

Introduction to Modeling

Learning Objectives

By the end of this session you should learn:

- How does infectious disease modelling fit into the field of epidemiology
- What are the different goals of ID mechanistic models
- What are the different types of ID models
- What are common data relied upon for modelling
- How are ID data and ID models related

Contextualizing Infectious Disease Modelling

Disease vs Infectious Disease

Disease - A deviation from the normal physiological status of an organism that negatively affects its survival or reproduction

Infectious Disease - A disease in one organism (the host) that is caused by another organism (pathogen or parasite) which has entered the host's body

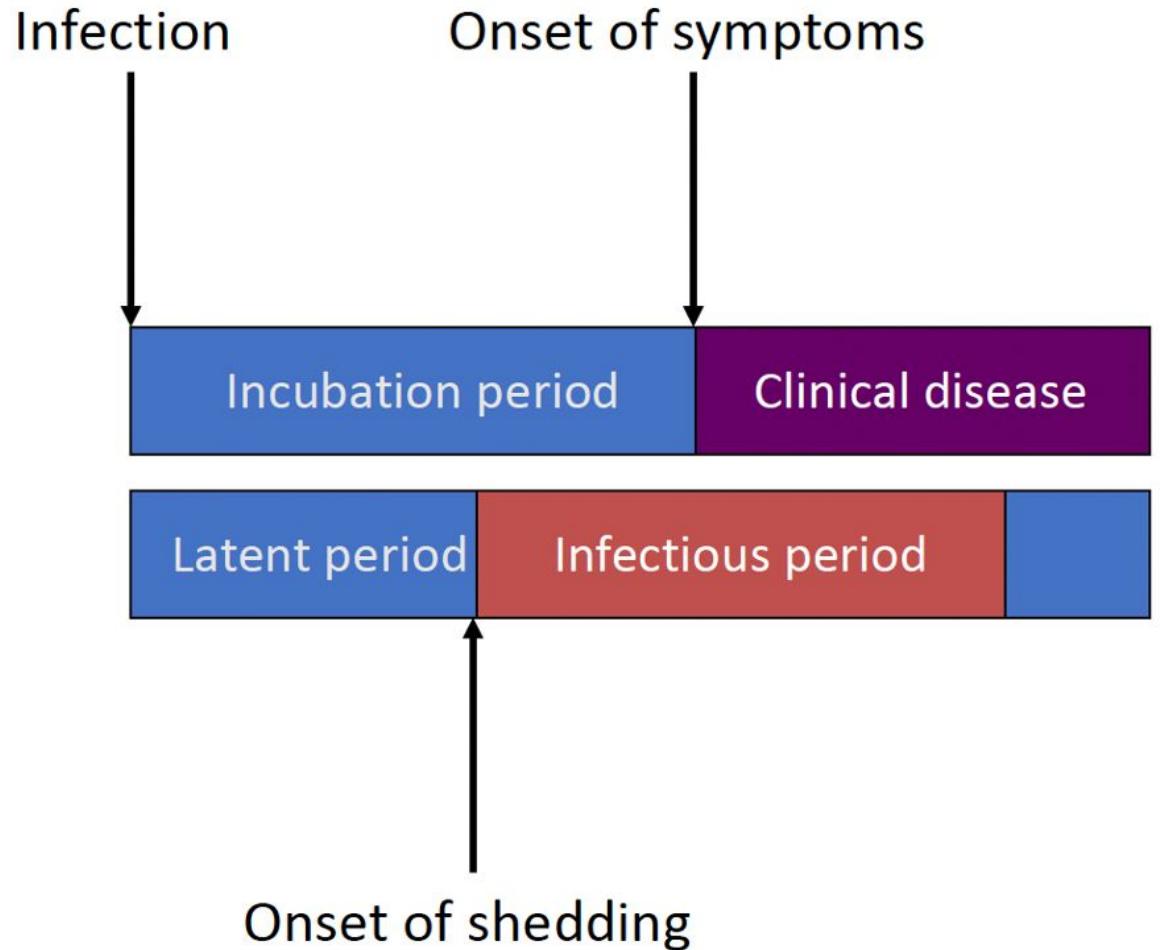
Agents of Infectious Diseases

Pathogens (agents) – organisms that are capable of producing diseases.

- Viruses (Examples: HIV -> AIDS, influenza -> flu, Measles morbillivirus -> measles)
- Bacteria (Examples: Vibrio cholerae -> Cholera, Yersinia pestis -> plague, Mycobacterium tuberculosis -> Tuberculosis)
- Fungi (Examples: Aspergillus -> Aspergillosis, tinea -> Athlete's foot)
- Protozoa (Examples: Plasmodium falciparum -> Malaria, Trypanosoma cruzi -> Chagas Disease)
- Helminths (Examples: Schistosoma mansoni -> Schistosomiasis, Hookworm -> hookworm infection)

parasites

From infection to disease



Tangent

We are modeling infections,
although we actually observe
clinical cases

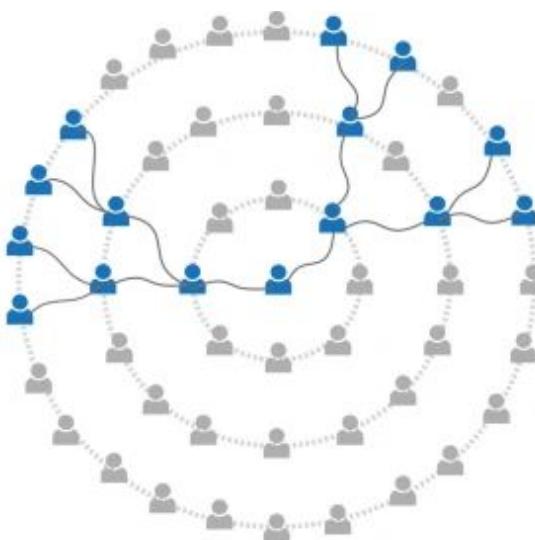
Clinical status

Infection status

Epidemiology focus on population level

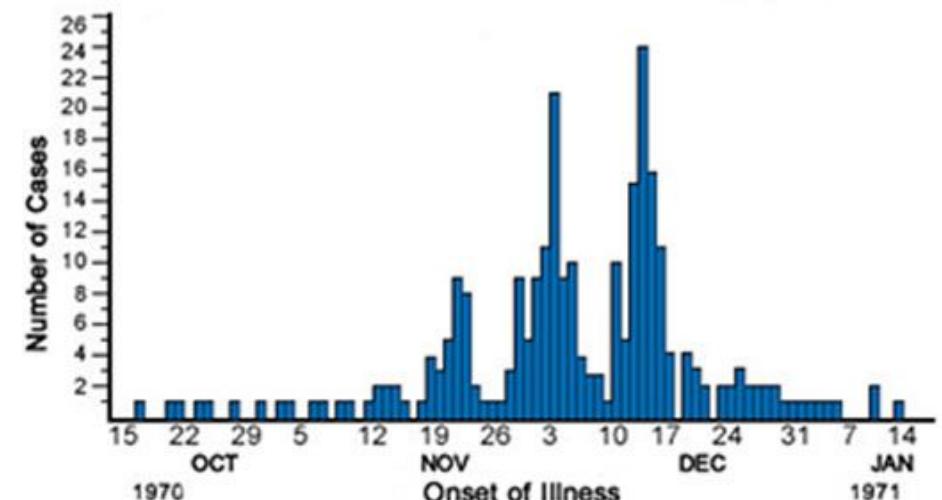
We can track the movement of pathogens throughout populations

Visualized easily via a transmission chain, which is the set of infection events that occur as a pathogen moves through a population



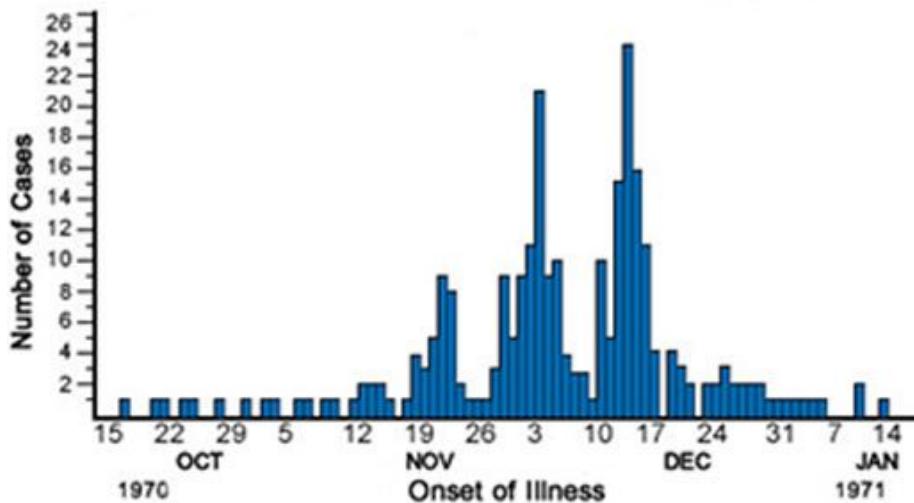
Wegehaupt et al. BMC Public Health 2023

Measles Cases by Date of Onset in Aberdeen, South Dakota, October 15, 1970 – January 16, 1971



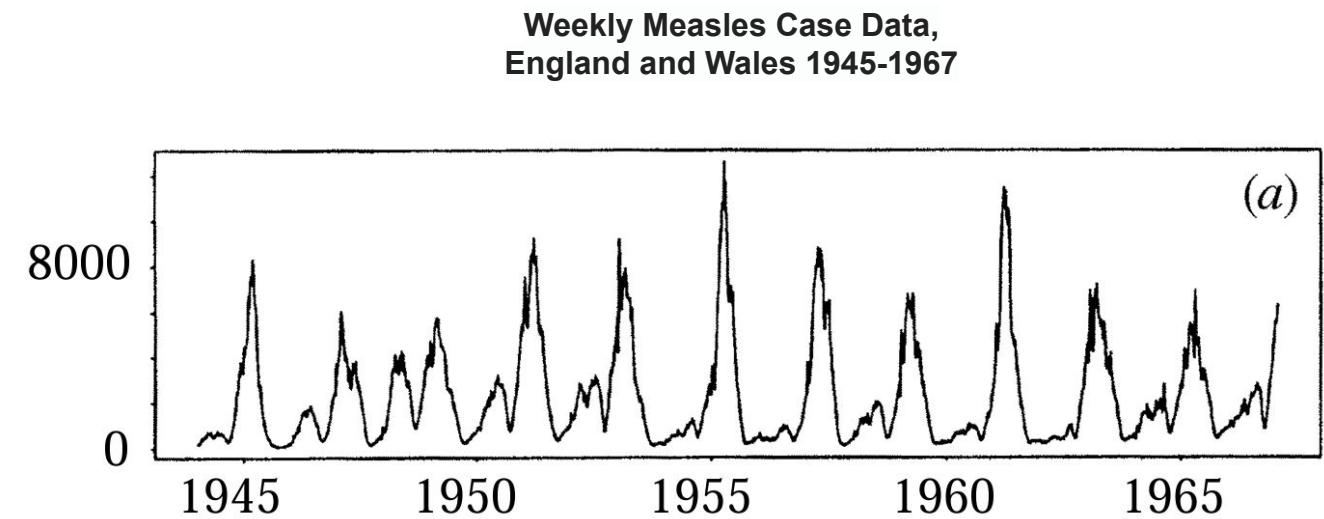
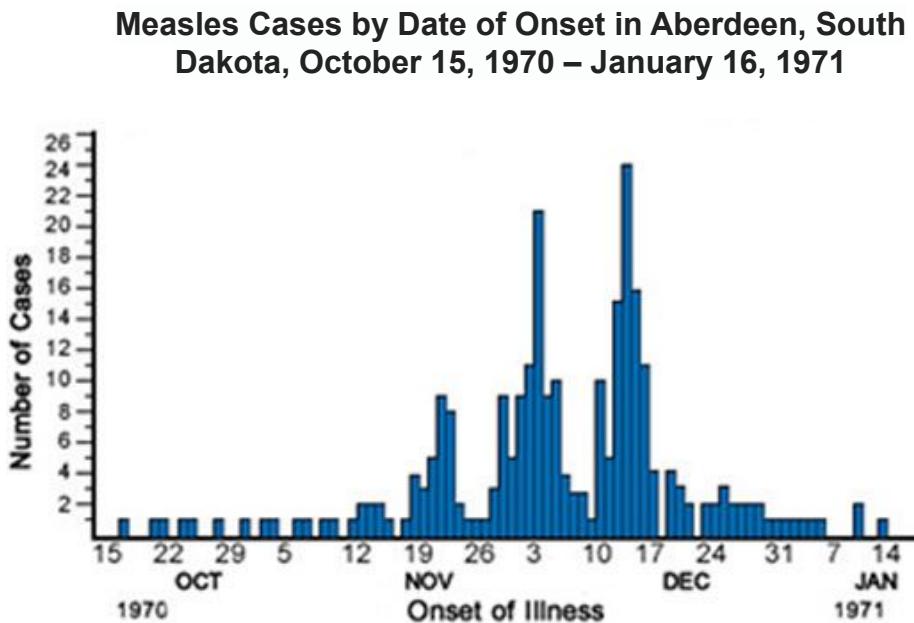
Use cases from time series data (Epi Curve)

Measles Cases by Date of Onset in Aberdeen, South Dakota, October 15, 1970 – January 16, 1971



Single outbreak vs Persistence

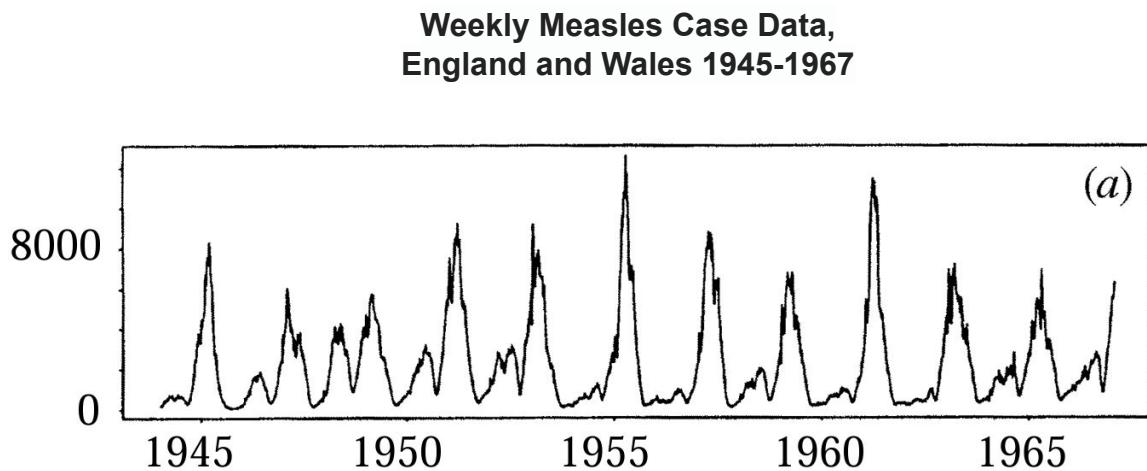
Closed population vs Open population



<https://www.cdc.gov/training/quicklearns/epimode/>

Finkenstädt B, Grenfell B. Proc Biol Sci. 1998

Use cases from long time series data



Epidemiological Dynamics

- What is the net reproduction number over time?
- How does seasonality shape transmission?
- Are there multi-annual cycles, and what might explain them?

Host-Pathogen Interactions

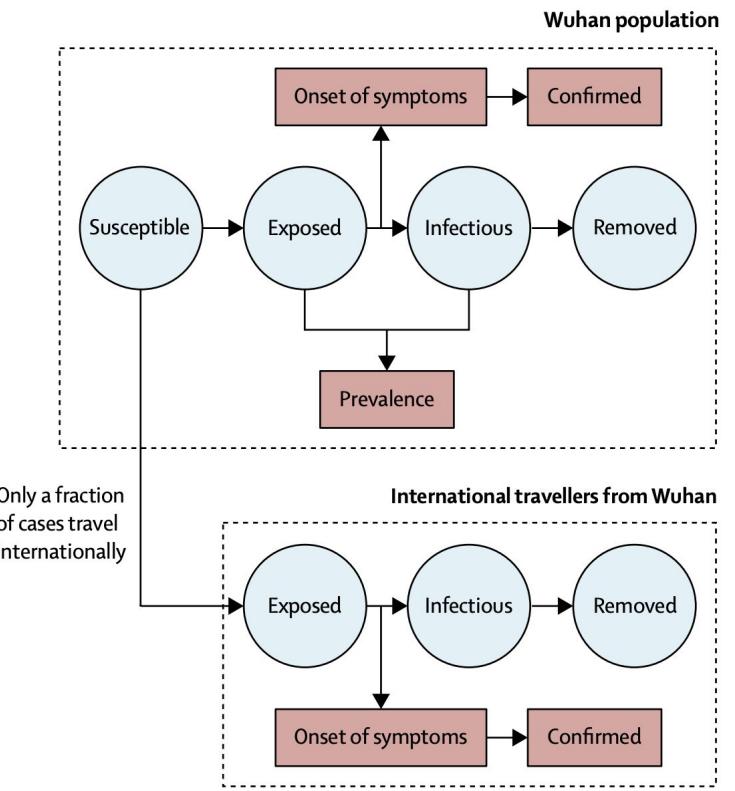
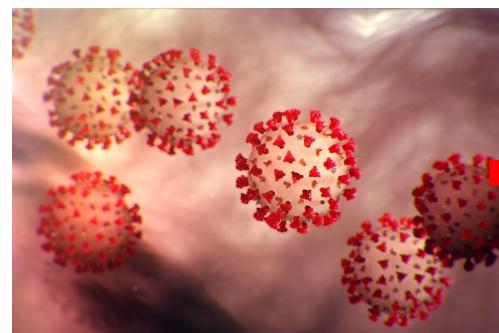
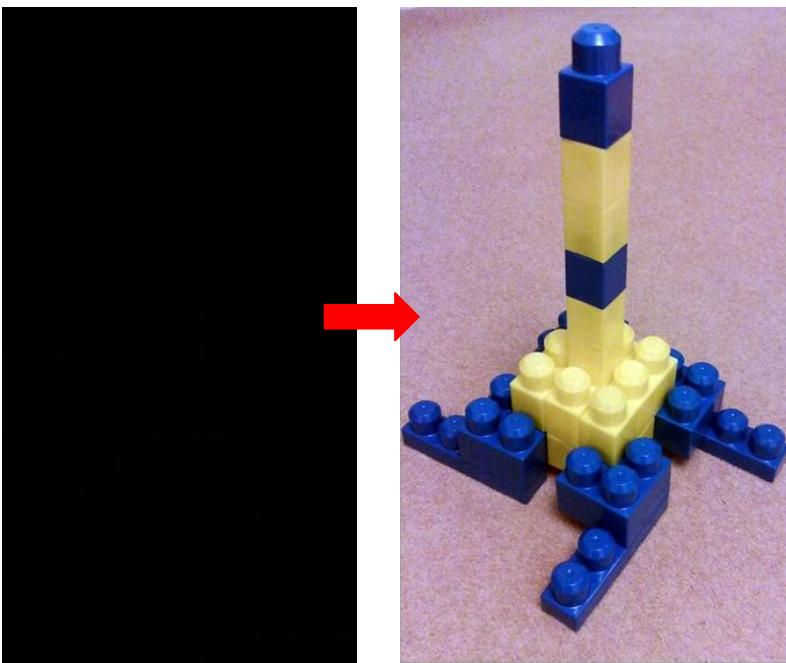
- What is the estimated duration of immunity following infection?
- Do re-infections contribute to sustained transmission?

Forecasting and Interventions

- Can we build a forecasting model to predict future peaks?
- When is best to implement control?

What is a model?

A model is a simplified representation of a more complex object/process, designed to address specific questions. It is an abstraction of reality.



Infectious disease models are not new

Daniel Bernoulli's 1766 analysis of smallpox might be the first published model of an infectious disease, although not a transmission model. <https://doi.org/10.1002/rmv.443>



The first counterfactual

- Bernoulli worked out solutions for a system of differential equations to determine life expectancy at birth with inoculation and without inoculation to smallpox

Results

- Inoculating everyone at birth increased overall life expectancy by about 3 years
- Effective as long as the probability of dying from smallpox right after inoculation is less than $\sim 11\%$, which Bernoulli estimated this risk to be $\sim 1\%$

Where does modelling fit in epidemiology?

Classical Epidemiology	Mechanistic Epidemiology
Data-Centric	Process-Centric
Public Health	Disease Ecology
Risk Factors	Infectious Disease Dynamics
Biostatistics	Mathematical Modelling

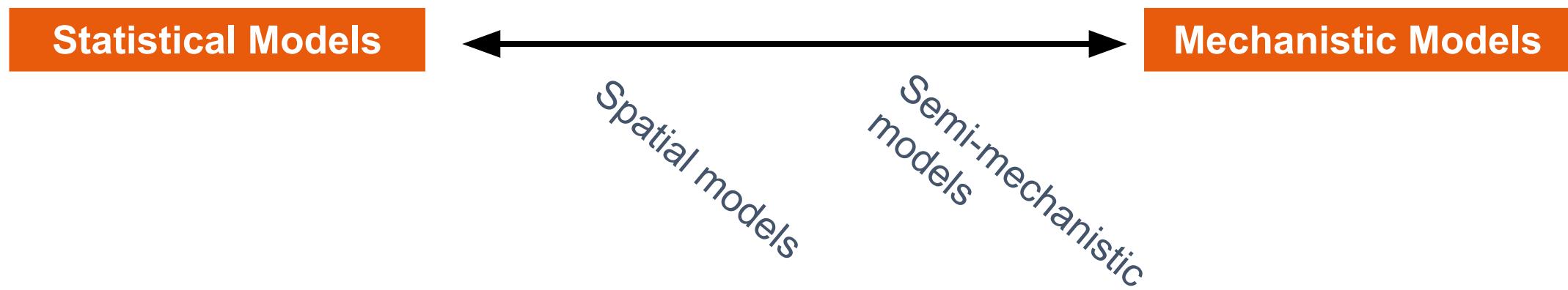
Where does modelling fit in epidemiology?

