Estimation

Goals:

- The basic recipe for estimation
- The method you use should be tailored to the data and to the use

Basic Recipe of Estimation

1. Make an observation of the world
2. Build a model that can replicate that observation
3. Define a measure of distance between observation and model
4. Search over many (all?) parameters to find the ones that minimize that distance

Basic Recipe of Estimation

1. Make an observation of the world
    1. Time series
    2. Proportion immune
2. Build a model that can replicate that observation
    - Can be dynamic or static
4. Define a measure of distance between observation and model
    - For a given set of parameters, how far apart are observation and the model?
5. Search over many (all?) parameters to find the ones that minimize that distance
    - Analytically, brute force, or algorithmically

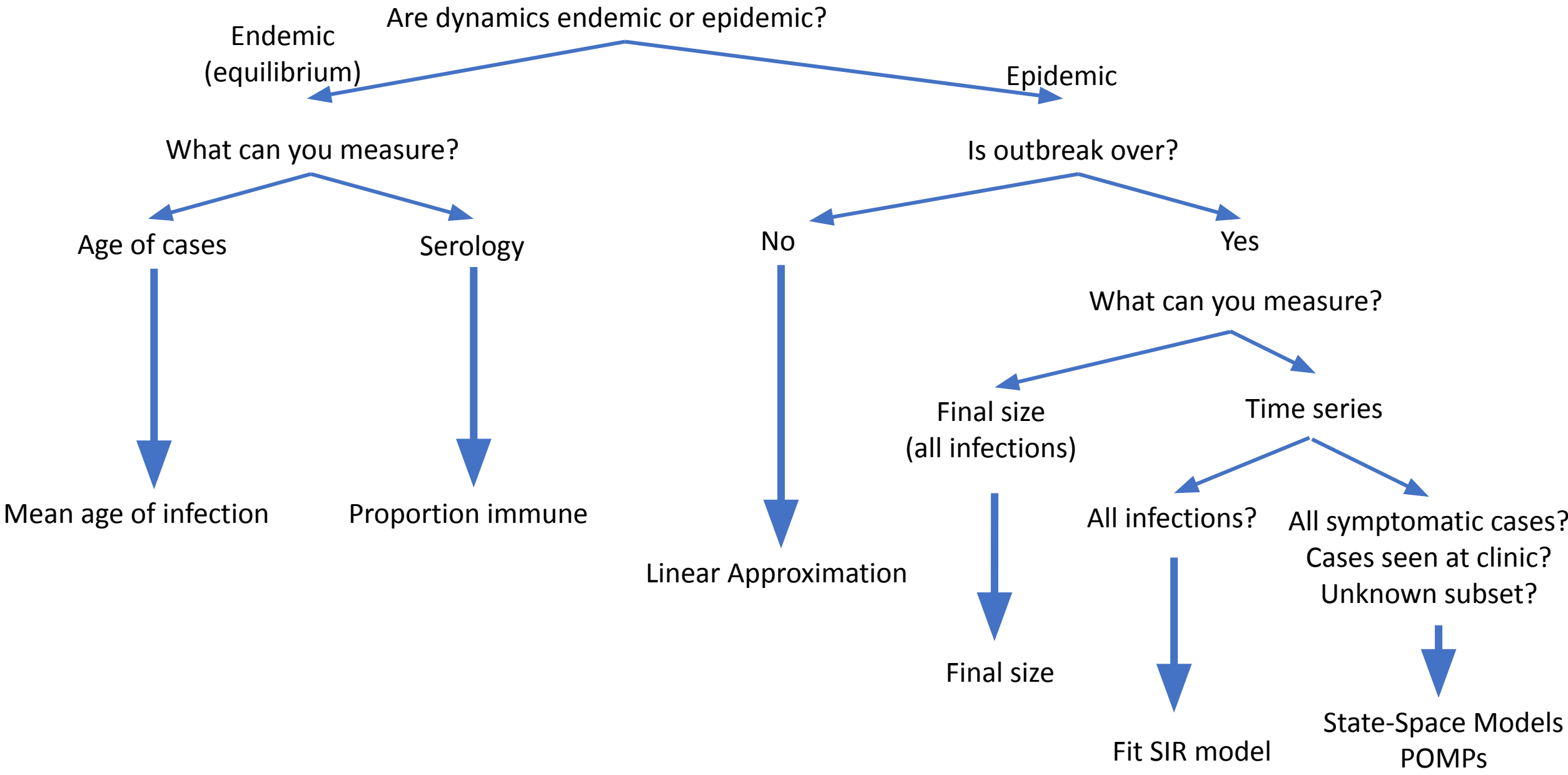
Basic Recipe of Estimation

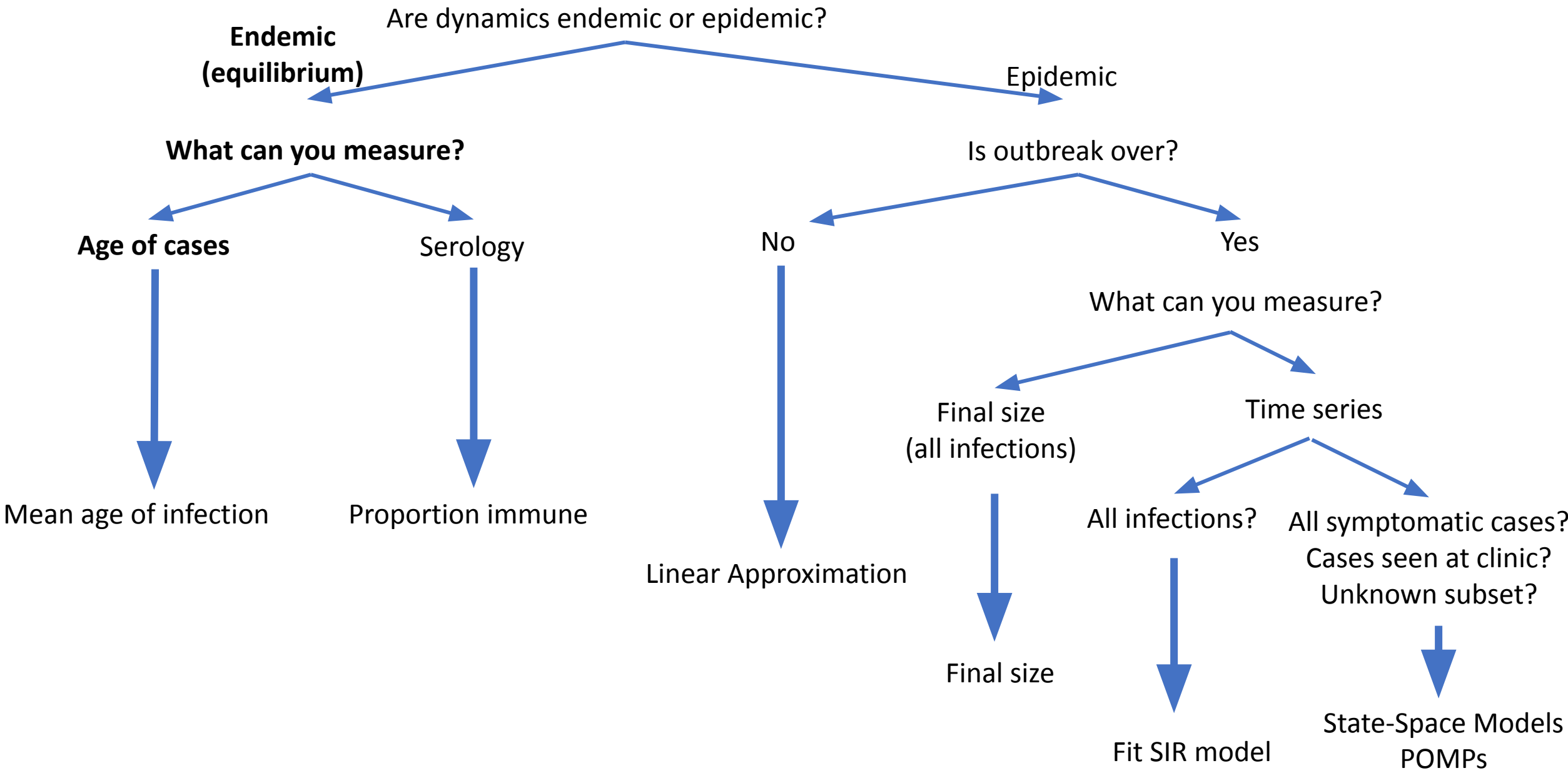
1. Make an observation of the world

What you can observe depends on where you are:

1. Are the dynamics at equilibrium?
2. What can you measure?
3. Is the outbreak over?
    - Is it still growing exponentially?

What you can observe depends on where you are:

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Endemic (equilibrium)
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Serology
Mean age of infection
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Linear Approximation
What can you measure?
Final size (all infections)
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Final size
All infections?
All symptomatic cases?
Cases seen at clinic?
Unknown subset?
Fit SIR model
State-Space Models
POMPs

