Conceptual models of cross-immunity, and practical applications

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Dynamical models of disease spread

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UNICEF McMaster's 2025 Panel Event

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Outline

What is dynamical modeling?

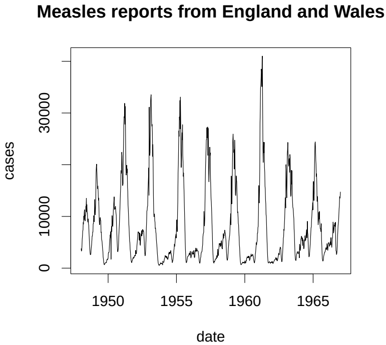
Modeling approaches

- Deterministic models
- Stochastic models
- Statistical fitting

Limitations

- Heterogeneity
- Behavioural changes

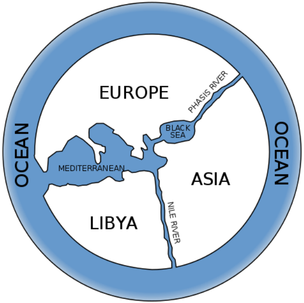
Dynamical modeling connects scales



- Start with rules about how things change in short time steps
  - Usually based on *individuals*
- Calculate results over longer time periods
  - Usually about *populations*
- Also known as “mechanistic” or “mathematical”

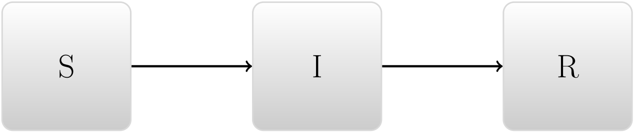
Model worlds

- A dynamical model is based on a model world
- The model world has *enough* assumptions to allow us to calculate dynamics
- The model world is *simpler* than the real world
- Essentially, all models are wrong, but some are useful. – Box and Draper (1987), *Empirical Model Building . . .*



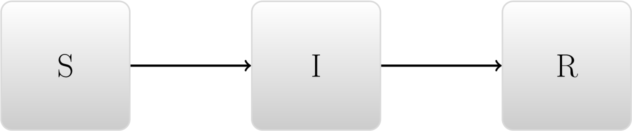
Simple models of disease spread

- Divide people into categories:

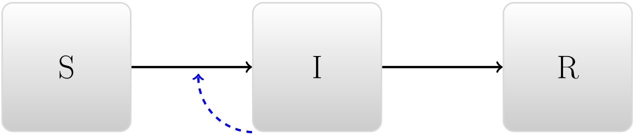


- Susceptible: can be infected
- Infectious: can infect others
- Recovered: cannot be infected

PRESLIDE What determines transition rates?



What determines transition rates?



- People get better independently
- People get infected by infectious people

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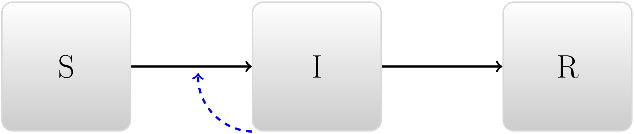
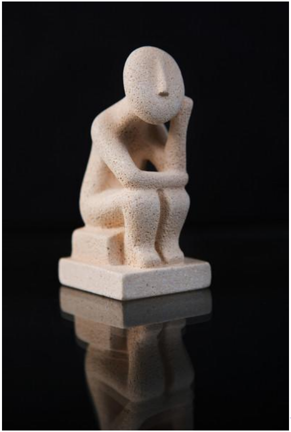
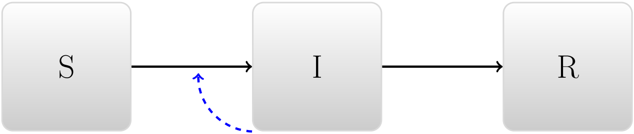
Conceptual modeling





Conceptual modeling



- What is the final result?
- How do disease levels change?
- When does disease increase, decrease?

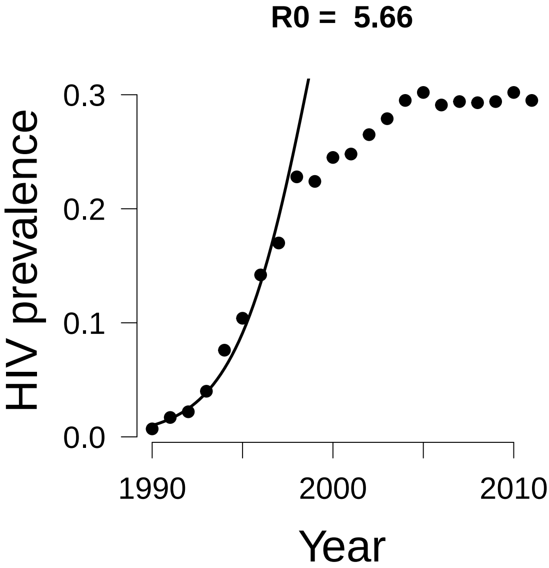
Result: change tends to be exponential

- The number of people recovering or becoming infected is *proportional* to the number infected
  - I infect three people, they each infect 3 people ...
  - How fast does disease grow?
  - How quickly do we need to respond?

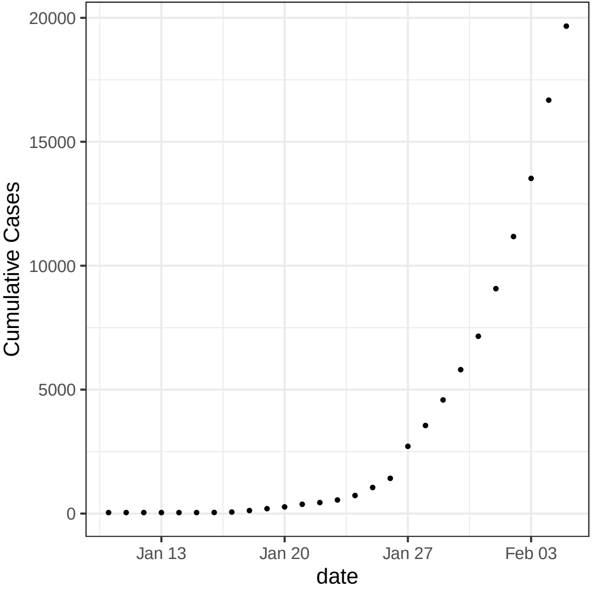
little r

- We measure epidemic *speed* using little r:
  - *Units*: [1/time]
  - Disease increases like e^{rt}
- Characteristic time scale is $C = 1/r$
  - Closely related to doubling time
  - COVID, $C \approx 1\mathrm{month}$
  - HIV in SSA, $C \approx 18\mathrm{month}$
- Often focus on initial period (may also say r_0)

