Week 1: Modeling Goals, Parameters, & Structures

Dr. Rachel Sippy
University of Cambridge

Objectives

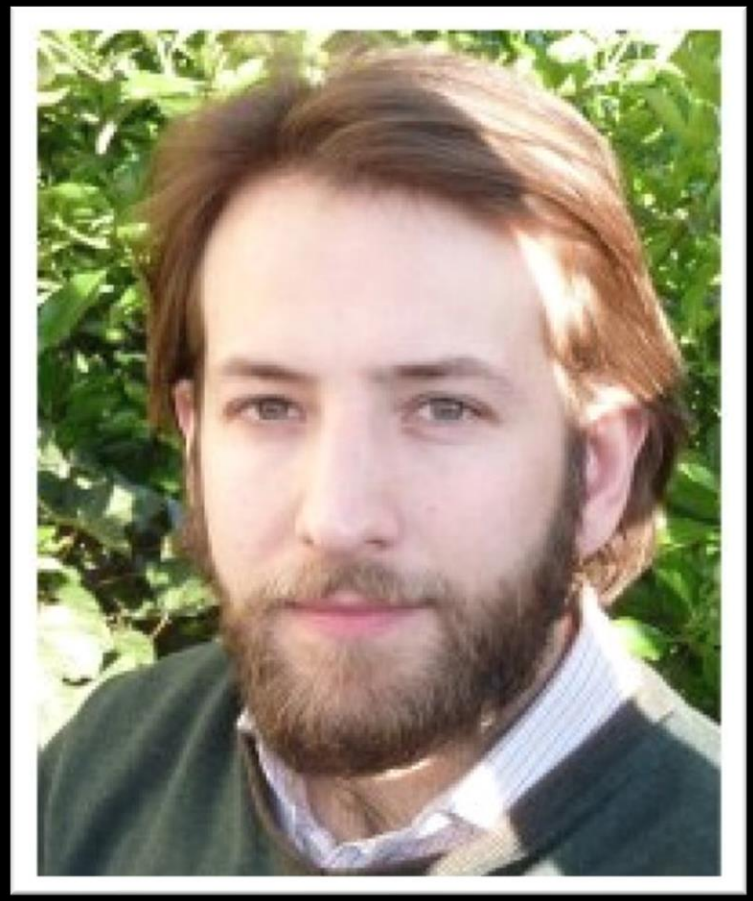
- Add your first bullet point here
- Add your second bullet point here
- Add your third bullet point here

Post Questions in the Chat!

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

Week 1 Instructors

- Dr. Rachel Sippy



- Dr. Henrik Salje

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

Workshop Schedule

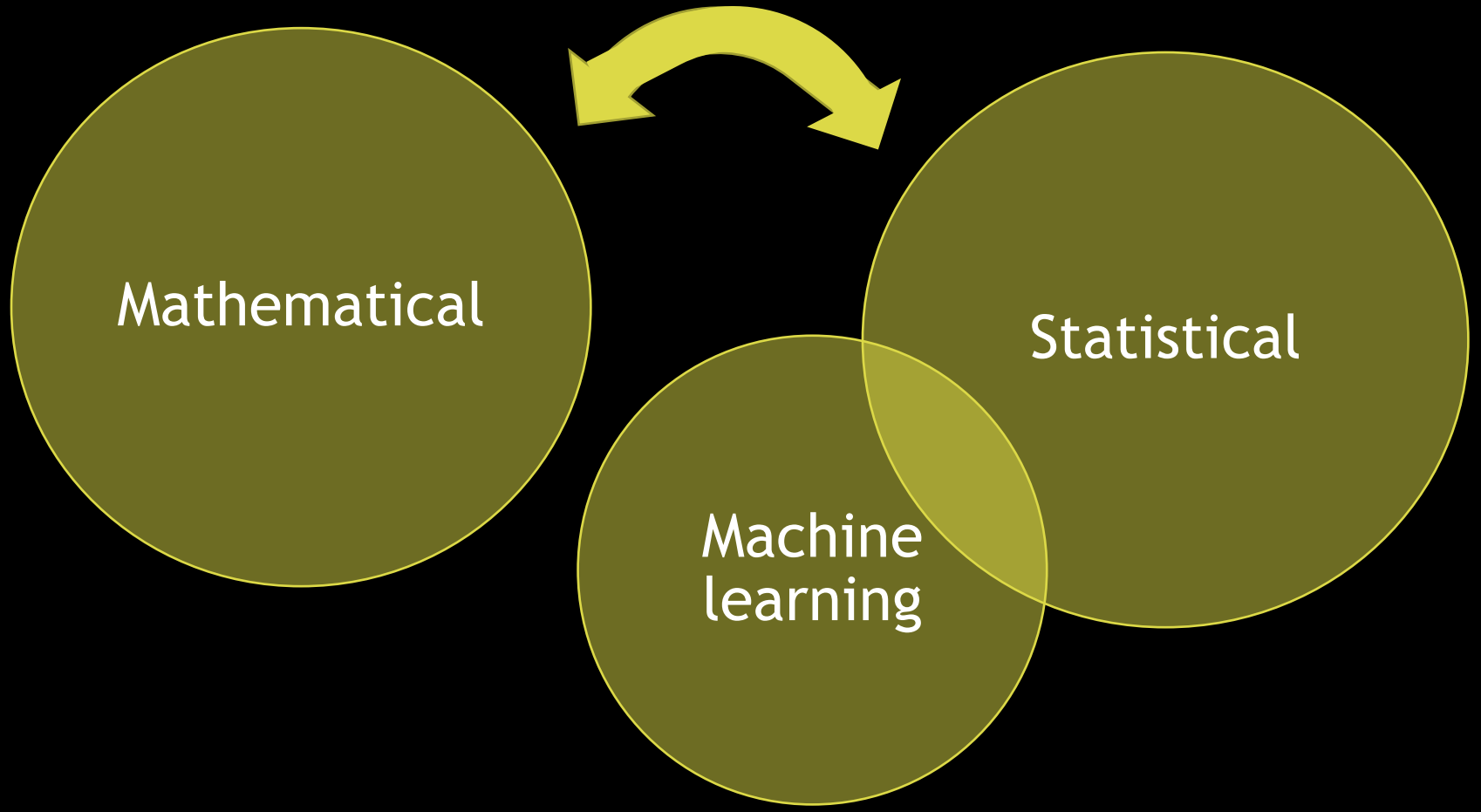
Time	Topics
2:00—2:10 pm	~~Outline & Introduction~~
2:10—3:00 pm	Defining Mathematical Models
3:00—3:30 pm	History of Mathematical Models
3:30—3:45 pm	Modern Modeling
3:40—3:50 pm	Break
3:50—5:00 pm	Introduction to R

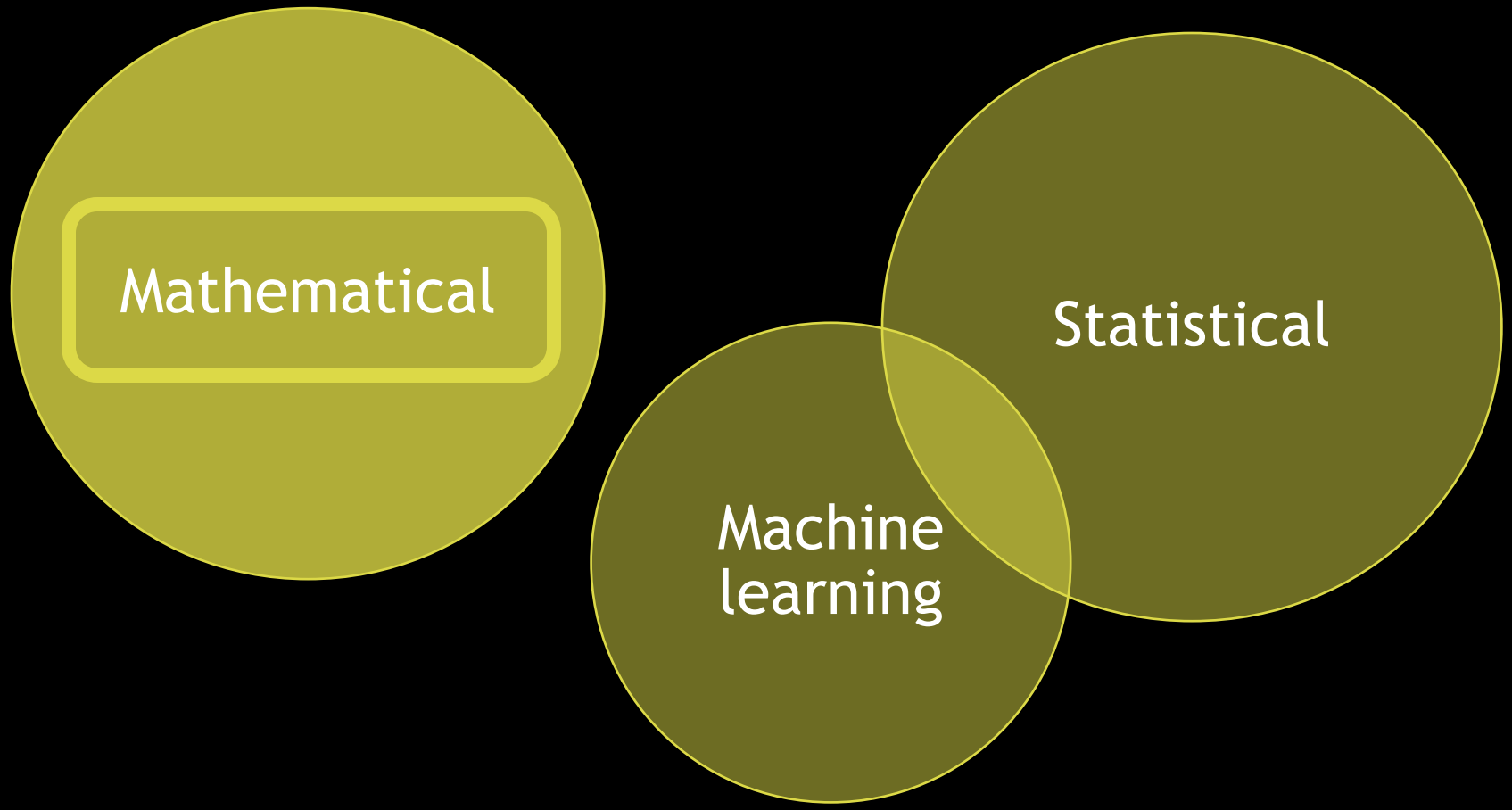
Three Major Model Types

(used in epidemiology)
(general modeling approaches)

- Statistical models
  - Regression (many!), time series
- Mathematical models
  - Compartmental, mechanistic, agent-based
- Machine learning
  - Uses algorithms and statistical models

Model Types are Related




Mathematical
Statistical
Machine learning

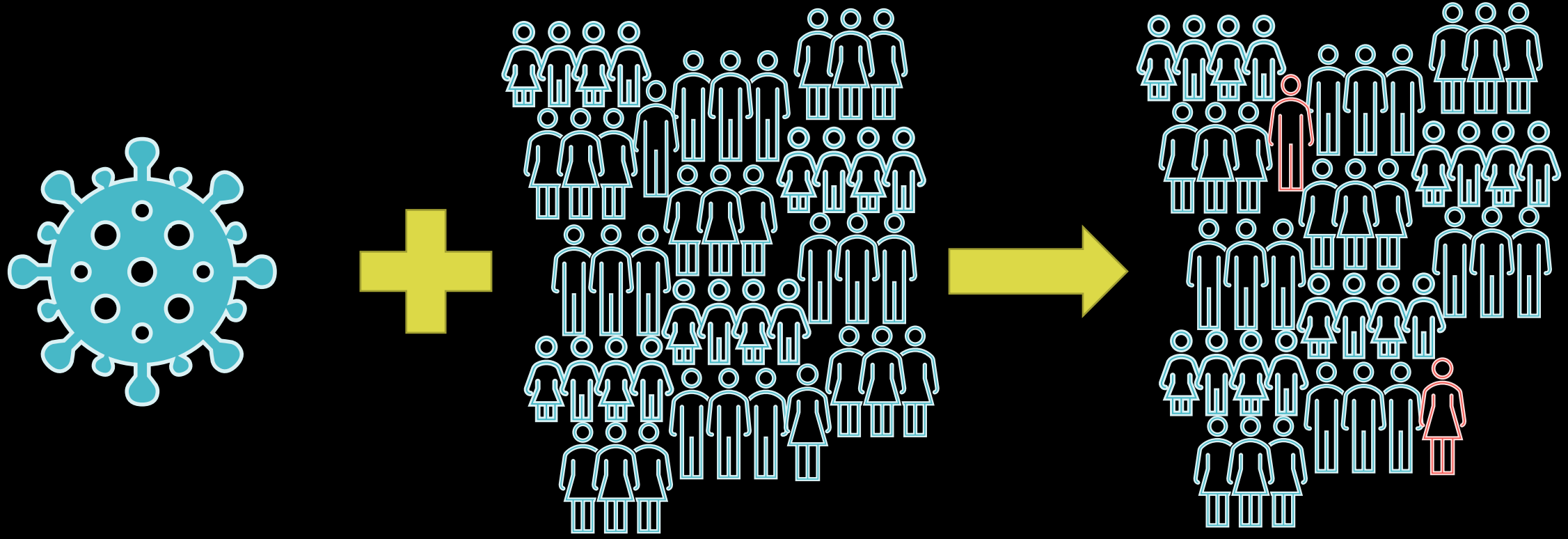
Mathematical Modeling

- Often called “mechanistic” modeling
- Used to assess explicit hypotheses about biological mechanisms of infection dynamics
- Model structure is critical first decision
- Models expressed as equations

Mathematical Modeling

- Used to estimate parameters/measures related to an epidemic
- Often, we use equations to create a scenario (set of conditions)
  - Example: population of city, level of interaction, certain disease, susceptibility of population
- If we can create a realistic model, then we can make changes to model and see what happens
  - Example: what happens when we vaccinate some people?
- This is similar to running an experiment and observing what happens
- Results from these observations can be compared to real data
  - Example: do model results match what happened in real life?

Epidemic Scenario



Public Health Applications

Mathematical Modeling

- Estimate transmission parameters from data
- Construct and build mechanistic models
- Build more realistic models

Public Health Questions

- How big will the final epidemic be?
- What is the R0 value?
- How will interventions impact the epidemic?

Public Health Applications: Example

Scenario

- Emergence of H5N1 (2006) and swine flu (2009)
- Vaccines take many months to develop
- Vaccines may improve during the pandemic
- Manu countries have no or low stockpiles of antivirals

Public Health Questions

Public Health Applications: Example

Scenario

- Emergence of H5N1 (2006) and swine flu (2009)
- Vaccines take many months to develop
- Vaccines may improve during the pandemic
- Manu countries have no or low stockpiles of antivirals

Public Health Questions

- How should we distribute vaccines?
- Should everyone use the first available vaccine or wait for a better one?
- Do travel restrictions impact spread?
- What is the impact of closing schools?
- How many cases would occur if we run out of antivirals?
- Is it better to use antivirals as prophylaxis or to treat cases?

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History of Mathematical Modeling of Infectious Disease

Early efforts & recent advances

History of Mathematical Models

1700 | 1800 | 1900 | 2000

History of Mathematical Models

1700 | 1800 | 1900 | 2000

- Daniel Bernoulli, 1760

It is, then, only the risk which is attributed to inoculation which should keep us undecided… 'What would be the state of the human race if, at the price of a certain number of victims, we could procure for it freedom from natural smallpox?' [**5**, p. 284]

History of Mathematical Models

1700 | 1800 | 1900 | 2000

Bernoulli

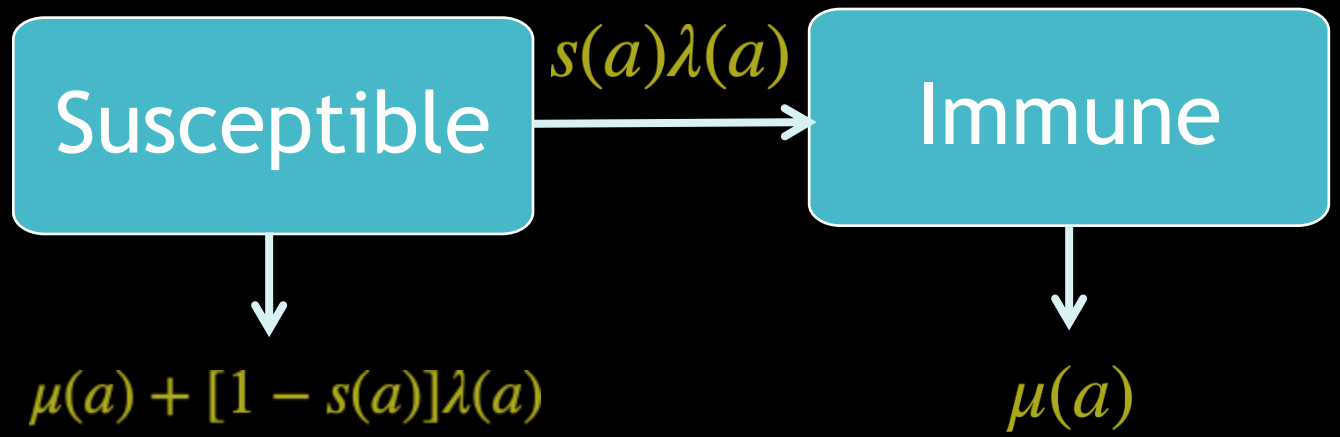
It is, then, only the risk which is attributed to inoculation which should keep us undecided... 'What would be the state of the human race if, at the price of a certain number of victims, we could procure for it freedom from natural smallpox?' [**5**, p. 284]

- What is the impact of inoculation against smallpox?

History of Mathematical Models

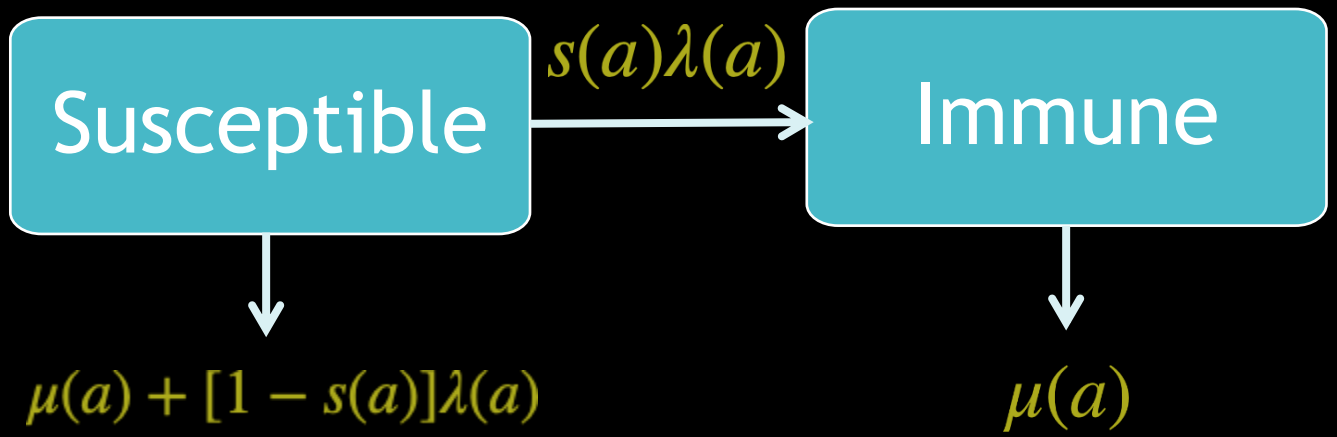
1700 | 1800 | 1900 | 2000

Bernoulli



- s(a)=probability of surviving infection
- λ(a)=force of infection
- μ(a)=death rate

History of Mathematical Models



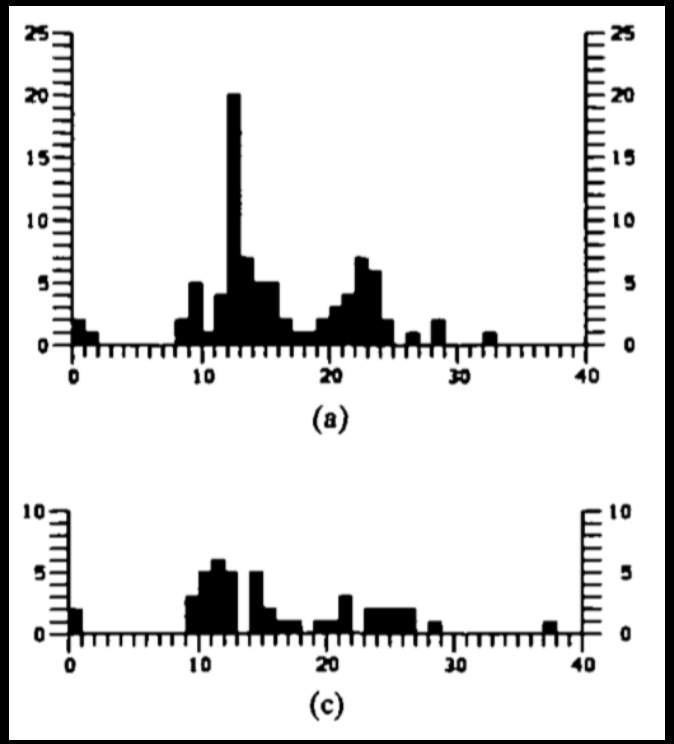
- Inoculation would increase life expectancy at birth by ~3 years

History of Mathematical Models

1700 | 1800 | 1900 | 2000

Bernoulli

- Pyotr En'ko, 1889
- How does contact between susceptible and infected people impact a measles epidemic?



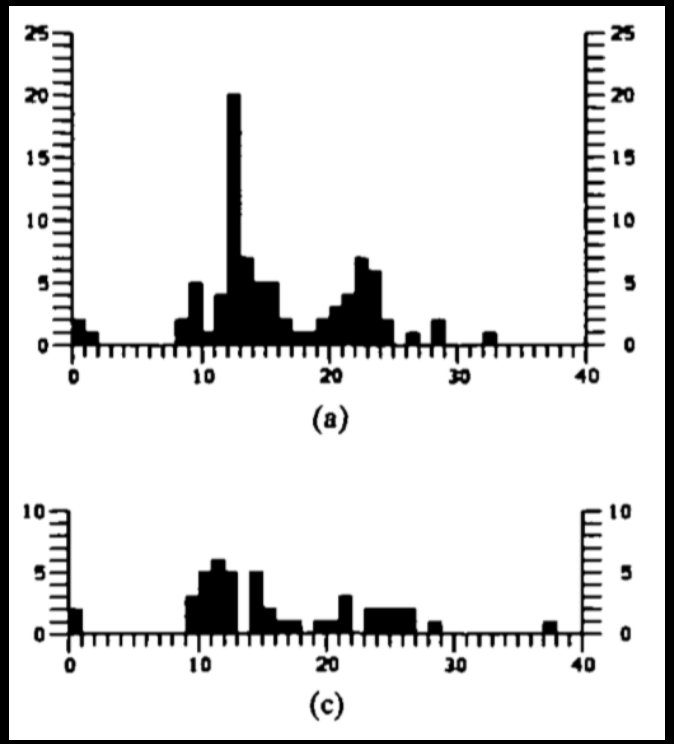
History of Mathematical Models

1700 | 1800 | 1900 | 2000

Bernoulli | En'ko

- How does contact between susceptible and infected people impact a measles epidemic?

The number of contacts depends on the way of life. For a solitary way of life—one's home, one's servants, a selected circle of acquaintances—the number of contacts is less. In schools the patients are isolated at the first signs of the disease and can infect their schoolmates only as long as they appear completely healthy; therefore it is assumed that a patient has contact with the same number of individuals as a healthy individual.



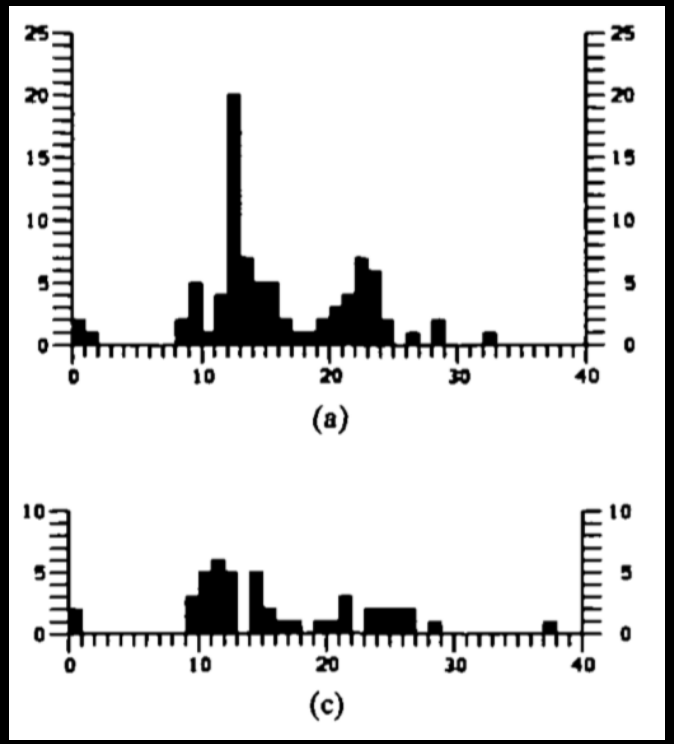
History of Mathematical Models

1700 | 1800 | 1900 | 2000

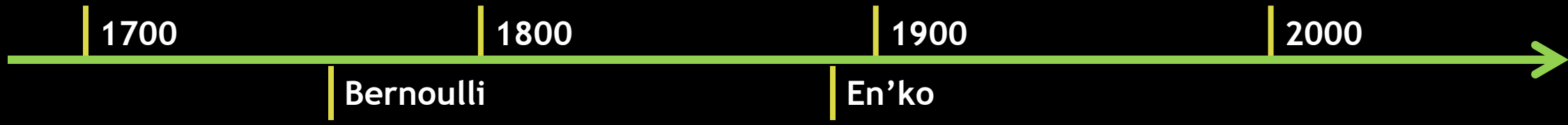
Bernoulli | En'ko

$$1 - ((N - 1 - x)/(N - 1))^A$$

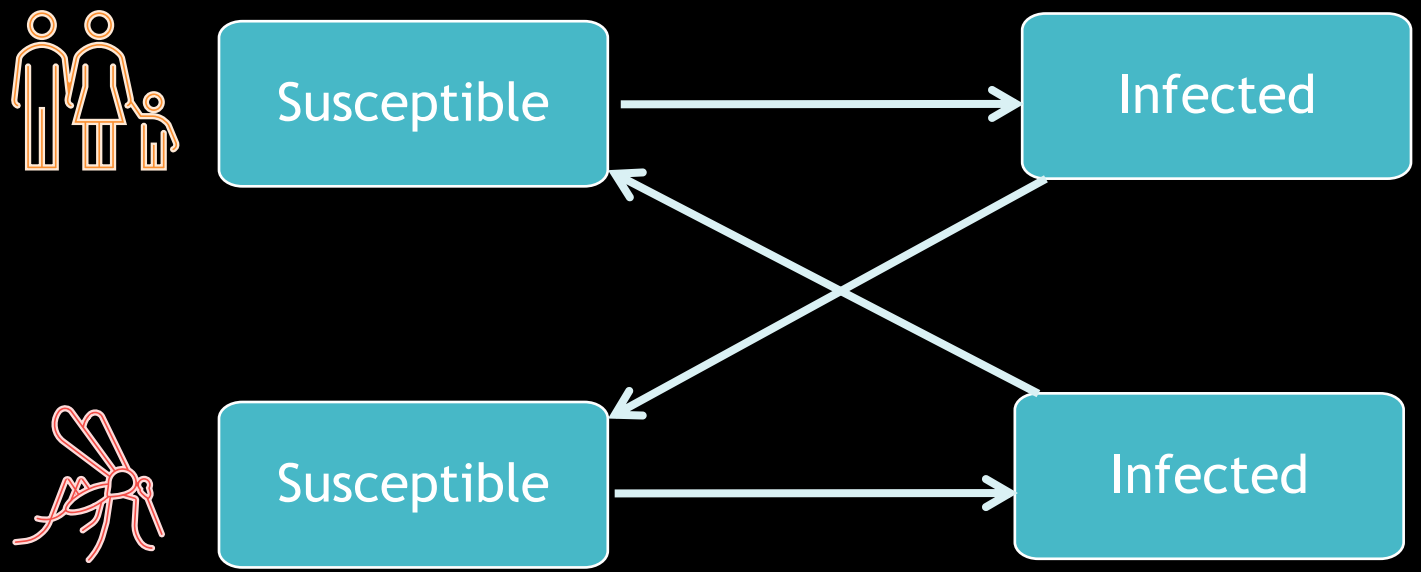
- N=population size
- x=number of infected
- A=number of contacts



History of Mathematical Models



- Ronald Ross, 1911



History of Mathematical Models

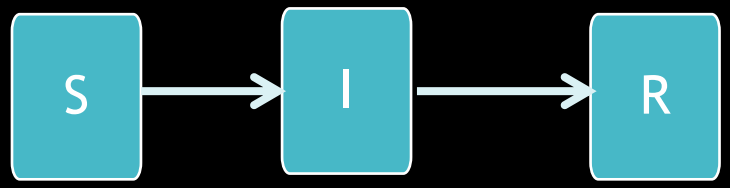
1700 | 1800 | 1900 | 2000

Bernoulli | En'ko | Ross

- How does vector control impact a malaria epidemic?
- If you increase mosquito mortality from 5% to 45% you could eradicate malaria in Africa
- Argued for establishment of new field of study, co-authored with Hilda Hudson

History of Mathematical Models

- Kermack and McKendrick, 1926



History of Mathematical Models

1700 | 1800 | 1900 | 2000

Bernoulli | En'ko | Ross | Kermack & McKendrick

- Evaluated plague and cholera epidemics
- Formalization of mechanistic models for epidemics

$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

$$\frac{dI(t)}{dt} = \beta S(t) I(t) - \gamma I(t)$$

$$\frac{dR(t)}{dt} = \gamma I(t)$$

History of Mathematical Models

1700 | 1800 | 1900 | 2000

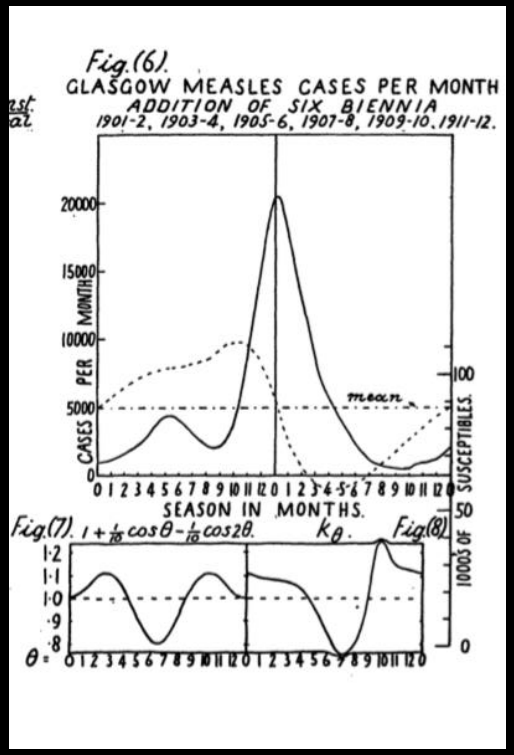
Bernoulli

En'ko

Ross

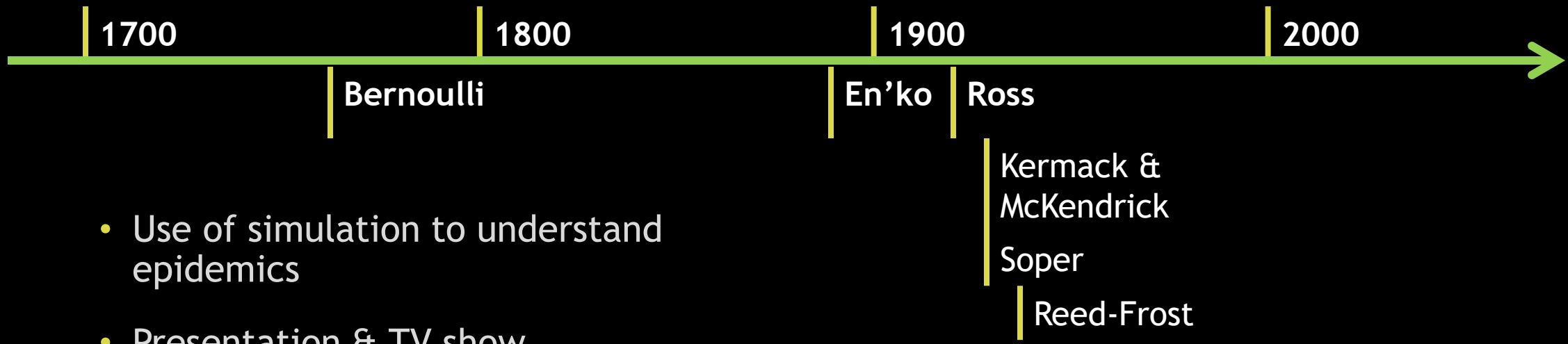
Kermack & McKendrick

Soper



- Evaluated seasonality of measles epidemics

History of Mathematical Models



- Use of simulation to understand epidemics
- Presentation & TV show
- Formally published by Helen Abbey
- Basis for modern epidemic modeling

History of Mathematical Models

- Extended Ross malaria models for use on computers
- Ross-MacDonald models, formalized by Smith & McKenzie, Aron & May, and Anderson & May

