Week 1: Determinants of Epidemic Growth

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Week 1 Overview

- ~~Monday, July 26:~~
  - ~~Introductory material, history of mathematical modeling~~
  - ~~Introduction to R~~
- Tuesday, July 27:
  - Epidemic determinants & parameters
  - Guided practice in R
- Wednesday. July 28:
  - Model structures
  - Plots & compartmental models in R

Objectives

- Learn the key determinants of epidemics
- Understand how these determinants are related to one another
- Learn to estimate these determinants in simple scenarios

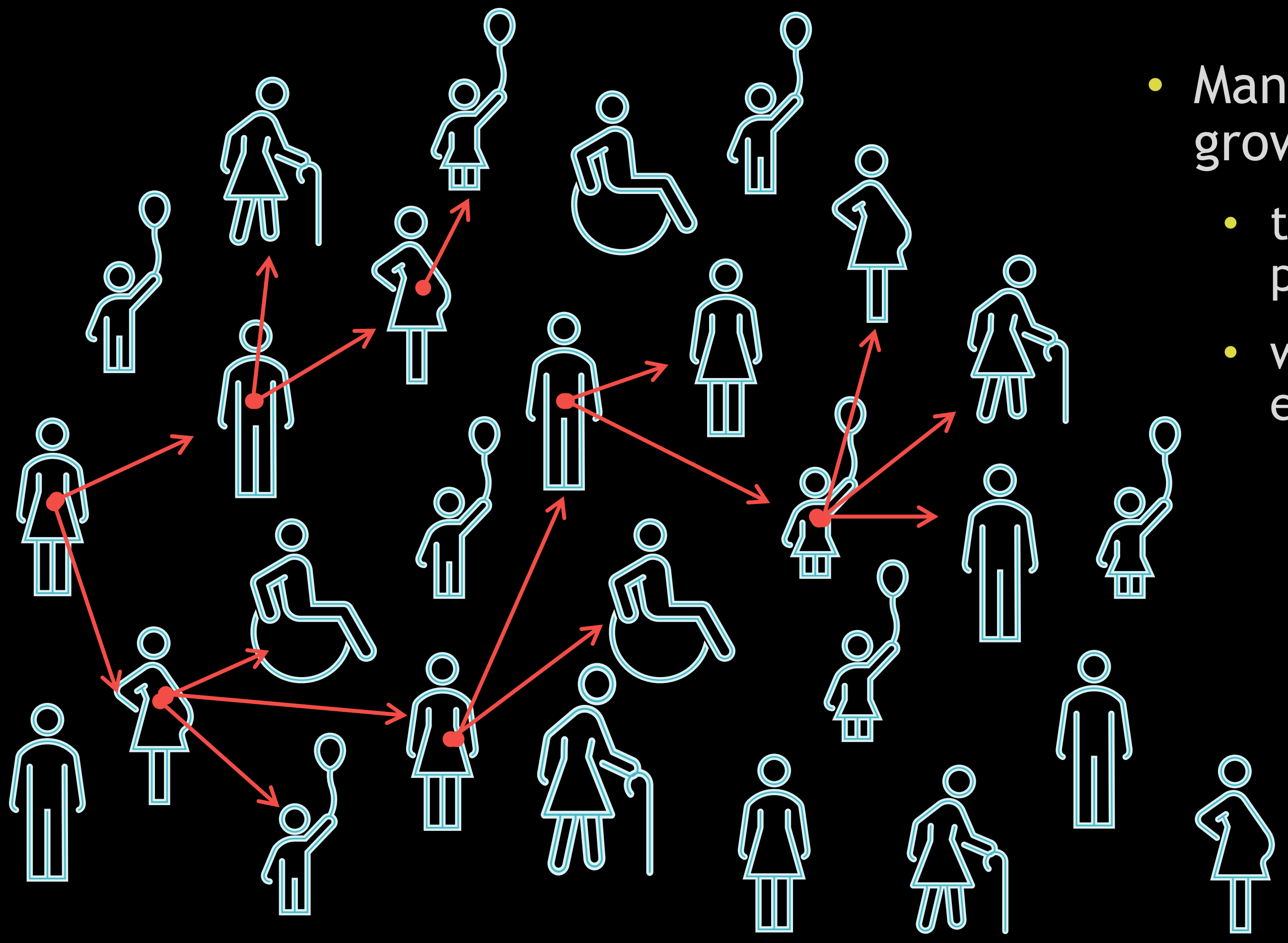
Post Questions in the Chat!

(we will have breaks to answer these during the workshop)

Workshop Schedule

Time	Topics
2:00—2:05 pm	Greetings
2:05—3:00 pm	Epidemic Determinants
3:00—3:10 pm	Break
3:10—4:00 pm	R Practical: Working with Data
4:00—4:10 pm	Break
4:10—5:00 pm	R Practical: Data Summaries

Determinants of Epidemic Growth



- Many factors contribute to the growth of an epidemic
  - these are often represented as parameters in our models
  - we are interested in trying to estimate these parameters

Doubling Time & Reproductive Number

Doubling Time

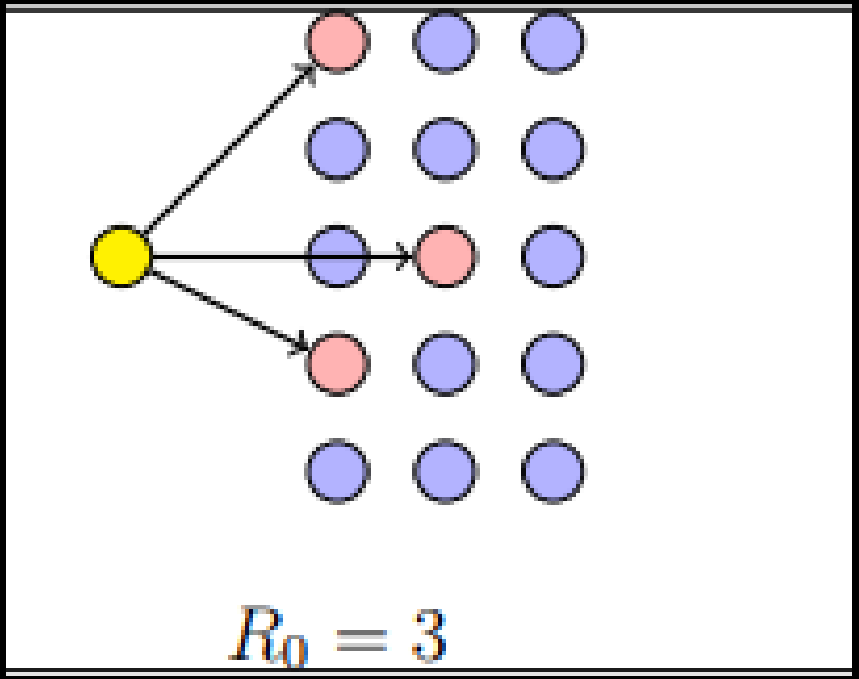
- Simple measure of growth
- The time it takes for the number of incident cases to double early in an epidemic
- Good measure of how quickly a disease spreads in a population

- $T_d = \dfrac{t_\tau - t_{\tau-1}}{\log_2\left(\dfrac{N_\tau}{N_{\tau-1}}\right)}$

- T_d : doubling time
- t_τ : time τ
- N_τ : number of incident cases at time τ

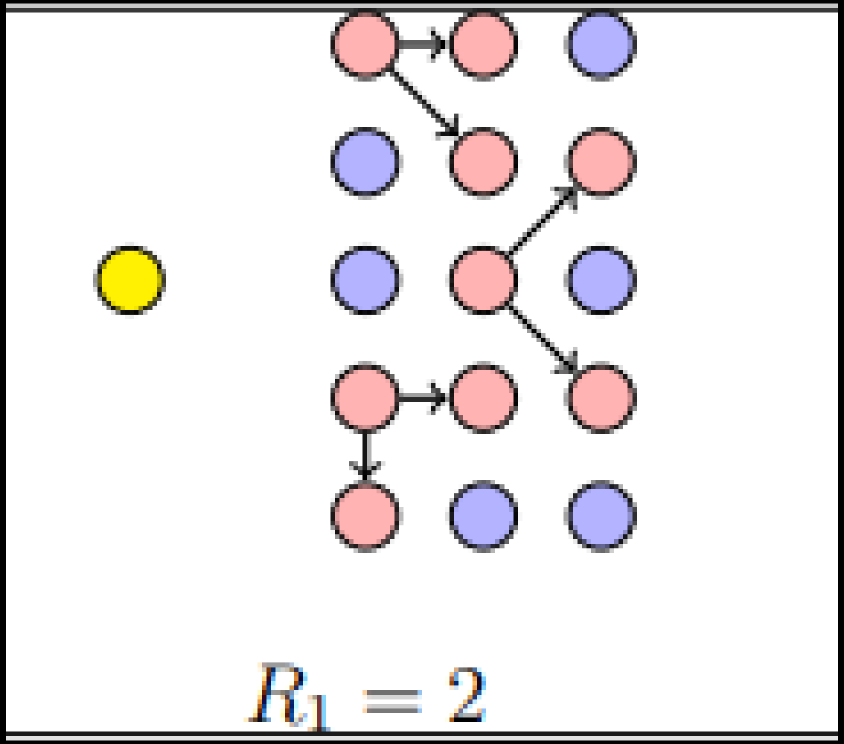
Reproductive Number

- Basic reproductive number (R_0), R-naught
  - the number of people a single case will infect in a completely susceptible population
  - the 0 indicates t=0, or the start of the epidemic when the population is completely susceptible and a case enters the population



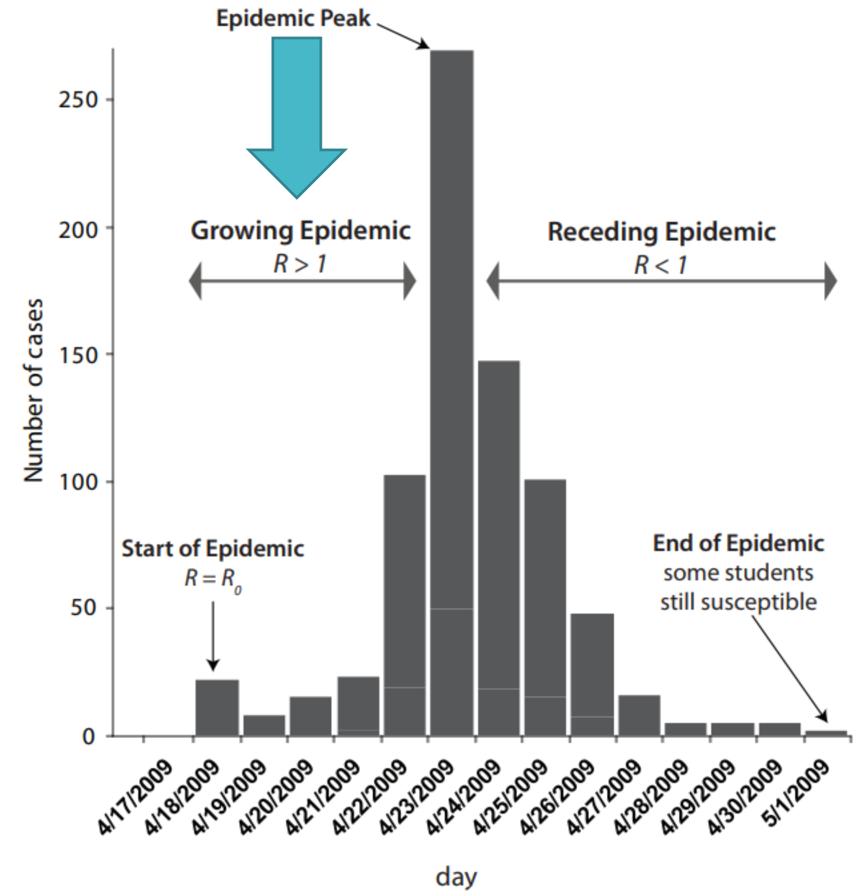
Reproductive Number

- Reproductive number (R_t)
  - sometimes called *net* reproductive number or *effective* reproductive number
  - the number of people a single infectious person will infect at time t, or when there is some immunity in the population
  - this has an impact on the doubling time



