

Introduction of Infectious Disease Modelling

Objectives

By the end of this session on **Intro to ID Modelling** 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 measles and rubella data relied upon for modelling, and what are potential issues with the data
- How are ID data and ID models related

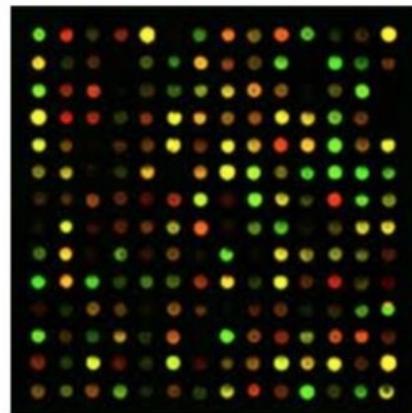
Contextualizing Infectious Disease Modelling

Many ways to study infectious diseases

Medicine



Genomics



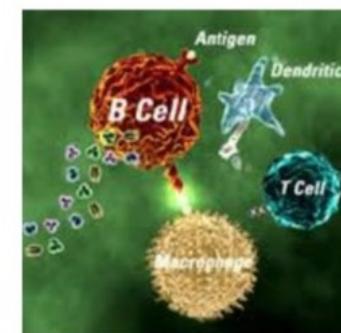
Microbiology



Some disciplines focus on infectious diseases from the:

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

Immunology



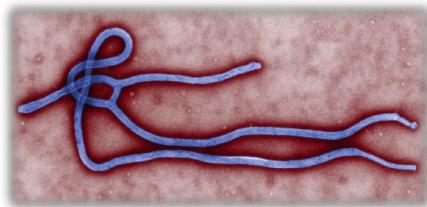
Vaccines & Drugs



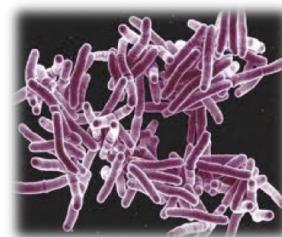
Disease vs Infectious Disease

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



Ebola Virus



Tuberculosis Bacteria



HIV

Pathogen: Microorganism that causes disease
(virus, bacteria, parasite)

Agents of Infectious Diseases

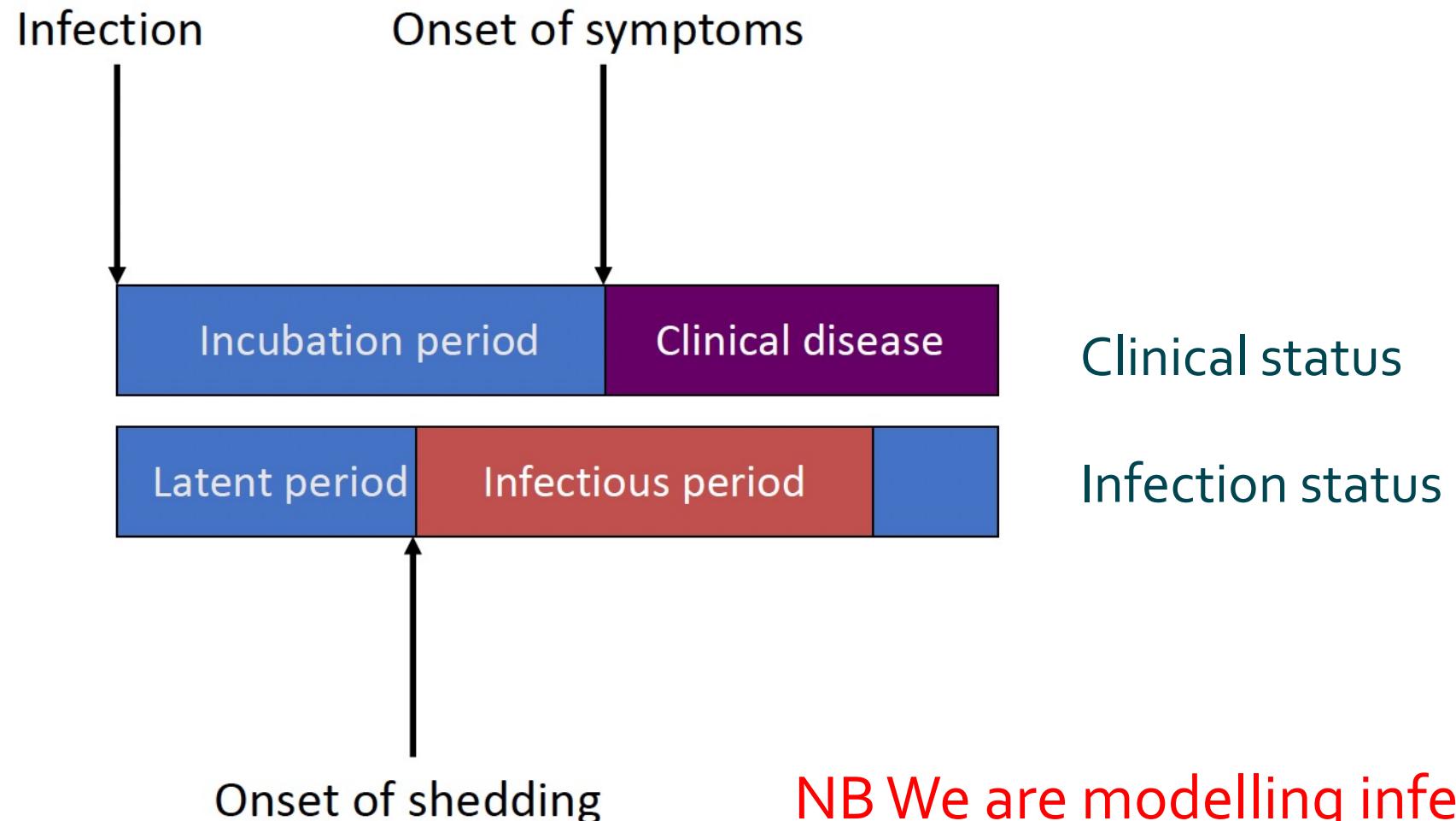
Infectious disease is a disease caused by a pathogen

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)

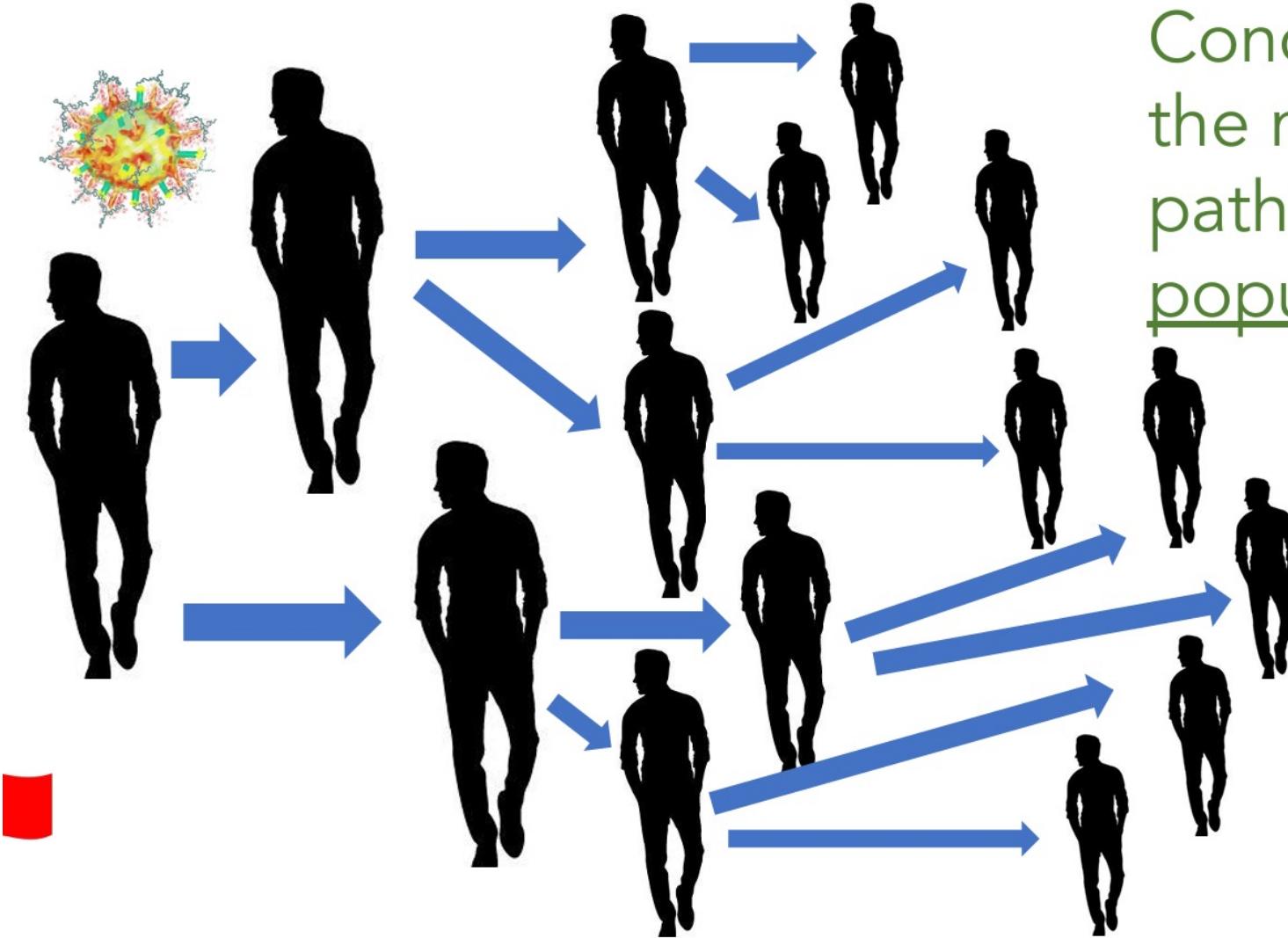
parasites

From infection to disease



NB We are modelling infections, although we actually observe clinical cases

Epidemiology Focus on Population Level

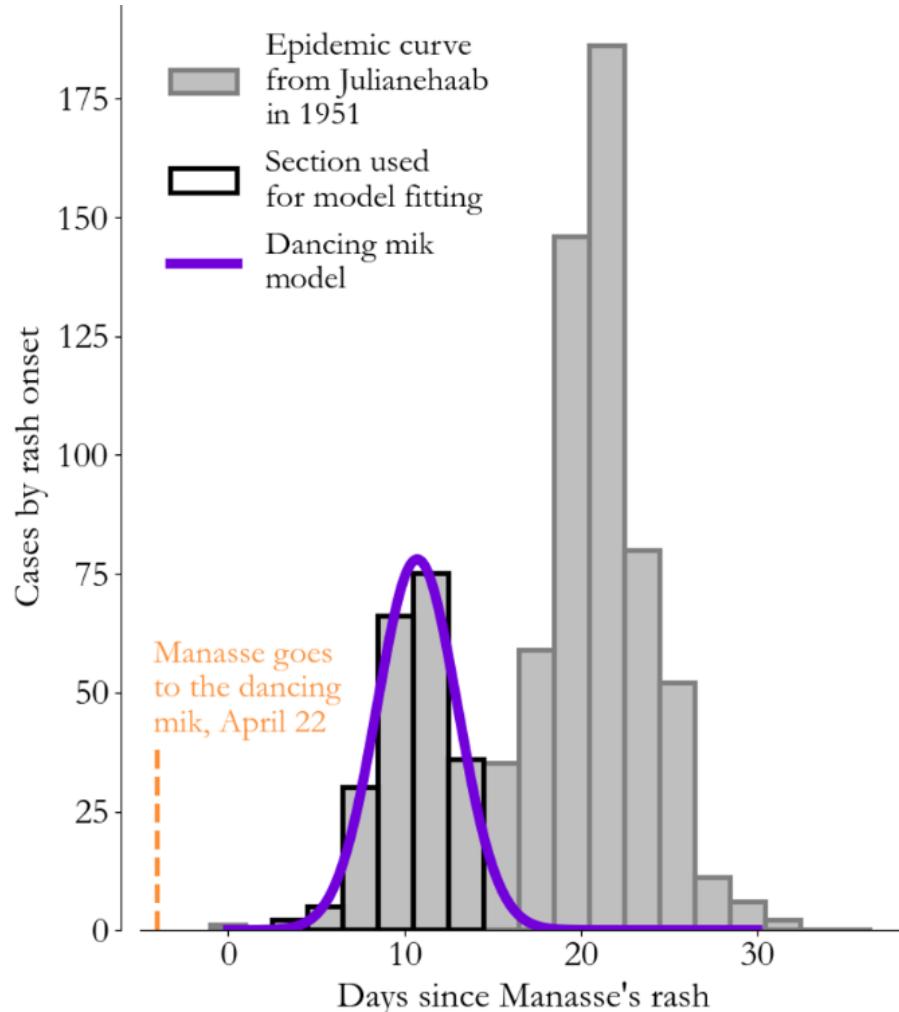


Concept: We can track the movement of pathogens throughout populations

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

The use of time series data

Measles Epidemic from Greenland



Epi Outbreak investigation:

- What pathogen is causing the illness?
- Is it a novel pathogen?
- Who is infected?

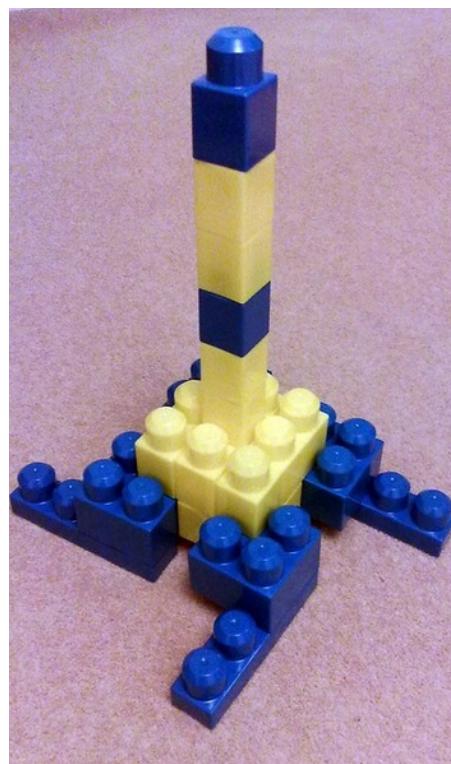
Biological questions:

- What allows a pathogen to enter the population?
- What does the growth rate tell us?
- Why does the epidemic turn over?
- Why are there two peaks?