Mean Age of Infection

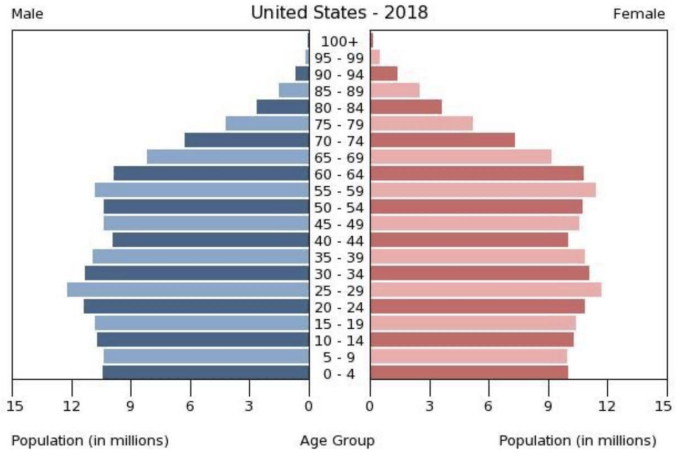
$$A = \frac{L}{R_0 - 1}$$

$$R_0 = \frac{L}{A} + 1$$

- A is the mean age of infection
- L is the life expectancy at birth

Basic Recipe of Estimation

1. Make an observation of the world
2. Build a model that can replicate that observation
   - Validity of the estimate depends on the match between the model and reality
   - $R_0 = {}^{L}/_{A}$ only holds if the age distribution of the population is exponentially distributed (e.g. constant death rate at all ages)
   - In many populations, mortality is low in the young and high in the elderly. This leads to a population age distribution that is more rectangular



Mean Age of Infection

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$$R_0 = \frac{L}{A}$$

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Not a big difference, but a bias that is generated by choosing the wrong model

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This part is trivial for mean age of infection IF the population has homogeneous mixing. Based on what we did earlier, how would you estimate R_0 for a population with age-specific mixing or force of infection?

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    1. Build SIR model with mixing matrix and demography that reflects the population of interest
    2. For a given R_0, simulate model to equilibrium and evaluate mean age of infection
    3. Do this for all R_0 and estimate is that which is closest to observed mean age

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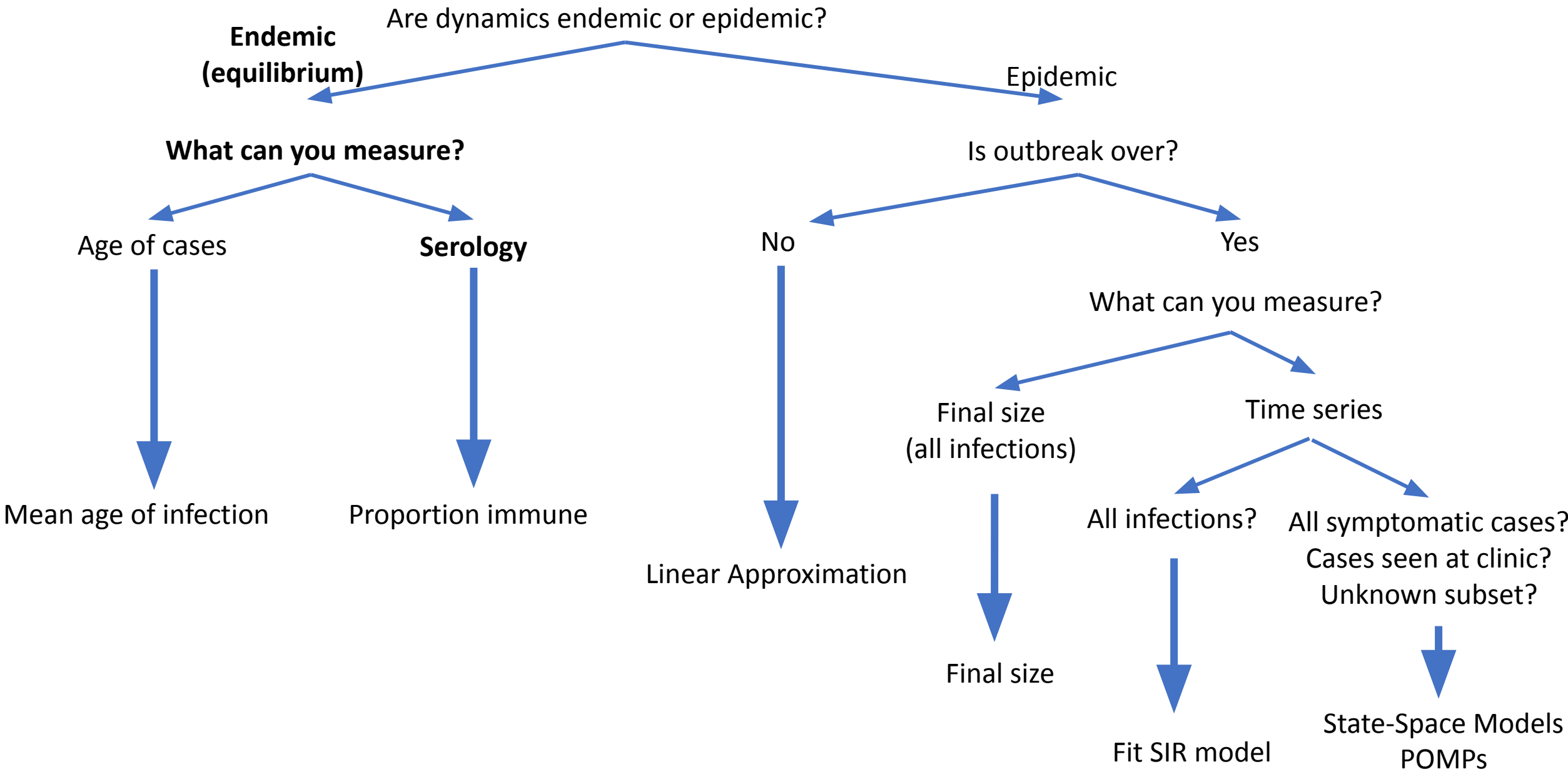
What if you have the whole age distribution of reported cases?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Proportion Immune