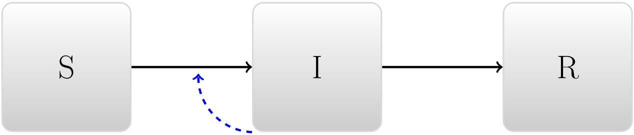
Exponential growth



Exponential growth



Result: disease does not always spread



- If rate out of I is faster than the rate into I
- I $\rightarrow$ 0 and the outbreak stops

Concept: reproductive number

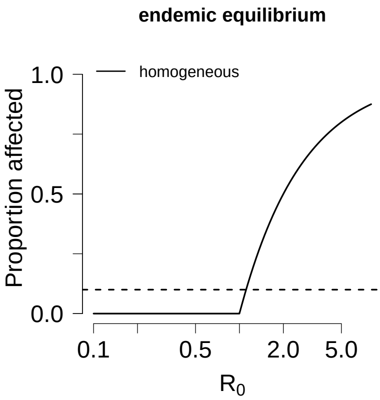
- $\mathcal{R}$ is the number of people who would be infected by an infectious individual *in a fully susceptible population.*

- $\mathcal{R} = \beta/\gamma = \beta D = (cp)D$
  - c: Contact Rate
  - p: Probability of transmission (infectivity)
  - D: Average duration of infection

- A disease can invade a population if and only if $\mathcal{R} > 1$.

- Often focus on initial period (may also say $\mathcal{R}_0$)

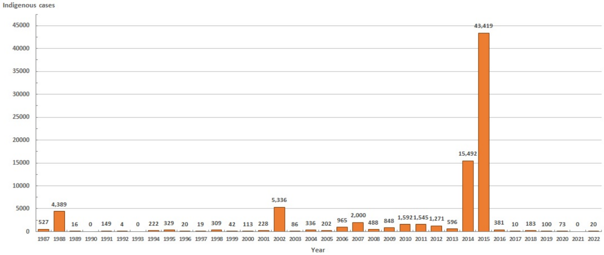
Yellow fever in Panama



Example: Dengue (Taiwan CDC)

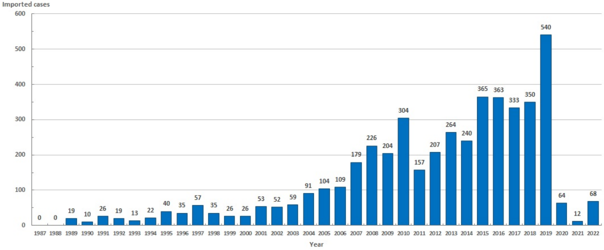
Indigenous cases

40,000

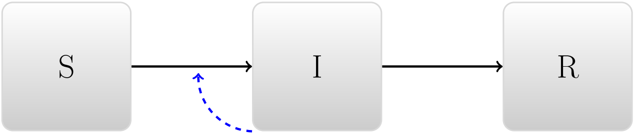


Imported cases

500



Result: not every one gets infected



- When S gets low, then I goes down and the outbreak stops
- There is not always a reason why you didn't get infected!
  - Remember the model world
  - Everyone in this model is assumed to be the same

Next steps

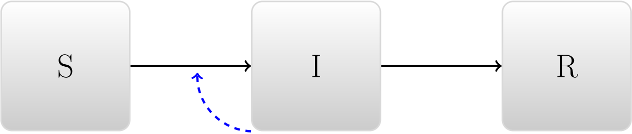
- We can *implement* the model and see what it's going to do
- This requires more assumptions, for example:
  - Time steps or continuous time?
  - Deterministic or stochastic?

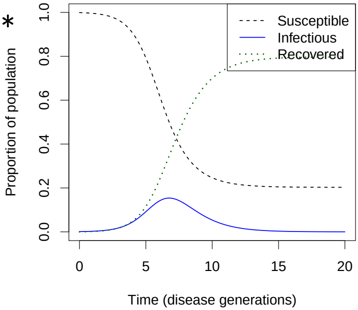
Outline

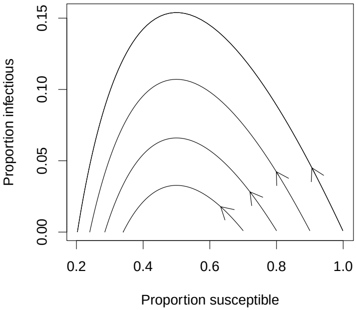
Deterministic models

- For a given set of assumptions, a deterministic model always predicts the same results
- In other words, our model world *determines* the outcome

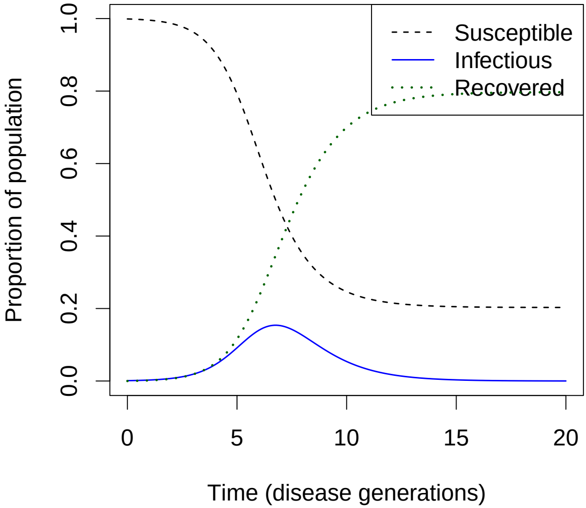
Simulations



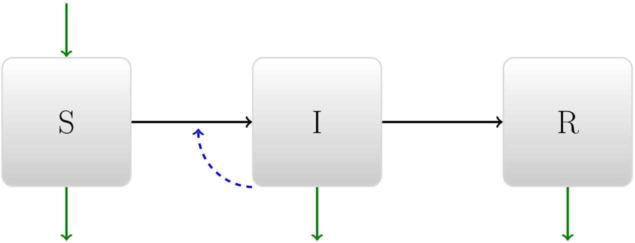




Simulations (repeat)