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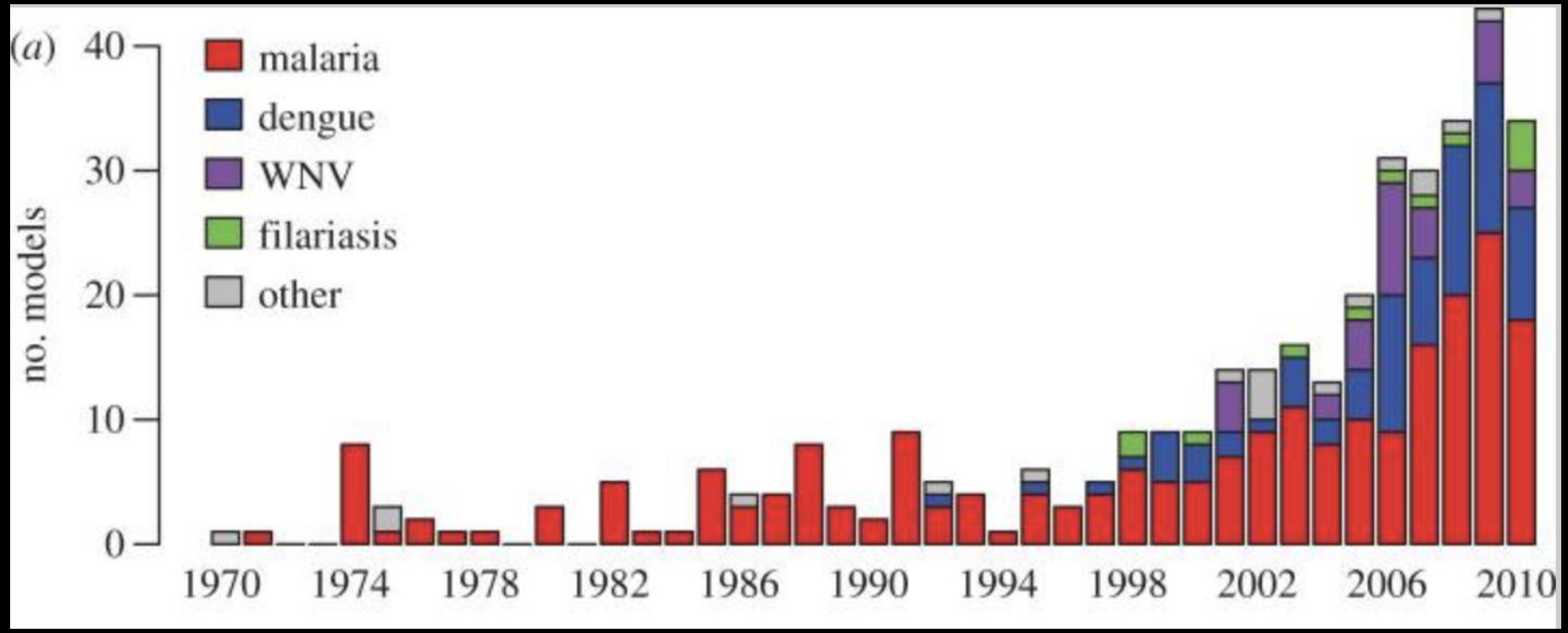
Modern Modeling

Modern Modeling

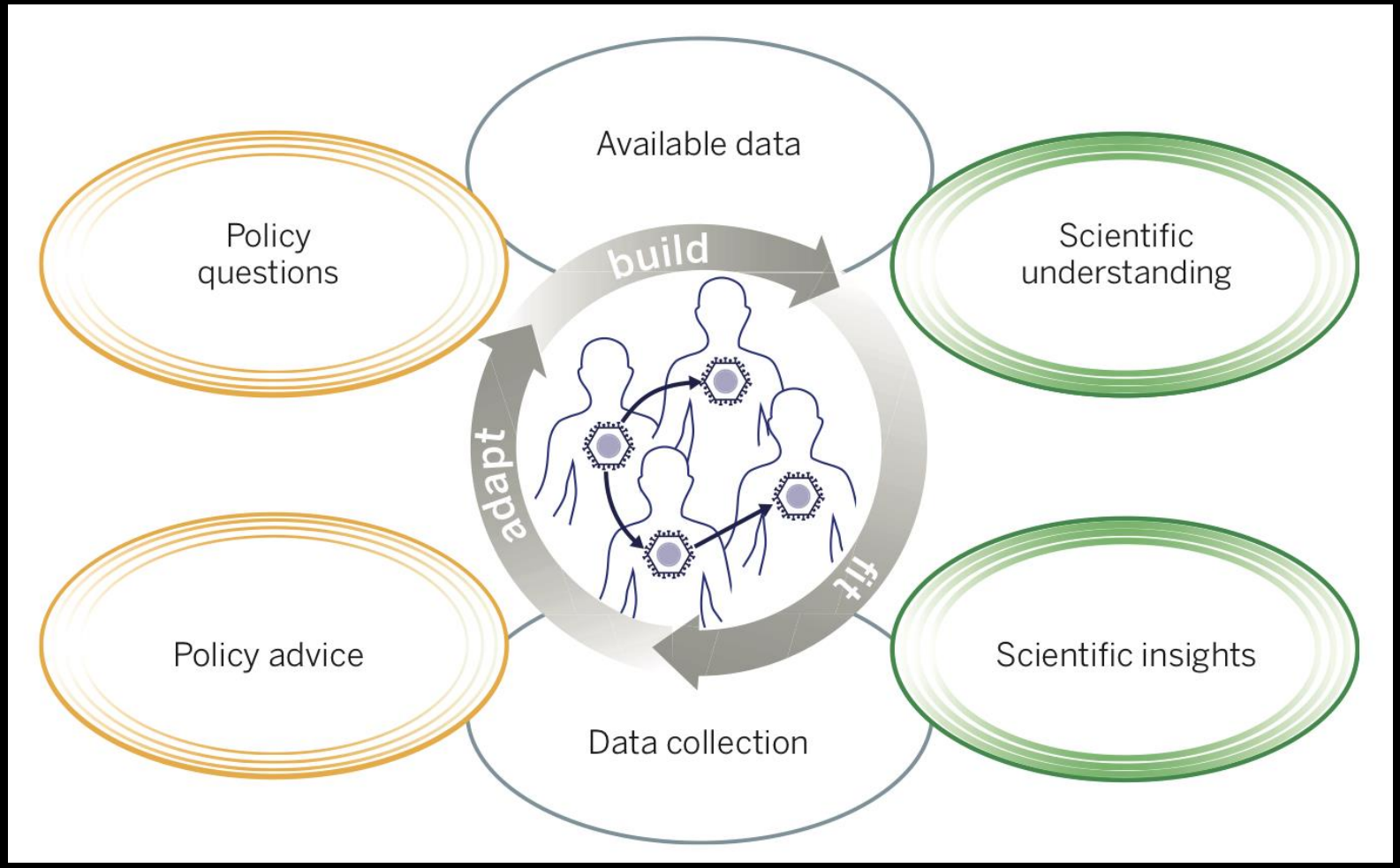


Reiner et al. 2013

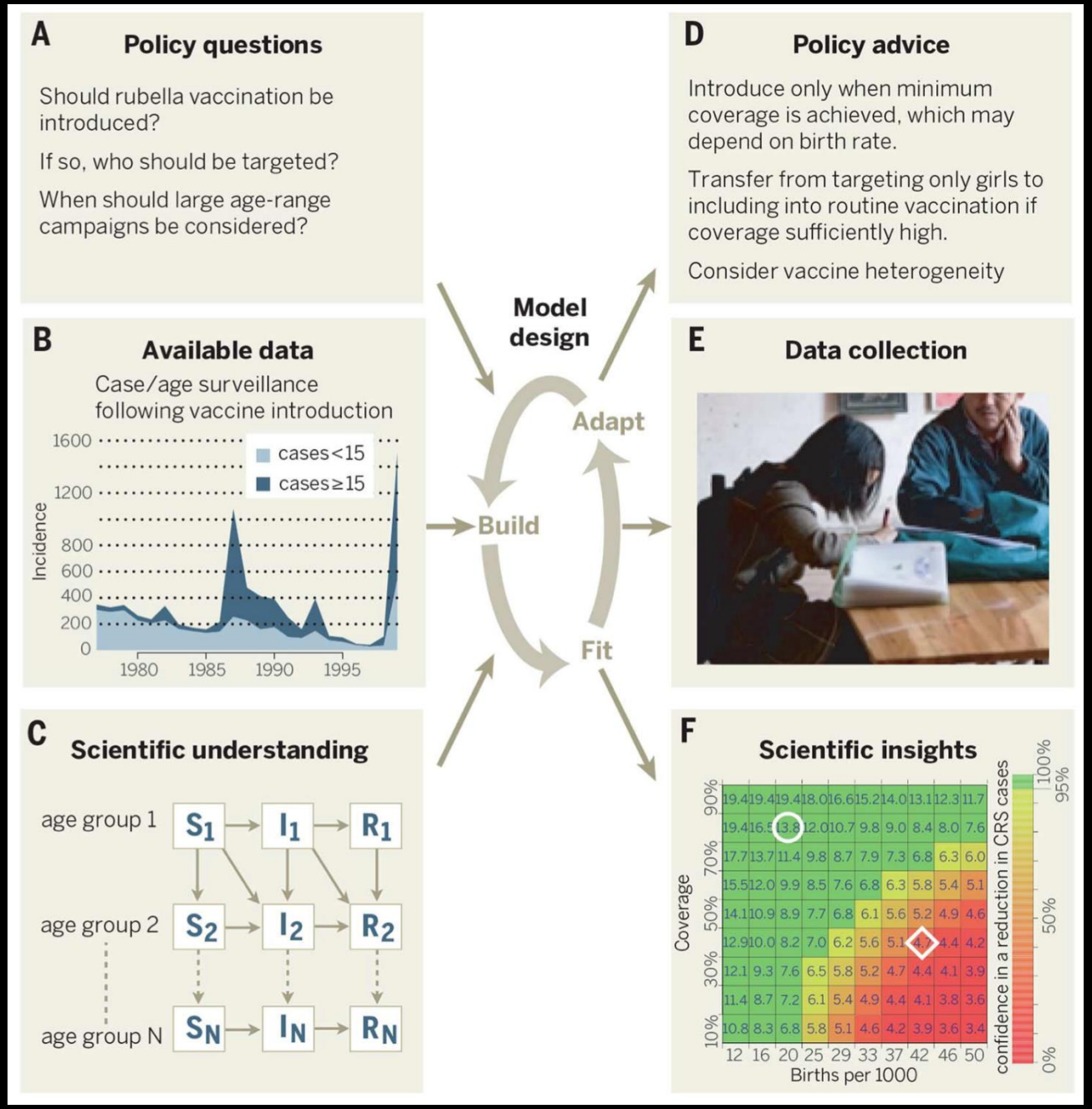
- Early models have been expanded and developed for a wide variety of scenarios and applications

Modern Modeling

- Modeling is used to fit and answer policy questions



Heesterbeek et al. 2015



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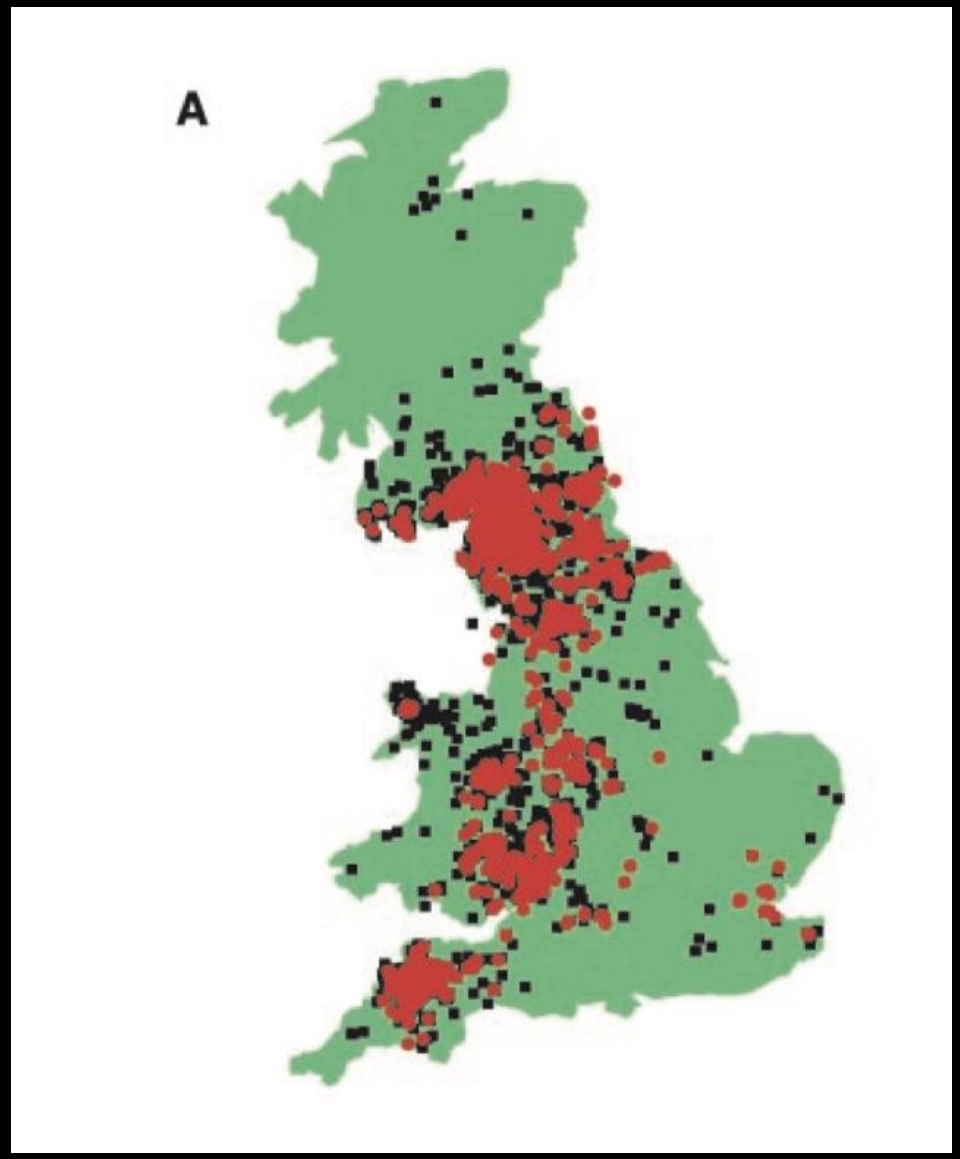
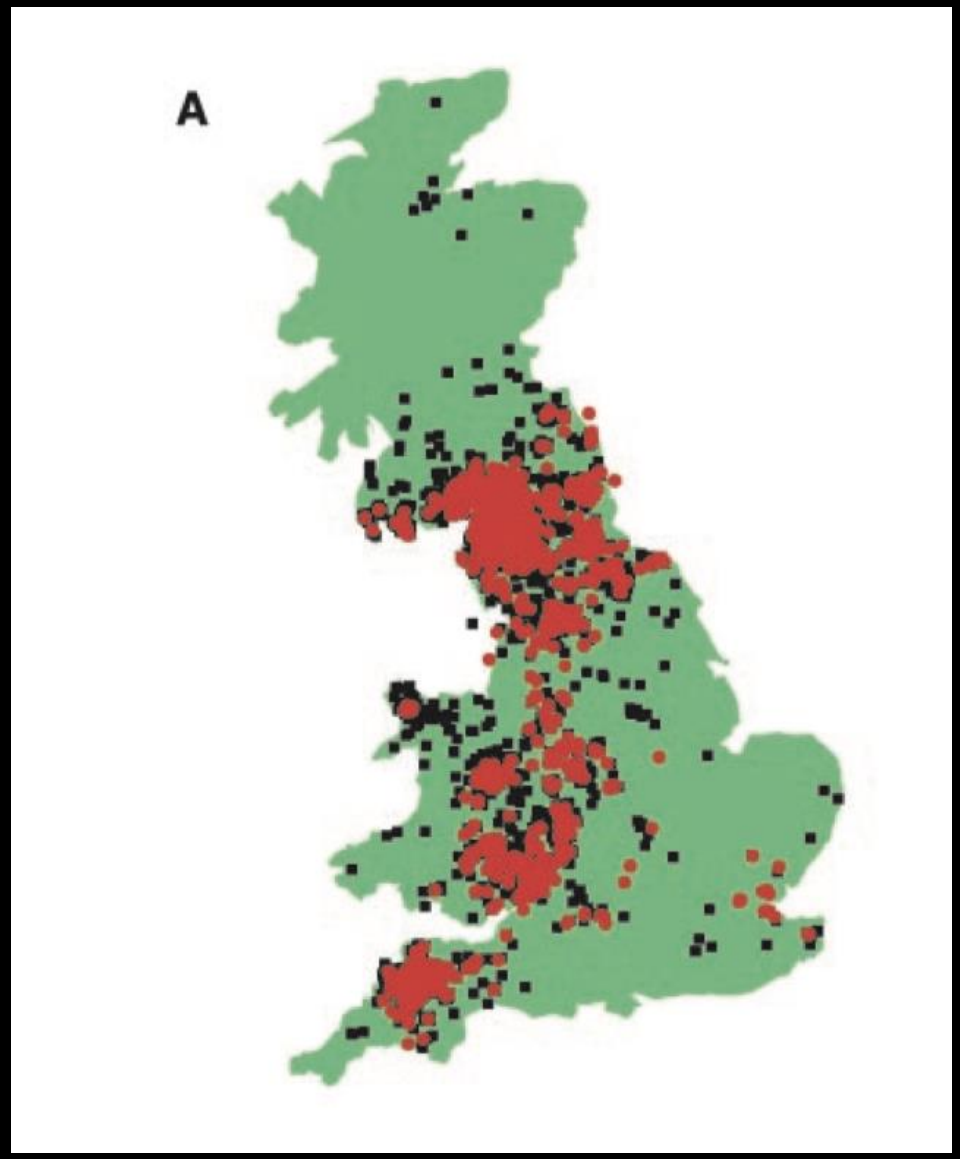
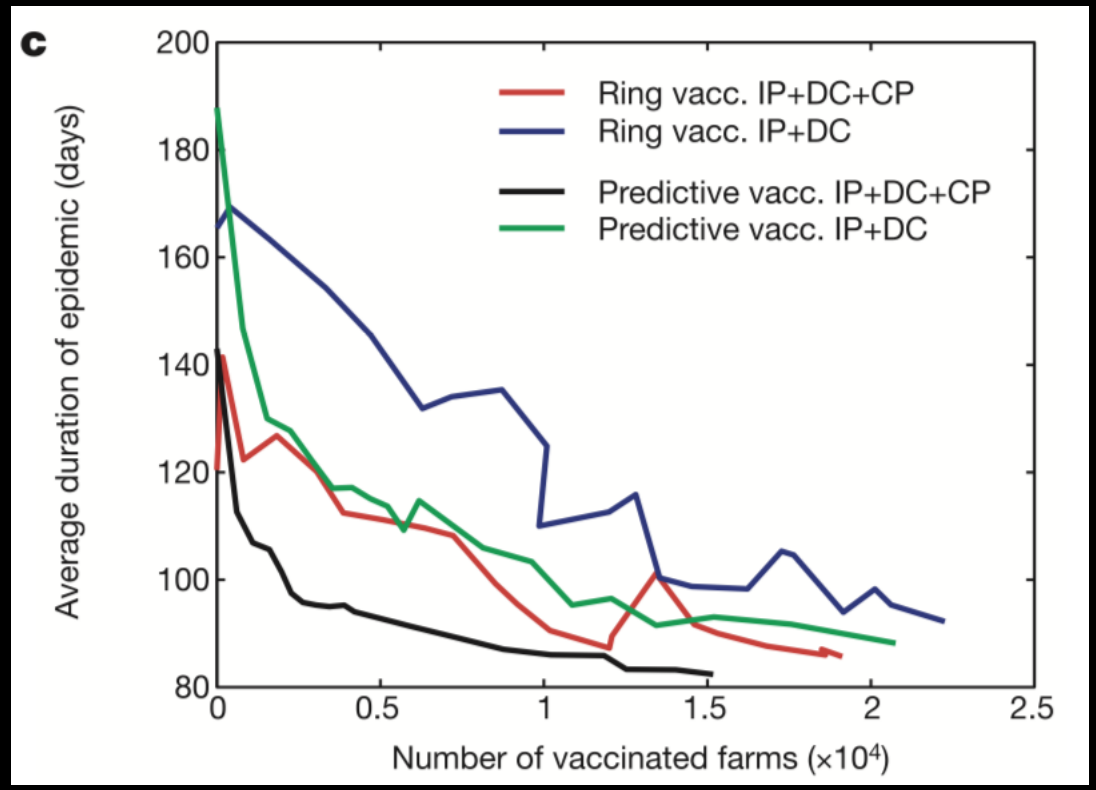


Foot & Mouth Disease, UK 2001

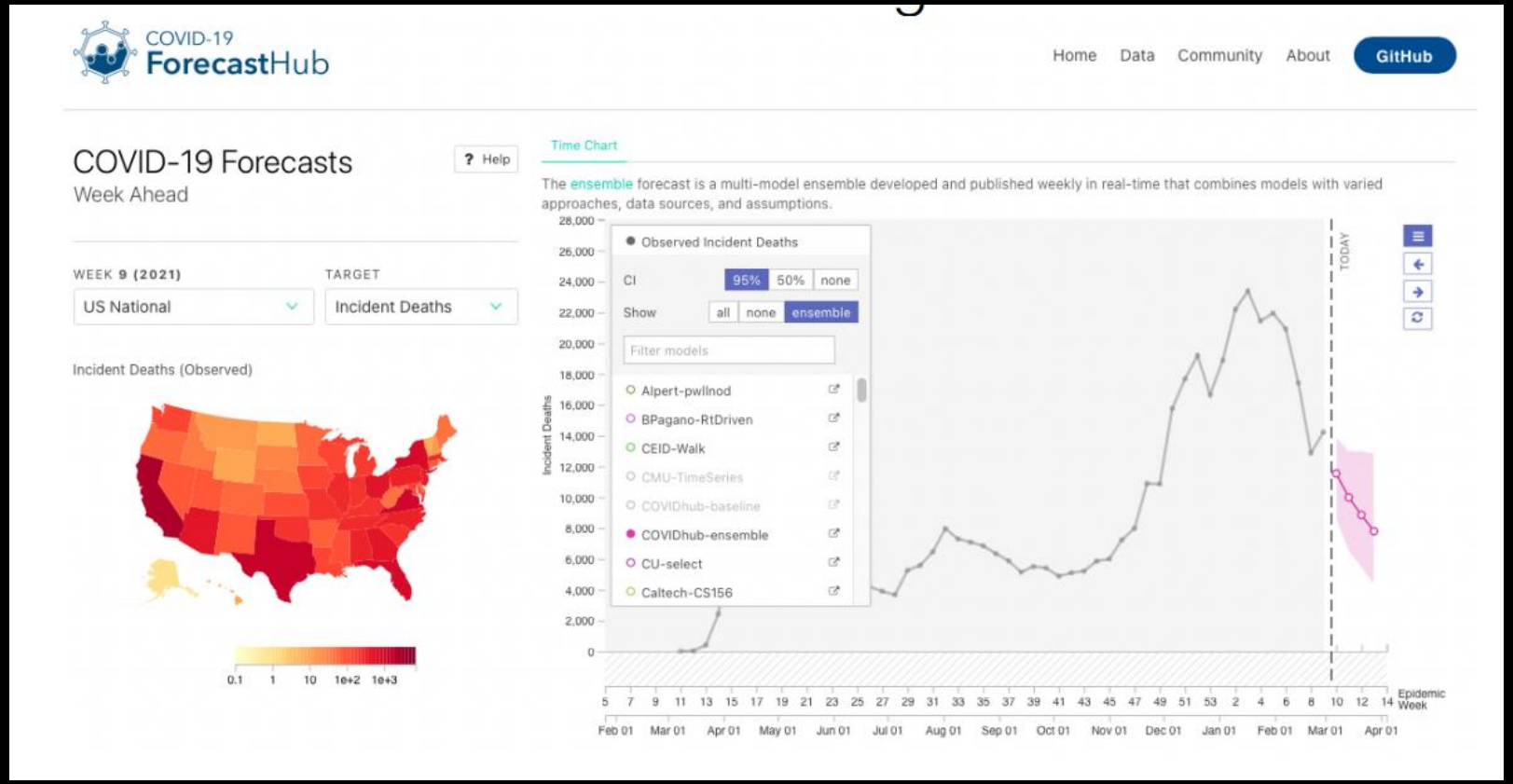
- Series of outbreaks among farms
- Questions around severity of control and which controls to implement
- Test the impacts of different control scenarios

Keeling et al. 2001, 2003





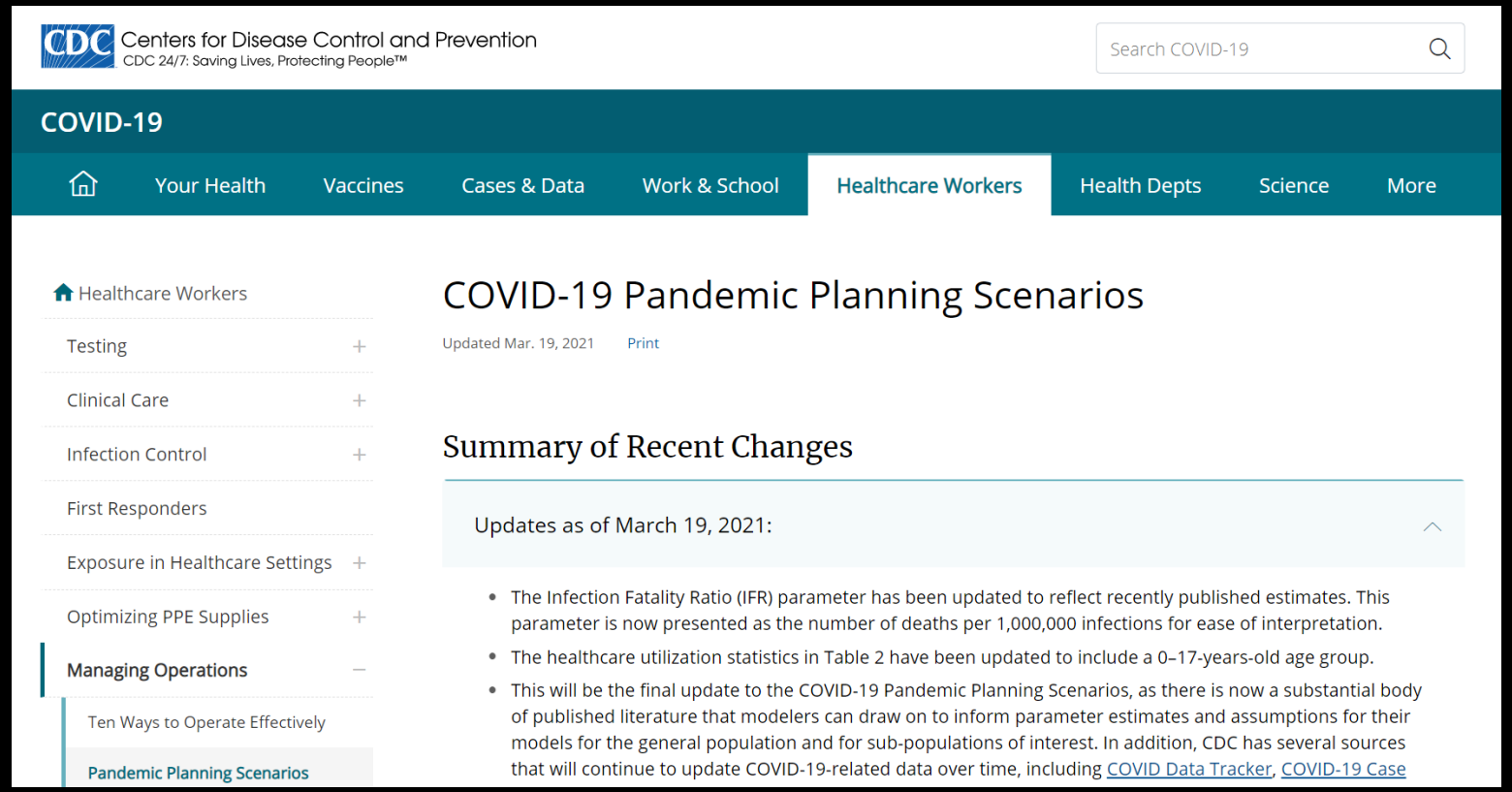
Keeling et al. 2001, 2003



COVID-19, Global 2020—2021

- Efforts to forecast disease incidence and deaths for different locations on a weekly basis

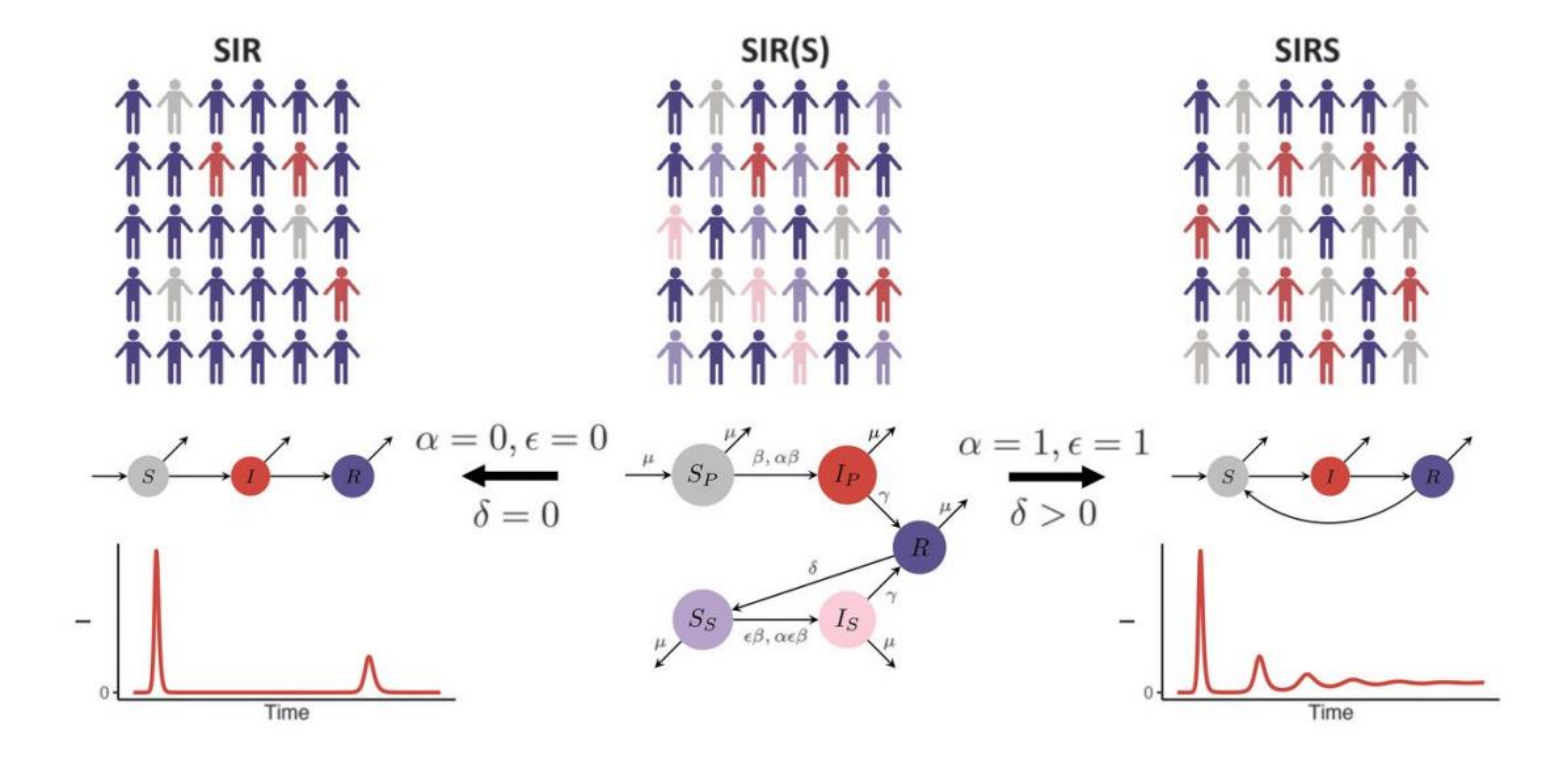
https://viz.covid19forecasthub.org



COVID-19, Global 2020—2021

- Scenario planning: estimates of outcomes using best-case, worst-case, and most-likely parameters for disease transmission and severity
- Based on biological and epidemiologic characteristics of SARS-CoV-2

https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html

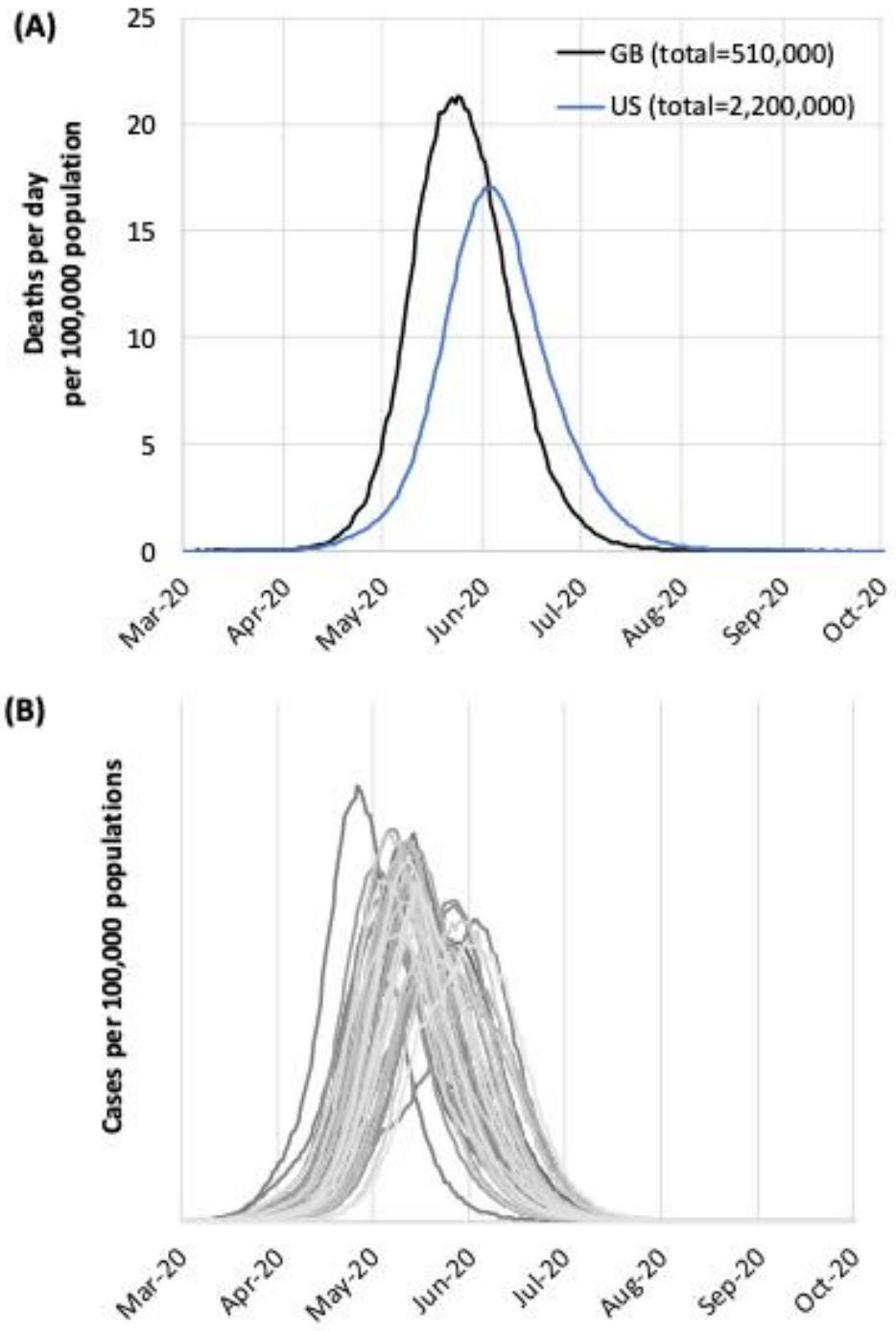


COVID-19, Global 2020—2021

- Understanding immunity, vaccination, and long-term dynamics

Saad-Roy et al. 2020

Ferguson et al. 2020



COVID-19, Global 2020—2021

- Questions around severity of control and which controls to implement
- Test the impacts of different control scenarios

Figure 1: Unmitigated epidemic scenarios for GB and the US.