- For the standard SIR model, the equilibrium proportion immune is

$$\text{P(immune)} = 1 - \frac{1}{R_0}$$

The proportion immune can be estimated using a serological survey.
This is less likely to be biased by access to care.

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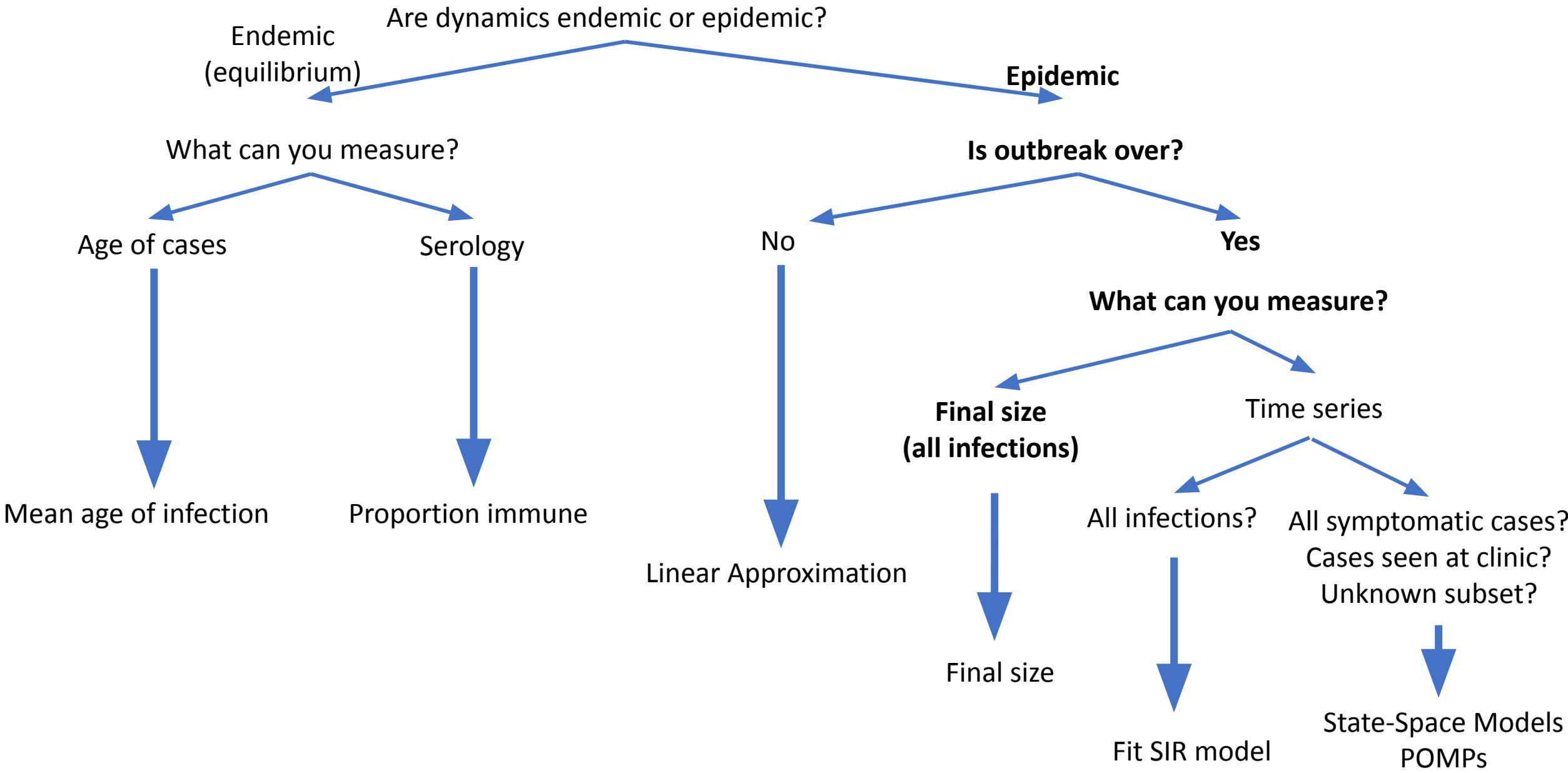
As with mean age of infection – this result holds for the simple case, but the equilibrium proportion immune at equilibrium (or the age-specific seroprevalence curve) can be simulated for any specific assumptions about model structure, age-specific mixing, demographics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Epidemic Final Size

$$R_\infty = 1 - e^{-R_0 R_\infty}$$

Use Newton's method for estimation !