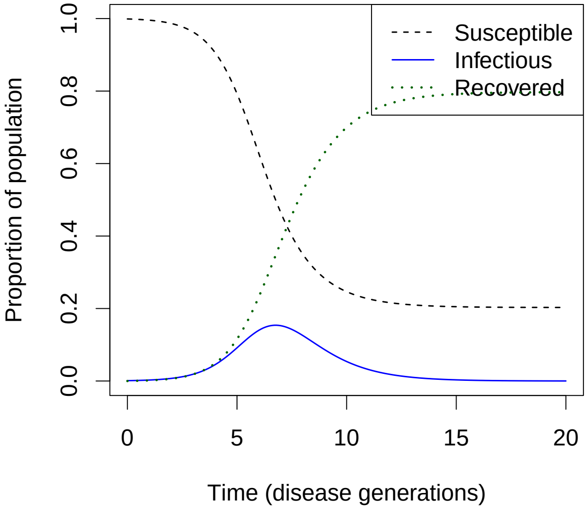


Closing the circle

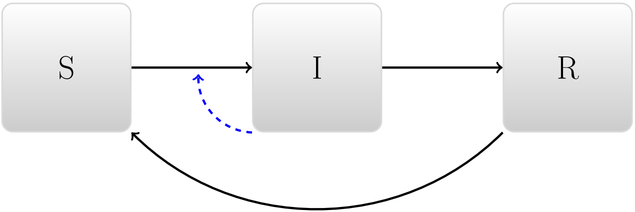


- * Births and deaths

Closing the circle (repeat)

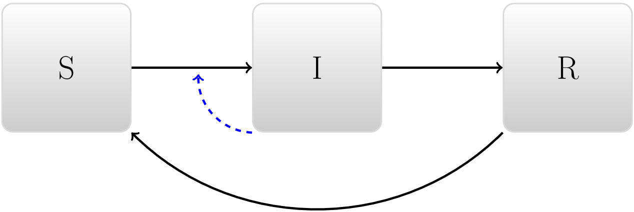


Closing the circle



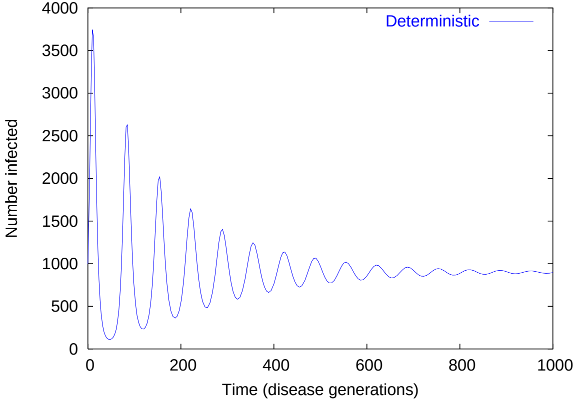
- * Loss of immunity

Processes and rates

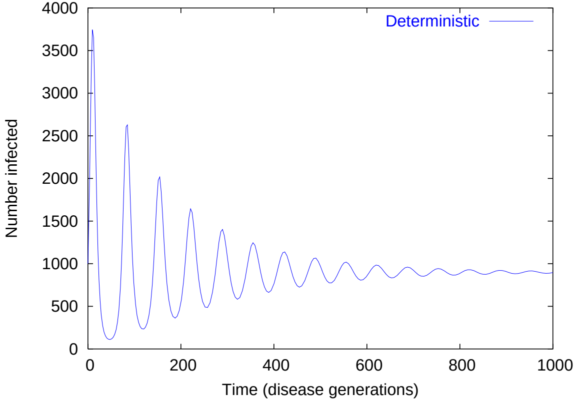


Event	**transition**	**rate**	**Effect** (S, I)
Infection	$S \to I$	$\beta SI/N$	$(-1, 1)$
Recovery	$I \to R$	γI	$(0, -1)$
Loss of immunity	$R \to S$	$\mu(N - S - I)$	$(1, 0)$

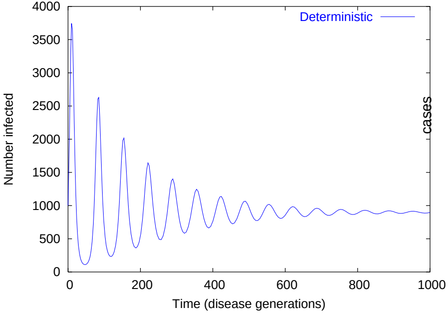
Result: Diseases tend to oscillate



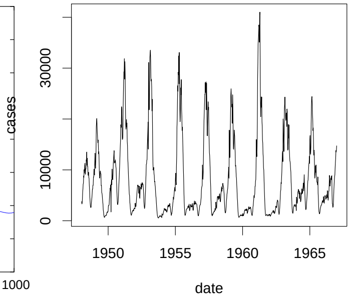
Result: Oscillations tend to be damped



What is missing from our model world? (repeat)

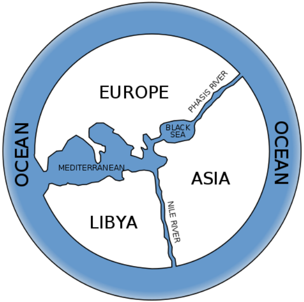


Measles reports from England and Wales



What is missing from our model world?

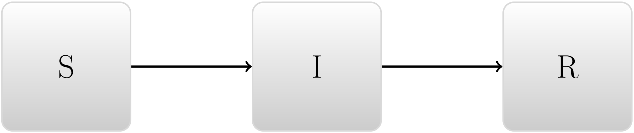
- Almost everything! So what's important?
- * Seasonality
- * Chinese New Year!
- * School terms
- * Randomness
- * *Any* of these things can amplify damped oscillations



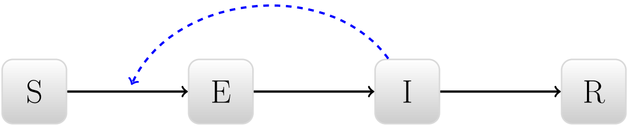
Example: Ebola transmission

- How much Ebola spread occurs before vs. after death
- Highly context dependent
  - Funeral practices, disease knowledge
- *Weitz and Dushoff Scientific Reports 5:8751.*

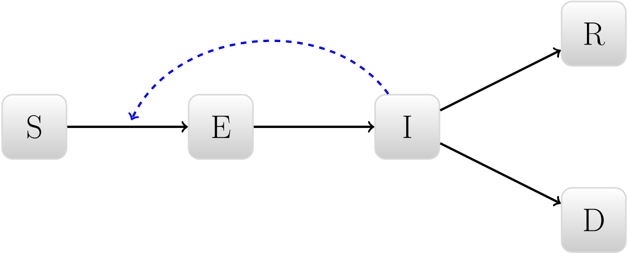
Simple disease model (repeat)