Reproductive Numbers & Epidemic Curve

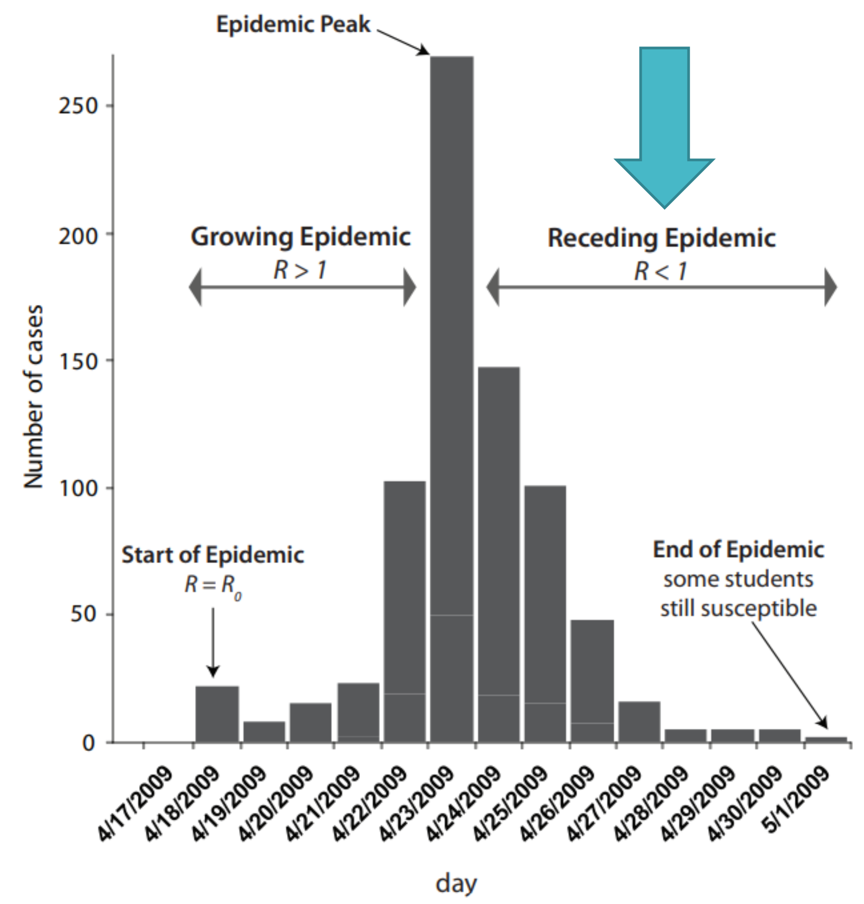
- Reproductive numbers change throughout an epidemic
  - Rt will correlate to trends in incidence
  - at the start, as long as Rt>1, the epidemic will grow
    - Rt>1 means each case causes more than one additional case



adapted from Lessler et al., NEJM 2009

Reproductive Numbers & Epidemic Curve

- Reproductive numbers change throughout an epidemic
  - as the epidemic continues, there will be fewer susceptible people and the reproductive number will decrease unless:
    - more susceptibles are added
    - something changes to increase transmission
  - if Rt=1, transmission will be stable
  - as soon as Rt<1, the epidemic will start to fade

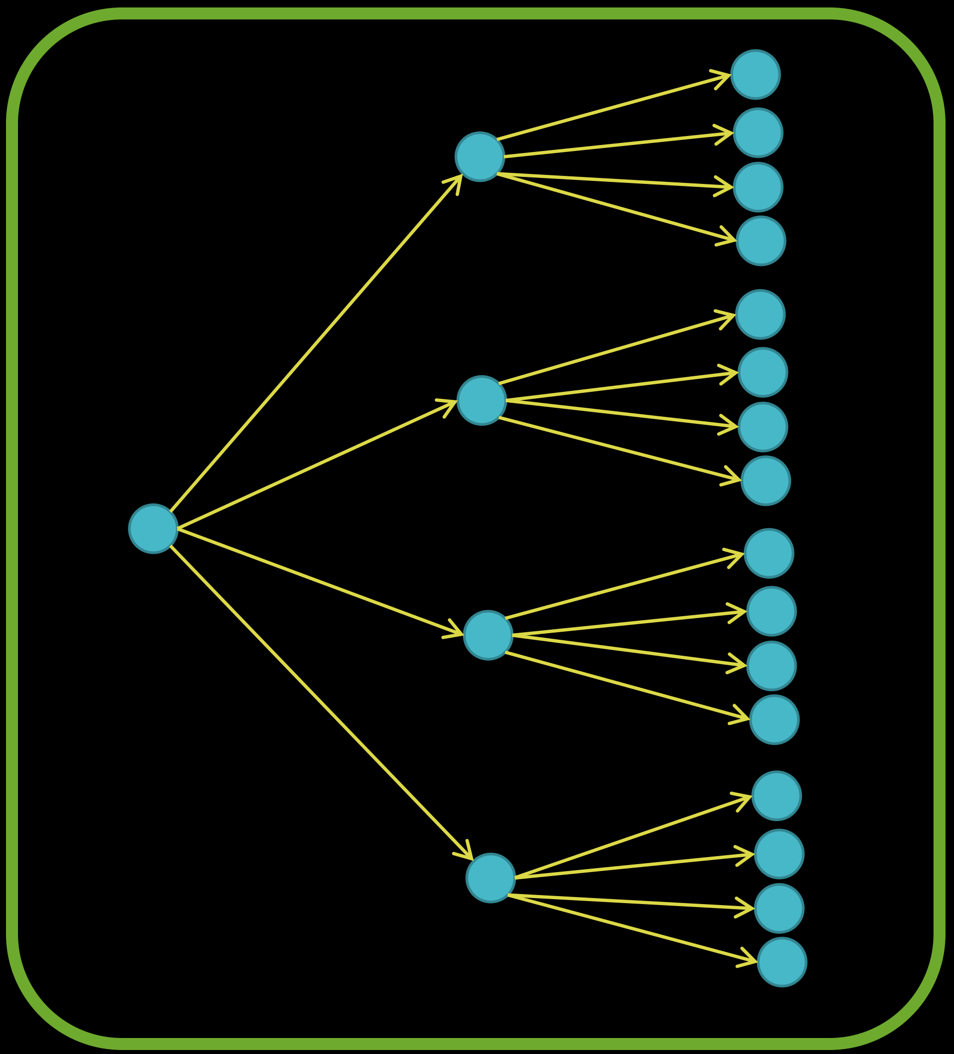


adapted from Lessler et al., NEJM 2009

What is the Reproductive Number?

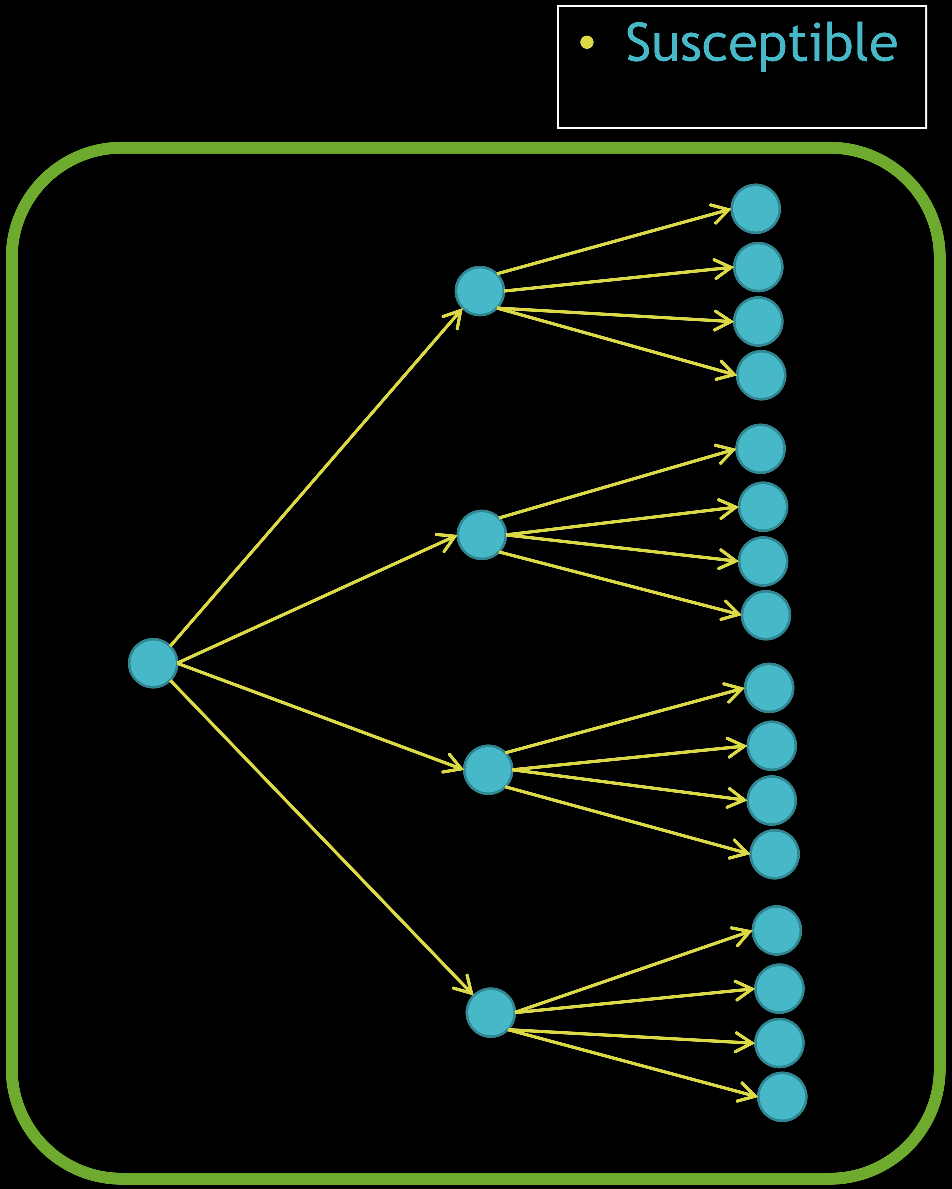
- Susceptible

- The entire population is susceptible
    - R0 or Rt?



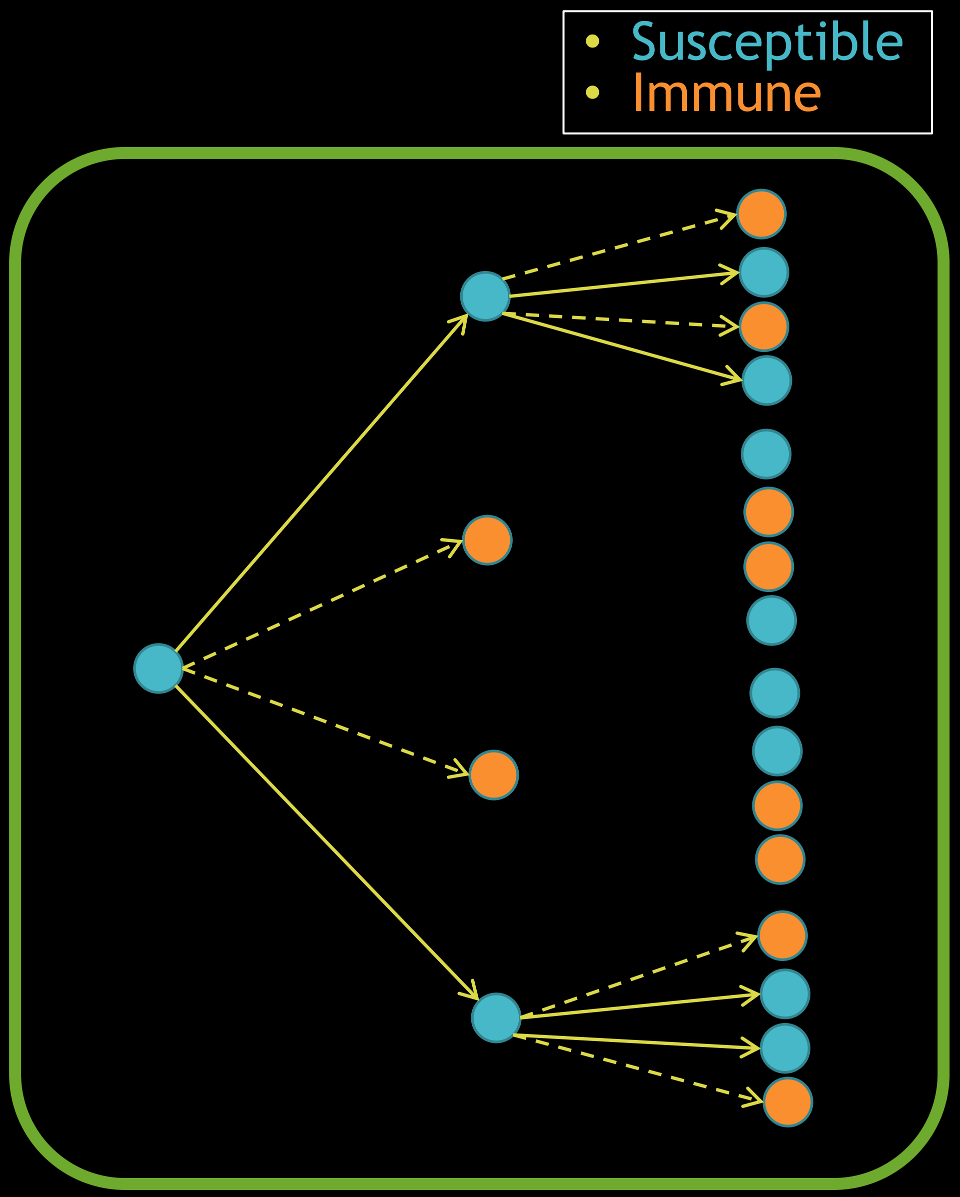
What is the Reproductive Number?