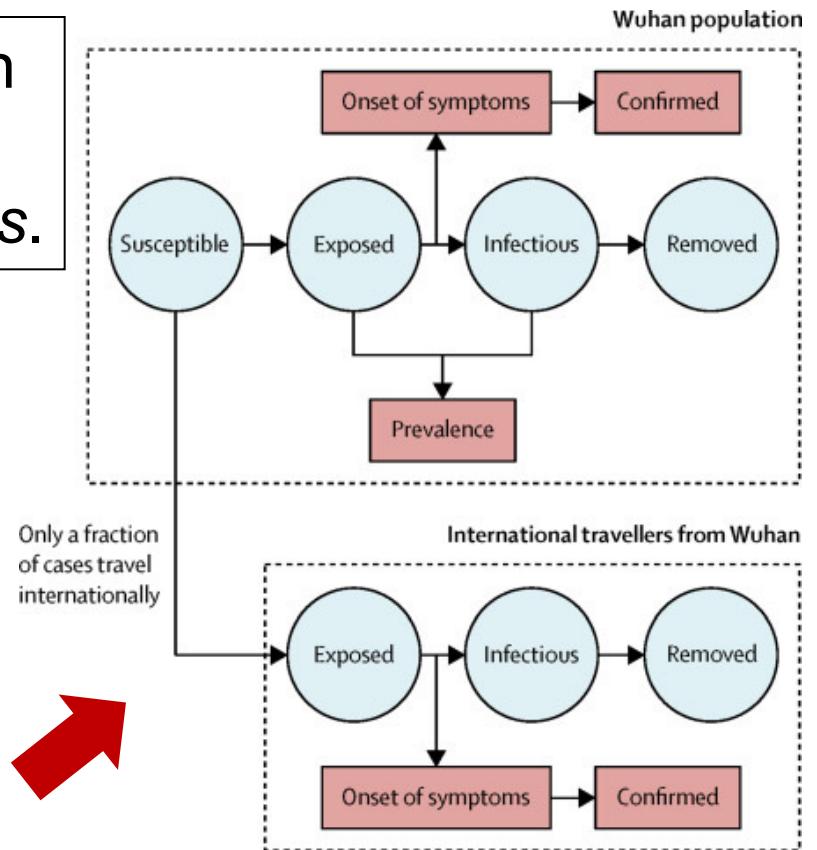
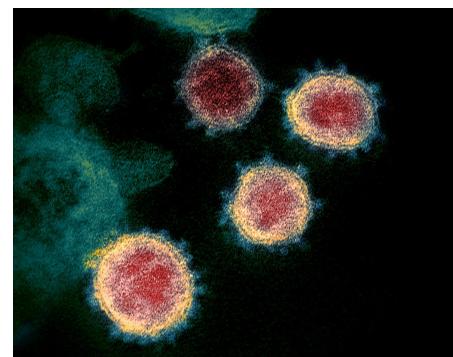
Intervention questions:

- How to prevent spread?
- When is best to implement control?
- Drugs, vaccines, or other control measures?

What is a model?

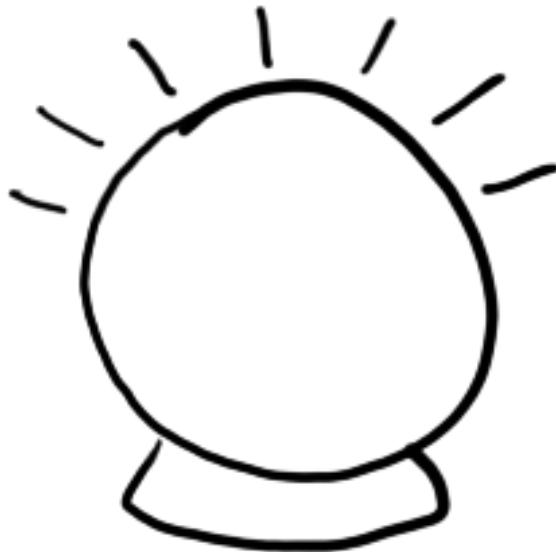


A model is a simplified representation
of a more complex object/process,
designed to address specific questions.



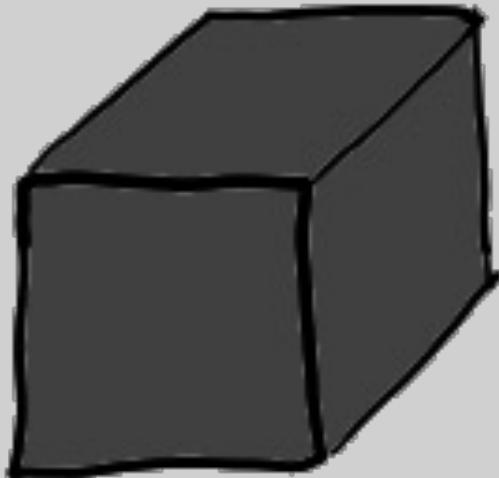
What model is not ...

A model is **not** a crystal ball.



(it can't create information out of nothing.)

A model is **not** a black box.



(it is only useful when you understand the assumptions and use it to guide thinking, not replace it.)

A model is **not** a perfect representation.
(the map is not the territory)

“Only *six inches!*” exclaimed Mein Herr. “We very soon got to *six yards* to the mile. Then we tried a *hundred* yards to the mile. And then came the grandest idea of all! We actually made a map of the country, on the scale of *a mile to the mile!*”

“Have you used it much?” I enquired. “It has never been spread out, yet,” said Mein Herr: “the farmers objected: they said it would cover the whole country, and shut out the sunlight! So we now use the country itself, as its own map, and I assure you it does nearly as well. Now let me ask you *another* question. What is the smallest *world* you would care to inhabit?”

Lewis Carroll. (1893) *Sylvie and Bruno Concluded*.

(it is only useful when it simplifies 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 ~ 11%, which Bernoulli estimated this risk to be ~1%

Infectious Disease Models are not new

The collage includes the following elements:

- Top Left:** A map of the UK showing the spread of foot-and-mouth disease in 2001, with a graph of weekly increases and total cases (514).
 - Top Center:** Two people riding horses in a field.
 - Top Right:** A box containing the text "2001 foot and mouth disease".
- Middle Left:** A newspaper clipping from April 26, 2006, titled "Scientific studies call for stronger action" regarding the 2001 foot-and-mouth outbreak.
 - Bottom Left:** A box containing the text "Early 2000s pandemic flu".
 - Bottom Left Text:** International, simulated a response to detailed population data and travel patterns.
- Middle Center:** A news article from The Atlantic magazine dated April 26, 2006, titled "Computer Simulations Help Nations Prepare for Flu Pandemic".
 - Bottom Center:** A box containing the text "2014 Ebola".
 - Bottom Center Text:** An animated map showing the spread of H5N1-like flu over a 120-day period, with red representing active infection and green representing recovery.
- Bottom Right:** A news article from The Atlantic magazine dated September 23, 2014, titled "Chasing Ebola".
 - Bottom Right Text:** Scientists are using computer models to predict the outbreak's next moves, but they can't account for human behavior.
 - Bottom Right Image:** A woman in a white tank top.
 - Bottom Right Text:** How to Fill In Crepey Skin On Arms, Chest, And Legs (Effortless 2 Min Remedy).
 - Bottom Right Text:** Recommended Reading.

Where does modelling fit in epidemiology?

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

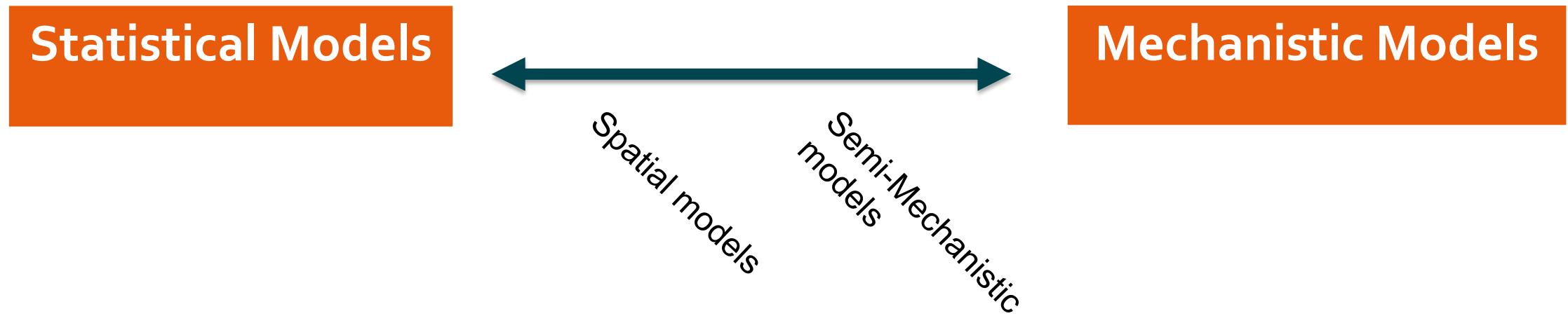
Where does modelling fit in epidemiology?

(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

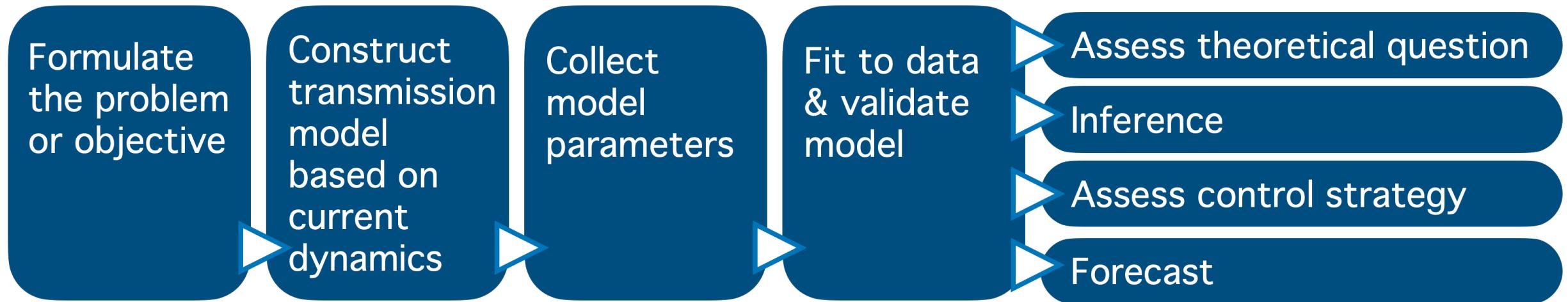
Where does modelling fit in epidemiology?

Statistical Models	Mechanistic Models
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 in Developing a Model



Model Utility and Types

- 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

Formulate
the problem
or objective

Model Utility

- We always 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 and cannot do

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

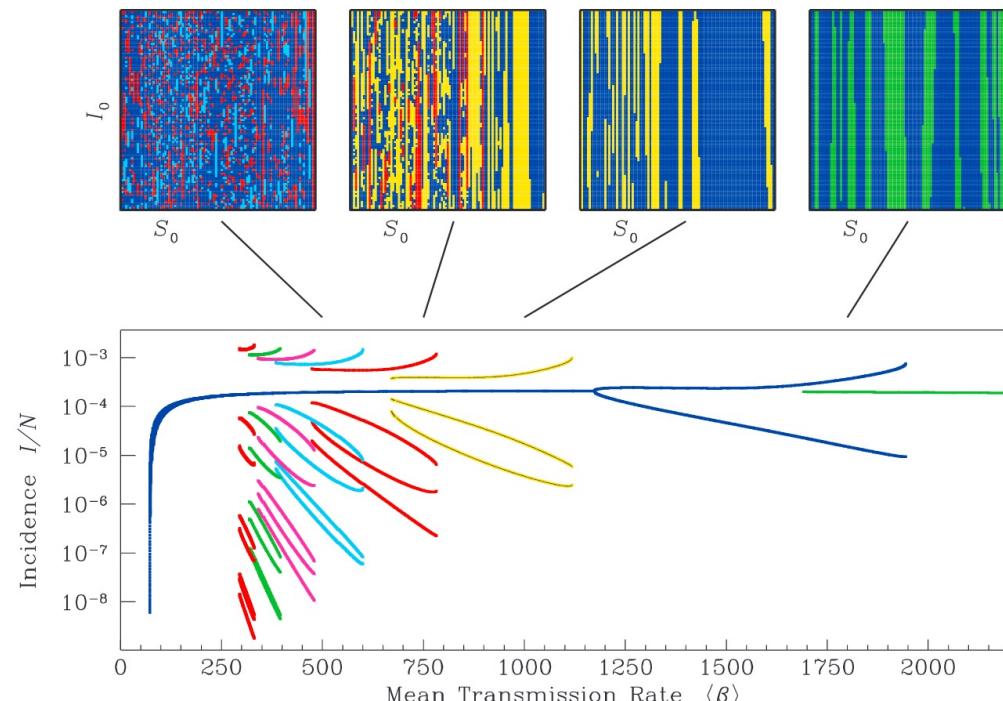
Earn et al. investigated the causes of transitions in measles epidemic patterns from regular (i.e., annual or biennial) to irregular outbreaks. The assumption under-investigation was the dynamical effect of changing birth rates and vaccination rates (i.e., changes in transmission) on incidence given 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](https://doi.org/10.1126/science.287.5453.667)]

REPORTS

A Simple Model for Complex Dynamical Transitions in Epidemics

David J. D. Earn,^{1,2*} Pejman Rohani,² Benjamin M. Bolker,³
Bryan T. Grenfell²

Dramatic changes in patterns of epidemics have been observed throughout this century. For childhood infectious diseases such as measles, the major transitions are between regular cycles and irregular, possibly chaotic epidemics, and from regionally synchronized oscillations to complex, spatially incoherent epidemics. A simple model can explain both kinds of transitions as the consequences of changes in birth and vaccination rates. Measles is a natural ecological system that exhibits different dynamical transitions at different times and places, yet all of these transitions can be predicted as bifurcations of a single nonlinear model.



