UNIT 8: Infectious disease

Outline

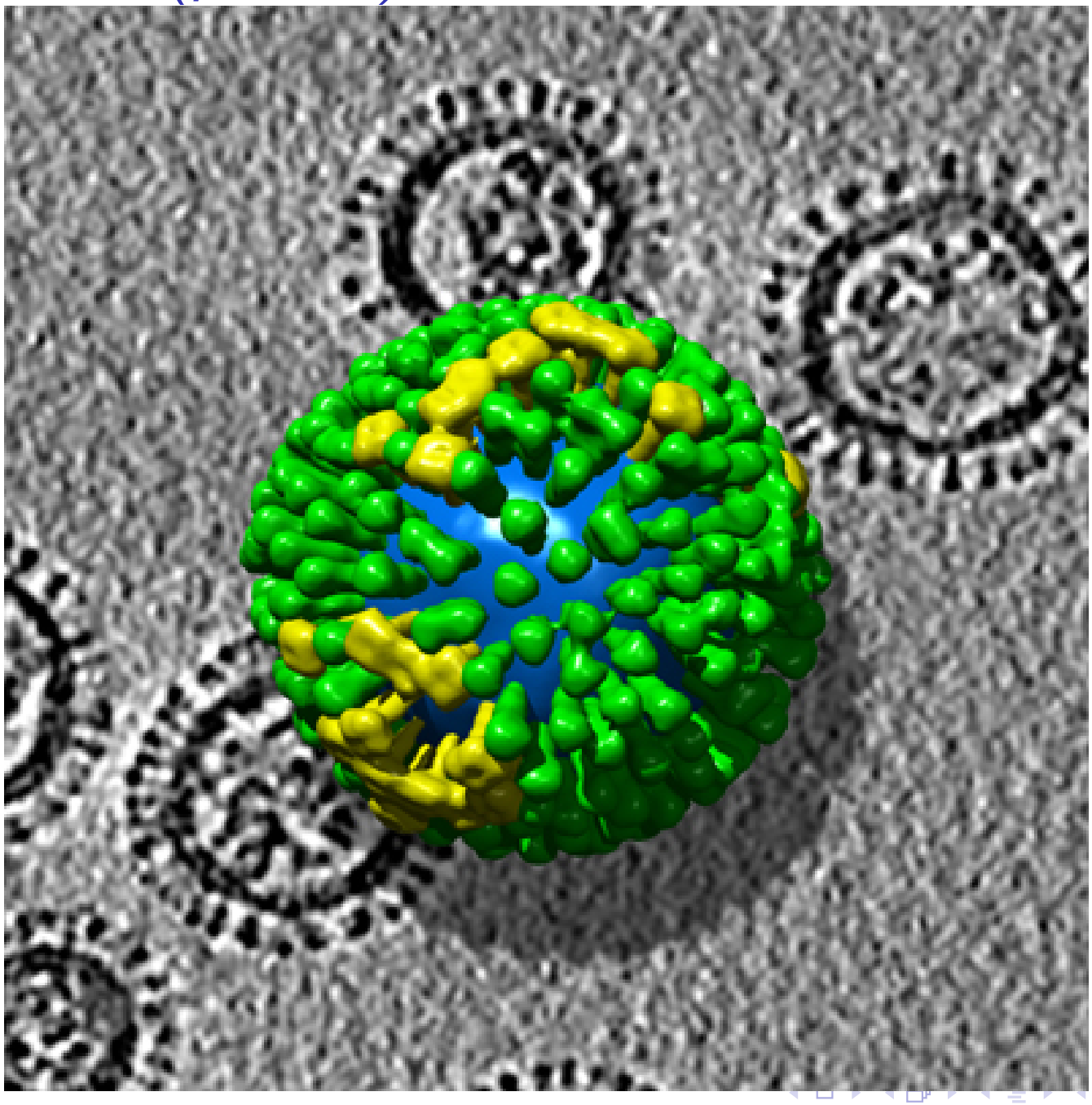
Infectious disease

- 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?

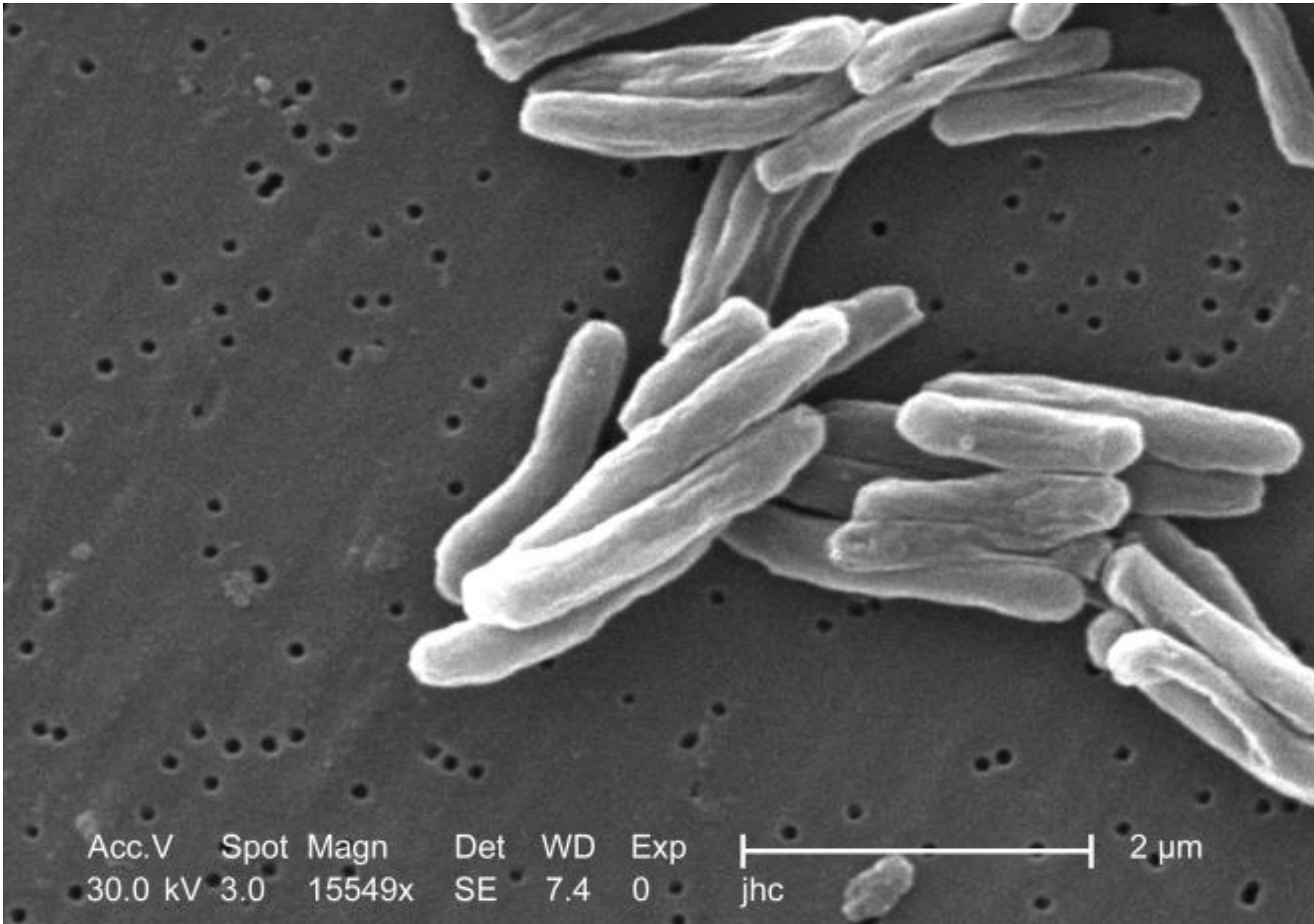
Disease agents

- 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
    - * influenza virus, Ebola virus, HIV, measles
  - **Bacteria** are independent, free-living cells with hundreds or thousands of chemical pathways
    - * Tuberculosis, anthrax, pertussis
  - **Eukaryotic** pathogens are nucleated cells who are more closely related to you than they are to bacteria
    - * Malaria, various worms

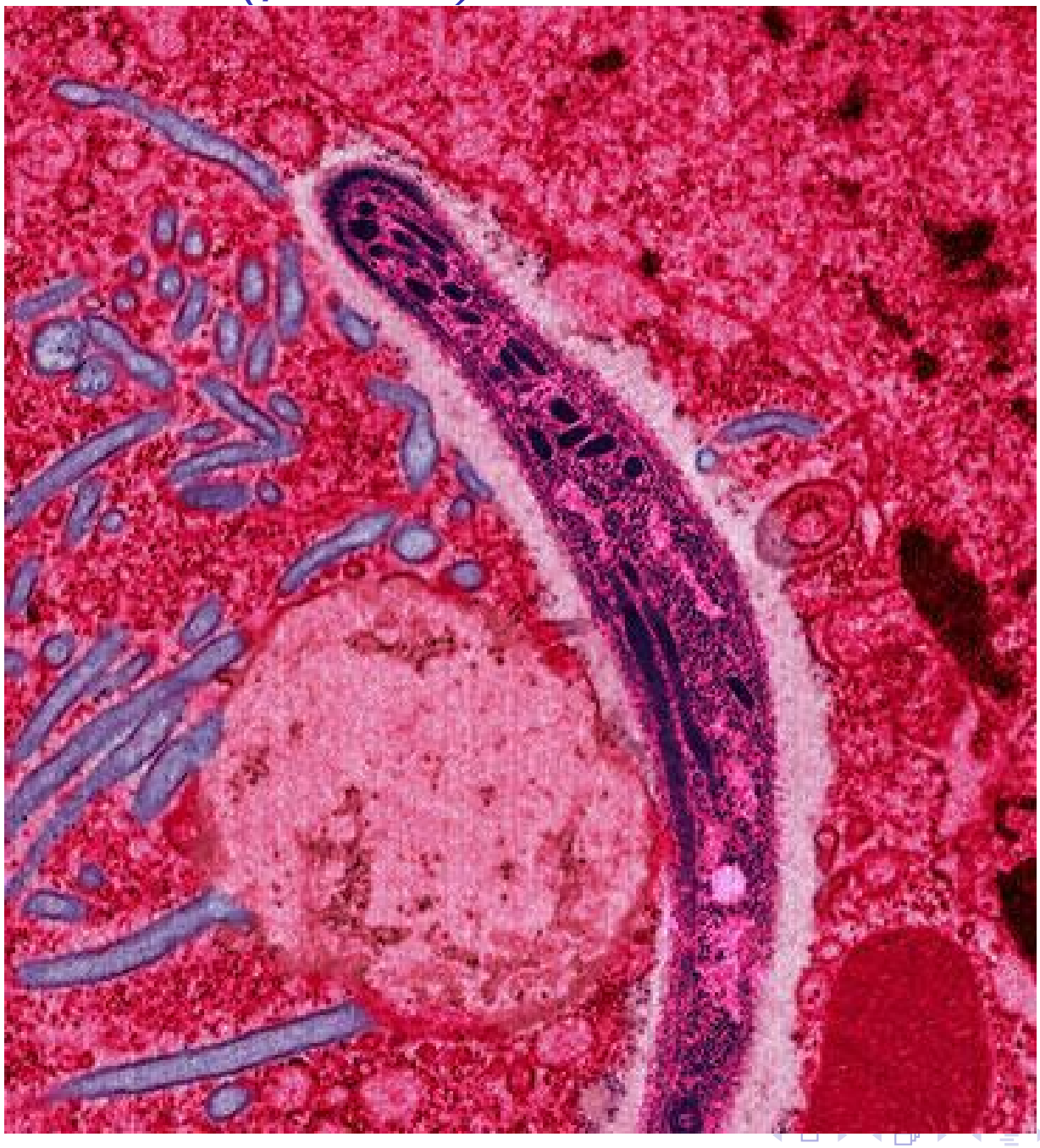
Influenza virus (present)



Tuberculosis bacilli (present)



Malaria sporozoite (present)