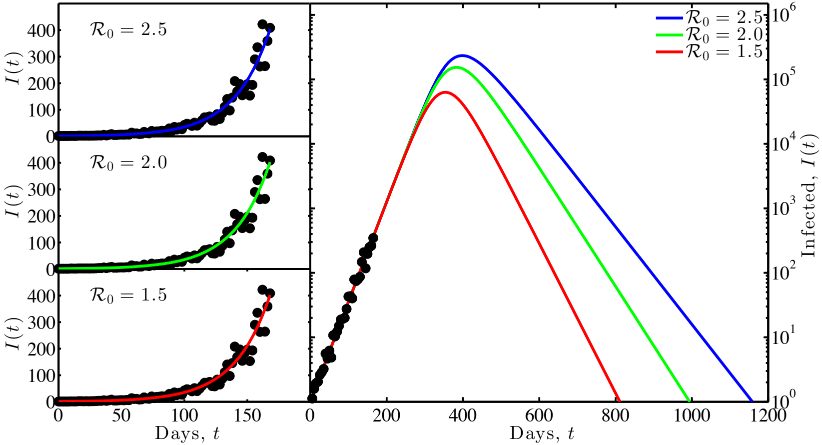
Model with latent period



Include post-death transmission

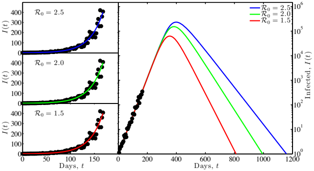


Result: generation interval links $r\mathcal{R}$(preview)

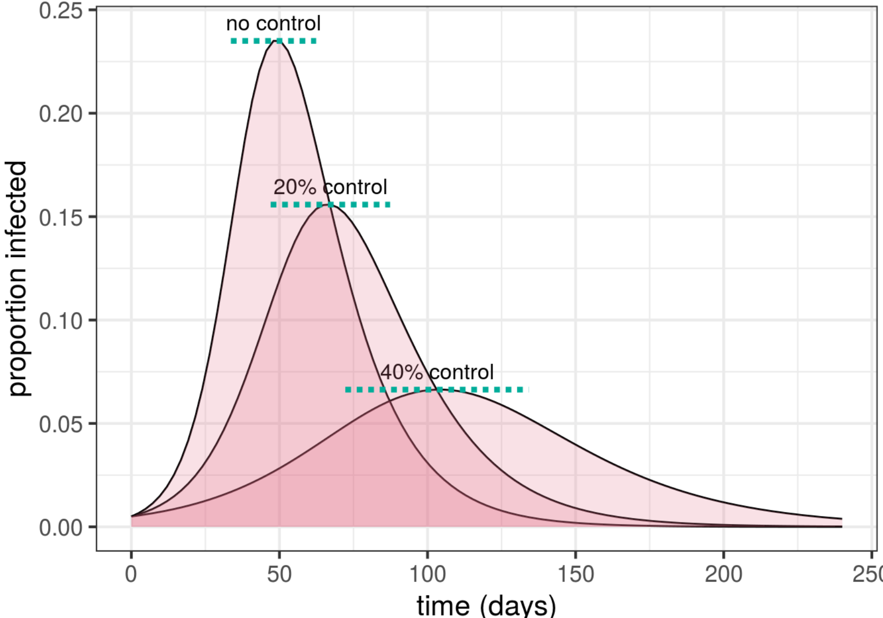


Result: generation interval links $r\mathcal{R}$

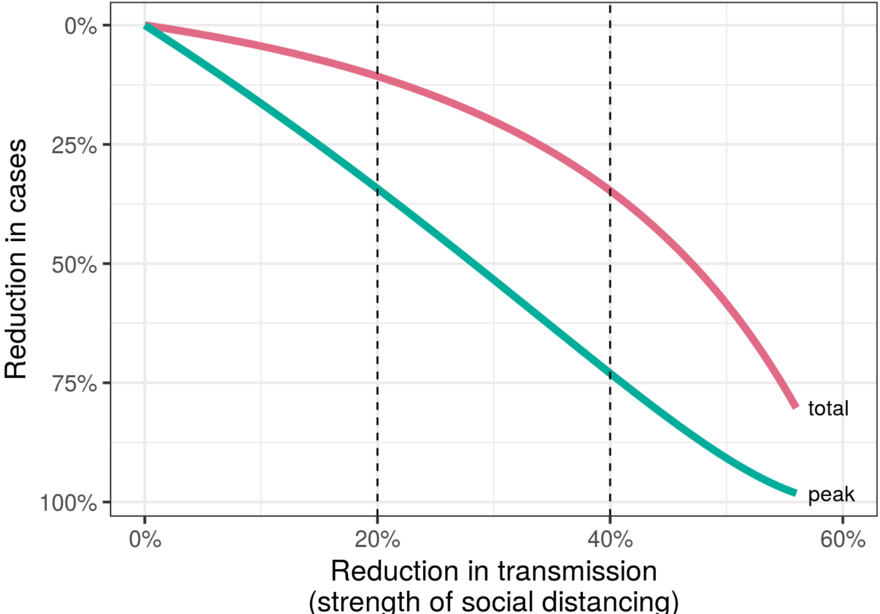
- Mechanistic view: If we know $\mathcal{R}$, faster generations mean faster spread (bigger r)
- Phenomenological view: If we know r, slower generations mean stronger spread (bigger $\mathcal{R}$)