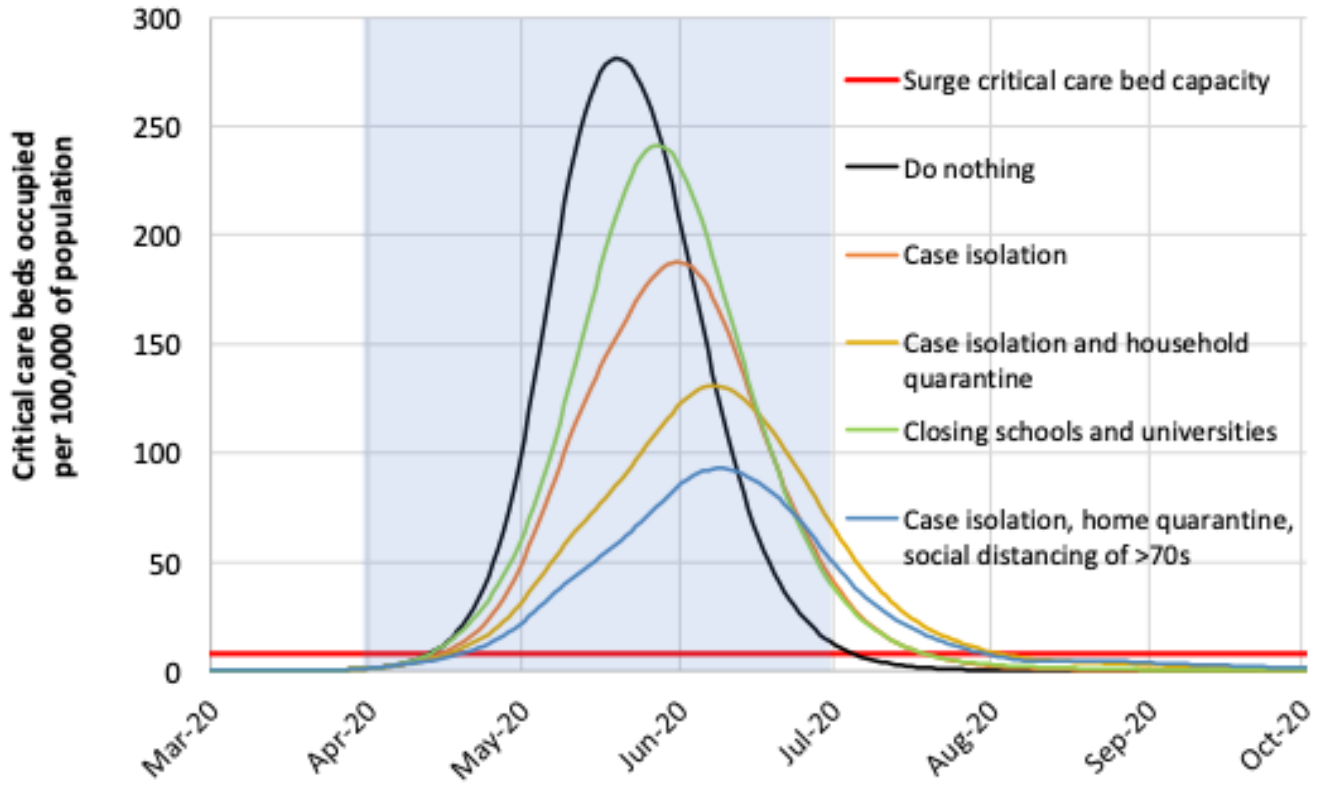


Figure 2: Mitigation strategy scenarios for GB showing critical care (ICU) bed requirements. The black line shows the unmitigated epidemic. The green line shows a mitigation strategy incorporating closure of schools and universities; orange line shows case isolation; yellow line shows case isolation and household quarantine; and the blue line shows case isolation, home quarantine and social distancing of those aged over 70. The blue shading shows the 3-month period in which these interventions are assumed to remain in place.

COVID-19, Global 2020—2021

- Questions around severity of control and which controls to implement
- Test the impacts of different control scenarios

Ferguson et al. 2020

“All models are wrong, but some are useful.”

-George Box

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Week 1: Determinants of Epidemic Growth

Dr. Henrik Salje
University of Cambridge

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Objectives

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

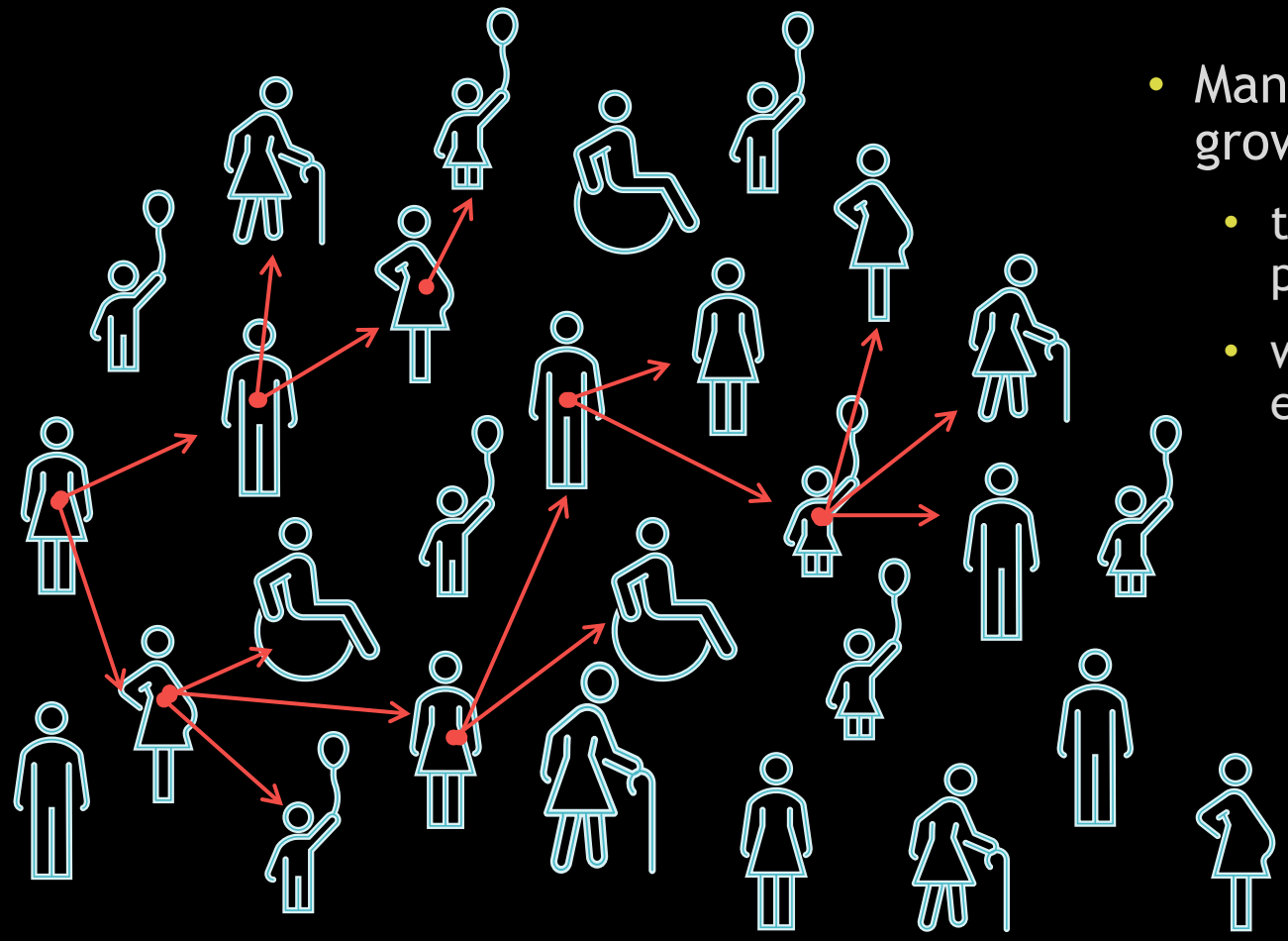
Post Questions in the Chat!

(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

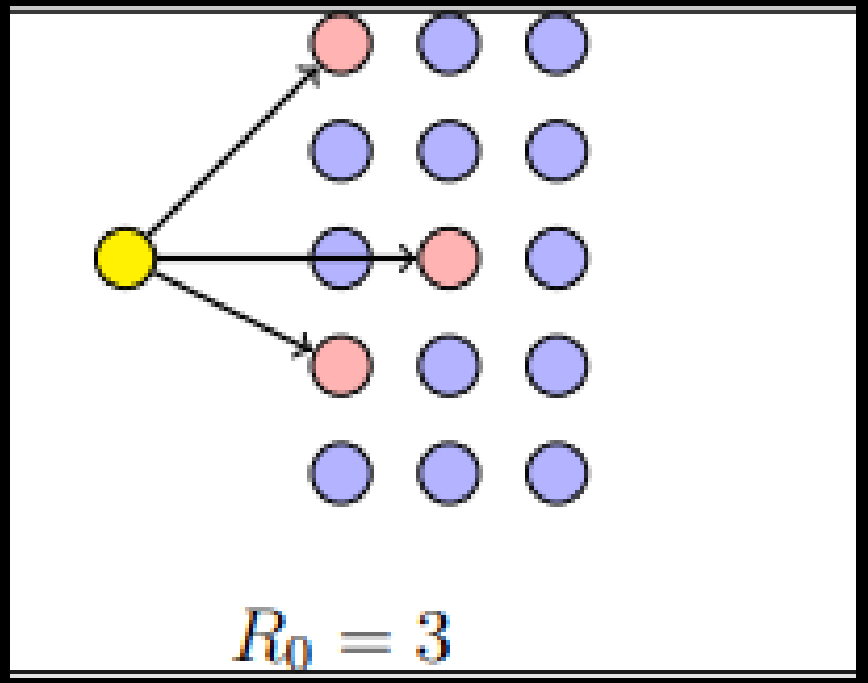
- Simple measure of growth
- The time it takes for the number of incident cases to double early in an epidemic
- Good measure of how quickly a disease spreads in a population

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

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

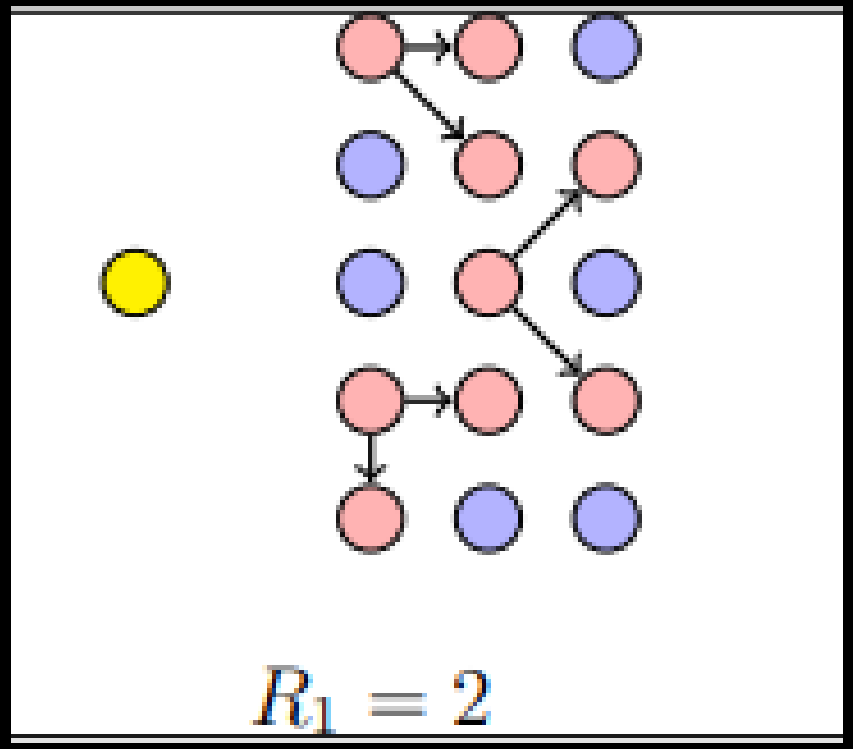
Reproductive Number

- 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



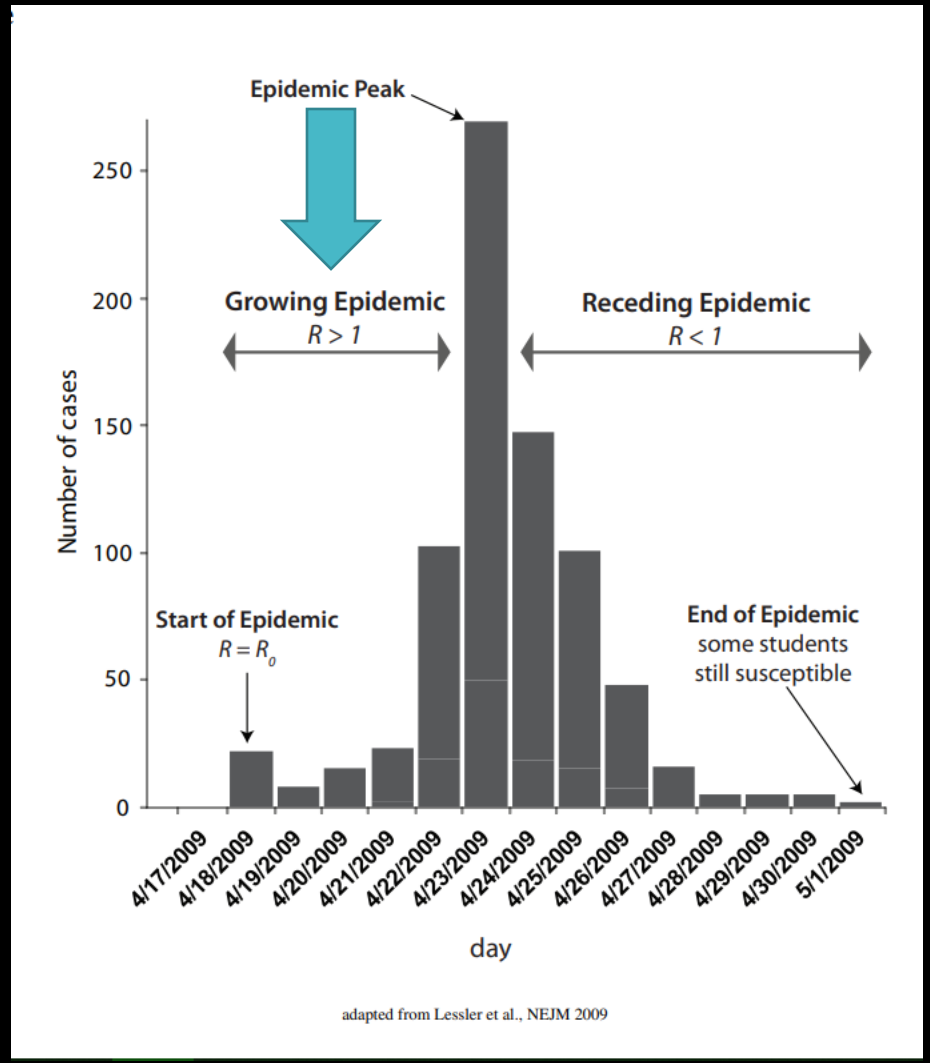
Reproductive Number

- 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



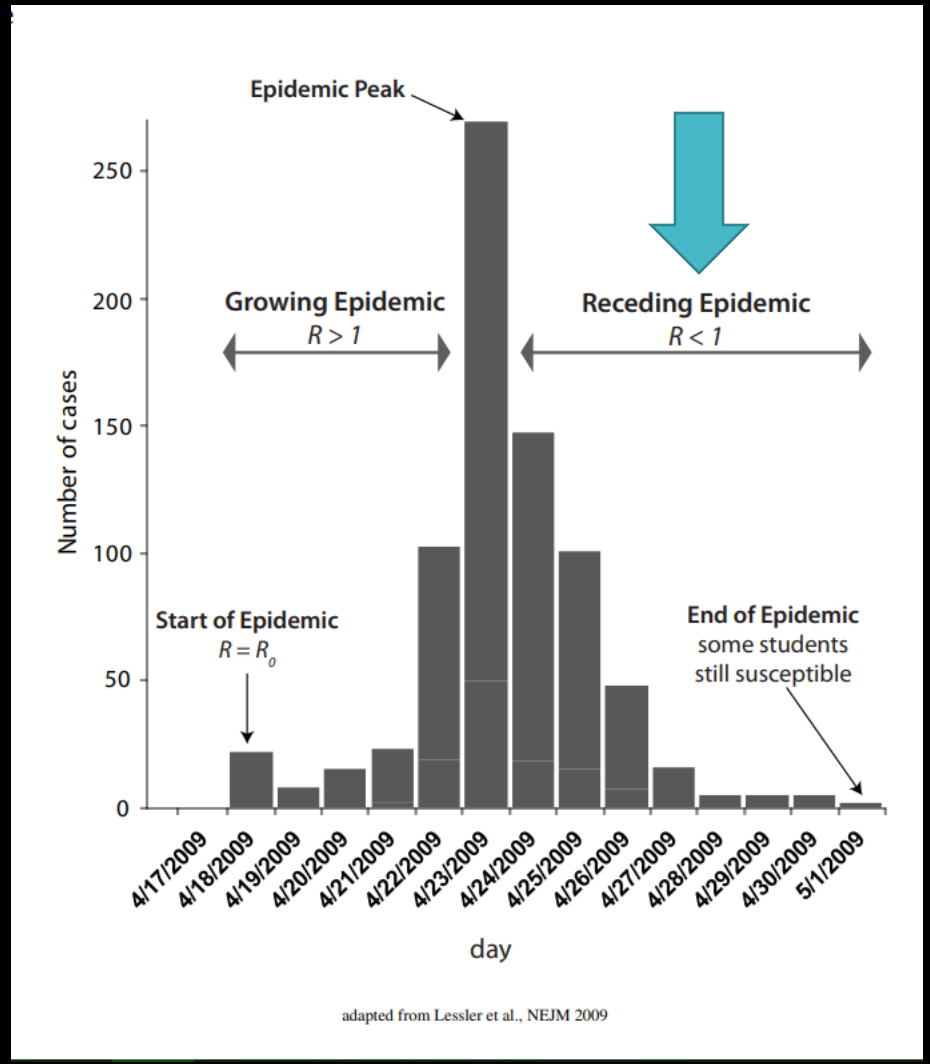
Reproductive Numbers & Epidemic Curve

- 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



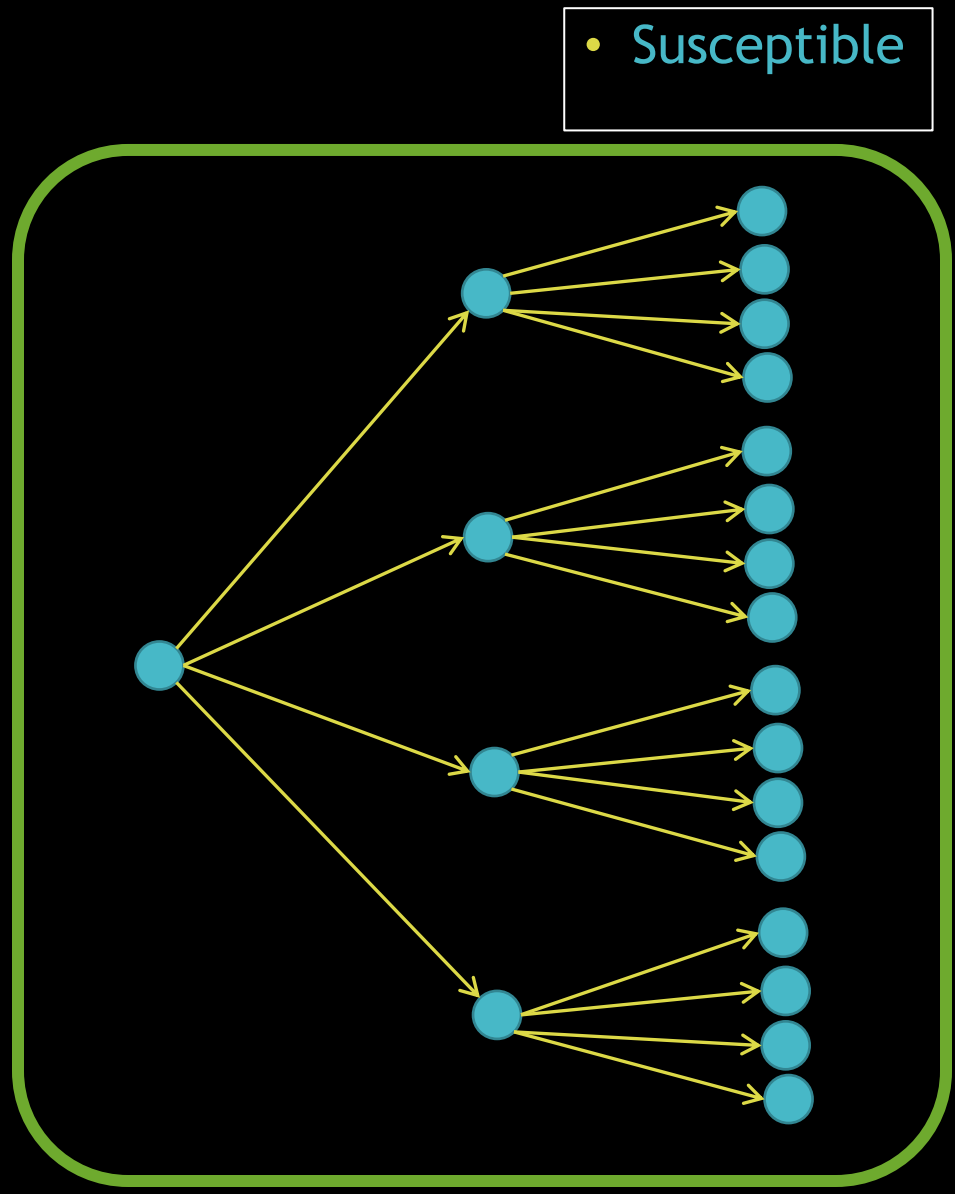
Reproductive Numbers & Epidemic Curve

- 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



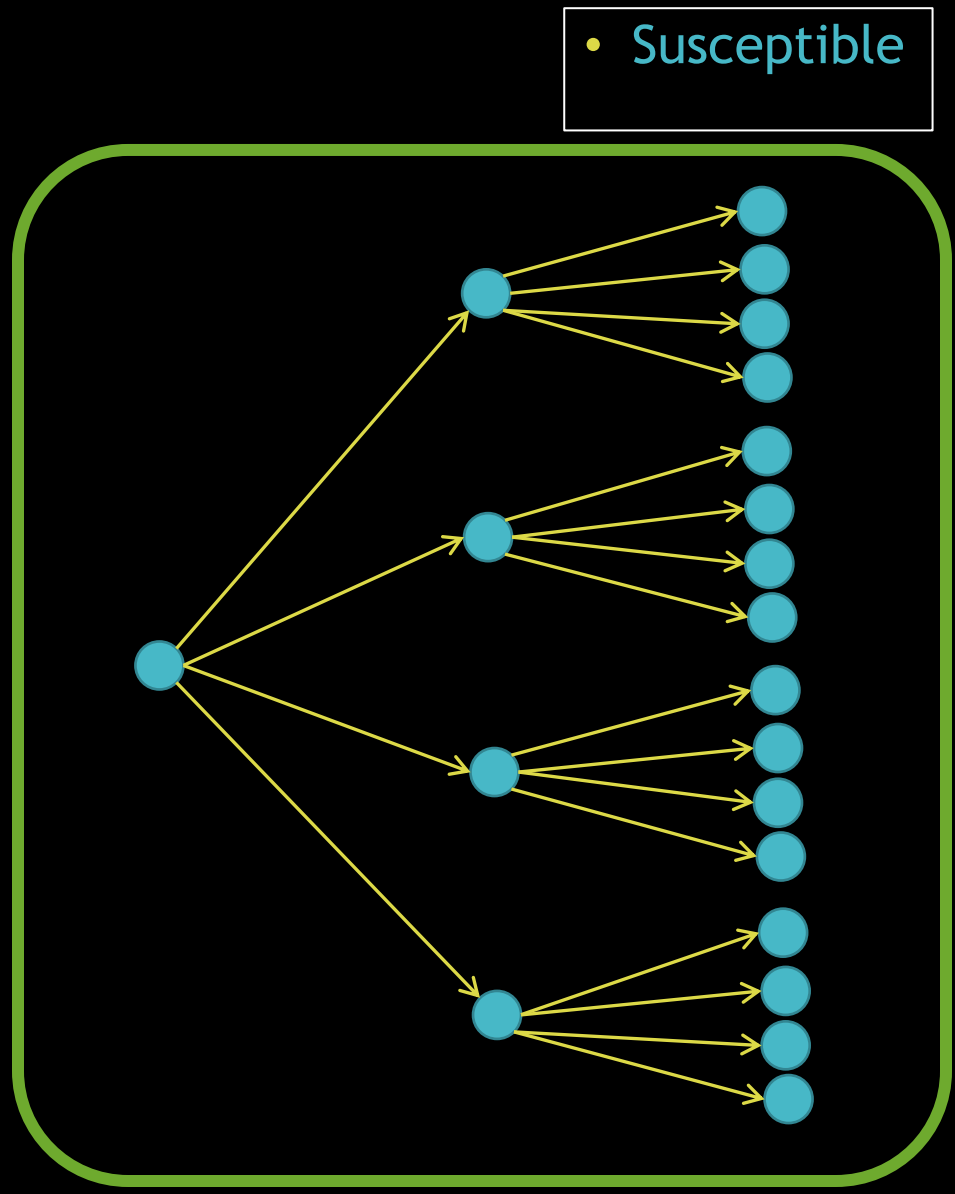
What is the Reproductive Number?

- The entire population is susceptible
  - R0 or Rt?



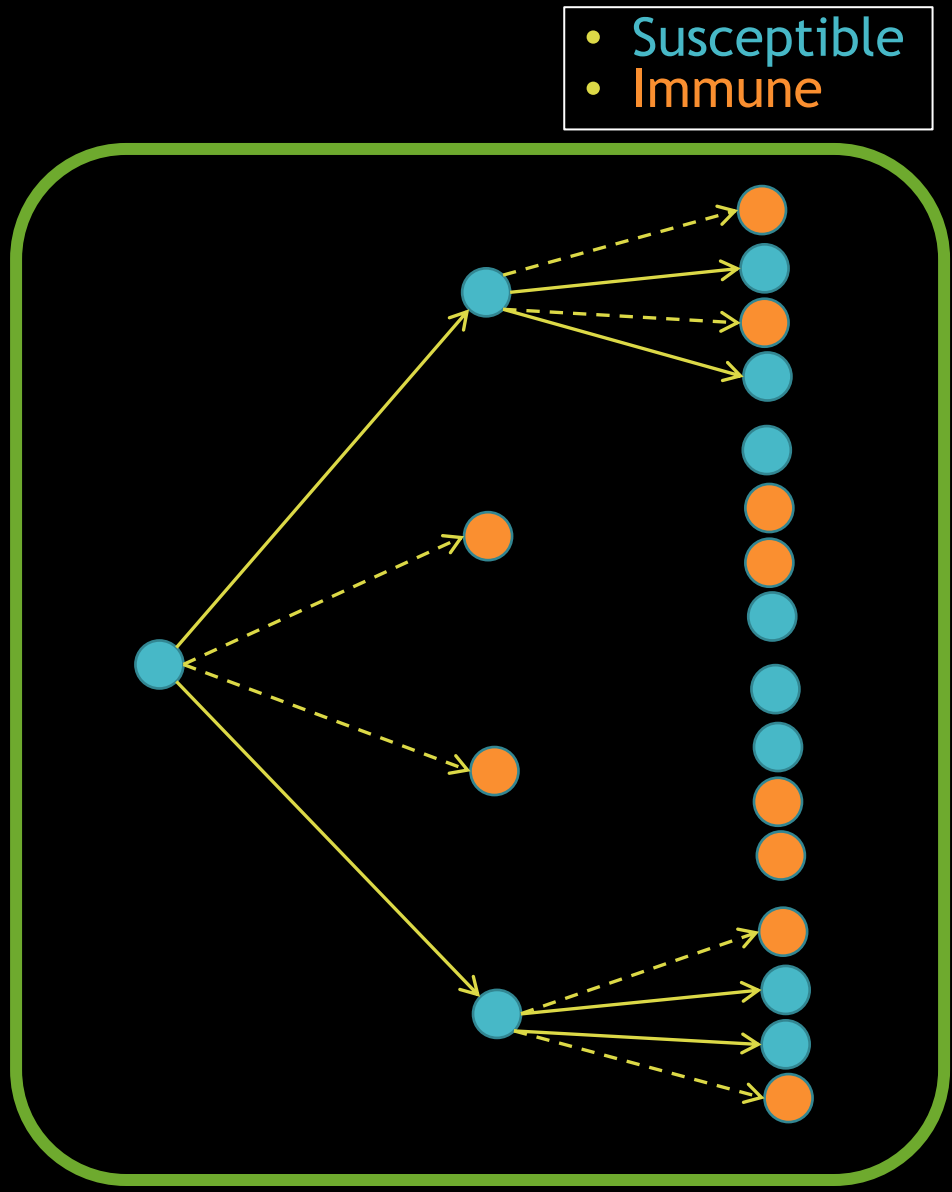
What is the Reproductive Number?

- The entire population is susceptible
  - R0=4



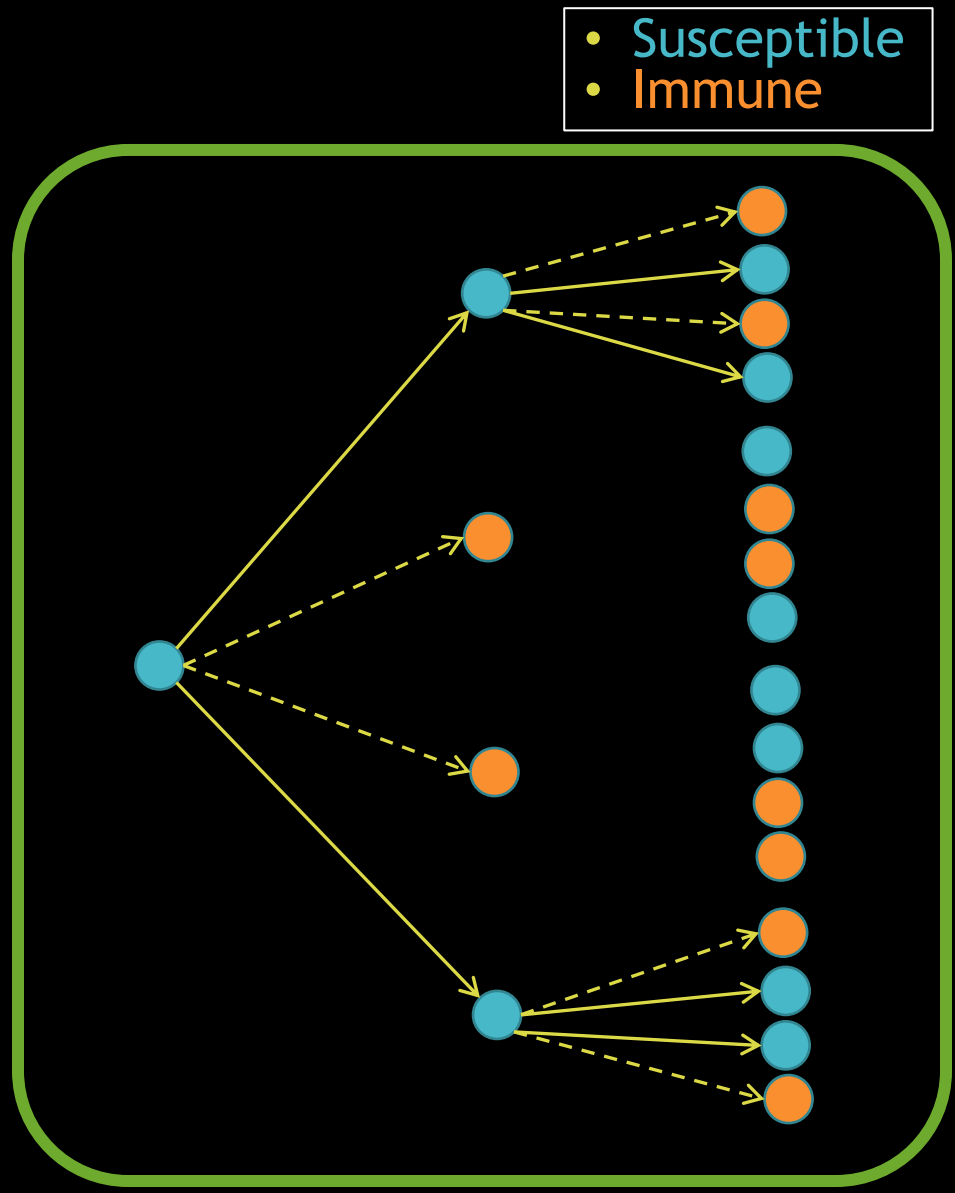
What is the Reproductive Number?