Microparasites

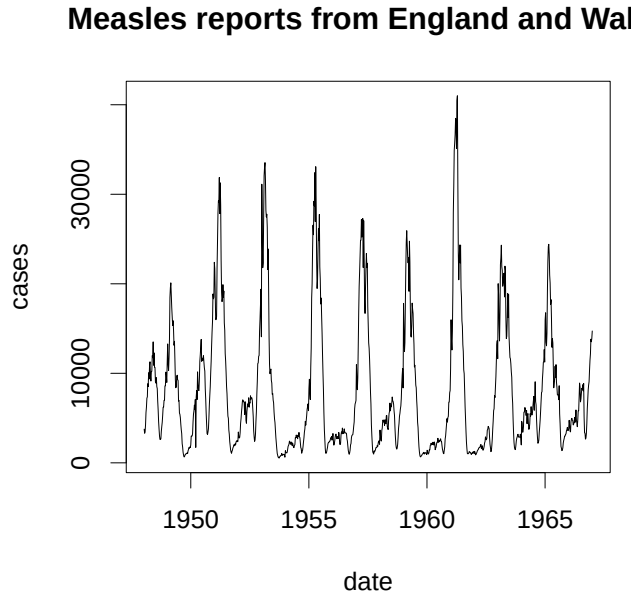
- For infections with small pathogens (viruses and bacteria), we don't attempt to count pathogens, but instead divide disease into stages
  - Latently infected
  - Productively infected
  - Recovered

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 include 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



Outline

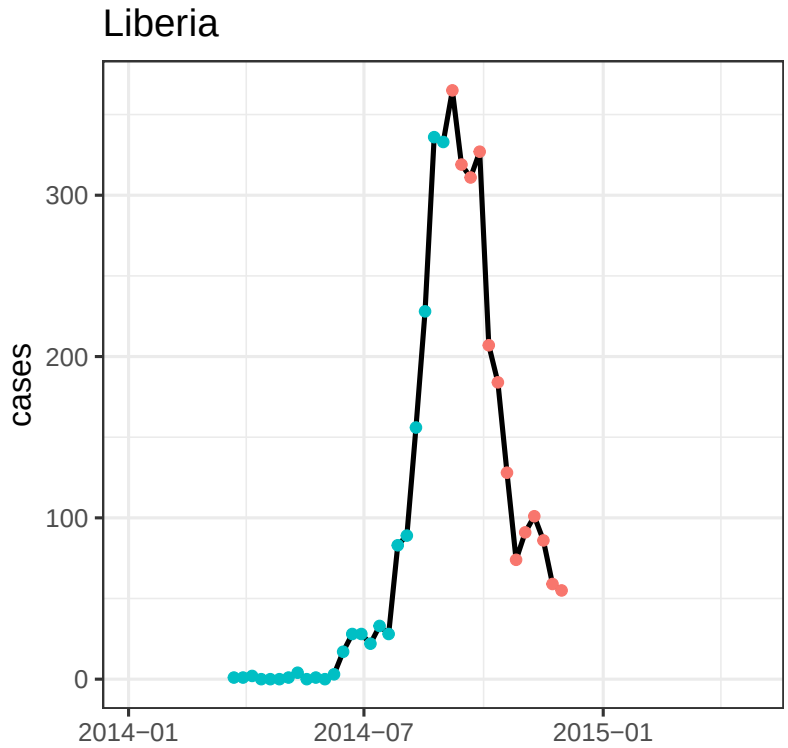
Rate of spread

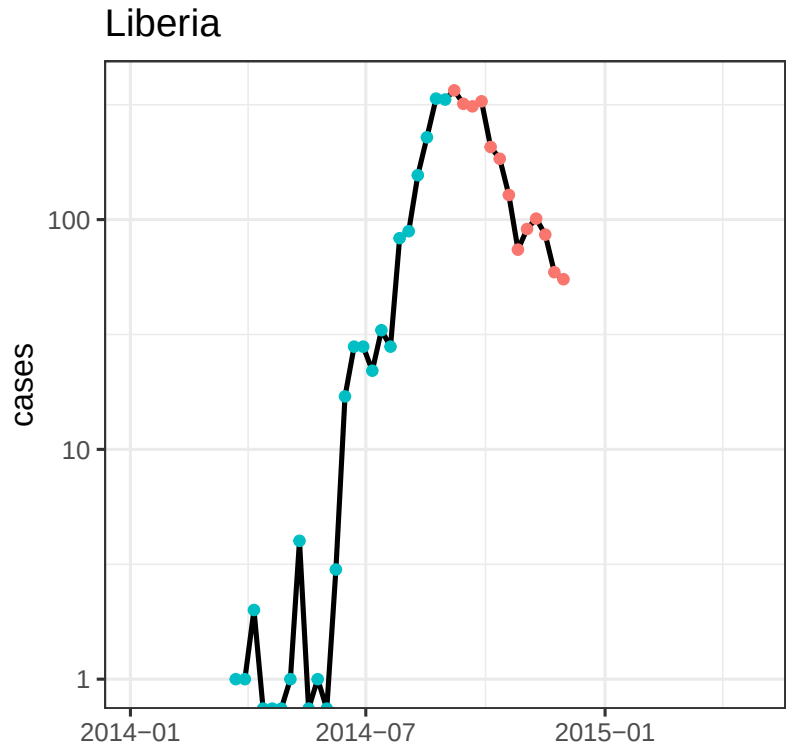
- For many diseases, especially new diseases, we can *observe* and *estimate* r.
  - * Instantaneous rate of increase (per capita)
    - * Units of $1/t$
    - * Gives the exponential rate of spread
- Want to know what factors contribute to that, and how it relates to $\mathcal{R}$.
  - * number of new cases per case
  - * Unitless

Basic reproductive number

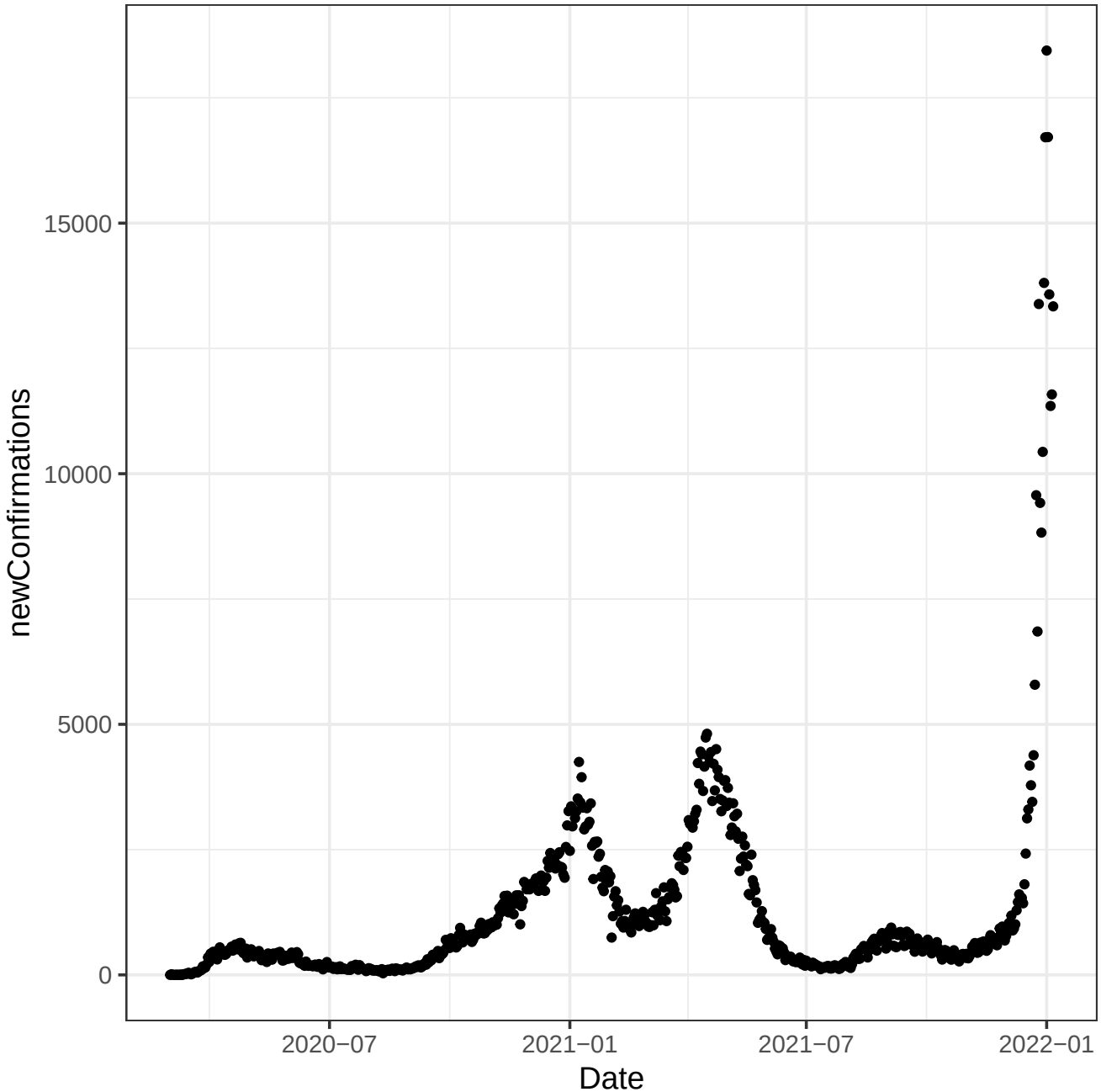
- People in the disease field love to talk specifically about $\mathcal{R}_0$
- But they don't always mean the same thing when they say $\mathcal{R}_0$:
  - Actual value of $\mathcal{R}$ before an epidemic
  - Hypothetical value assuming no immunity
  - Hypothetical value assuming no immunity and no control efforts whatsoever
- Often easier to talk simply about $\mathcal{R}$.