- The entire population is susceptible
  - R0=4



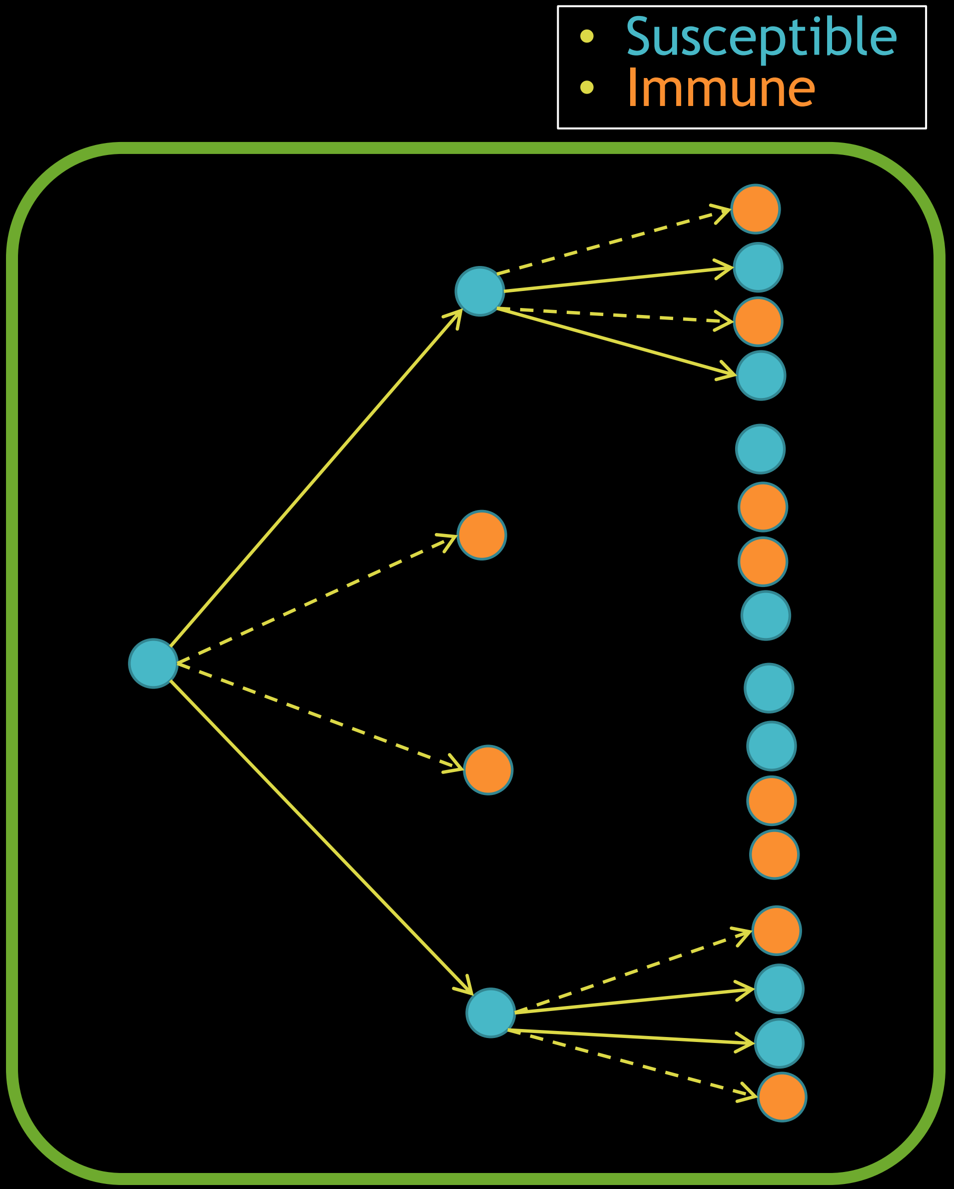
What is the Reproductive Number?

- Same population, but now 50% of the population is immune
    - R0 or Rt?



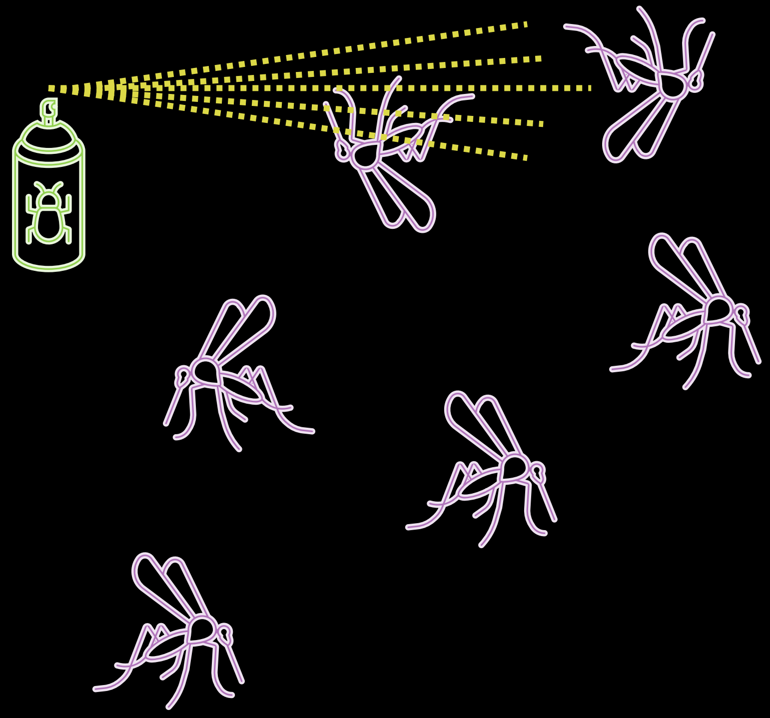
What is the Reproductive Number?

- Same population, but now 50% of the population is immune
  - R0=4
  - Rt=2
  - if there is random mixing, then the reproductive number is R0 time the proportion of susceptibles in the population
  - $R_t = R_0 s_t$



Reproductive Number & Disease Control

- our ability to control disease arises from knowledge that a reproductive number below 1 will results in decreasing incidence
- if we can calculate the reproductive number from its determinants, we can assess which control measures will cause a decline in the reproductive number
- estimating the reproductive number is a common modeling goal



Reproductive Number & Disease Control

- Do we need to eliminate mosquitoes to eliminate malaria?
  - malaria elimination was thought to be impossible
  - MacDonald demonstrated mathematically that an increase in mosquito mortality would eliminate malaria

- $R_0 = b^2 sa$

- b: mosquito biting rate
- s: time τ
- a: number of incident cases at time τ

Reproductive Numbers are Disease- and Setting-specific

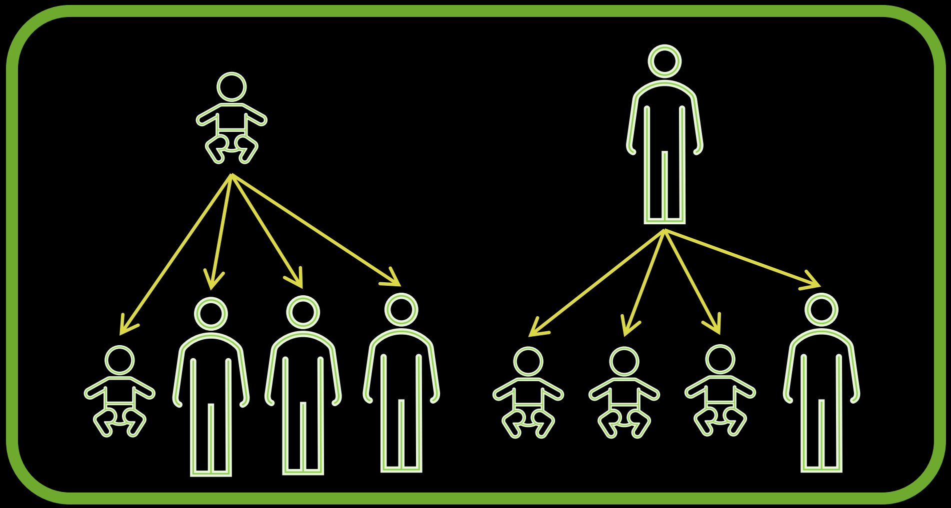
Pathogen	R0
Cholera	2.6, 5.0, 4.0—15.0
Dengue	1.3—6.3
Influenza	1.5—2.0
Malaria	1—10, 100—1000, 1—3000
Measles	7.7, 7.1—29.3, 11.0—18.0
Rubella	2.9—7.8, 3.4—5.6
SARS	1.2, 2.7, 2.2—3.6
Smallpox	3.2, 6.9, 3.5—6.0

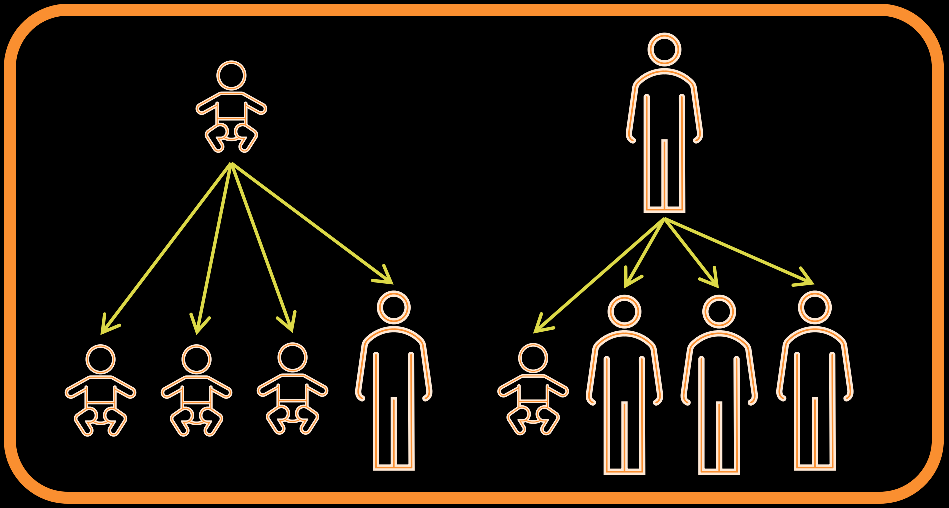
- For many diseases, the reproductive number will be very similar across different settings

Reproductive Number

- If there is not random mixing, R0 is more difficult to calculate, but models can help achieve this
  - it is more likely that there is heterogenous mixing
  - not everyone has an equal chance of encountering everyone else in the population

- Population A
  - each infected child leads to 3 infections in adults, and 1 infection in children
  - each infected adult leads to 1 infection in adults and 3 infections in children
- Population B
  - each infected child leads to 1 infection in adults, and 3 infections in children
  - each infected adult leads to 3 infections in adults and 1 infection in children





Reproductive Number

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- Population B
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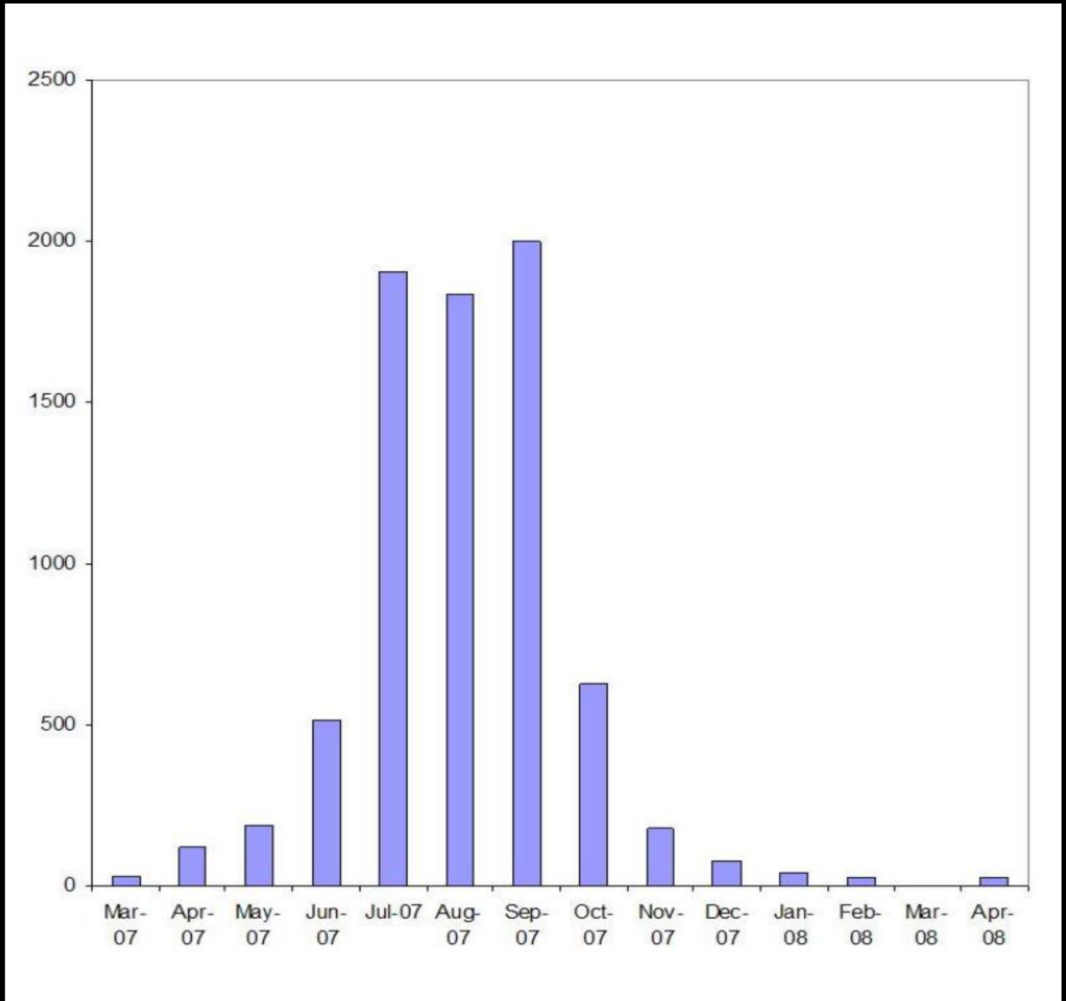
  - each infected adult leads to 3 infections in adults and 1 infection in children
- If we vaccinate children, which population would see the biggest effect?

