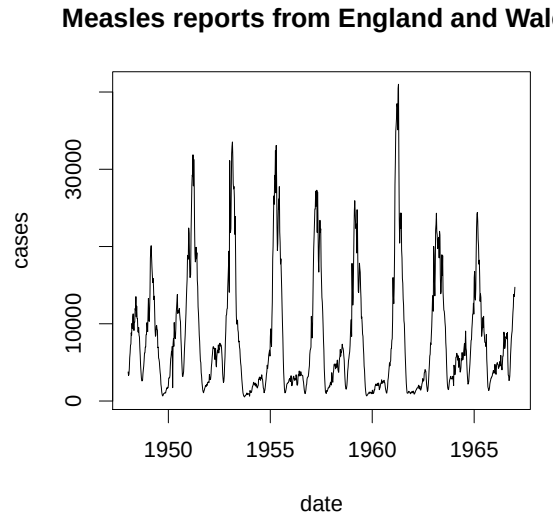
What limits epidemics?

- What limits epidemics in our simple models?
  - **Answer:** Depletion of susceptibles
- What else limits epidemics in real life?
  - **Answer:** Interventions
  - **Answer:** Behaviour change
  - **Answer:** Heterogeneity (differences between hosts, locations, etc.)

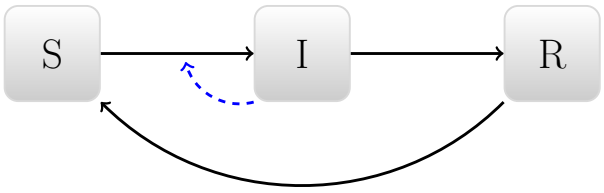
4 Recurrent epidemic models

- If epidemics tend to burn out, why do we often see repeated epidemics?
  - **Answer:** People might lose immunity
  - **Answer:** Births and deaths

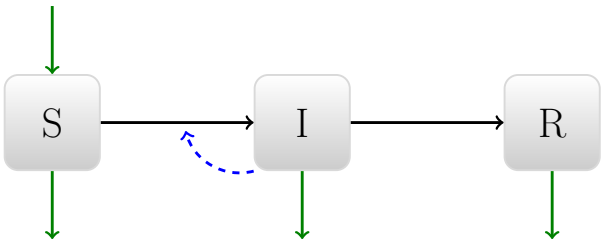
Recurrent epidemics



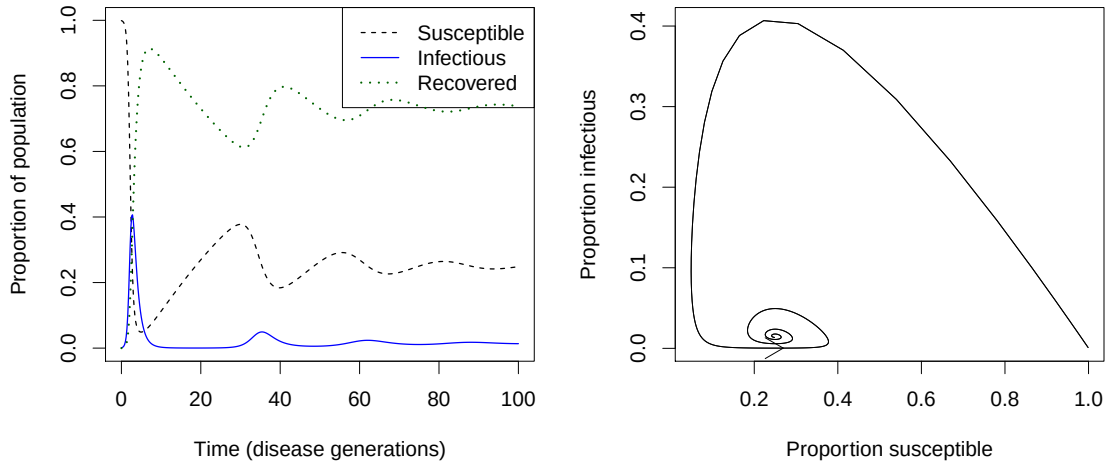
Closing the circle



Births and deaths



Tendency to oscillate



Tendency to oscillate

- "Closed-loop" SIR models (ie., with births or loss of immunity):
  - Tend to oscillate
  - Oscillations tend to be damped
    - System reaches an **endemic** equilibrium – disease persists