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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

May 2002

BRYAN T. GRENFELL,^{1,4} OTTAR N. BJØRNSTAD,² AND BÁRBEL F. FINKENSTÄDT^{1,3}

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University Park, Pennsylvania 16802 USA

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SCALING OF MEASLES DYNAMICS

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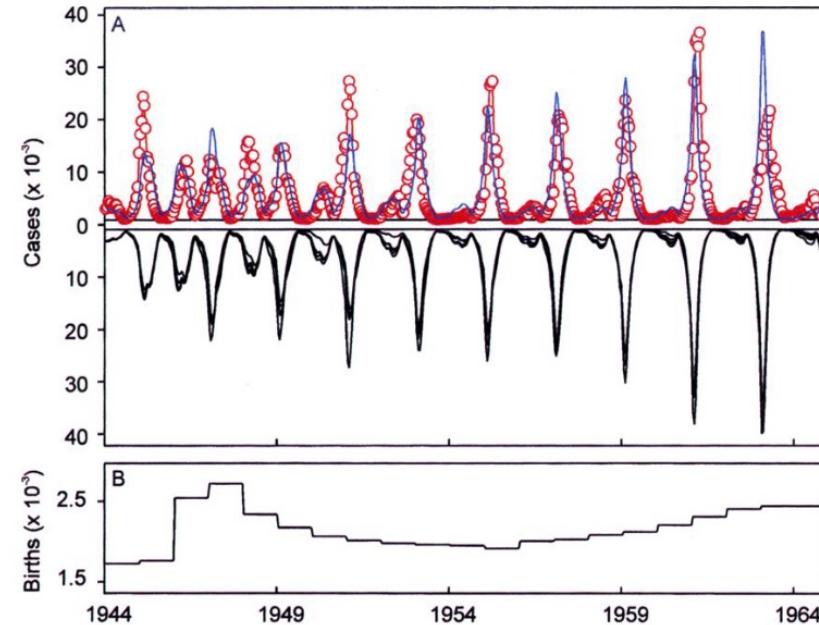


FIG. 1. (A) Measles incidence in 2-wk periods (in hundreds) in London from 1944 to 1965. The circles and the red line represent observed incidence (corrected for underreporting). The blue line represents the deterministic prediction from the TSIR model (using the susceptible and infected density in the 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 Modelling Example



Article

Rubella Vaccine Introduction in the South African Public Vaccination Schedule: Mathematical Modelling for Decision Making

Nkengafac Villyen Motaze ^{1,2,*}, Ijeoma Edoka ³, Charles S. Wiysonge ^{2,4,5},

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

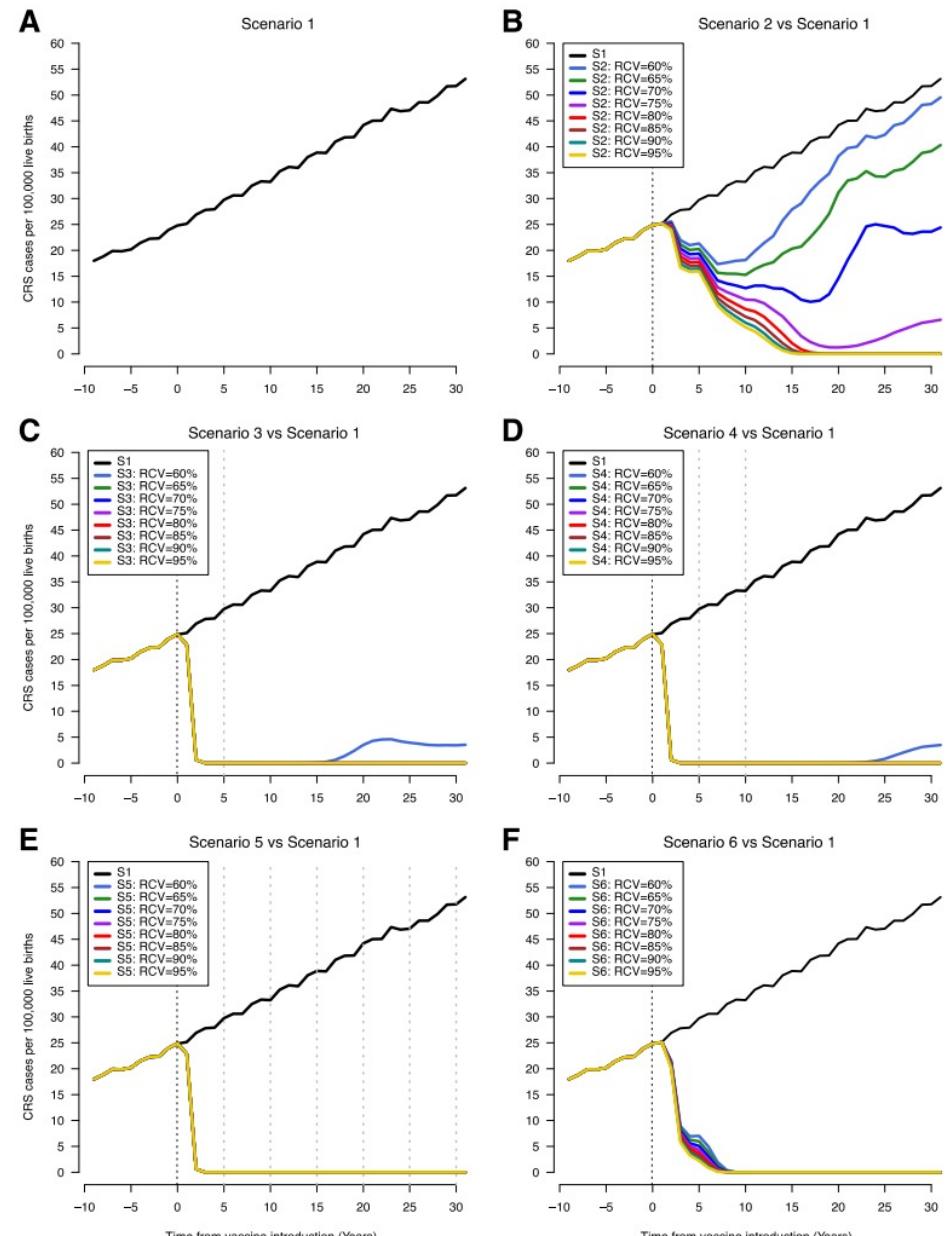


Figure 2. Time series of congenital rubella syndrome (CRS) incidence (CRS cases per 100,000 live births) showing scenario 1 (A) and comparing scenario 1 with scenarios 2–6 (B–F). The vertical black dotted

Four Goals for Mechanistic ID Models

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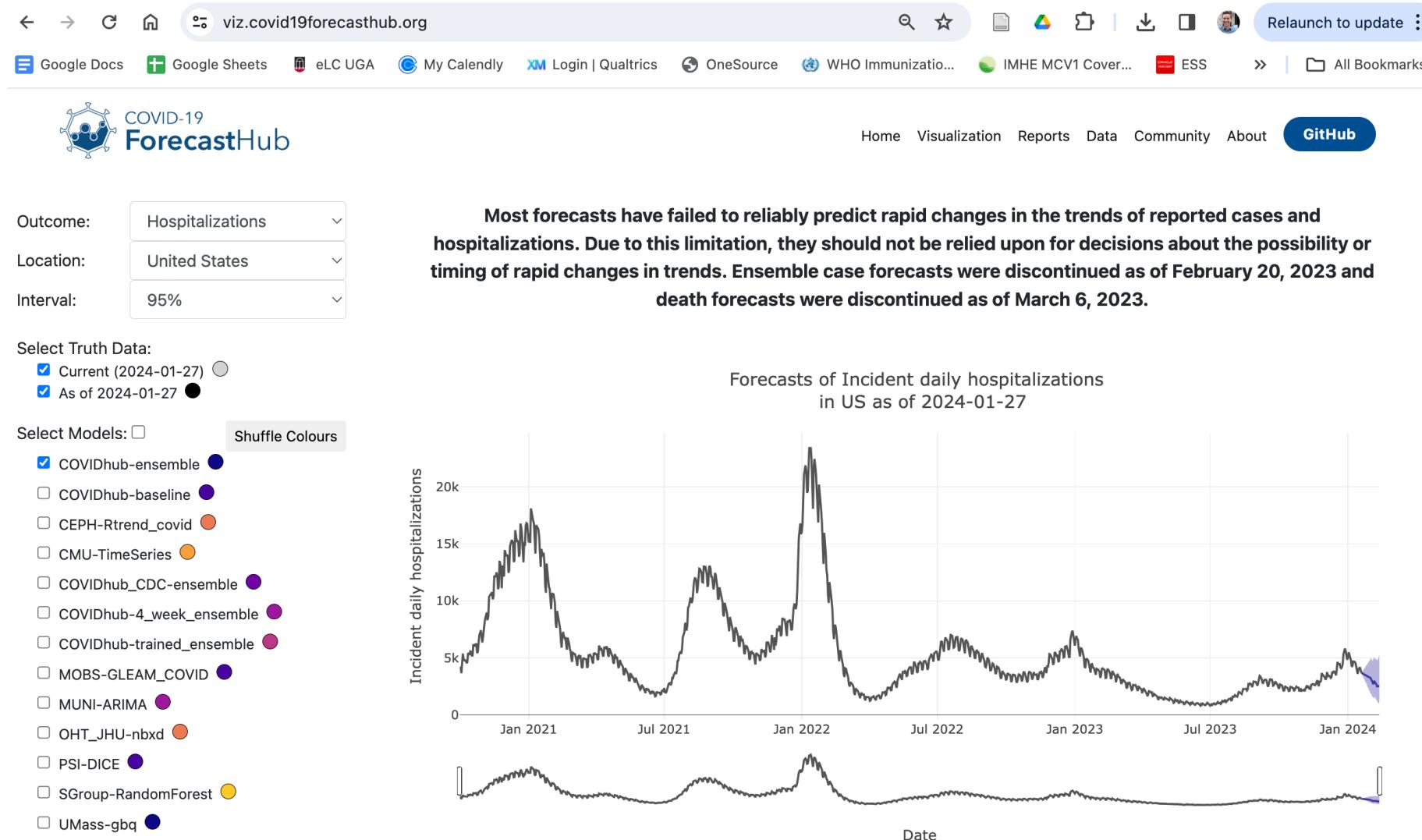
- Conditional predictions of what could happen under specific scenarios
- *Focus on contrast's between scenarios*

Forecast Modelling

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

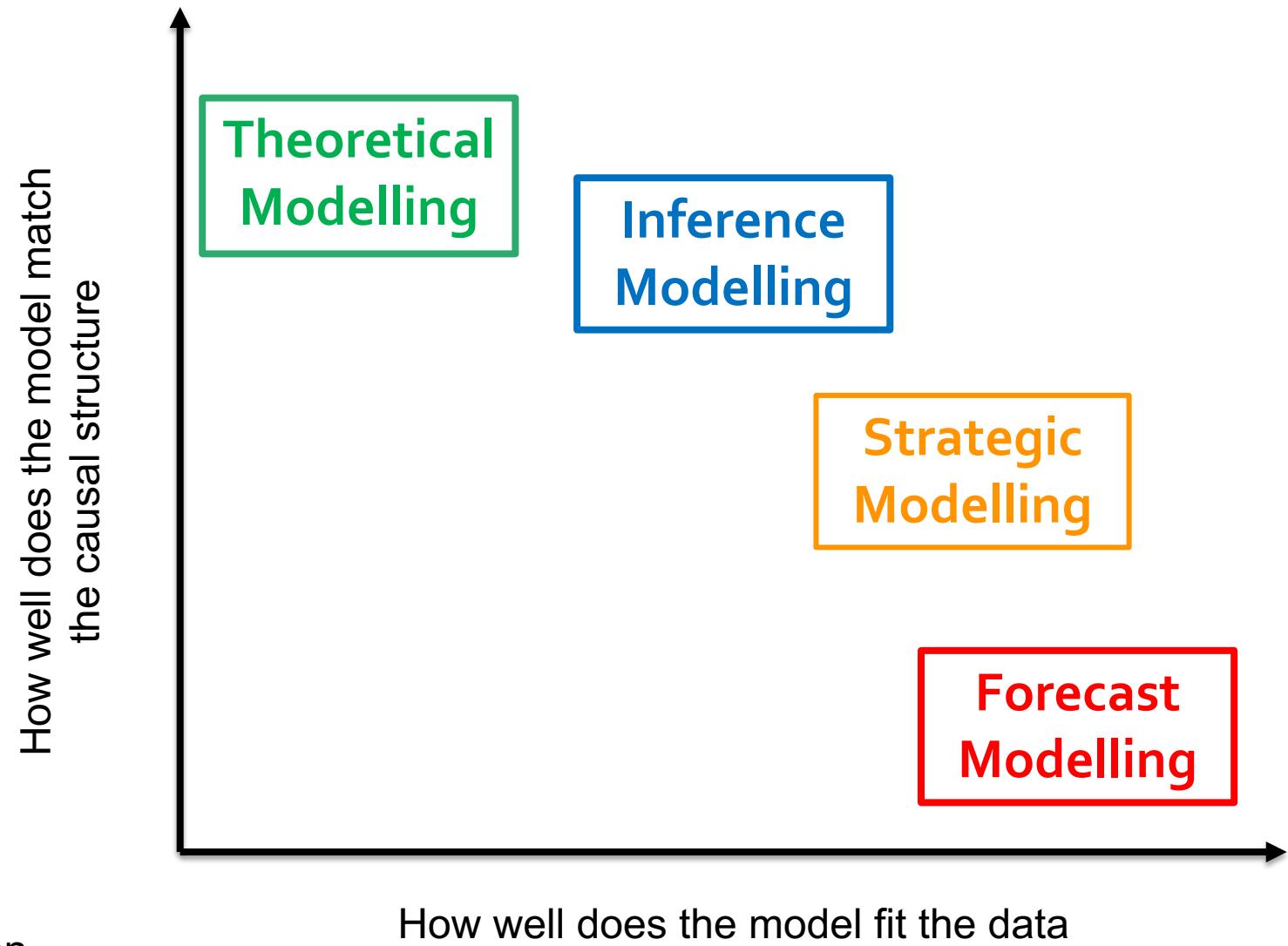
- Unconditional prediction of what will happen
- Choice of specific metrics

Forecast Model Example



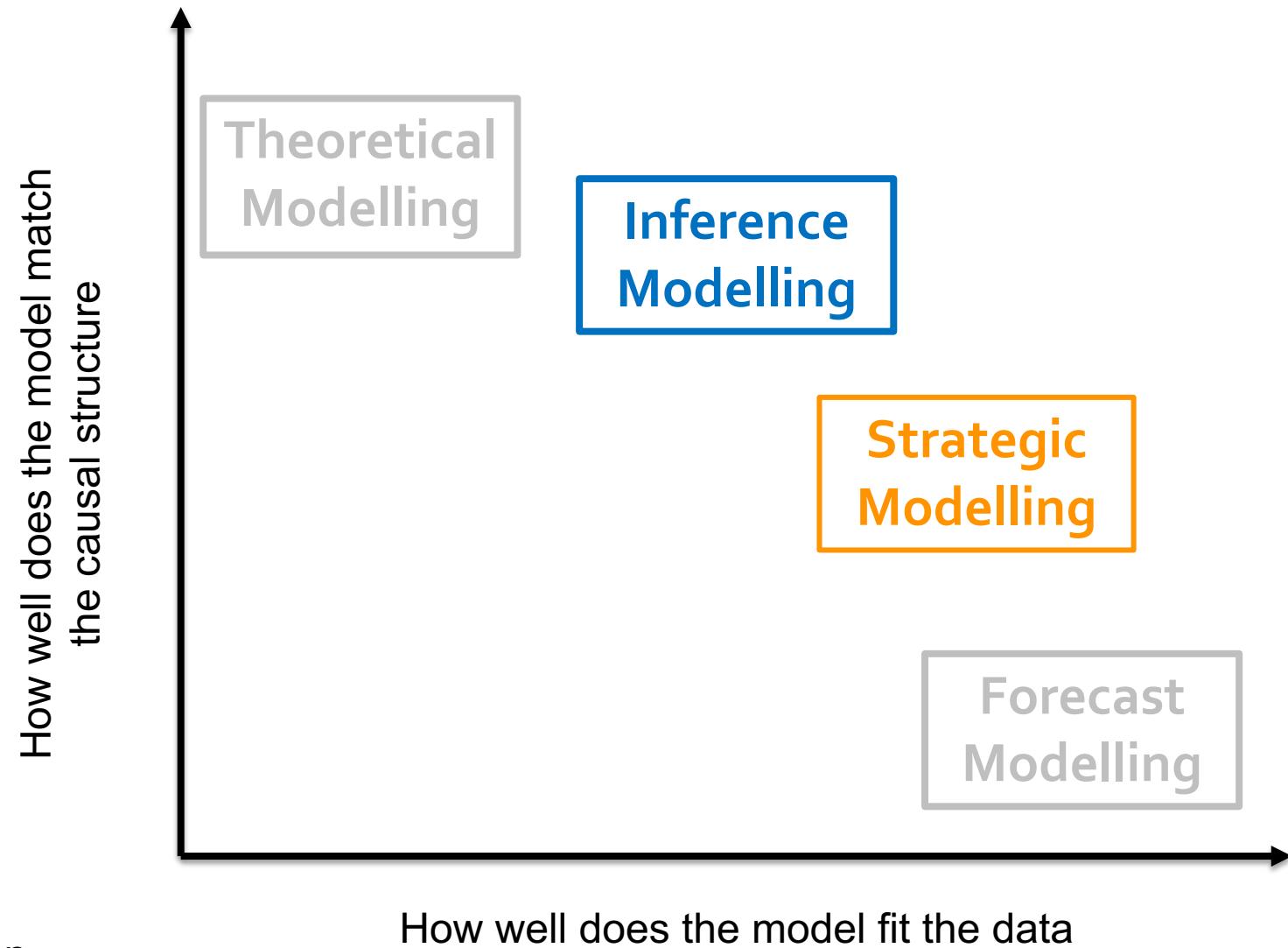
Four Goals for Mechanistic ID Models

Formulate
the problem
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Four Goals for Mechanistic ID Models