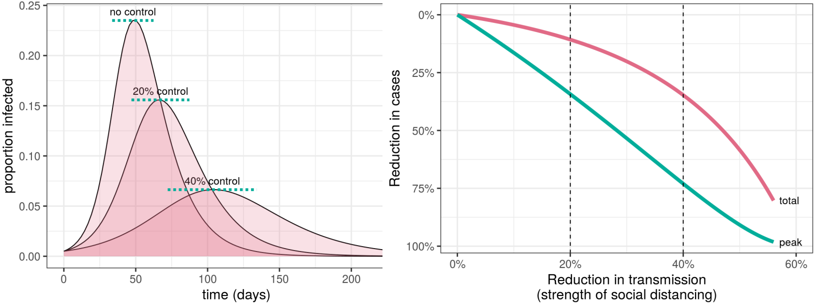
Example: COVID: flatten the curve



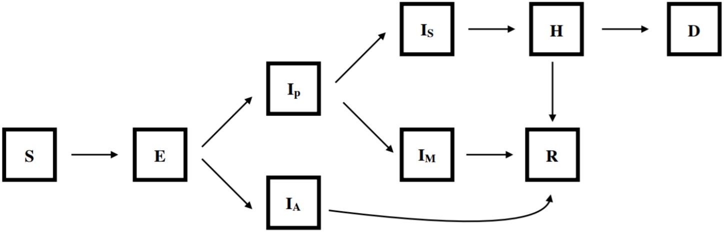
Example: COVID



Result: It is easier to reduce the peak than the total cases



More box models



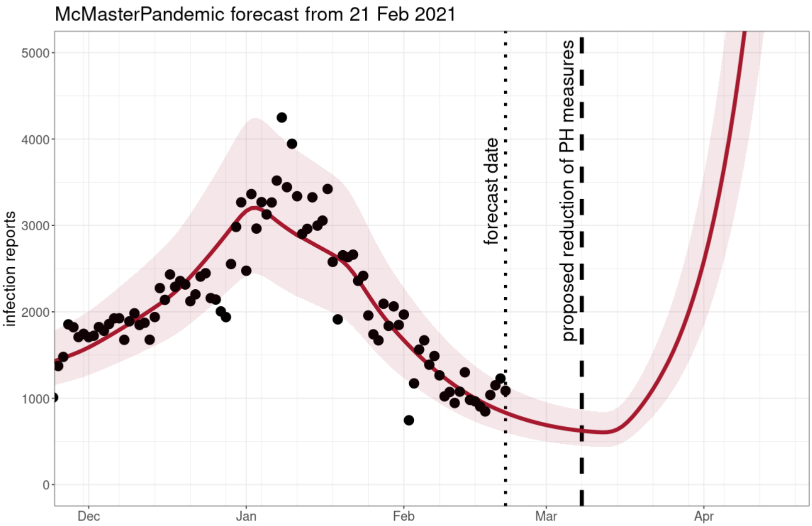
S = susceptible
E = exposed

I_P = pre-symptomatic
I_A = asymptomatic
I_S = symptomatic, severe case
I_M = symptomatic, minor case

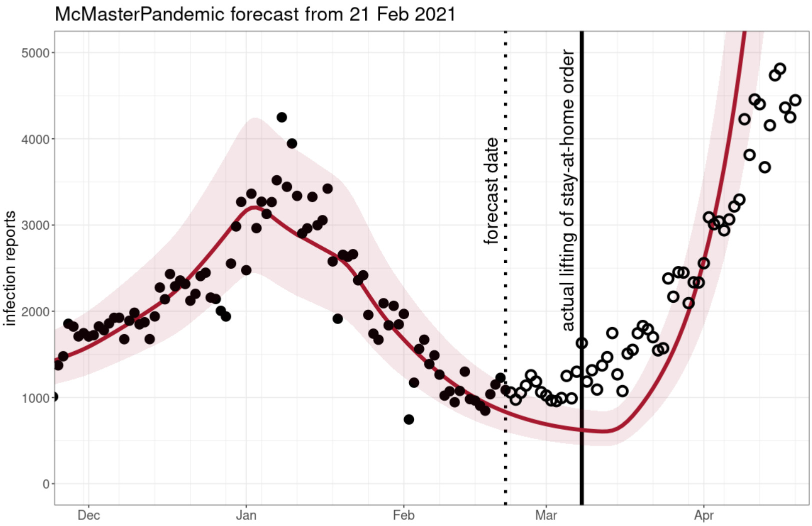
H = hospitalized
R = recovered
D = dead

Childs et al., http://covid-measures.stanford.edu/

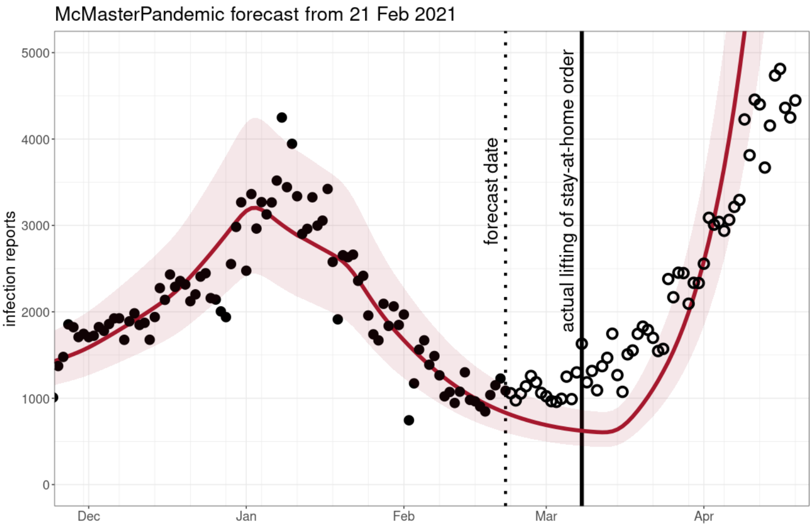
Example: COVID waves (preview)



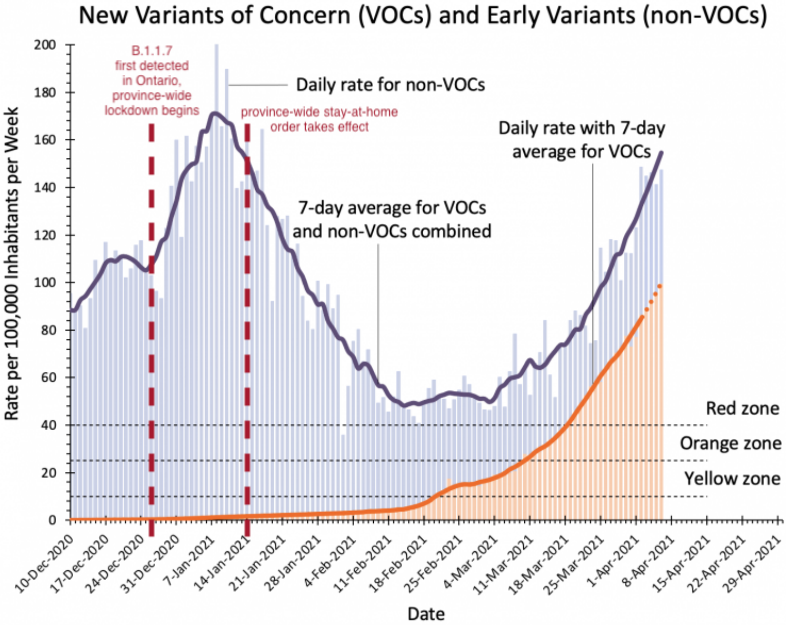
Example: COVID waves (preview)



Example: COVID waves

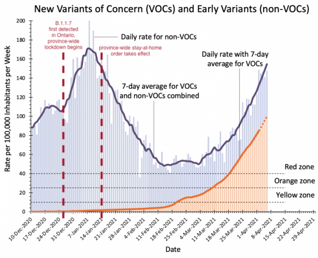


Example: COVID waves (preview)



Example: COVID waves

- alpha variant was increasing even though total was decreasing
- using a dynamical perspective allows us to project the effect of this



The daily rates of new variants of concern (VOCs) for the last 4 days are predicted.