(Bio)Statistical Epidemiology (data-centric)	Mechanistic Epidemiology (process-centric)
Account for bias and random error to find correlations that may imply causality	Systems Approach: Explicitly model multiple mechanisms to understand their interactions
Often the first step to assessing relationships	Links observed relationship at different scales
Assume independence of individuals (as some scale)	Explicitly focus on dependence of individuals

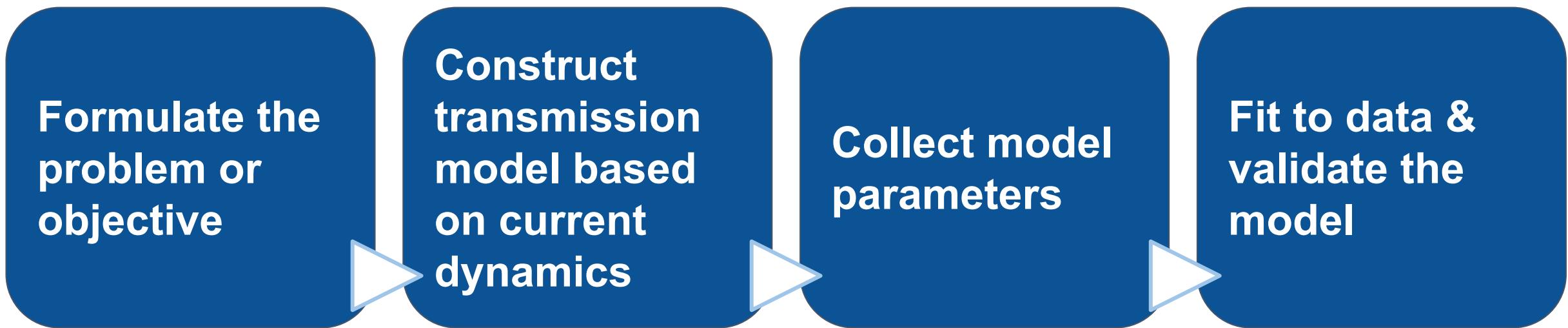
Where does modelling fit in epidemiology?

(Bio)Statistical Epidemiology (data-centric)	Mechanistic Epidemiology (process-centric)
Is HIV positively associated with the risk of TB infection?	Based on increased TB due to HIV, how much should we expect increase in TB to increase given HIV prevalence?
Are insecticide treated bednets (ITN) or indoor residual spraying (IRS) more effective for controlling malaria?	How do we expect the spatial distribution of malaria incidence to change after implementing ITB or IRS?
What are risk factors for dying from measles infection?	What is the impact of vaccination on the age profile of measles infection and deaths?

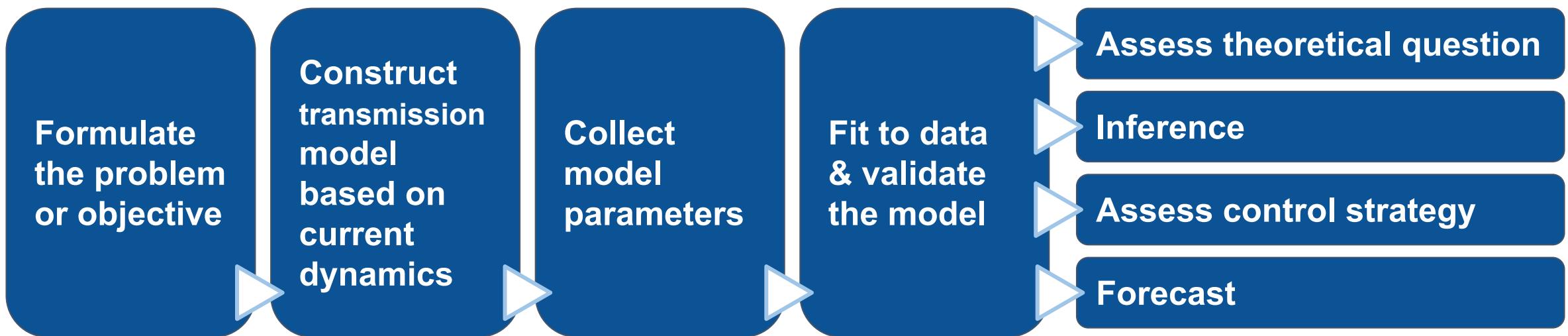
Where does modelling fit in epidemiology?



Steps of developing a model



Steps of developing a model



Model Utility

Model utility

Formulate
the problem
or objective

- We develop models based on a specific goal or objective
- When setting model goals with public health practitioners, it is critical to set and communicate realistic expectations about what the model can

Four goals for mechanistic ID models

Formulate
the problem
or objective

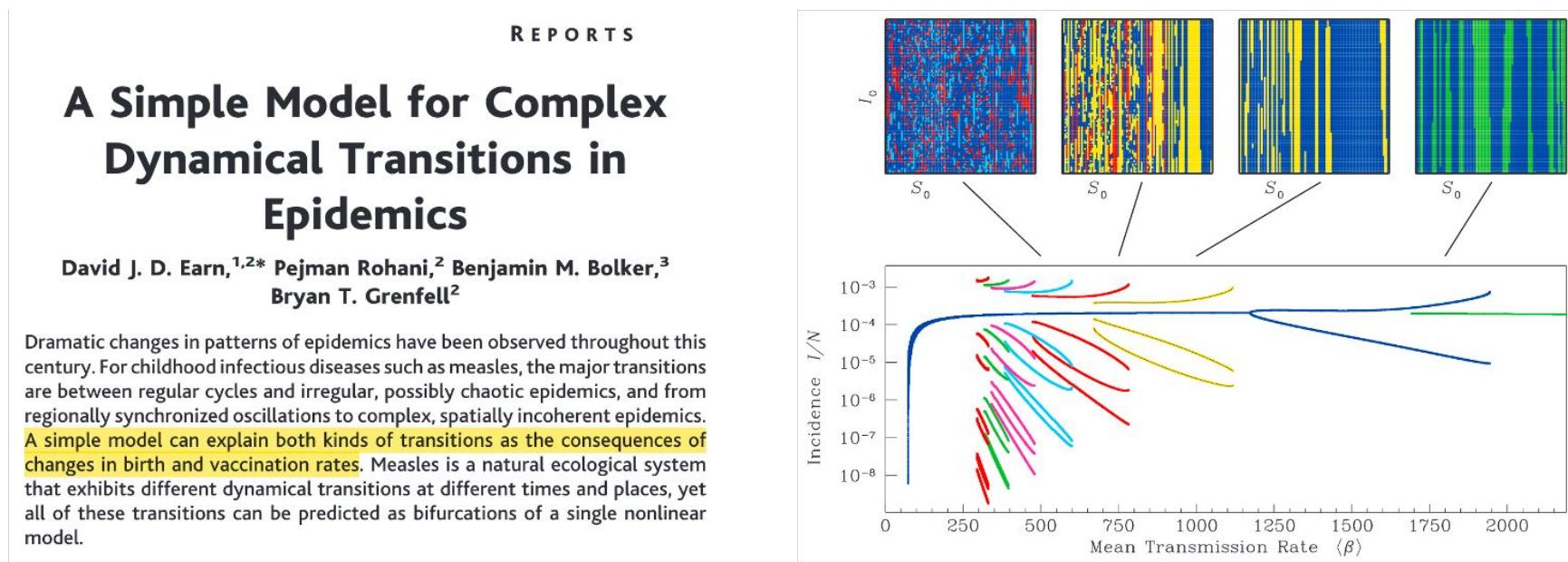
Theoretical Modelling

What type of emergence behavior is produced by disease systems with different properties?

- What-if type questions
- Highly abstract
- Explore consequences of hypothetical mechanisms

Theoretical model example

Earn et al. investigated the causes of transitions in measles epidemic patterns from regular (i.e., annual or biennial) to irregular outbreaks. The assumption under-investigation was the dynamical effect of changing birth rates and vaccination rates (i.e., changes in transmission) on incidence given term-time forcing. As a result, the authors displayed a bifurcation diagram looking across multiple transmission rates on incidence patterns and found more stochastic dynamics at lower transmission rates.
[10.1126/science.287.5453.667]



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Inference Modelling

What is the true nature of the disease processes that are producing the observed health metrics?

- Understand specific mechanisms of transmission
- Quantify value of specific parameters
- Account for epistemic and sampling process

Inference model example

Ecological Monographs, 72(2), 2002, pp. 185–202
© 2002 by the Ecological Society of America

DYNAMICS OF MEASLES EPIDEMICS: SCALING NOISE, DETERMINISM, AND PREDICTABILITY WITH THE TSIR MODEL

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May 2002

SCALING OF MEASLES DYNAMICS

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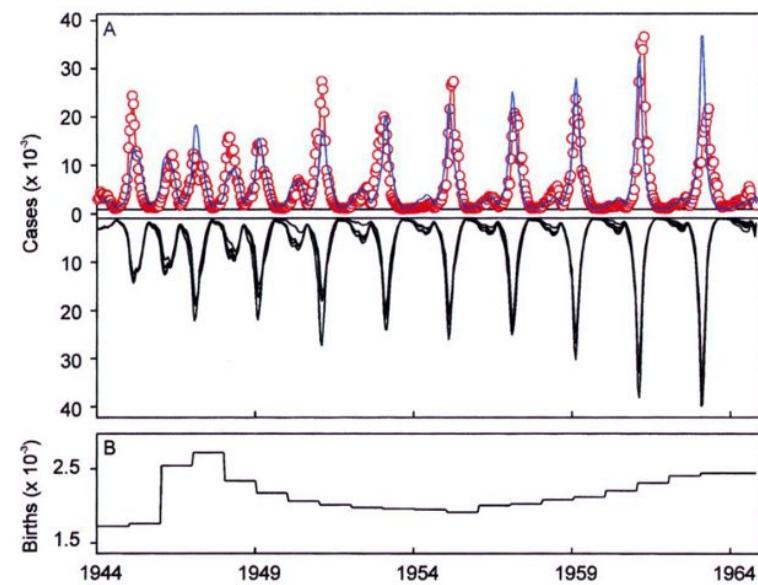


FIG. 1. (A) Measles incidence in 2-wk periods (in hundreds) in London from 1944 to 1965. The circles and the red line represent observed incidence (corrected for underreporting). The blue line represents the deterministic prediction from the TSIR model (using the susceptible and infected density in the first 2-wk period of 1944 as initial conditions). The black lines (and inverted scale) represent five stochastic realizations of the TSIR model. (B) The biweekly number of births (in hundreds) in London. The numbers are averaged within each year. The post-World War II baby boom in the late 1940s is associated with a period of annual cycles in measles incidence.

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Strategic Modelling

How will an epidemic unfold and different control strategies work under various conditions?

- Conditional predictions of what could happen under specific scenarios
- *Focus on contrast's between scenarios*

Strategic modeling example

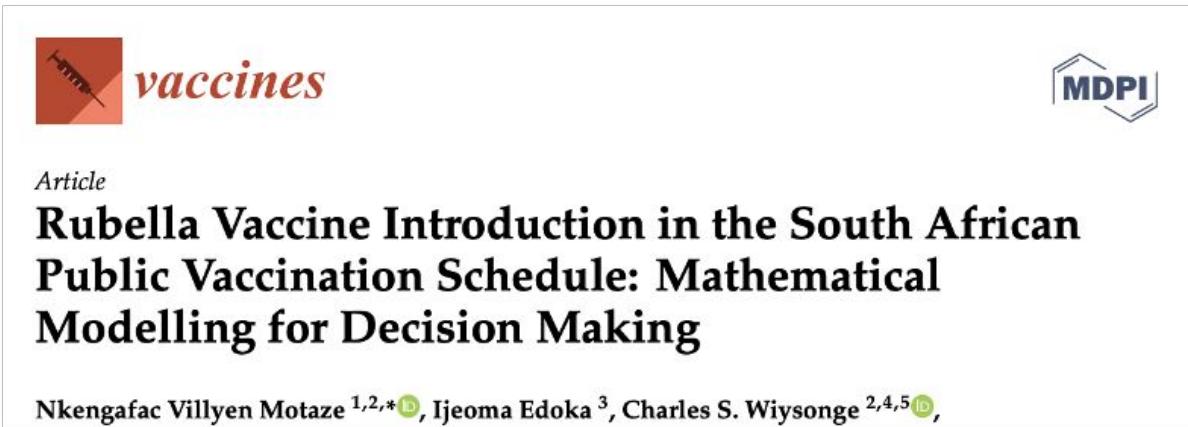


Table 1. Possible scenarios for rubella-containing vaccine (RCV) introduction in South Africa.

Scenario	Routine Vaccination in Expanded Program on Immunization (EPI)	Target Age Group for Routine Vaccination	Target Age Group for Initial Mass Campaign	Follow-Up Mass Campaigns	
				Target Age Group	Timing
1			No RCV in EPI		
2	RCV introduction	1 year	No initial campaign	No follow-up campaign	N/A
3	RCV introduction	1 year	1 to 14 years	No follow-up campaign	N/A
4	RCV introduction	1 year	1 to 14 years	1 to 4 years	One follow-up campaign 5 years after initial campaign
5	RCV introduction	1 year	1 to 14 years	1 to 4 years	Six follow-up campaigns every 5 years after initial campaign for 30 years
6	RCV introduction	1 year and 9 years	No initial campaign	No follow-up campaign	N/A

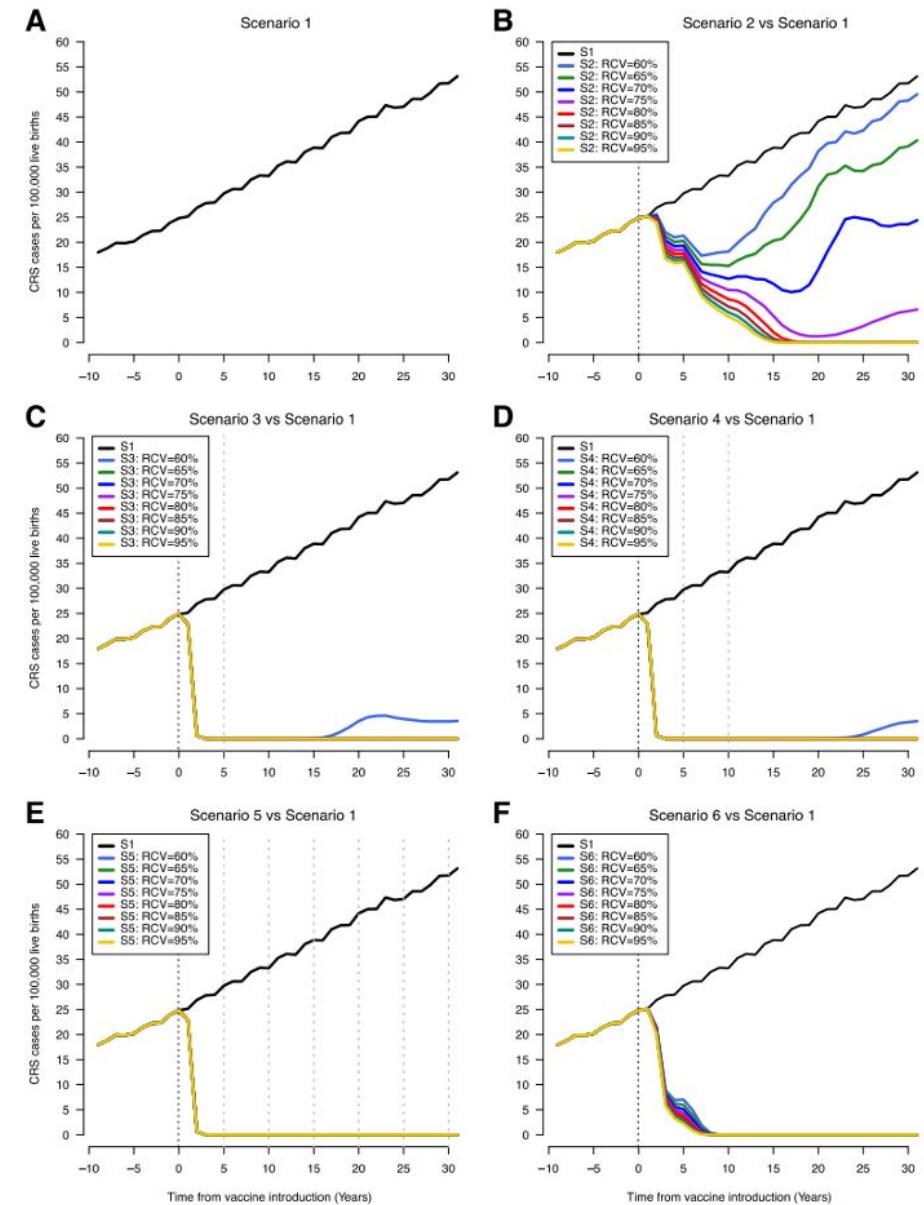


Figure 2. Time series of congenital rubella syndrome (CRS) incidence (CRS cases per 100,000 live births) showing scenario 1 (A) and comparing scenario 1 with scenarios 2–6 (B–F). The vertical black dotted

Four goals for mechanistic ID models

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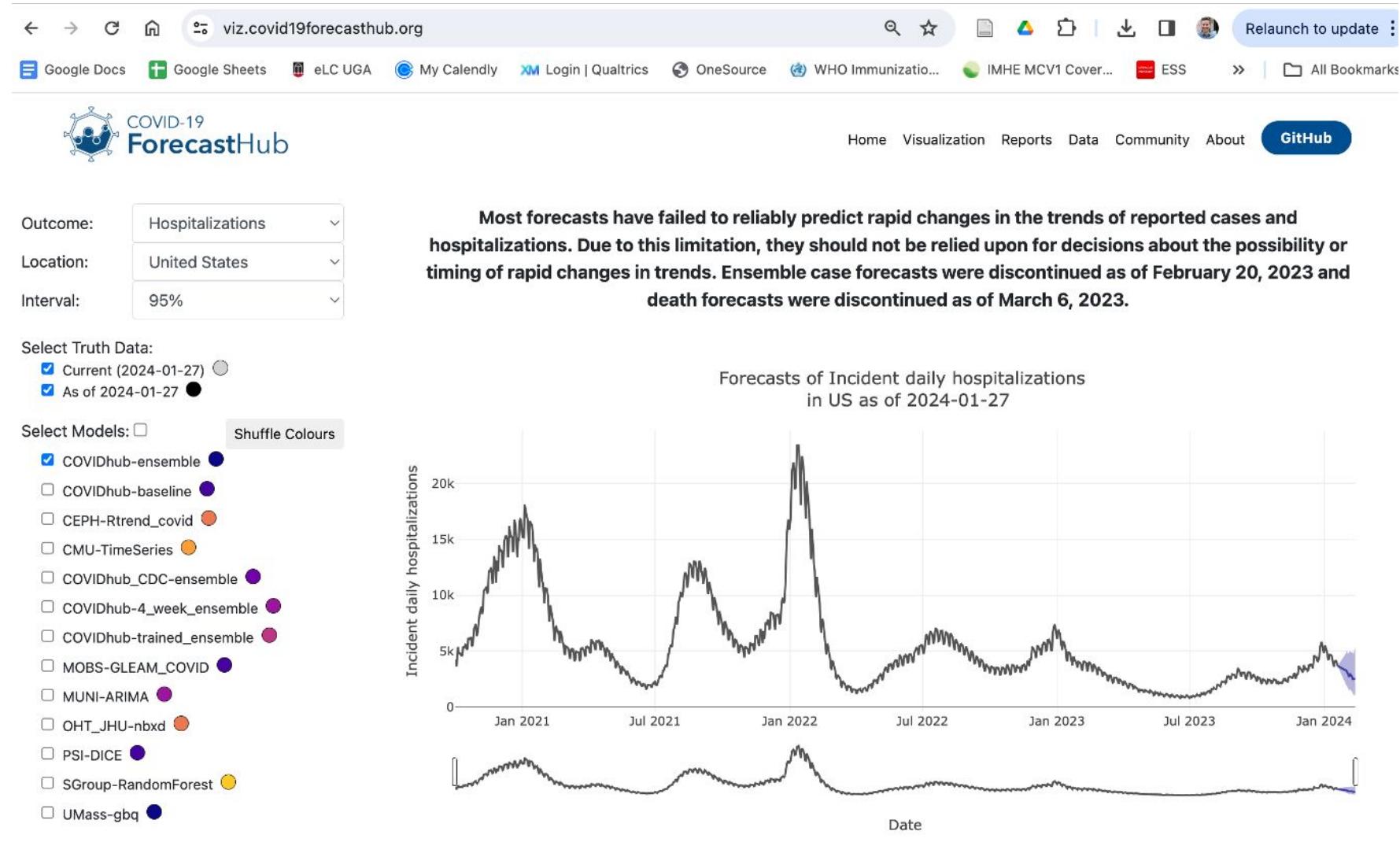
- Conditional predictions of what could happen under specific scenarios
- *Focus on contrast's between scenarios*

Forecast Modelling

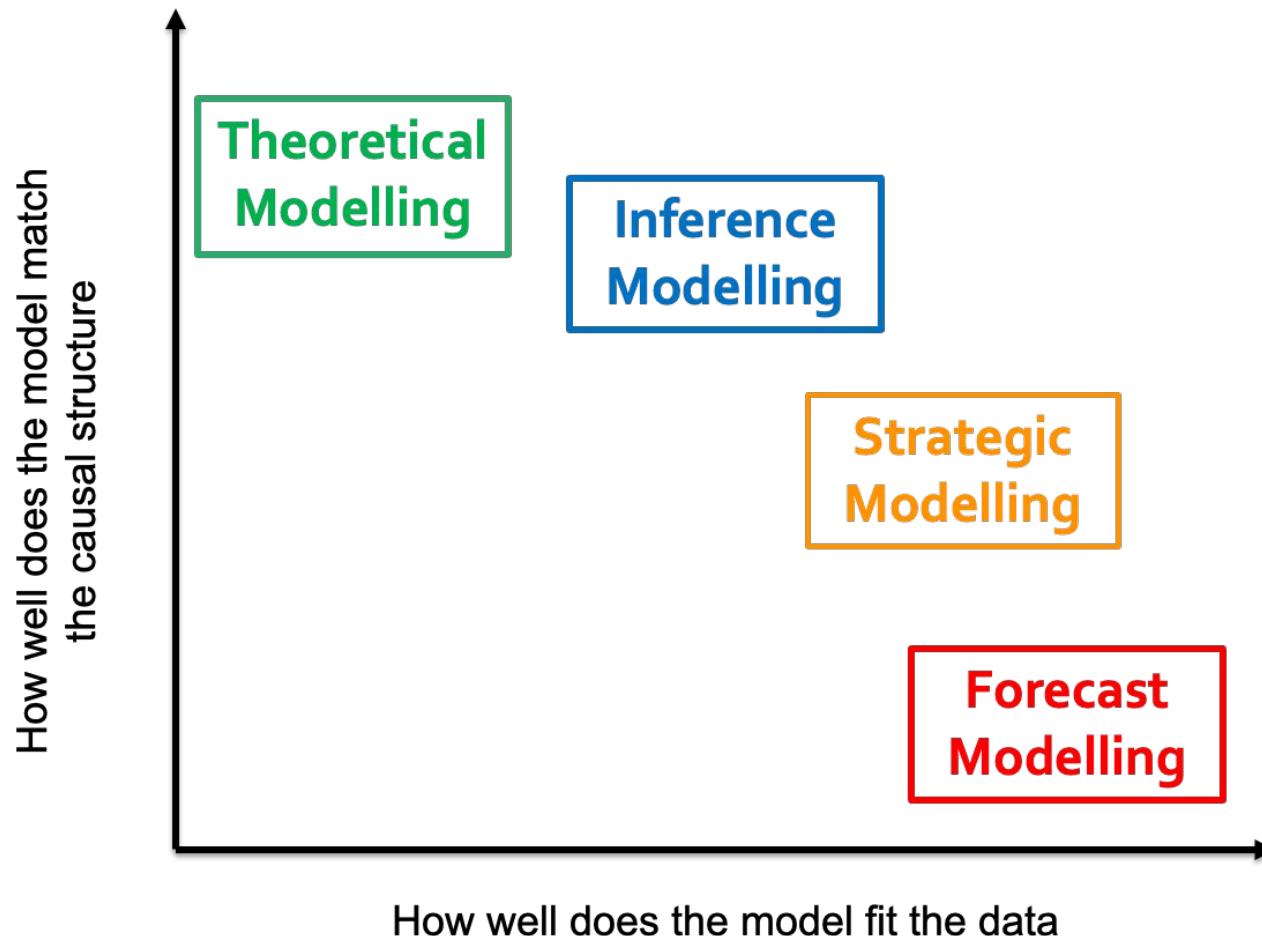
How will an epidemic unfold in the coming weeks or months?