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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

Construct transmission model based on current dynamics

Scale of modelling

INTERFACE

rsif.royalsocietypublishing.org

Research



Cite this article: Klepac P, Megiddo I, Grenfell BT, Laxminarayan R. 2016 Self-enforcing regional vaccination agreements. *J. R. Soc. Interface* 13: 20150907. <http://dx.doi.org/10.1098/rsif.2015.0907>

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Self-enforcing regional vaccination agreements

Petra Klepac¹, Itamar Megiddo², Bryan T. Grenfell^{3,4,5} and Ramanan Laxminarayan^{2,6}

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IM, 0000-0001-8391-6660

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

Social, political, economic, health systems

Populations (“between host models”)

Individuals, physiological systems

Cells, genes, proteins (“within host models”)

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 modeling the natural history of HPV infection and disease. Key words: cervical intraepithelial neoplasms; mathematical model; Markov process; papillomavirus infections; uncertainty. (*Med Decis Making* 2010;30:84–98)

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 Group¹, Mark Jit, Petra Klepac

Summary

Background In December, 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel coronavirus, emerged in Wuhan, China. Since then, the city of Wuhan has taken unprecedented measures in response to the outbreak, including extended school and workplace closures. We aimed to estimate the effects of physical distancing measures on the progression of the COVID-19 epidemic, hoping to provide some insights for the rest of the world.



Lancet Public Health 2020; 5:e264–70
Published Online March 25, 2020
[https://doi.org/10.1016/S2468-7667\(20\)30073-6](https://doi.org/10.1016/S2468-7667(20)30073-6)

ARTICLES

<https://doi.org/10.1038/s41559-018-0786-x>

nature ecology & evolution

Within-host dynamics shape antibiotic resistance in commensal bacteria

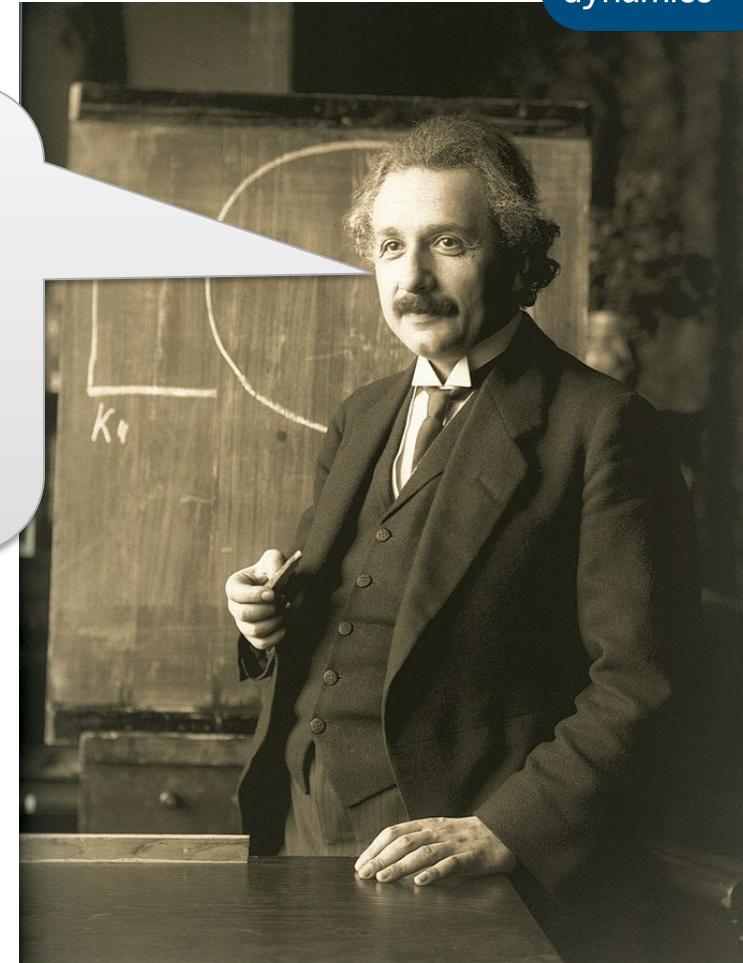
Nicholas G. Davies^{1,2*}, Stefan Flasche^{1,2}, Mark Jit^{1,2,3} and Katherine E. Atkins^{1,2,4}

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.

What type of model will be 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.”

*Everything
should be as
simple as
possible, but no
simpler.*



Einstein 1921 by F Schmutzler, public domain

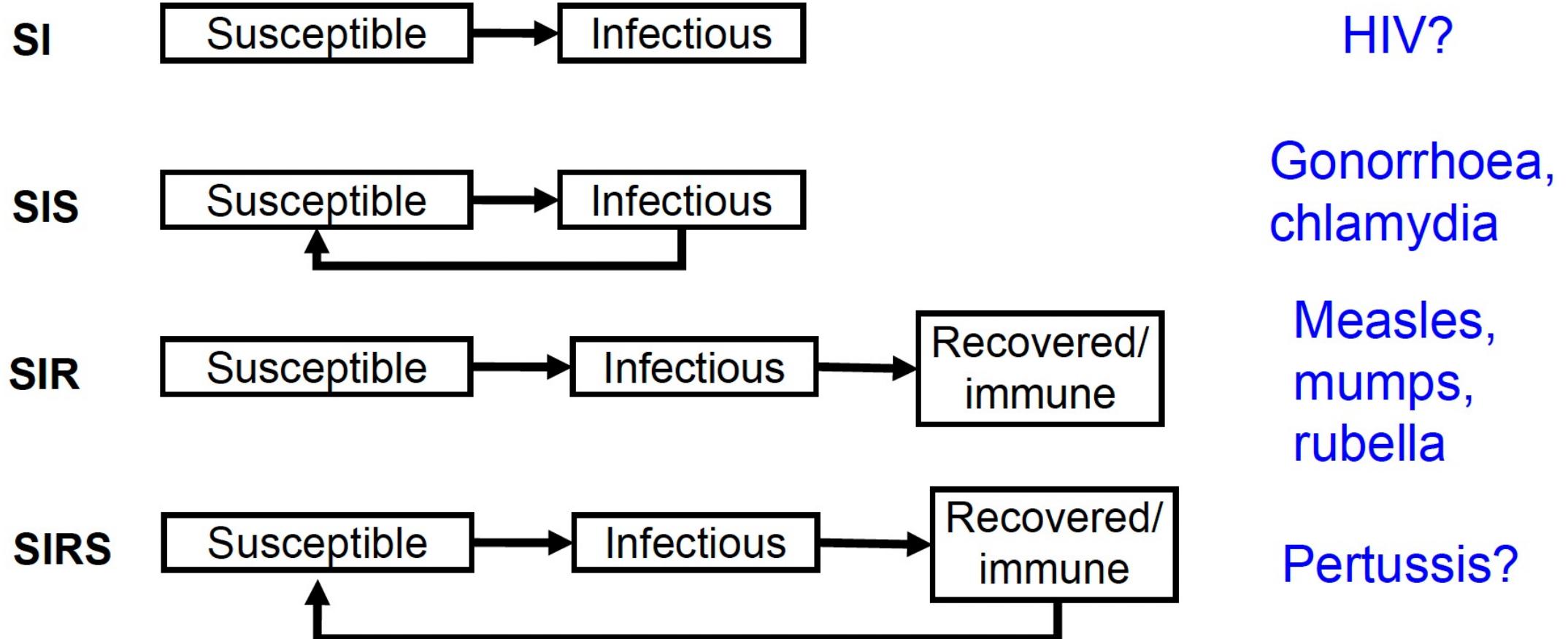
Model structure

Construct transmission model based on current dynamics

- **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.

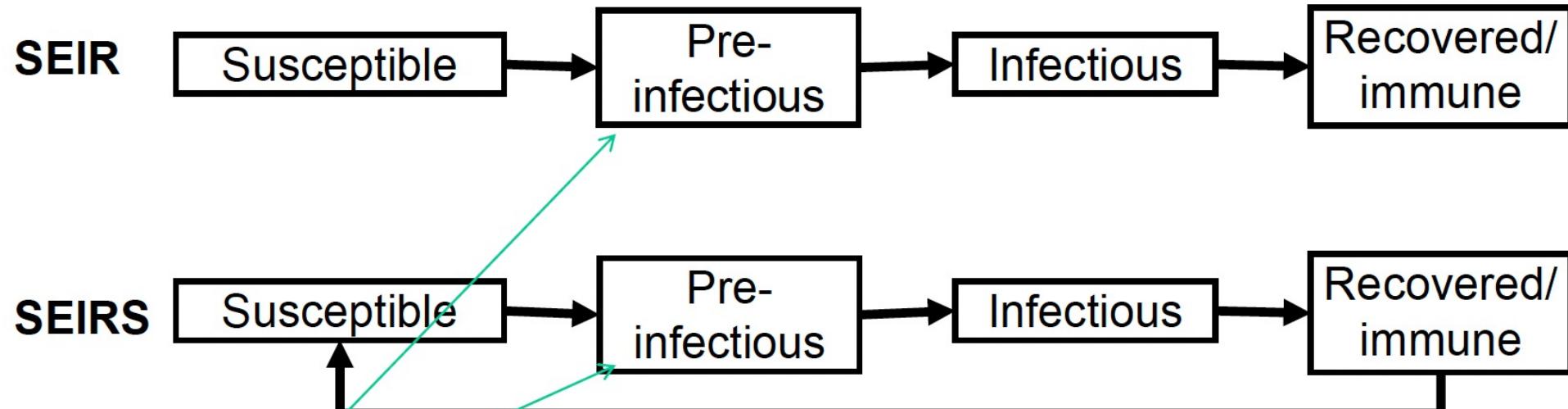
Model structure

Construct transmission model based on current dynamics



Construct transmission model based on current dynamics

Model Structure – Common Mistake

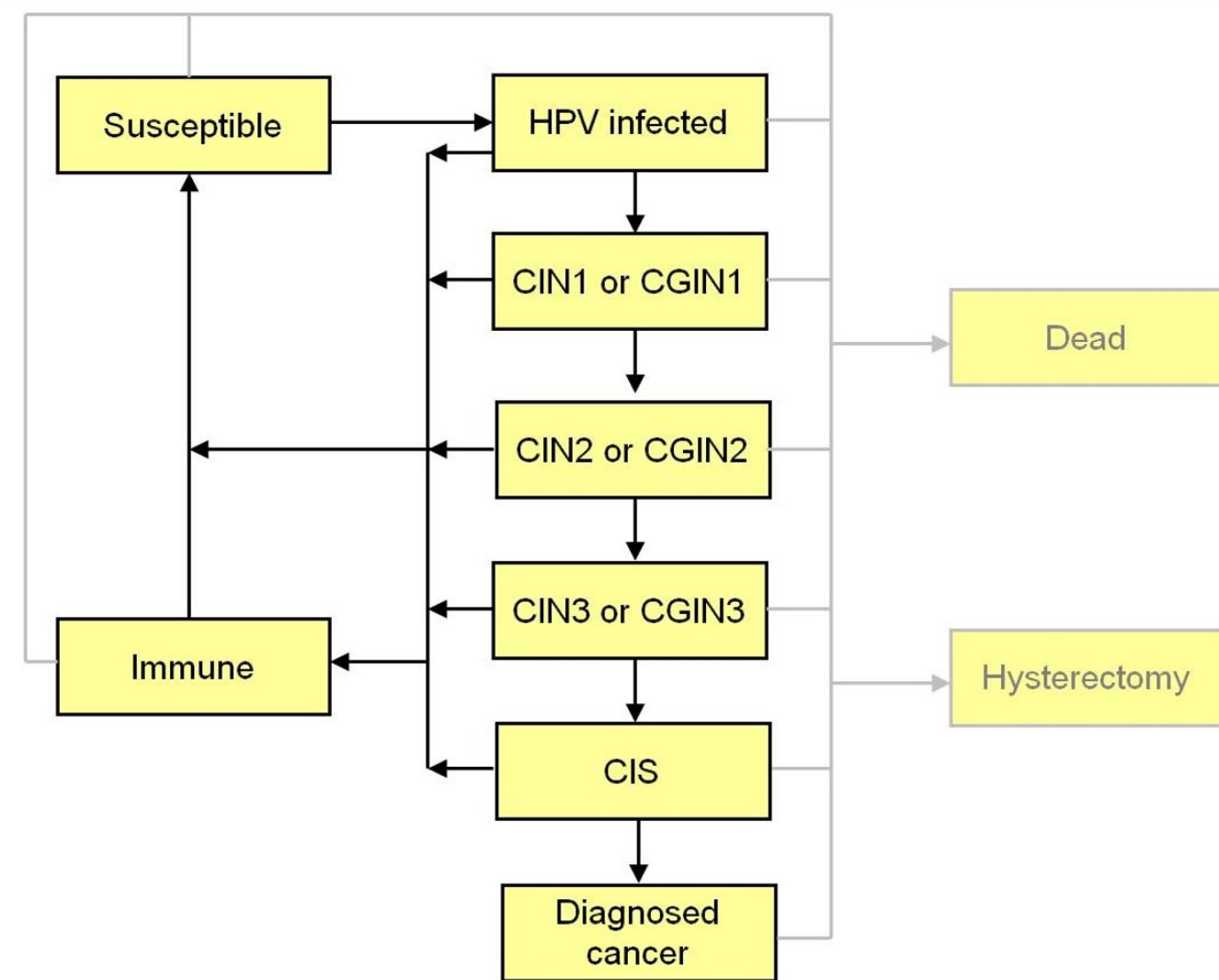


NB Often referred to as the “Infected” or “Exposed” category in the modelling literature...