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Stochastic models

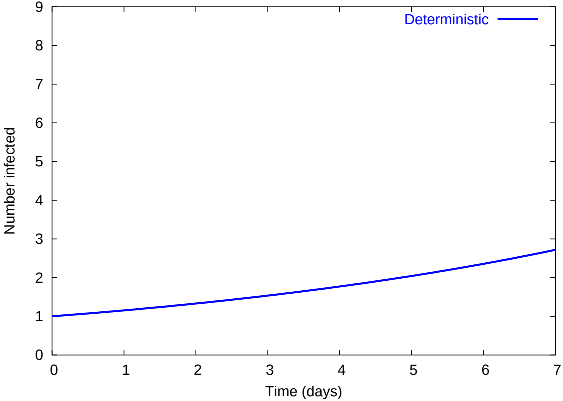
- For a given set of assumptions, a stochastic model predicts a variety of possible results
- In other words, there is room for randomness (stochasticity) inside our model world
  - We may think the world is really stochastic
  - Or simply that there are things we can't predict ...

Types of stochasticity

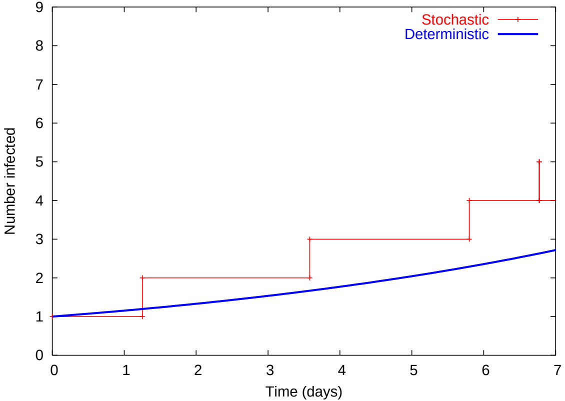
Event	**transition**	**rate**	**Effect** (S, I)
Infection	$S \to I$	$\beta SI/N$	$(-1, 1)$
Recovery	$I \to R$	γI	$(0, -1)$
Loss of immunity	$R \to S$	$\mu(N - S - I)$	$(1, 0)$

- We can add random changes to the rates
  - Contact rate (β), for example, may go up and down for reasons we can't predict
- We also get a stochastic model even by just treating individuals as individuals!

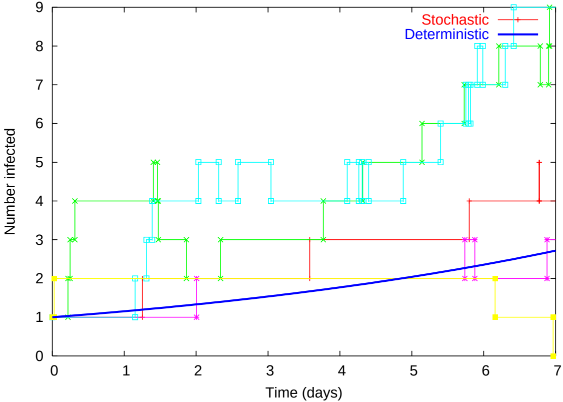
Deterministic spread



Demographic spread



Demographic spread



- Demographic refers to the *minimum* stochasticity corresponding to treating individuals as individuals

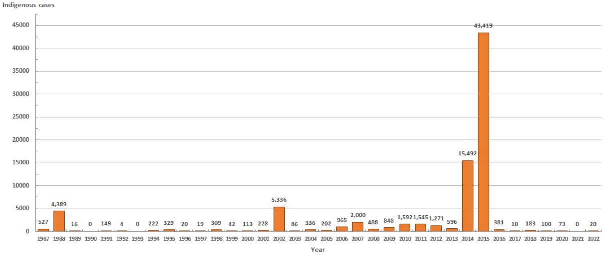
Result: outbreaks can die out at random

- In simple models, the probability of a single introduction going extinct at random is $1/\mathcal{R}$
- If an introduction does not lead to an outbreak, there's not always a reason

Result: Pattern of outbreak sizes is related to $\mathcal{R}$(repeat)

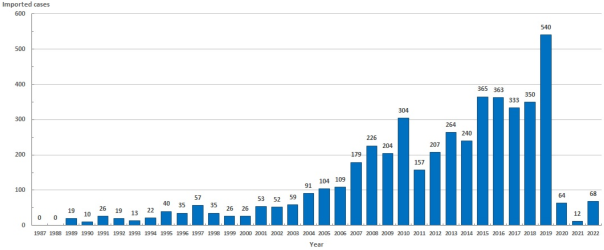
Indigenous cases

40,000

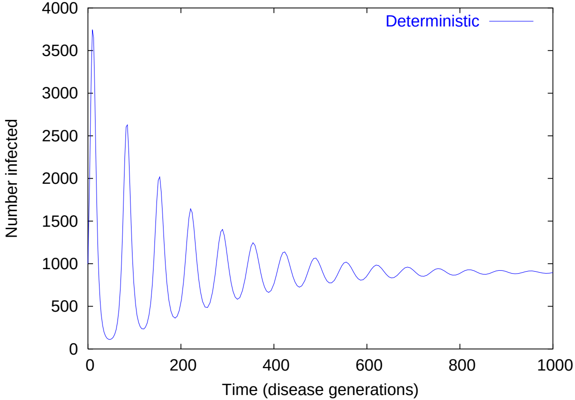


Imported cases

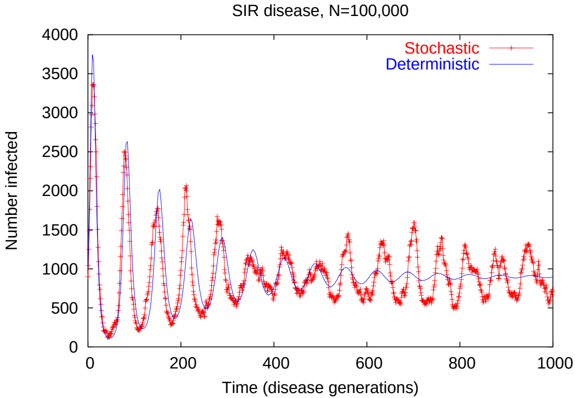
500



Result: stochasticity interacts with oscillations (preview)

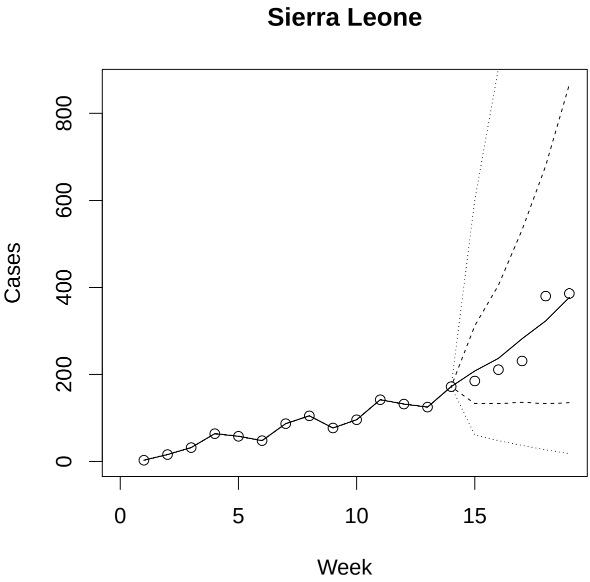


Result: stochasticity interacts with oscillations



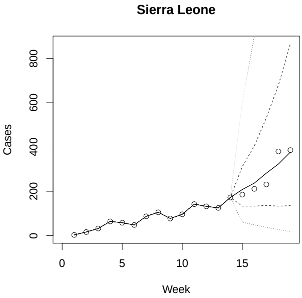
Outline

Statistical fitting



Statistical fitting

- How certain or uncertain are our projections?
- What else do we need to know?