- Unconditional prediction of what will happen
- Choice of specific metrics

Forecast modeling example



Four goals for mechanistic ID models



Reporting standards based on model goals

Theoretical Modelling

- Clear description of mechanistic mapping b/w model and phenomena
- Clear description of assumptions and model structure
- Evaluation of how non-target model components influence results

Inference Modelling

- Clear description of how models are linked to data
- Description of sources of uncertainty
- Description of how threats to inference addressed (e.g., confounding)

Strategic Modelling

- Clear description of how interventions are mechanistically modeled
- Definition and justification of scenarios
- Clear definition of what outcomes will be used to make contrasts b/w scenarios

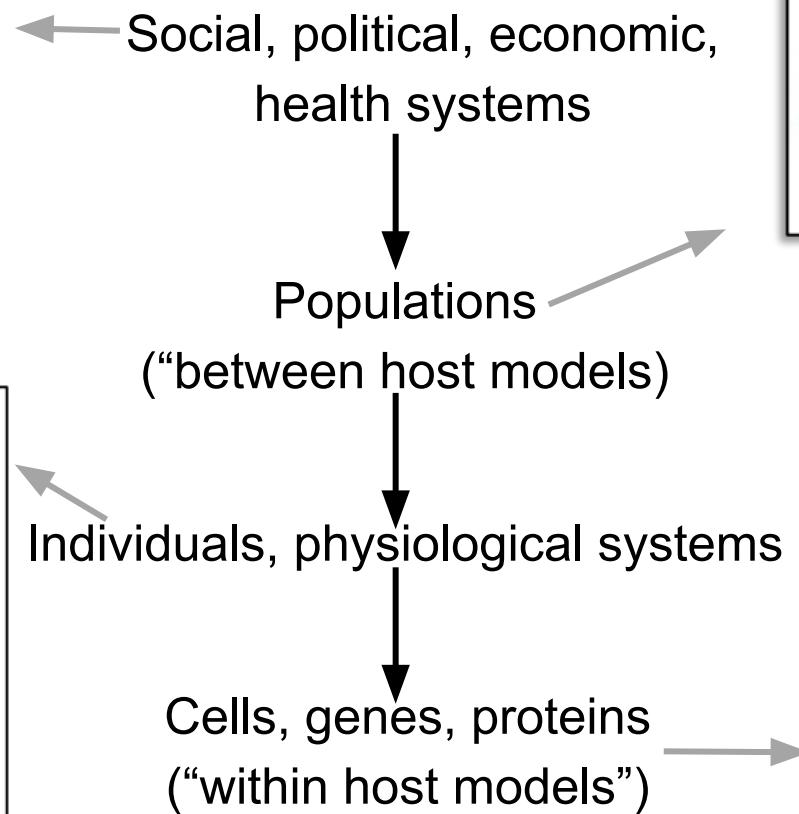
Forecast Modelling (Pollet et al 2021)

- Describe forecasting targets
- Define time horizon
- Describe how forecasts were validated

Model Type

Scale of modelling

Construct transmission model based on current dynamic



INTERFACE
rsif.royalsocietypublishing.org

Self-enforcing regional vaccination agreements

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⁶Public Health Foundation of India, New Delhi 110071, India

IM, 0009-0001-8391-6660

In a highly interconnected world, immunizing infections are a transboundary problem, and their control and elimination require international cooperation and coordination. In the absence of a global or regional body that can impose a universal vaccination strategy, each individual country sets its own strategy. Mobility of populations across borders can promote

Received: 22 October 2015
Accepted: 23 December 2015

The effect of control strategies to reduce social mixing on outcomes of the COVID-19 epidemic in Wuhan, China: a modelling study



Kiesha Prem*, Yang Liu*, Timothy W Russell, Adam J Kucharski, Rosalind M Eggo, Nicholas Davies, Centre for the Mathematical Modelling of Infectious Diseases COVID-19 Working Group, Mark Jit, Petra Klepac

Lancet Public Health 2020; 5:e261–70
Published Online
March 25, 2020
<https://doi.org/10.1016/j.lph.2019.12.003>

PREVENTION AND SCREENING

Estimating Progression Rates for Human Papillomavirus Infection From Epidemiological Data

Mark Jit, PhD, Nigel Gay, MSc, Kate Soldan, PhD, Yoon Hong Choi, PhD, William John Edmunds, PhD

A Markov model was constructed in order to estimate type-specific rates of cervical lesion progression and regression in women with high-risk human papillomavirus (HPV). The model was fitted to age- and type-specific data regarding the HPV DNA and cytological status of women undergoing cervical screening in a recent screening trial, as well as cervical cancer incidence. It incorporates different assumptions about the way lesions regress, the accuracy of cytological screening, the specificity of HPV DNA testing, and the age-specific prevalence of HPV infection. Combinations of assumptions generate 162 scenarios for squamous cell carcinomas and 54 scenarios for adenocarcinomas. Simulating an unscreened cohort of women infected with high-risk HPV indicates that the probability of an infection continuing to persist and to develop into invasive cancer depends on the length of time it has already persisted. The scenarios and parameter sets that produce the best fit to available epidemiological data provide a basis for modelling the natural history of HPV infection and disease.

Key words: cervical intraepithelial neoplasia; mathematical model; Markov process; papillomavirus infections; uncertainty. (*Med Decis Making* 2010;30:84–98)

ARTICLES
<https://doi.org/10.1038/s41559-018-0786-x>
nature ecology & evolution

Within-host dynamics shape antibiotic resistance in commensal bacteria

Nicholas G. Davies ^{1,2*}, Stefan Flasche ^{1,2}, Mark Jit ^{1,2,3} and Katherine E. Atkins ^{1,2,4}

The spread of antibiotic resistance, a major threat to human health, is poorly understood. Simple population-level models of bacterial transmission predict that above a certain rate of antibiotic consumption in a population, resistant bacteria should completely eliminate non-resistant strains, while below this threshold they should be unable to persist at all. This prediction stands at odds with empirical evidence showing that resistant and non-resistant strains coexist stably over a wide range of antibiotic consumption rates. Not knowing what drives this long-term coexistence is a barrier to developing evidence-based strategies for managing the spread of resistance. Here, we argue that competition between resistant and sensitive pathogens within individual hosts gives resistant pathogens a relative fitness benefit when they are rare, promoting coexistence between strains at the population level. To test this hypothesis, we embed mechanistically explicit within-host dynamics in a structurally neutral pathogen transmission model. Doing so allows us to reproduce patterns of resistance observed in the opportunistic pathogens *Escherichia coli* and *Streptococcus pneumoniae* across European countries and to identify factors that may shape resistance evolution in bacteria by modulating the intensity and outcomes of within-host competition.

Construct
transmission
model based
on current
dynamic

What type of model is most useful?

“Selecting the correct level of detail is one of the most difficult decisions a modeler faces. Models that are too simple may lose face validity because they do not incorporate aspects that content experts feel are required, but models that are too complex may be difficult to build, debug, analyze, understand, and communicate.”

Model structure

Construct
transmission
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dynamic

Model structure is usually determined by considering the **relationship between**:

- **Inputs** relevant to the natural history of disease, clinical pathways, intervention effectiveness etc.
- **Outputs** most useful to decision makers eg. cases of disease, deaths, hospital admissions, life years gained, QALYs, DALYs.

Model structure

SI



Chronic infection (e.g., HIV, Hep B, Hep C)

SIS



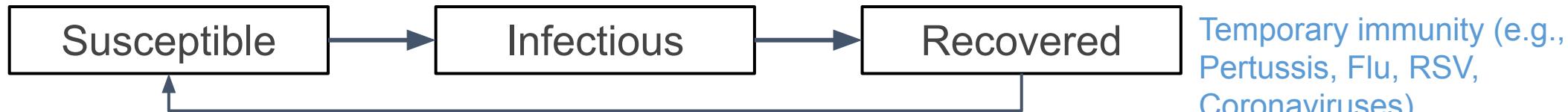
Reinfection possible (e.g., Gonorrhea, Chlamydia, Malaria)

SIR



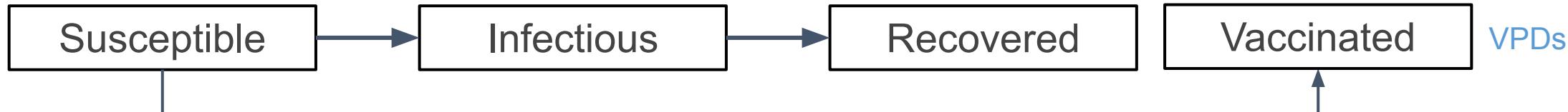
Lifelong immunity (e.g., Measles, Rubella, Mumps, Varicella zoster, Ebola)

SIRS



Temporary immunity (e.g., Pertussis, Flu, RSV, Coronaviruses)

SIRV



Construct transmission model based on current dynamic

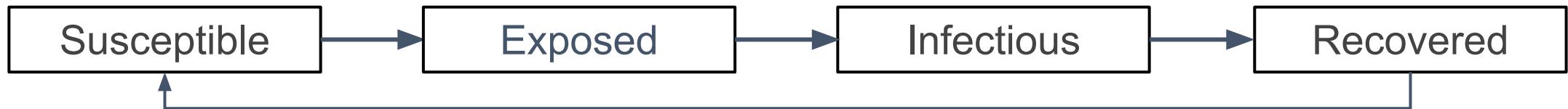
Model structure - Common mistake

Construct transmission model based on current dynamic

SEIR



SEIRS

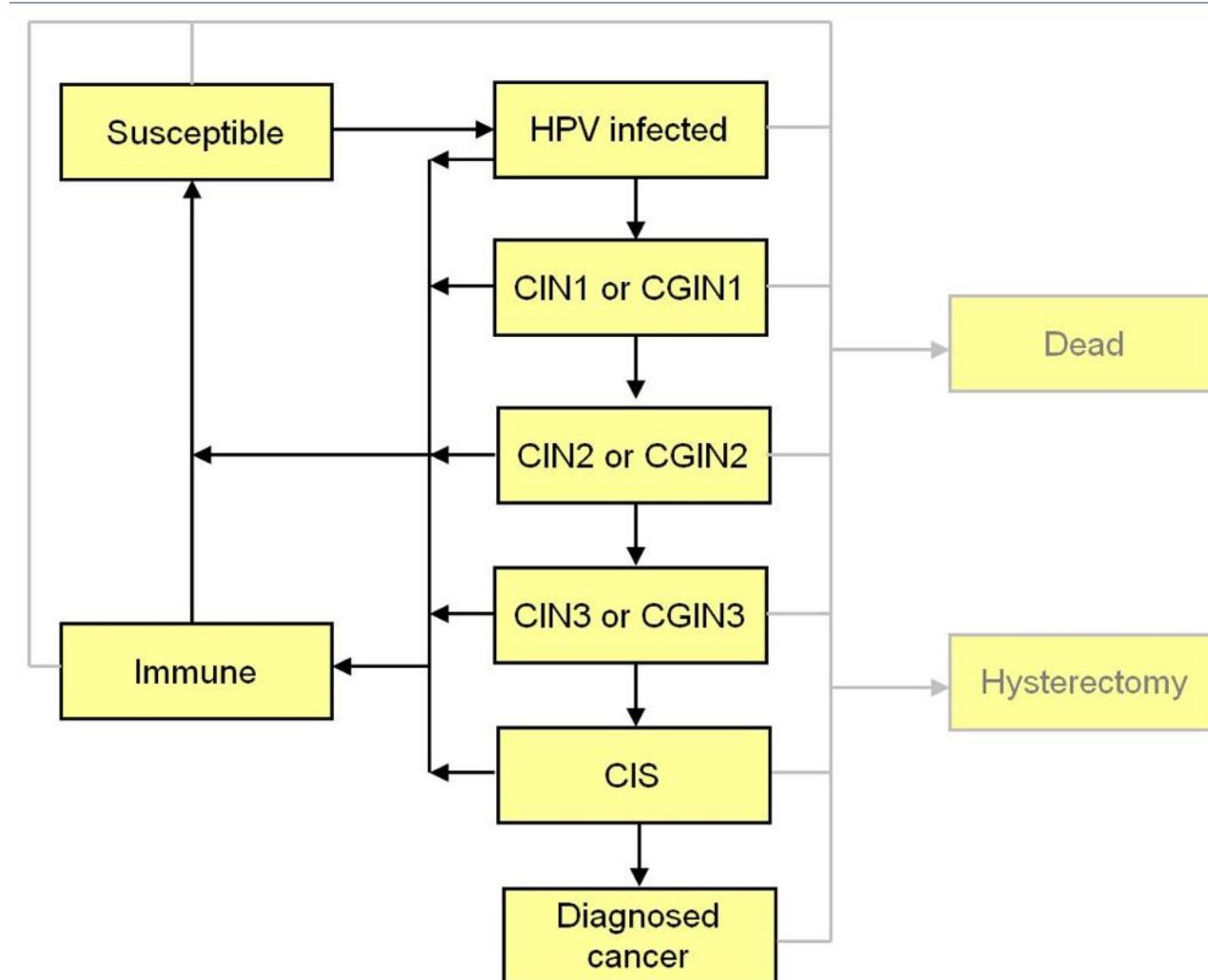


Tangent

“Exposed” is misleading. Really it means infected but not yet infectious. Think “pre-infectious”

Model structure - Can get complicated

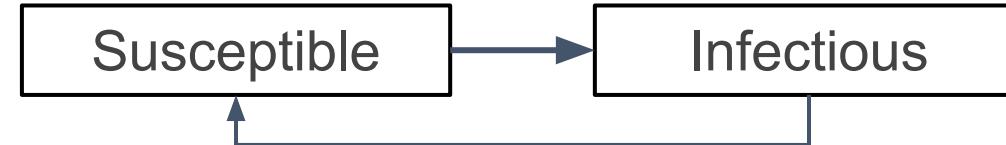
Construct transmission model based on current dynamic



Types of models

Construct transmission model based on current dynamic

Compartmental model



↑
Non-homogenous mixing
↓

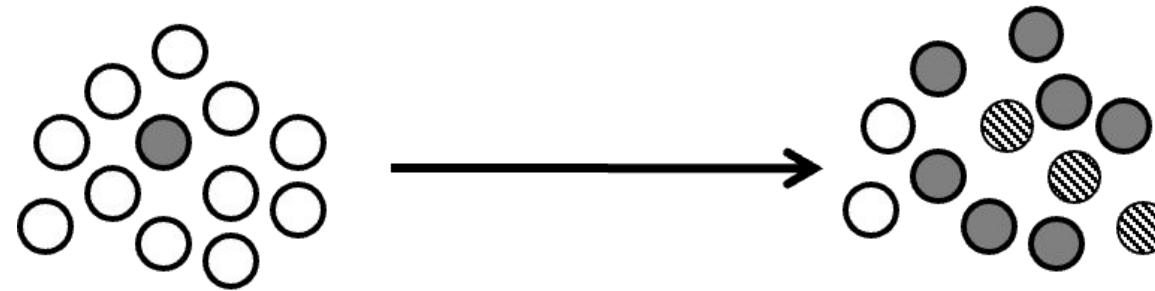
Structured compartmental model (e.g. age, sex)

Meta-population model (i.e., spatially structured)

Network model

Multi-scale model

Individual- (agent-) based model



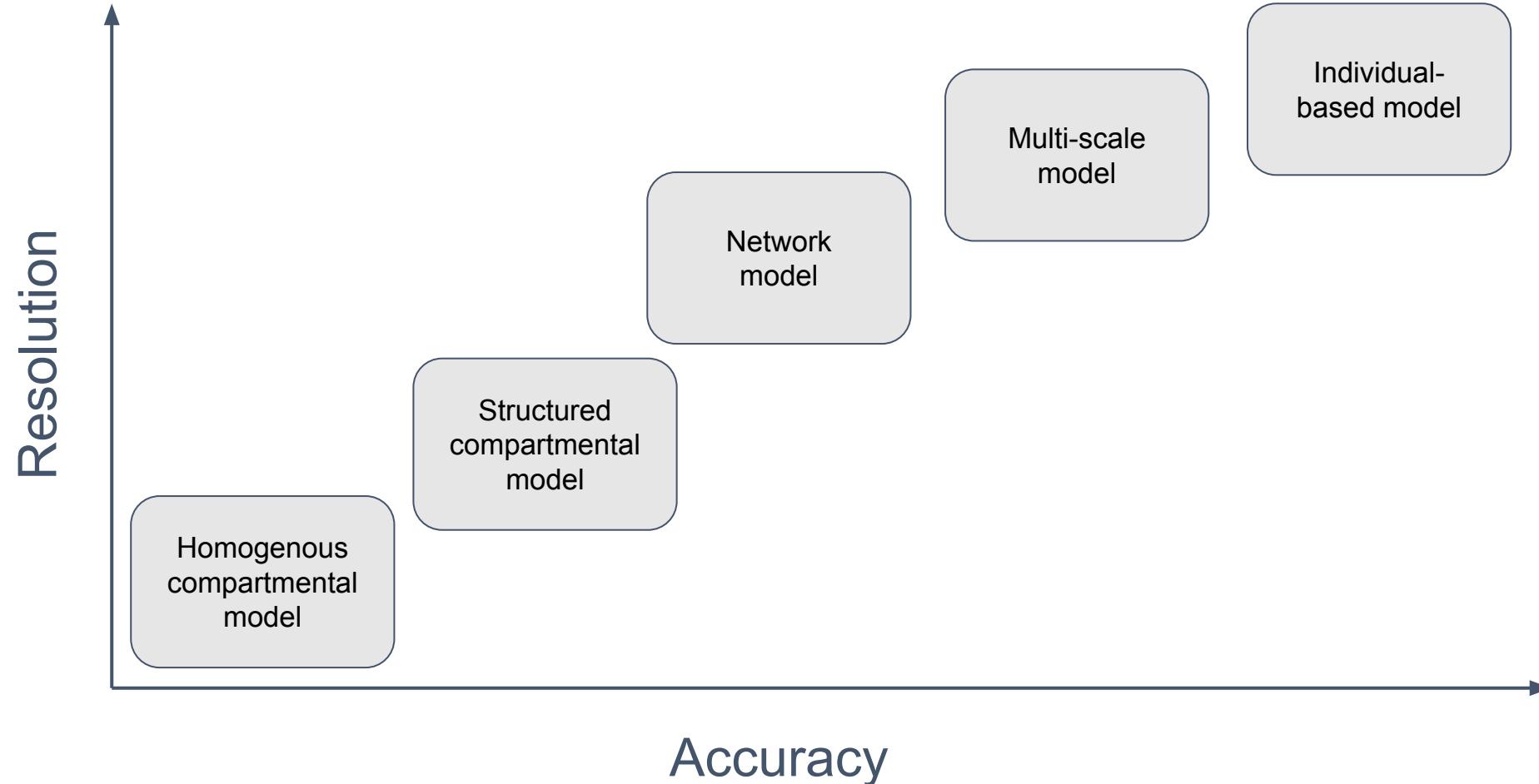
○ Susceptible

● Infected

▨ Immune

Model type depends on modelling objective

Construct transmission model based on current dynamic



What makes a good model?

Three model features...