BUT....this can be misleading : everyone is “Exposed” and infectious individuals can be considered “infected”.

Construct
transmission
model
based on
current
dynamics

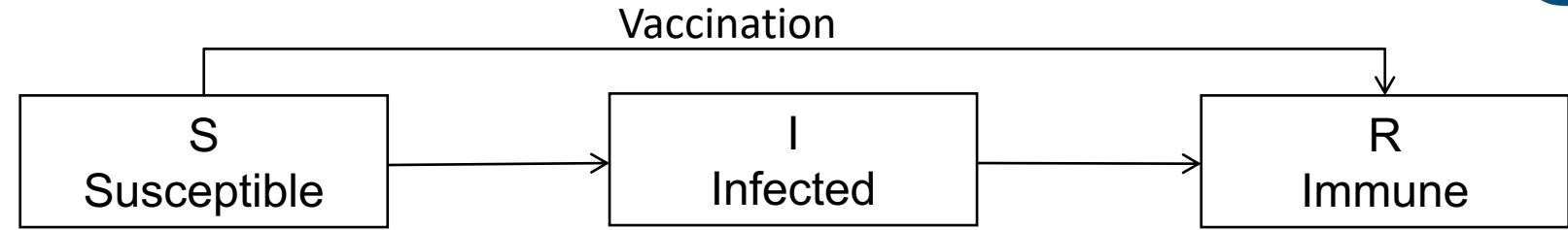
Model structure



Construct transmission model based on current dynamics

Types of models

Compartmental transmission dynamic model



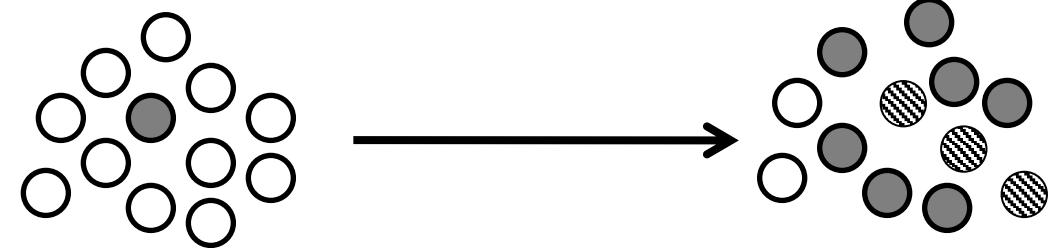
Structured compartmental model (e.g., age or sex structured)

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

Network model

Multi-scale model

Individual-(agent-) based model:



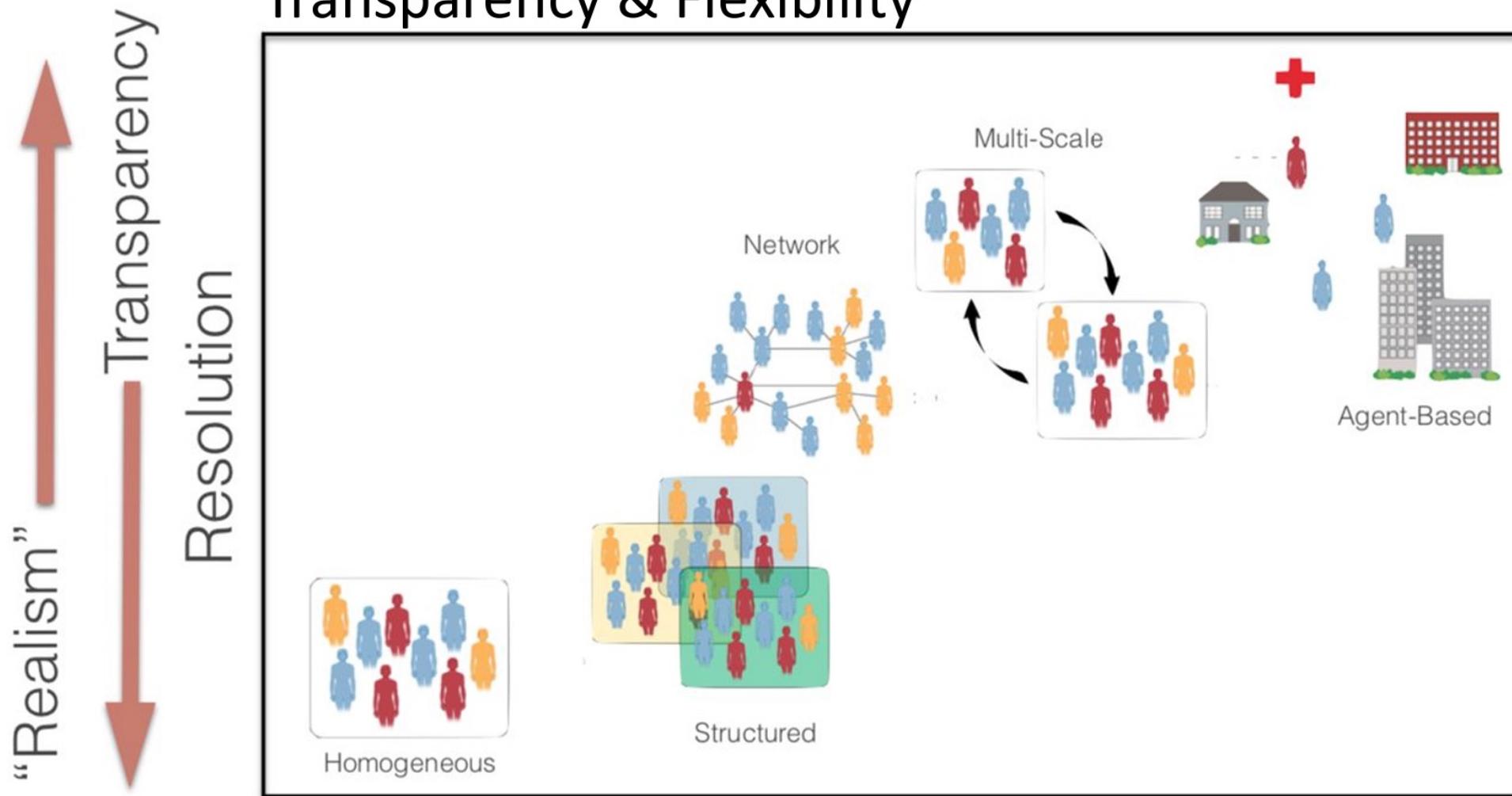
Non-homogenous mixing

- Susceptible
- Infected
- ▨ Immune

Construct transmission model based on current dynamics

Model type depends on modelling objective

Realism & Complexity vs. Transparency & Flexibility



Construct
transmission
model
based on
current
dynamics

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

2 Types Modelling Methods

2 main types:

Stochastic

- incorporate chance variation
- provide the probability of a given outcome or range in which the outcome is likely to occur eg
 - probability that transmission ceases
 - 95% certain that 10-15 cases will be seen

To be discussed in detail in block 2

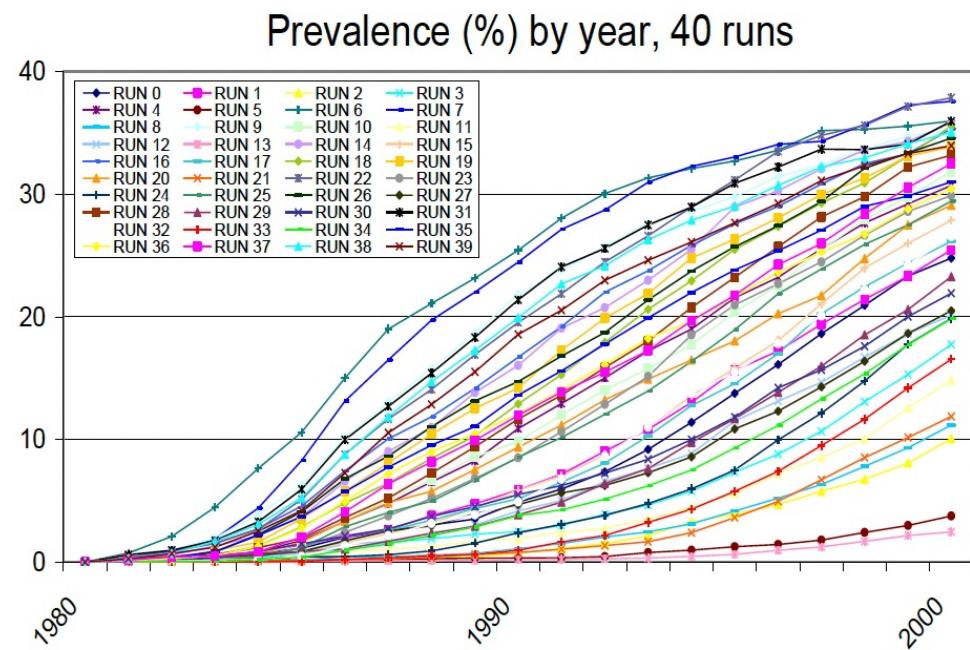
Deterministic models

- describe what will happen on average in a population
- individuals are subdivided into categories (“compartments”)
- describe transitions between compartments

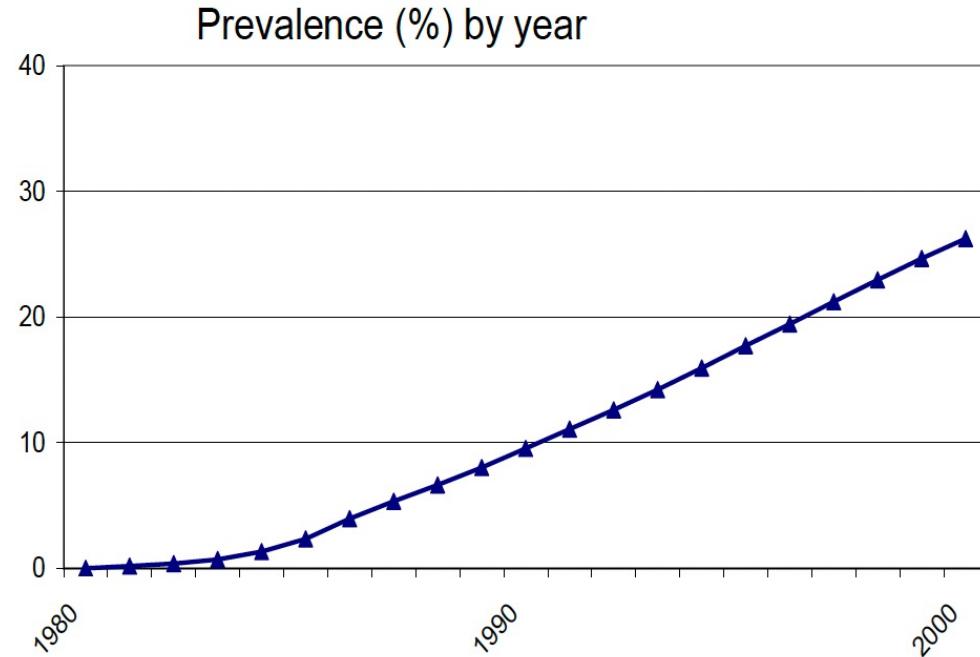
2 Types Modelling Methods

Examples of output from a deterministic and a stochastic model

Stochastic model



Deterministic model



Deterministic Models

Deterministic models are set up using either difference or differential equations

Difference equations calculate the number in each infection category using **discrete time** steps e.g. 1, 2, 3 days etc

number of cases tomorrow =
number of cases today
+ number of new cases with onset between today and tomorrow
– the number of cases who recover between today and tomorrow

Differential equations calculate the number in each infection category using time steps which are “infinitesimally” small, i.e. in continuous time

How to 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*)

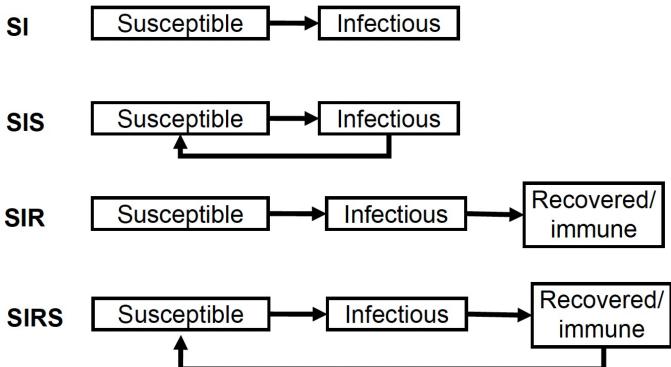


Overview

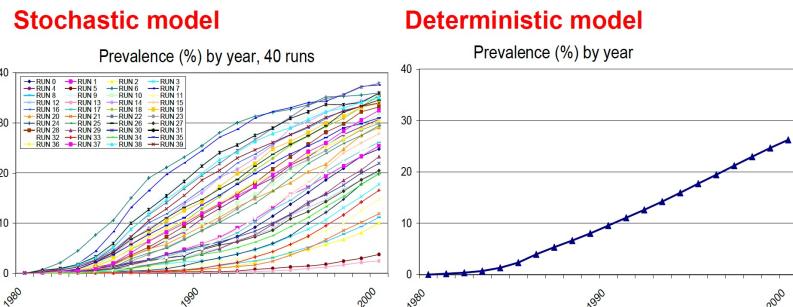
Model Scale

→ Social, political, economic, health systems
↓
Populations ("between host models")
↓
→ Individuals, physiological systems
↓
Cells, genes, proteins ("within host models")

Model Structure



Model Processes



Model Type

Compartmental transmission dynamic model

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

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

Network model

Multi-scale model

Individual-(agent-) based model:

Measles and Rubella Data

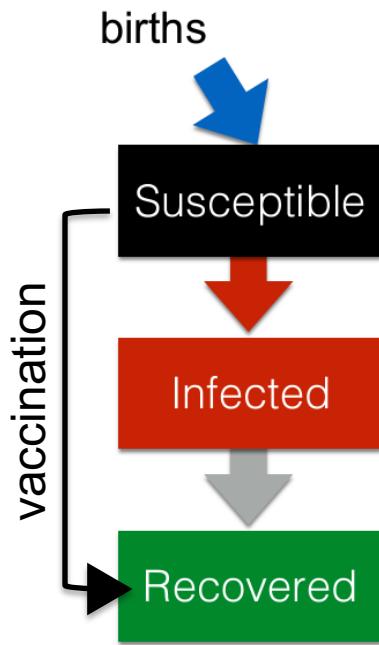
Four most common sources of data for measles and rubella modelling