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



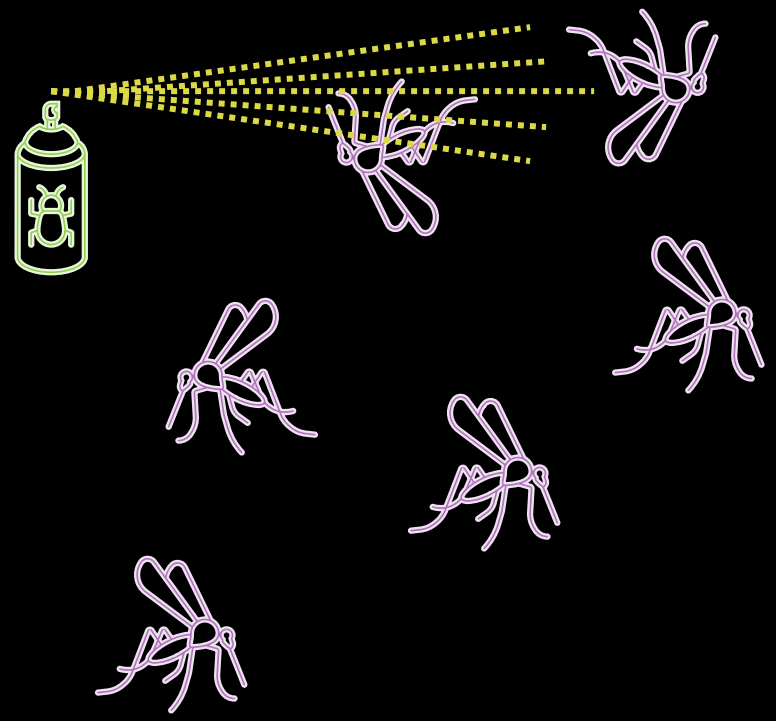
What is the Reproductive Number?

- 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

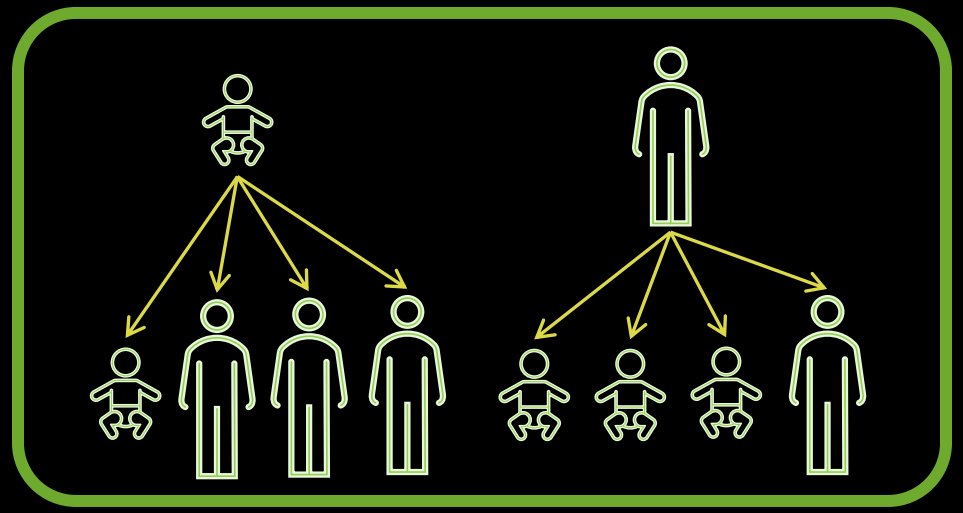
Pathogen	R0
Cholera	2.6, 5.0, 4.0—15.0
Dengue	1.3—6.3
Influenza	1.5—2.0
Malaria	1—10, 100—1000, 1—3000
Measles	7.7, 7.1—29.3, 11.0—18.0
Rubella	2.9—7.8, 3.4—5.6
SARS	1.2, 2.7, 2.2—3.6
Smallpox	3.2, 6.9, 3.5—6.0

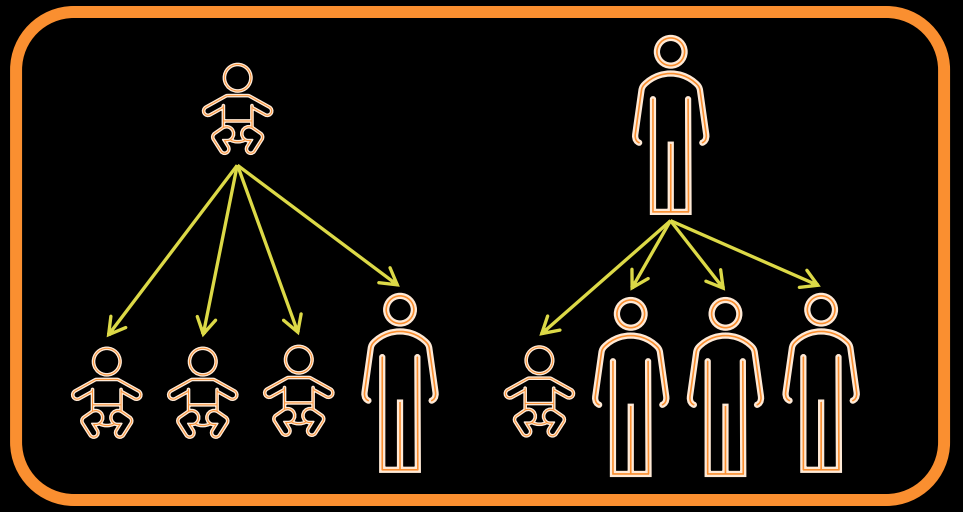
- For many diseases, the reproductive number will be very similar across different settings

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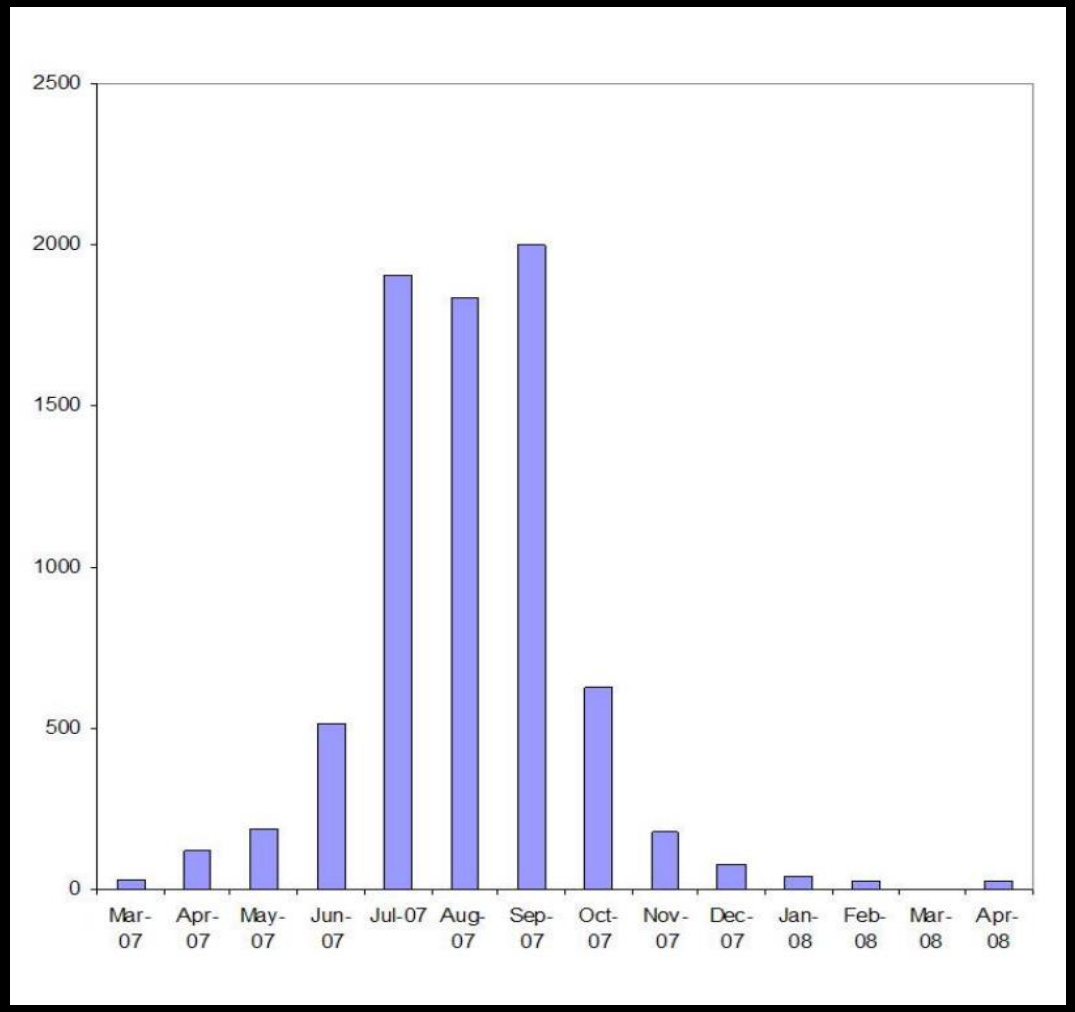
  - each infected adult leads to 1 infection in adults and 3 infections in children
- Population B
  - each infected child leads to 1 infection in adults, and 3 infections in children
  - each infected adult leads to 3 infections in adults and 1 infection in children
- If we vaccinate children, which population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

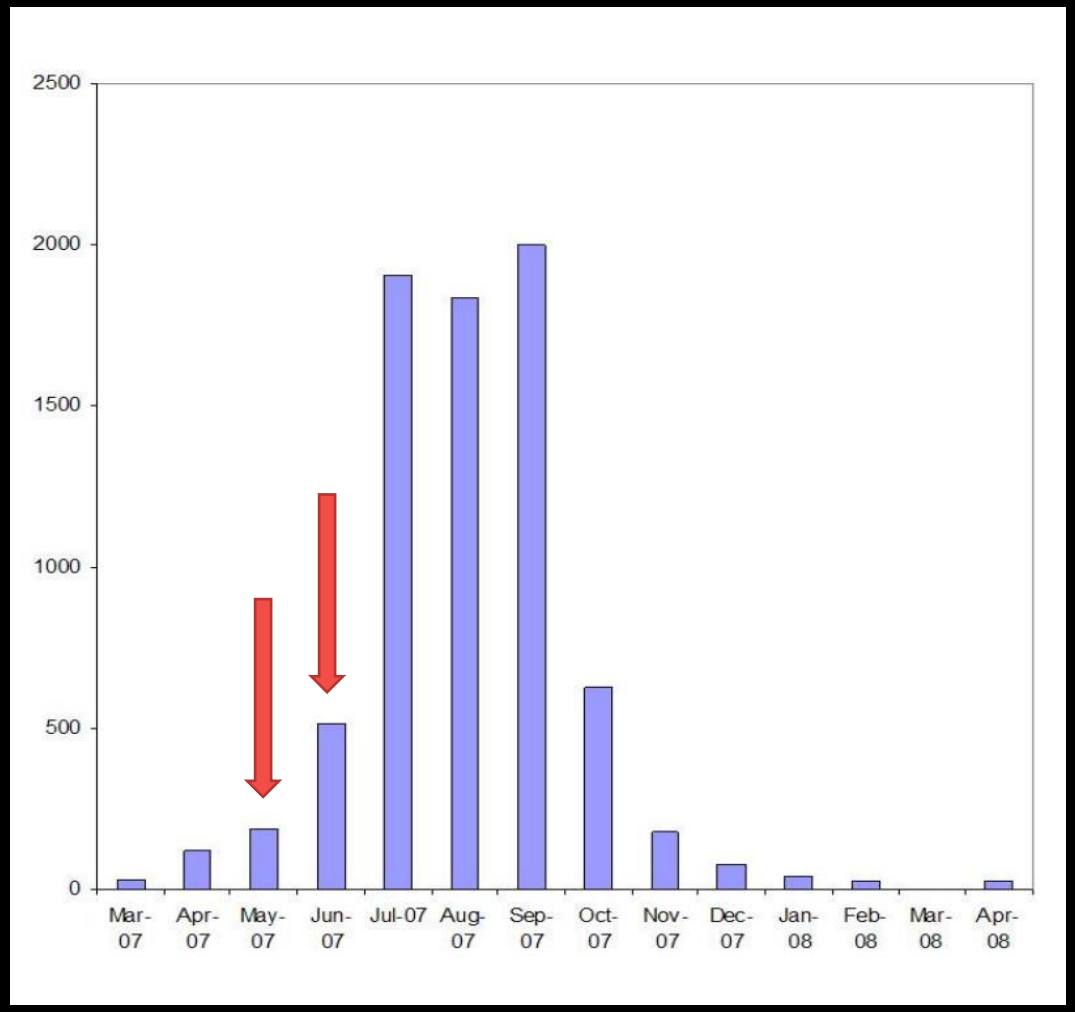
Generation Time & Serial Intervals



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

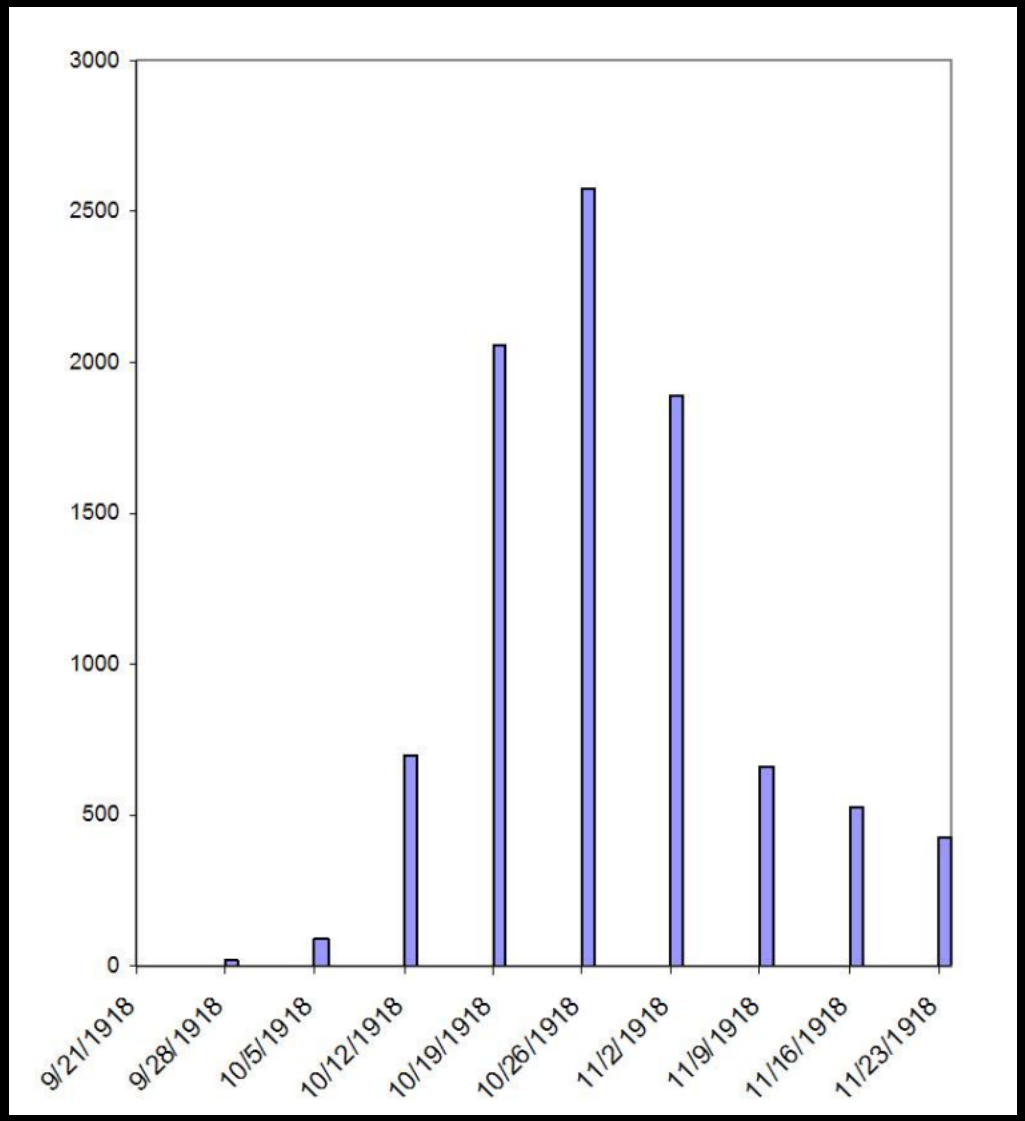
- Measles outbreak in Iceland

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

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

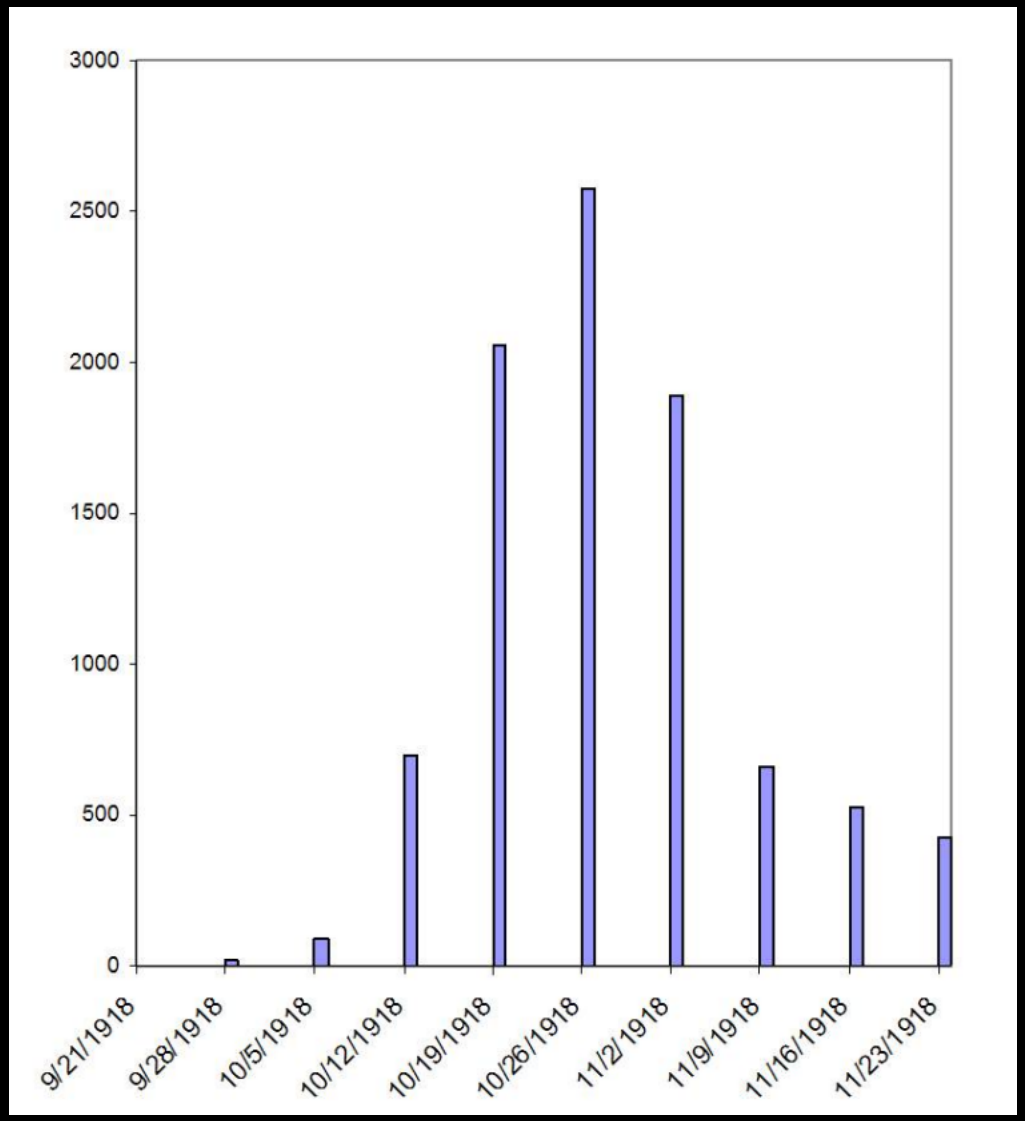
$$= 0.7\ months$$

- 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
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- Comparing the two epidemics:
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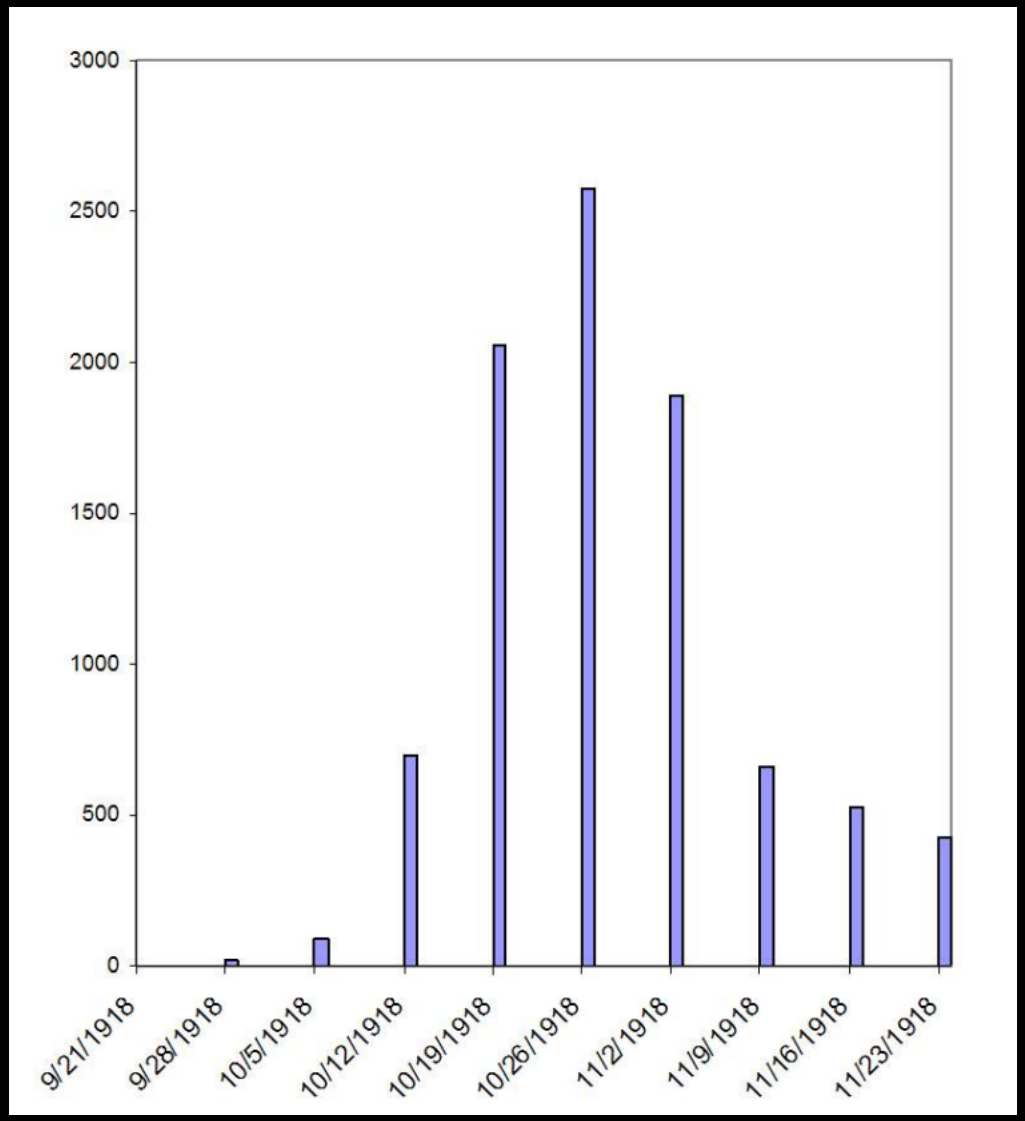
- But
  - Measles R_0=15
  - Influenza R_0=2

?



Generation Time & Epidemic Growth

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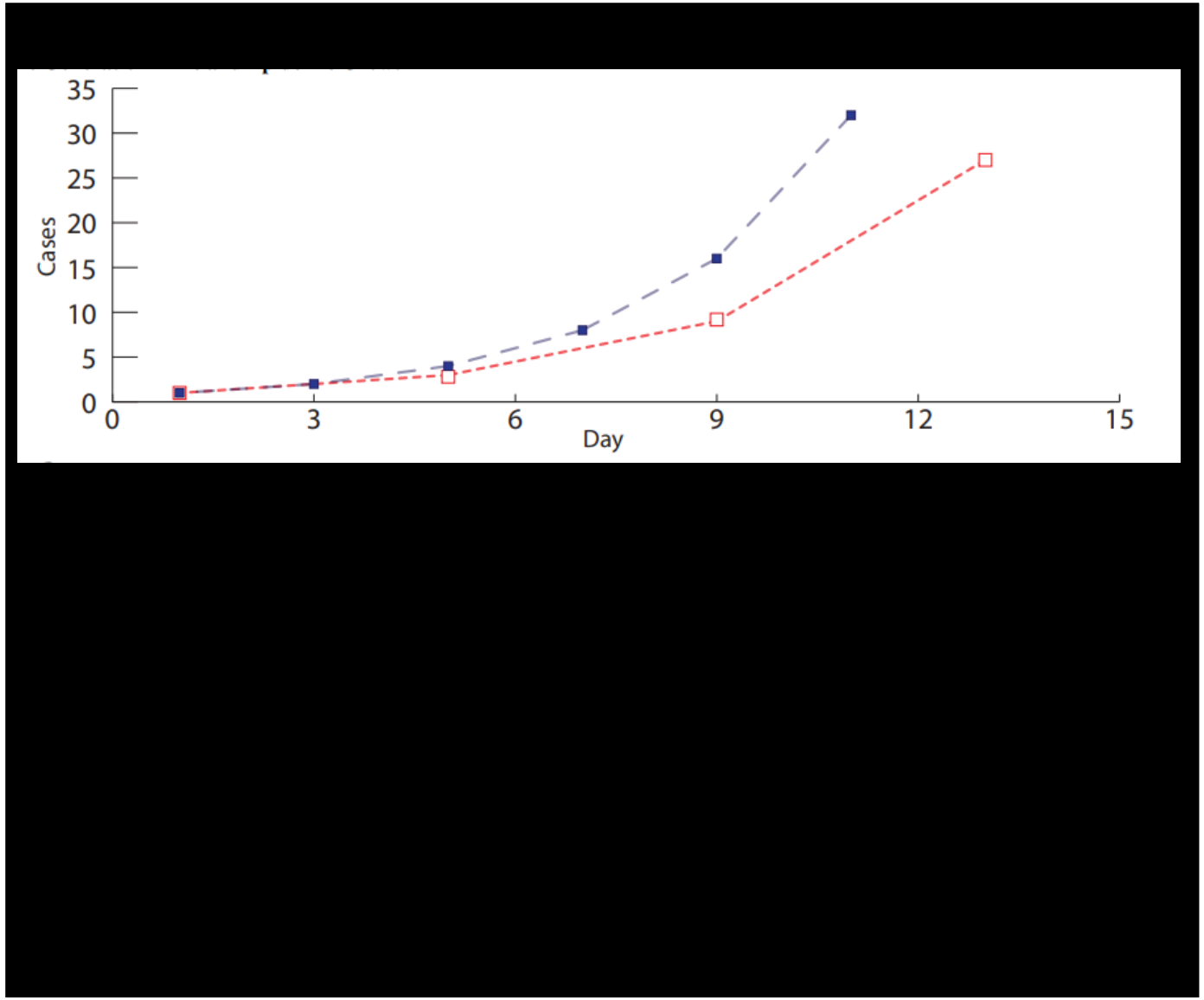
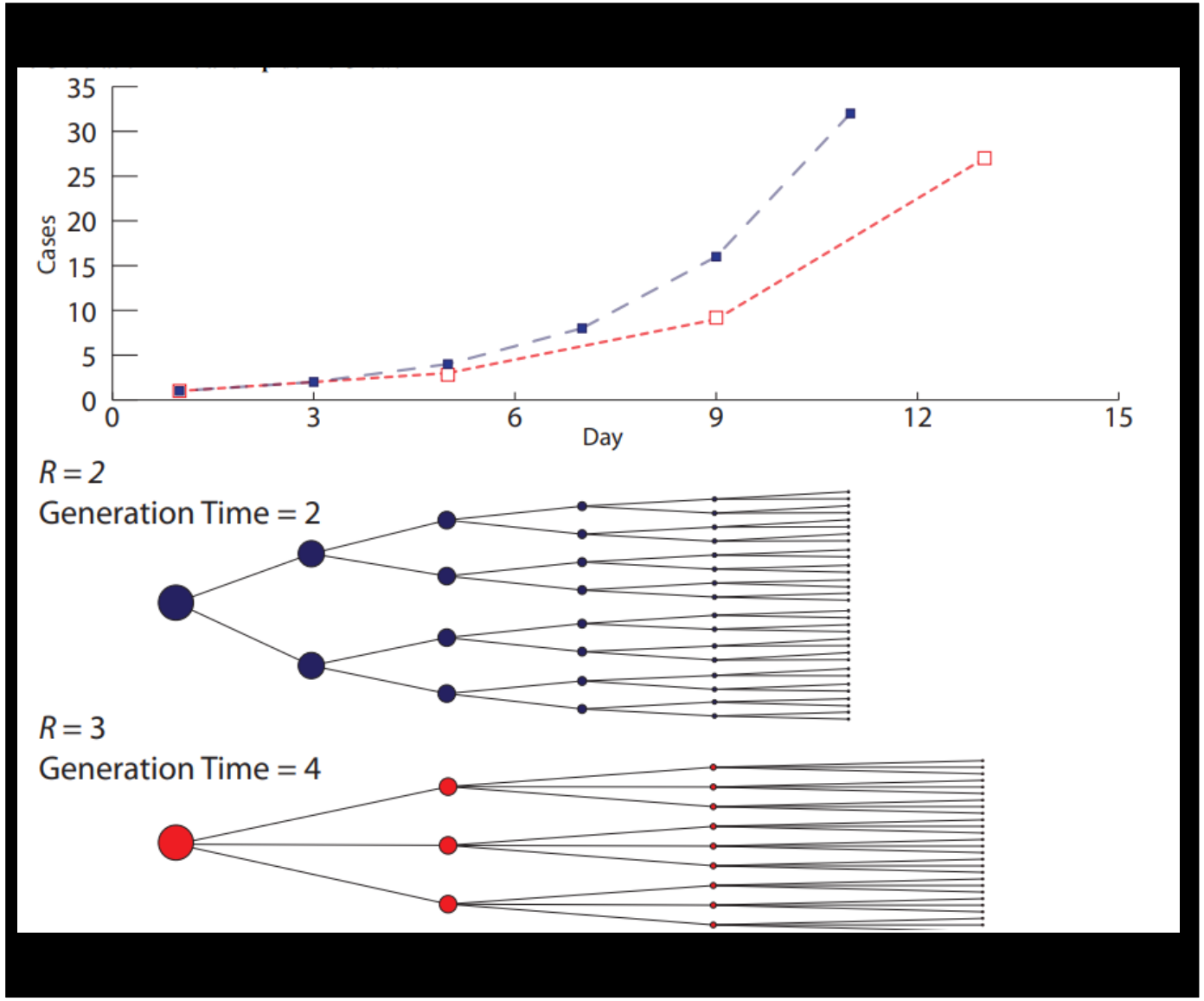