Construct
transmission
model based
on current
dynamic

1. **Accuracy:** ability to capture observed patterns (qualitative or quantitative) and make predictions
2. **Transparency:** ability to understand model components. Decreases with model complexity
3. **Flexibility:** How easily the model can be adapted to new scenarios. Decreases model complexity

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2 Types of Modeling Methods

1. Deterministic:

- **No randomness**
- Models give you the **same output** every time you run/solve (assuming same starting parameters/conditions)
- Relies on average rates to describe what will happen on **average** in a population

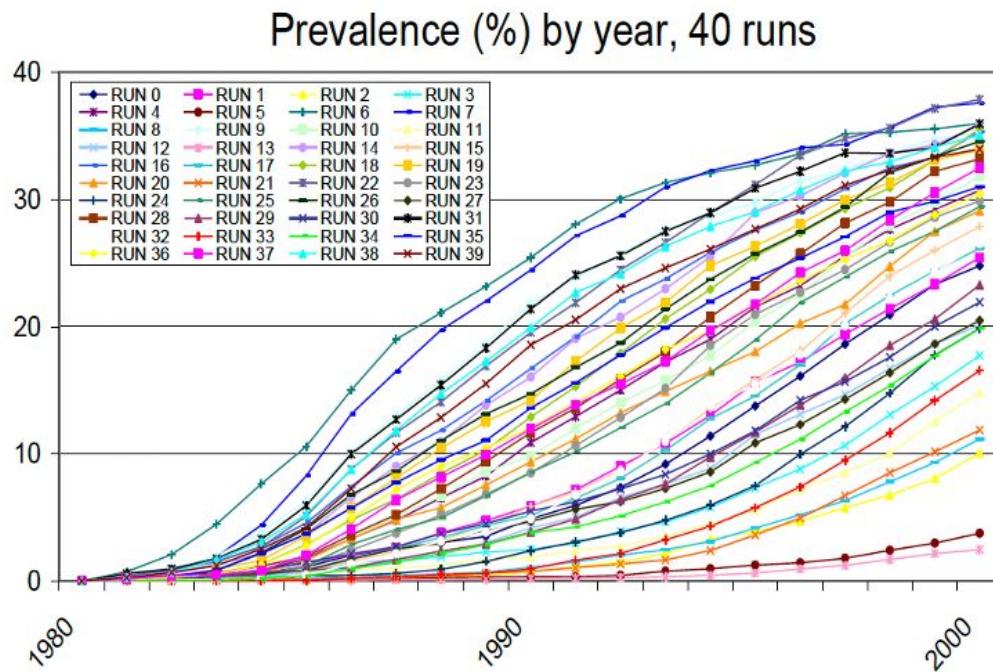
2. Stochastic:

- Incorporate chance variation or **randomness**
- Running the model multiple times can give **different output**
- Provide the probability of a given outcomes of range in which the outcome is likely to occur (e.g., probability that transmission ceases)

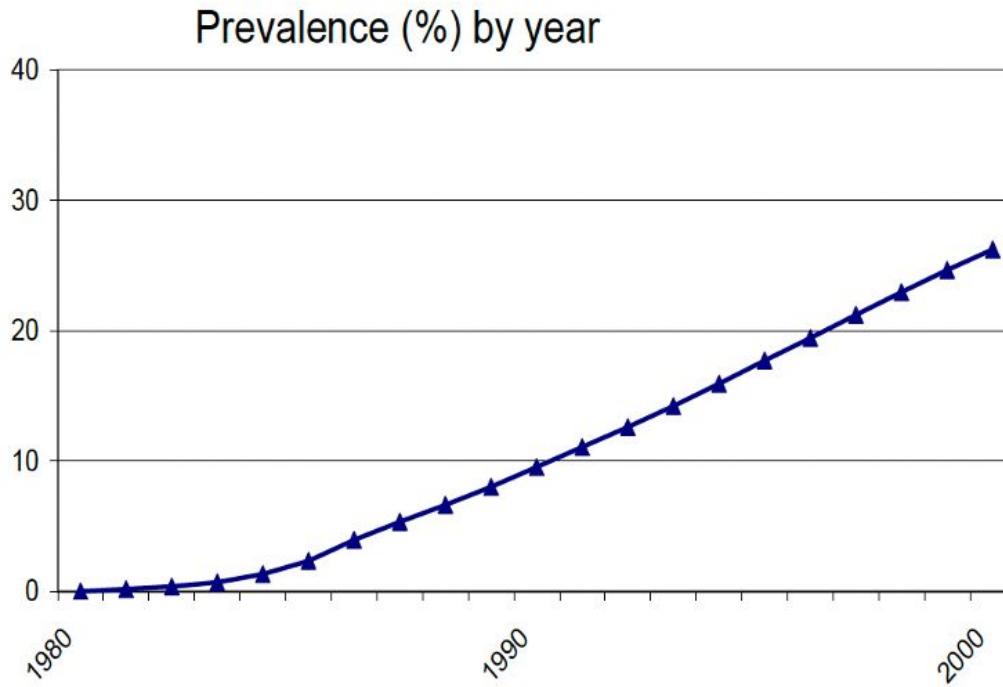
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2 Types of modeling methods

Stochastic model



Deterministic model



Deterministic Models: Difference vs Differential Equations

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1. Difference Equations:

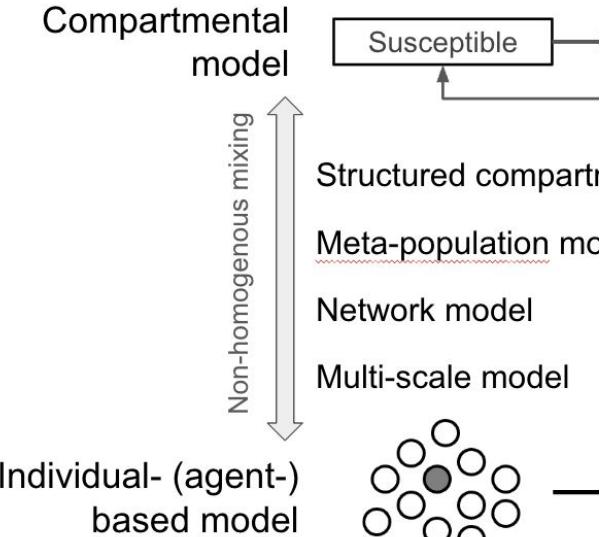
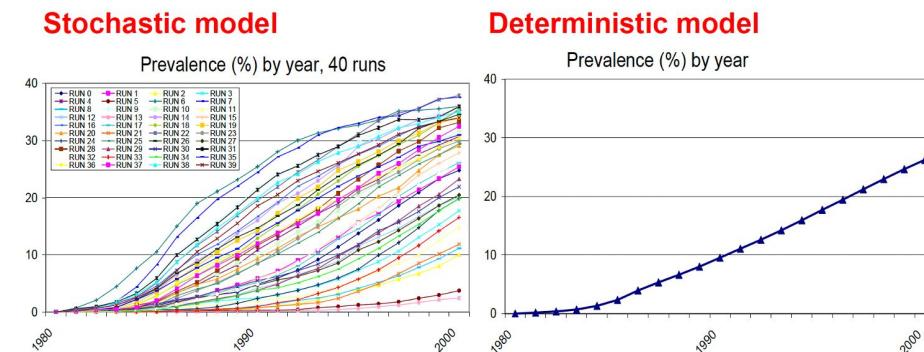
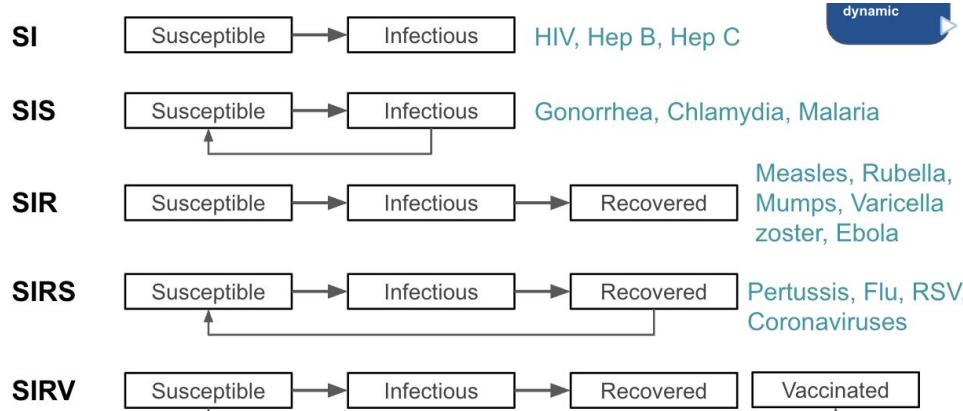
- Calculate the number in each infected category using discrete time steps

2. Differential Equations:

- Calculate the number in each infection category using time steps with are “infinitesimally” small (i.e., continuous time)

Model Type Overview

**Construct
transmission
model based
on current
dynamic**



How to implement (run/solve) a model

Analytical Models (i.e. **pure math**)

- Often working with differential equations
- Aim to find exact solutions or expressions: e.g., what is final outbreak size
- Good for **fundamental principles**
- Can't easily handle complexity like heterogeneity or time-specific changes

Computational Models (i.e., **computer simulations**)

- You can incorporate **real-world data**, changes over time, randomness, networks, spatial structure, etc

Data

Data Types

- Case Surveillance Data (passive vs active; suspected vs epi linked vs clinical vs confirmed)
- Genetic Surveillance Data
- Serological Surveillance Data
- Mortality Surveillance Data
- Vaccination Data (admin, survey)
- Socio-Demographic Data
- Epidemiological studies

Data Scales

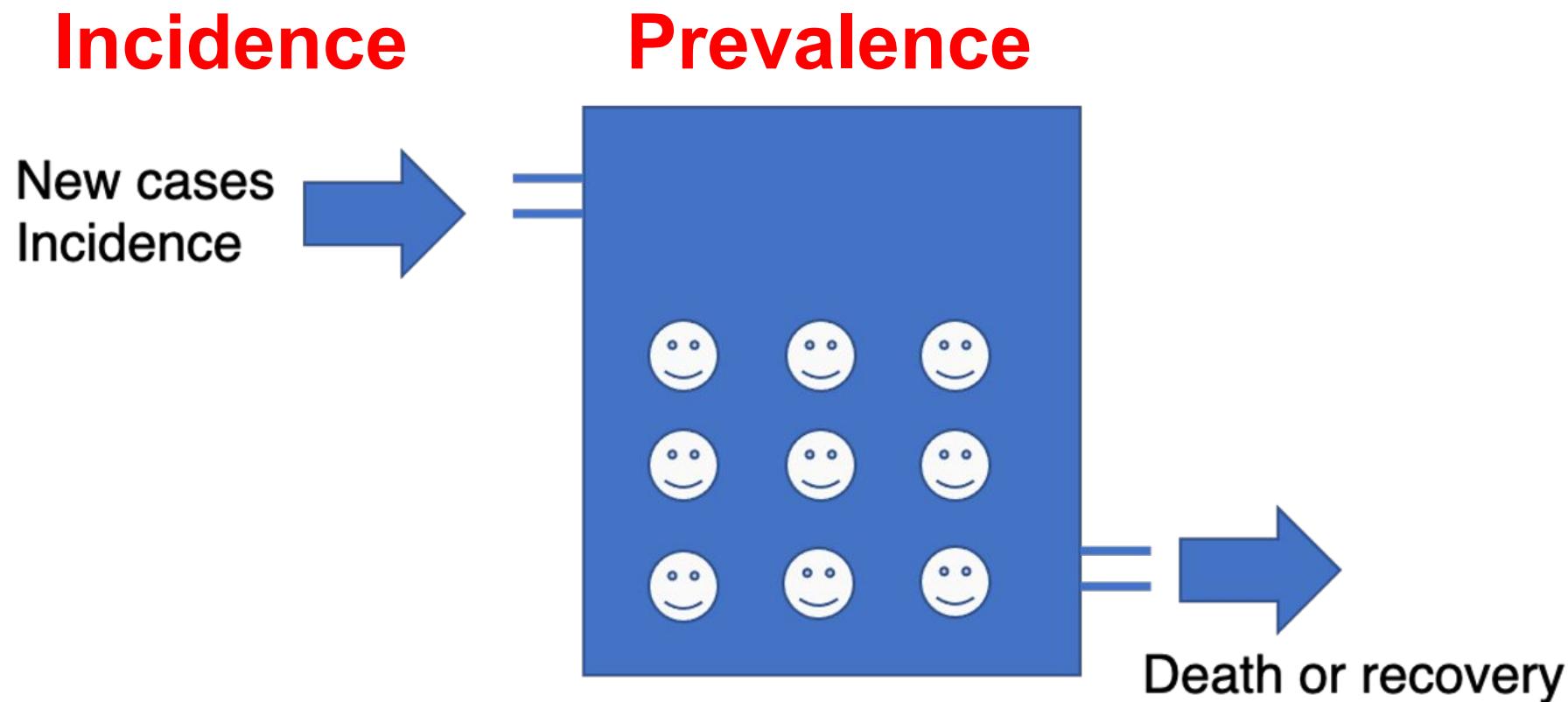
- Individual data (e.g., line list, survey observations)
- Aggregate data
- Spatial data

How are data related to ID models?

Discovery comes from testing ideas (models) against observations (data)

Models drive empirical development and vice versa

Measures of disease frequency

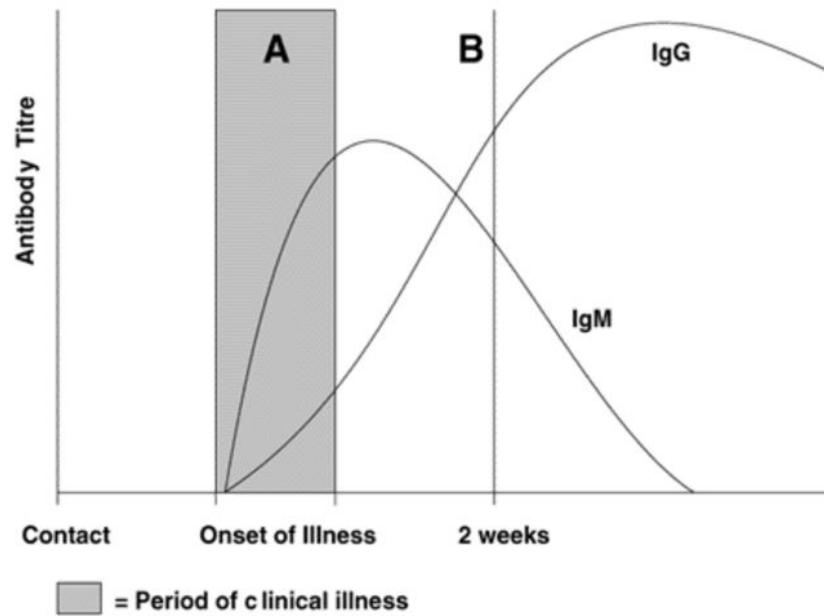


Disease **prevalence** is influenced by:

- **Incidence** of disease
- Duration of disease (time to recovery or death)

Measures of disease frequency

- Incidence of infection
- Prevalence of infection
- Seroprevalence (prevalence of antibody)

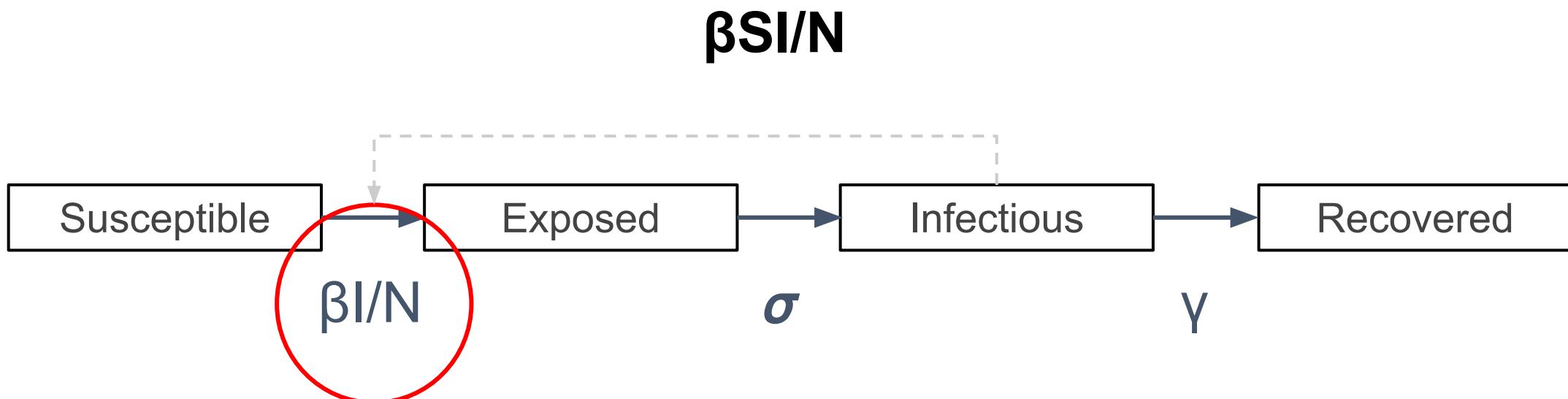


IgG antibodies persist from years to decades and are a correlate of immunity

IgM antibodies persist for a few weeks, and are often used as to confirm infection.

Measures of disease frequency

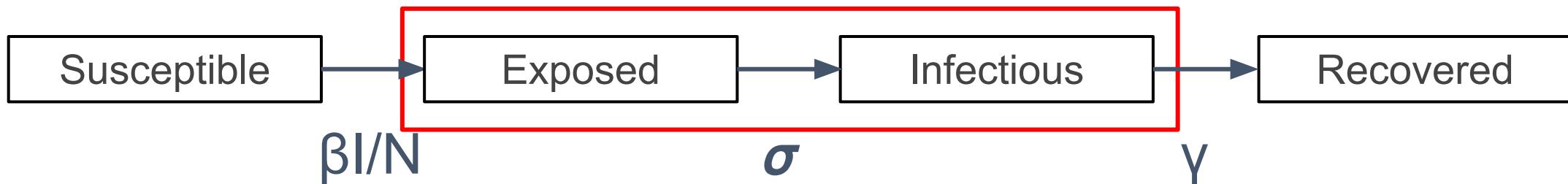
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Measures of disease frequency

- Incidence of infection
- Prevalence of infection
- Seroprevalence (prevalence of antibody)

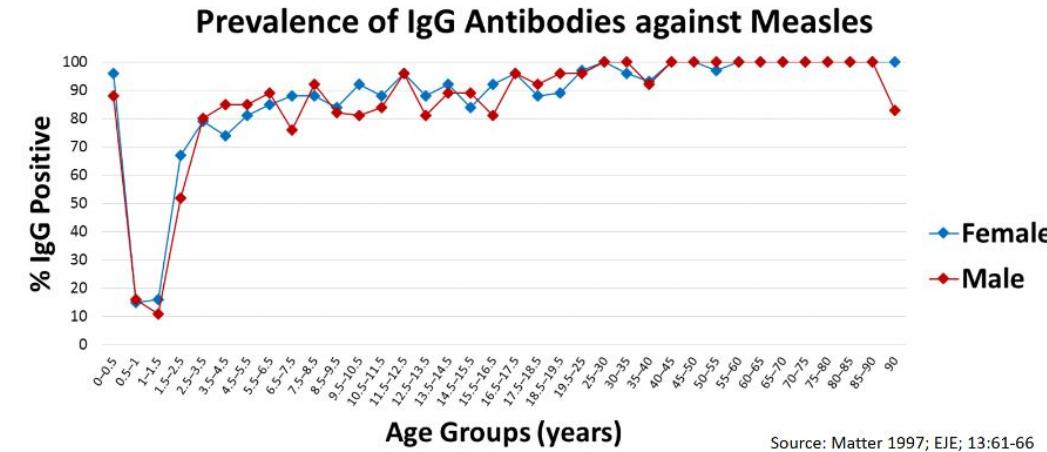
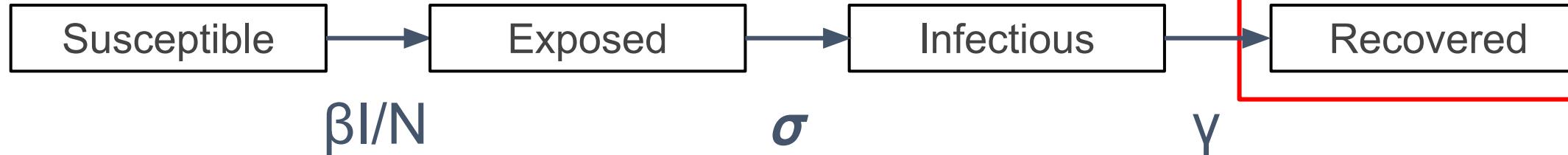
$$(E+I)/N$$



Measures of disease frequency

- Incidence of infection
- Prevalence of infection
- Seroprevalence (prevalence of antibody)

R/N



Risk vs Rate

Incidence risk = $\frac{\text{Number of new cases in a time period}}{\text{Population at risk at the start}}$

Cumulative incidence

Attack rate

Incidence rate = $\frac{\text{Number of new cases}}{\text{Total person-time at risk}}$

Incidence density rate

Risk vs Rate

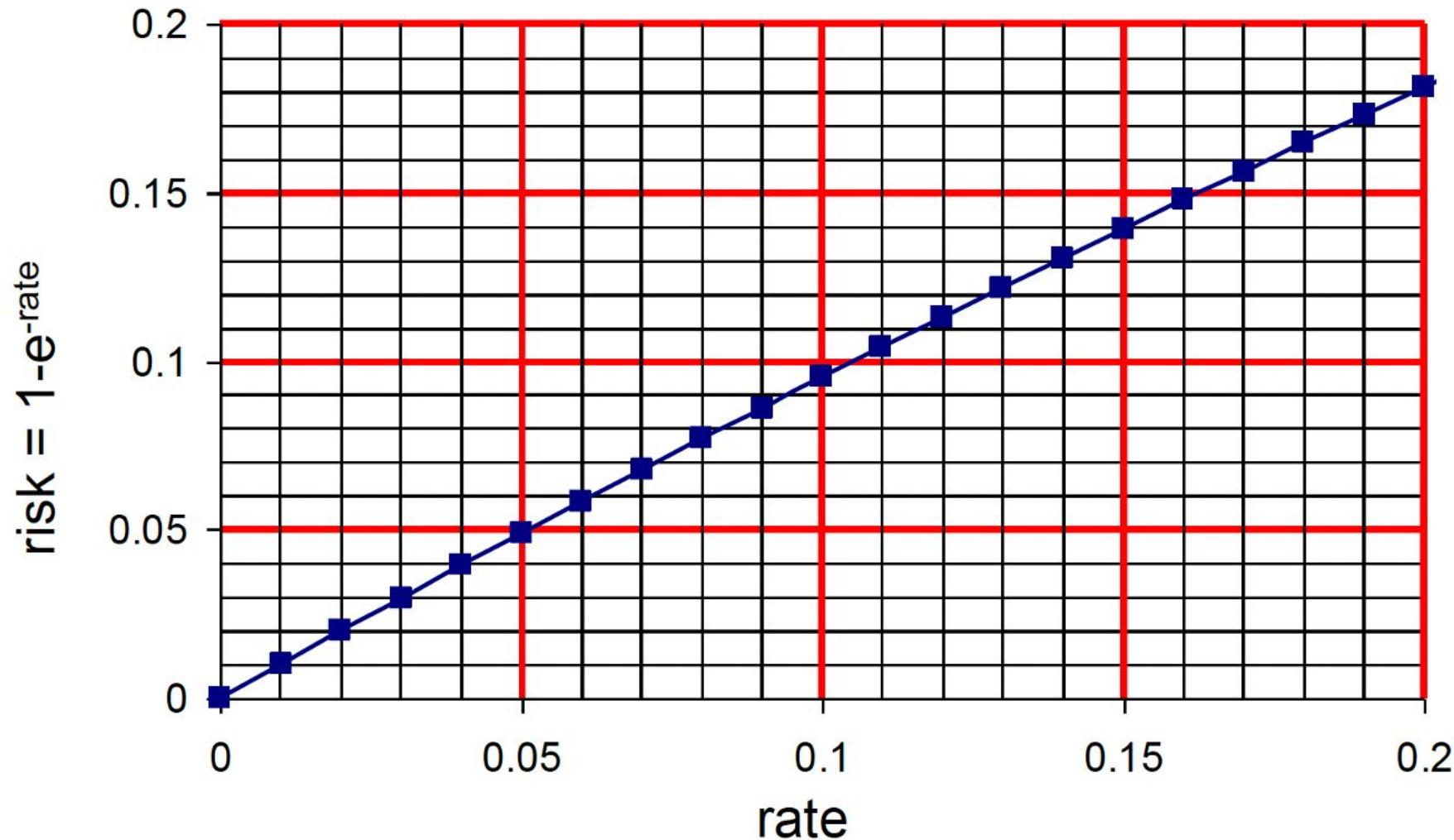
The parameters that go into **difference equations** should be **risks**