Example: the West African Ebola epidemic

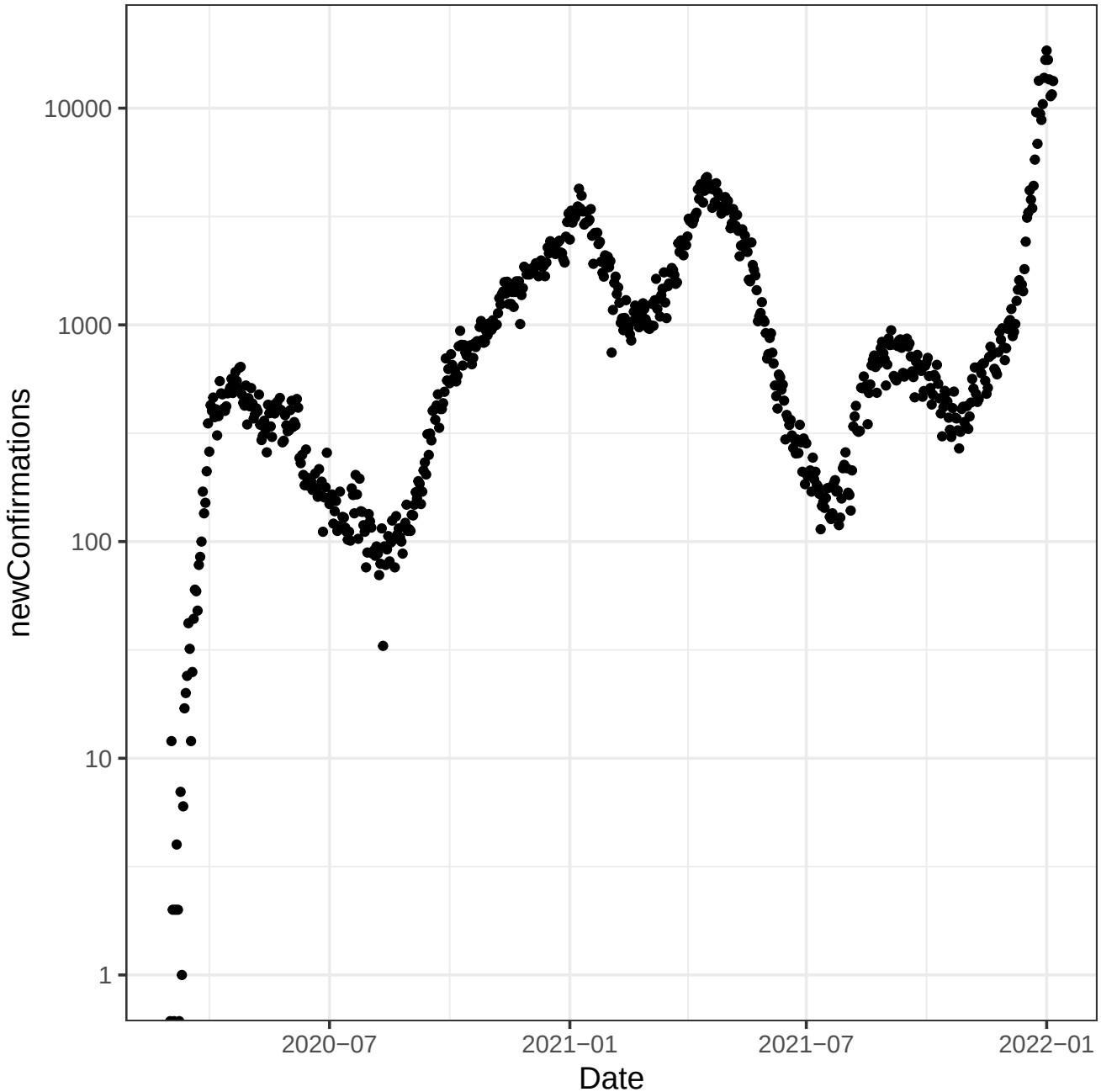




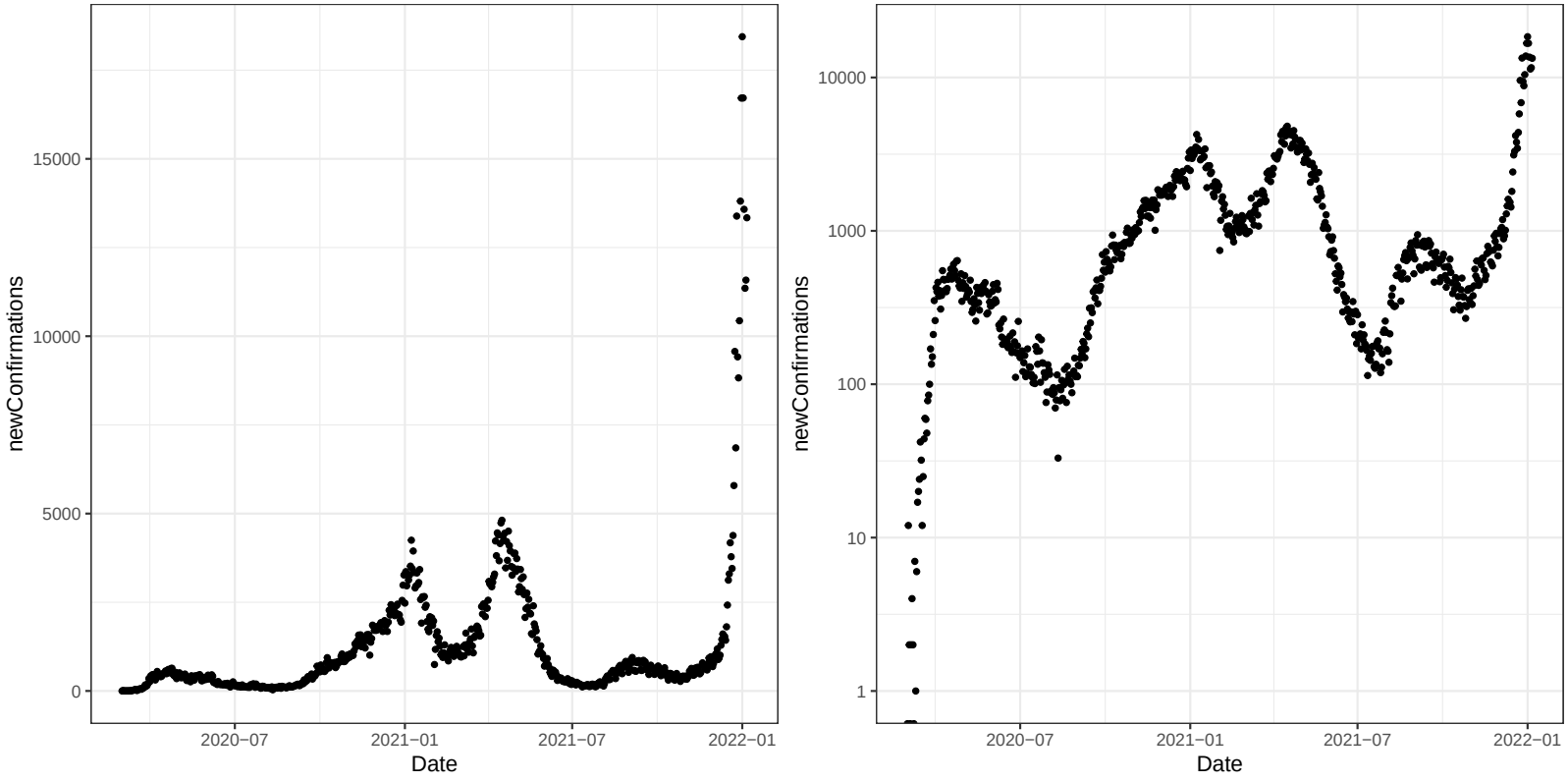
COVID in Ontario (repeat)



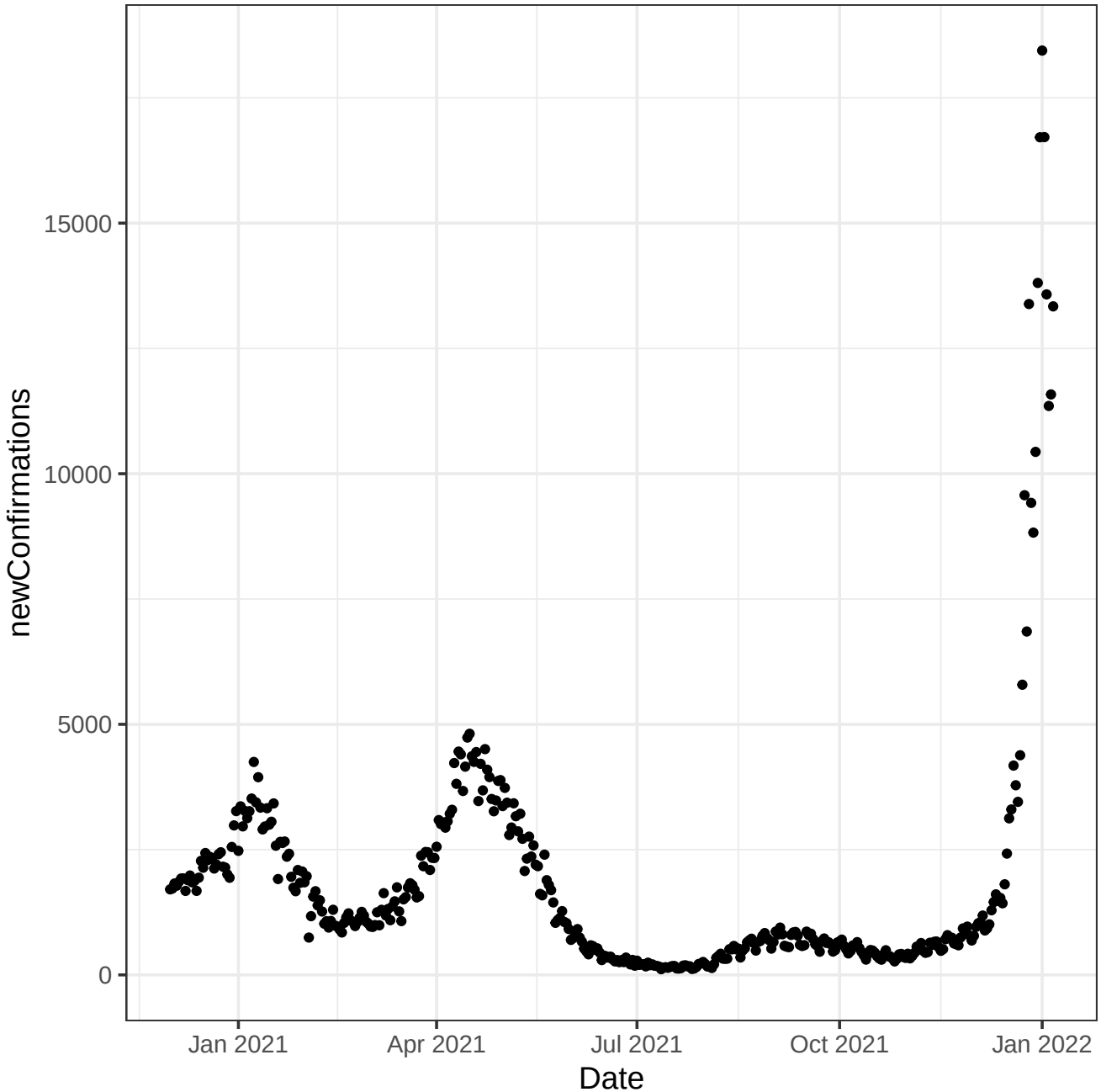
COVID in Ontario (repeat)