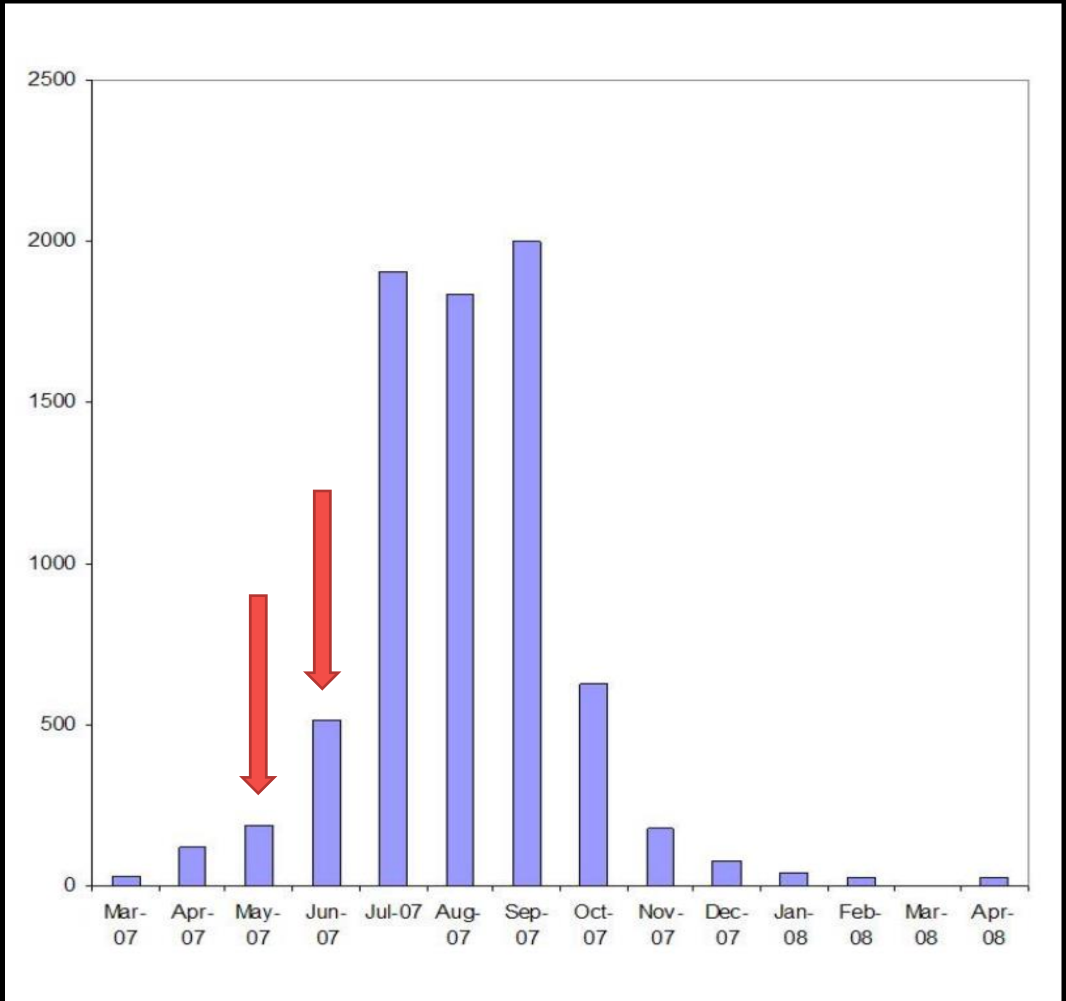
Generation Time & Serial Intervals



Generation Time & Epidemic Growth

- Measles outbreak in Iceland

$$T_d = \frac{t_\tau - t_{\tau-1}}{\log_2\left(\frac{N_\tau}{N_{\tau-1}}\right)}$$



Generation Time & Epidemic Growth

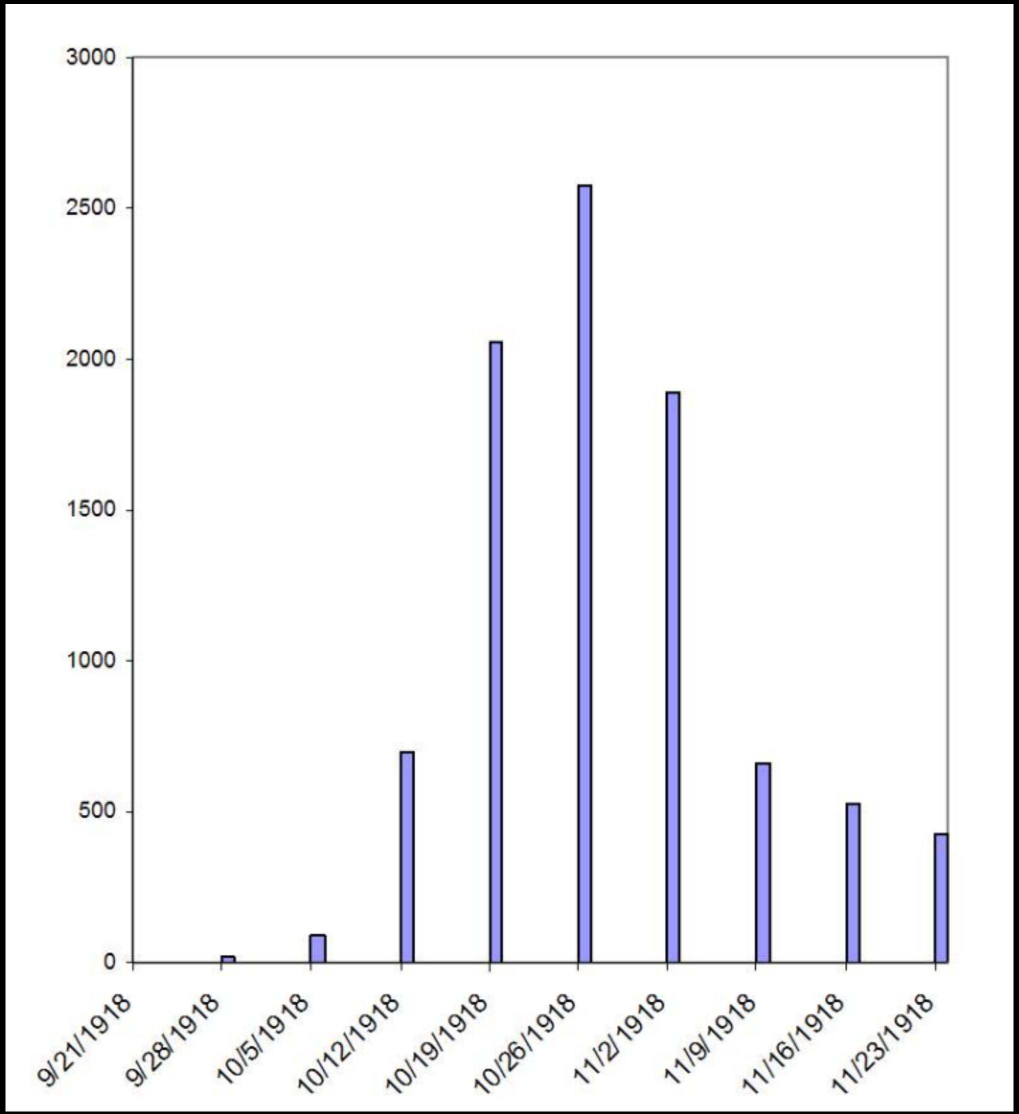
- Measles outbreak in Iceland

$$T_d = \frac{t_\tau - t_{\tau-1}}{\log_2\left(\frac{N_\tau}{N_{\tau-1}}\right)}$$

$$T_d = \frac{1\ month}{\log_2\left(\frac{514}{191}\right)}$$

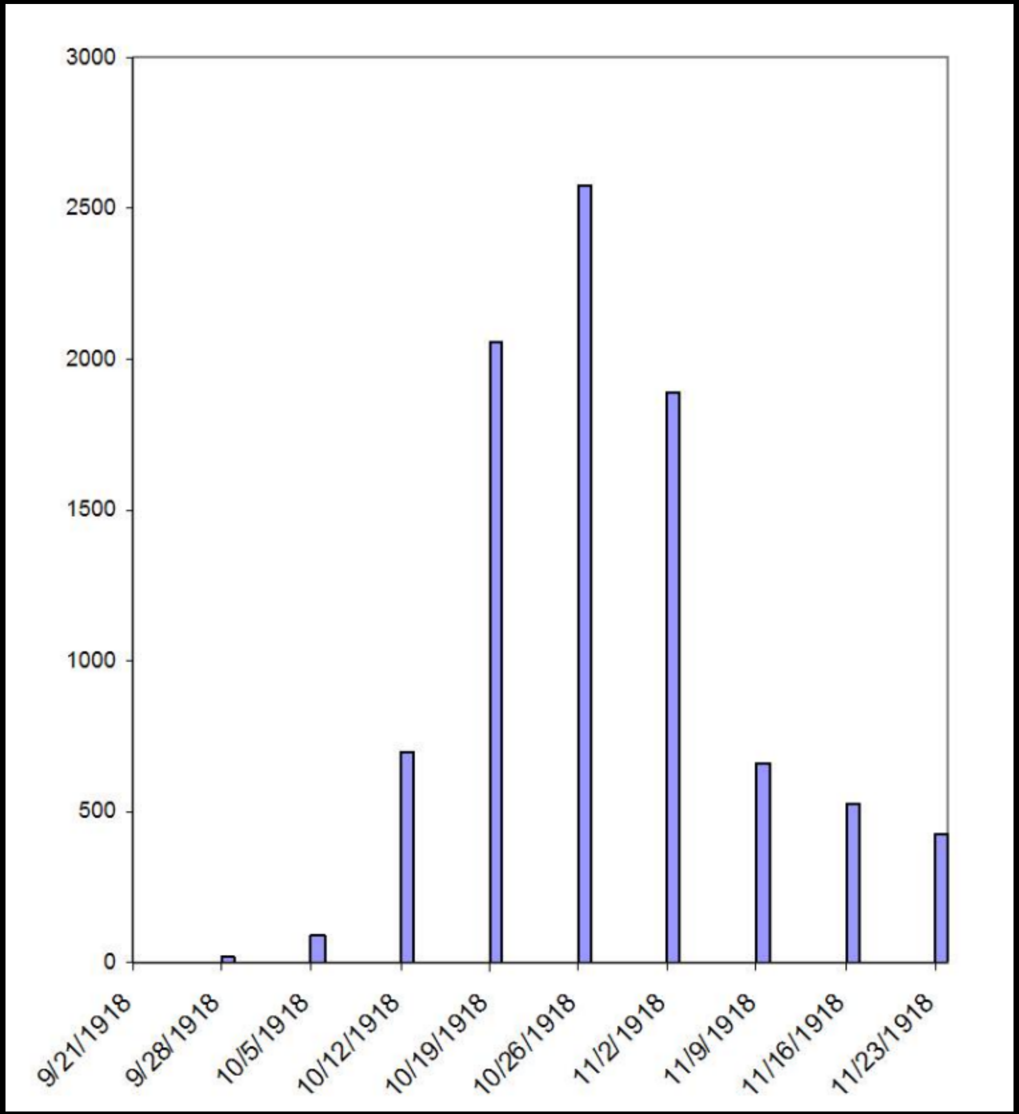
$$= 0.7\ months$$

- Doubling time ranges from 0.5—1.5 months during epidemic



Generation Time & Epidemic Growth

- Influenza outbreak in USA
- Doubling time ranges from 0.3—0.6 weeks during epidemic
- Comparing the two epidemics:
  - Measles: 0.7 months
  - Influenza: 0.6 weeks