Risk and rate are related via the following expression:

$$\text{risk} = 1 - e^{-\text{rate}}$$

However, if rate is small then $e^{-\text{rate}} \approx 1 - \text{rate}$ therefore, **risk \approx rate**

Risk vs Rate



Rates and Average Time

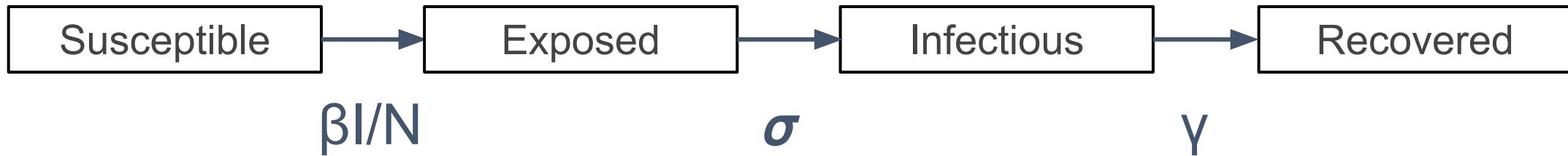
The **rate** at which something occurs
= $1/\{\text{average time to the event}\}$

The **average time** to event
= $1/\{\text{rate at which event occurs}\}$

Rates and Average Time Examples

Examples:

- The rate at which individuals recover from being infectious (γ)
 $= 1/\{\text{average duration of infectiousness}\}$
- The average duration of infected but not yet infections period
 $= 1/\sigma$



Acknowledgments

Emilia Vynnycky

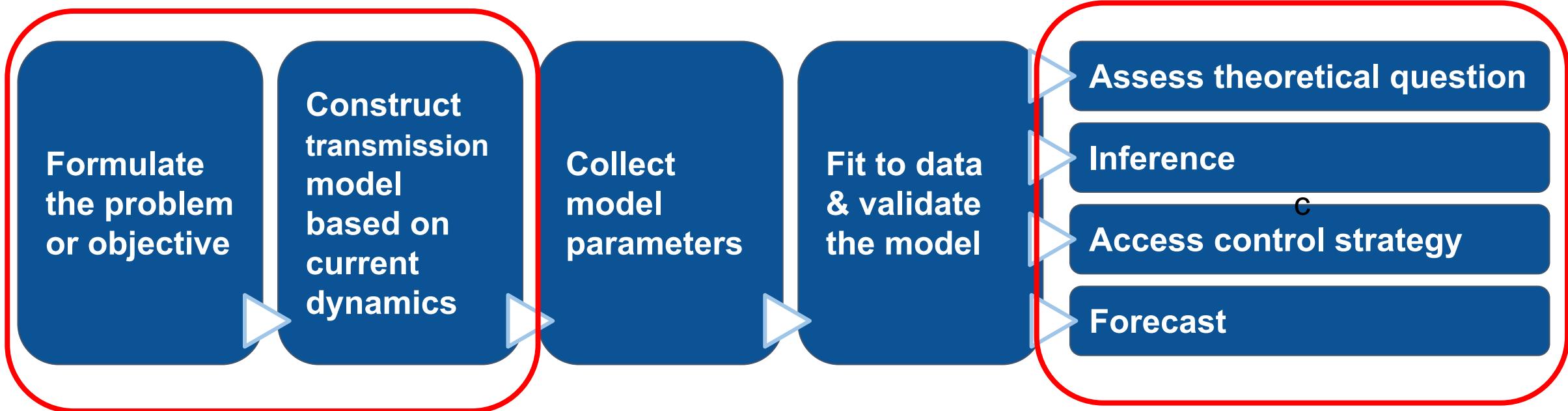
Mark Jit

Learning Objectives

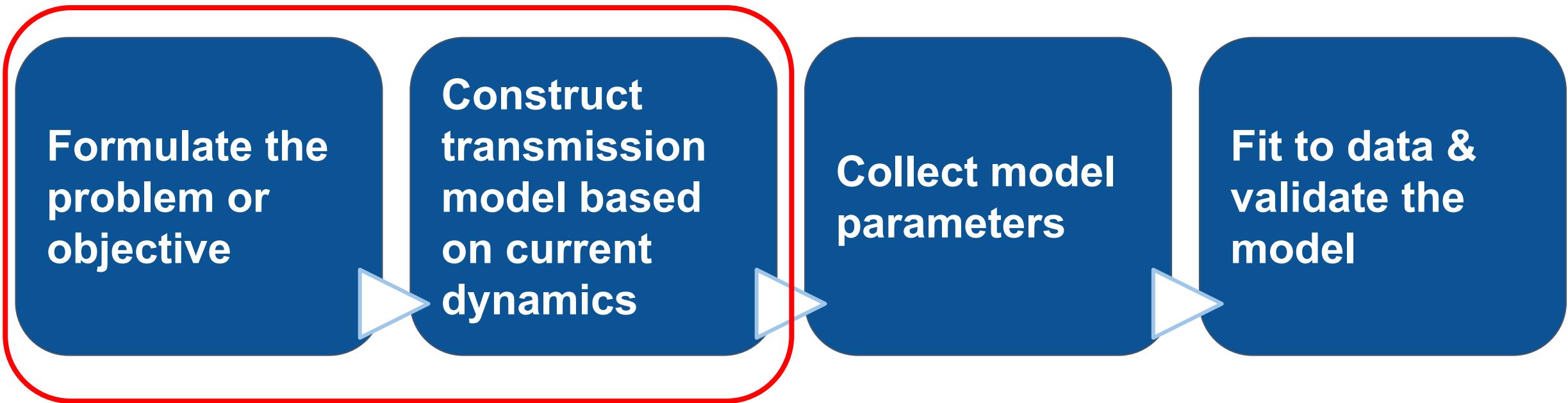
You should have learned:

- How does infectious disease modelling fit into the field of epidemiology
- What are the different goals of ID mechanistic models
- What are the different types of ID models
- What are common data relied upon for modelling
- How are ID data and ID models related

Steps of developing a model



Steps of developing a model



OLD

Lecture 1

Intro to Modeling

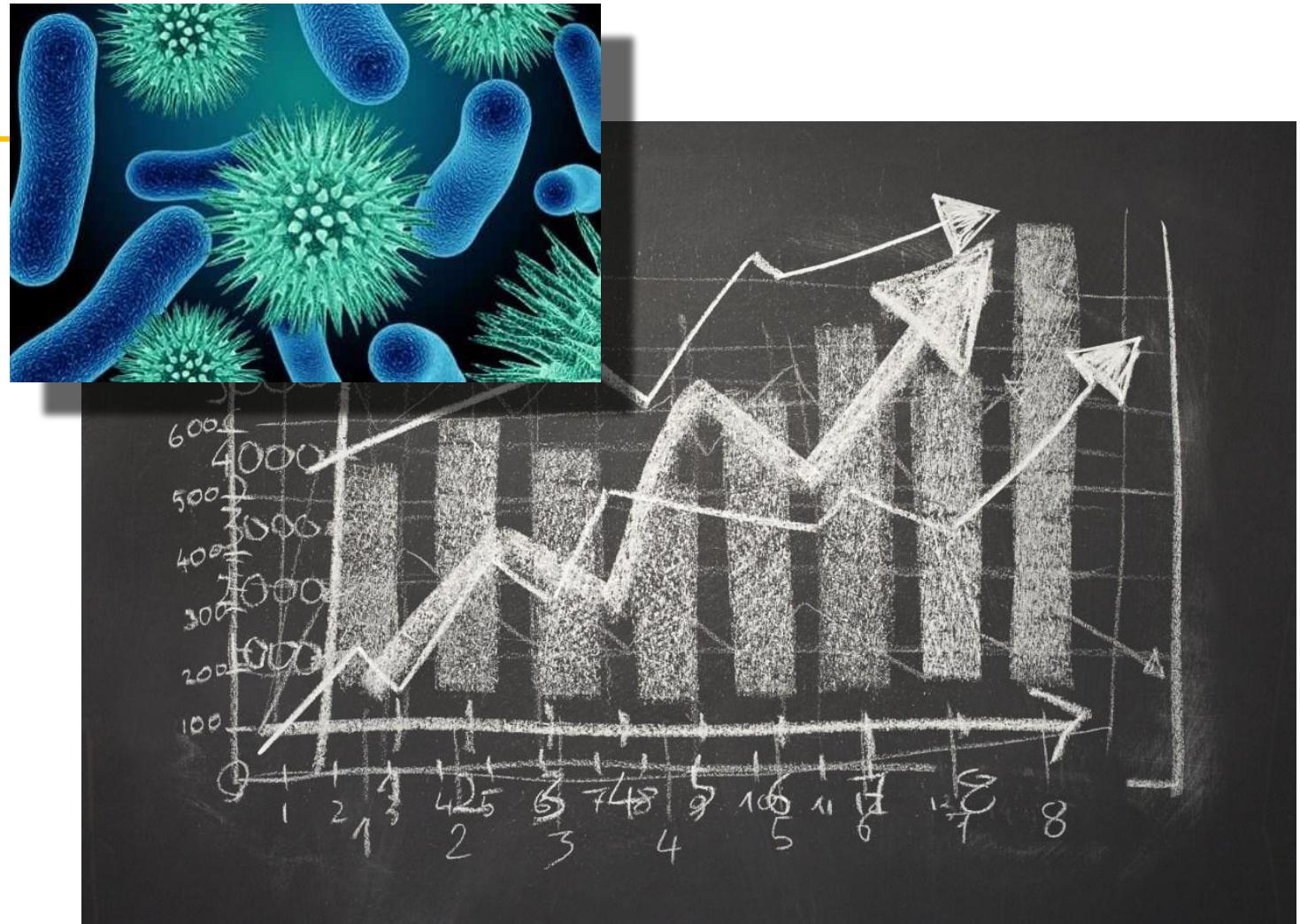
Micaela E. Martinez
Emory University

slides in part adapted from Pej Rohani & John Drake's SISMID 2019 course materials

Modeling Infectious Diseases

Course Objectives:

- Modeling 101
- Basic Reproduction Ratio (R_0)
- Simple Epidemic Dynamics
- Vaccination & interventions
- Heterogeneity
- Modeling during a pandemic
- Informing models with data
- Stochasticity and uncertainty

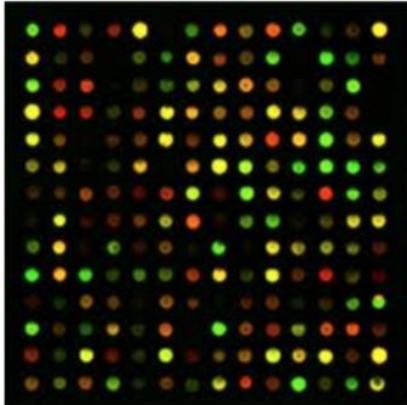


Many ways to study infectious diseases

Medicine



Genomics



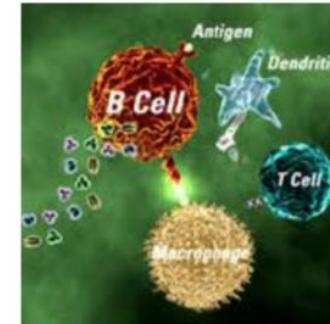
Microbiology



Some disciplines focus on infectious diseases from the:

- (1) individual level
- (2) within-host scale
- (3) microbe perspective

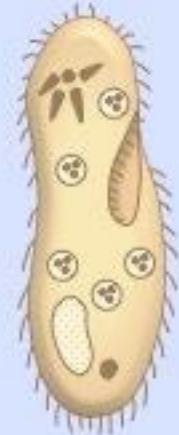
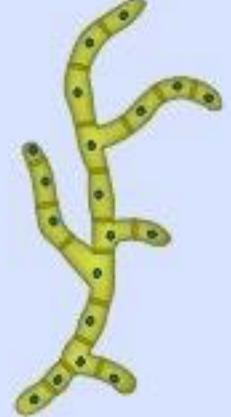
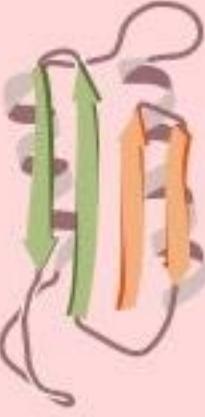
Immunology



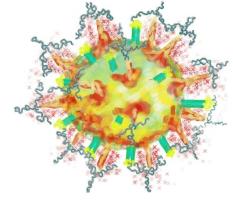
Vaccines & Drugs



Agents of infectious diseases

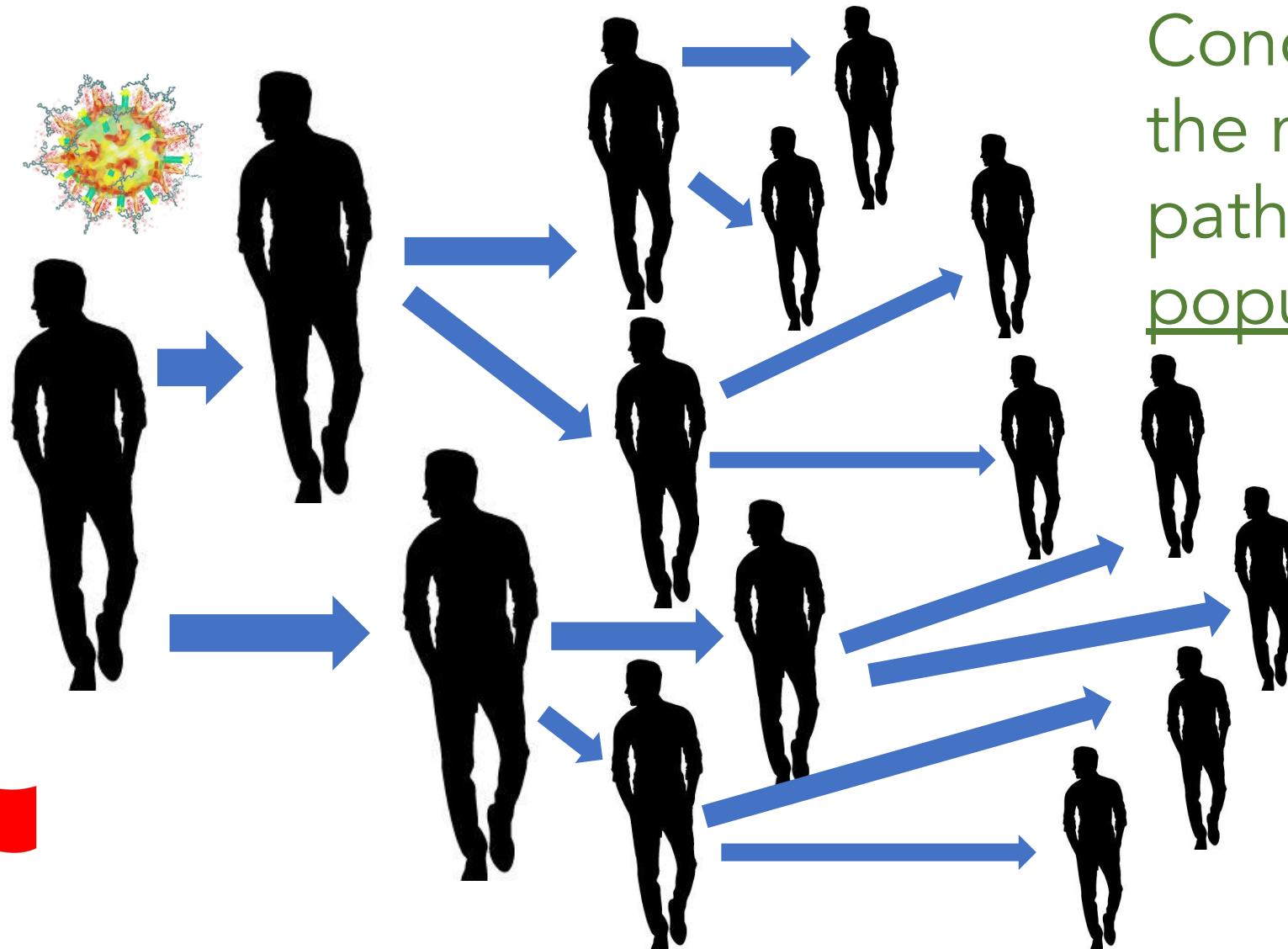
CELLULAR				ACELLULAR	
					
Parasites (e.g. helminthes) ⇒ Tapeworm	Protozoa (e.g. plasmodia) ⇒ Malaria	Fungi (e.g. tinea) ⇒ Athlete's foot	Prokaryote (i.e. bacteria) ⇒ Leprosy	Virus (e.g. HIV) ⇒ AIDS	Prion ⇒ CJD

Epidemiology & Disease Ecology focus on the population-level



Concept: We can track
the movement of
pathogens throughout
populations

Epidemiology & Disease Ecology focus on the population-level



Concept: We can track the movement of pathogens throughout populations

A transmission chain is the set of infection events that occur as a pathogen moves through a population.



The use of time series data

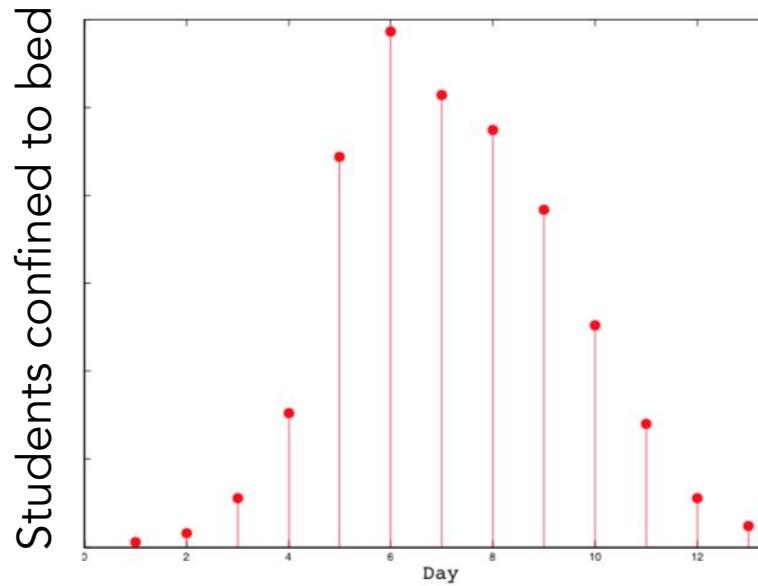


What pathogen is causing the illness?

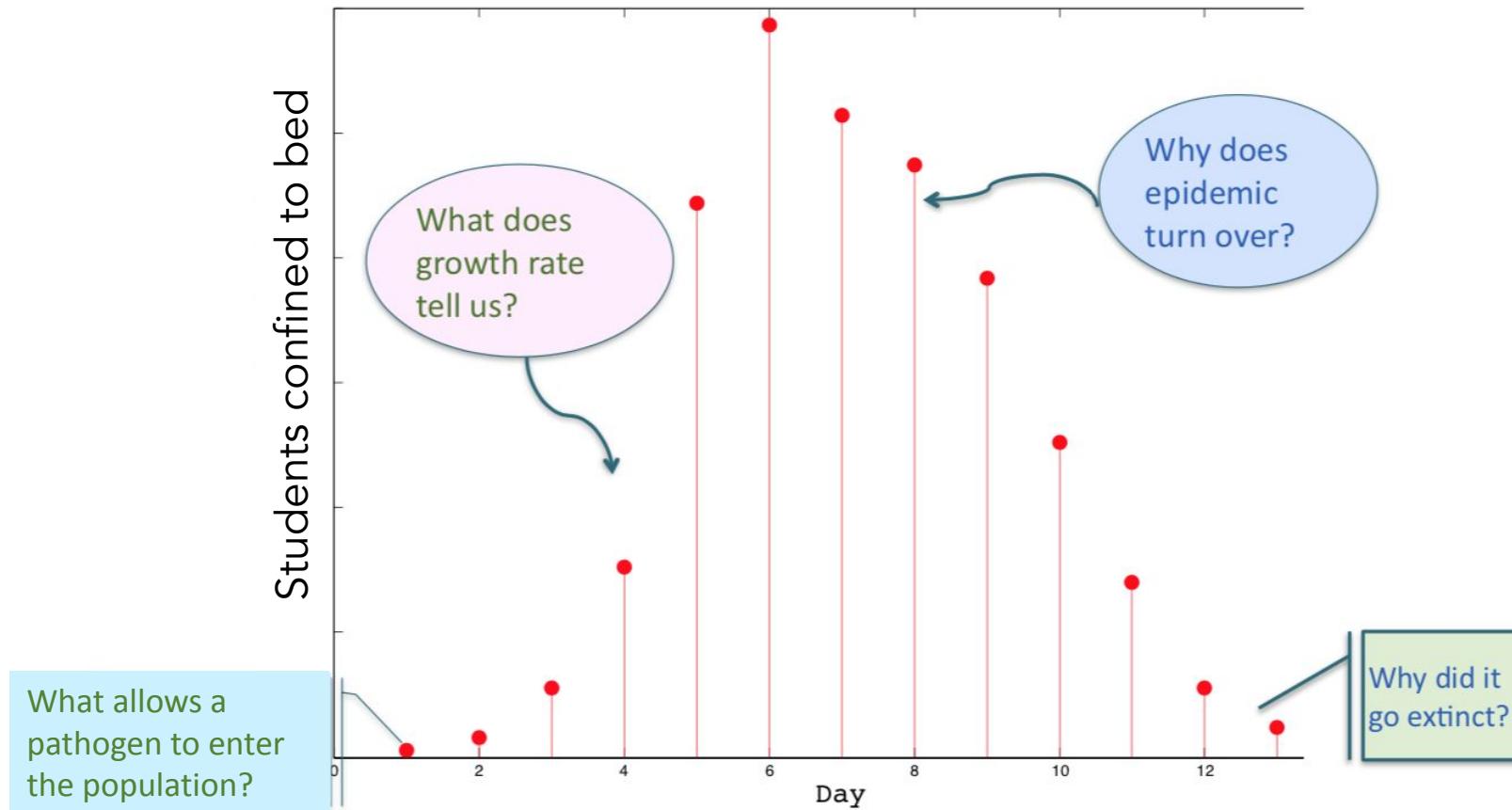
Is it a novel pathogen?