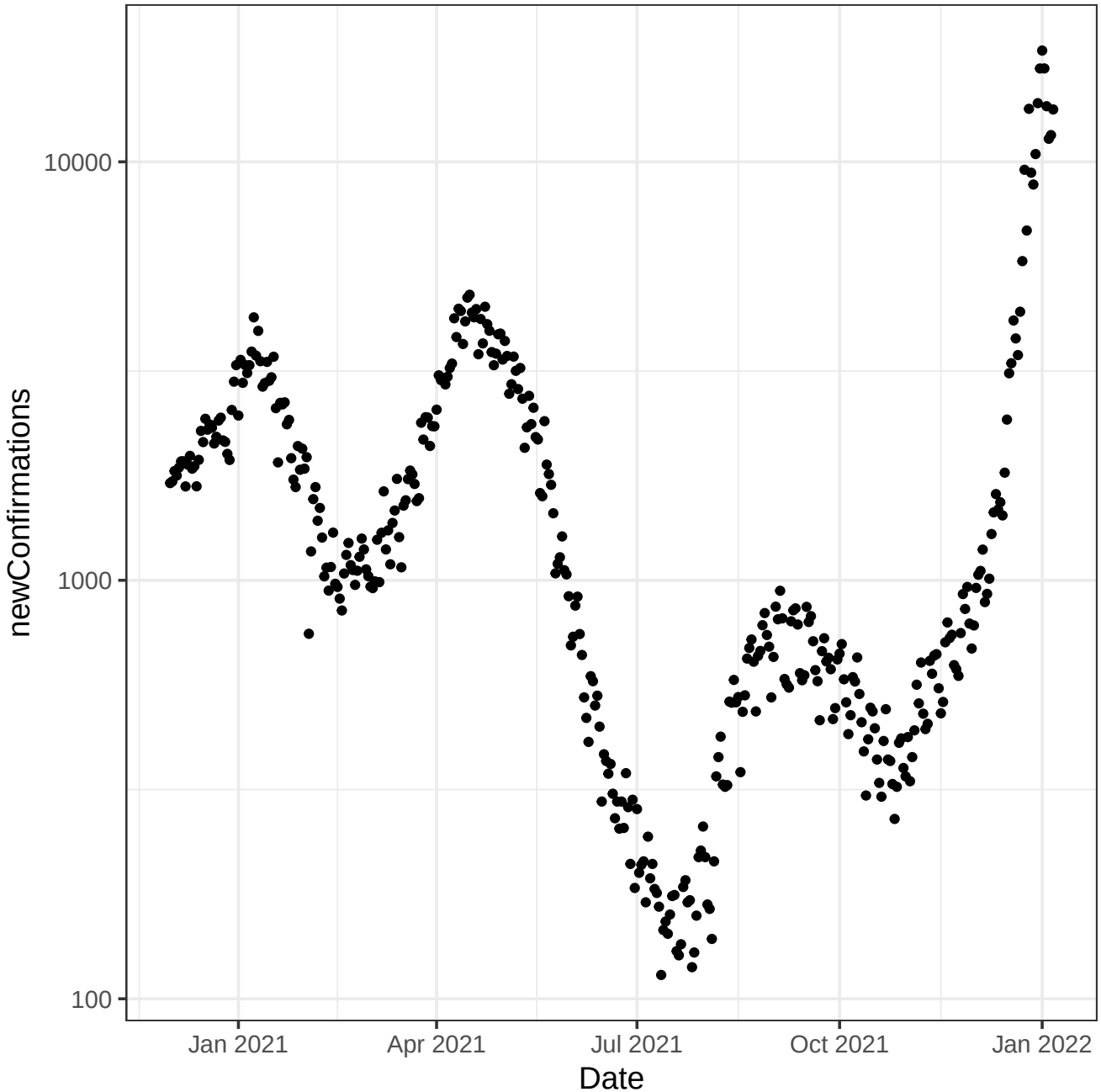
COVID in Ontario



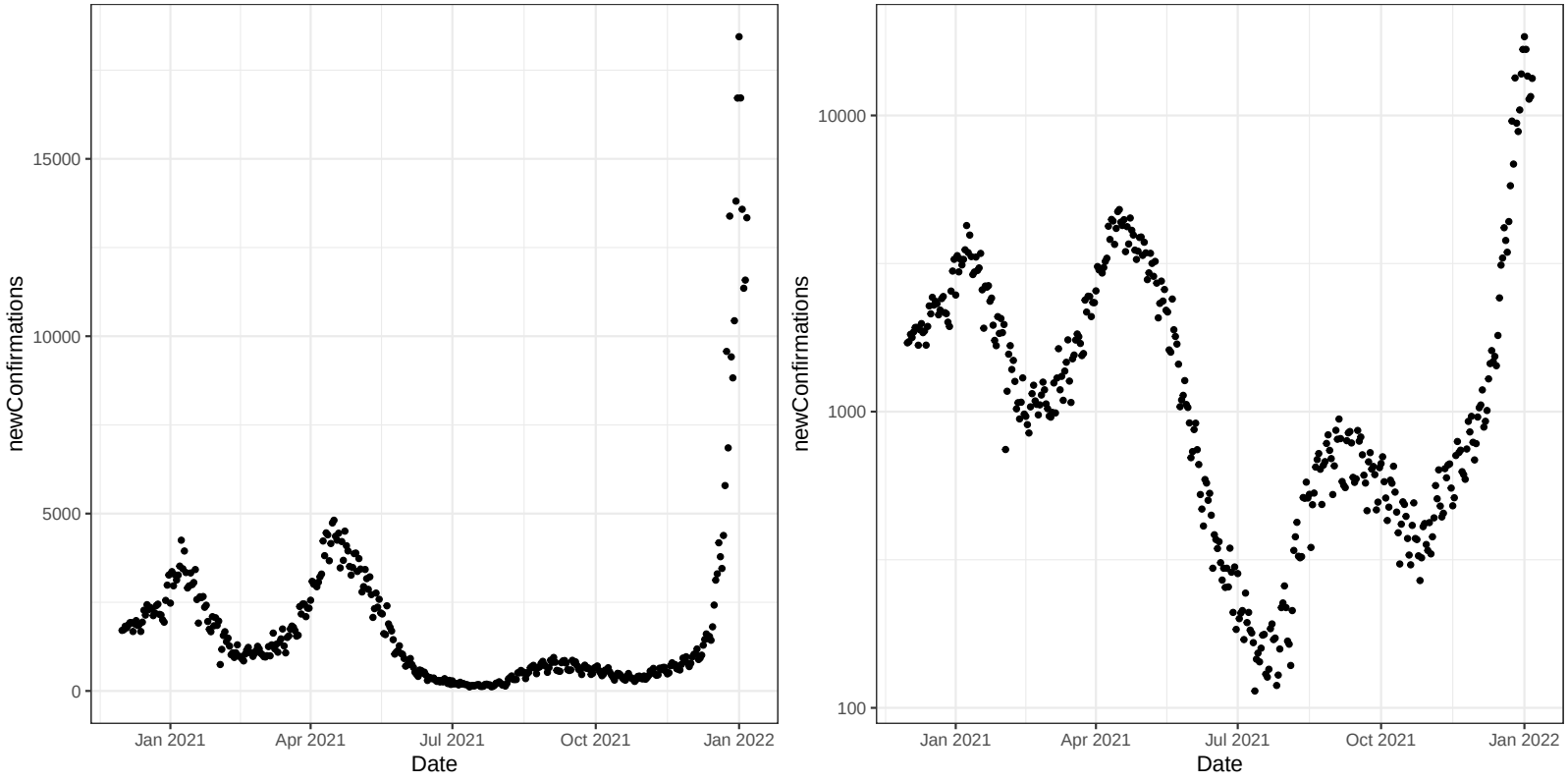
COVID in Ontario (repeat)



COVID in Ontario (repeat)



COVID in Ontario



Scales

- Which scale should we look at?
  - * Log scale is better for looking at trends
  - * Linear scale is better for looking at impacts

Population biology

- What quantities do we want to look at?
  - * Speed of exponential growth r
  - * Finite rate of increase λ
    - * Skipped this year
  - * Lifetime reproduction

Instantaneous rate of growth r

- What are the components?
  - * Birth rate
    - * Instantaneous rate of a case producing new cases
    - * [case/(case · time]
  - * Death rate
    - * Virus-centered!
    - * Rate of death, recovery, or effective quarantine
- How do you think we estimate?
  - * We estimate r from the population-level increase in disease
    - * Then using that to estimate b
  - * Models go both directions!
    - Individuals $\leftrightarrow$ Populations

Finite rate of growth λ

- Why do we want this?
  - * to communicate with policy-makers or the public
  - * maybe to make concrete predictions, though we could use r
- How do we calculate it?
  - * Pick a time step (week? year?)
  - * Use a formula $\lambda = \exp(r\Delta t)$

Example

- $r \approx 0.14/$ day for early COVID spread
- What is λ?
  - At a time scale of a day?
  - At a time scale of a week?

Reproductive number $\mathcal{R}$

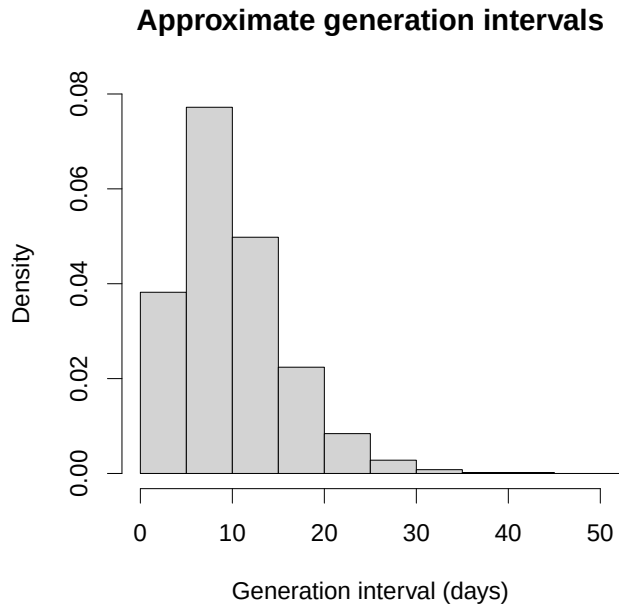
- What is it?
  - * Expected number of new cases per case over the lifetime of a case
- Why do we want this?
  - * An important measure of how hard the epidemic will be to stop
- How do we calculate it?
  - * $\mathcal{R} = b/d$; if we can estimate those

Example

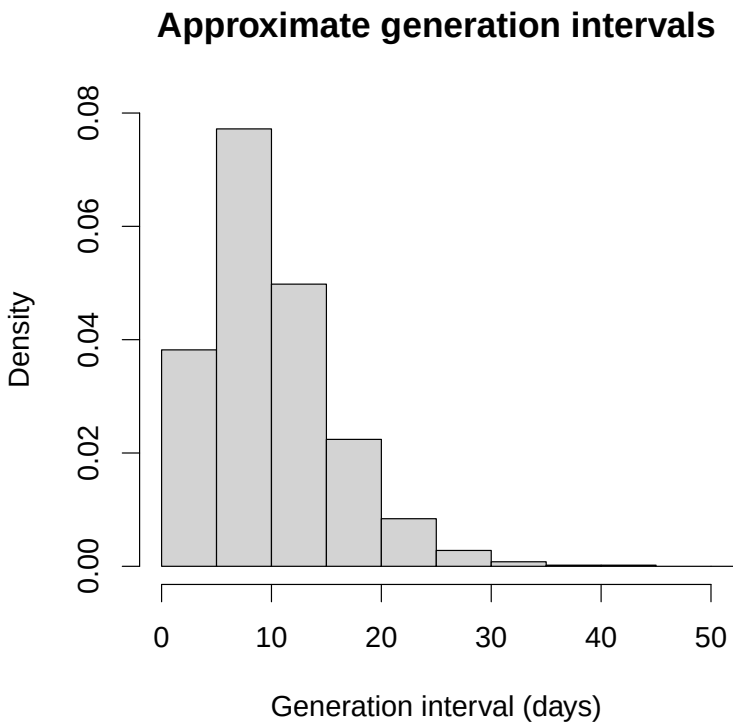
- $r \approx 0.14/\,\text{day}$
- What is our estimate of $\mathcal{R}$?
  - When average length of infection $L = 5\,\text{day}$?
  - When average length of infection $L = 10\,\text{day}$?