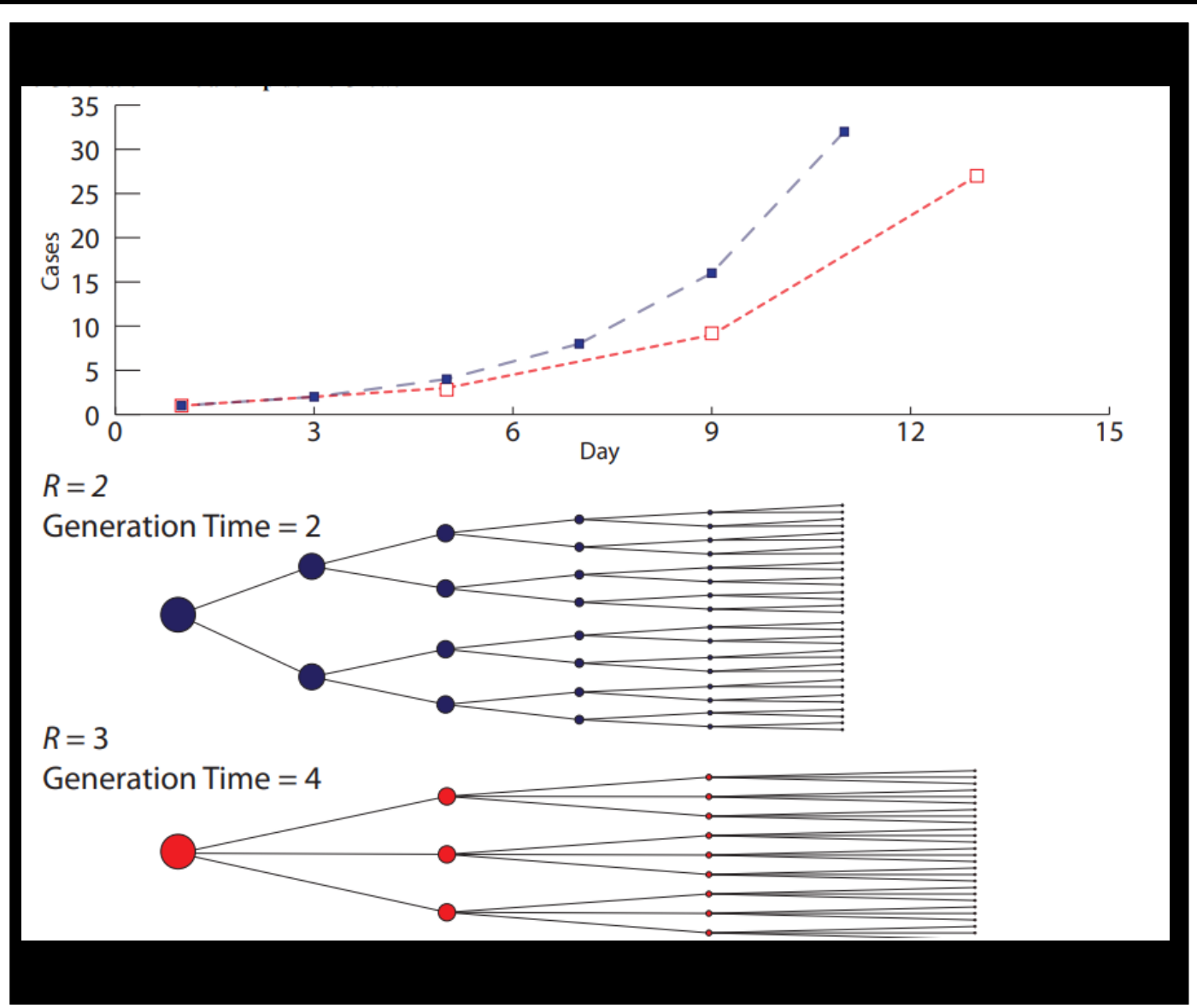
Generation Time & Epidemic Growth

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



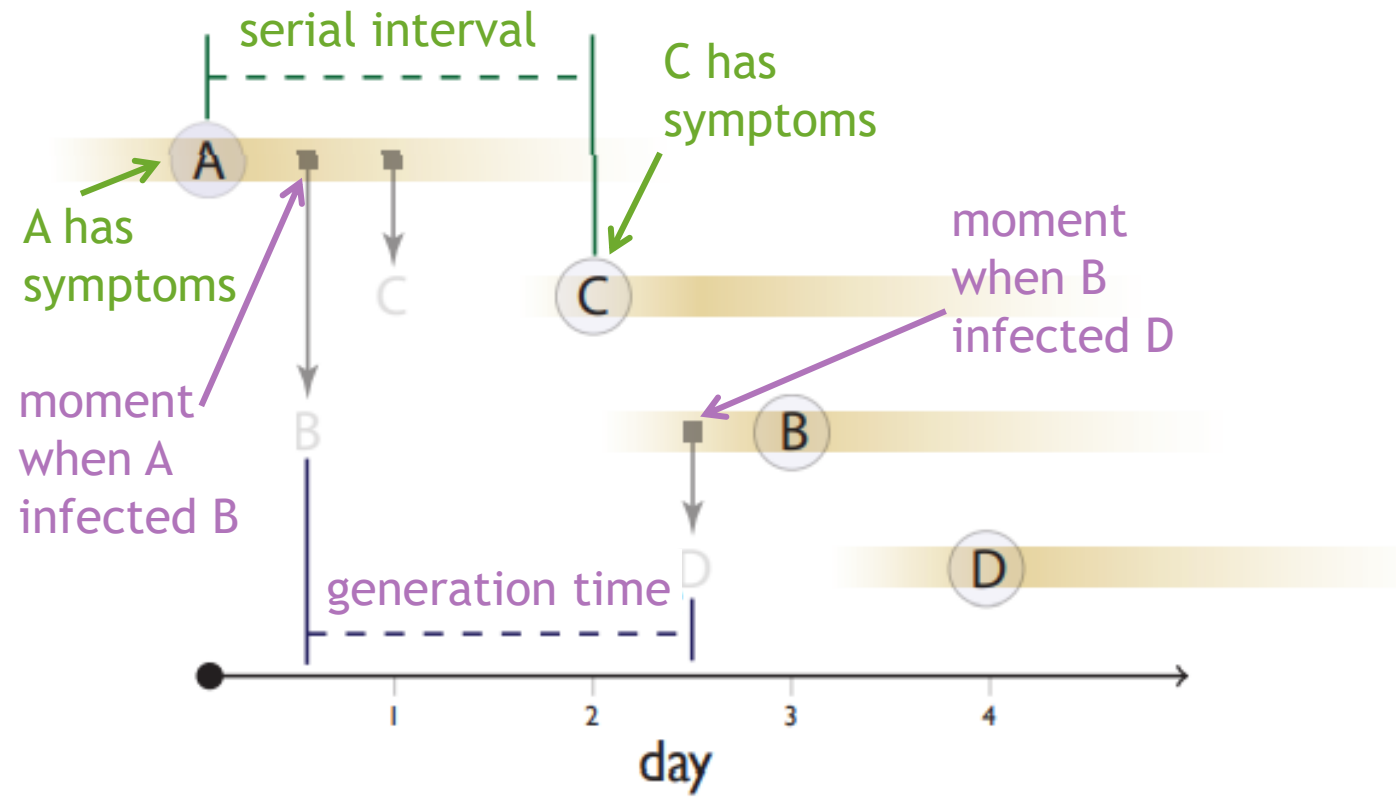
Generation Time & Epidemic Growth

- 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



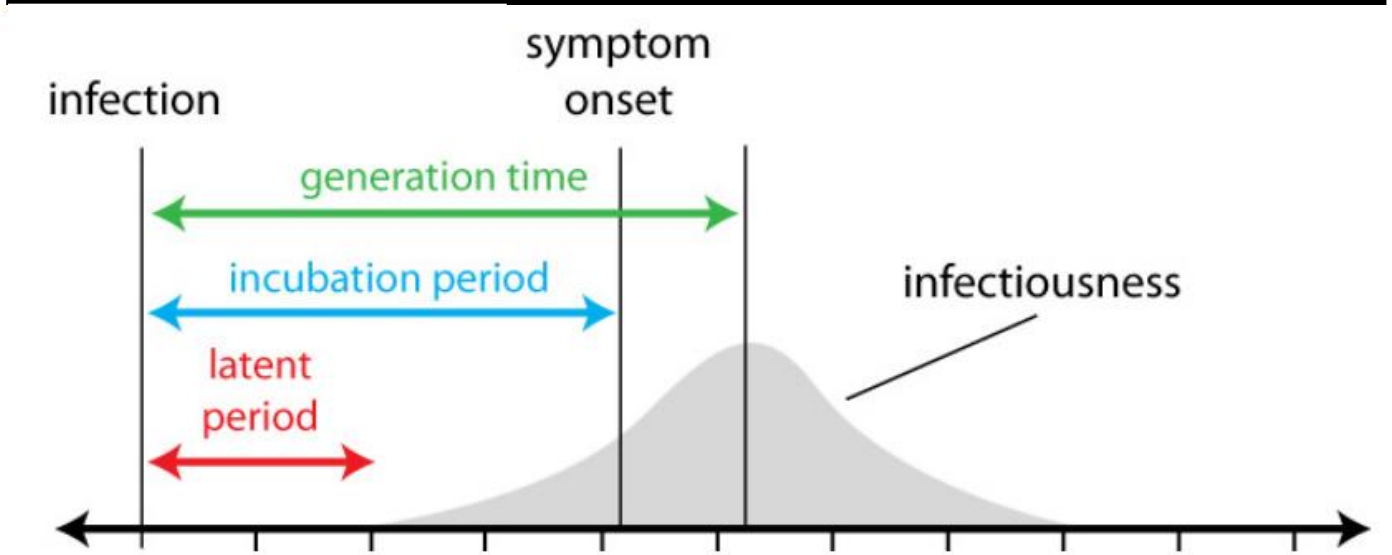
Generation Time & Epidemic Growth

- 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
  - $T_d = 4.7\ days$
  - $T_g = 18\ days$

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

- 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

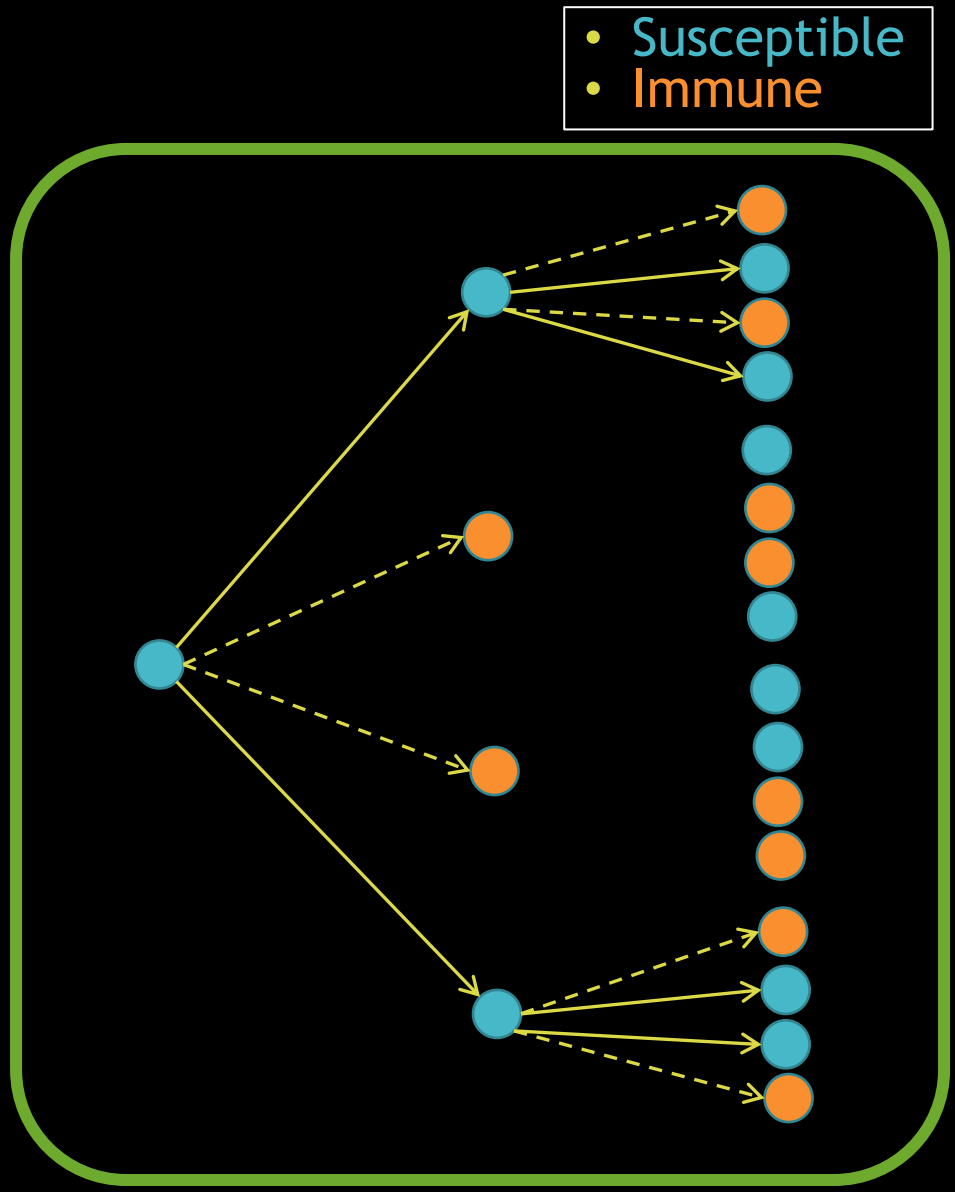
- $R = 2^{T_g/T_d}$

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

Herd Immunity

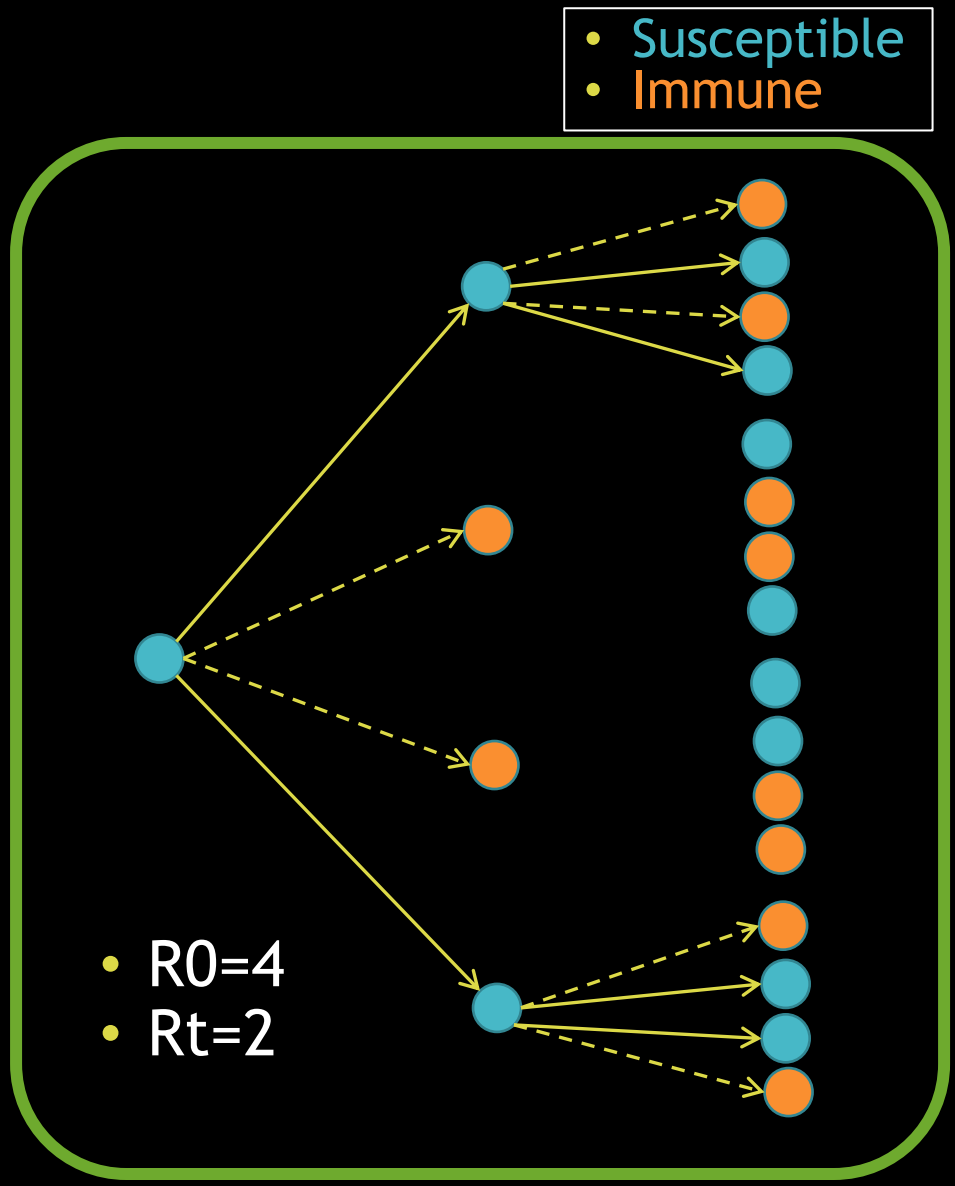
Reproductive Number & Herd Immunity

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



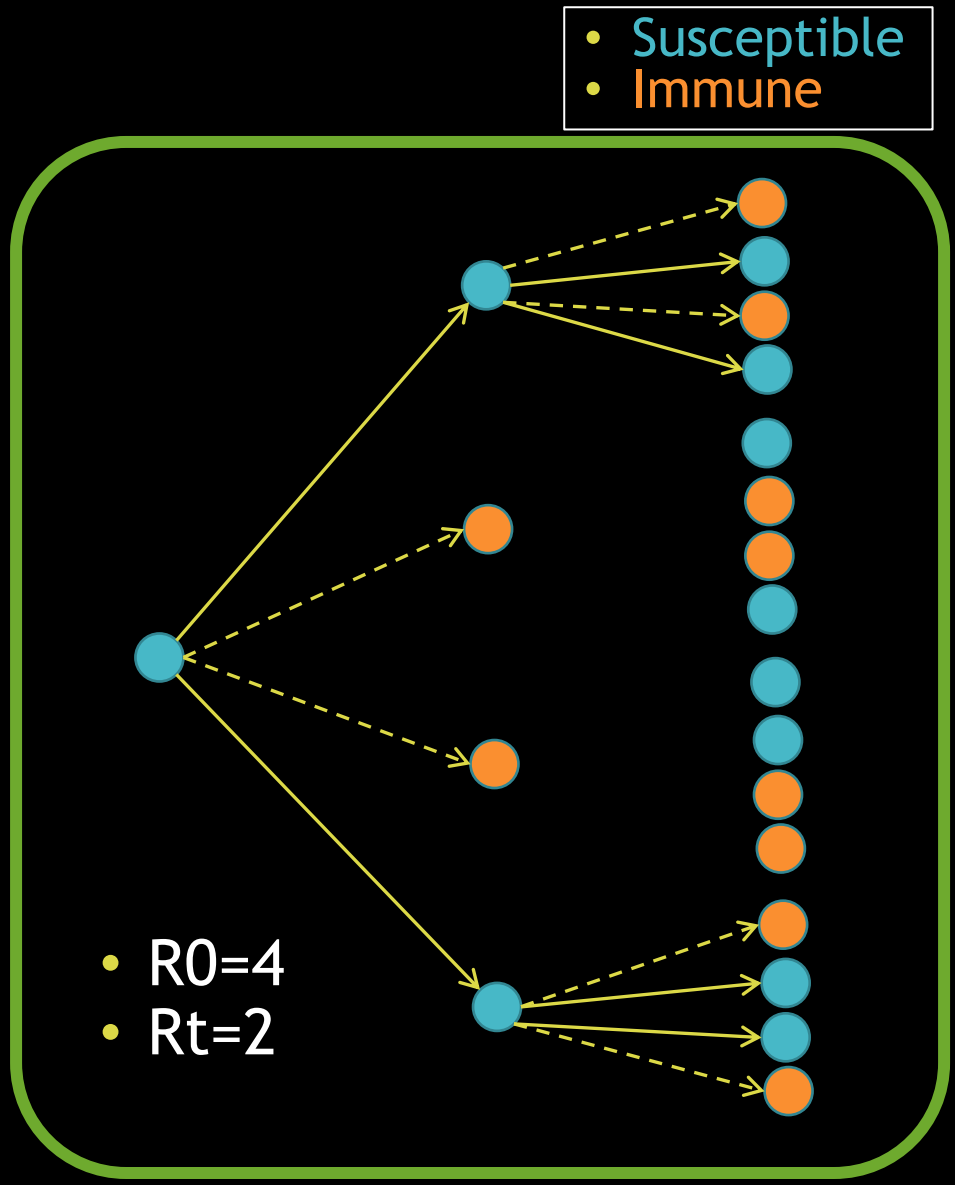
Reproductive Number & Herd Immunity

- 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)
  - $R_t = R_0 s_t$



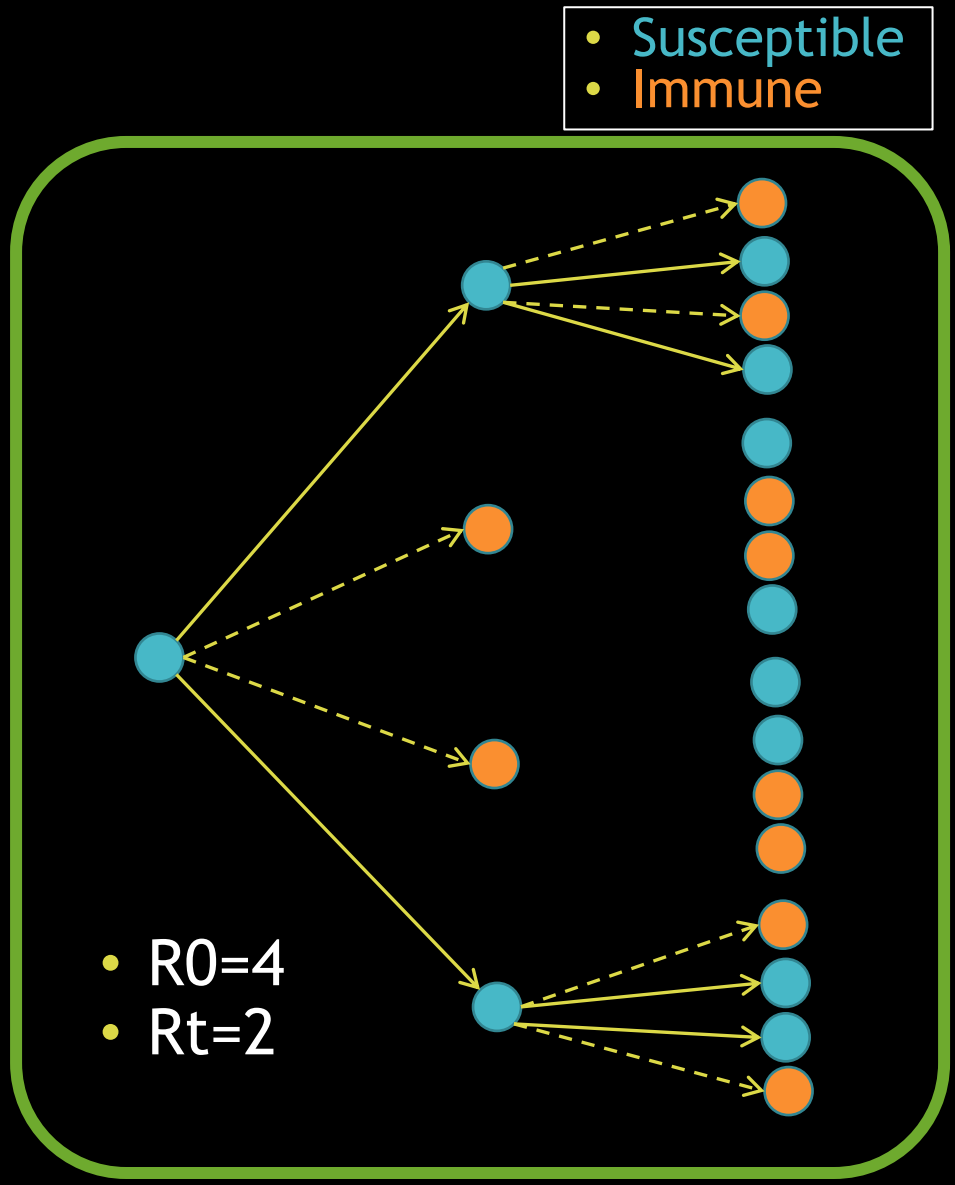
Reproductive Number & Herd Immunity

- 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



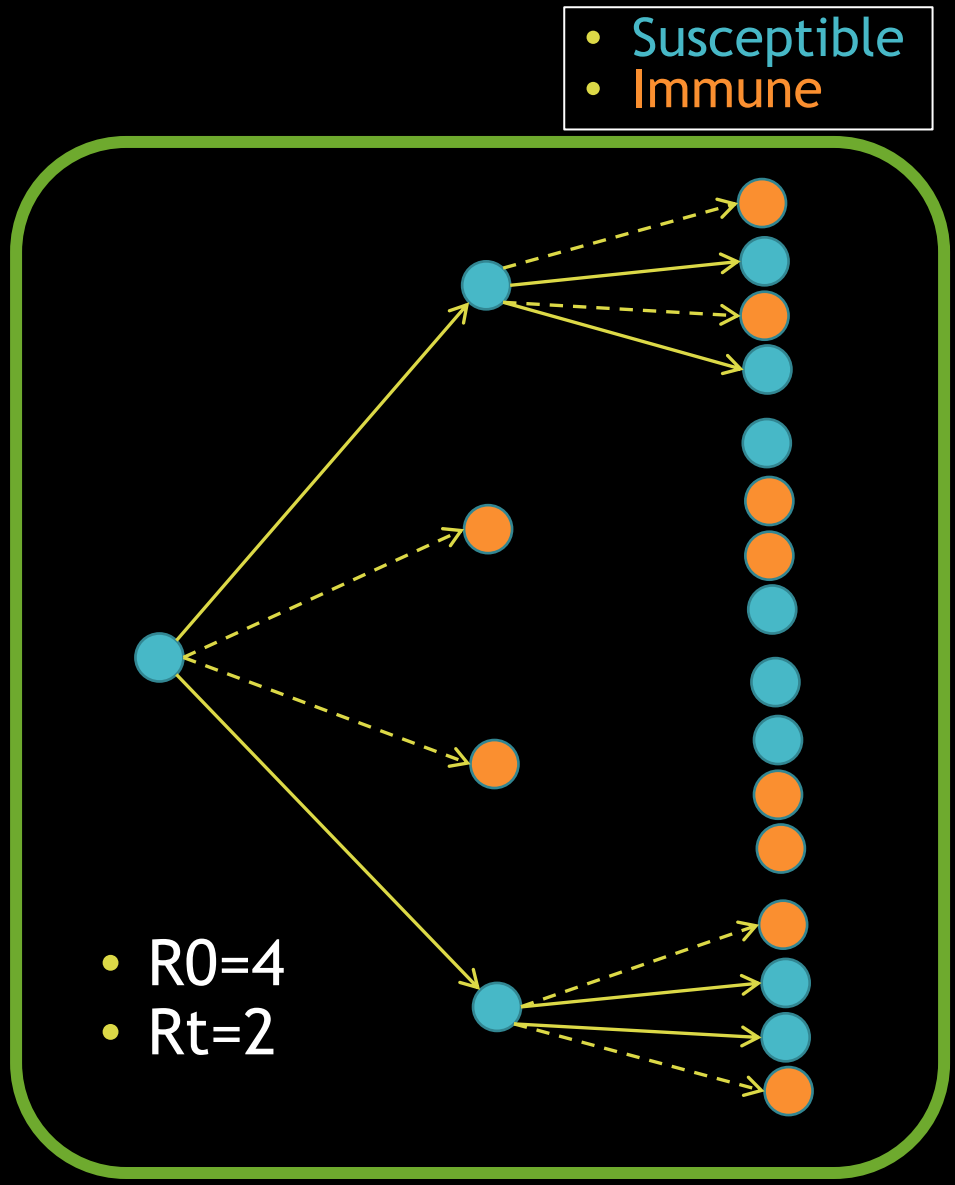
Reproductive Number & Herd Immunity

- 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?

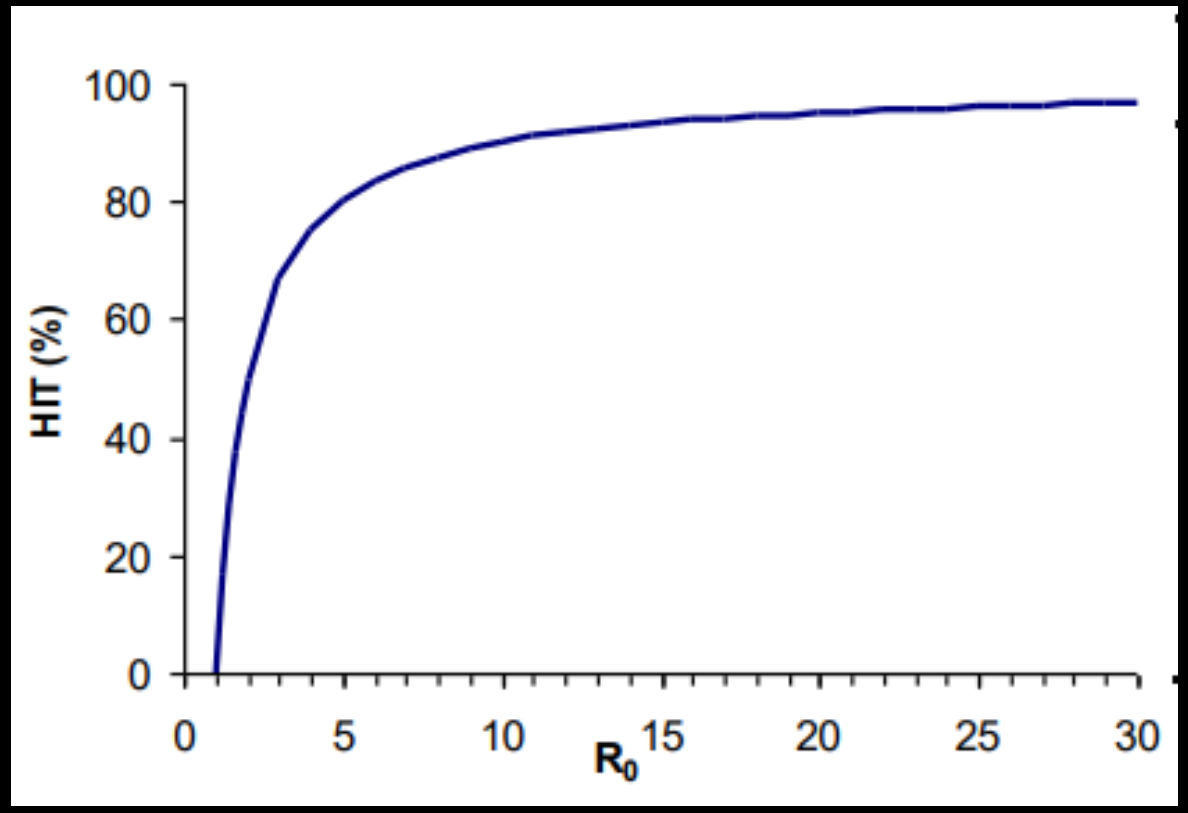


Reproductive Number & Herd Immunity

- 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%

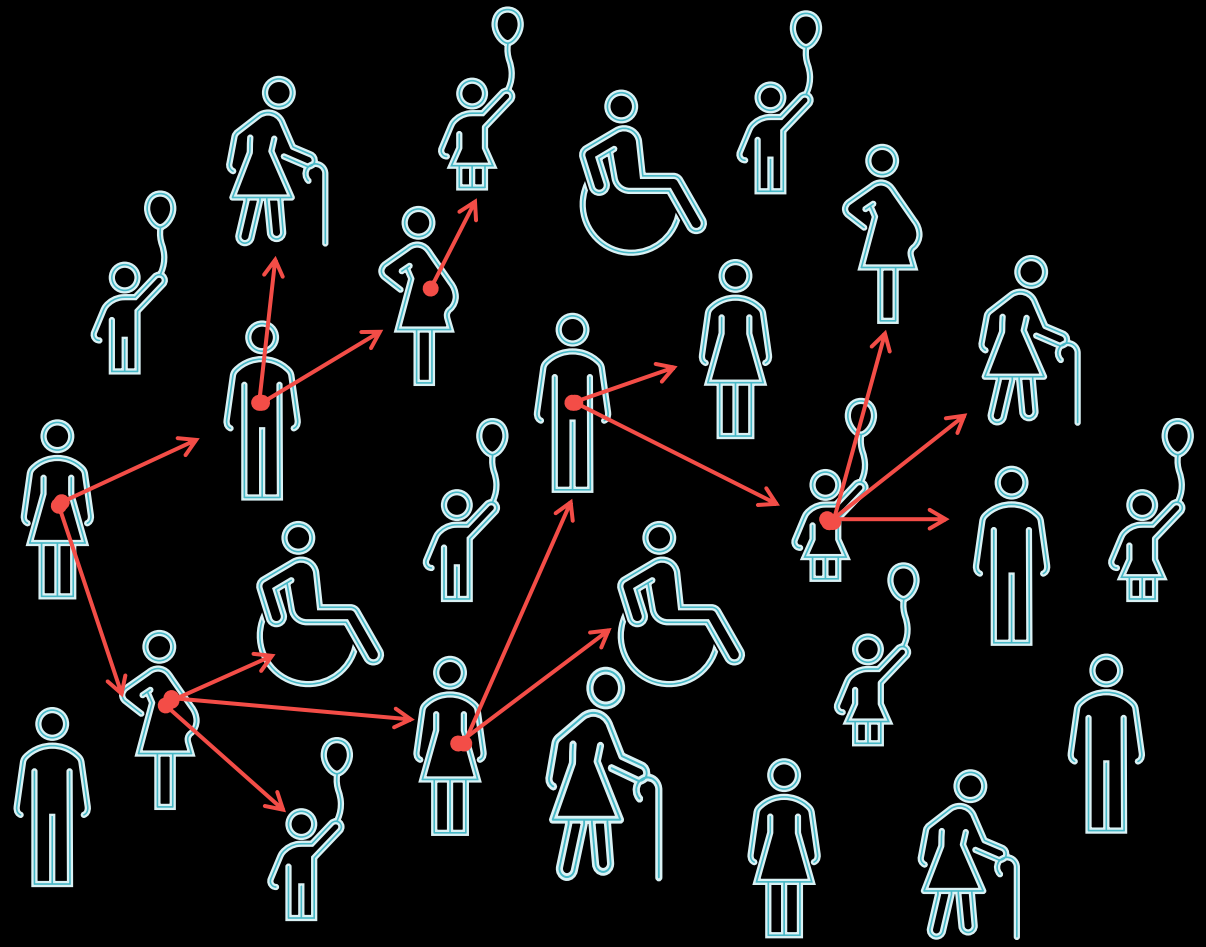


Herd Immunity Threshold



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

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

Week 1: SIR Models

Dr. Rachel Sippy
University of Cambridge

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 structure and assumptions of a basic SIR model
- Understand how a graphic representation can be expressed mathematically

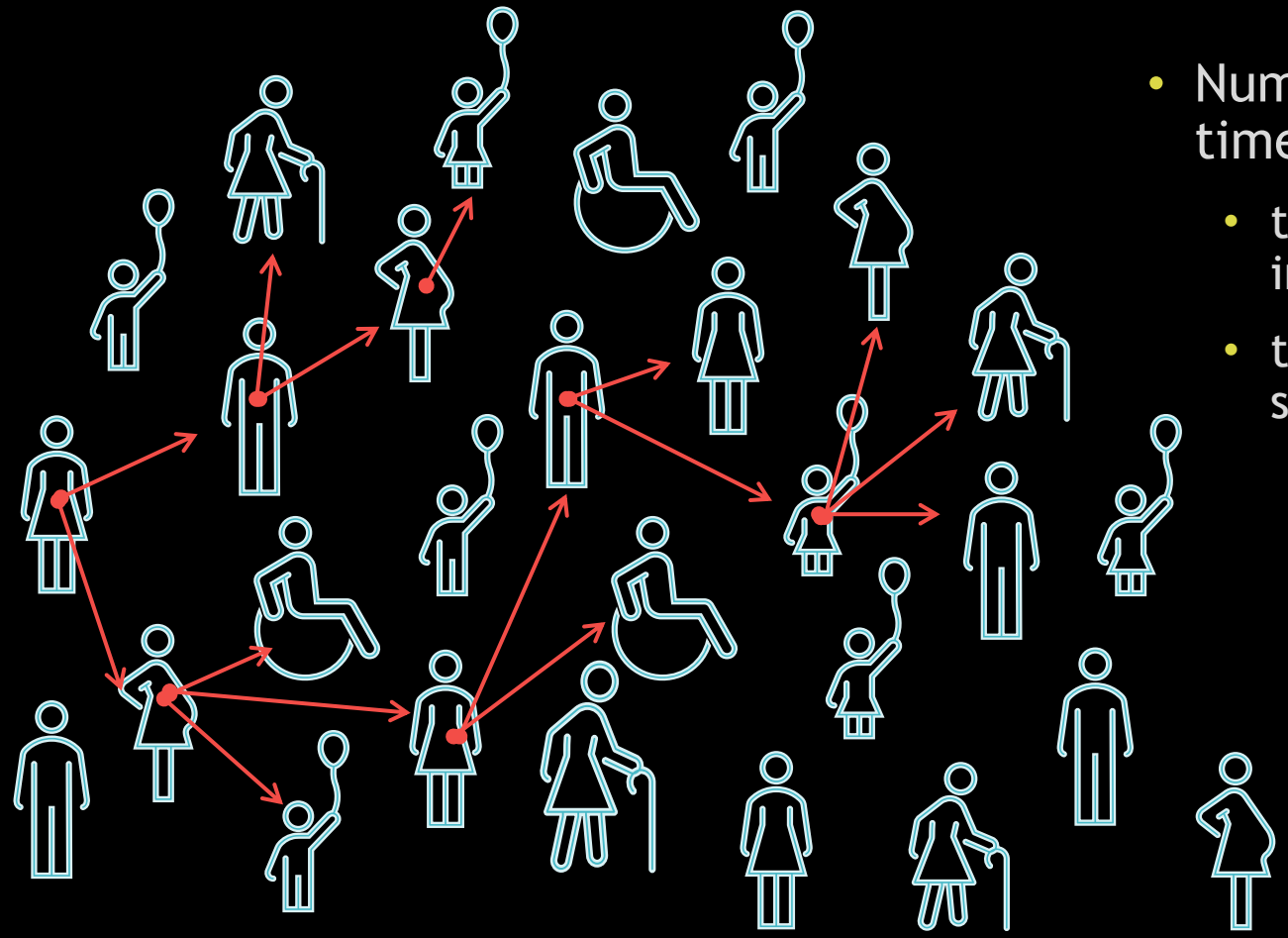
Post Questions in the Chat!