Generation Time & Epidemic Growth

- Influenza outbreak in USA
- Doubling time ranges from 0.3—0.6 weeks during epidemic
- Comparing the two epidemics:
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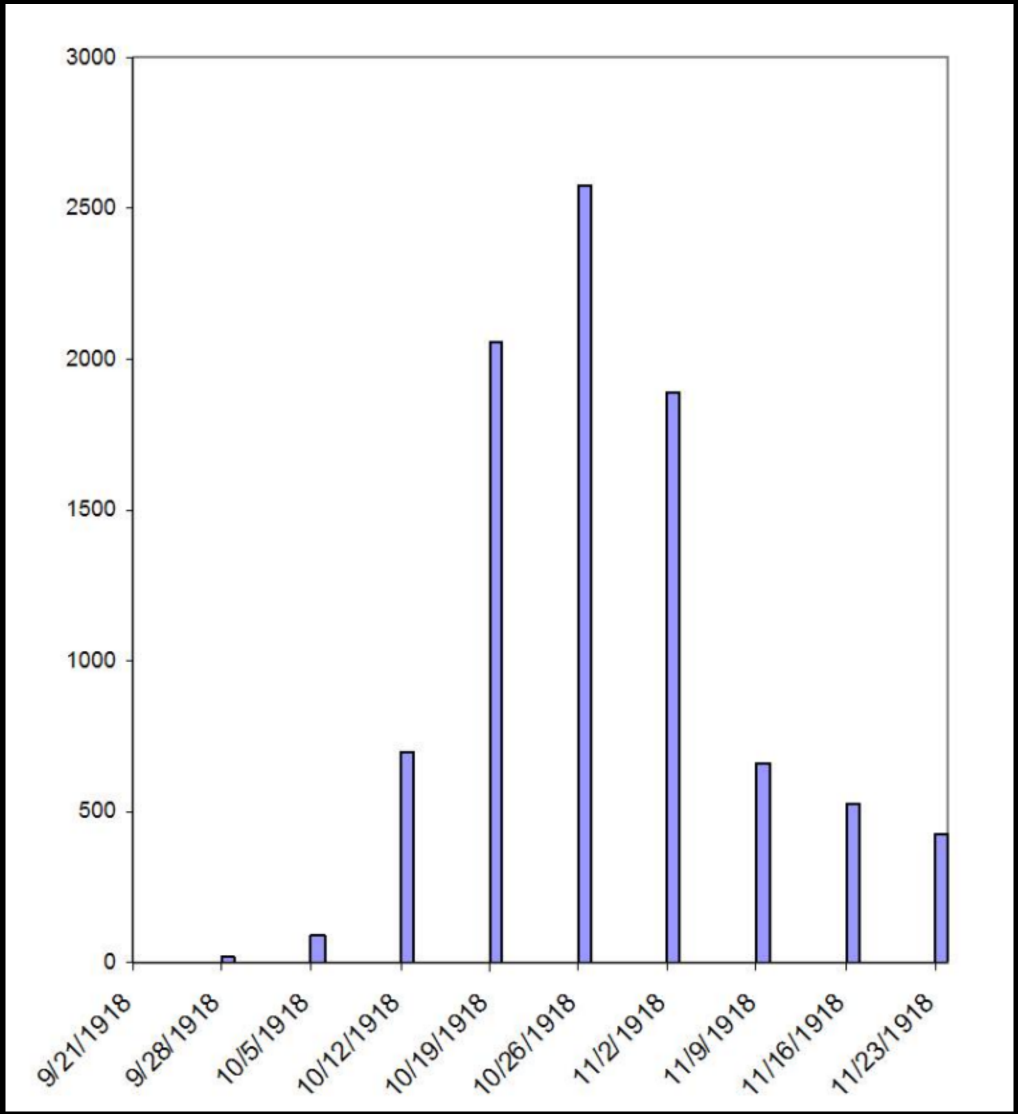
- But
  - Measles R_0=15
  - Influenza R_0=2



Generation Time & Epidemic Growth

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- Comparing the two epidemics:
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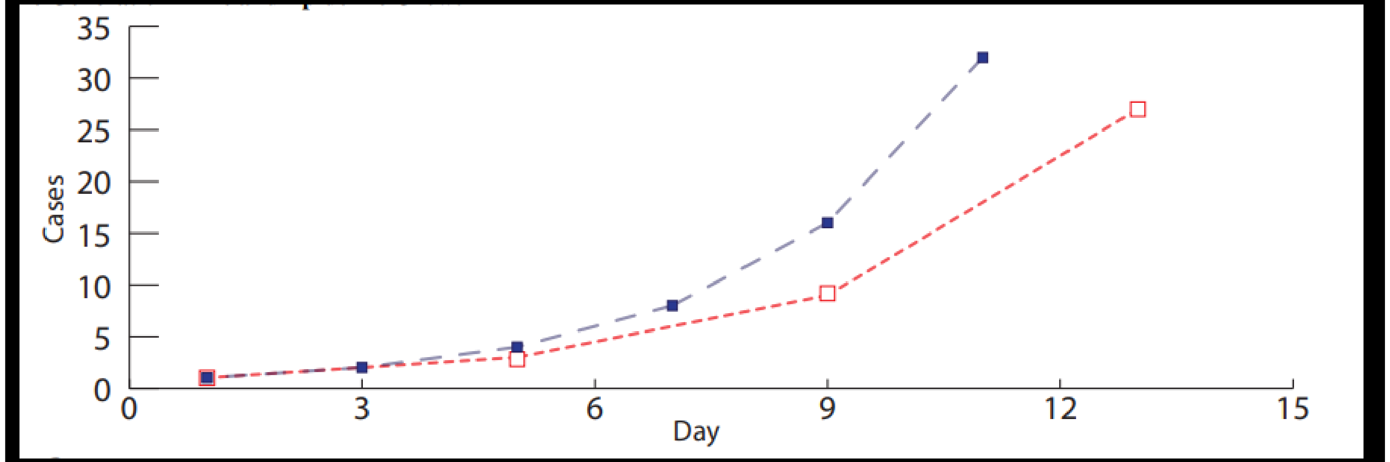
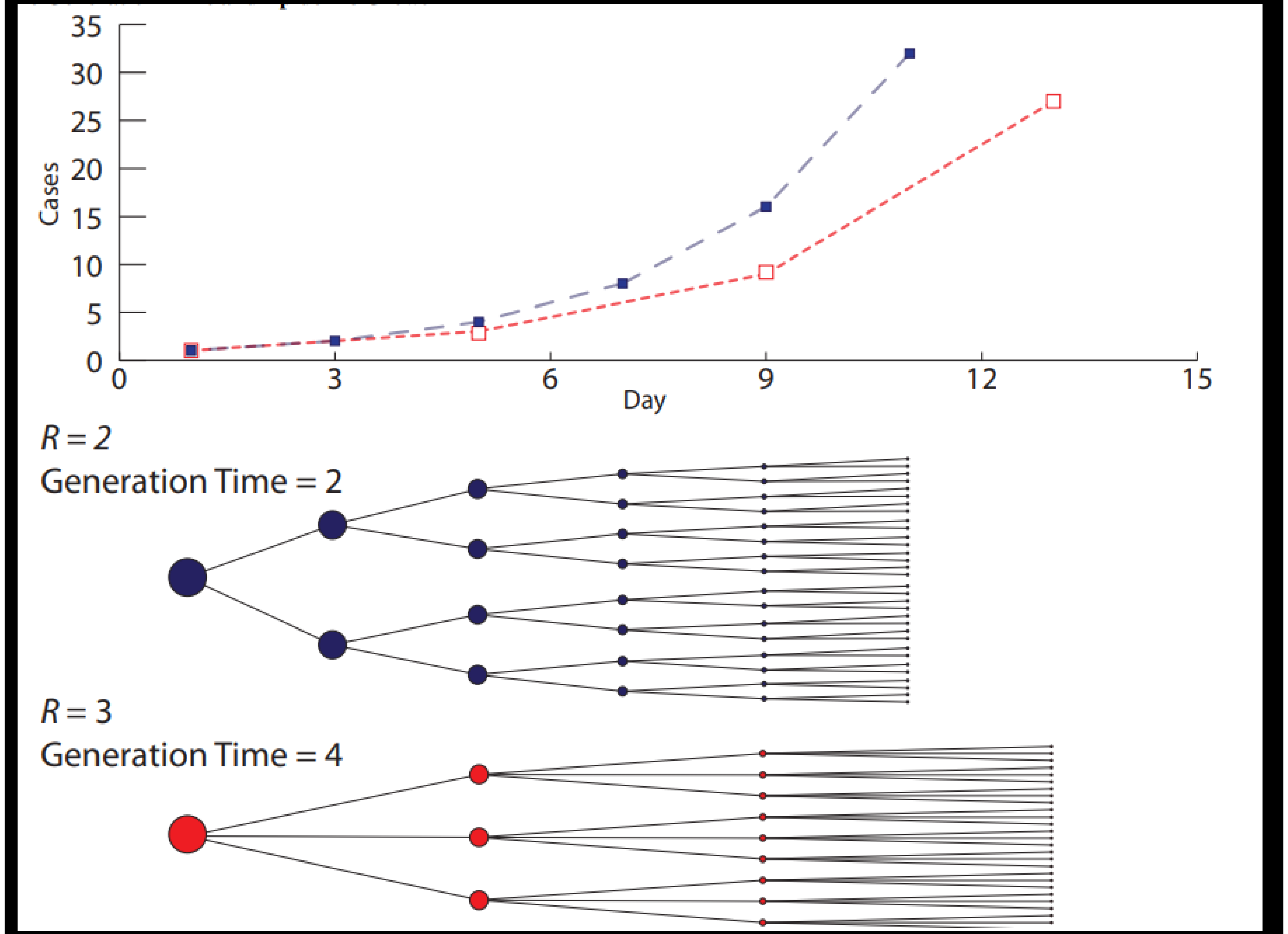
?