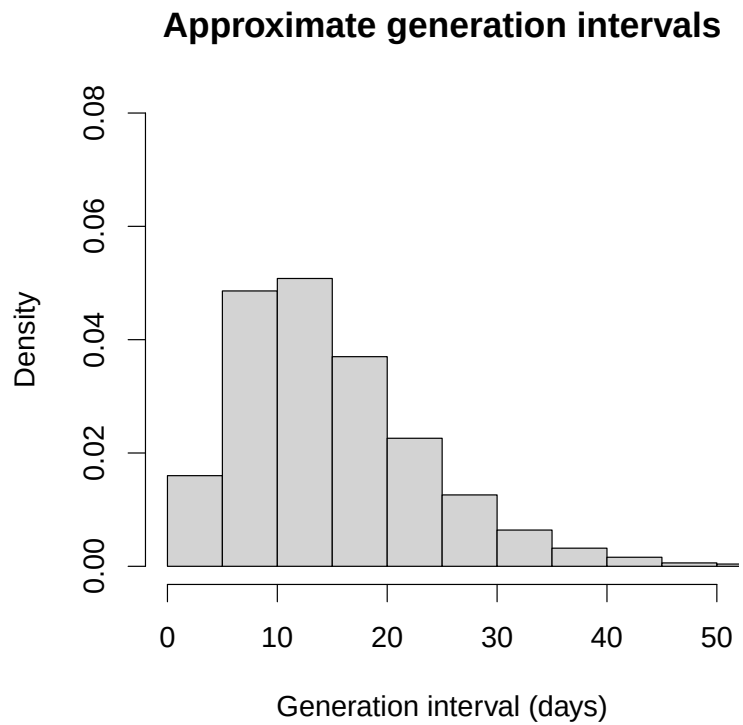
Generation intervals

- 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



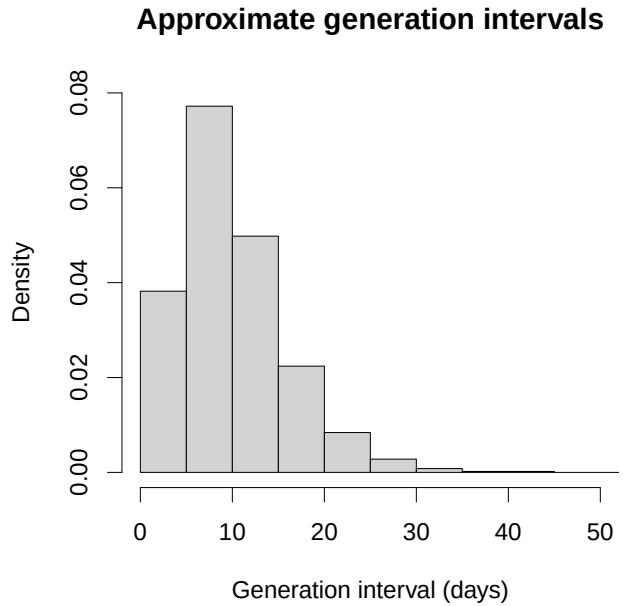
Generation intervals





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?*

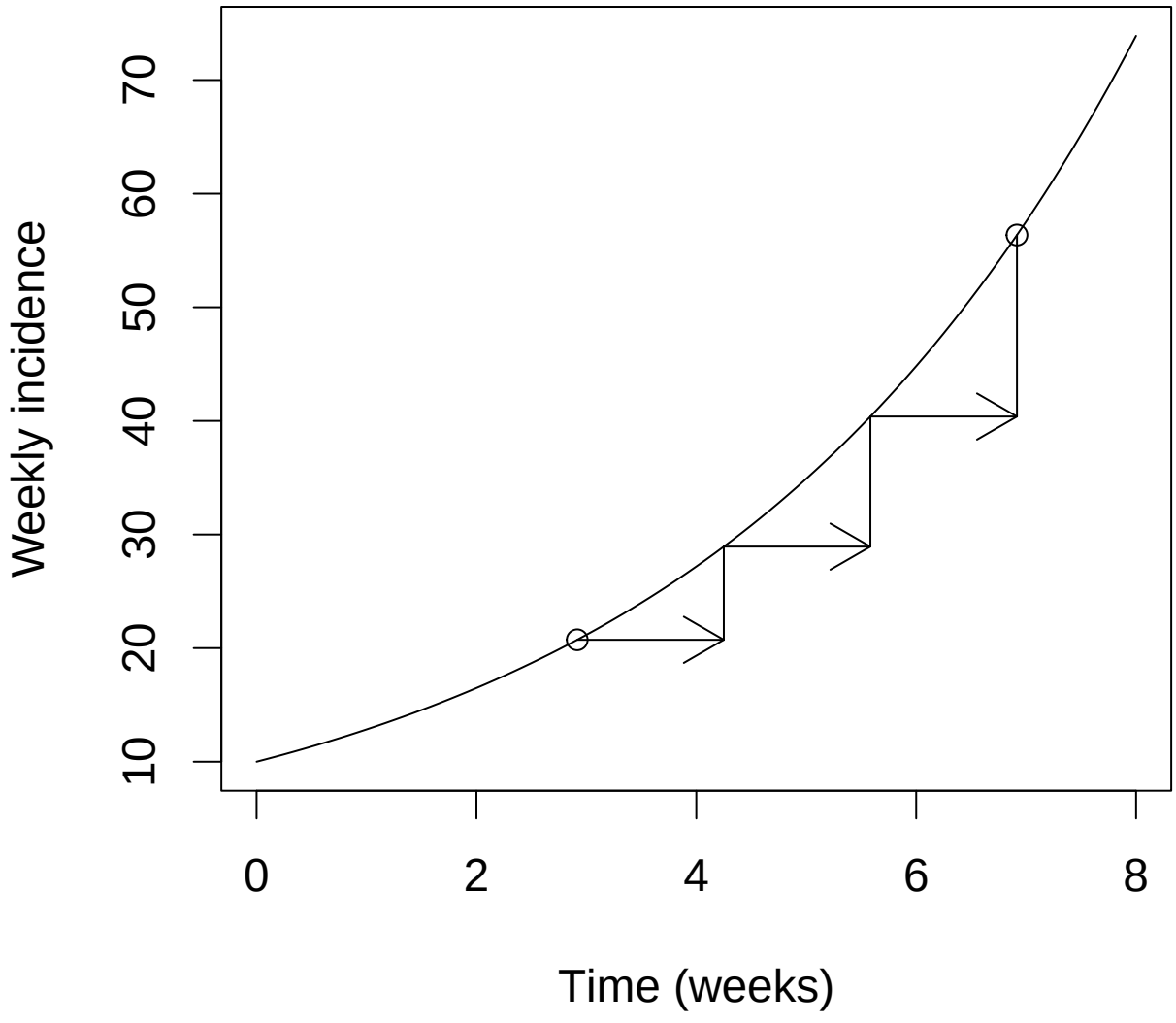


Fighting Ebola (present)

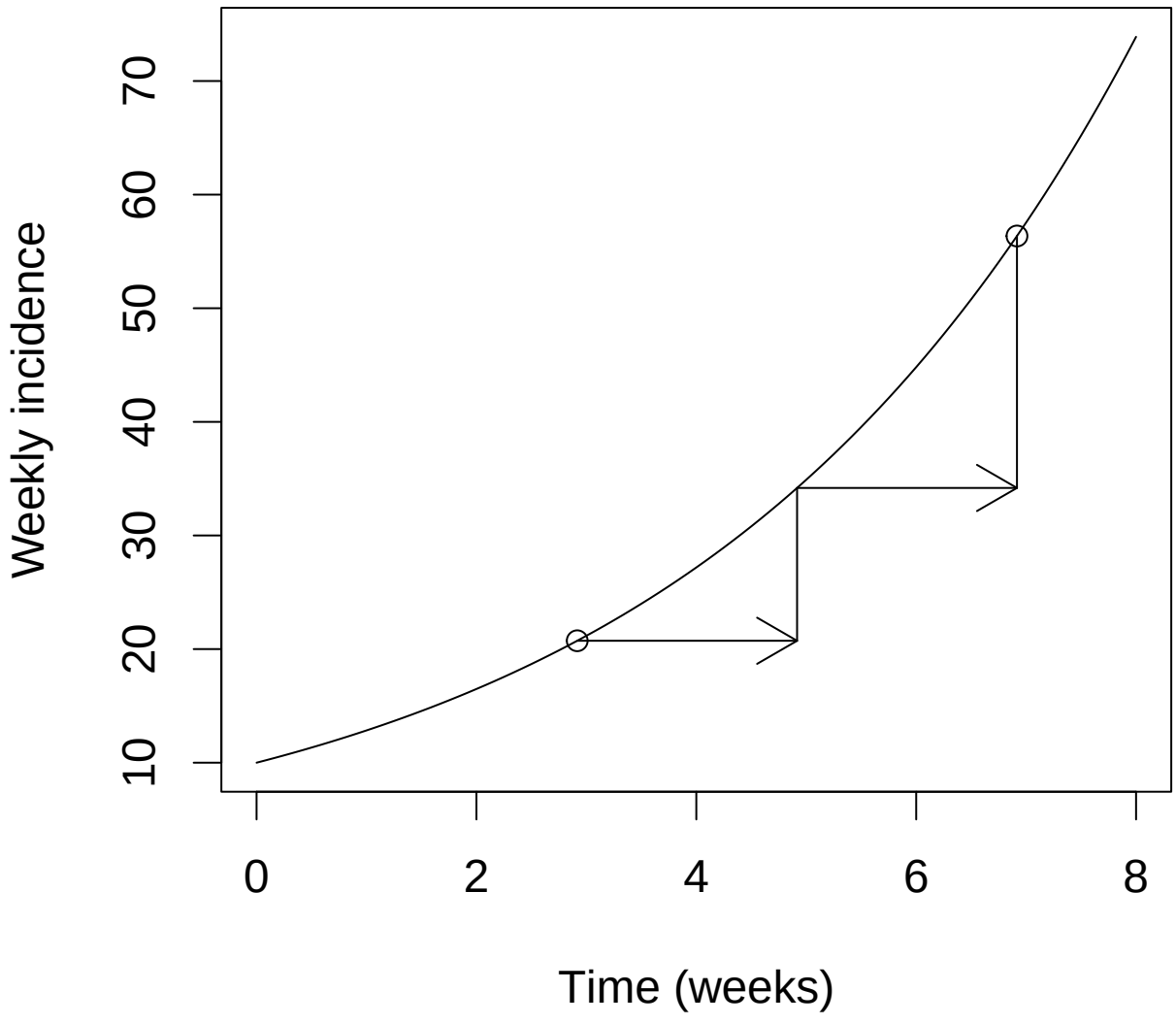
Generation time and risk

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

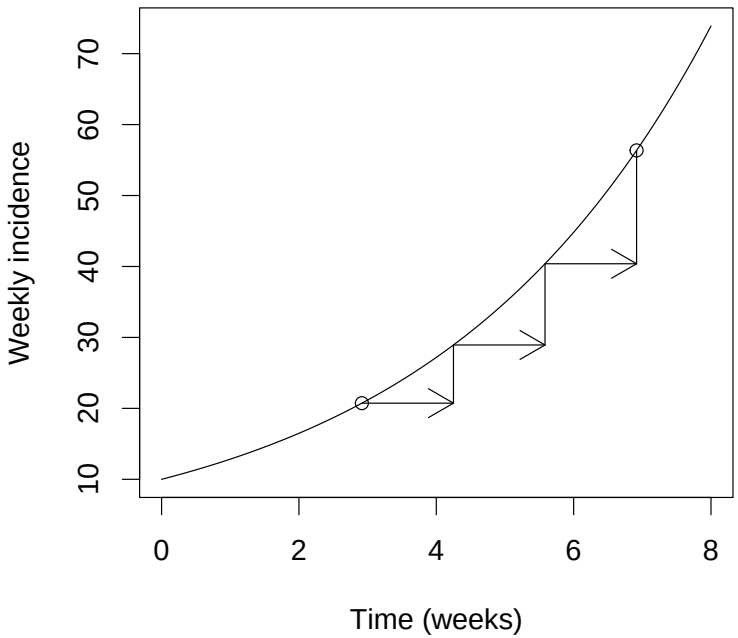
Generation time and risk (preview)

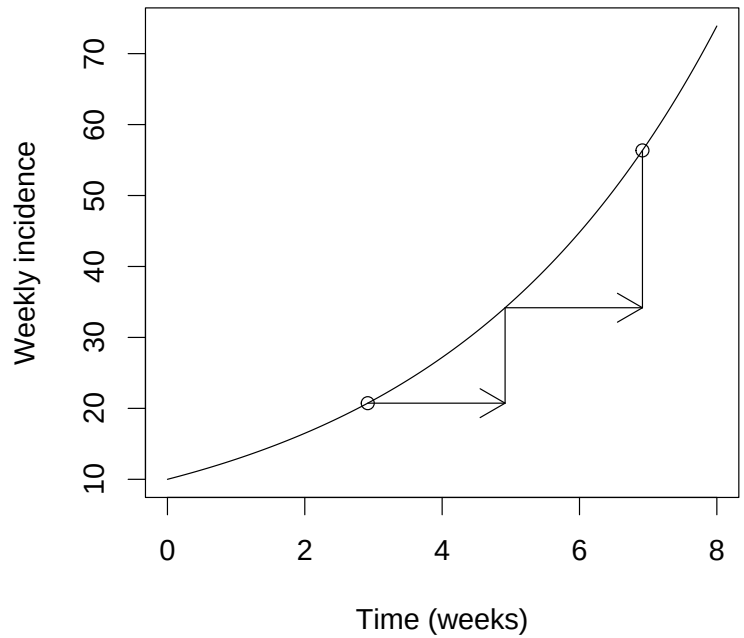


Generation time and risk (preview)



Generation time and risk



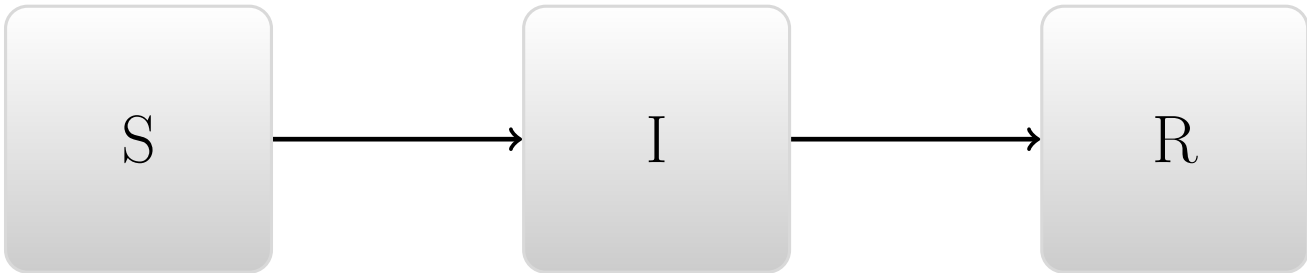


Generation time and risk

- $\mathcal{R} = \exp(r\hat{G})$
- An intuitive view:
  - Epidemic speed = Generation strength $\times$ Generation speed
  - *Mathematically:* $r = \log(\mathcal{R}) * (1/\hat{G})$
- If we know generation speed, then a faster epidemic speed means:
  - * More strength required (greater $\mathcal{R}$)
- If we know epidemic speed, a faster generation speed means
  - * Less strength required (smaller $\mathcal{R}$)