- Citation: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3506030/

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- A useful result but challenging for estimation because we rarely can see ALL infections.

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- Requires an assumption that dynamics don't change during outbreak
- More commonly applied AFTER R_0 is estimated by another method to predict final size*
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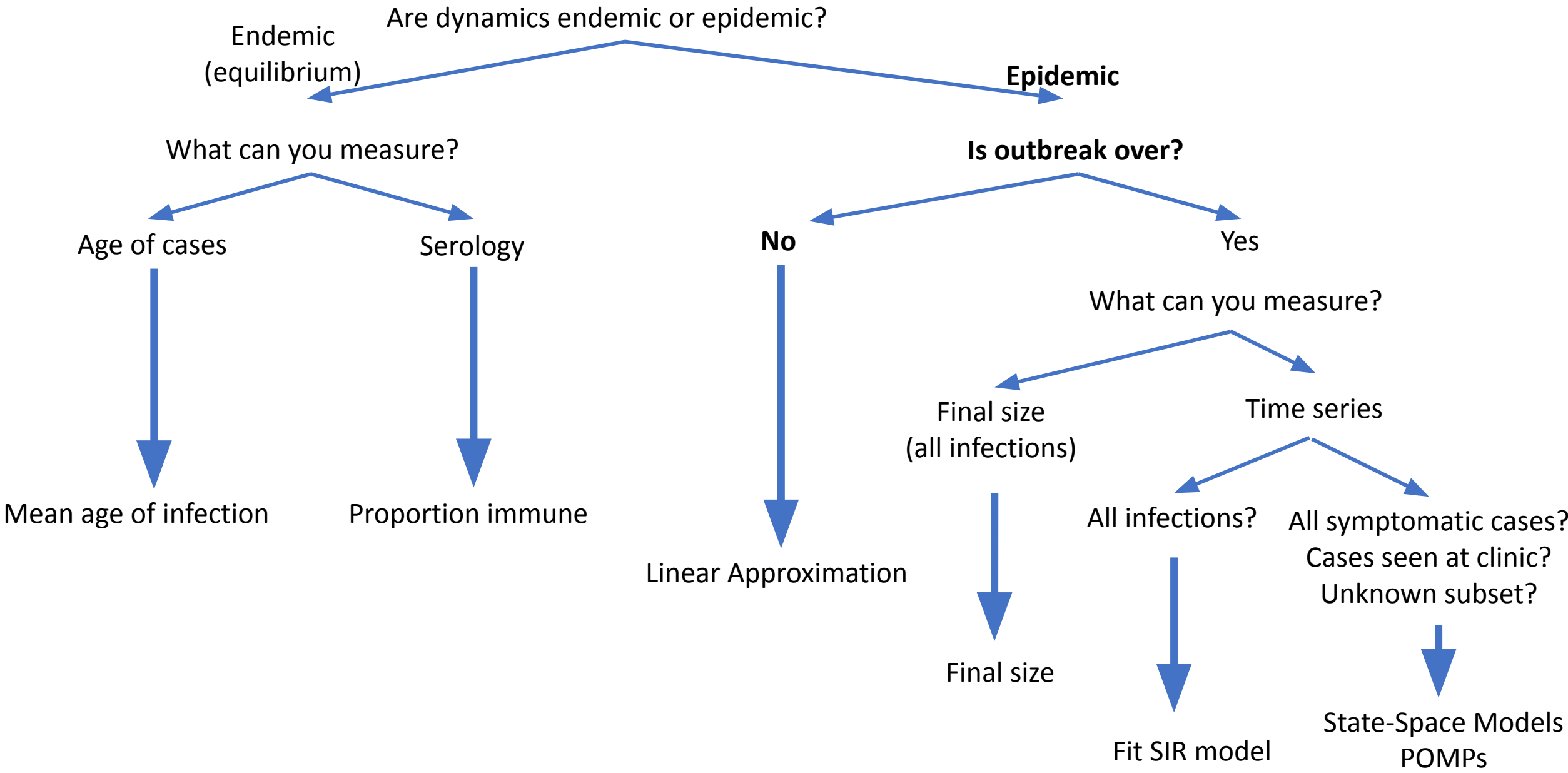
* What assumption does this require?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Fitting Time Series

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  How does herd immunity change this?