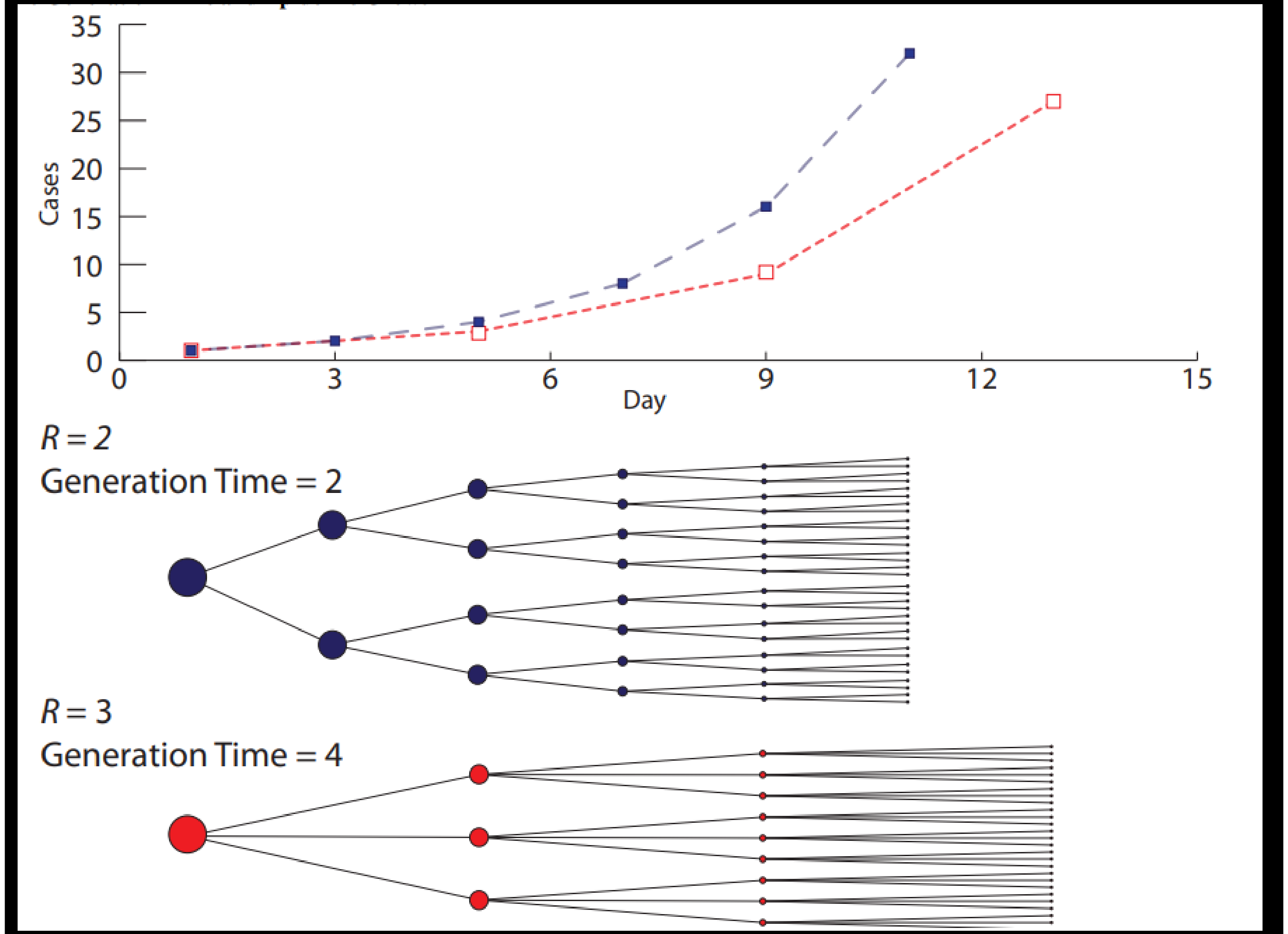
Generation Time & Epidemic Growth

- Consider two outbreaks:
  - Blue: R=2
  - Red: R=3



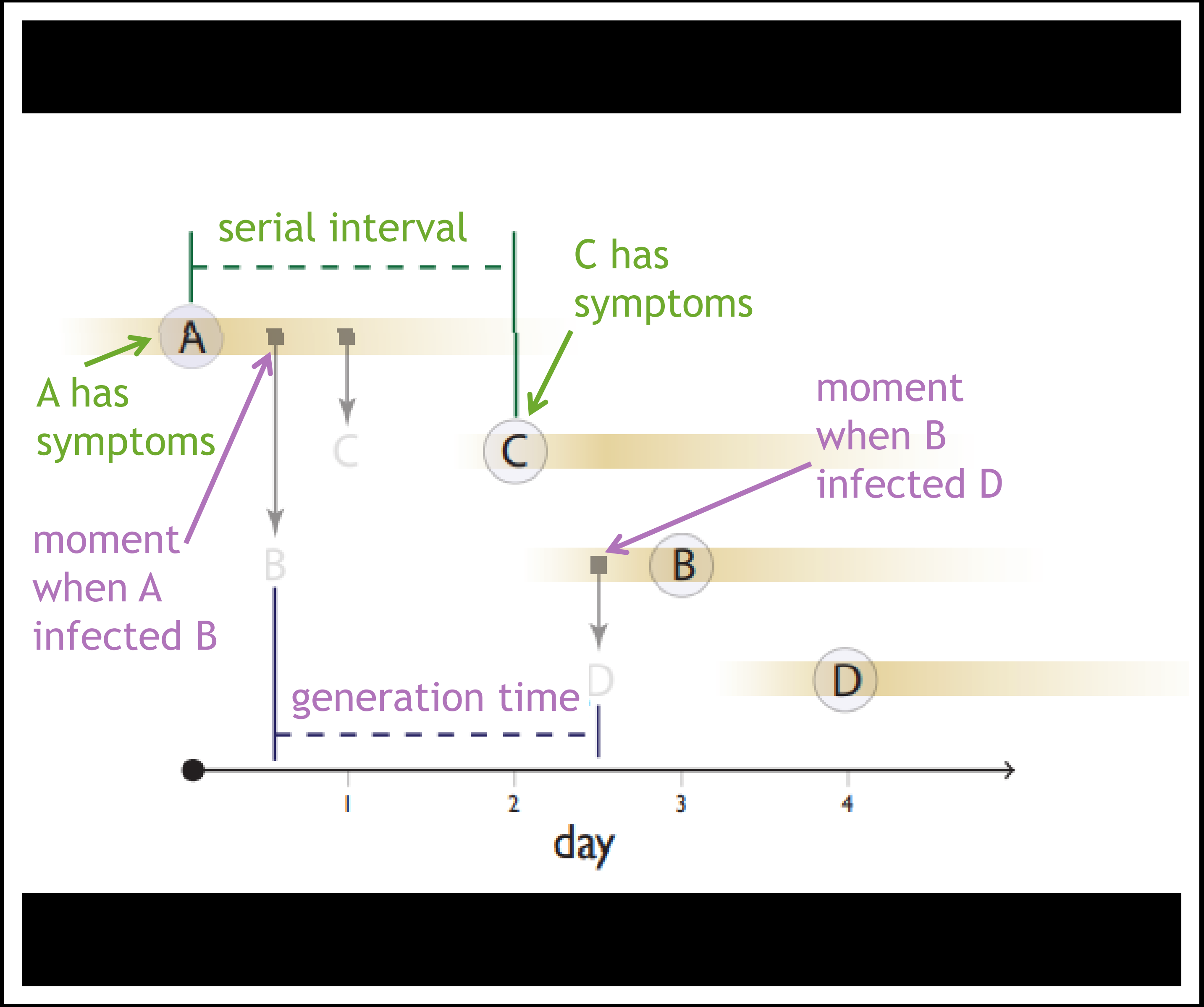
Generation Time & Epidemic Growth

- Consider two outbreaks:
  - Blue: R=2
  - Red: R=3
- Because blue grows more rapidly, we may think it has a higher reproductive number
- The outbreaks have different generation times
  - Blue: Generation T=2
  - Red: Generation T=4



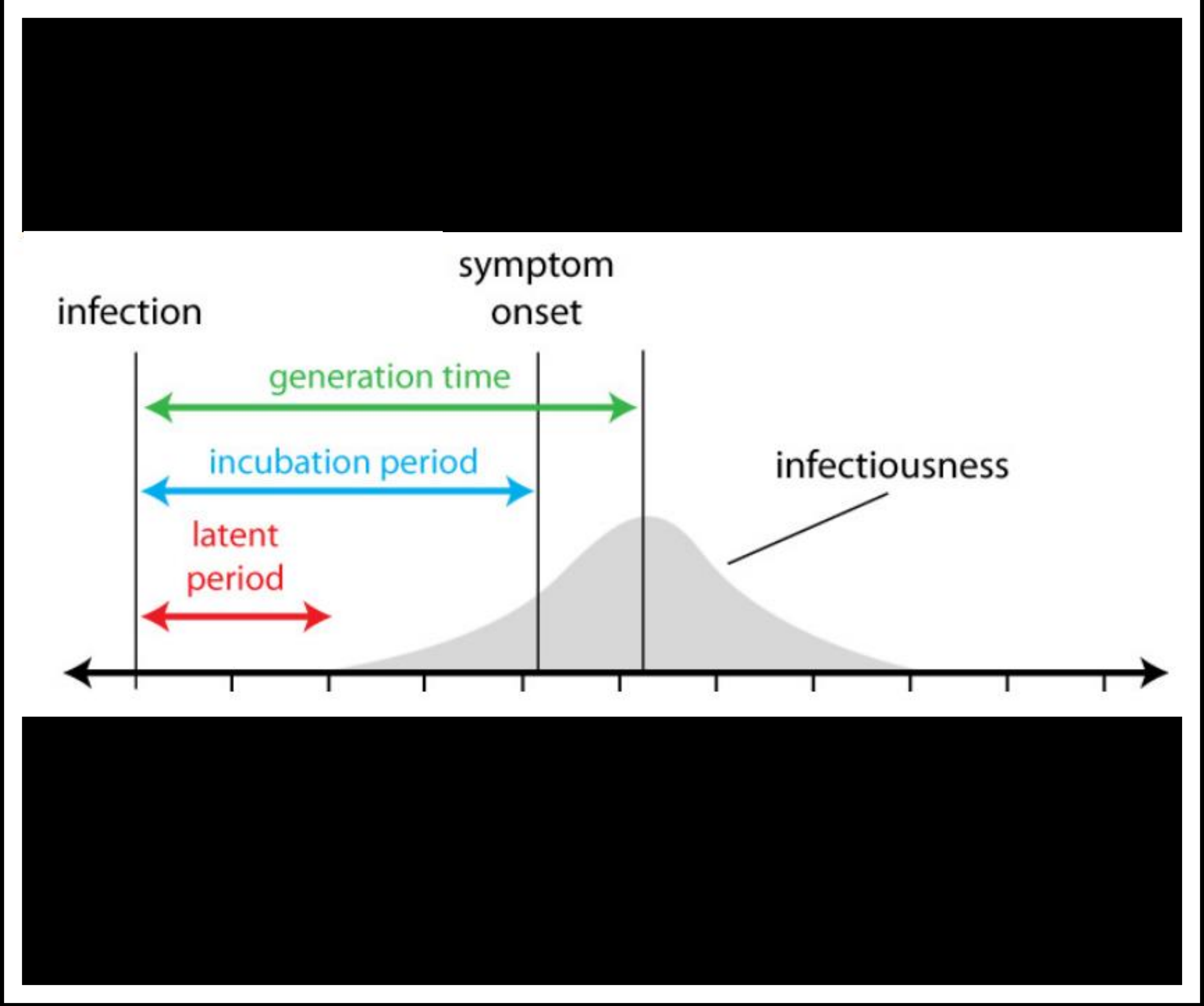
Generation Time & Epidemic Growth

- Generation time
  - time between time of infection in subsequent generations of infection
  - time between becoming infected and infecting others
- Both R_0 and generation time are important for the disease growth rate early in an epidemic



Generation Time & Serial Intervals

- Serial Interval
  - time between symptom onset in subsequent generations of cases
  - often used as a proxy for generation time



Generation Time & Epidemics

- Incubation period
  - time between infection and development of symptoms
- Latent period
  - time between infection and becoming infectious
- Infectious period
  - period when a case is infectious
- Generation time is most important
  - depends on biological factors and number of contacts

Reproductive Numbers & Generation Times

Pathogen	R0	Generation Time (days)
Cholera	2.6, 5.0, 4.0–15.0	7.1–9.3, 7–10
Dengue	1.3–6.3	19–22, 24
Influenza	1.5–2.0	3.6, 1.5–2.7, 3.1, 2.2–4, 2.7
Malaria	1–10, 100–1000, 1–3000	60–120, >200
Measles	7.7, 7.1–29.3, 11.0–18.0	9–17, 12
Rubella	2.9–7.8, 3.4–5.6	22, 15–23
SARS	1.2, 2.7, 2.2–3.6	8.4
Smallpox	3.2, 6.9, 3.5–6.0	14–16, 16, 14–20

- Generation time is also disease- and setting-specific
- Easier to understand why influenza grows more quickly than measles

Doubling Time & Generation Time

- R, doubling time, and generation time are related
- Influenza
  - $T_d = 2.5\ days$
  - $T_g = 2.5\ days$
- Measles
  - $T_d = 4.7\ days$
  - $T_g = 18\ days$

- $T_d = \dfrac{\ln 2}{\ln\left(\frac{R}{T_g}\right)}$

- T_d : doubling time
- T_g : generation time
- R: reproductive number

Doubling Time & Generation Time

Disease	R_0	T_g (days)	T_d (days)
Cholera	2.6	8.5	6.4
Dengue	4.0	20	10
Influenza	2.0	2.5	2.5
Measles	15.0	18	4.7
Rubella	5.0	22	9.5
SARS	2.7	8.4	5.8
Smallpox	4.0	16	8