Cases surveillance data

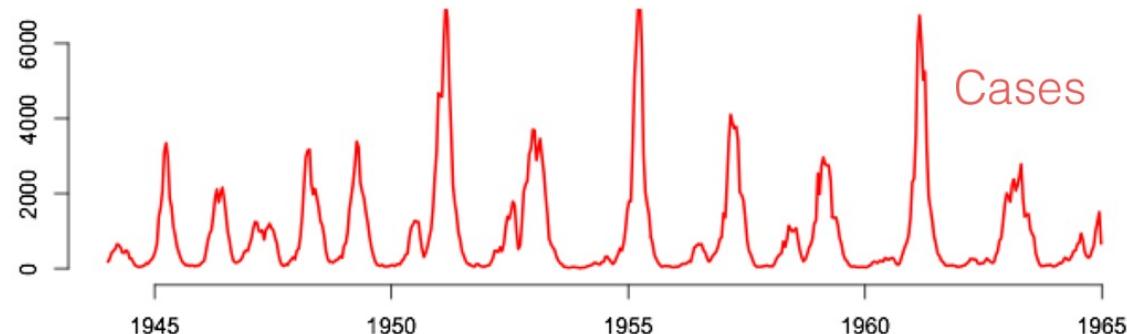
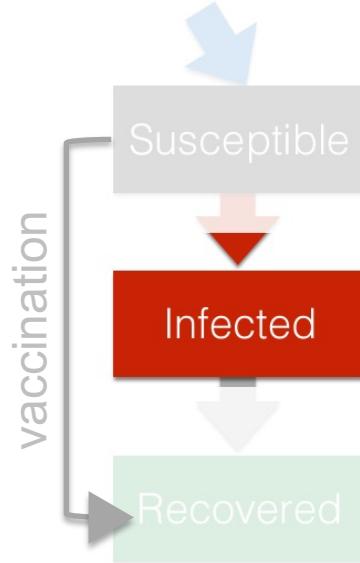
Vaccination coverage data

Serological data

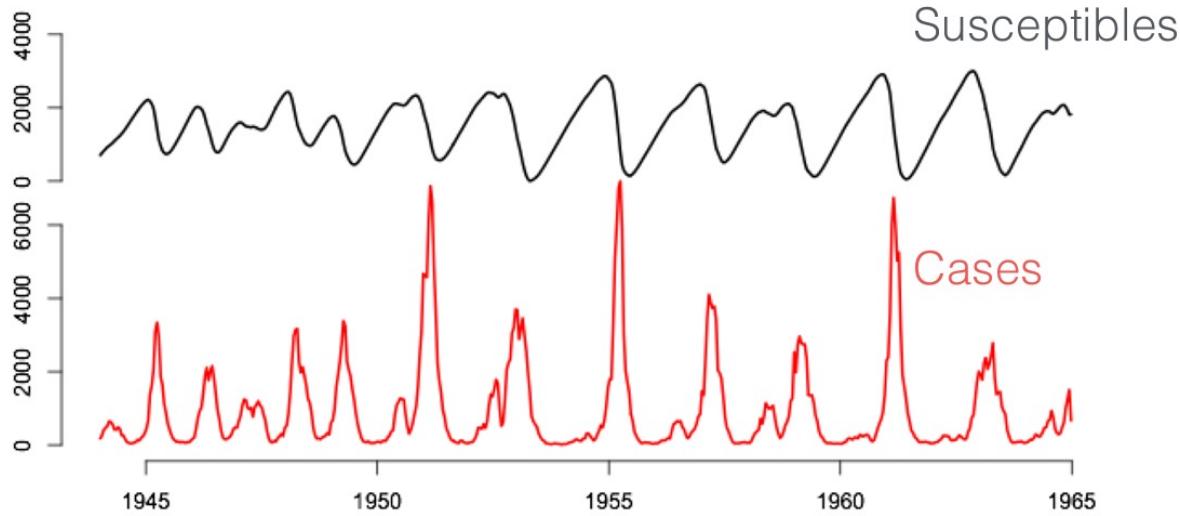
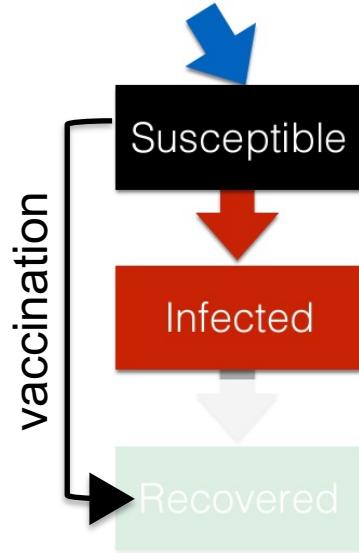
Demographic data



The **central process** in infectious disease epidemiology

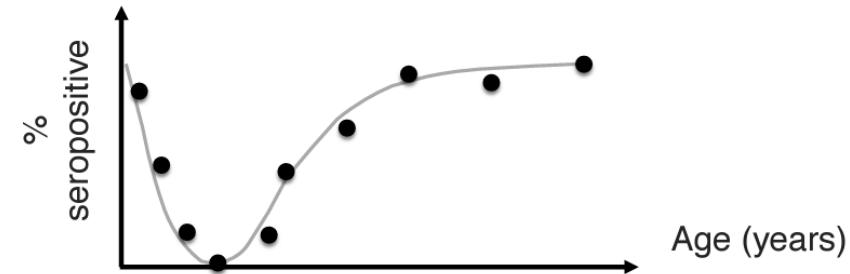
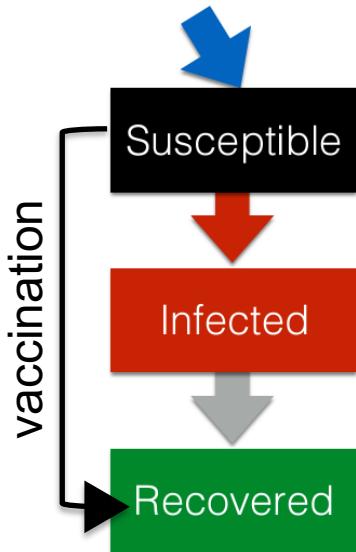


Only **cases** are directly observed



Only **cases** are directly observed
 Susceptibles can be **inferred** with
 sufficiently robust data on births,
 vaccination, and cases through time

Serology can directly measure susceptibles



Only **cases** are directly observed
Susceptibles can be **inferred** with
sufficiently robust data

Focal Questions

	Measles	Rubella
Biology	Directly transmitted, completely immunising Inexpensive, safe and completely immunising vaccination	Directly transmitted, completely immunising Inexpensive, safe and completely immunising vaccination
Burden	Case fatality rate can be high, especially in children.	Mild infection in children, infection during the first trimester of pregnancy can result in birth of a child with CRS.
Current public health context	Control is gathering pace globally, eliminated, or near elimination in many contexts	Introduction of RCV into new contexts , following opening of a GAVI funding window.

Measles

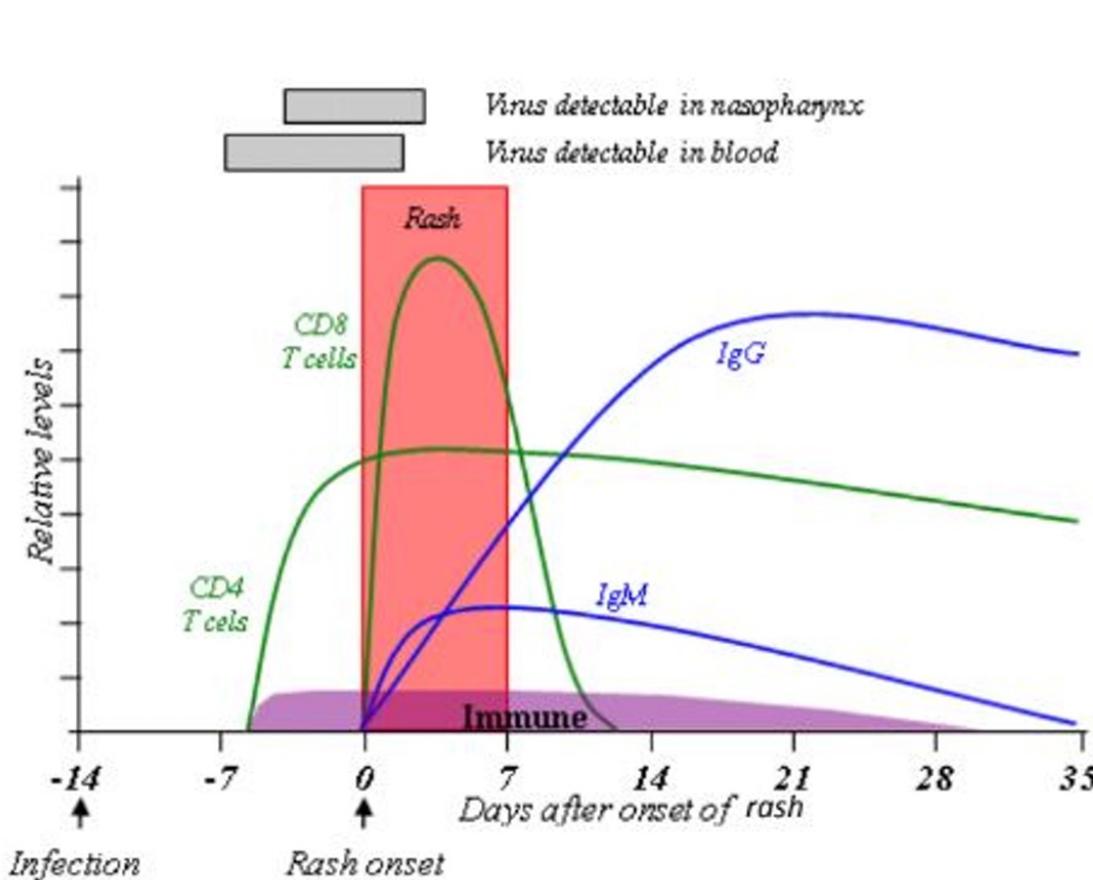
Measles has an R_0 of 12-18

Incubation period: 10-14 days (range 7-23)

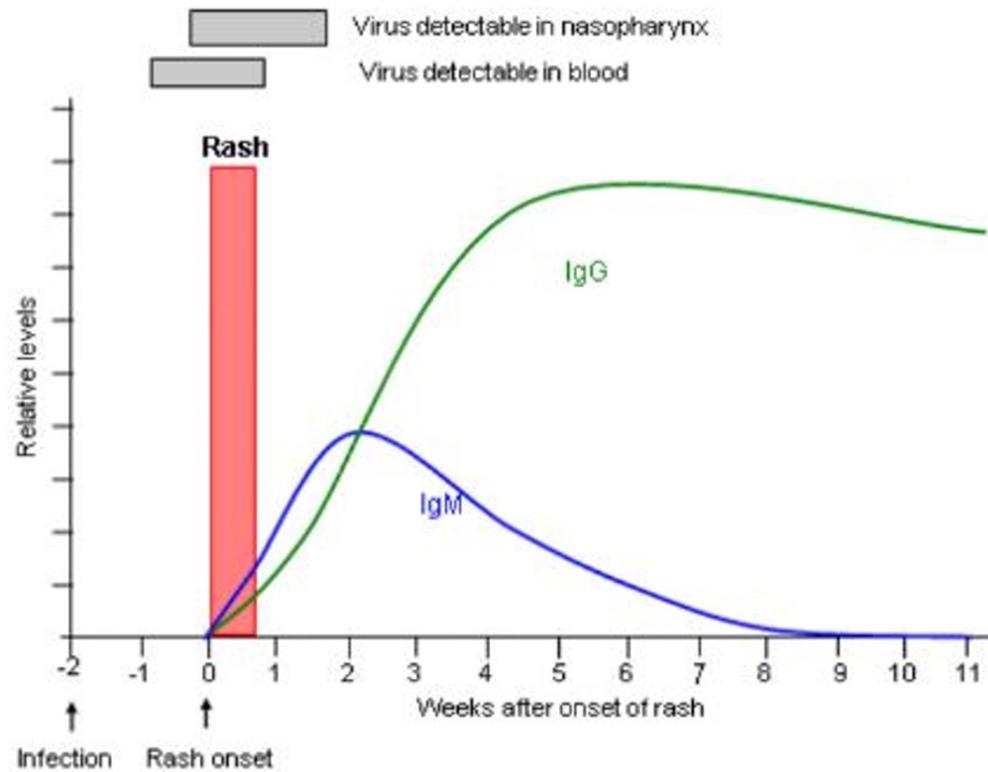
Latent period: 6-9 days

Generation time: 11-12 days

Vaccine effectiveness:
9-11 months old: 84% (IQR 72-95%)
12+ months old: 92.5% (IQR 85-97%)
MCV1 failure => MCV2 95%



Rubella



Rubella has an R_0 of 5-7

Incubation period: 14 days
(range 12-23)

Generation time: 18 days
40-50% of cases are **subclinical**

Vaccine effectiveness:
9+ months old: 95-100%
90-100% in outbreak situations

Slow immune response to vaccines, wait 6-8 weeks after vaccination to assess seroconversion