Fitting Time Series

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Initial Geometric Growth on time scale of infectious period

$$I_1 = I_0 * R_0$$
$$I_2 = I_1 * R_0$$
$$I_2 = I_0 * R_0^2$$
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$$I_T = I_0 R_0^T$$

$$\log(I_T) = \log(I_0) + T\log(R_0)$$

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Exponential growth on arbitrary time scale

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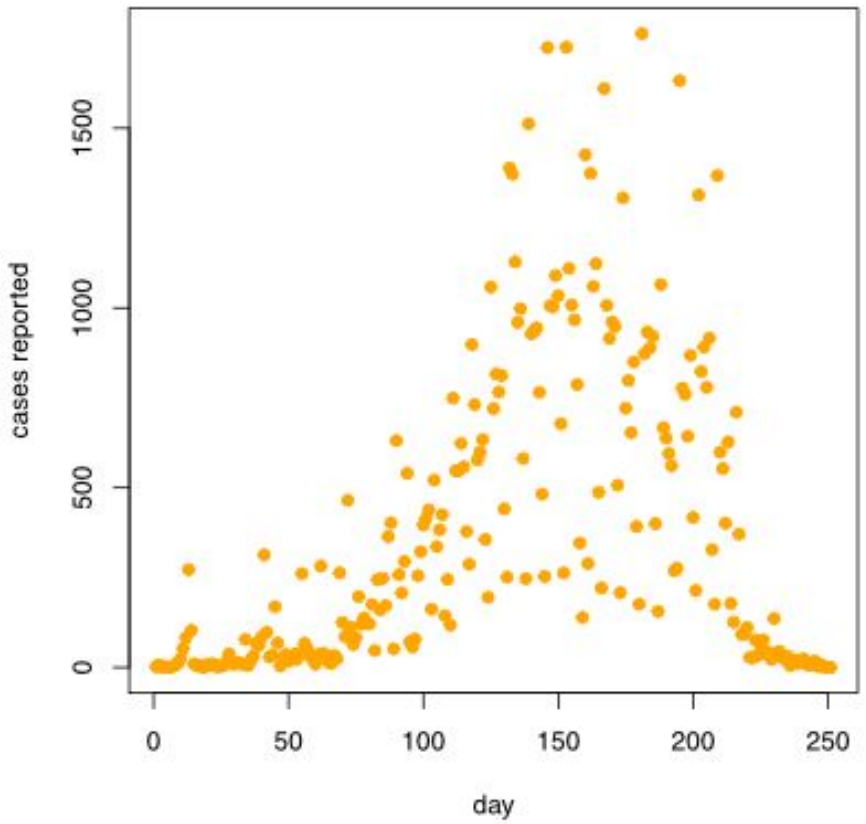

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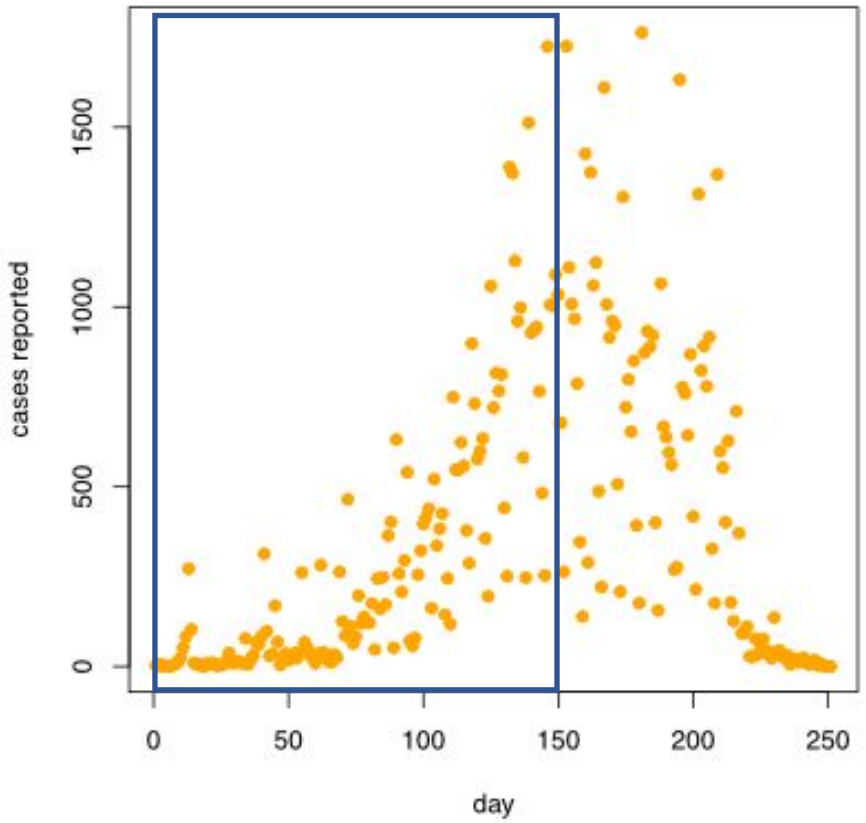