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

Workshop Schedule

Time	Topics
2:00—2:10 pm	~~Greetings~~
2:10—3:00 pm	SIR Model & Differential Equations
3:00—3:10 pm	Break
3:10—3:30 pm	SIR Model & Time Steps
3:30—3:40 pm	Break
3:40—5:00 pm	R Session

Core Concept



- Number of new infections per unit time is a function of:
  - the number of people who are infectious in a population
  - the number of people who are susceptible

SIR Model

- We want to build a model of transmission (scenario) for a completely immunizing infection
- We are going to develop a mechanistic (compartmental) model where individuals can be classified as:
  - susceptible
  - infected
  - recovered

SIR Model

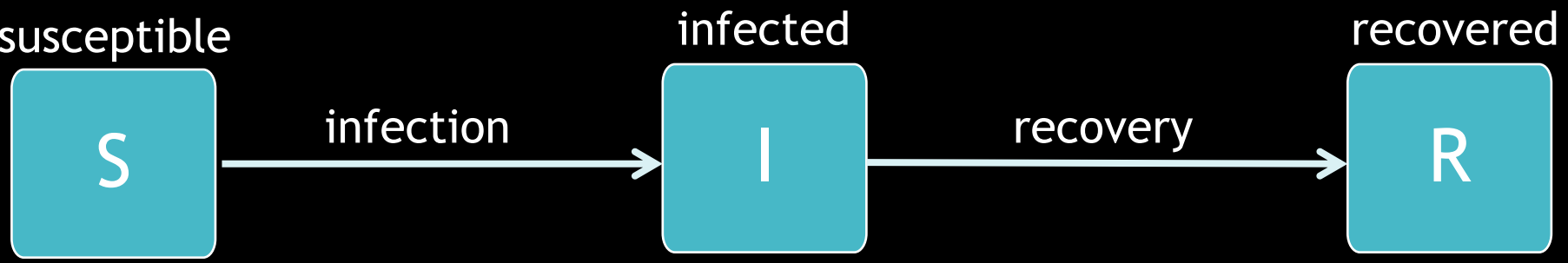
- Compartmental/mechanistic models
  1. Populations are divided into compartments
  2. Compartments and transition rates are determined by biological systems
  3. Transition rates between compartments are expressed mathematically

SIR Model

- What are the major assumptions?

SIR Model

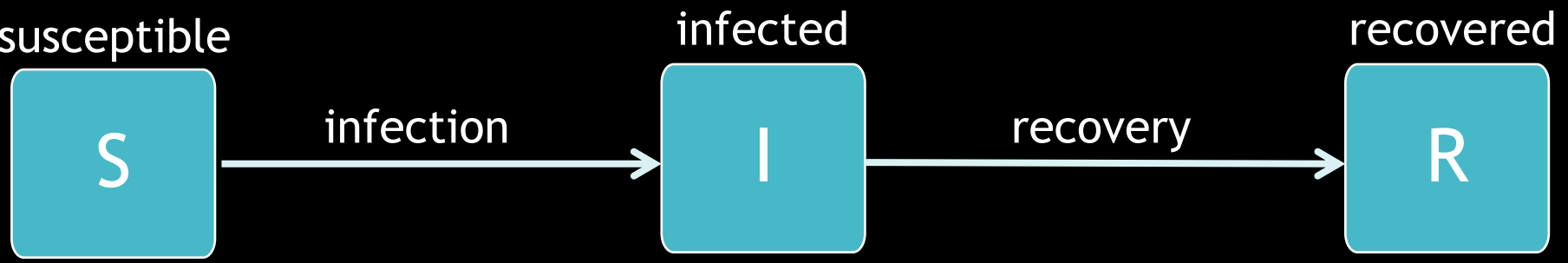
- Everyone is either:



- Population size is constant
  - no births
  - no deaths
  - no migrations

SIR Model

- Everyone is either:

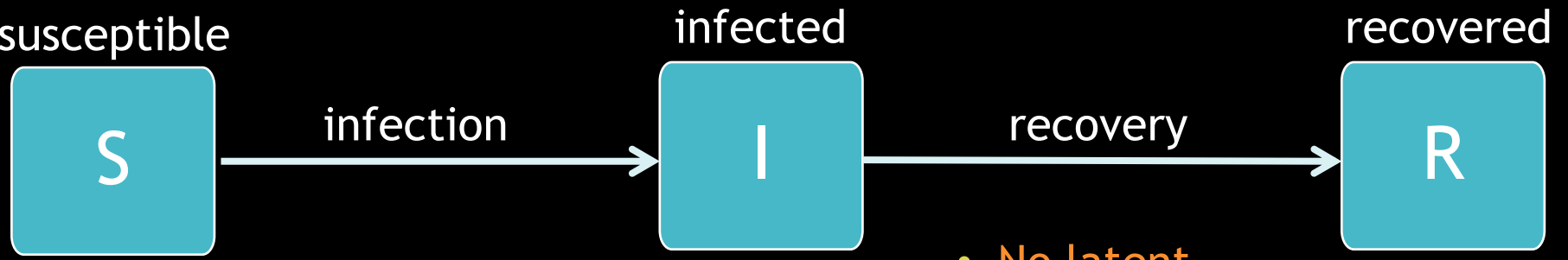


- Recovery is permanent

- Population size is constant
  - no births
  - no deaths
  - no migrations

SIR Model

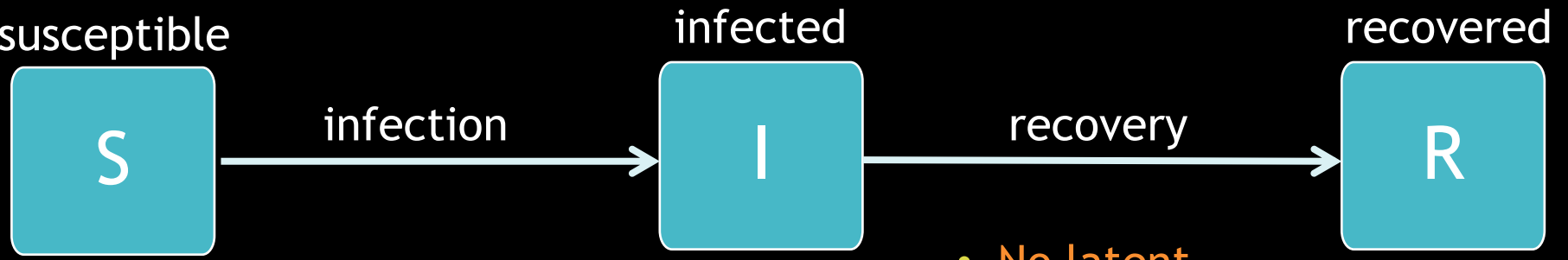
- Everyone is either:



- Recovery is permanent
- Population size is constant
  - no births
  - no deaths
  - no migrations
- No latent period
  - if you are infected, you are infectious

SIR Model

- Everyone is either:

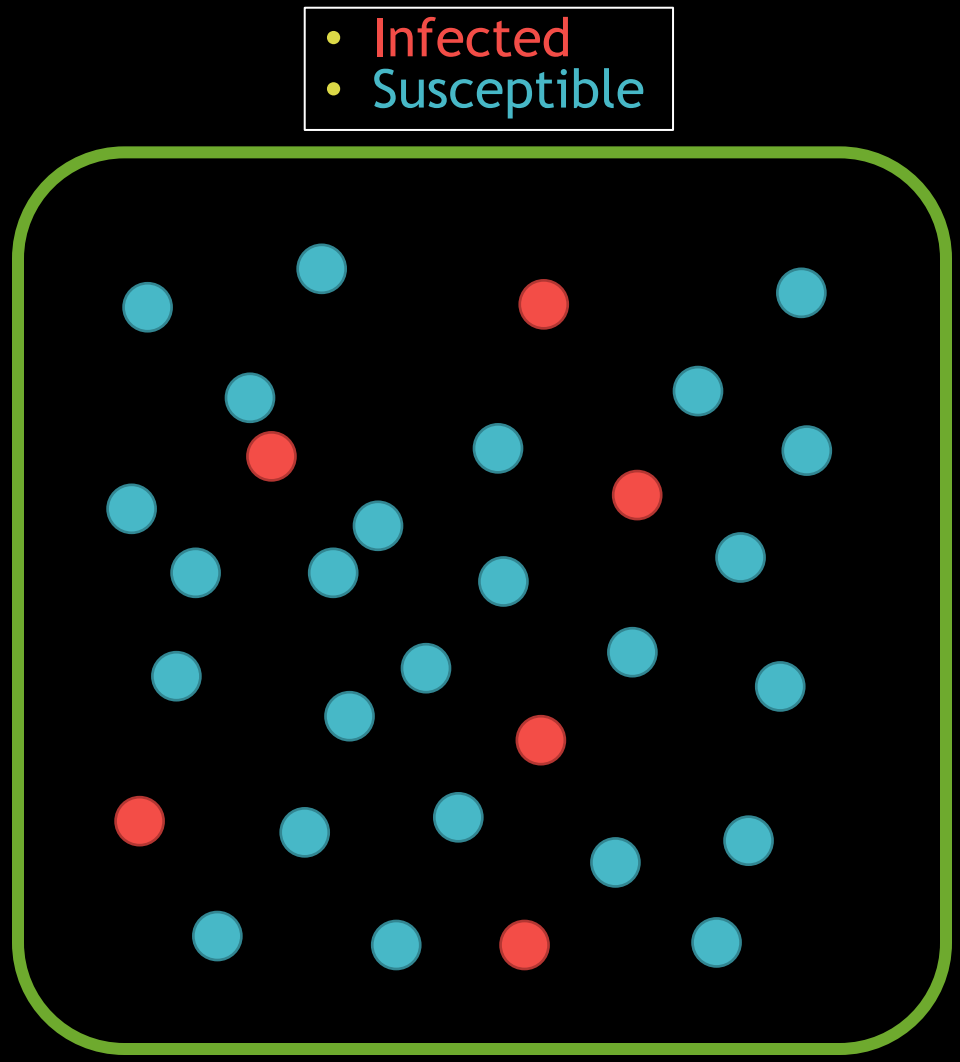


- Recovery is permanent

- Population size is constant
  - no births
  - no deaths
  - no migrations
- People mix uniformly
  - homogeneous mixing
  - random mixing
  - mass action
- No latent period
  - if you are infected, you are infectious

Law of Mass Action

- The rate at which individuals of two types contact one another in a population is proportional to the product of their densities



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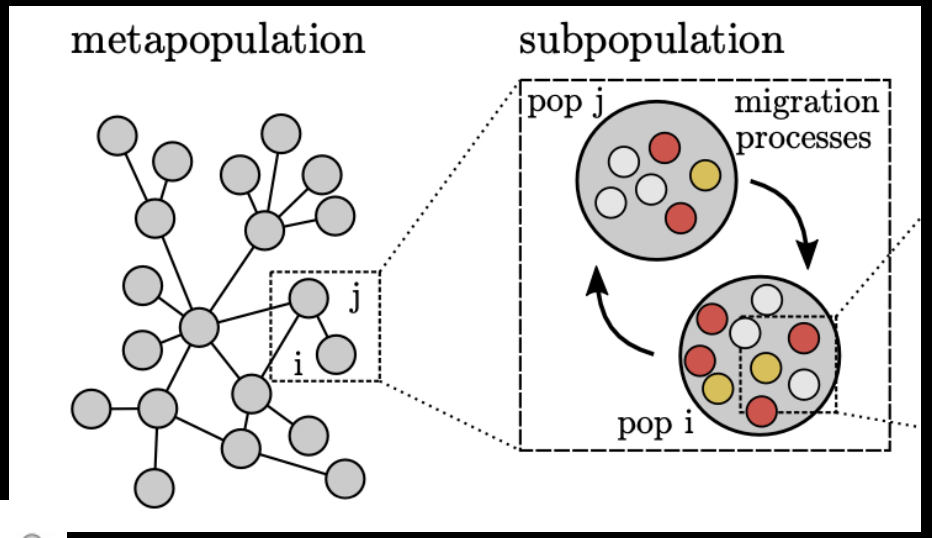
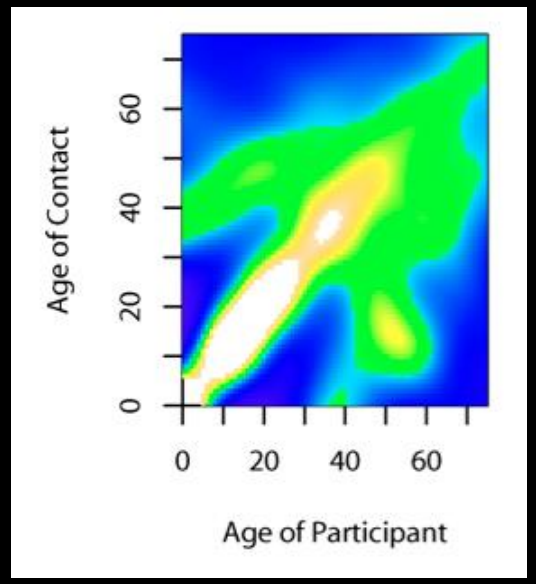


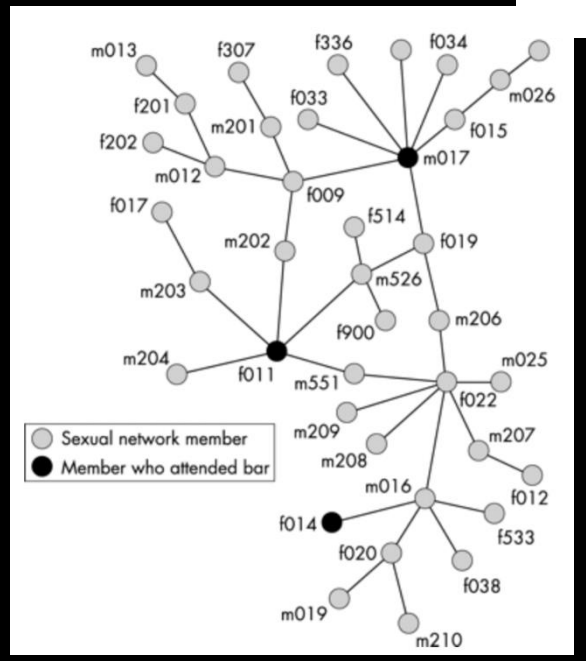
Hackl, et al (2019)

Metapopulations (spatial)



Mossong, et al. (2008)

Age Mixing

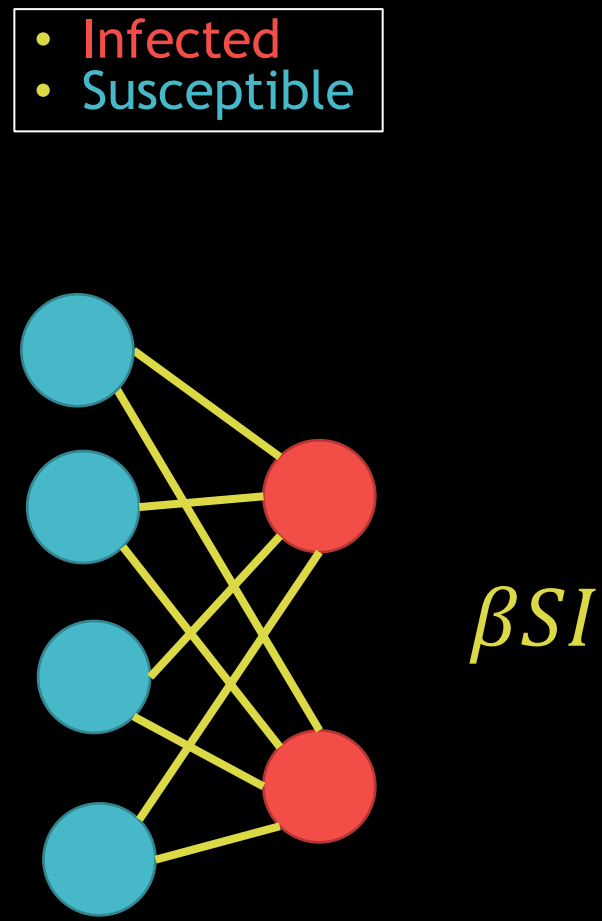


De, et al. (2004)

Network Contacts

Law of Mass Action

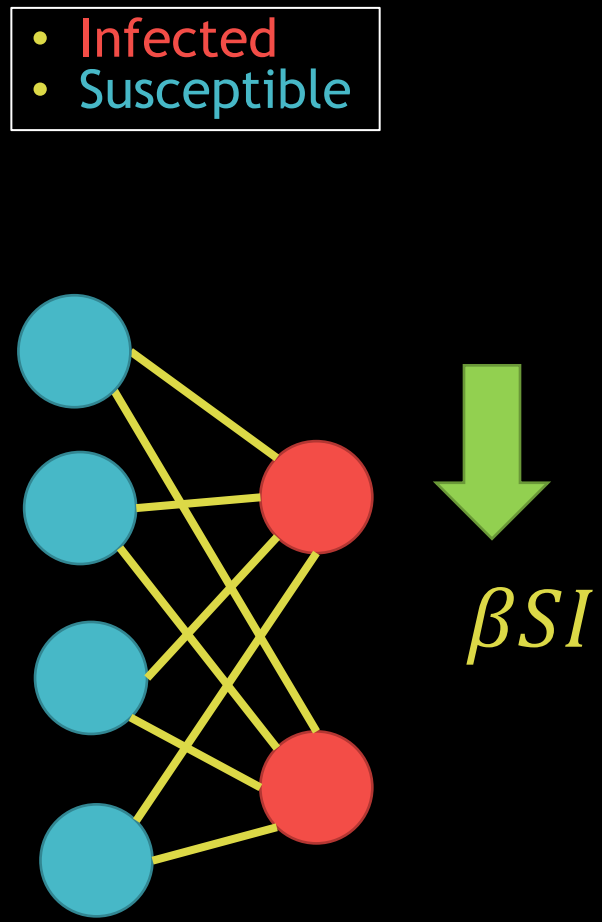
- Random mixing
- S x I is the number of unique contacts between the susceptible and infectious individuals
  - 2 infected
  - 4 susceptible
  - 8 unique contacts



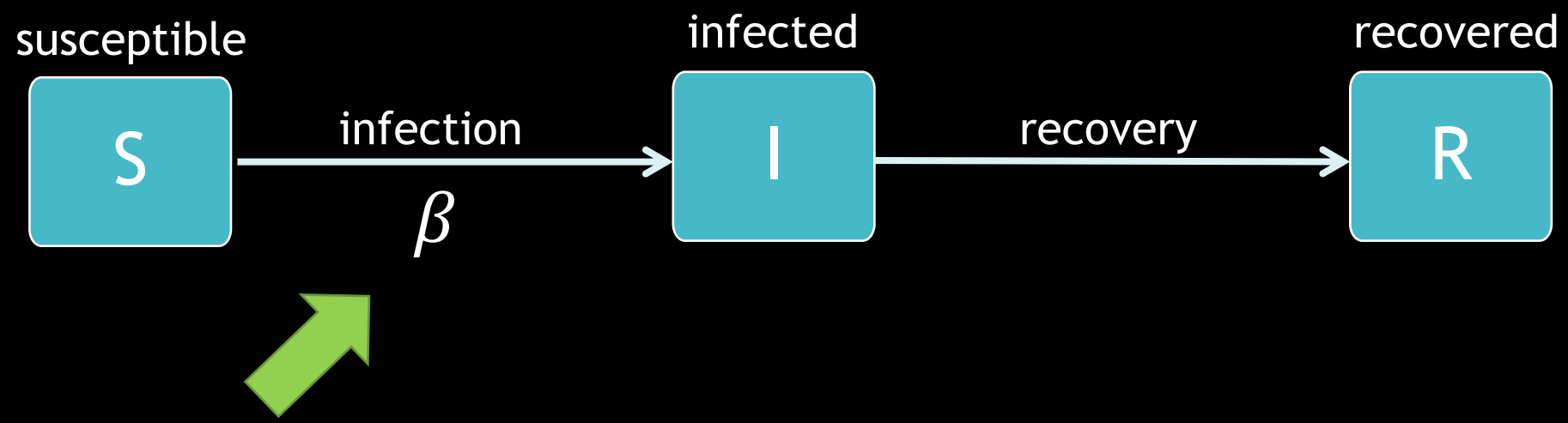
$$\beta SI$$

Law of Mass Action

- Random mixing
- S x I is the number of unique contacts between the susceptible and infectious individuals
  - 2 infected
  - 4 susceptible
  - 8 unique contacts
- ß is a transmission coefficient
  - it is the probability of a susceptible becoming infected if they contact an infected person



SIR Model: Kermack & McKendrick



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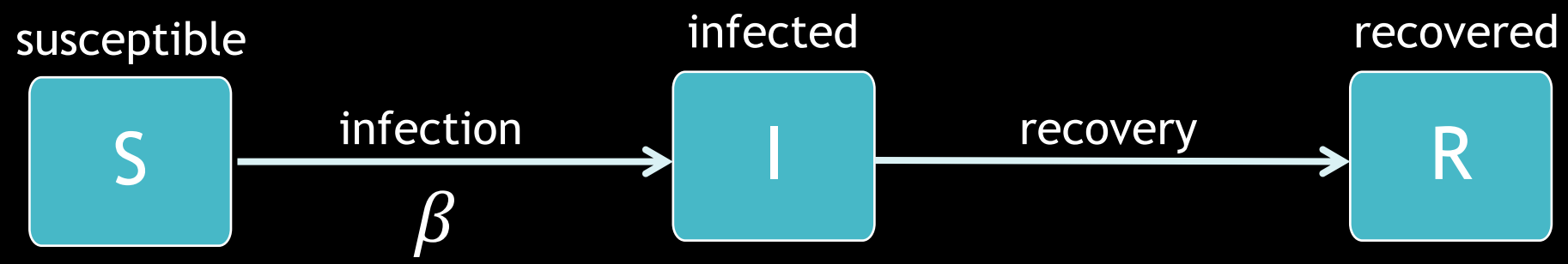
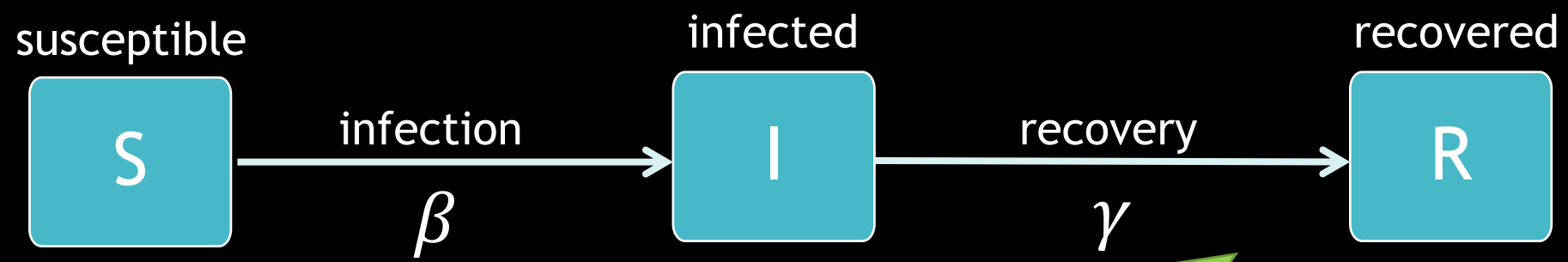


$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

SIR Model: Kermack & McKendrick

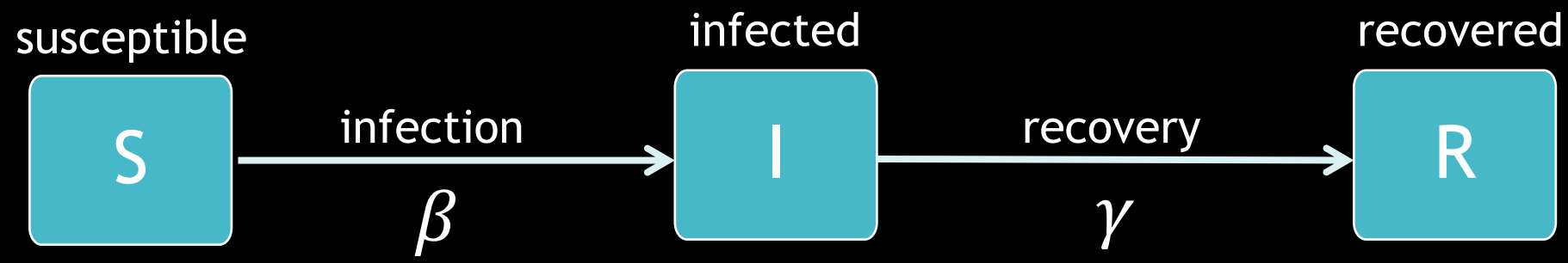


$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

$$\frac{dI(t)}{dt} = \beta S(t) I(t) - \gamma I(t)$$

$$\frac{dR(t)}{dt} = \gamma I(t)$$

SIR Model: Kermack & McKendrick



- β is a transmission coefficient
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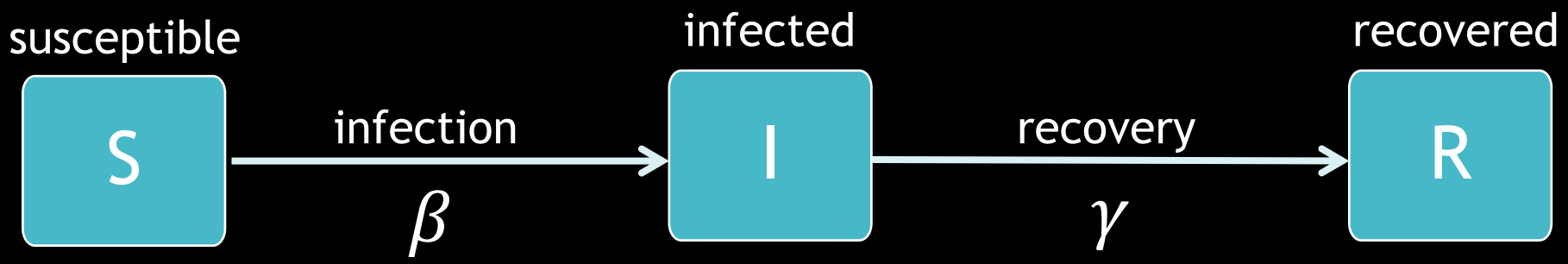
$$\frac{dR(t)}{dt} = \gamma I(t)$$

- γ is the recovery rate
  - 1/ γ is the duration of infectiousness

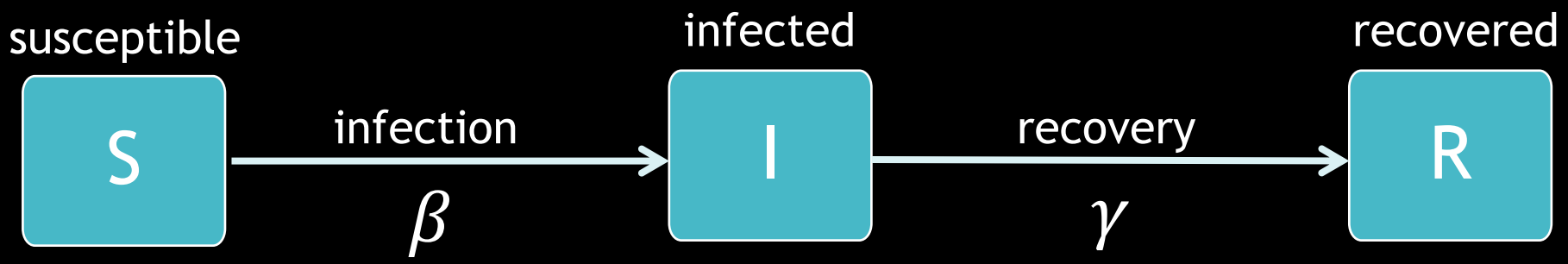
SIR Model: Kermack & McKendrick



- system of ordinary differential equations
  - ODE
  - mathematical expression of transition rates between compartments

$$\begin{cases} \frac{dS(t)}{dt} = -\beta S(t) I(t) \\ \frac{dI(t)}{dt} = \beta S(t) I(t) - \gamma I(t) \\ \frac{dR(t)}{dt} = \gamma I(t) \end{cases}$$

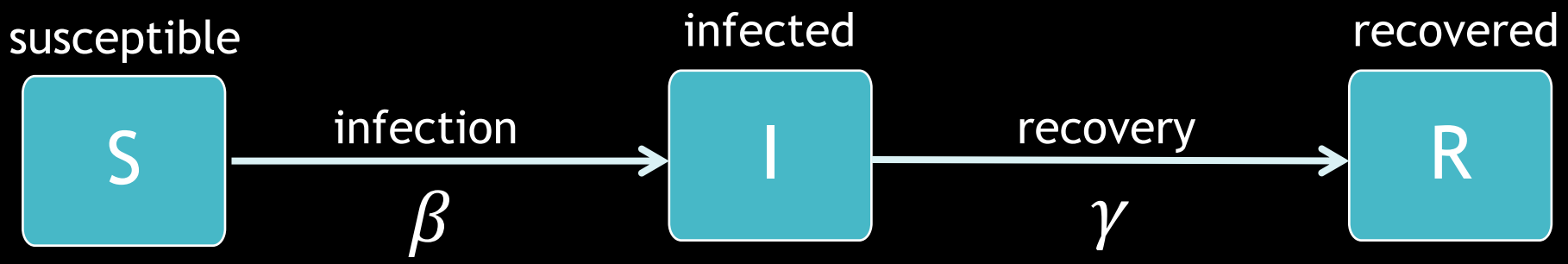
SIR Model: Kermack & McKendrick



- system of ordinary differential equations
  - multiply compartments by transition rates to express change

$$\begin{cases} \frac{dS(t)}{dt} = -\beta S(t) I(t) \\ \frac{dI(t)}{dt} = \beta S(t) I(t) - \gamma I(t) \\ \frac{dR(t)}{dt} = \gamma I(t) \end{cases}$$

SIR Model: Kermack & McKendrick



- rate of change in number of **susceptible** individuals at time t

$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

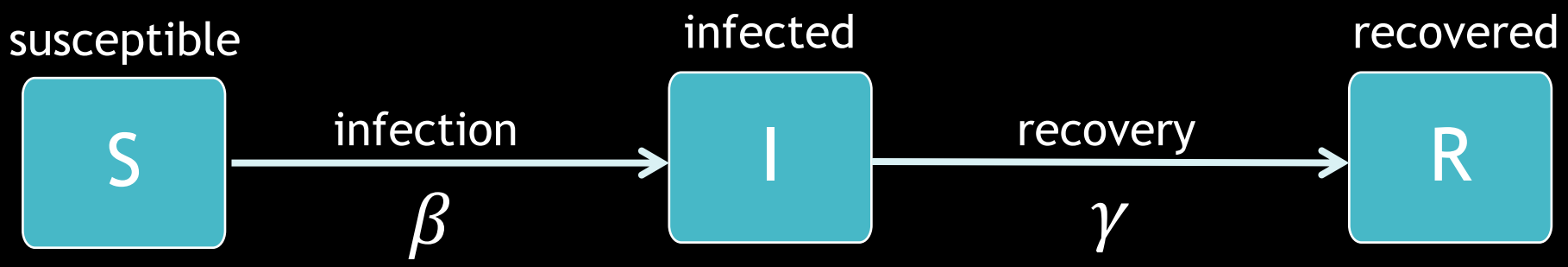
- rate of change in number of **infected** individuals at time t

$$\frac{dI(t)}{dt} = \beta S(t) I(t) - \gamma I(t)$$

- rate of change in number of **recovered** individuals at time t

$$\frac{dR(t)}{dt} = \gamma I(t)$$

SIR Model: Kermack & McKendrick

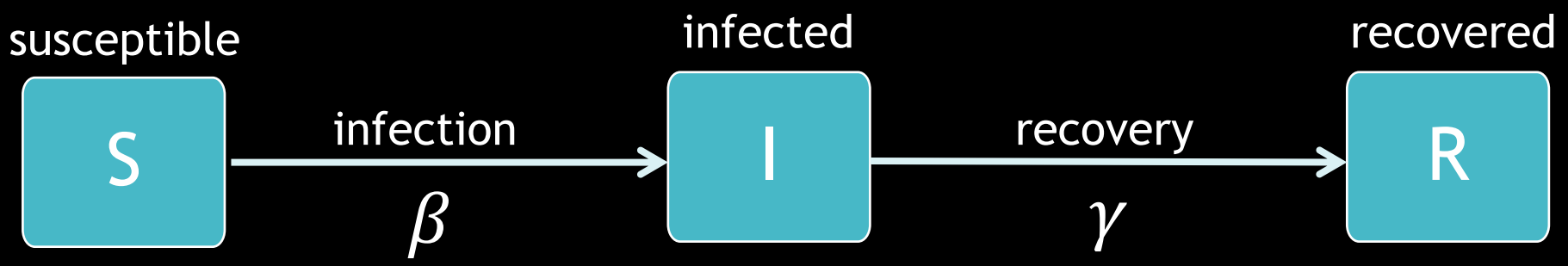


- How do we calculate the rate of change for a compartment?