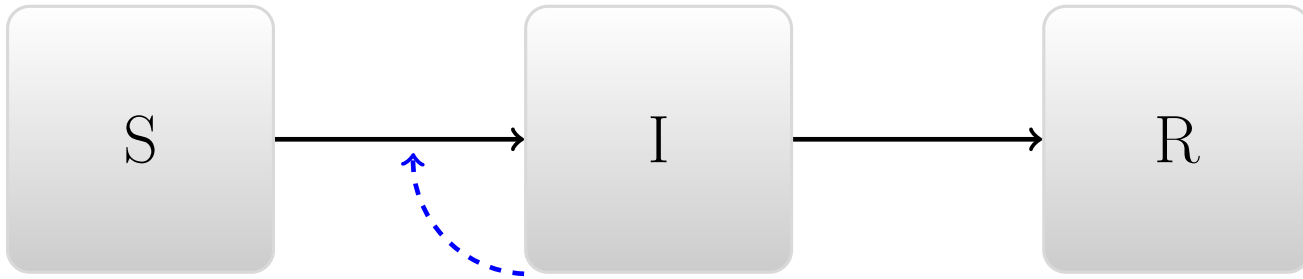
Outline

Single-epidemic model



- Susceptible $\rightarrow$ Infectious $\rightarrow$ Recovered
- We also use N to mean the total population

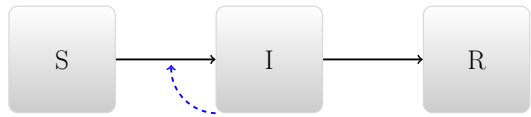
Transition rates



- 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?
  - * The *may be* an **epidemic** – an outbreak of disease
  - * Disease burns out
  - * Everyone winds up either recovered
    - * . . . or susceptible

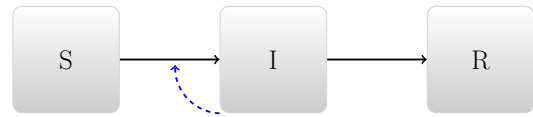


Interpreting

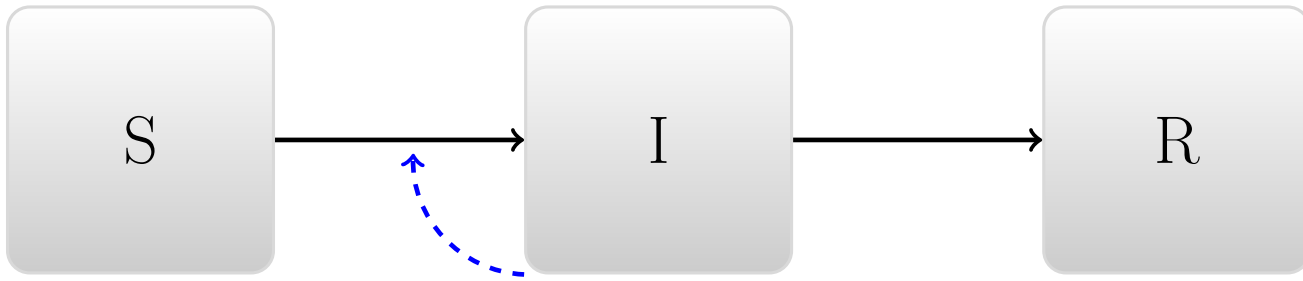
- Why might there not be an epidemic?
  - * If the disease can't spread well enough in the population
    - * Could depend on season, or immunity . . .
  - * Demographic stochasticity: if we only start with one individual, we expect an element of chance
- Why doesn't everyone get infected?
  - * NOANS

Implementing the model

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



Quantities



State variables

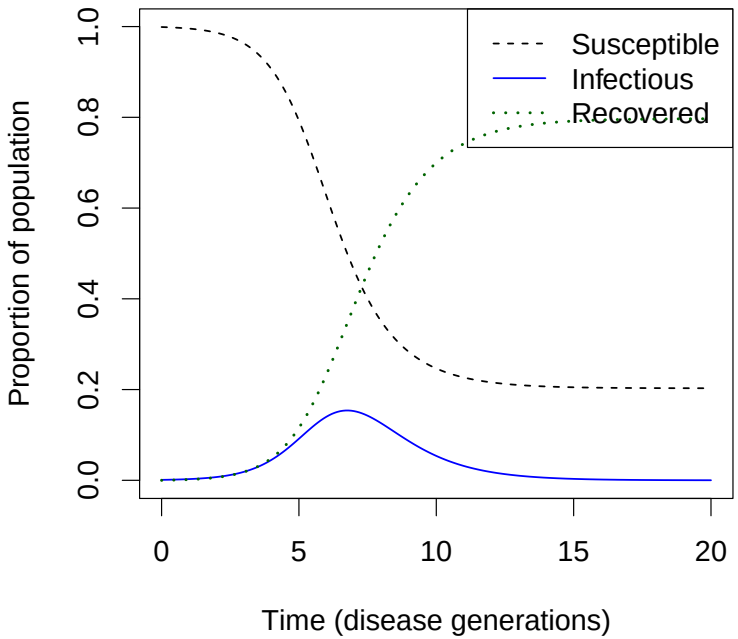
- S, I, R, N: [people] or [people/ha]

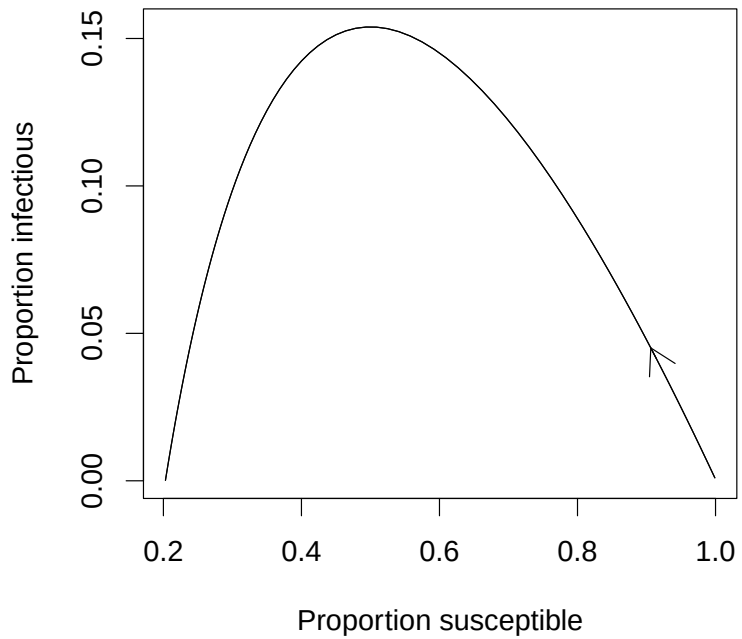
Quantities

Parameters

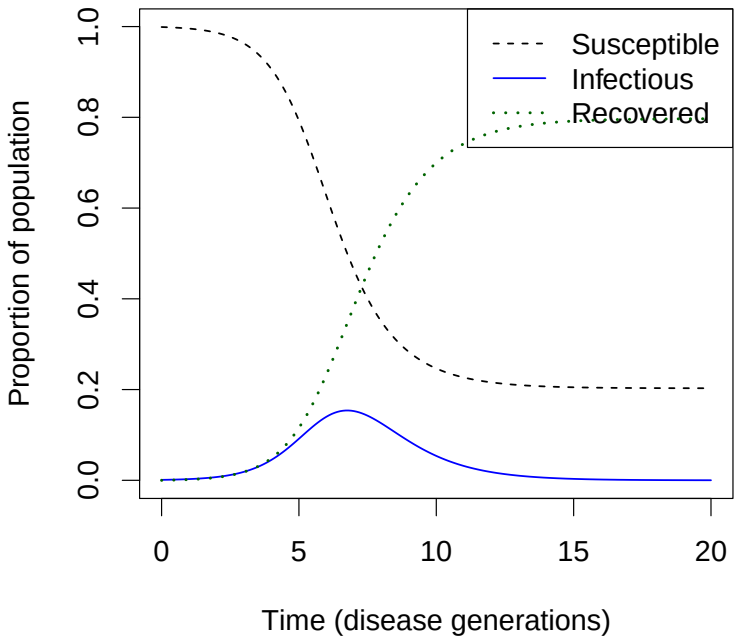
- Susceptible people have **potentially effective** contacts at rate β (units [1/time])
  - These are contacts that would lead to infection if the person contacted is infectious
  - Total infection rate is $\beta I/N$, because I/N is the proportion of the population infectious
- Infectious people recover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

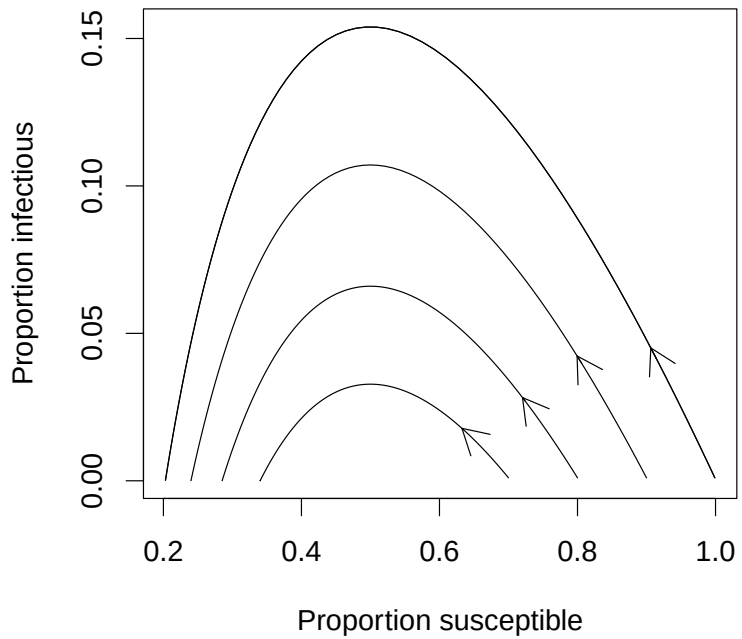
Simulating the model (preview)





Simulating the model





Basic reproductive number

- What *unitless* parameter can you make from the model above?
  - * $\mathcal{R}_0 = \beta D = \beta/\gamma$ is the **basic reproductive number**
  - * The *potential* number of infections caused by an average infectious individual
    - * That is: the number they would cause on average if everyone else were susceptible
  - * The product of the rate β (units [1/t]) and the duration D ([t])

Basic reproductive number implications

- What happens early in the epidemic if $\mathcal{R}_0 > 1$?
  - * Number of infected individuals grows exponentially
- What happens early in the epidemic if $\mathcal{R}_0 < 1$?
  - * Number of infected individuals does not 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:
  - * $\mathcal{R}_{\text{eff}} = \mathcal{R}_0 S/N$
- Is the disease increasing or decreasing?
  - * It will increase when $\mathcal{R}_{\text{eff}} > 1$ (more than one case per case)
  - * This happens when $S/N > 1/\mathcal{R}_0$
- Why doesn't everyone get infected?
  - * When susceptibles are low enough $\mathcal{R}_{\text{eff}} < 1$
  - * When $\mathcal{R}_{\text{eff}} < 1$, the disease dies out on its own (less than one case per case)