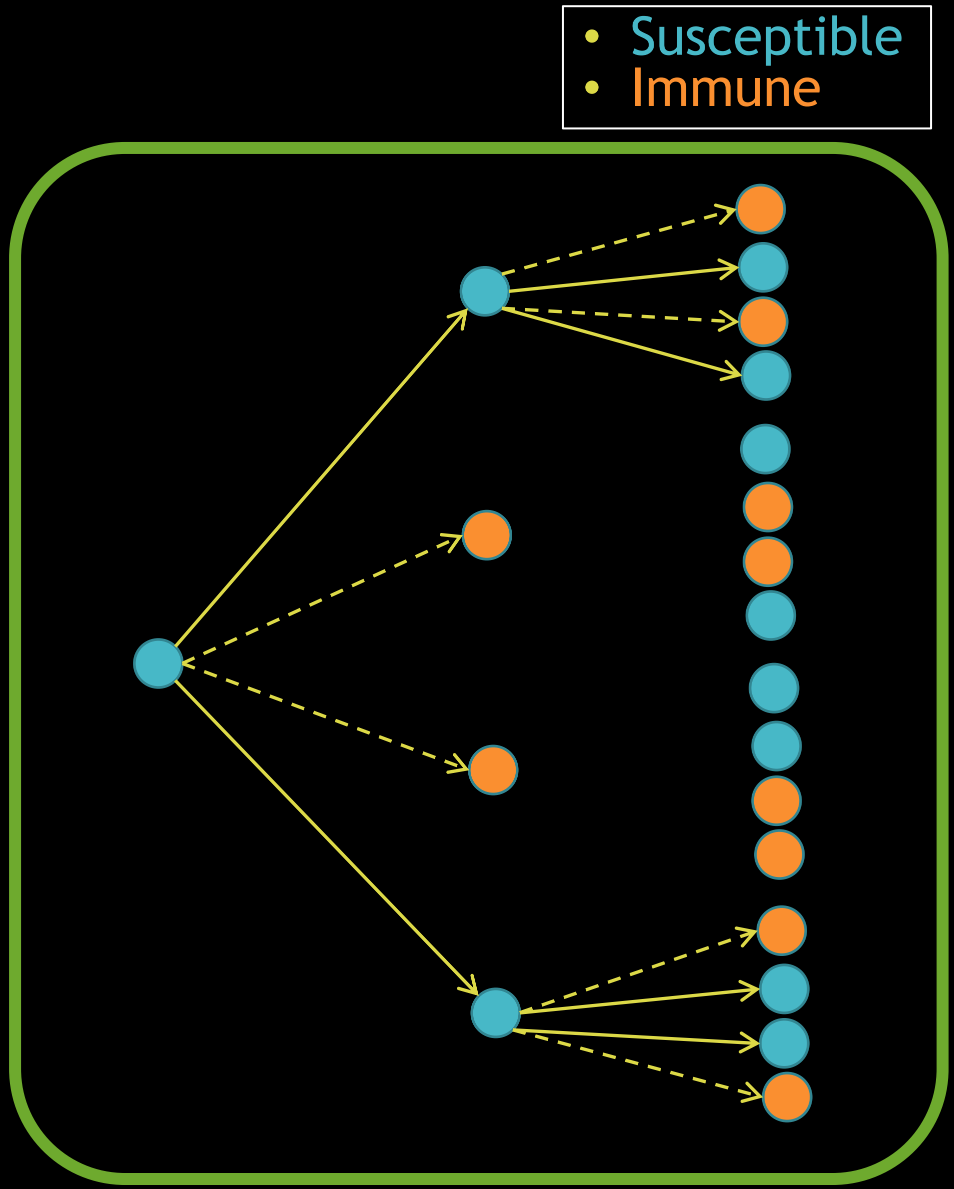
- $R = 2^{T_g/T_d}$

- We can use doubling time and generation time to estimate R

Herd Immunity

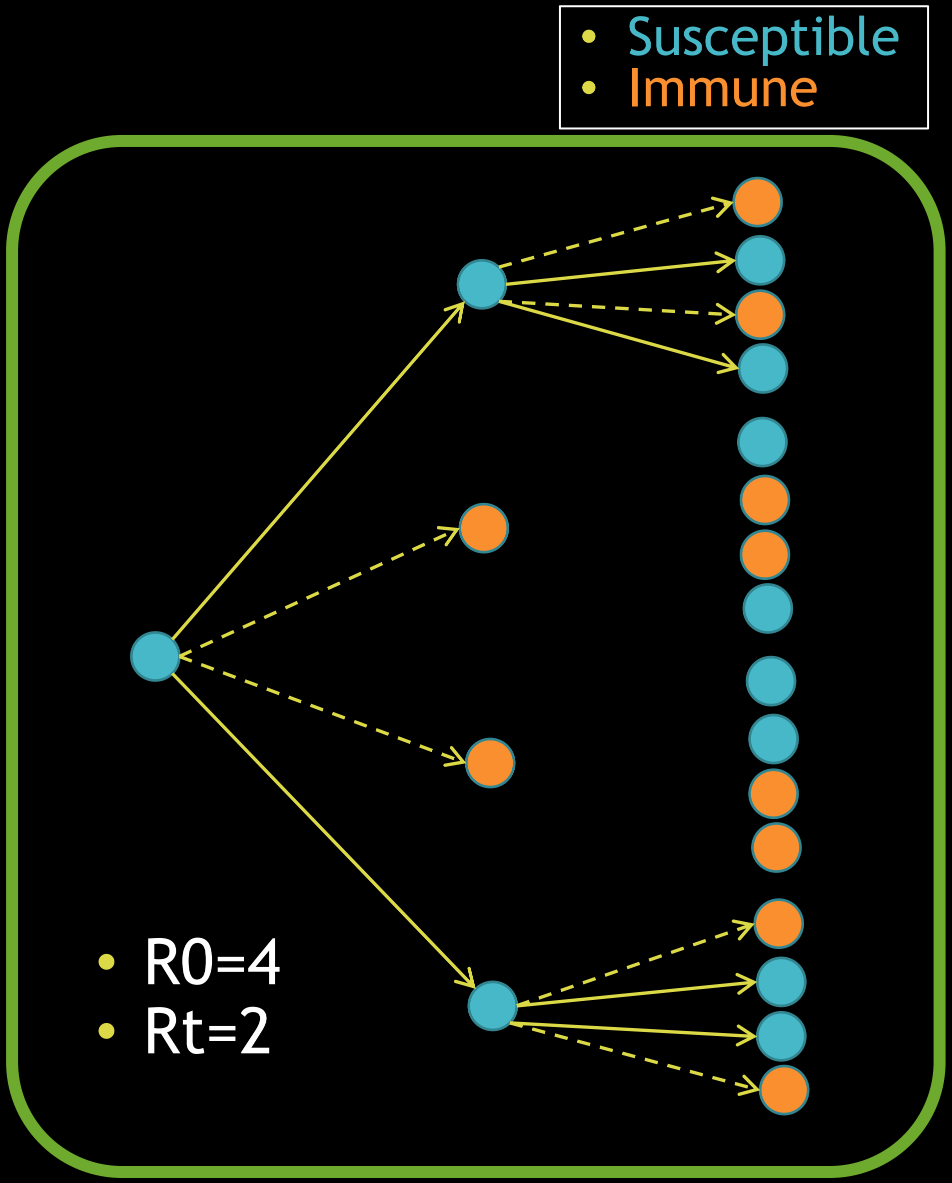
Reproductive Number & Herd Immunity

- Herd immunity
  - proportion of the population that is immune to infection
  - indirect protection resulting from immune individuals in the population
  - $HI = 1 - s$



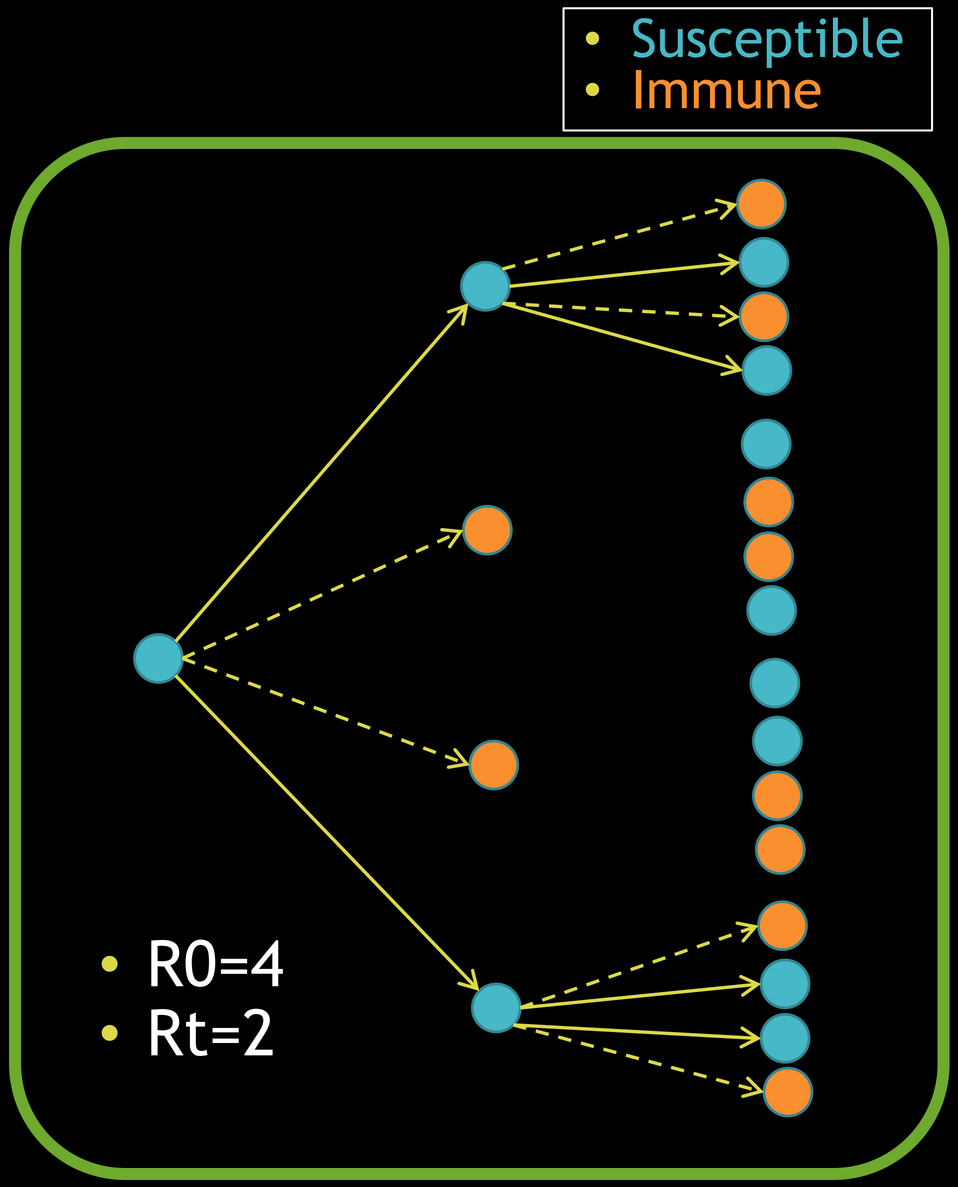
Reproductive Number & Herd Immunity

- Herd immunity
  - recall that the number of new cases depends on the presence of infected persons (to cause infection) but also the presence of susceptible persons (to become infected)
  - $R_t = R_0 s_t$



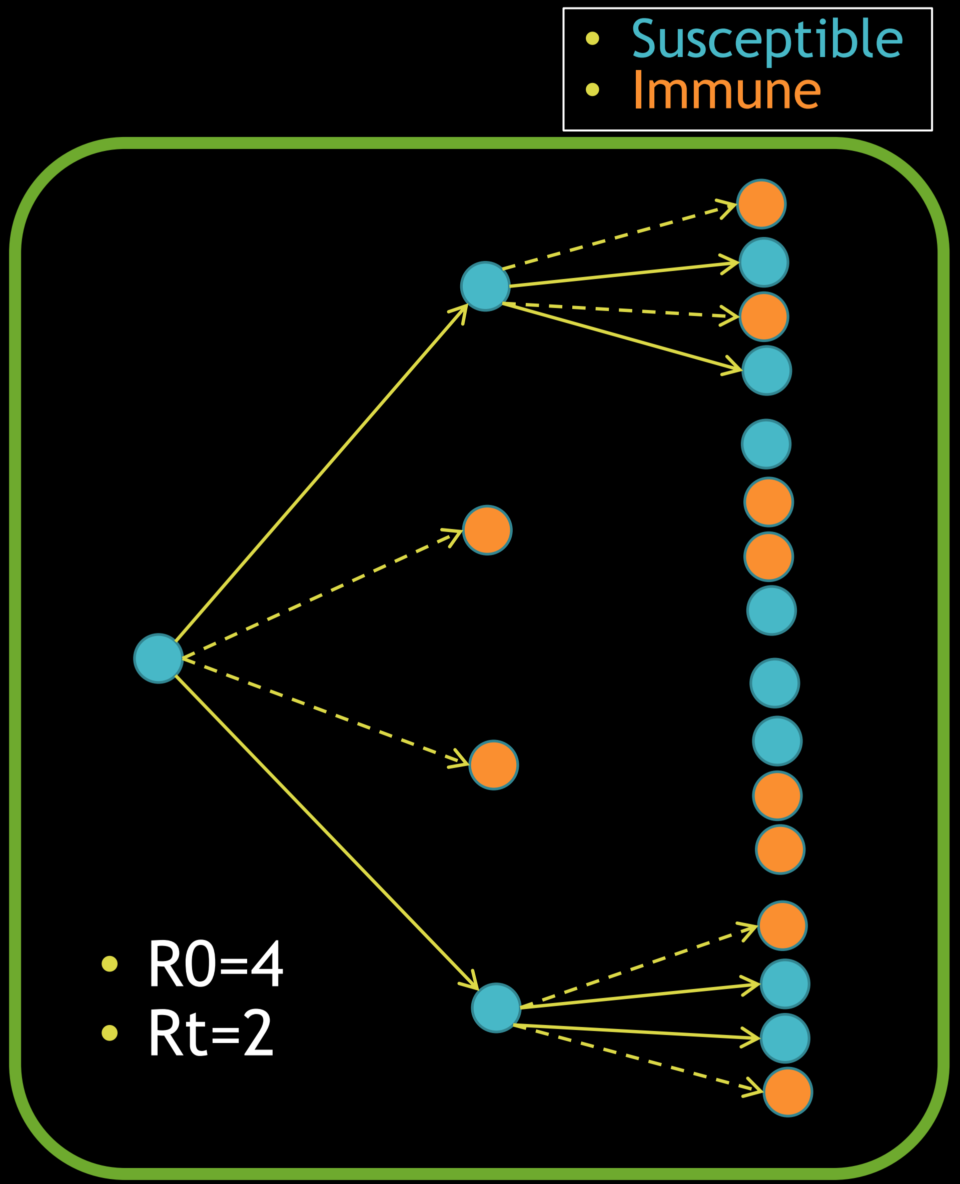
Reproductive Number & Herd Immunity

- Herd immunity
  - recall that the number of new cases depends on the presence of infected persons (to cause infection) but also the presence of susceptible persons (to become infected)
  - $R_t = R_0 s_t$
  - if half of the population is immune, the reproductive number is cut in half
  - if there are enough immunes, we can control transmission