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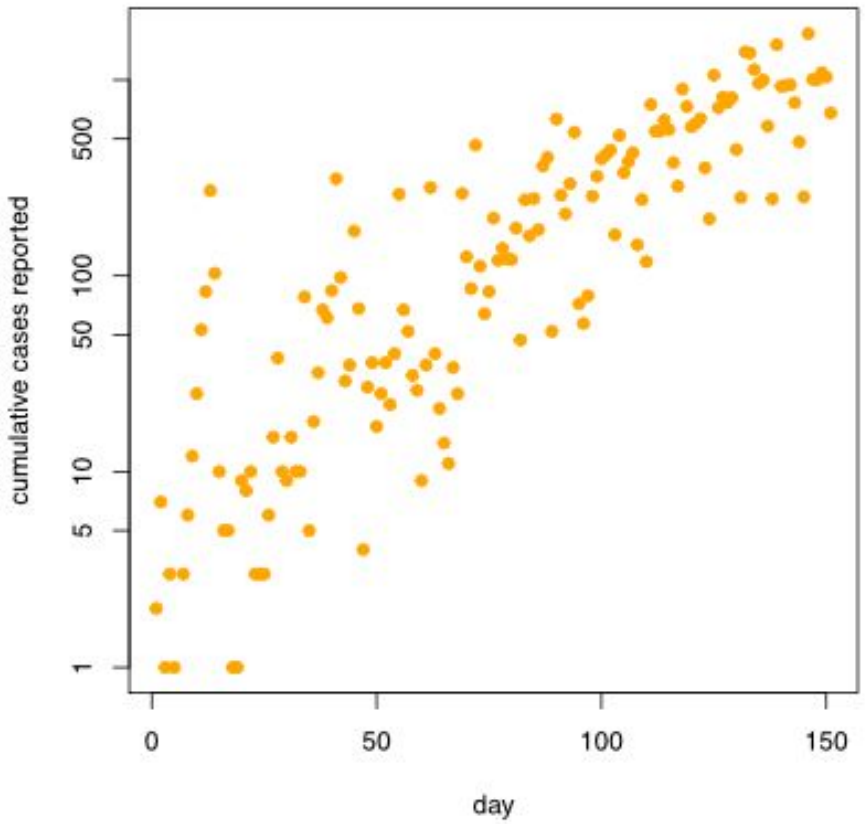

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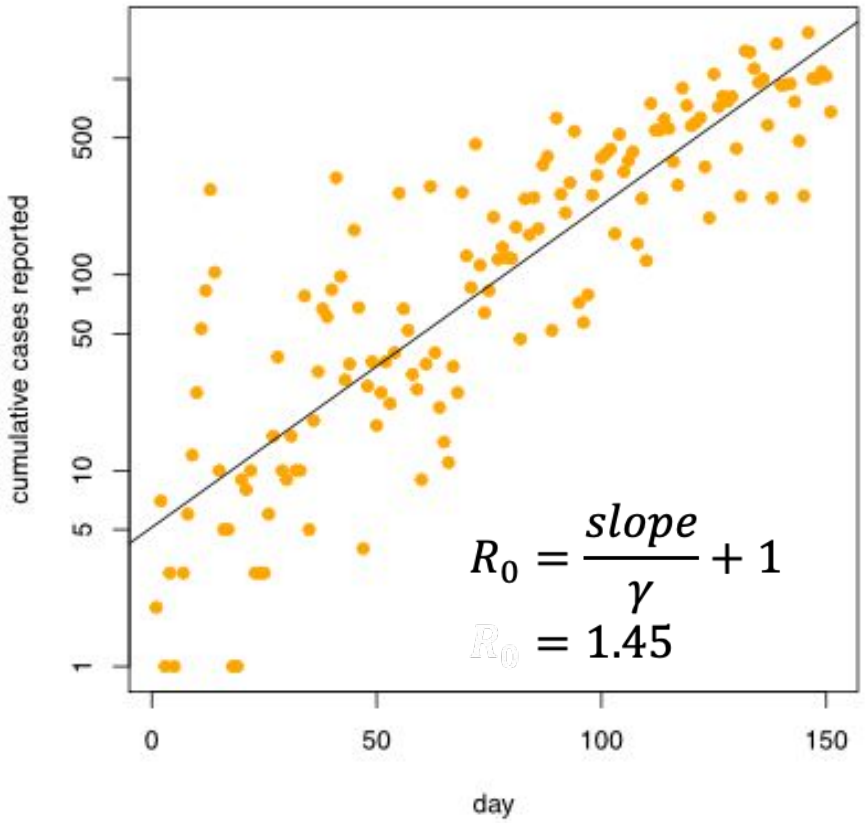