Is there a vaccine or treatment?

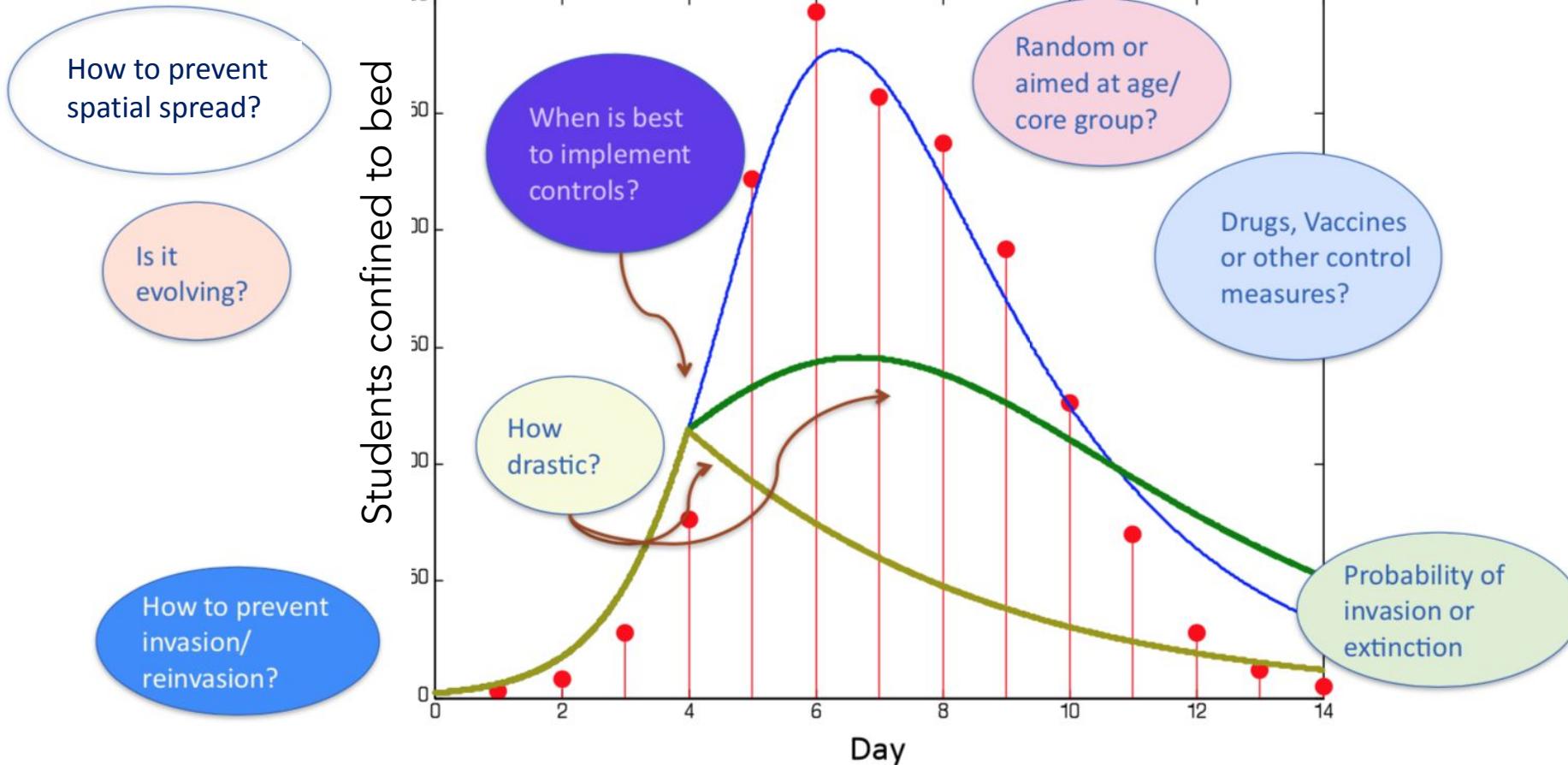
1978 outbreak in a British boarding school



Biological questions we can ask of time series

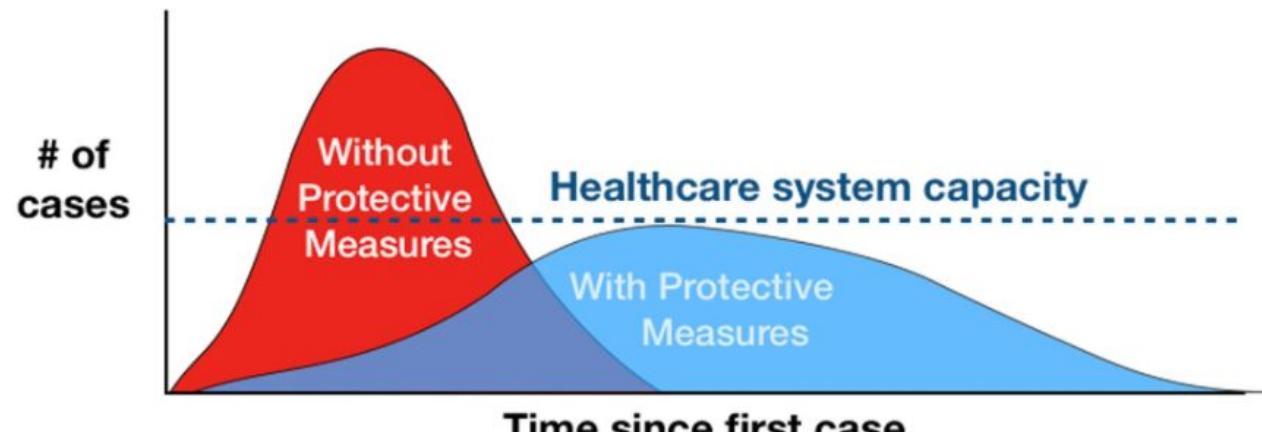


Questions about interventions we can ask of time series



Flattening the Coronavirus Curve

One chart explains why slowing the spread of the infection is nearly as important as stopping it.



Adapted from CDC / The Economist

The shape of the epidemic curve contains information about transmission

Different types of models:

A mathematical model is a set of equations that describe behavior of a system; such as a biological system, a physical system, a technology or social system.

A statistical model describes relationships between observed quantities and independent variables

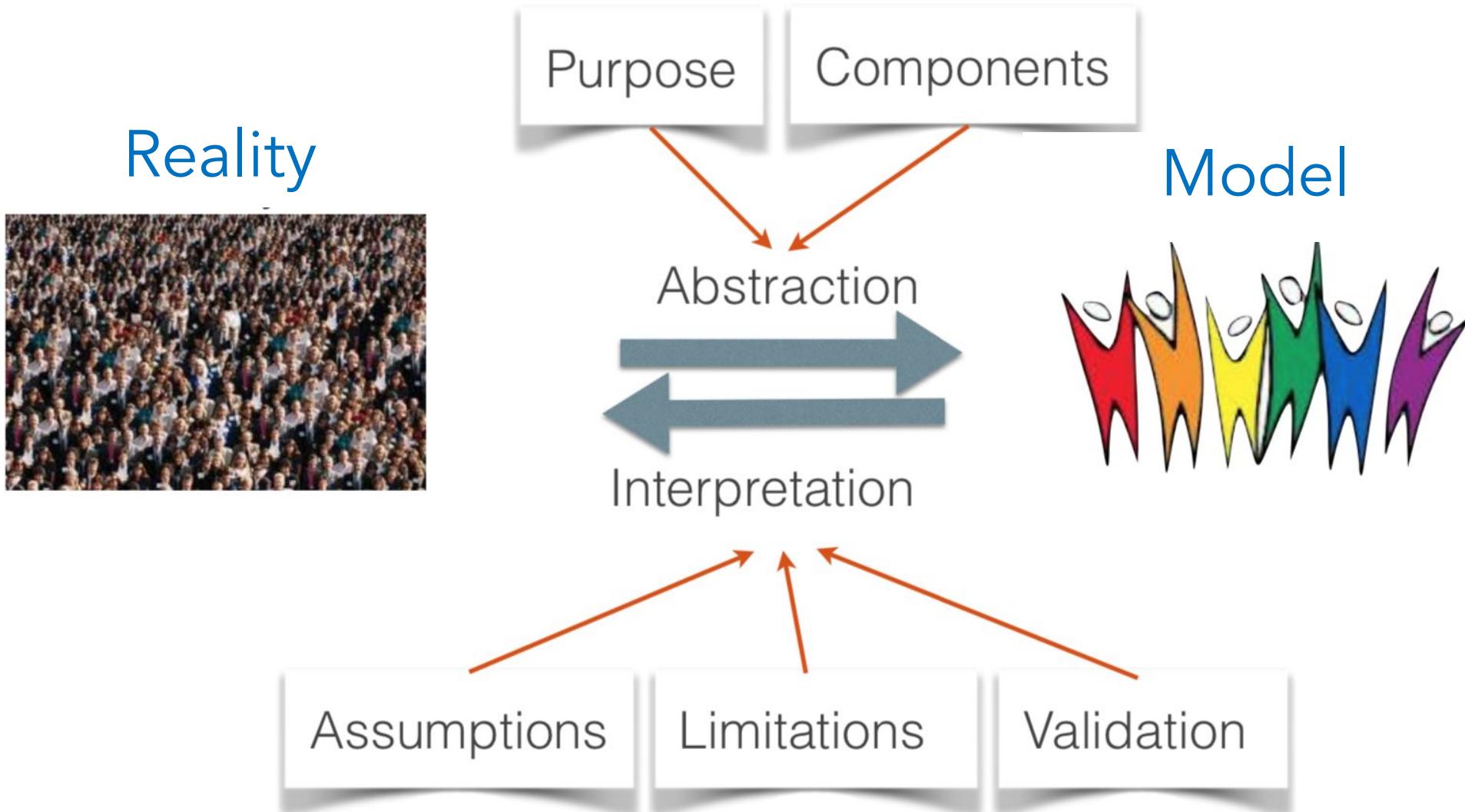
Developing a mathematical model is different from statistical analyses of data



What is a model?



Mathematical models are abstractions of reality



- Choice of model depends crucially on focal question and available data
- Models are a tools and typically several types of models can be deployed for any given disease system
- Models are used principally for understanding nature or making projections under various scenarios



What is a
“good”
model?



Judging a Model...

Three fundamental features of models, often opposing forces:

Accuracy: ability to capture observed patterns (qualitative or quantitative) and make predictions

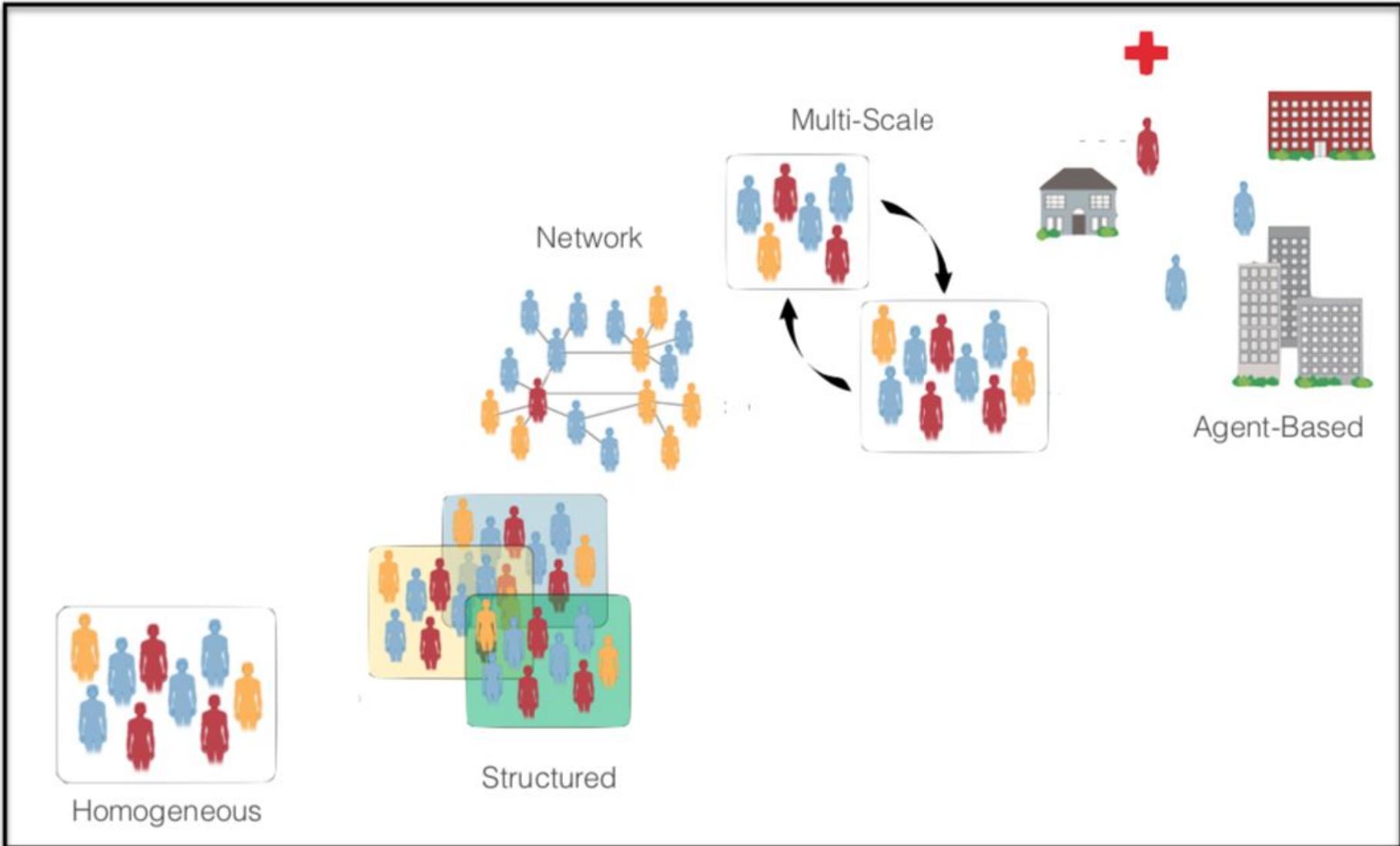
Transparency: Ability to understand model components. Decreases with model complexity

Flexibility: How easily the model can be adapted to new scenarios. Decreases with model complexity



What is a
“good”
model?

Realism & Complexity vs. Transparency & Flexibility



How do you implement a mathematical model?

Analytical Models

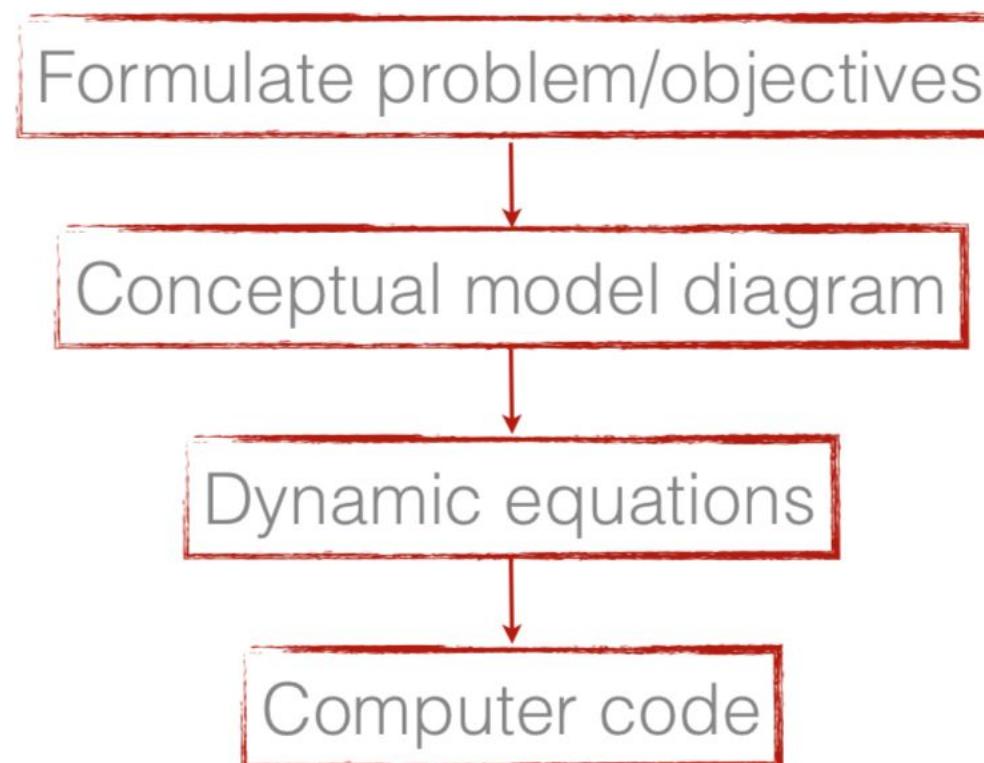
Concentrate on problems that can be expressed and analyzed fully using analytical approaches (*i.e., pure math*)

Computational Models

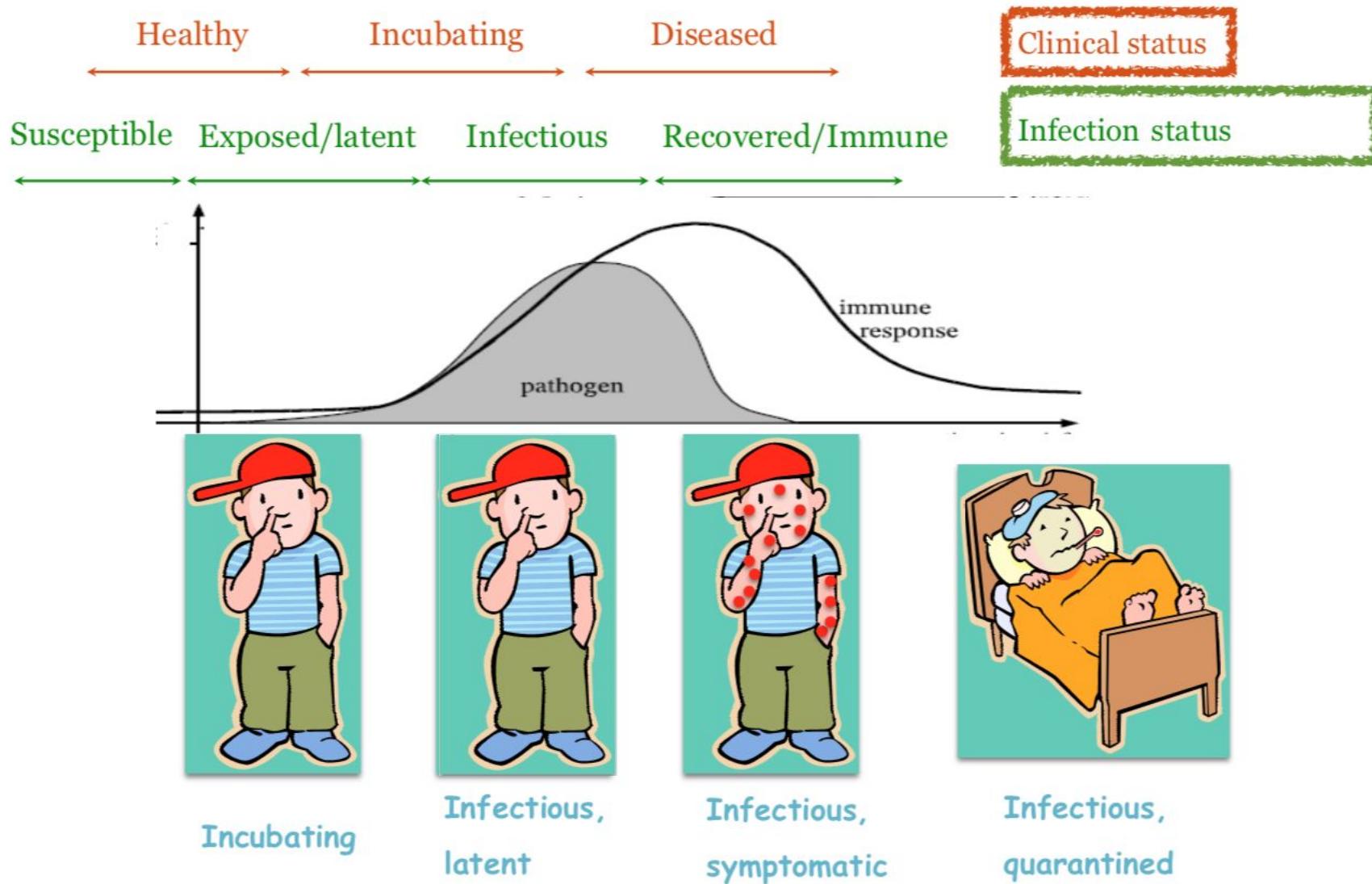
Construct an appropriate model for the system and use a combination computational methods for analysis and scenario analysis (*i.e., computer simulations*)



Steps in Developing a Model



Categories of Disease Status & Infection



Simple Models

Pragmatic choice: categorize individuals in population according to their infection status:

- Susceptible (S)
- Infectious (I)
- Recovered/Immune (R)

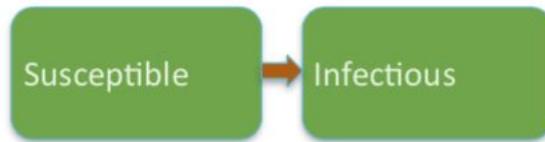
These are called state variables, they represent different states of the system that we are modeling



Simple Models

What model structure?