Outline

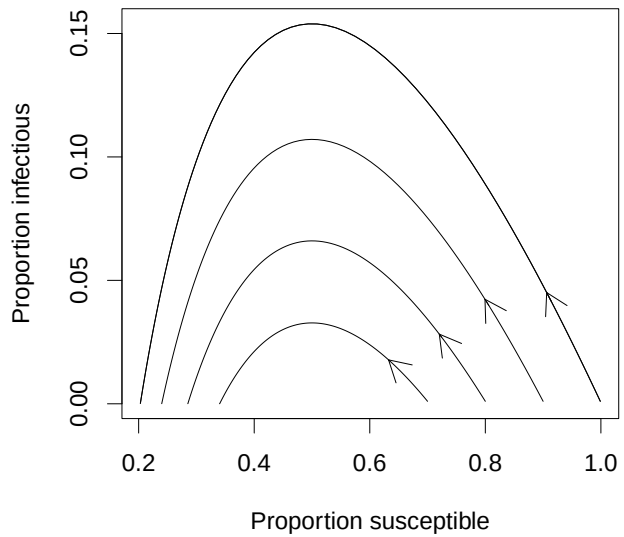
Epidemic size

- In this model, the epidemic always burns out
  - No source of new susceptibles
- Epidemic size is determined by:
  - * $\mathcal{R}_0$: larger $\mathcal{R}_0$ leads to a bigger epidemic
  - * The number of susceptibles at the beginning of the epidemic
    - * More susceptibles leads to a bigger epidemic
    - * . . . and *fewer* susceptibles at the end
  - * The number of infected individuals at the beginning of the epidemic
    - * Usually relatively small (and a relatively small effect)

Overshoot

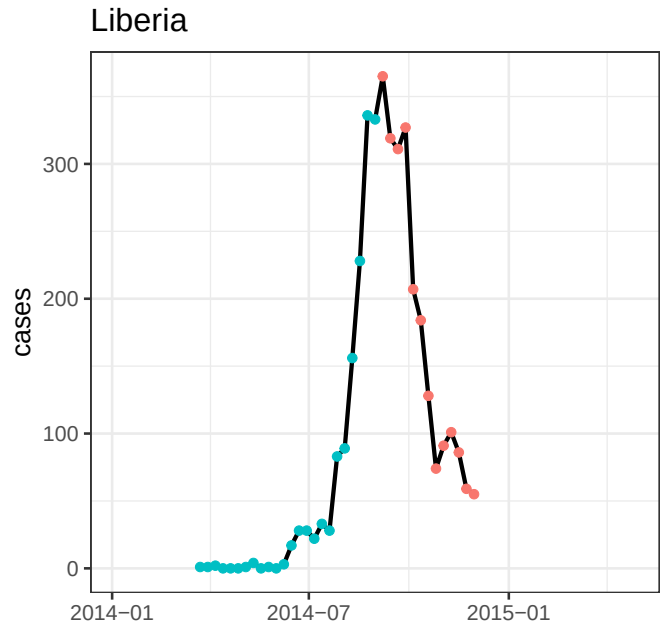
- Why does more susceptibles at the beginning mean fewer susceptibles at the end?
  - * More susceptibles $\Longrightarrow$
  - * Faster initial growth $\Longrightarrow$
  - * Bigger epidemic $\Longrightarrow$
  - * More infections at peak (same number of susceptibles) $\Longrightarrow$
  - * More generations needed for disease to fade out $\Longrightarrow$
  - * More infections after peak

    ...



Ebola example

- In September, the US CDC predicted "as many as" 1.5 million Ebola cases in Liberia by January
- In fact, their model predicted many *more* cases than that by April
- What happened?



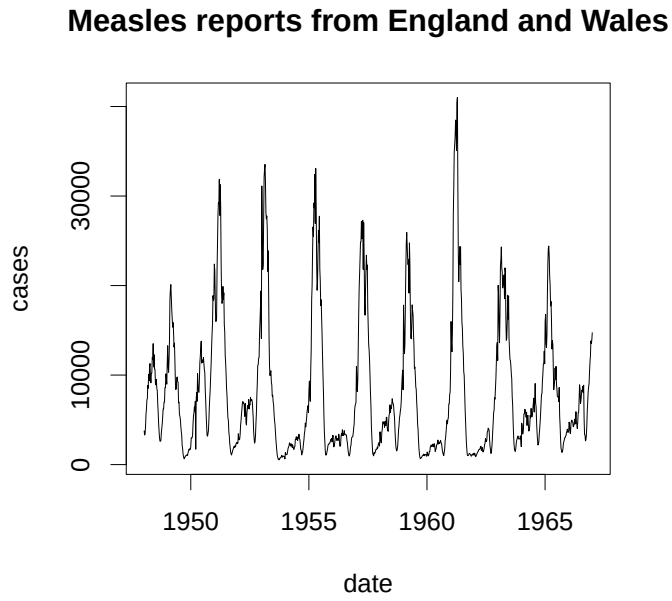
What limits epidemics?

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

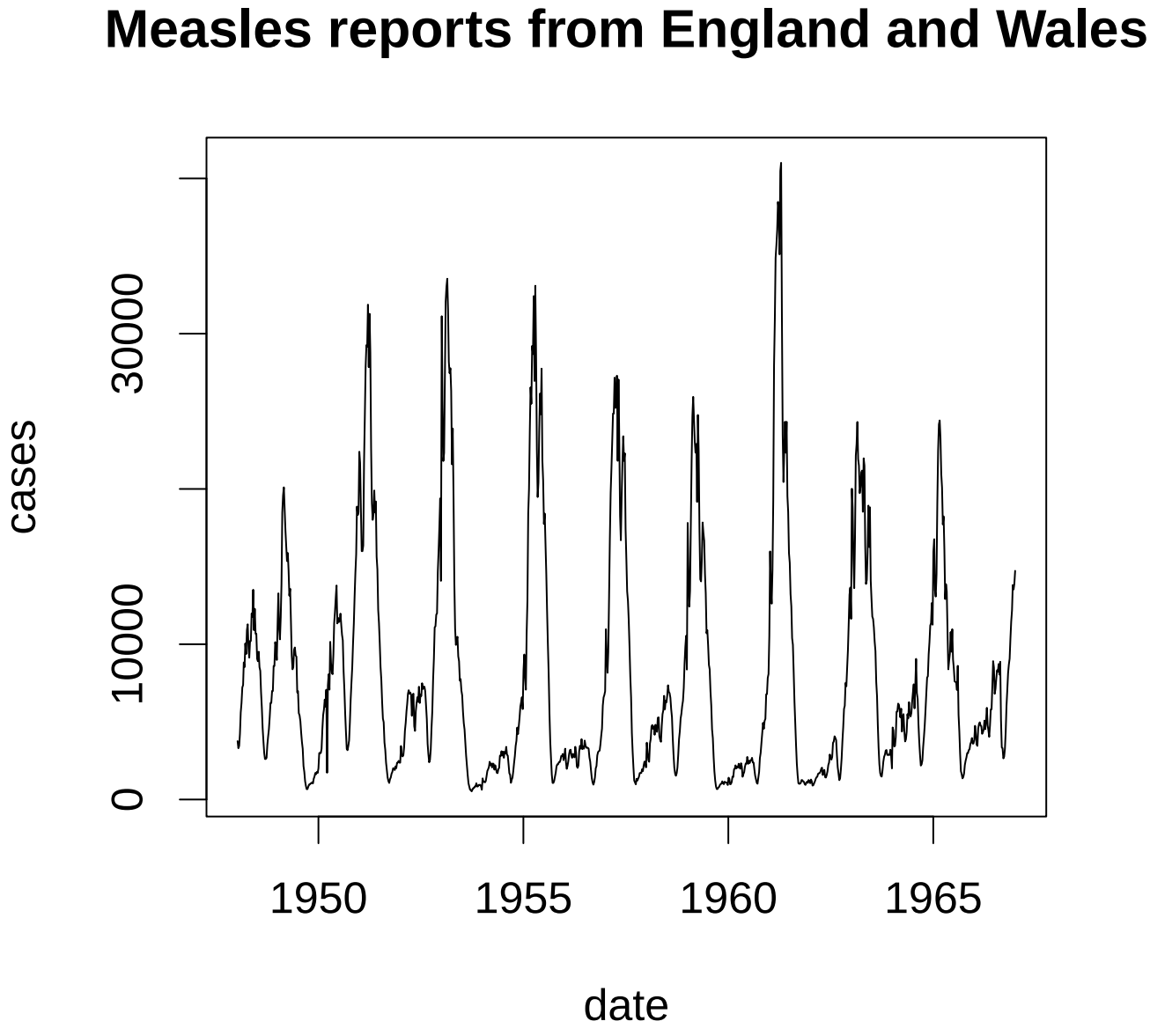
Outline

Recurrent epidemic models

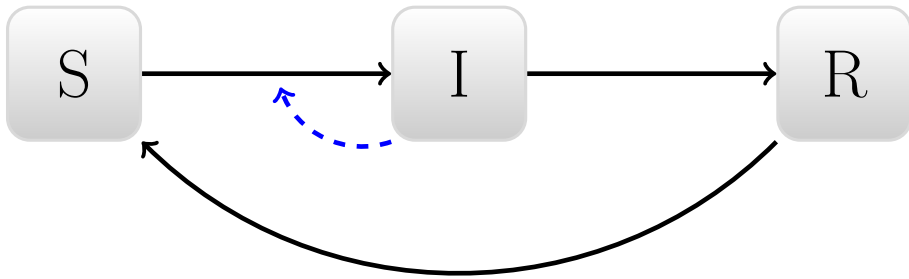
- If epidemics tend to burn out, why do we often see repeated epidemics?
  - * People might lose immunity
  - * Births and deaths; newborns are susceptible



Recurrent epidemics

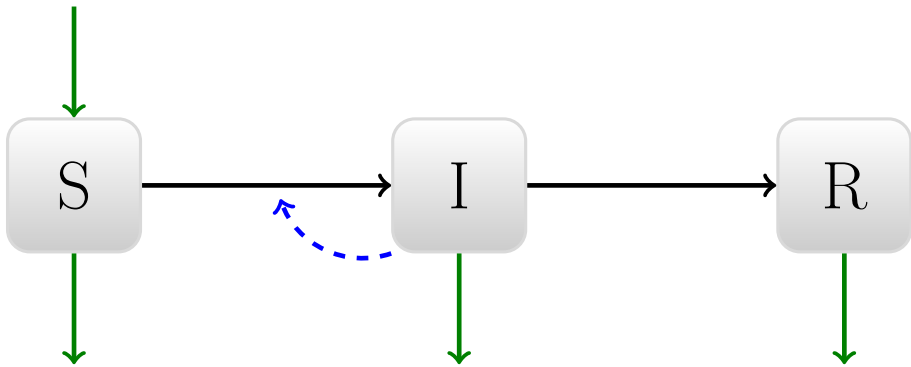


Closing the circle



- * Loss of immunity

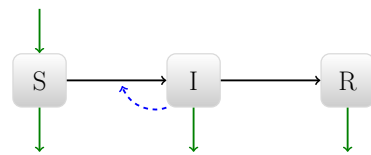
Closing the circle



- * Births and deaths
  - * Effect on dynamics is similar to loss of immunity

Births and deaths

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



- We often assume $b = d$
  - $\Longrightarrow$ population is constant

Outline

Equilibrium

- At equilibrium, we know that $\mathcal{R}_{\text{eff}} = 1$
  - One case per case
  - Number of susceptibles at equilibrium determined by the number required to keep infection in balance
    - $S/N = 1/\mathcal{R}_0$
- What does this remind you of?
  - * Reciprocal control!