$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

- For each compartment:
  - + number of individuals entering per unit time
  - - number of individuals leaving per unit time

SIR Model: Kermack & McKendrick



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- For each compartment:
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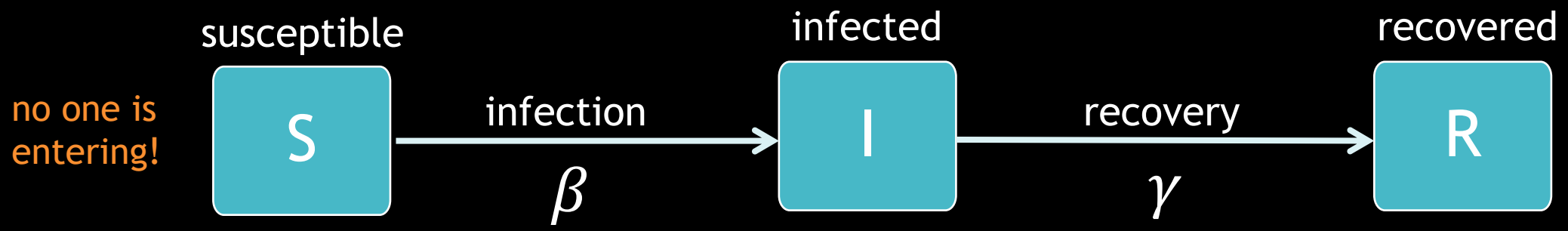
$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

rate of change

SIR Model: Kermack & McKendrick



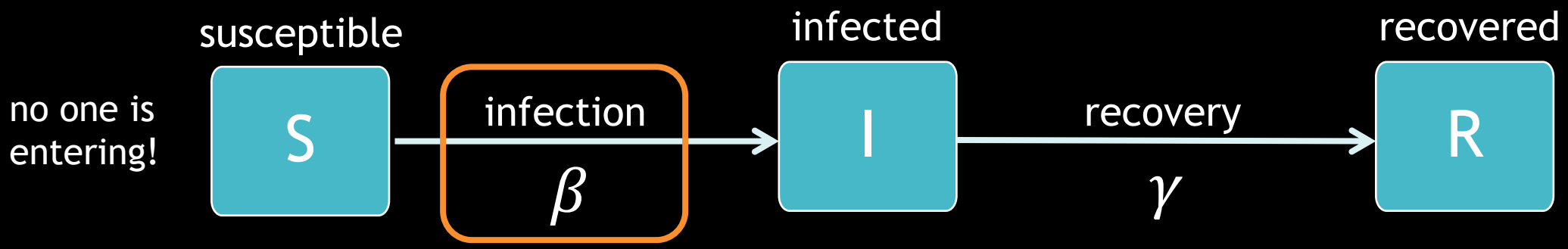
- How do we calculate the rate of change for a compartment?
- For each compartment:
  - + number of individuals entering per unit time
  - - number of individuals leaving per unit time

$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

rate of change

no one to add

SIR Model: Kermack & McKendrick



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- For each compartment:
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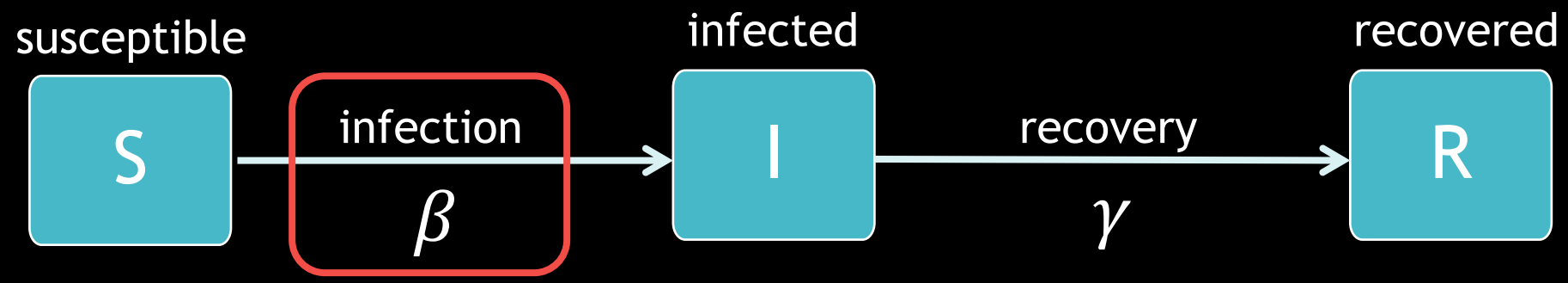
$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

rate of change

no one to add

the number infected depends on contact between S and I, and the probability of transmission

SIR Model: Kermack & McKendrick



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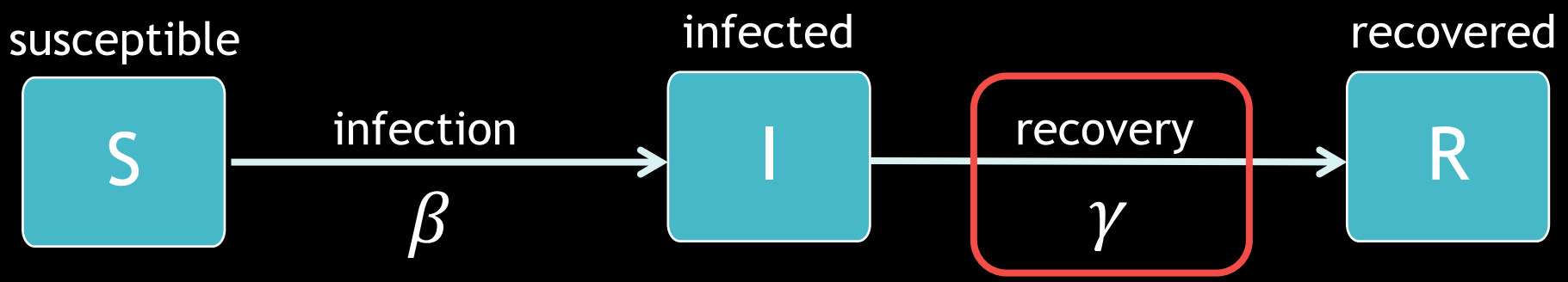
the number infected depends on contact between S and I, and the probability of transmission

SIR Model: Kermack & McKendrick



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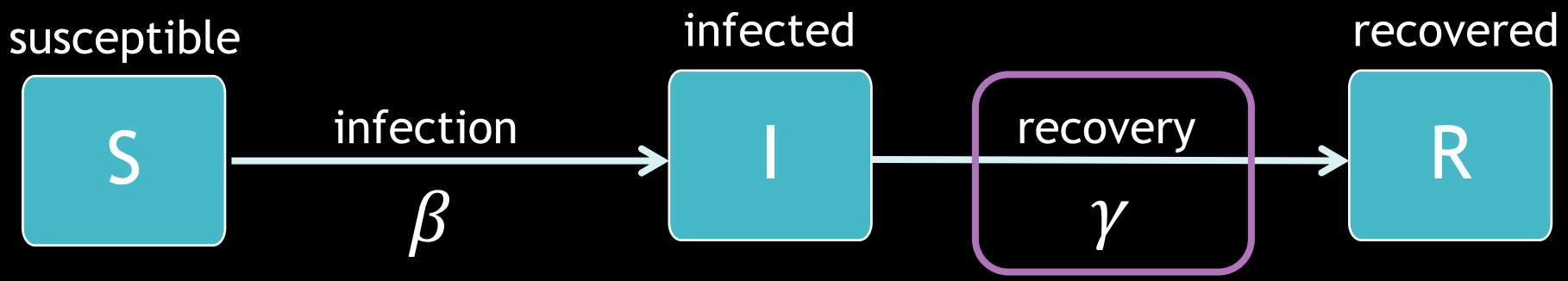
$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

$$\frac{dI(t)}{dt} = \beta S(t) I(t) - \gamma I(t)$$

the number who recover only depends on I and the recovery rate

SIR Model: Kermack & McKendrick



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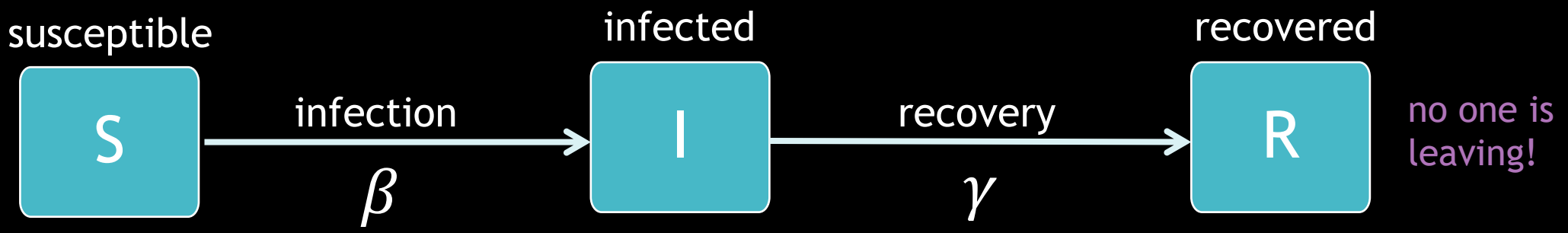

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$$\frac{dR(t)}{dt} = \gamma I(t)$$

no one to subtract

Questions & Break

Workshop Schedule

Time	Topics
2:00—2:10 pm	~~Greetings~~
2:10—3:00 pm	SIR Model & Differential Equations
3:00—3:10 pm	Break
3:10—3:30 pm	SIR Model & Time Steps
3:30—3:40 pm	Break
3:40—5:00 pm	R Session

SIR Model

- ODEs are solved to give us the rate of change for each compartment for each unit of time
- Units of time are meant to be infinitesimally small
  - larger time units have more inaccurate results
  - we want to model continuous time or instantaneous time units

$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

$$\frac{dI(t)}{dt} = \beta S(t) I(t) - \gamma I(t)$$

$$\frac{dR(t)}{dt} = \gamma I(t)$$

SIR Model

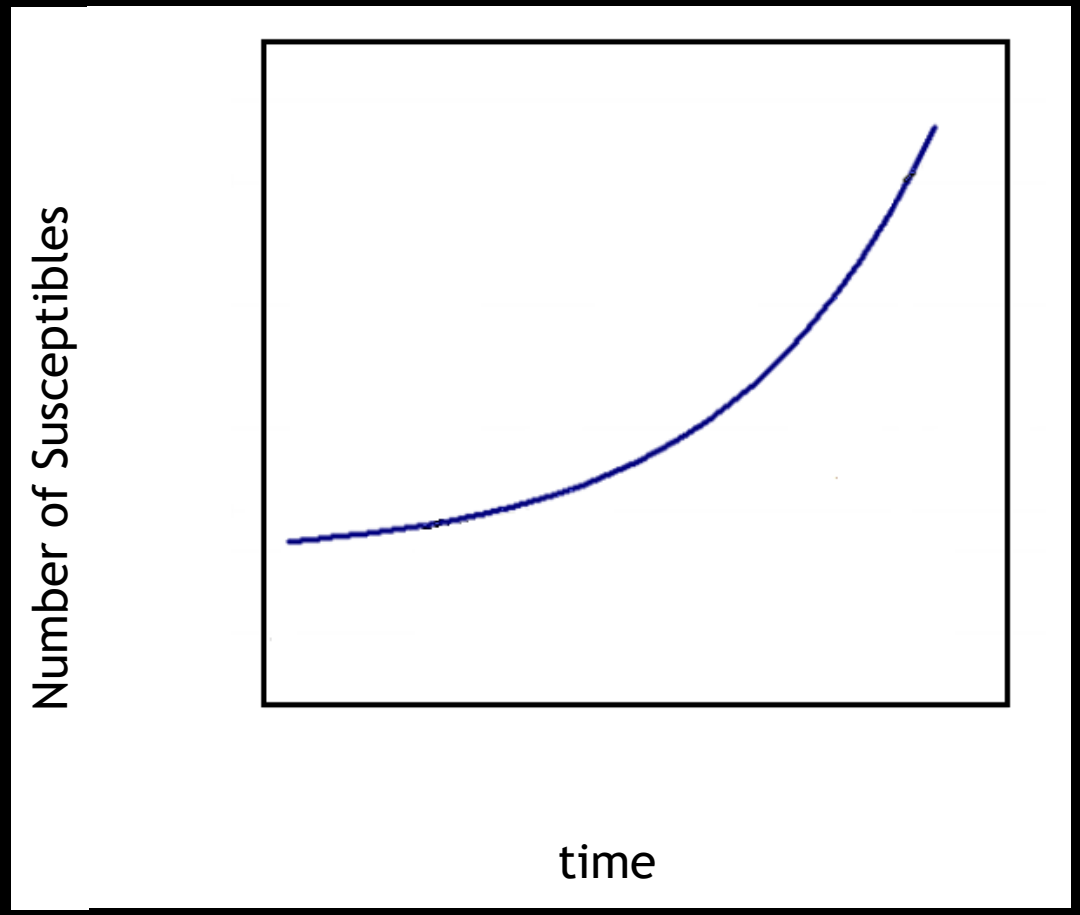
$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

$$\frac{dS(t)}{dt} = \frac{S(t+\delta t) - S(t)}{\delta t}$$

$$as\ \delta t \to 0$$

- rate of change can be expressed another way
  - δt is our unit time

SIR Model



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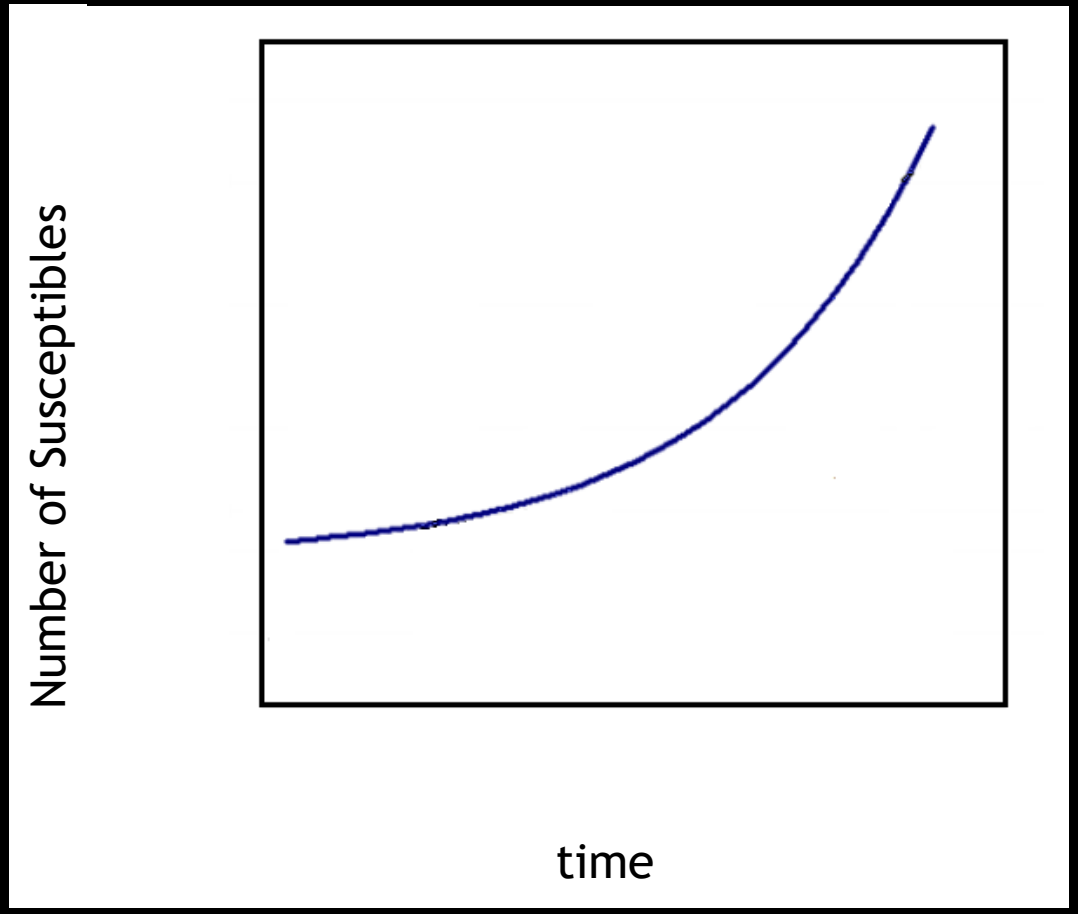

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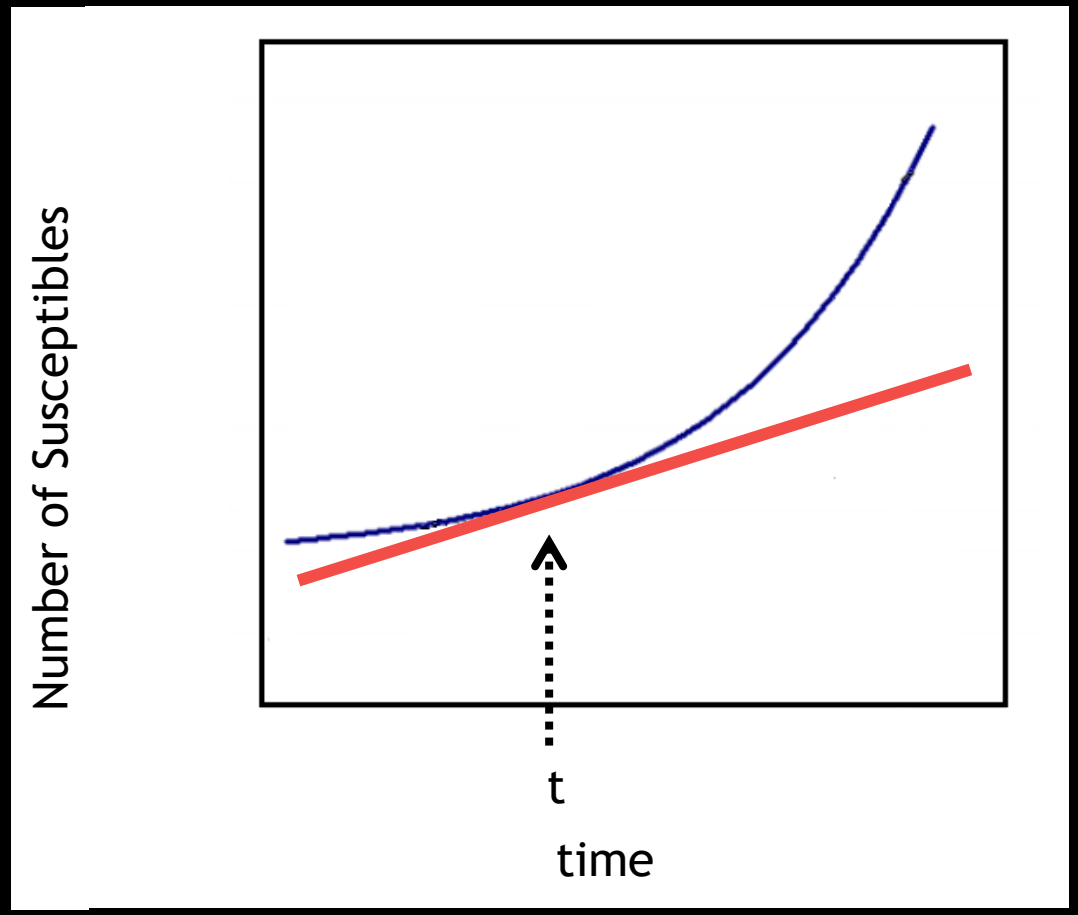
$$as\ \delta t \to 0$$

- δt is our unit time
- tangent of curve is rate for instantaneous time

SIR Model



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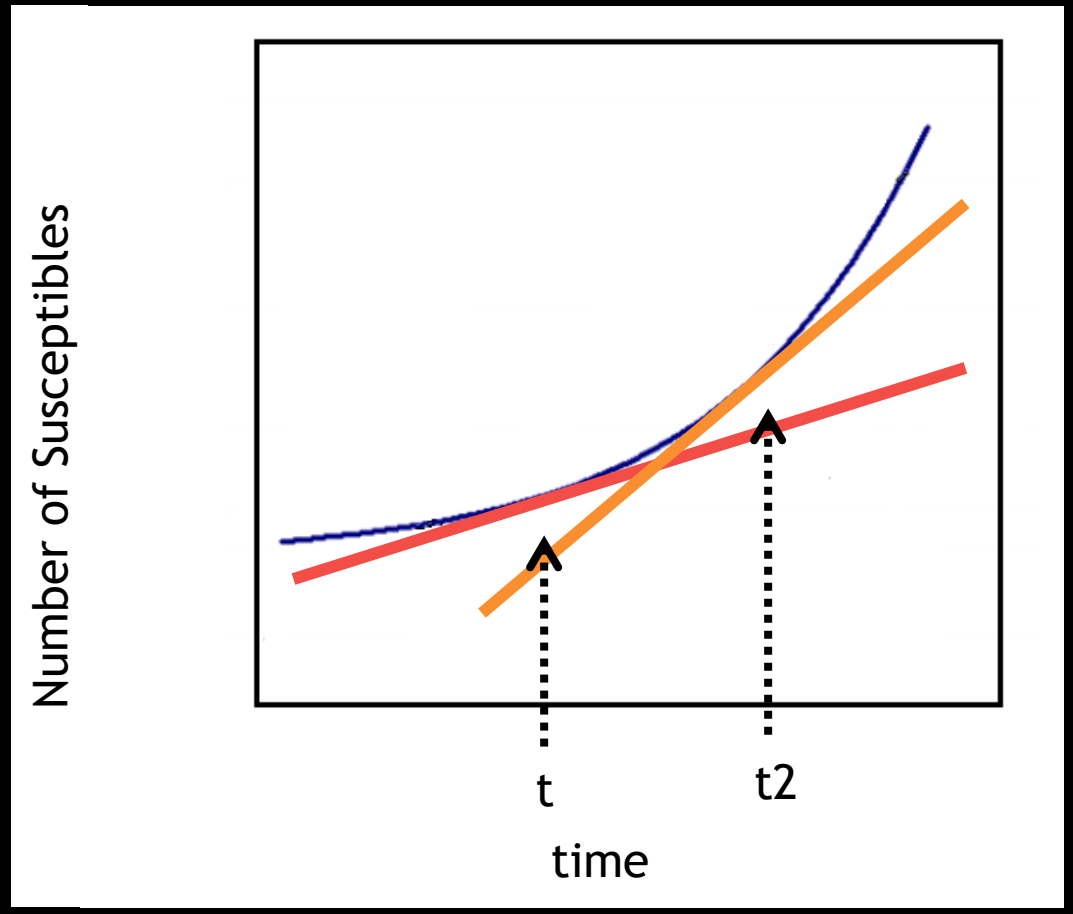

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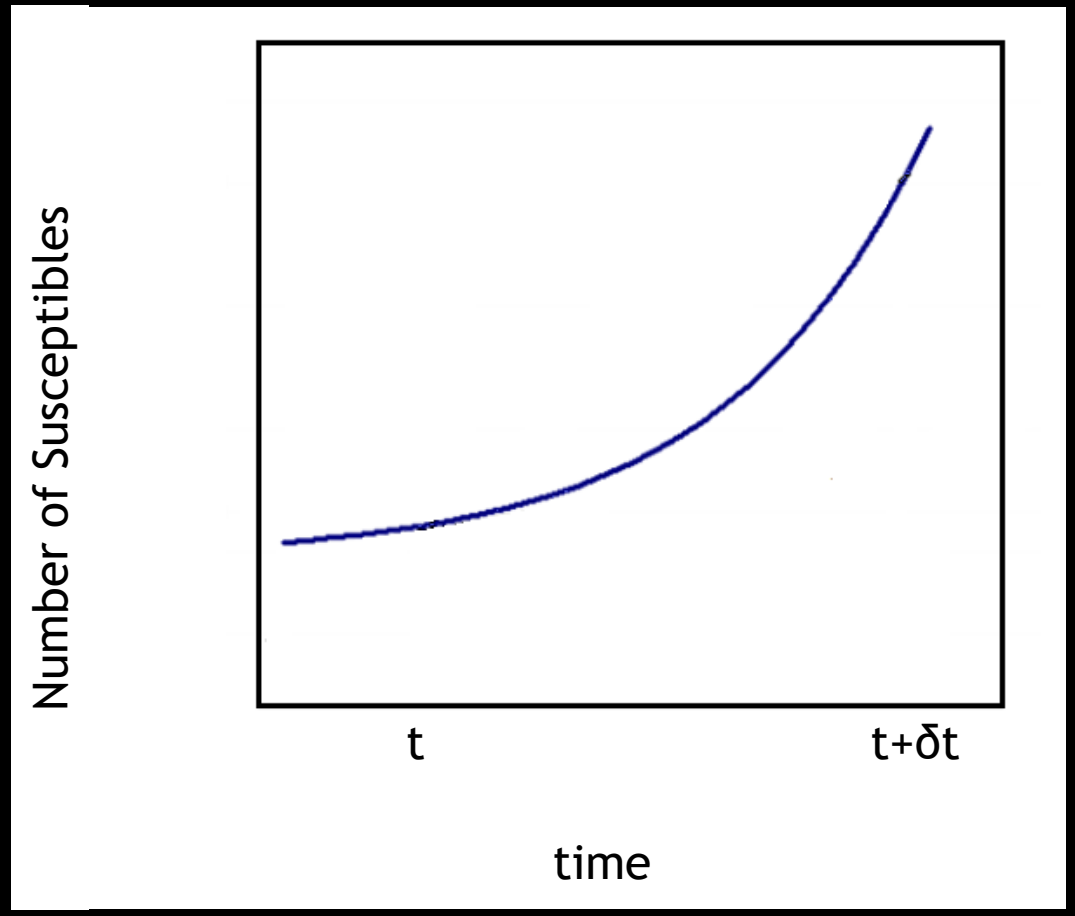

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- δt is our unit time, change in time
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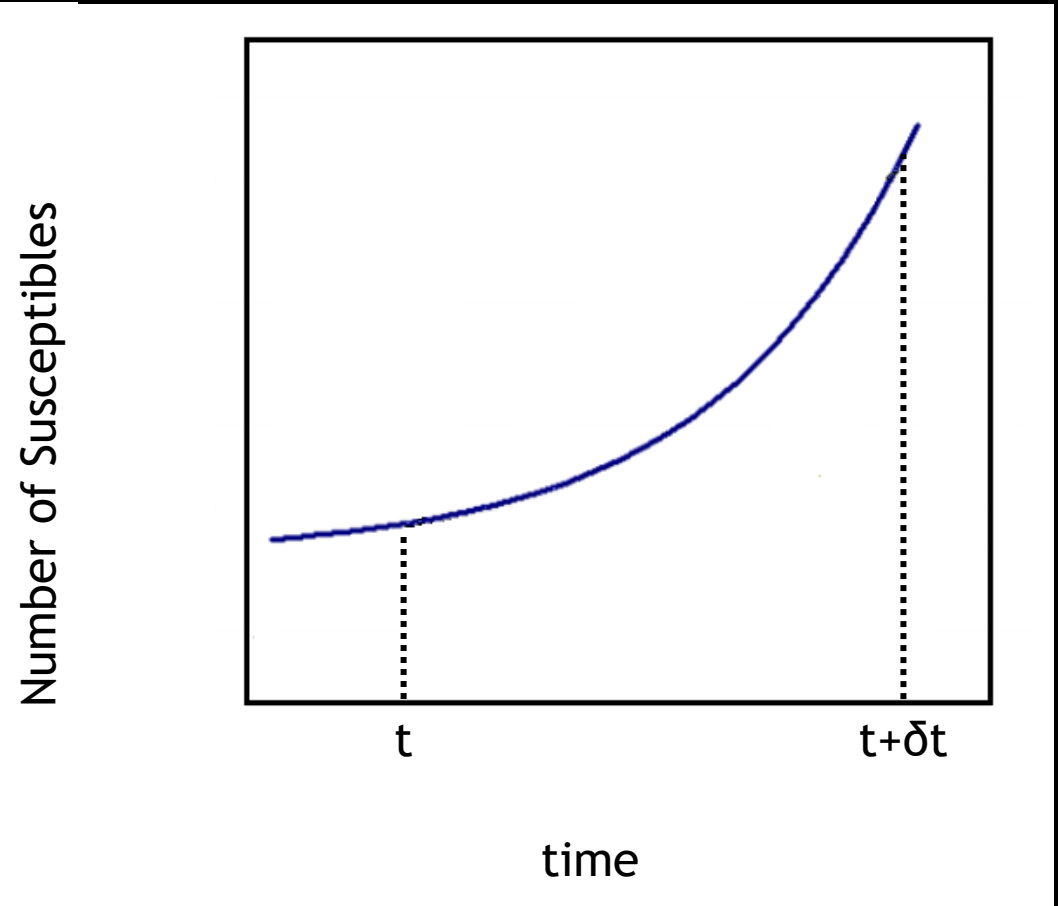
SIR Model



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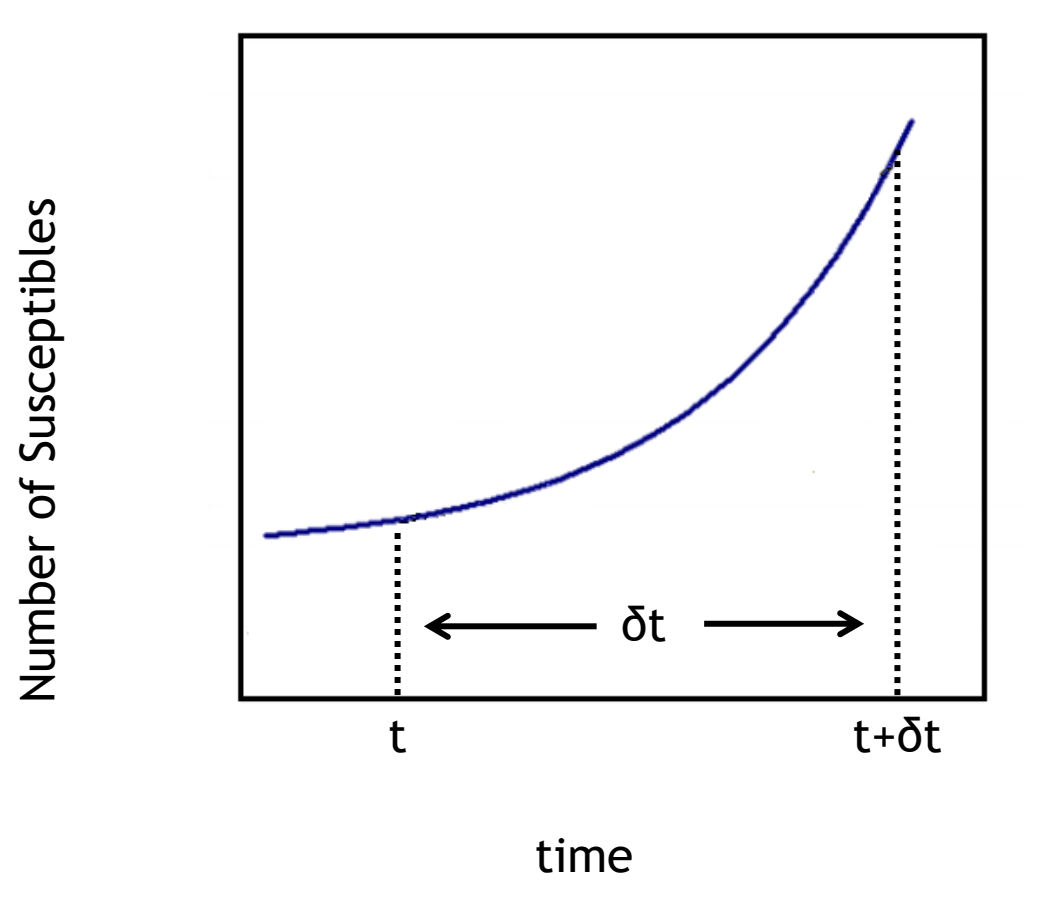
SIR Model



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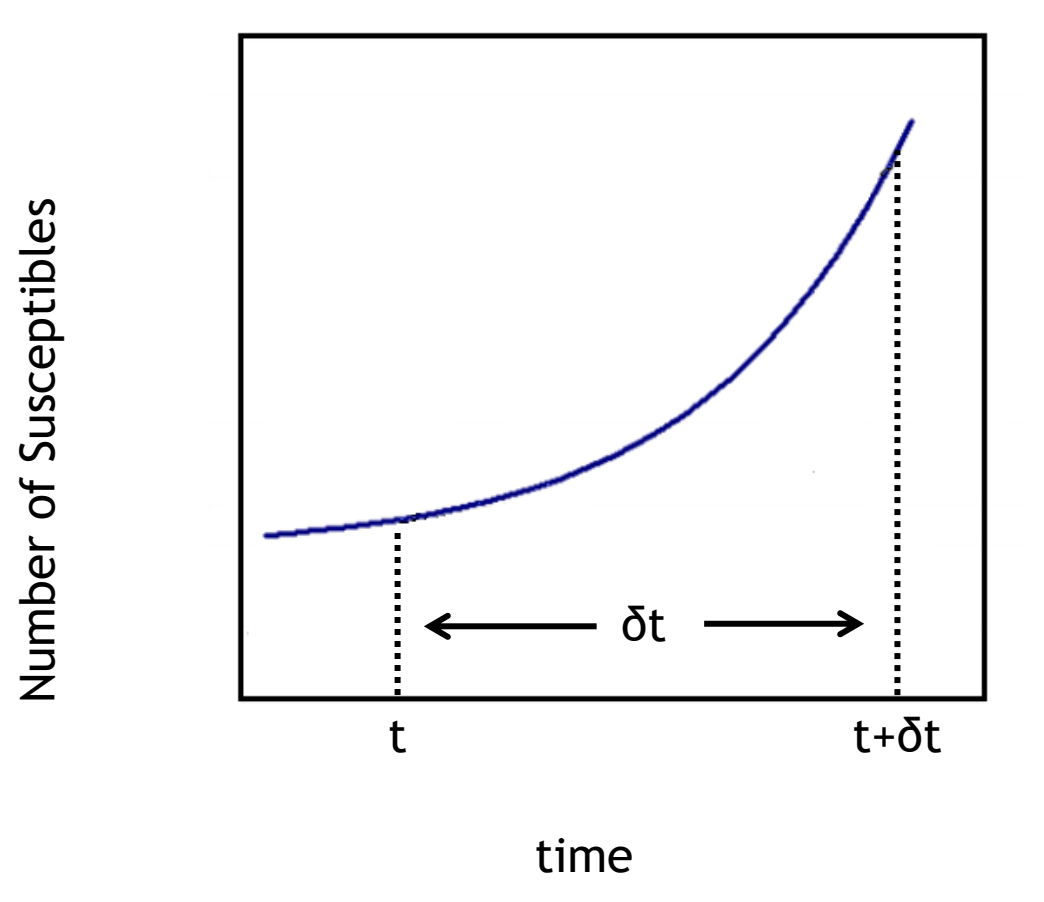