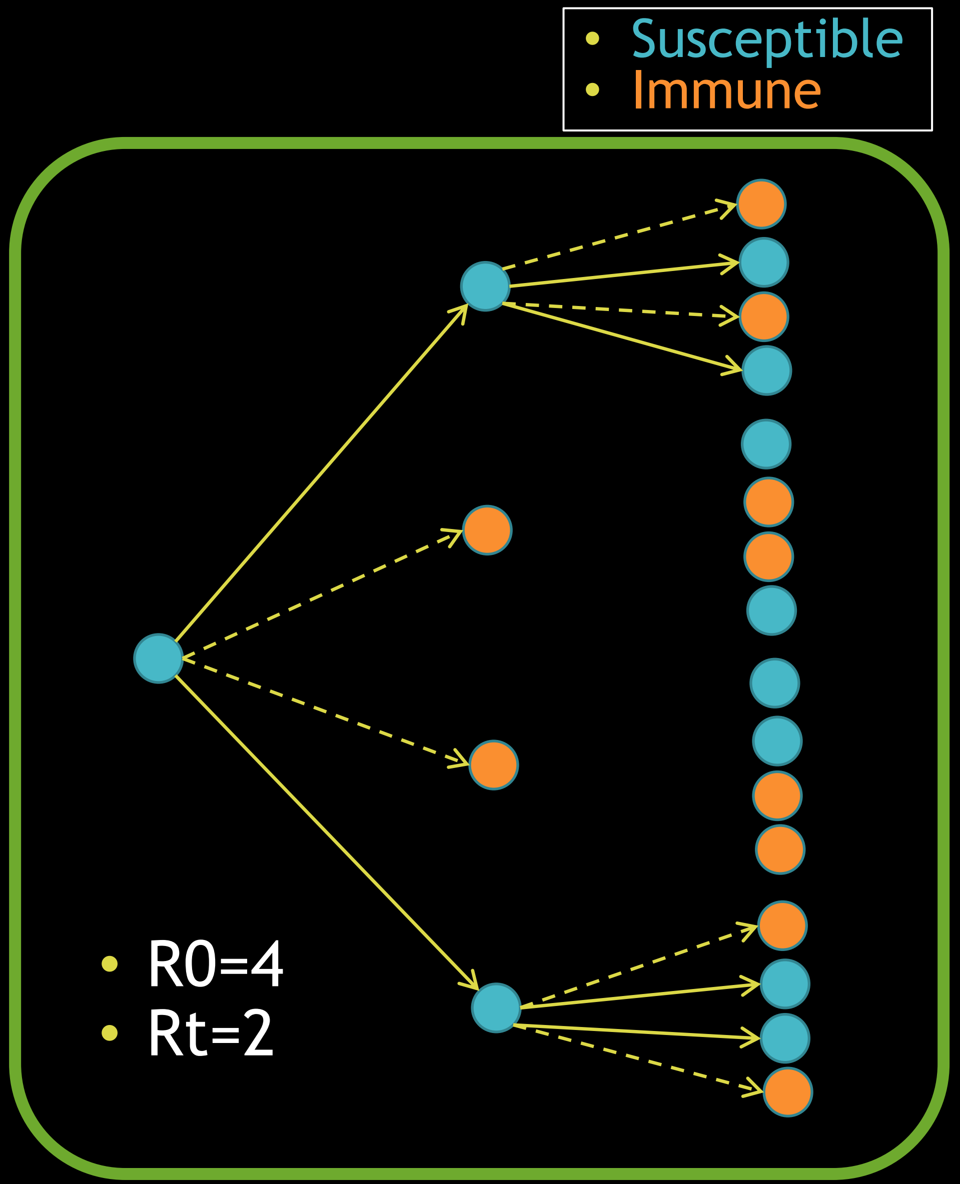
Reproductive Number & Herd Immunity

- Herd immunity threshold (HIT)
  - the proportion of the population that would need to be immune to control transmission
  - transmission is controlled when Rt=1
  - $HIT = 1 - \frac{1}{R_0}$
  - What is the HIT for this population?

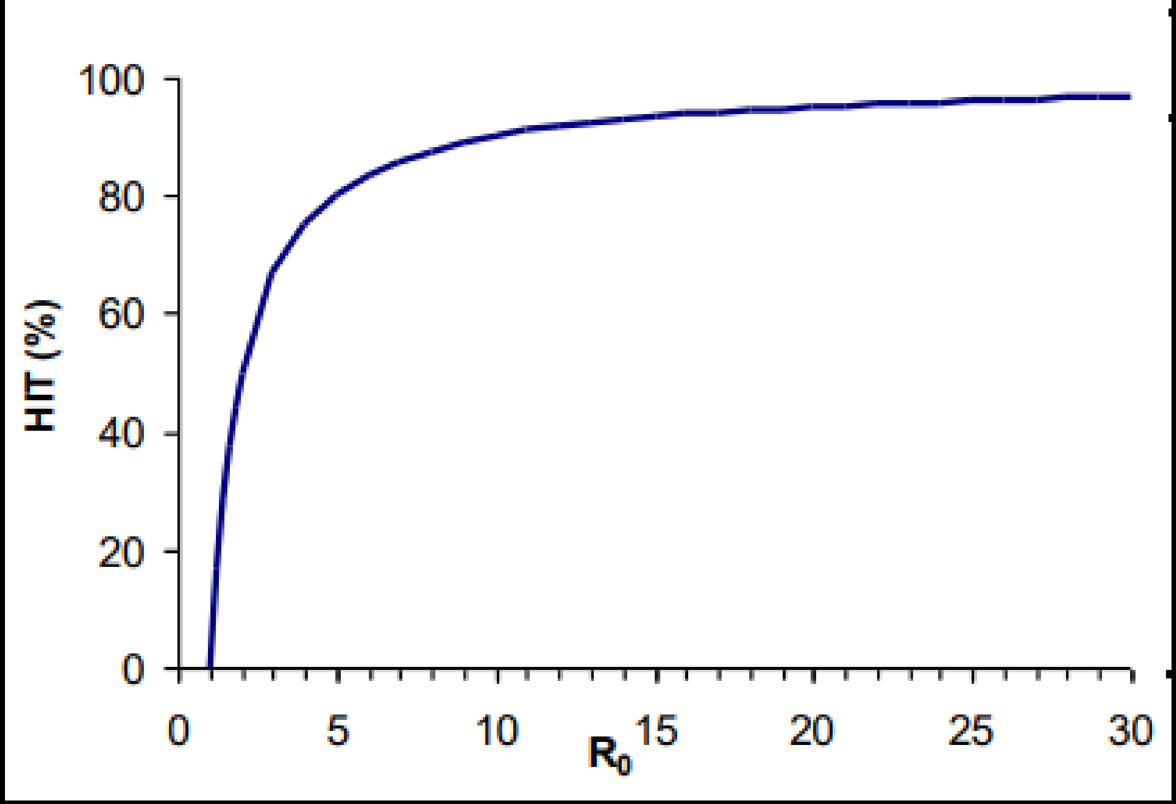


Reproductive Number & Herd Immunity

- Herd immunity threshold (HIT)
  - the proportion of the population that would need to be immune to control transmission
  - transmission is controlled when Rt=1
  - $HIT = 1 - \frac{1}{R_0}$
  - What is the HIT for this population?
  - HIT=75%

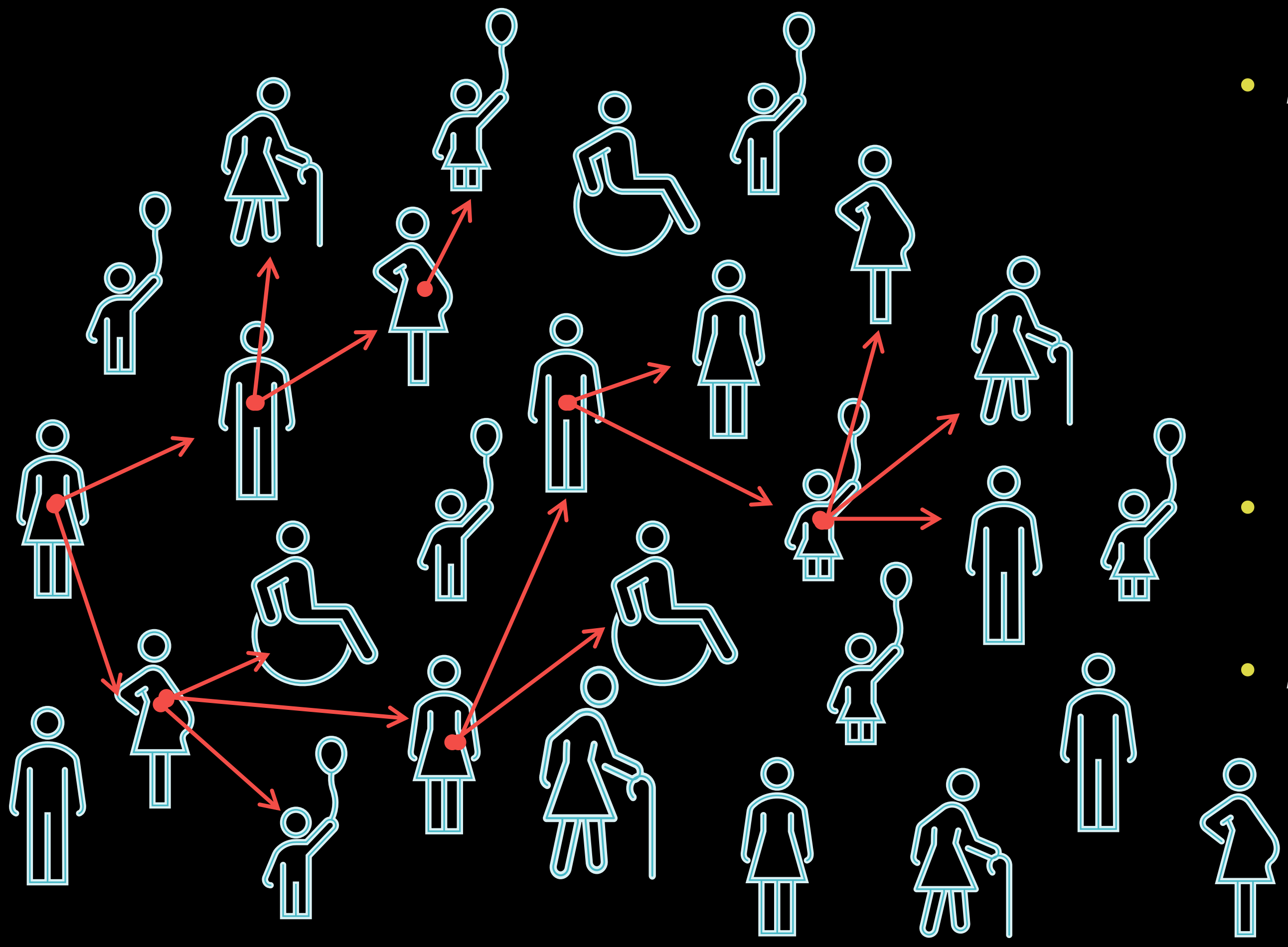


Herd Immunity Threshold



Disease	R_0	HIT (%)
Diphtheria	7.2	82-87
Malaria	100	99
Measles	15.0	90-95
Pertussis	15.0	90-95
Poliomyelitis	6.0	82-87
Rubella	5.0	82-87
Smallpox	4.0	70-80

Determinants of Epidemic Growth



- Many factors contribute to the growth of an epidemic
  - we are interested in trying to estimate these parameters
  - these give us an idea of how much control/intervention is needed
- In simple scenarios (e.g. random mixing), R is easier to estimate
- More complex scenarios require the use of modeling

Workshop Schedule

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2:00–2:05 pm	~~Greetings~~
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