Ways of collecting case data

Surveillance

- Passive
- Active

Epidemiological Studies

- Case series
- Case control
- Outbreak investigation

Levels of Data Aggregation

Aggregated data

De-identified data

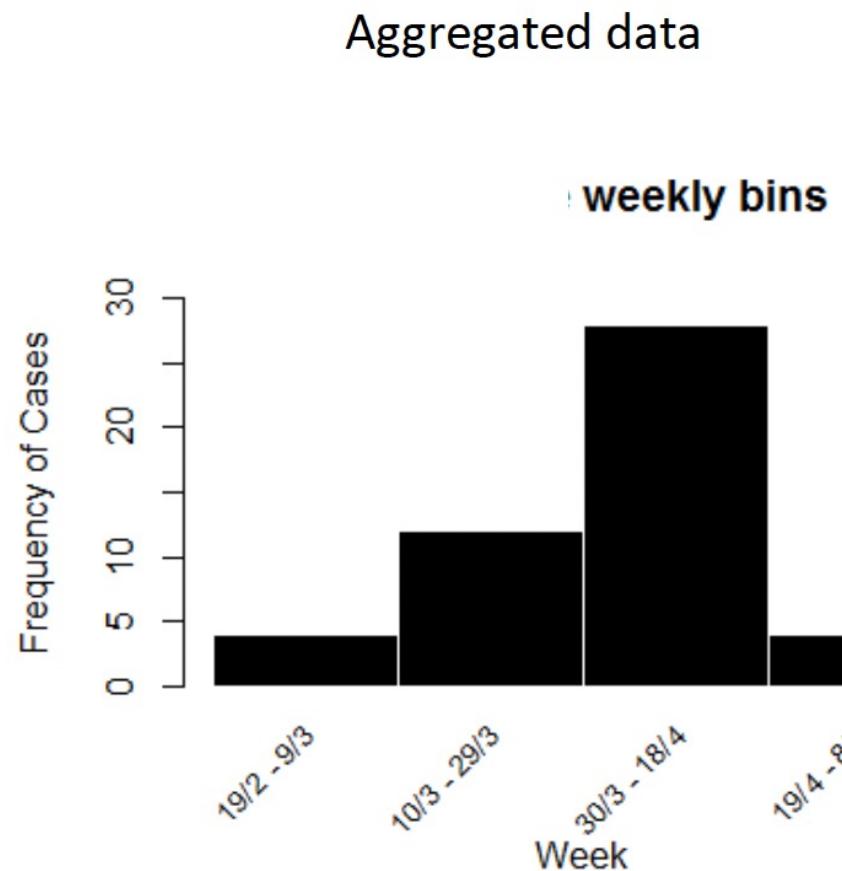
Personally identifying data

Levels of Data Aggregation

Aggregated data

De-identified data

Personally identifying data



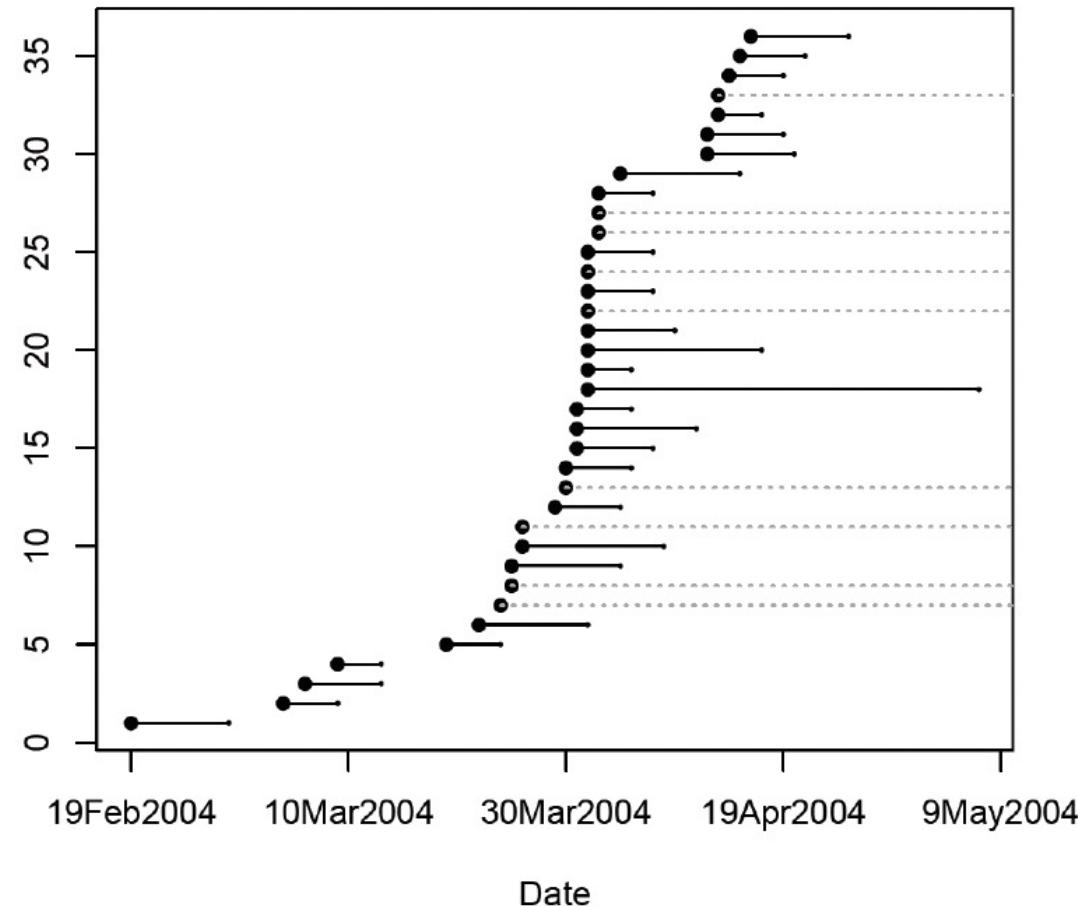
Levels of Data Aggregation

Aggregated data

De-identified data

Personally identifying data

De-identified data



Levels of Data Aggregation

Aggregated data

De-identified data

Personally identifying data

CaselD	Date of birth	Date Symptom Onset	Date Lab Received	Lab Test result
543	17 June 2010	4 Jan 2024	10 Jan 2024	Eq
544	9 July 2023	2 Jan 2024	10 Jan 2024	Pos
545	28 Nov 2021	8 Jan 2024	18 Jan 2024	Neg

Fever-Rash Surveillance System



Under-reporting (non-constant)

NB Rubella: Up to 50% of infections are sub-clinical

What is a measles “case”

Suspected Case = **Clinically compatible case**: fever, rash, 3 Cs (cough, corzya, conjunctivitis)

Epidemiologically linked: clinically compatible +

Confirmed case: clinically compatible + measles-IgM test positive

Other: clinically compatible + measles-IgM test negative

What is a rubella "case"?

Suspected Case = Clinically compatible case: fever, rash, 3 Cs (cough, corzya, conjunctivitis)

Epidemiologically linked: clinically compatible + contact with suspected measles cases

Confirmed case: clinically compatible + rubella-IgM test positive

Bias in measles suspected cases

Other acute infections that may be confused with measles:

- Rubella!
- Scarlet fever
- Human herpes virus type 6 and 7
- Entero- and adenoviruses
- Epstein-Barr virus
- Coxsackievirus
- Parvovirus B19
- Dengue viruses
- Cytomegalovirus
- Chikungunya-virus
- Zika-virus
- West-Nile-virus
- Ross River-virus
- Sindbis-virus

Measles and Rubella Line List

Individual level data made up of the following variables (plus or minus)

- Sex
- Age
- DateOfBirth
- DateSpecimenCollected
- DateSpecimenSentLab
- DateLastVaccination
- DateOfOnset
- DateSpecimenRecInLab
- DistrictOfResidence
- SpecimenCondition
- ReportingFacilty
- StateOfResidence
- DistrictOfResidence
- MeaslesIgM
- RubellaIgM
- FinalClassification

MR Vaccination Coverage

Survey data –

- Population-based survey design
- Include denominator and numerator

Administrative vaccination data –

- Number of doses administered
- Numerator only

Administrative vaccination coverage –

- # doses / population size of target birth cohort
- Denominator from census projections

MR Vaccination Coverage Biases

- Migrant populations captured? If so, where?
- Numerator issues: 2 doses to one child, doses to children not in the target cohort, mis-reporting
- Denominator issues: census mis-reporting, projection uncertainty, population movement

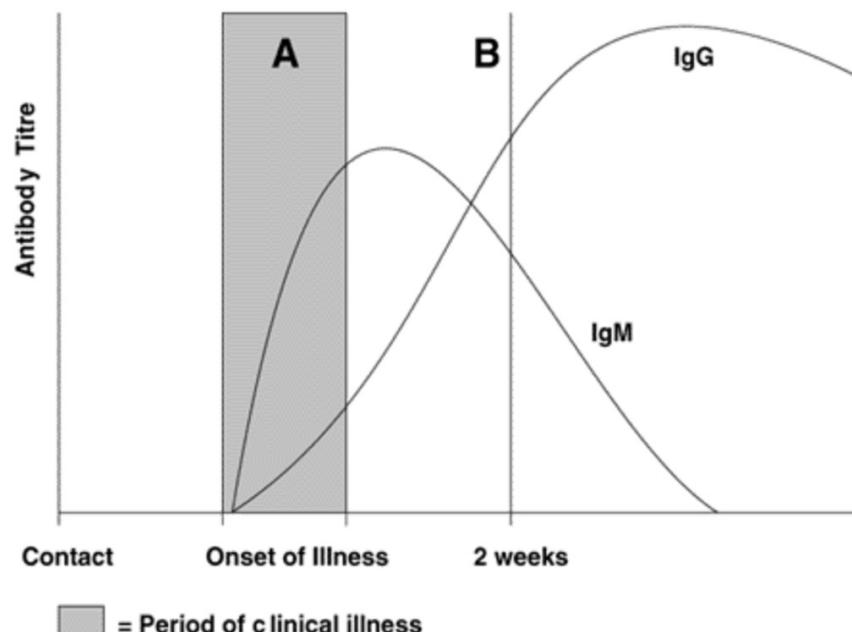
Serological Data

EIA IgM vs PCR

EIA IgG vs PRNT

Strengths

Limitations



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

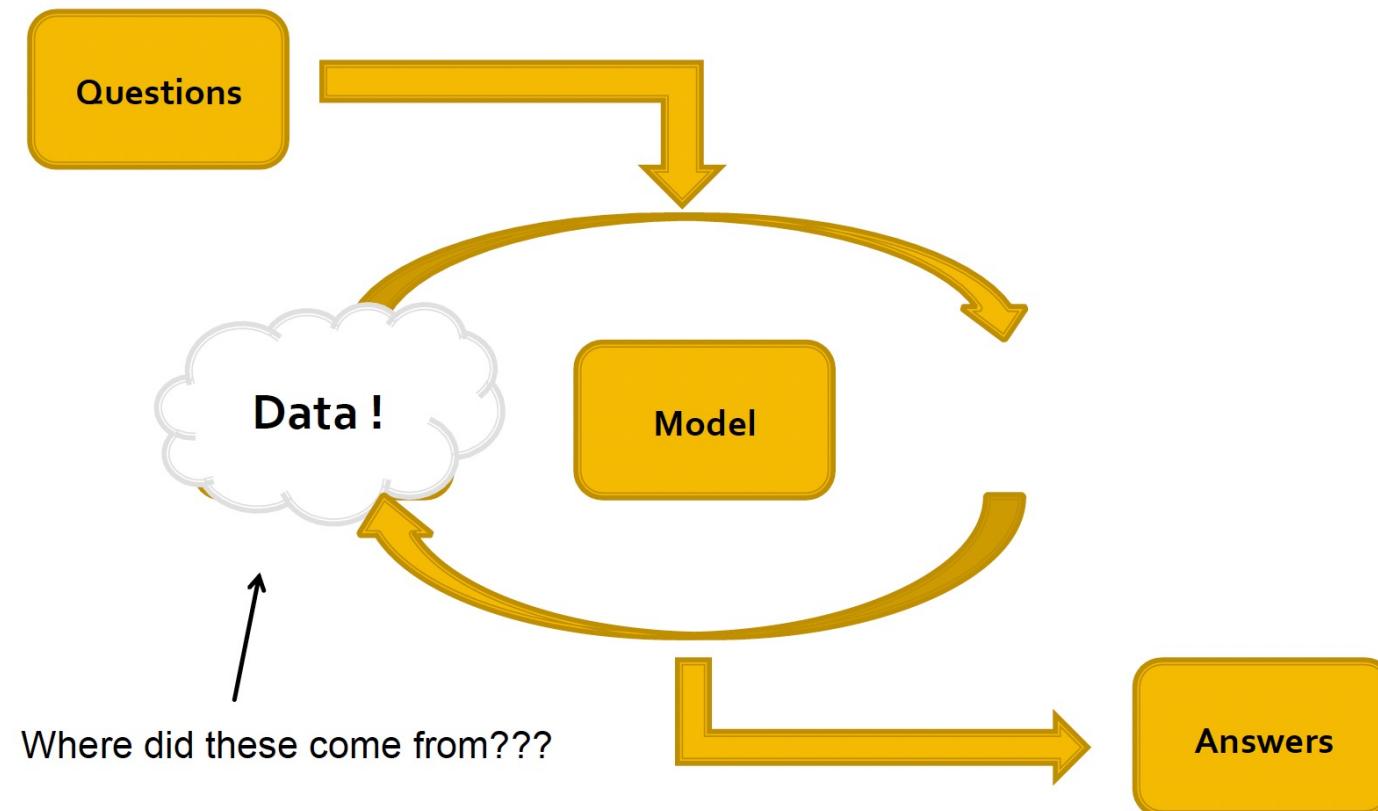
IgM antibodies persist for a few weeks, and are often used as to confirm infection.

How are data related to ID models?

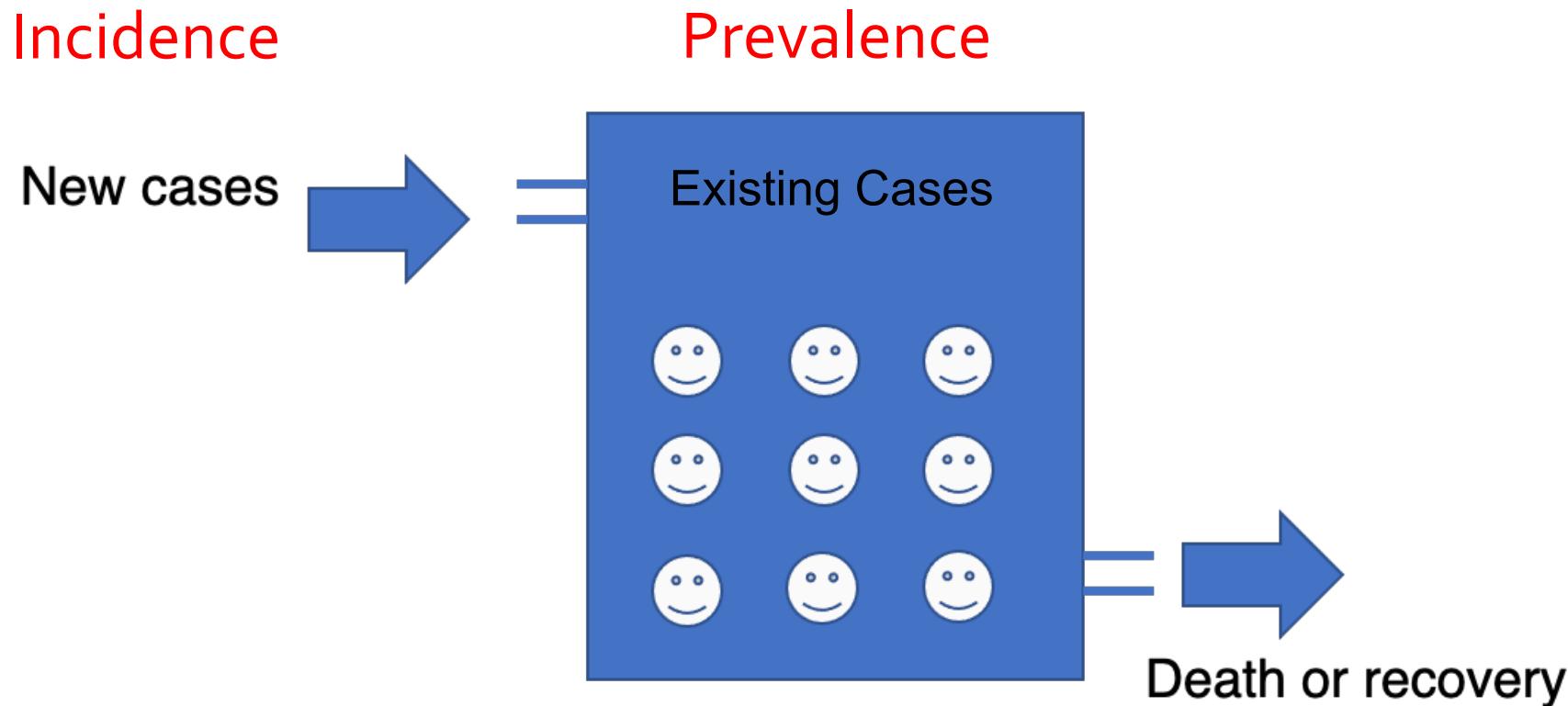
Models and Data

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 for non-fatal disease or survival time for fatal disease)