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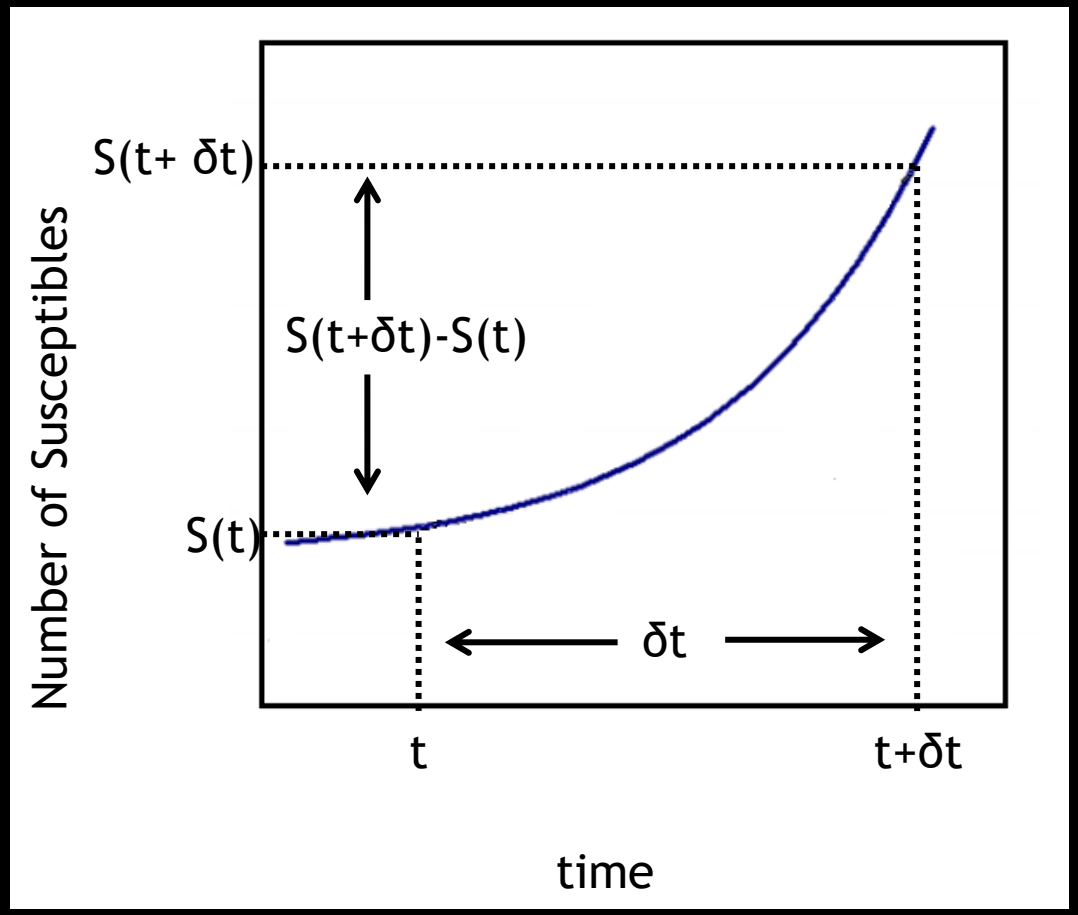

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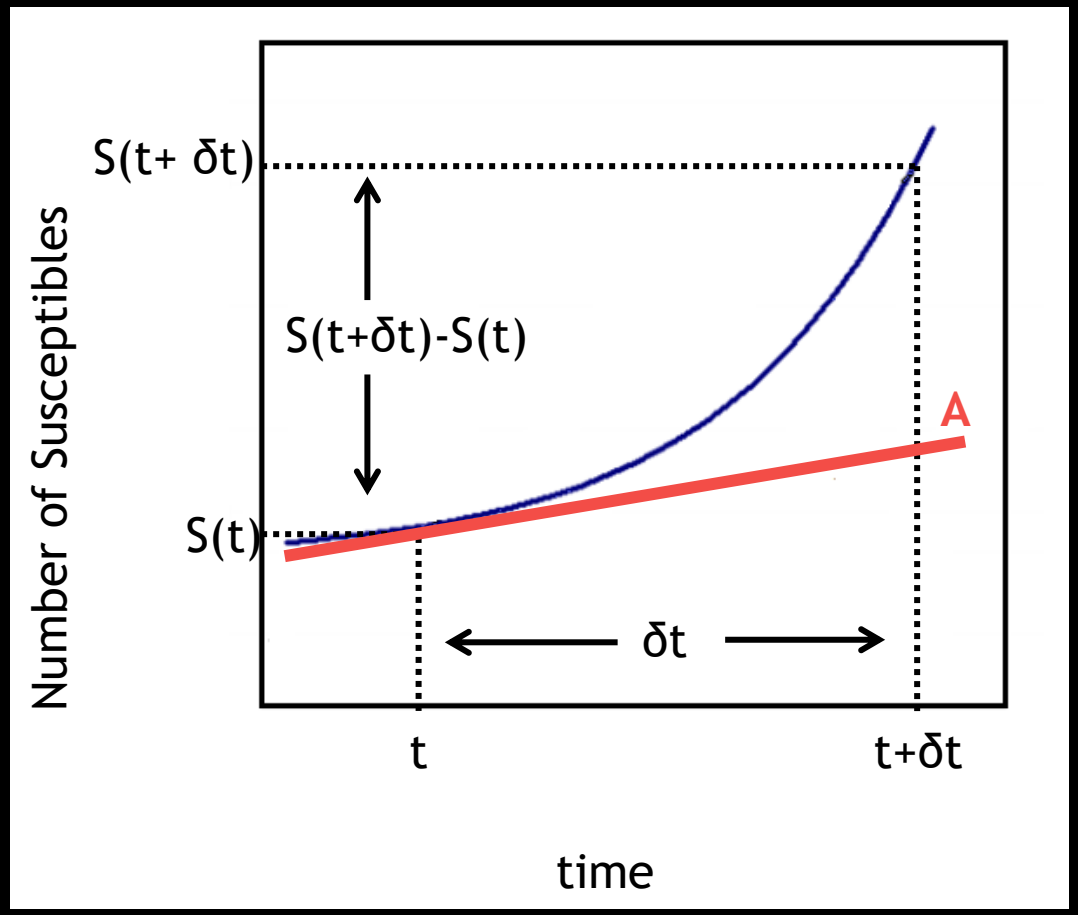
SIR Model



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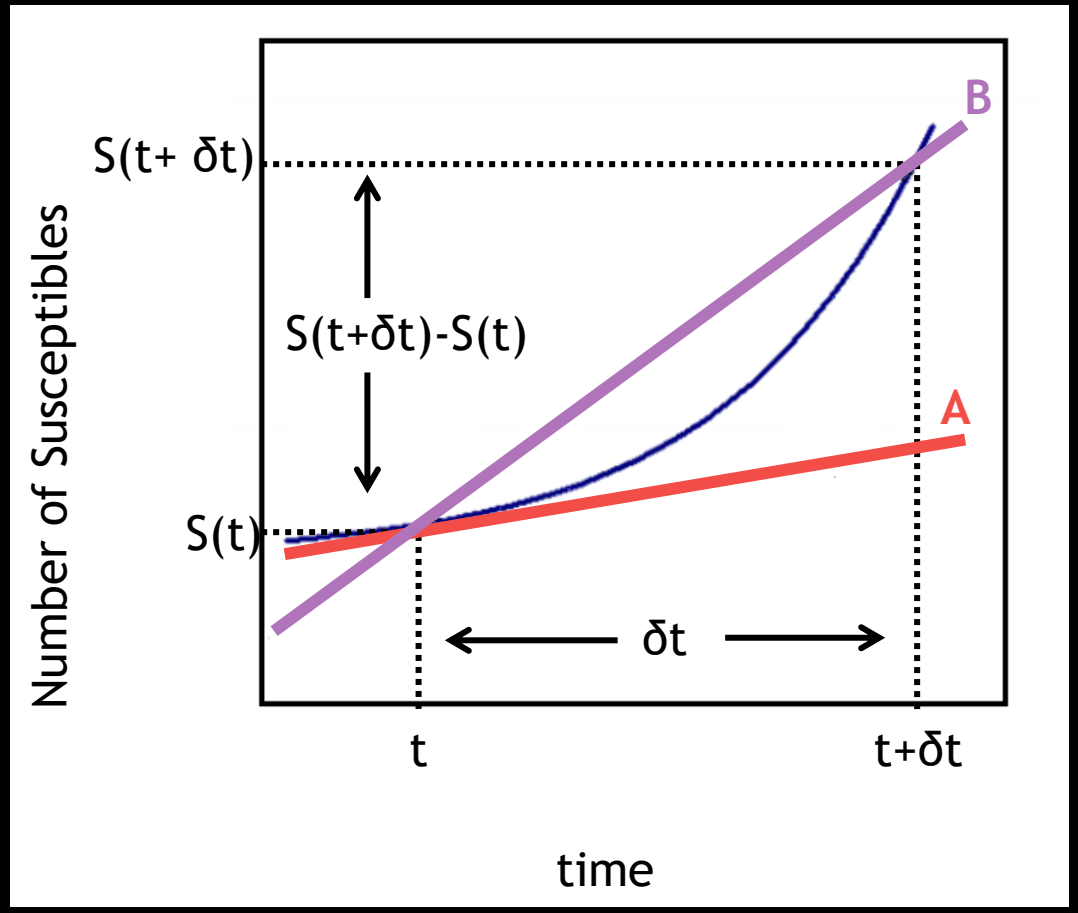
$$as\ \delta t \to 0$$

- tangent of curve is rate for instantaneous time
- we want to know slope A

SIR Model



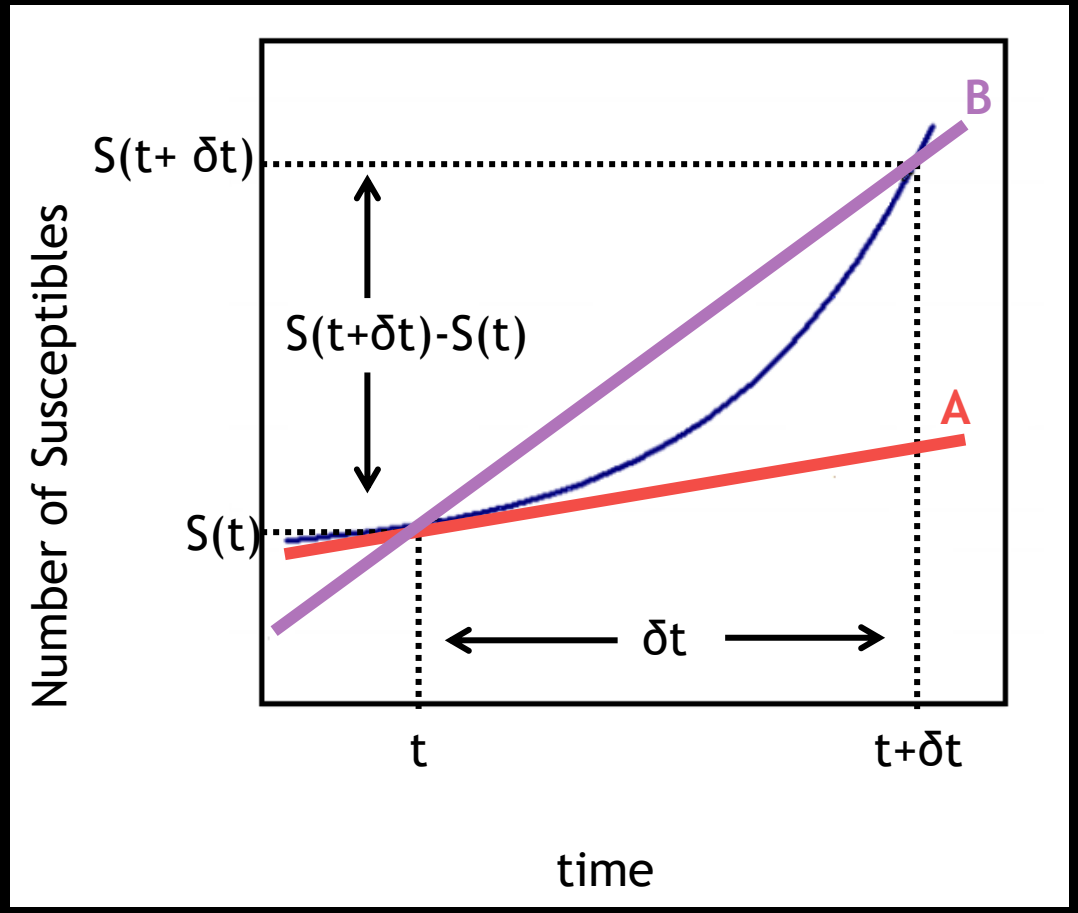
$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

$$\frac{dS(t)}{dt} = \frac{S(t+\delta t) - S(t)}{\delta t}$$

$$as\ \delta t \to 0$$

- we want to know slope A
- we can calculate slope B

SIR Model



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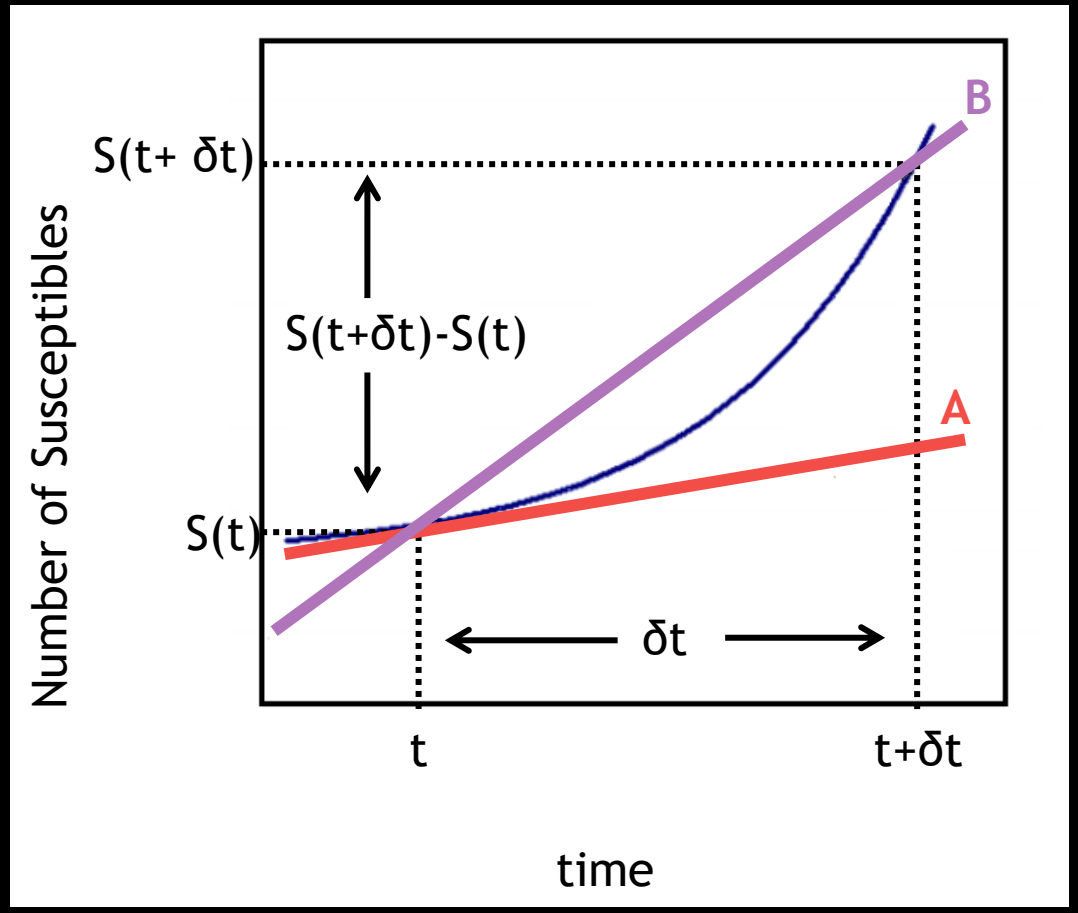
$$\frac{dS(t)}{dt} = \frac{S(t+\delta t) - S(t)}{\delta t}$$

$$as\ \delta t \to 0$$

- A and B look very far apart

SIR Model



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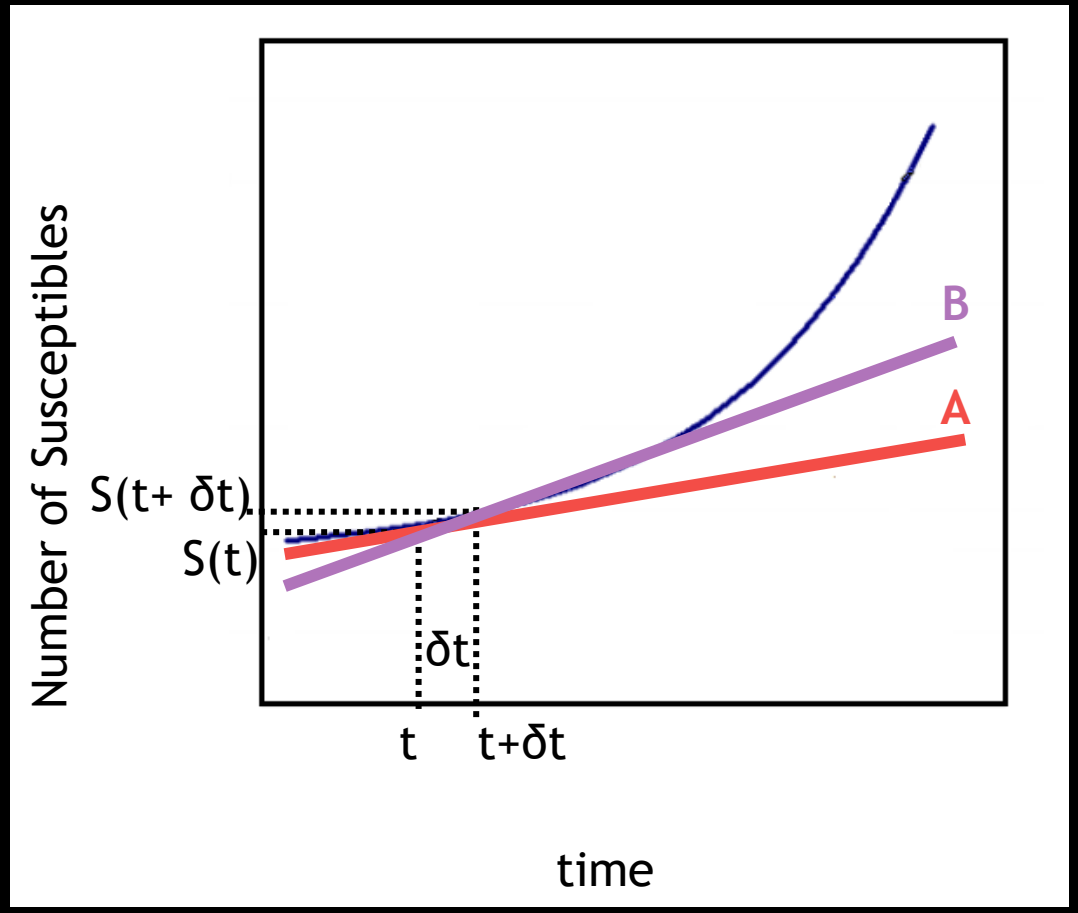

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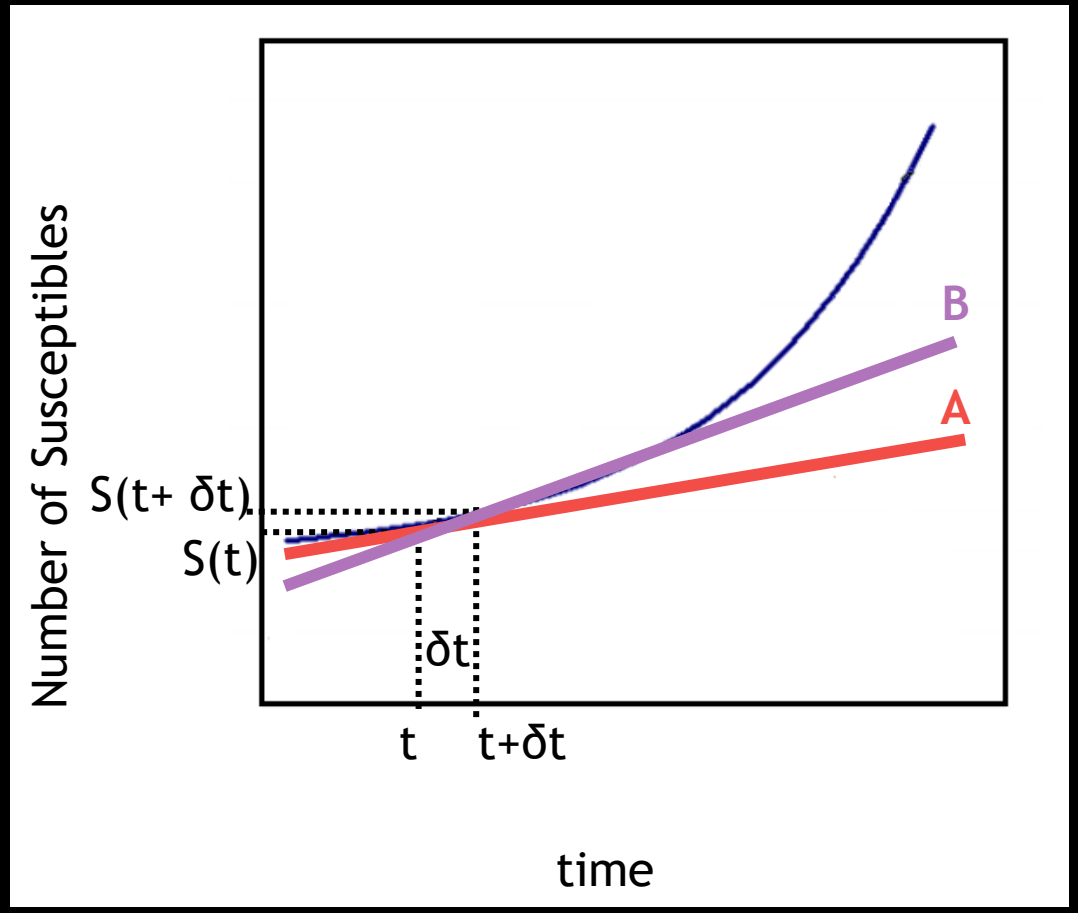
$$\frac{dS(t)}{dt} = \frac{S(t+\delta t) - S(t)}{\delta t}$$

$$as\ \delta t \to 0$$

- A and B look very far apart
- unless δt is very small!

SIR Model



$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

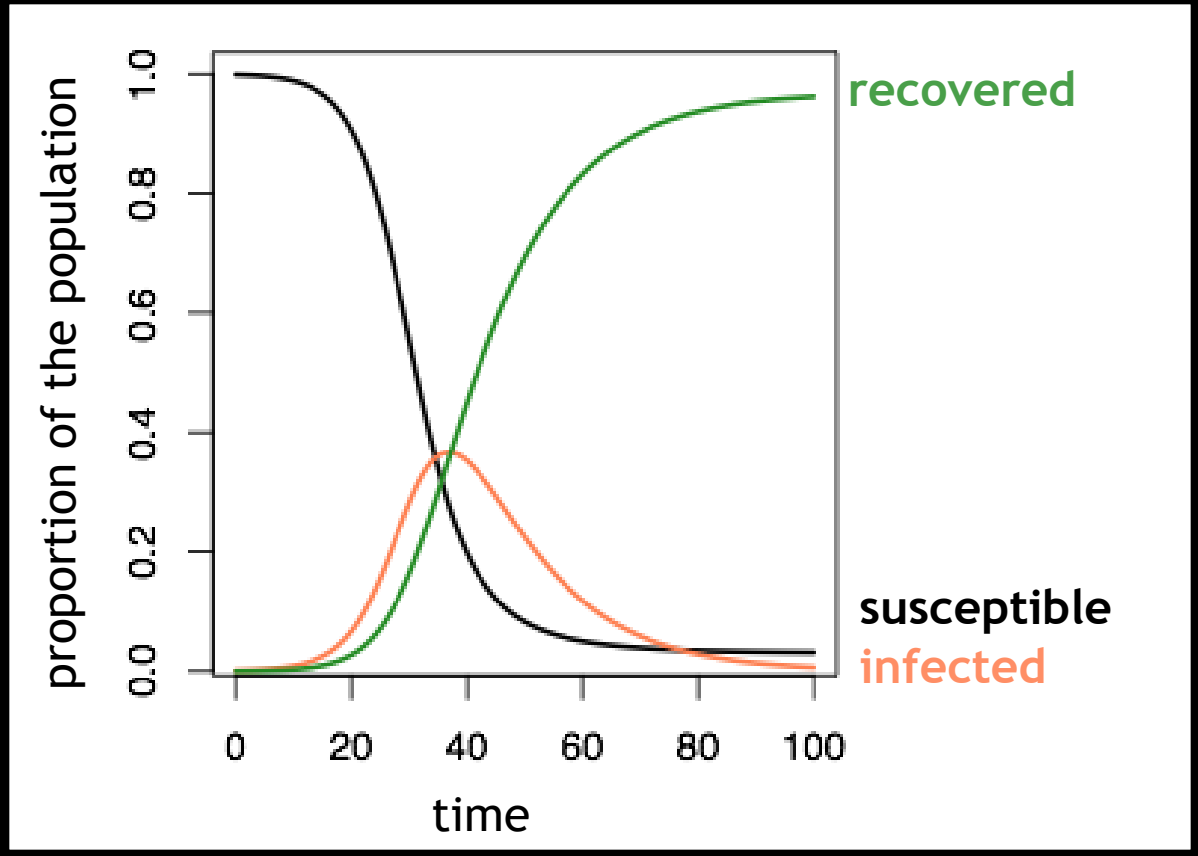
$$\frac{dS(t)}{dt} = \frac{S(t+\delta t) - S(t)}{\delta t} \quad as\ \delta t \to 0$$

- we can only solve for B, and B is only a good approximation for A if δt is very small

Solving Differential Equations

- Specialized software/programs
  - Berkeley Madonna
  - Stella
  - MatLab
  - Mathematica
  - Maple
  - R
- Software solves differential equations with different techniques (Euler, Runge-Kutta, Burlirsch-Stoer, etc.)
  - numerical integration

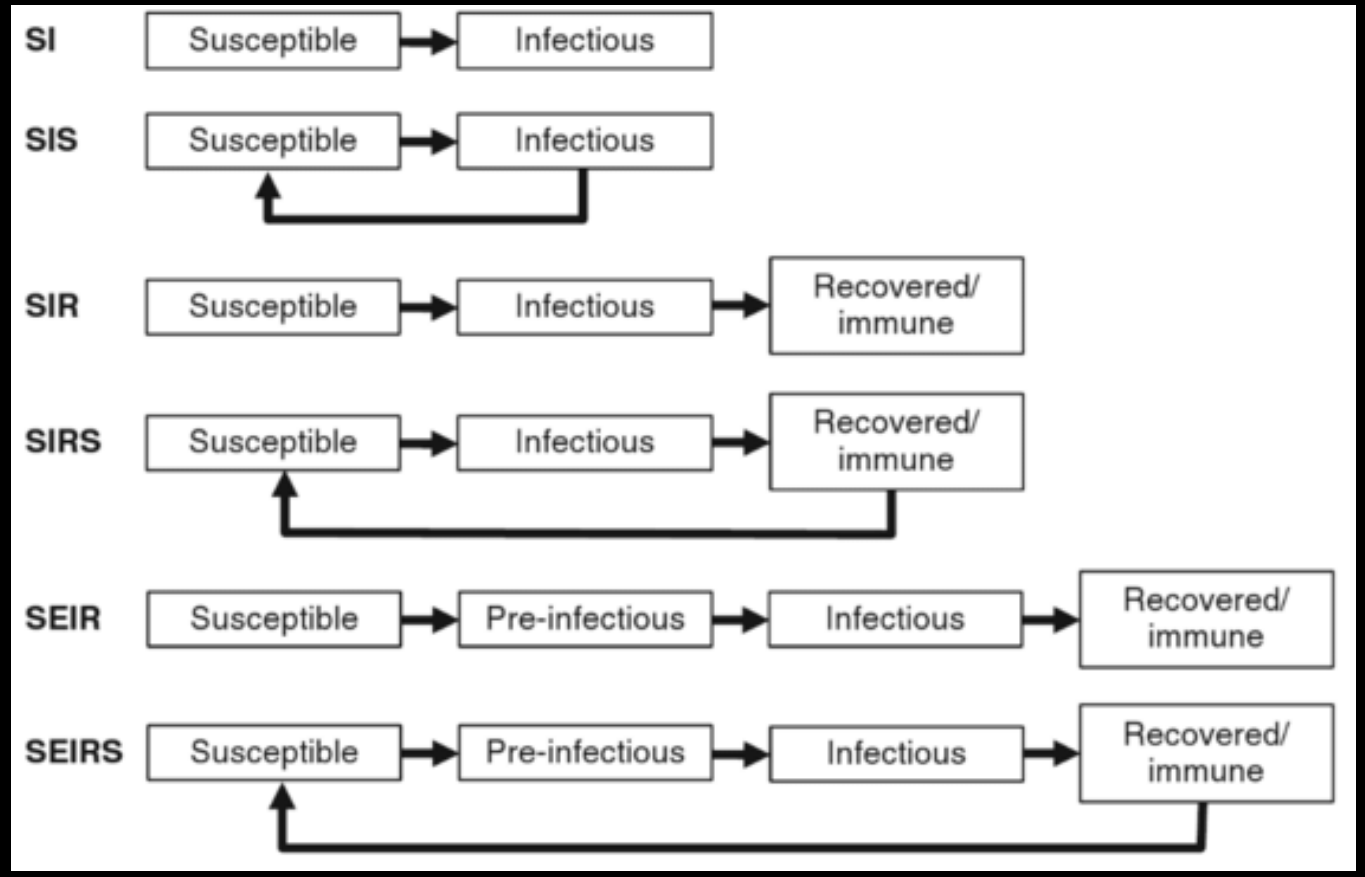
SIR Model Output



- We can examine the epidemic dynamics
- We will have values for S(t), I(t), and R(t) for each time step t
  - these can be expressed as population proportions and plotted
  - we can also find totals for each compartment at the end of the epidemic

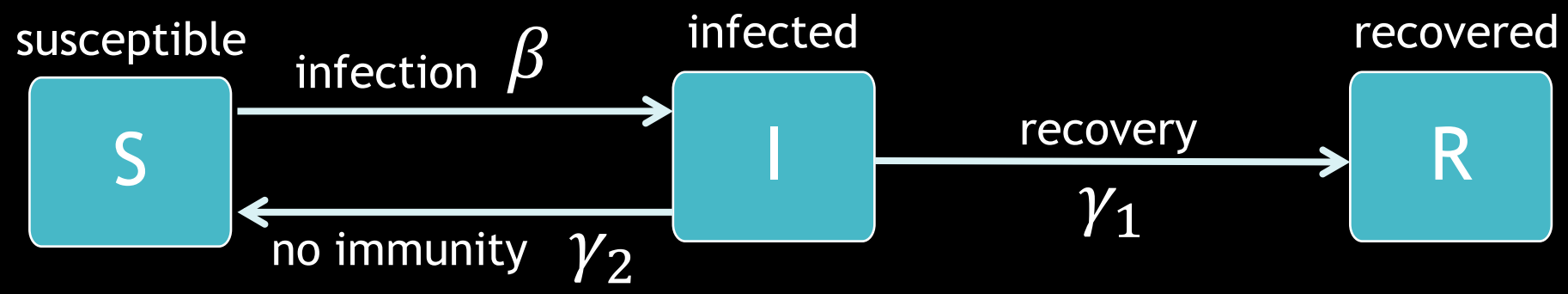
SIR Model Key Points

- Basic SIR model is the most commonly discussed compartmental/mechanistic model
- Models can be built to represent many disease systems, pathogen dynamics, and scenarios
  - Model building requires you to make assumptions – consider if the assumptions are valid for your situation
- Models are translated to mathematical expressions (ODEs) that are solved using numerical integration
- Output from models helps us understand dynamics of an epidemic



More Compartmental Models

Example: Hookworm Infection



$$\frac{dS(t)}{dt} = \gamma_2 I(t) - \beta S(t) I(t)$$

$$\frac{dR(t)}{dt} = \gamma_1 I(t)$$

$$\frac{dI(t)}{dt} = \beta S(t) I(t) - \gamma_1 I(t) - \gamma_2 I(t)$$

Workshop Schedule

Time	Topics
2:00–2:10 pm	~~Greetings~~
2:10–3:00 pm	~~SIR Model & Differential Equations~~
3:00–3:10 pm	~~Break~~
3:10–3:30 pm	~~SIR Model & Time Steps~~
3:30–3:40 pm	Break
3:40–5:00 pm	R Session