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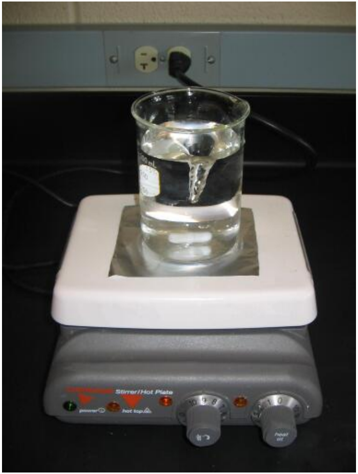
Heterogeneity



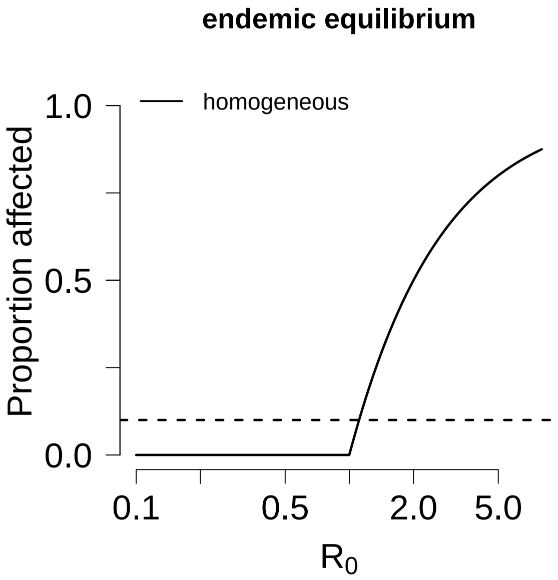
- Simple models treat the world like this cup
- People are all the same
- Perfectly mixed
- *Lots of people*
  - (for deterministic models)

Human heterogeneity

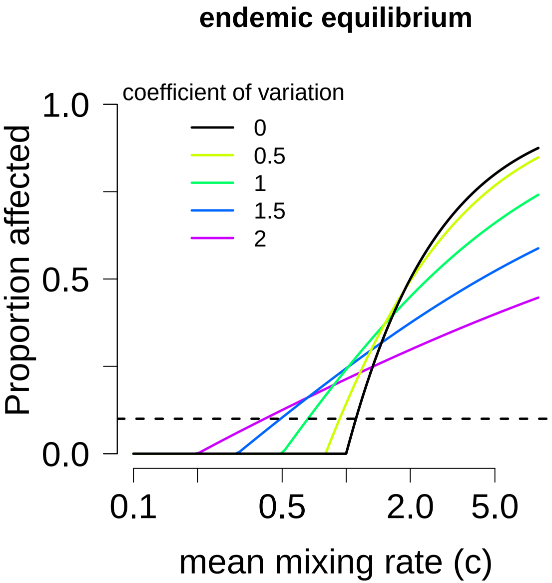
Human heterogeneity

Human heterogeneity

Example: Gonorrhea

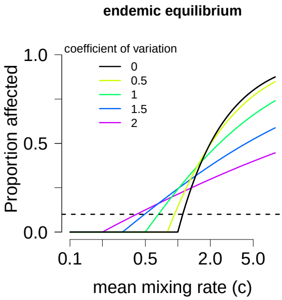


Example: Gonorrhea

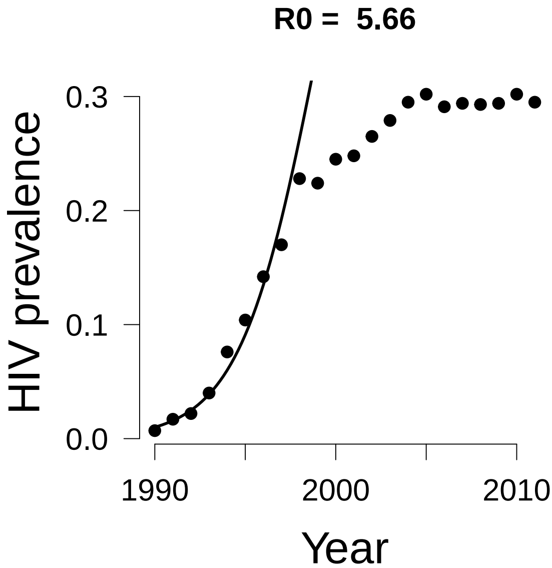


Result: heterogeneity makes incidence robust

- Disease levels are more resistant to change
- Higher when averaged transmission is low
- Lower when averaged transmission is high



Example: HIV



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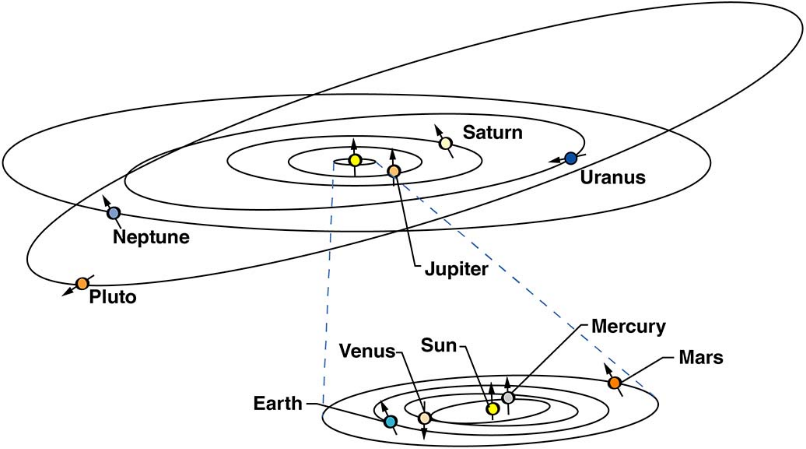
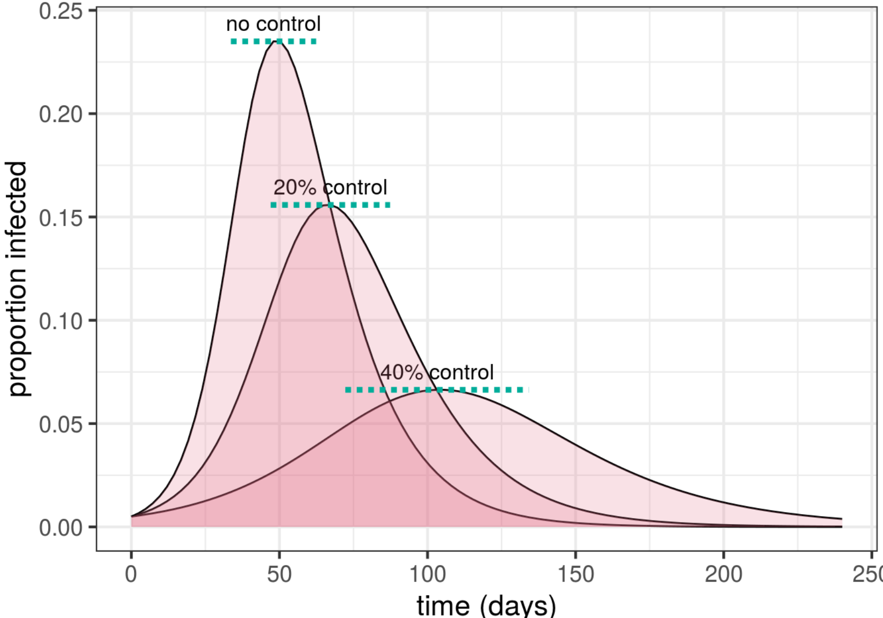
Behavioural changes