Source of oscillations

- Similar to predator-prey systems
- What happens if we start with too many susceptibles?
  - **Answer:** There will be a big epidemic
  - **Answer:** ...then a very low number of susceptibles
  - **Answer:** ...then a very low level of disease
  - **Answer:** ...then an increase in the number of susceptibles

Persistent oscillations

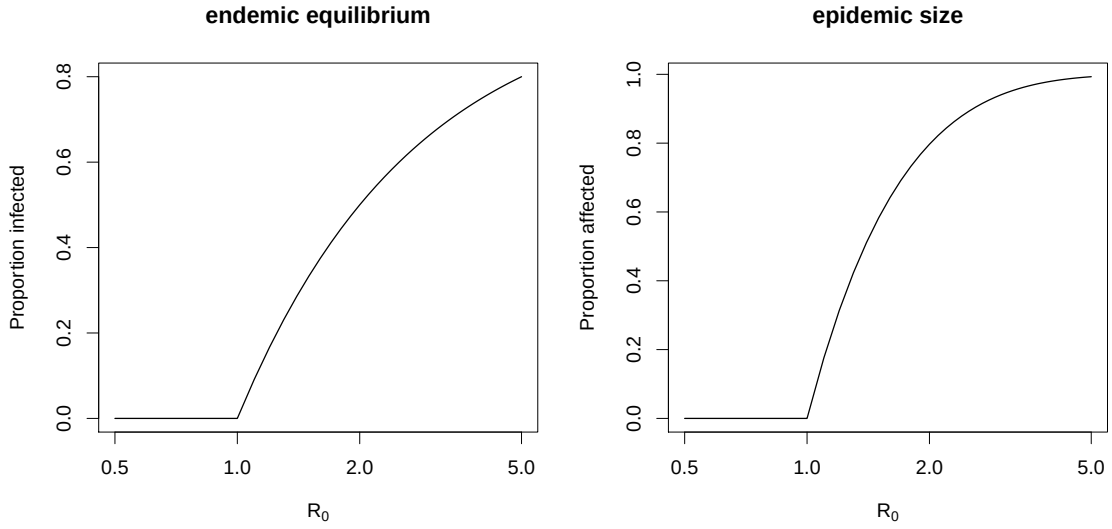
- If oscillations tend to be damped in simple models, why do they persist in real life?

- **Answer:** Weather
- **Answer:** School terms
- **Answer:** Demographic stochasticity
- **Answer:** Behaviour: if people are scared of the disease, it goes away, and then they stop being scared

5 Reproductive numbers and risk

- At equilibrium, the proportion of people who are susceptible to disease should be approximately $S/N = 1/\mathcal{R}_0$
- Proportion "affected" (infectious or immune) should be approximately $V/N = 1 - 1/\mathcal{R}_0$
- If you have a single, fast epidemic, the size is also predicted by $\mathcal{R}_0$.

Reproductive numbers and risk



Examples

- Ronald Ross predicted 100 years ago that reducing mosquito densities by a factor of 5 or so would *eliminate* malaria

- Gradual disappearance of polio, typhoid, etc., without risk factors going to zero
- Eradication of smallpox!

Threshold for elimination

- What proportion of the population should be vaccinated to eliminate a disease?
  - **Answer:** Transmission should be reduced by a factor of $\mathcal{R}$, so a fraction $1 = 1/\mathcal{R}$ should be vaccinated

Examples:

- Polio has an $\mathcal{R}_0$ of about 5. What proportion of the population should be vaccinated to eliminate polio?
  - **Answer:** 1-1/5 = 80%
- Measles has an $\mathcal{R}_0$ of about 20. What proportion of the population should be vaccinated to eliminate measles?
  - **Answer:** 1-1/20 = 95%

Persistence of infectious disease

- Why have infectious diseases persisted?
  - The pathogens *evolve*
  - Human populations are **heterogeneous**
    - People differ in: nutrition, exposure, access to care

Heterogeneity and persistence

- Heterogeneity *increases* $\mathcal{R}_0$
  - When disease is rare, it is concentrated in the most vulnerable populations
    - Cases per case is high
    - Elimination is harder

- Marginal populations
  - Heterogeneity could make it easier to concentrate on the most vulnerable populations and eliminate disease
  - Humans rarely do this, however: the populations that need the most support typically have the least access