Measures of Disease Frequency

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

Cumulative incidence
Attack rate

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

Incidence density rate

Risk vs Rate

The parameters which go into difference equations should be risks

e.g. the number of individuals who are infectious at time $t+1$ =
{number who were infected at time t }

\times

{proportion who became infectious between t and $t+1$ }

However, under for most situations, the risk \approx rate

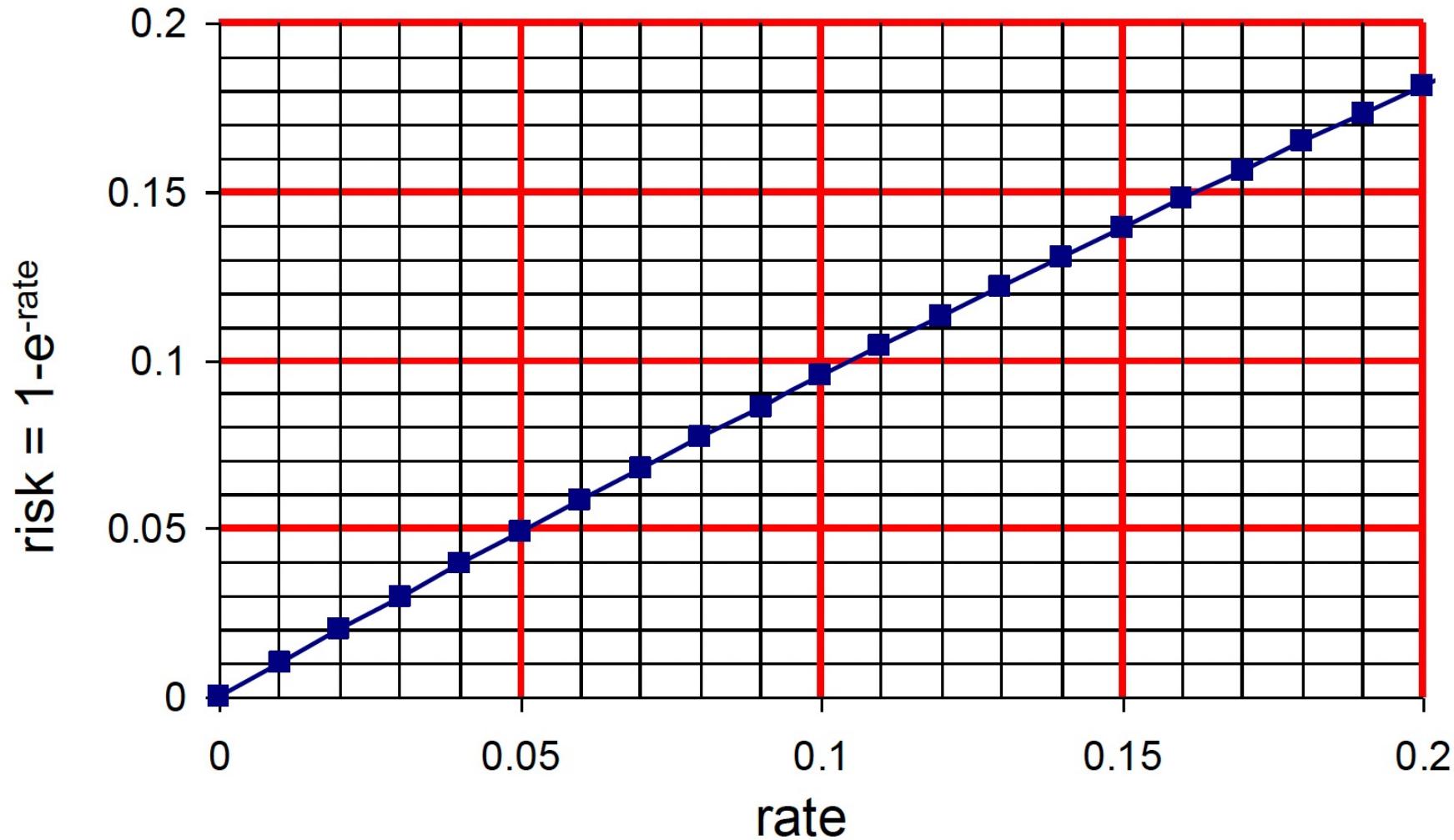
From previous training you may recall:

Risks and rates are related through the following expression:

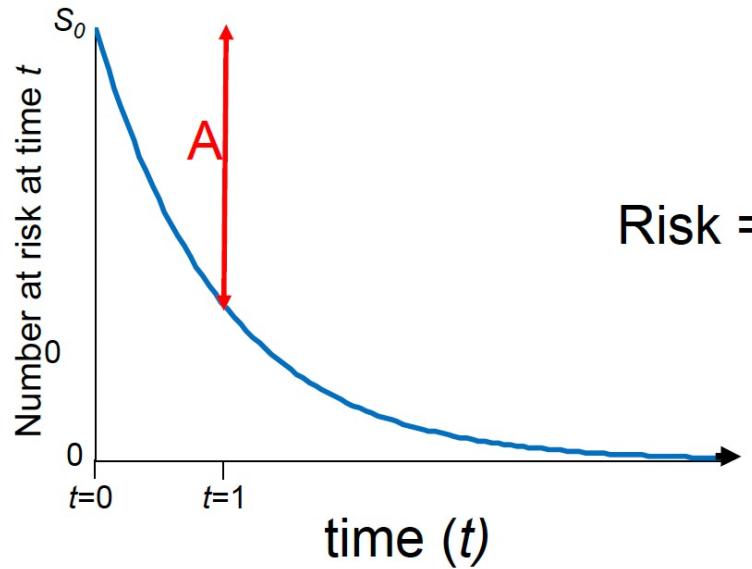
$$\text{risk} = 1 - e^{-\text{rate}}$$

If the rate is small, then $e^{-\text{rate}} \approx 1 - \text{rate}$, and so risk \approx rate

Risk vs Rate



Risk vs Rate



Risk = $\frac{\text{number who became cases (A)}}{\text{number at risk at the start } (S_0)}$

Rate = $\frac{\text{Number of new cases (A)}}{\text{Total person-time at risk}}$

Accounts for fact that those who develop disease by point A would have become cases in the meantime

Rate to Average Time

The rate at which something occurs

$$= 1/\{\text{average time to the event}\}$$

The rate at which individuals become infectious

$$= 1/\{\text{average pre-infectious period}\}$$

The rate at which individuals recover from being infectious

$$= 1/\{\text{average duration of infectiousness}\}$$

The mortality rate

$$= 1/\{\text{average "duration of life" or the life expectancy}\}$$

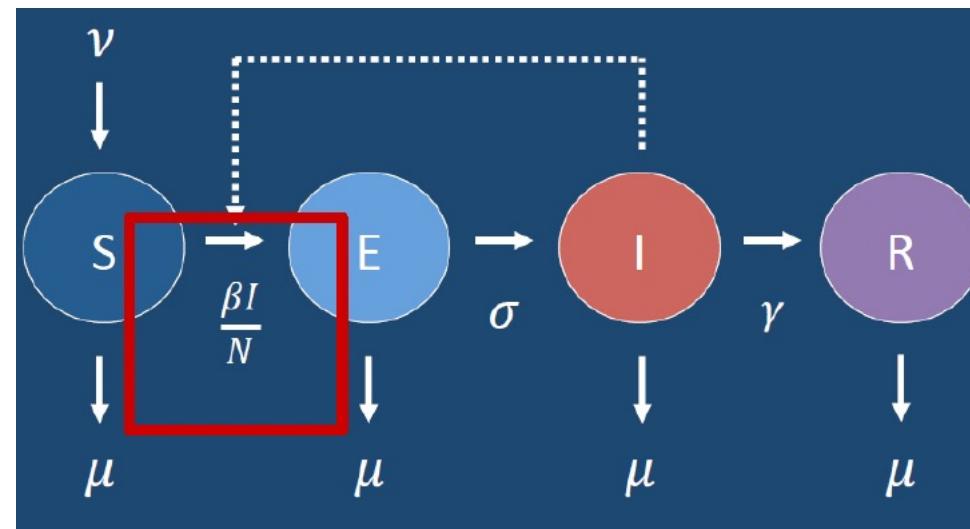
Metrics to measure disease presence and spread of disease

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

Metrics to measles presence and spread of disease

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

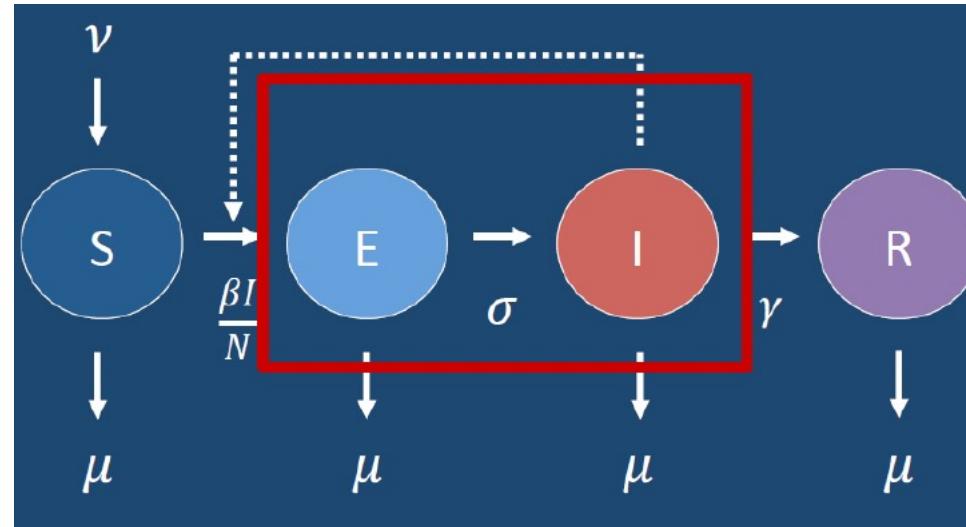
Reminder: E (exposed) class = infected but pre-infectious
 $\beta SI/N$



Metrics to measles presence and spread of disease

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

$$(E+I) / N$$

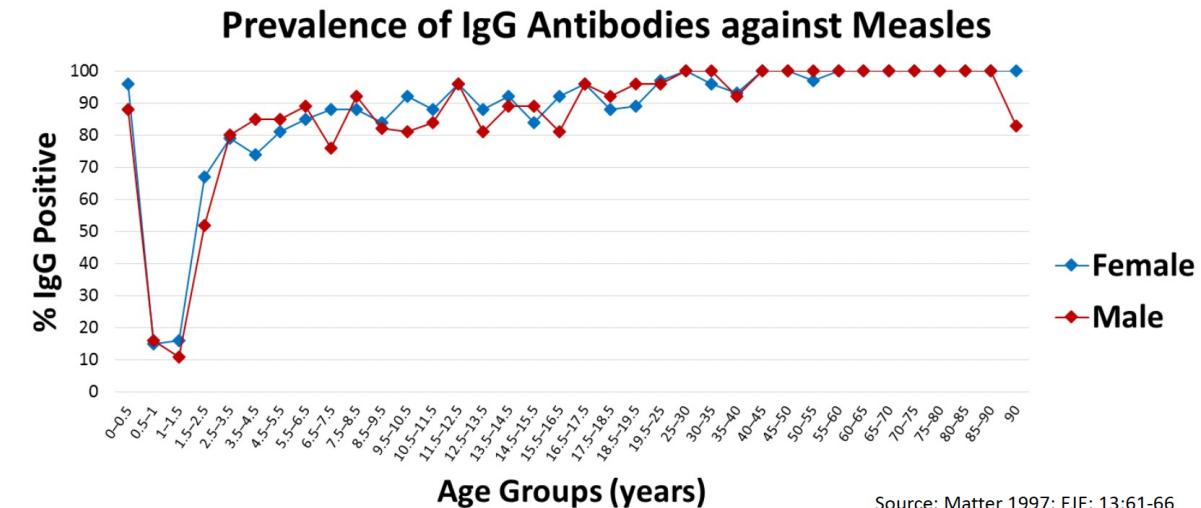
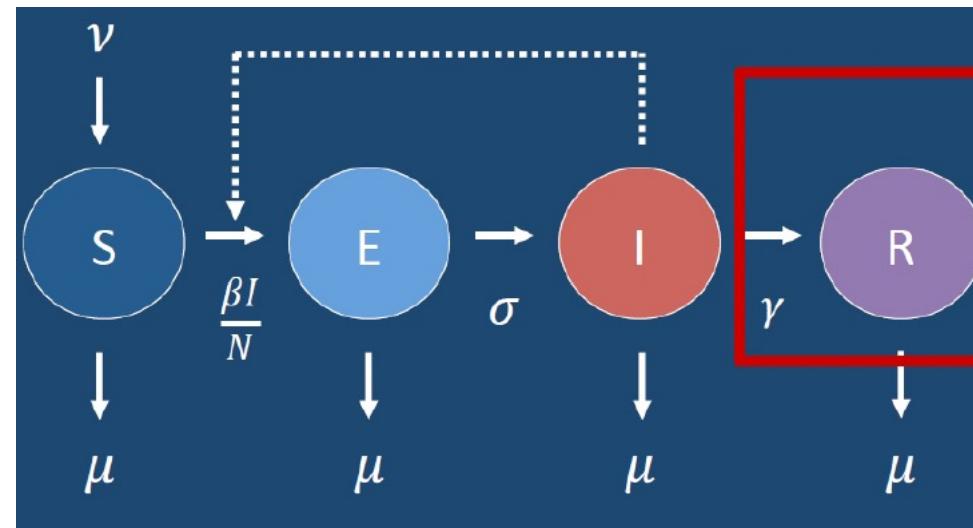


Metrics to measles presence and spread of disease

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

Can be related to:
• Prevalence of infection or
• Past infection

R / N



Source: Matter 1997; EJE; 13:61-66

Citations – These Slides were modified from the following:

Thunbi SM, Bruce F, Bellan SE, Pulliam JRCP.
“Introduction to Infectious Disease Data” Clinic on the
Meaningful Modeling of
Epidemiological Data.
<https://doi.org/10.6084/m9.figshare.5044603.v4>

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Mark Jit, LSHTM

Bellan, Steven; Borcherding, Rebecca; Bruce, Faikah;
Dushoff, Jonathan; Grebe, Eduard; Hargrove, John; et al.
(2017). International Clinics on Infectious Disease
Dynamics and Data. figshare. Collection.
<https://doi.org/10.6084/m9.figshare.c.3788224.v13>

Emilia Vynnycky, UKHSA