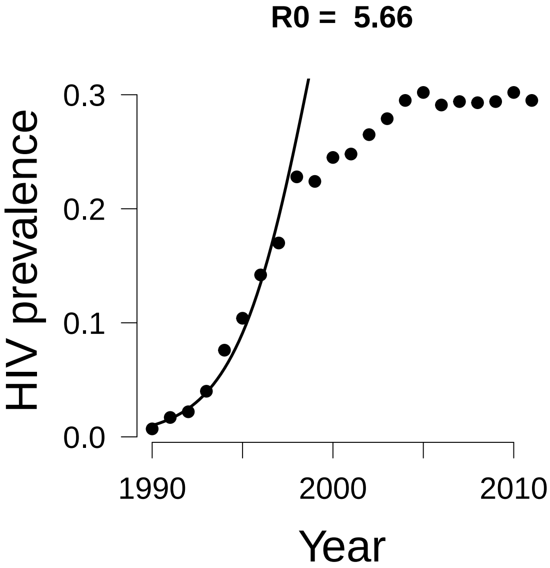
- I can calculate the motion of heavenly bodies, but not the madness of people. – Isaac Newton



Example: COVID



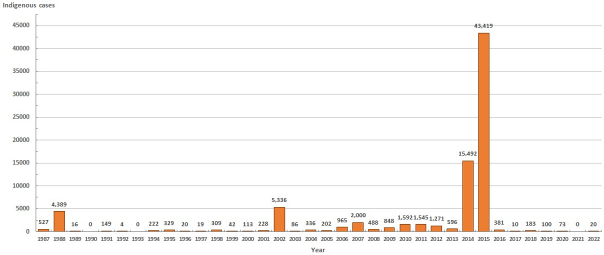
Example: HIV



Example: Dengue (Taiwan CDC)

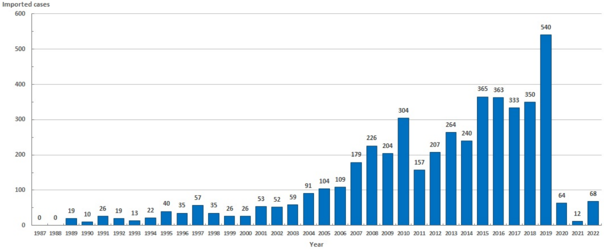
Indigenous cases

40,000

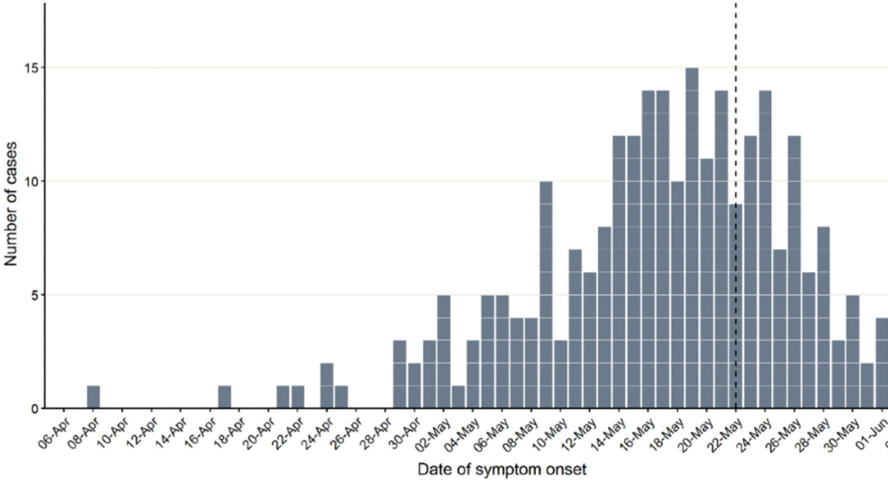


Imported cases

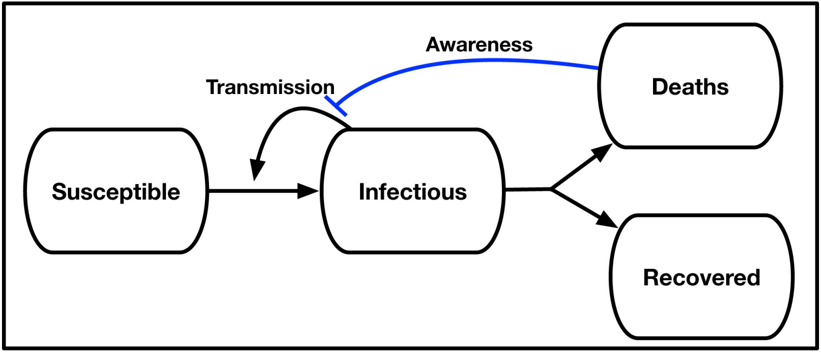
500



Example: mpox



Example: COVID awareness



Weitz et al.

https://www.pnas.org/doi/10.1073/pnas.2009911117

Summary

- Dynamical models are an essential tool to link scales
- Very simple models can provide useful insights
- More complex models can provide more detail, but also require more assumptions, and more choices
  - Statistical fitting can guide in interpretation
- We can evaluate assumptions
  - What was right, what was wrong?
  - What else do we need to know?

Thanks

- Organizers
- Collaborators
- Funders
- Audience