- Determined by pathogen biology



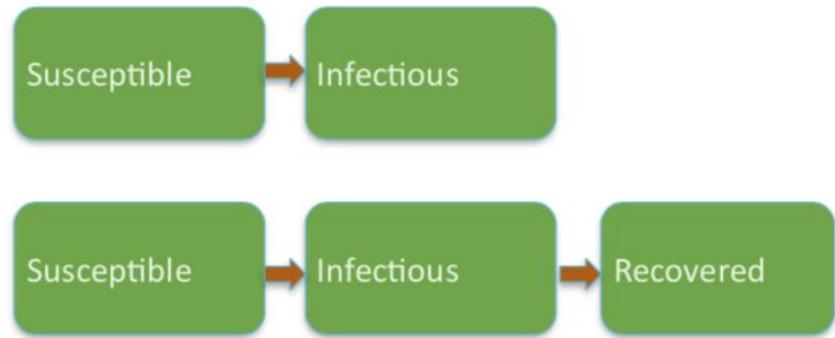
SI models can be used for fatal or chronic infections



Simple Models

What model structure?

- Determined by pathogen biology



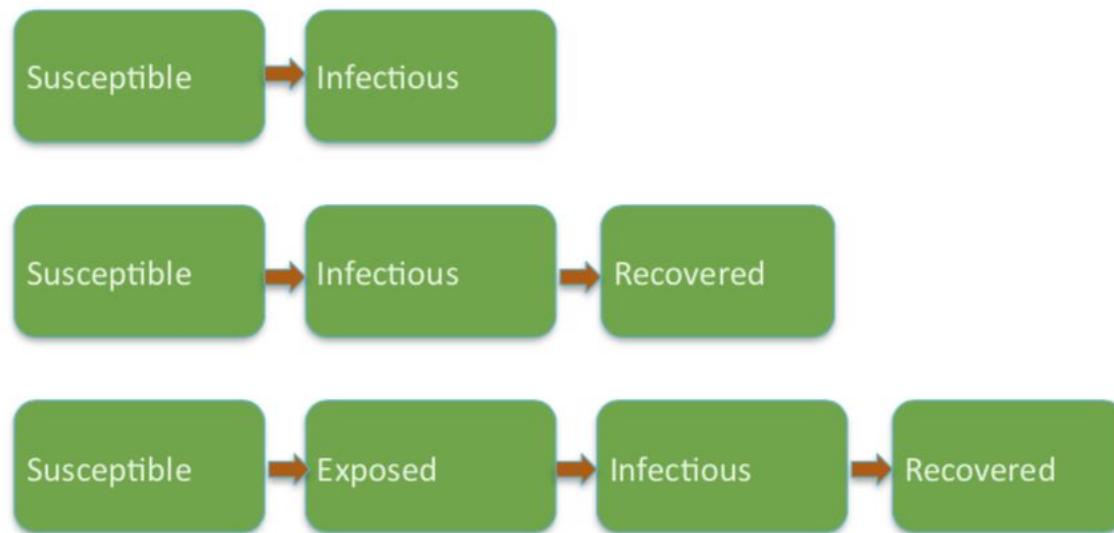
SIR models can be used for infections where there is recovery and immunity



Simple Models

What model structure?

- Determined by pathogen biology



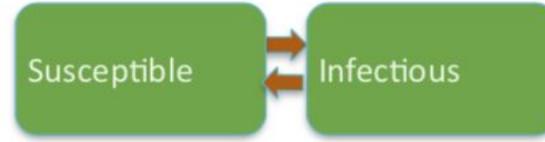
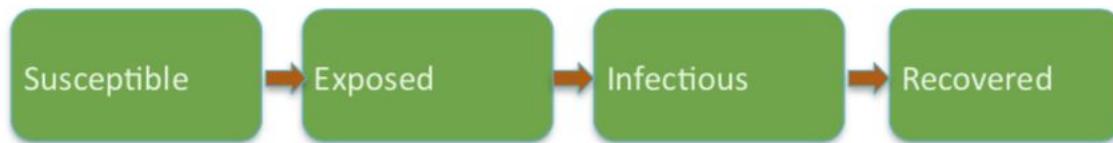
SEIR models can be used for infections where there is a non-negligible latent period when individuals are infected but not infectious. This can be a good category to have, for example for COVID-19, when considering testing and quarantine early on in infection.



Simple Models

What model structure?

- Determined by pathogen biology

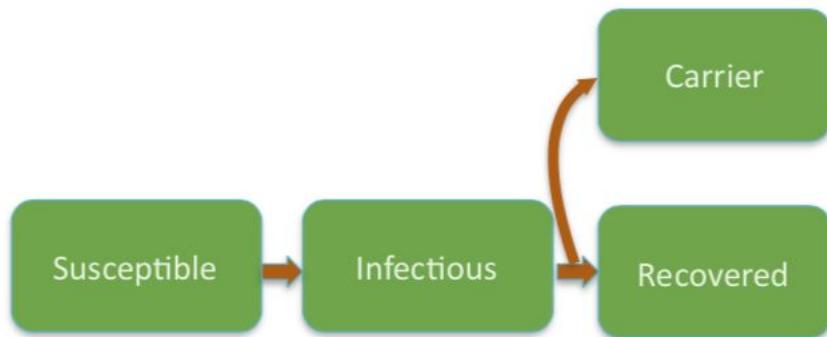


SIS models are appropriate when there is little immunity elicited, or the immunity elicited will not protect from reinfection in the near-future.

Simple Models

What model structure?

- Determined by pathogen biology



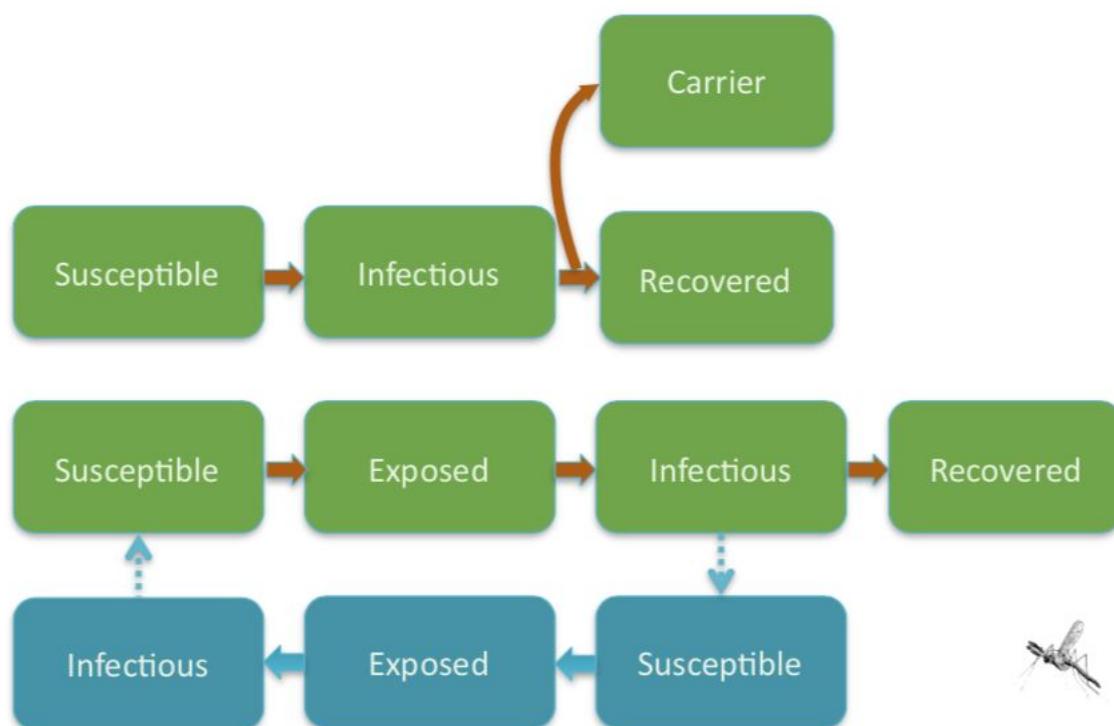
SIR – with carriers



Simple Models

What model structure?

- Determined by pathogen biology



SIR – with carriers

Vectored transmission



Simple Models

- **What model structure?**
- Depends on what do we know about the pathogen (eg, influenza)
 - It's directly transmitted (aerosol)
 - An acute infection
 - Lifelong immunity (to that strain)



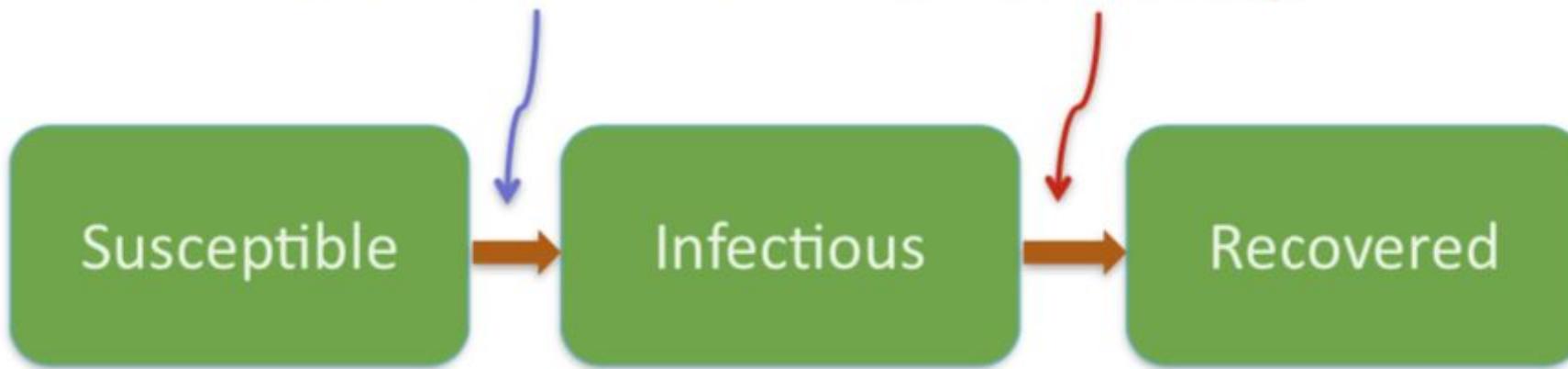
Break

LECTURE 1 INTRO TO MODELING: CONTINUED

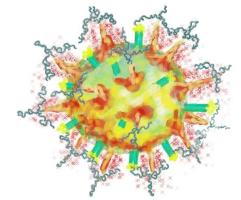
MICAEAL E. MARTINEZ

EMORY UNIVERSITY

Transmission Recovery

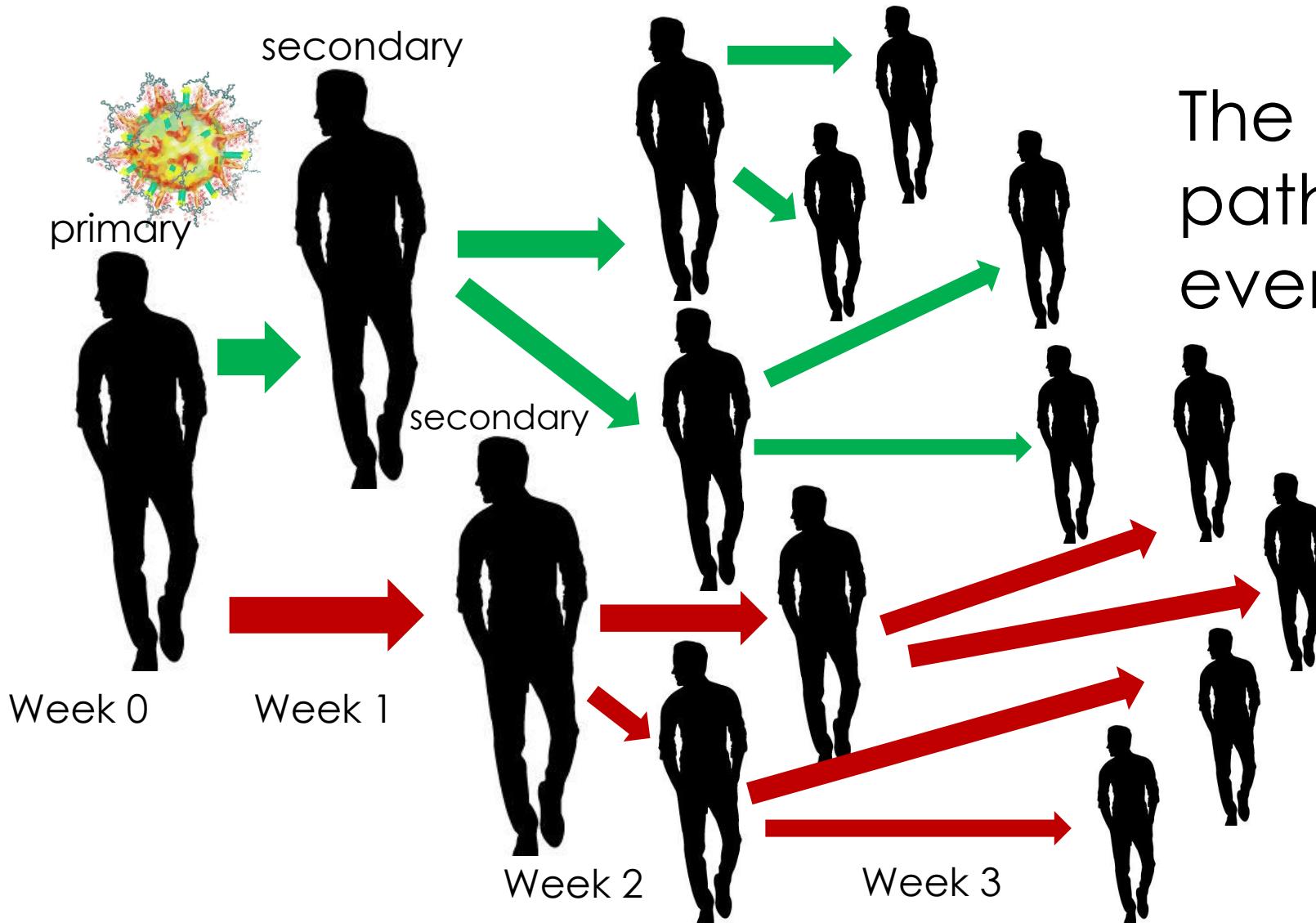


Transmission Chain



Concept: The set of host-to-host pathogen transmission events

Transmission Chain



The set of host-to-host pathogen transmission events

Each individual infected two others

The Basic Reproductive Number

- **basic reproduction number, R_0 :** average number of infections caused by a typical infected individual in a population consisting only of susceptibles; if $R_0 > 1$, the infectious agent can start to spread.

infection	Geographic location	Time period	R_0
measles	England & Wales	1950-1968	16-18
measles	Kansas, USA	1918-1921	5-6
pertussis	Maryland, USA	1943	16-17
chicken pox	New Jersey, USA	1912-1921	7-8
mumps	Netherlands	1970-1980	11-14
rubella	West Germany	1970-1977	6-7
polio	USA	1955	5-6

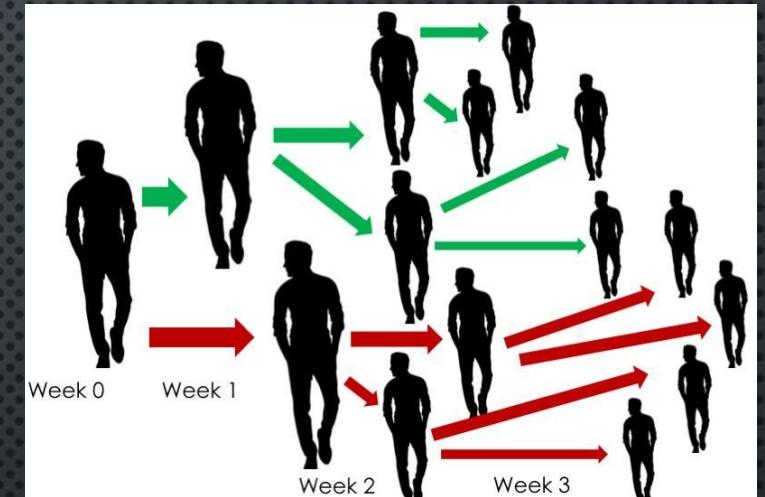
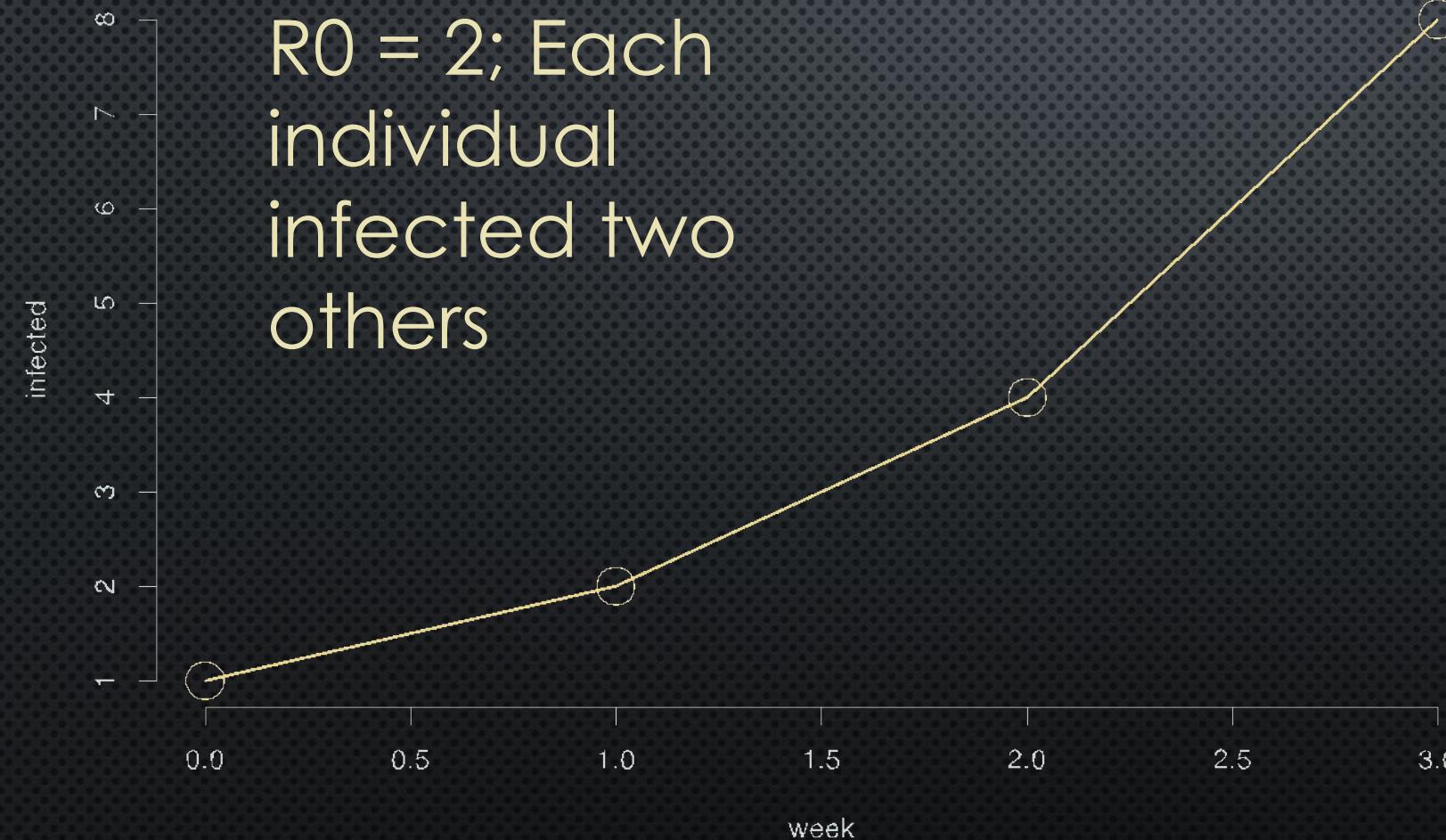
R_0 varies among:

1. diseases
2. populations
3. time periods

(Heesterbeek et al. 2015;
Anderson & May 1991)

Infections in the population

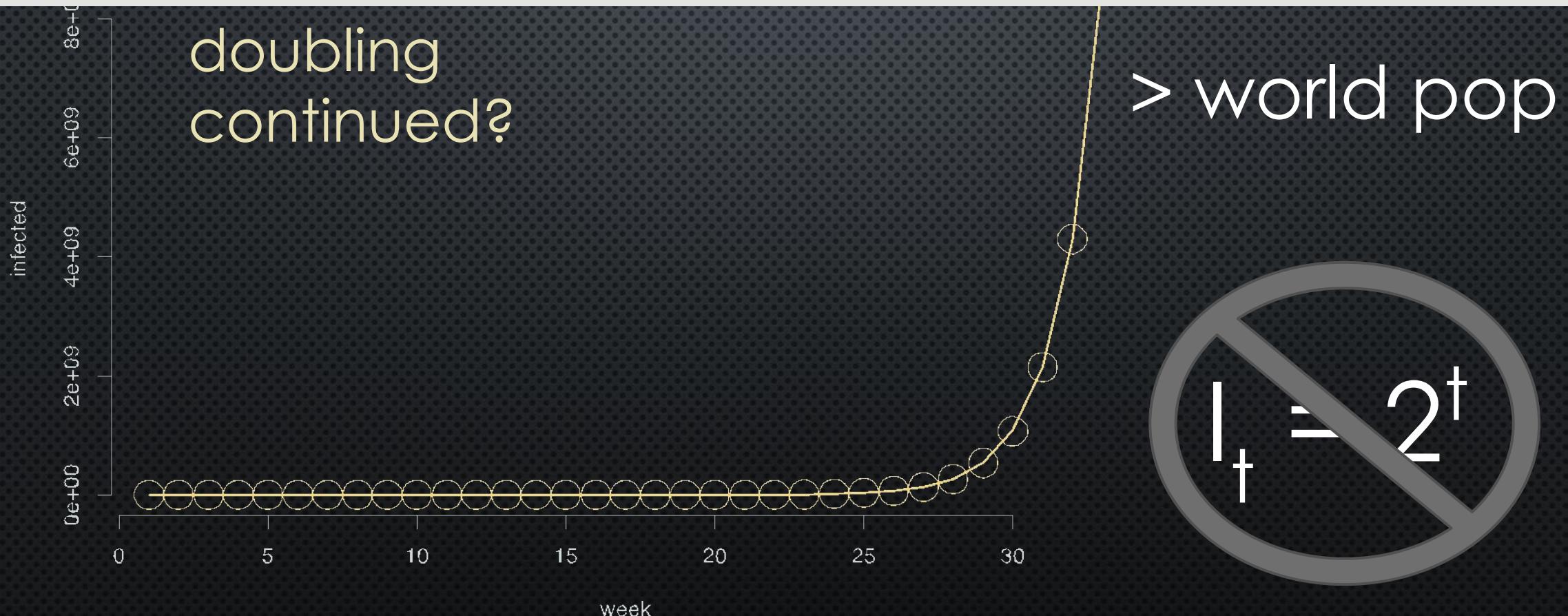
$R_0 = 2$; Each individual infected two others