Equilibrium

- Number of infectious individuals determined by number required to keep susceptibles in balance.
- As susceptibles go up, what happens?
  - Per capita replenishment goes down
  - Infections required goes down

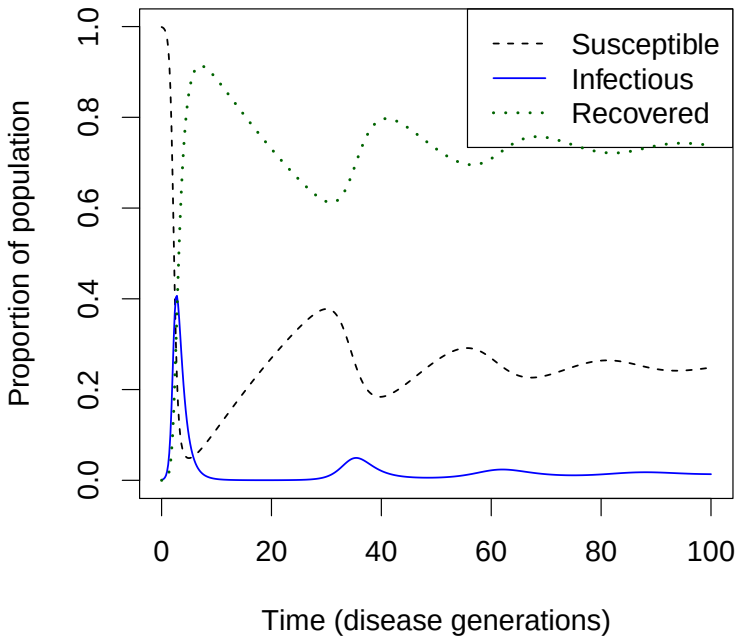
Reciprocal control

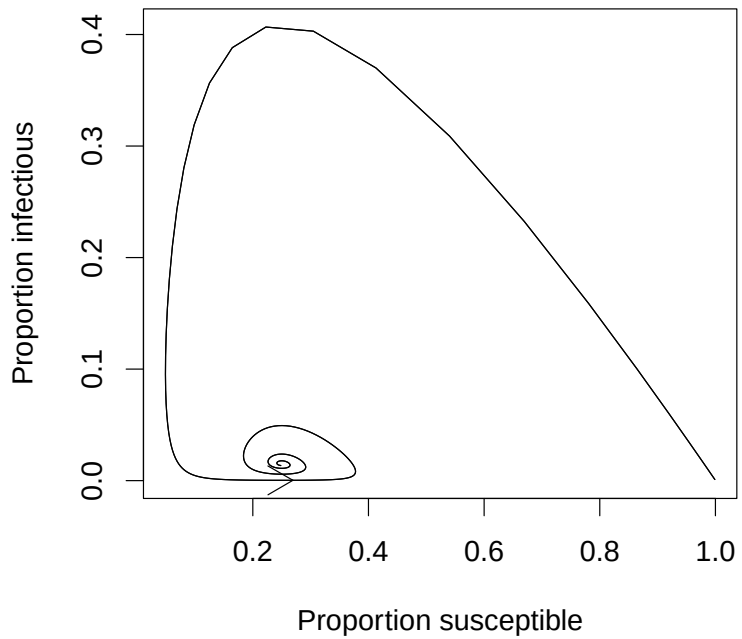
- What happens to *equilibrium* if we protect susceptibles (move them to R class)?
  - * Equation for dI/dt does not change
  - * Number of susceptibles at equilibrium does not change
  - * Fewer susceptibles removed by infection (some are removed by us)
  - * Less disease
- What else could happen?
  - * If we remove susceptibles fast enough, infection could go extinct
  - * If we keep increasing the rate ...
    - * Number of susceptibles goes down

Reciprocal control

- What happens if we remove infectious individuals at a constant rate (find them and cure them or isolate them)?
  - * We need more susceptibles to balance dI/dt
  - * If we have more susceptibles, then per capita replenishment goes down
    - * So the number of infectious individuals required for balance goes down
  - * If we remove infectious individuals fast enough, the infection could go extinct

Tendency to oscillate





Tendency to oscillate

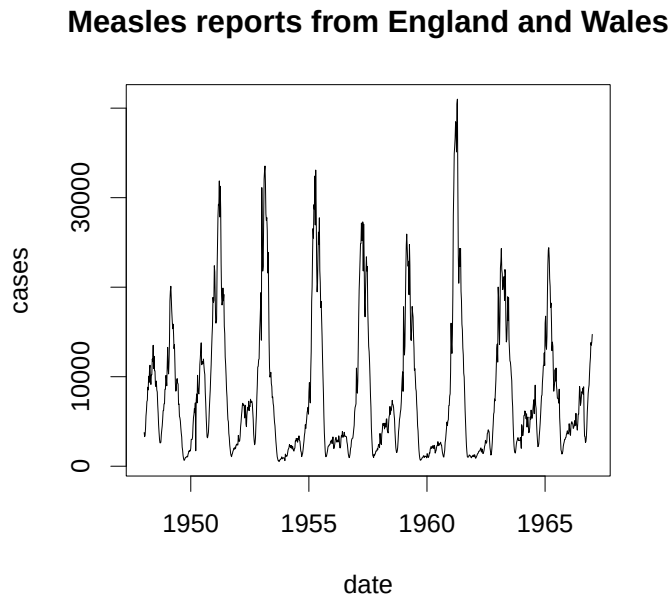
- "Closed-loop" SIR models (ie., with births or loss of immunity):
  - Tend to oscillate
  - Oscillations tend to be damped
    - System reaches an **endemic** equilibrium – disease persists

Source of oscillations

- Similar to predator-prey systems
- What happens if we start with too many susceptibles?
  - * There will be a big epidemic
  - * . . . then a very low number of susceptibles
  - * . . . then a very low level of disease
  - * . . . 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?
  - * Weather
    - * Seasonality
    - * Environmental stochasticity
  - * School terms
  - * Demographic stochasticity
  - * Changes in Behaviour
    - * People are more careful when disease levels are high

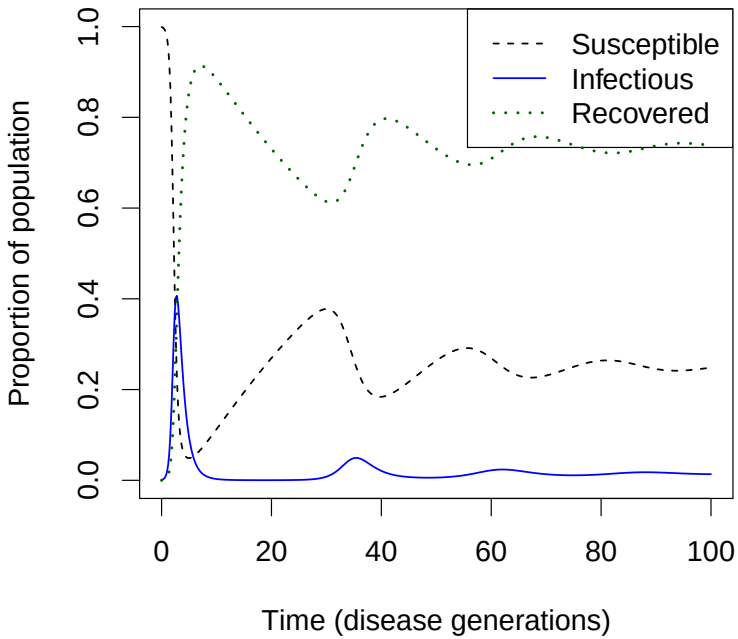


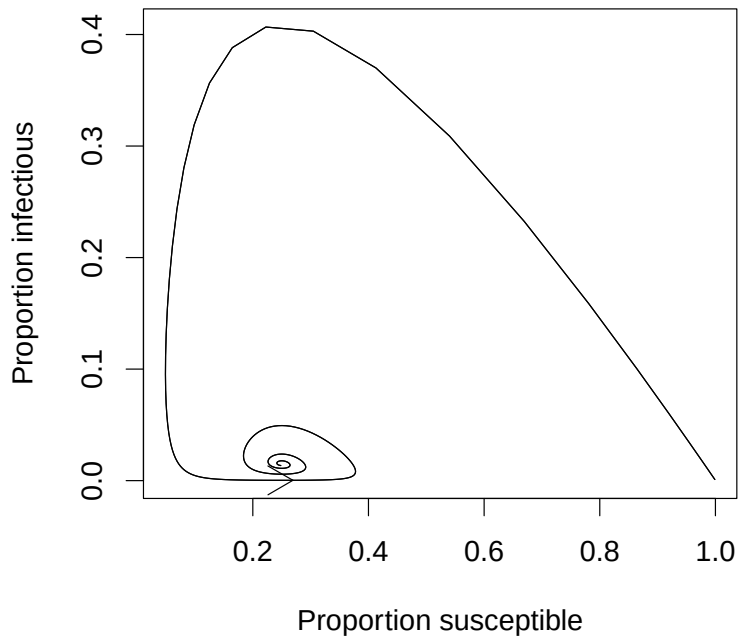
Outline

Reproductive numbers and risk

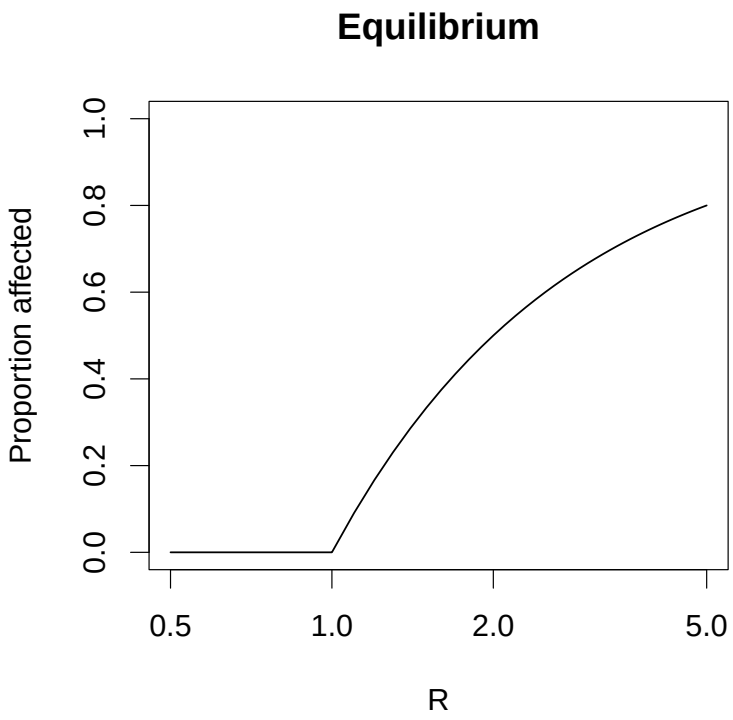
- At equilibrium, the proportion of people who are susceptible to disease should be approximately $S/N = 1/\mathcal{R}_0$
- Proportion "affected" (infectious or immune) should be approximately $V/N = 1 - 1/\mathcal{R}_0$
- If you have a single, fast epidemic, the size is also predicted by $\mathcal{R}_0$.

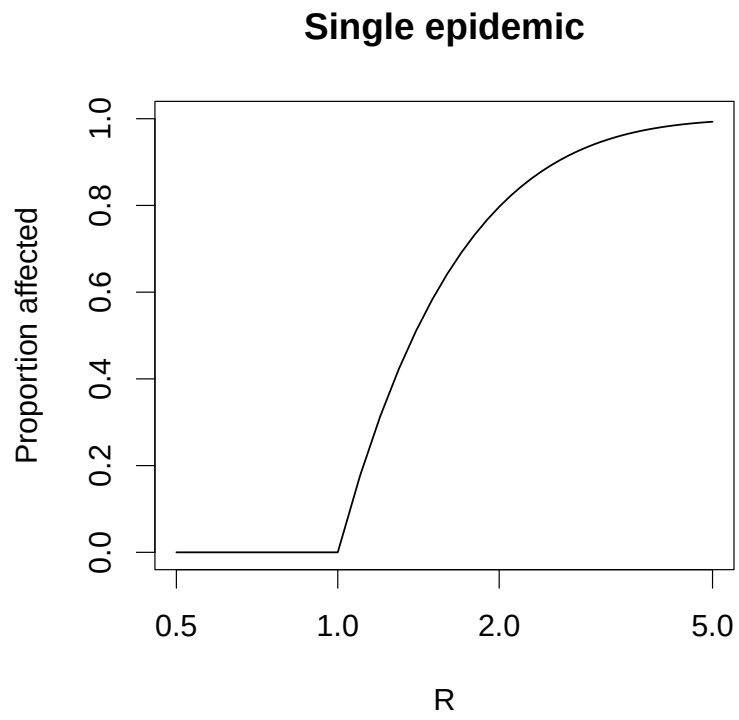
Reproductive numbers and risk (repeat)





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?
  - * Transmission should be reduced by a factor of $\mathcal{R}$, so at least 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?
  - * At least 1-1/5 = 80%
- Measles has an $\mathcal{R}_0$ of about 20. What proportion of the population should be vaccinated to eliminate measles?
  - * At least 1-1/20 = 95%
- If gonorrhea has an $\mathcal{R}_0$ of about 2, what proportion of unprotected sexual encounters should be protected to eliminate gonorrhea?
  - * At least 1-1/2 = 50%

Persistence of infectious disease

- Why have infectious diseases persisted?
  - The pathogens *evolve*
  - Human populations are **heterogeneous**
    - People differ in: nutrition, exposure, access to care
  - Information and misinformation
    - Vaccine scares, trust in health care in general

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