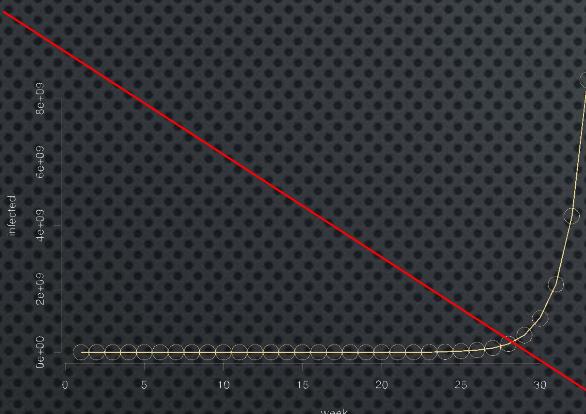
$$I_t = 2^t$$

Infections in the population

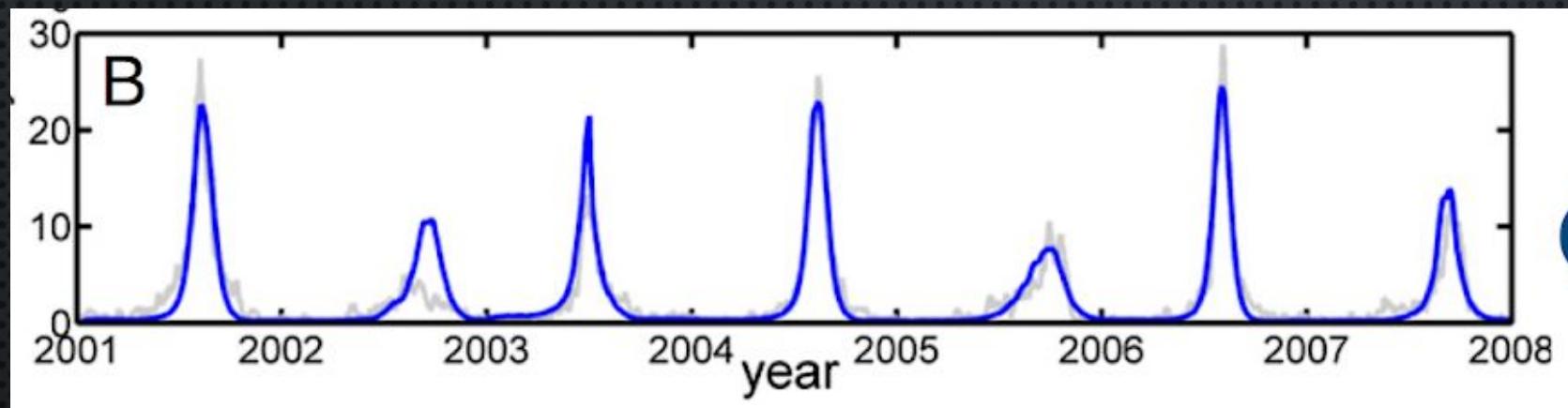
- **basic reproduction number, R_0 :** average number of infections caused by a typical infected individual in a population consisting only of susceptibles; if $R_0 > 1$, the infectious agent can start to spread.



Structure of Epidemics



Influenza in Jerusalem



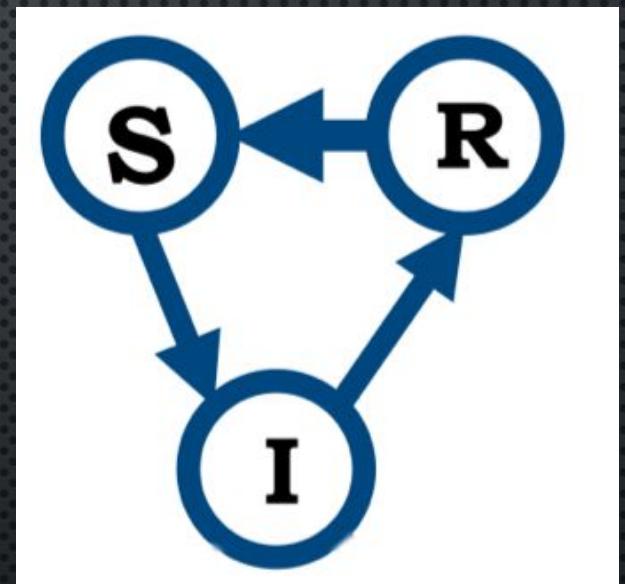
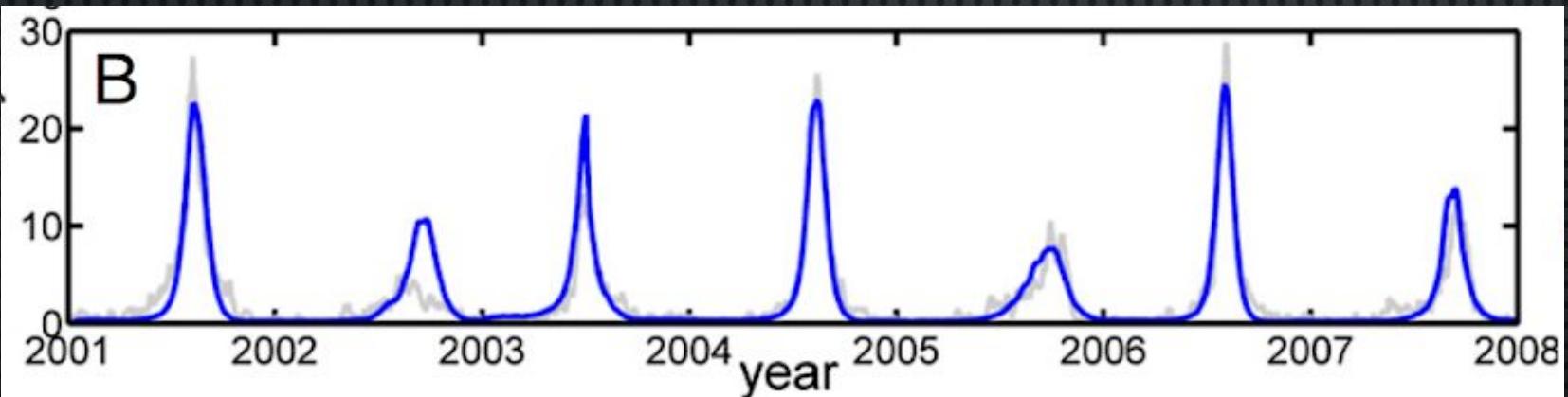
Features:

1. Exponential growth
2. Curtails (susceptible depletion and/or transmission decline)
3. Inter-epidemic period



Recurrent Epidemics

S: Susceptible
I: Infected
R: Recovered



Immunological Memory

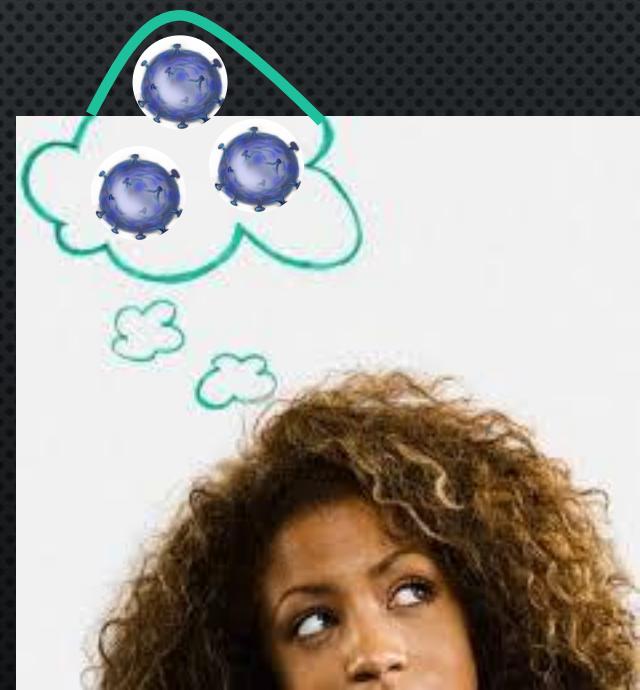
IMMUNOLOGICAL MEMORY REFERS TO THE ABILITY OF THE IMMUNE SYSTEM TO RESPOND MORE RAPIDLY AND EFFECTIVELY TO A PATHOGEN THAT HAS BEEN ENCOUNTERED PREVIOUSLY.

S: Susceptible

I: Infected

R: Recovered class
contains individuals
with immunological
memory

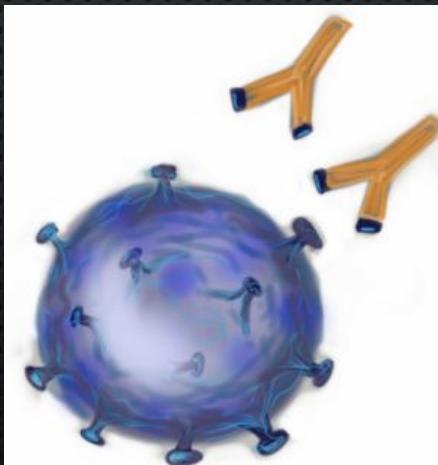
Immune
system
remembering
pathogens



Immunological Memory: Antibodies

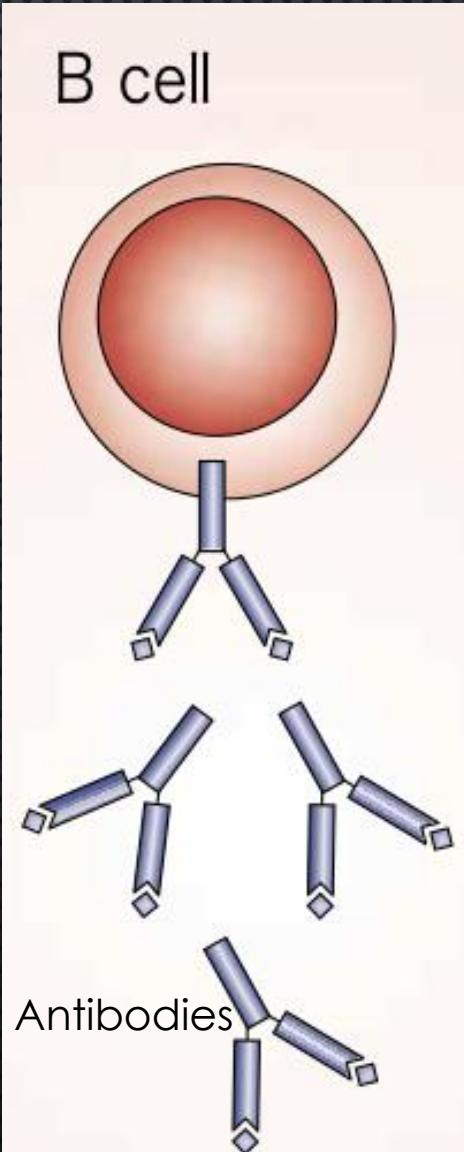
Antibodies are found in the fluid component of blood, or plasma, and in extracellular fluid

The simplest and most direct way in which **antibodies** can protect from pathogens is by binding to them and blocking their access to cells that they might infect or destroy. This is known as **neutralization**.



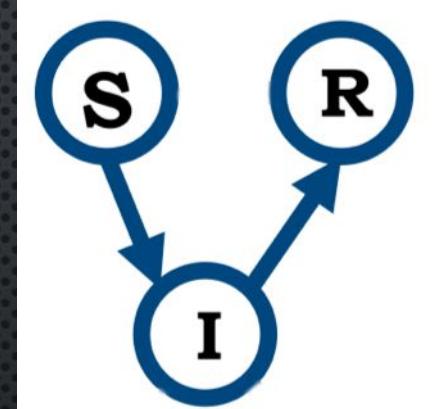
Antibodies

Virus to be neutralized



Susceptible-Infected-Recovered Models

Math



Susceptible-Infected-Recovered Models

(1) Population size

$$N = S + I + R$$

(2) Change in susceptible over time

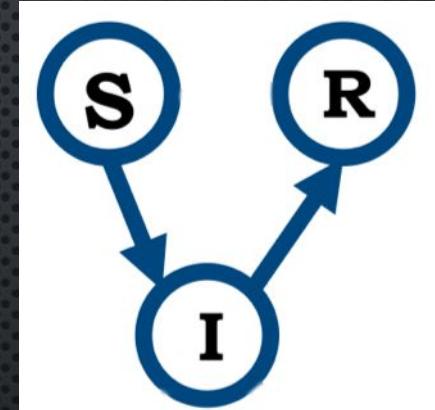
$$\frac{dS}{dt} = \mu N - \beta IS - \delta S$$

(3) Change in infected over time

$$\frac{dI}{dt} = \beta IS - \gamma I - \alpha I - \delta I$$

(4) Change in recovered over time

$$\frac{dR}{dt} = \gamma I - \delta R$$



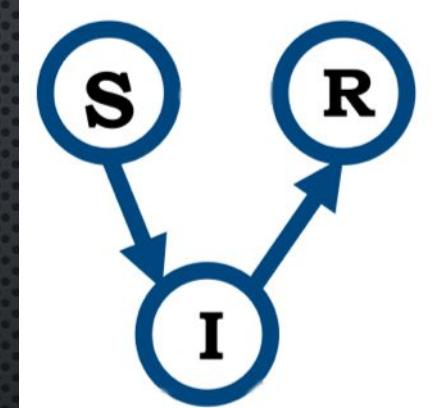
Susceptible-Infected-Recovered Models

- + individuals added to the class
- individuals leaving the class

(2) Change in susceptible over time

$$\frac{dS}{dt} = \mu N - \beta IS - \delta S$$

New infections
New births
Natural death



Susceptible-Infected-Recovered Models

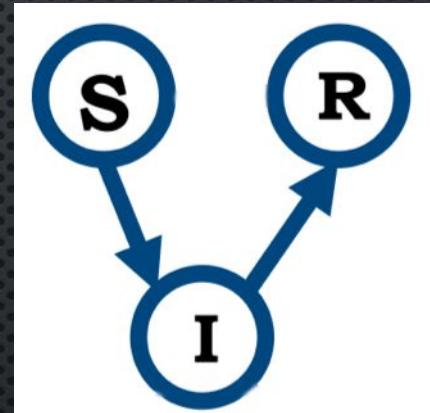
- + individuals added to the class
- individuals leaving the class

(3)

Change in infected over time

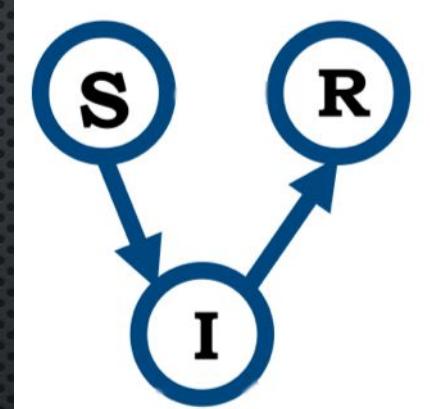
$$\frac{dI}{dt} = \beta I S - \gamma I - \alpha I - \delta I$$

New infections
recovery Infection-induced mortality
Natural death



Susceptible-Infected-Recovered Models

- + individuals added to the class
- individuals leaving the class



(4)

Change in recovered over time

$$\frac{dR}{dt} = \gamma I - \delta R$$

Natural
death
recovery

Growth of the Infected Class

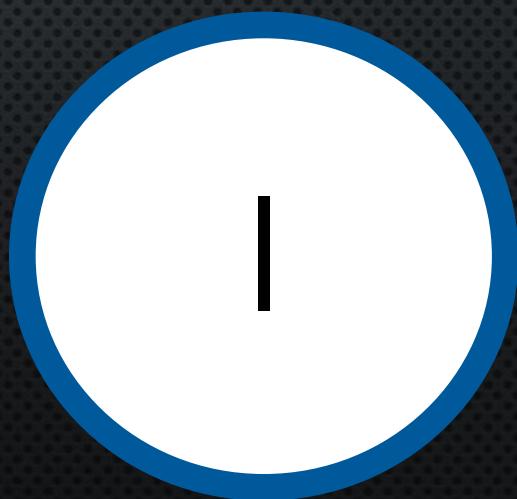
$$\frac{dI}{dt} = \beta IS - \gamma I - \alpha I - \delta I$$

$$\frac{dI}{dt} = \underbrace{\beta SI}_{\text{Rate in}} - \underbrace{(\gamma + \alpha + \delta)I}_{\text{Rate out}}$$

Rate
in

Rate
out

Rate
in



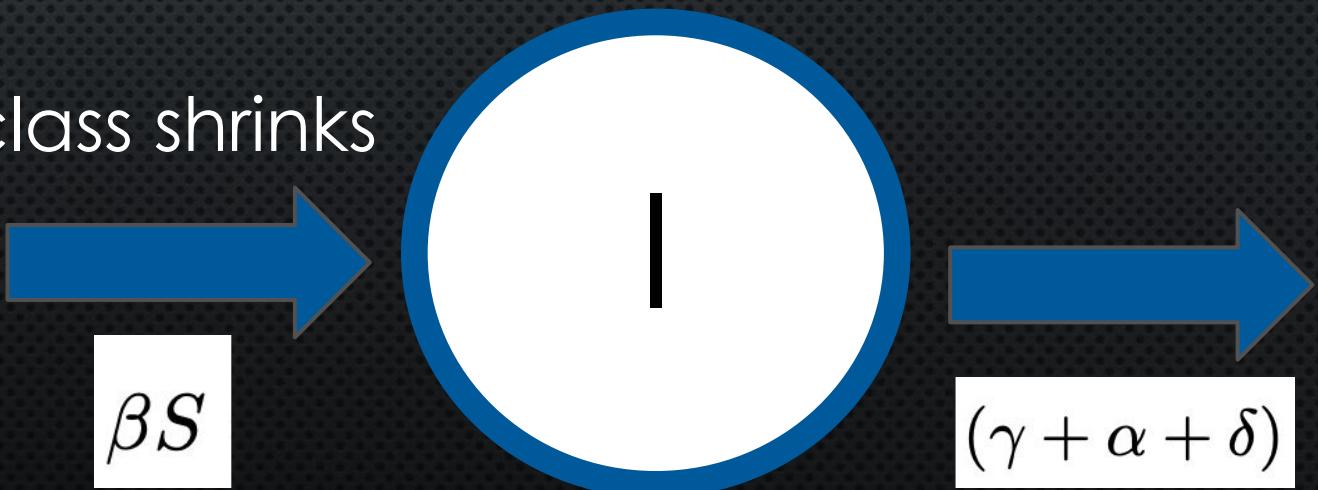
Rate
out

Change in Infected Class

Size of infected class remains constant

Infected class grows (rate in > rate out)

Infected class shrinks



Change in Infected Class

$$\beta S = (\gamma + \alpha + \delta)$$

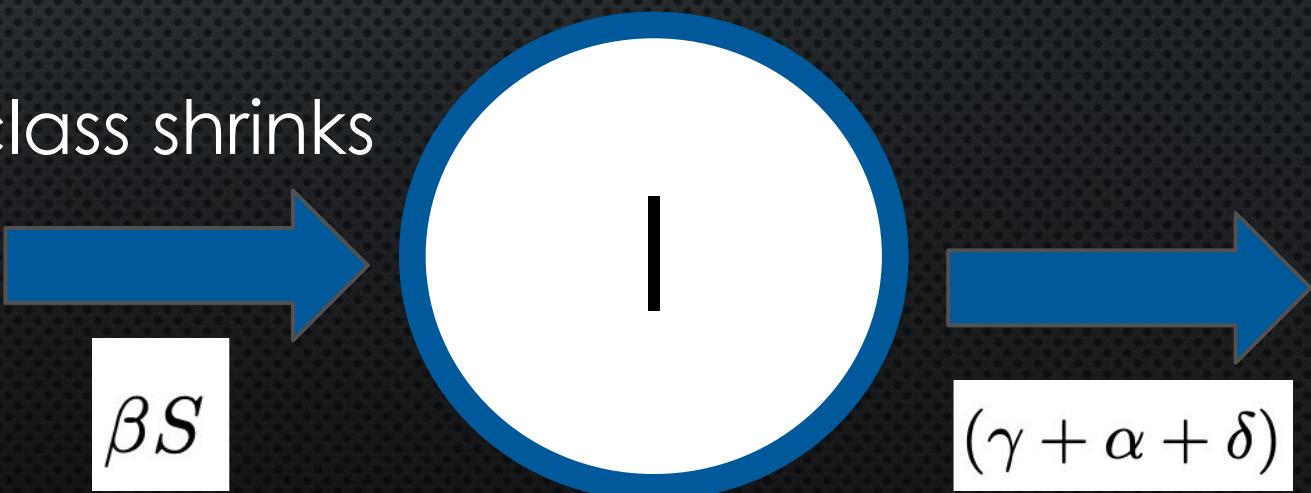
Size of infected class remains constant

$$\beta S > (\gamma + \alpha + \delta)$$

Infected class grows (rate in > rate out)

$$\beta S < (\gamma + \alpha + \delta)$$

Infected class shrinks



Calculating the Reproductive Ratio

$$\frac{\beta S}{(\gamma + \alpha + \delta)}$$

Called the reproductive ratio because it tells us how many new infections “reproduced” by each infected individual before they leave the infected class

If greater than 1, the infectious agent is successfully spreading and the infected class grows in size