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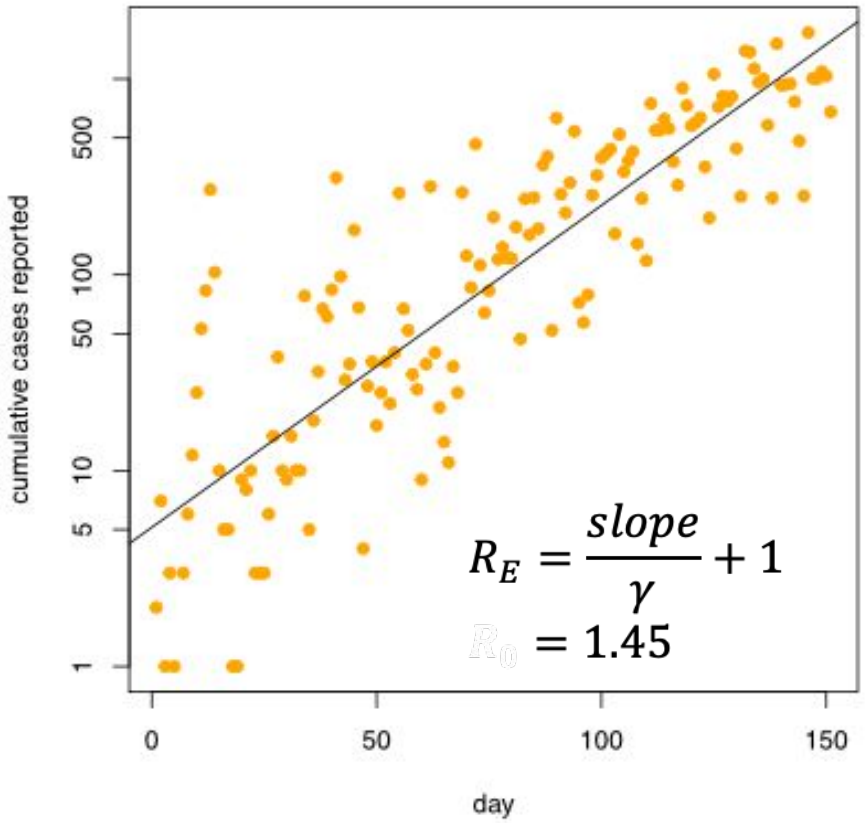

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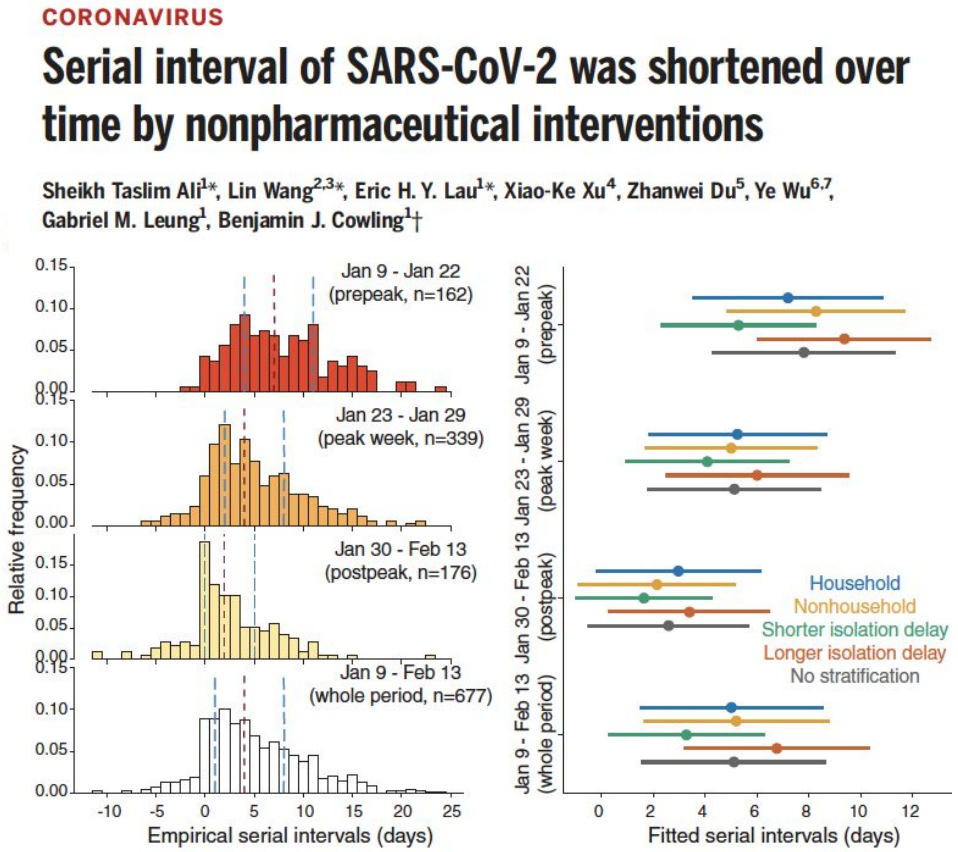

Fig. 1. Serial intervals of SARS-CoV-2 substantially shortened over time in mainland China. (A) Empirical

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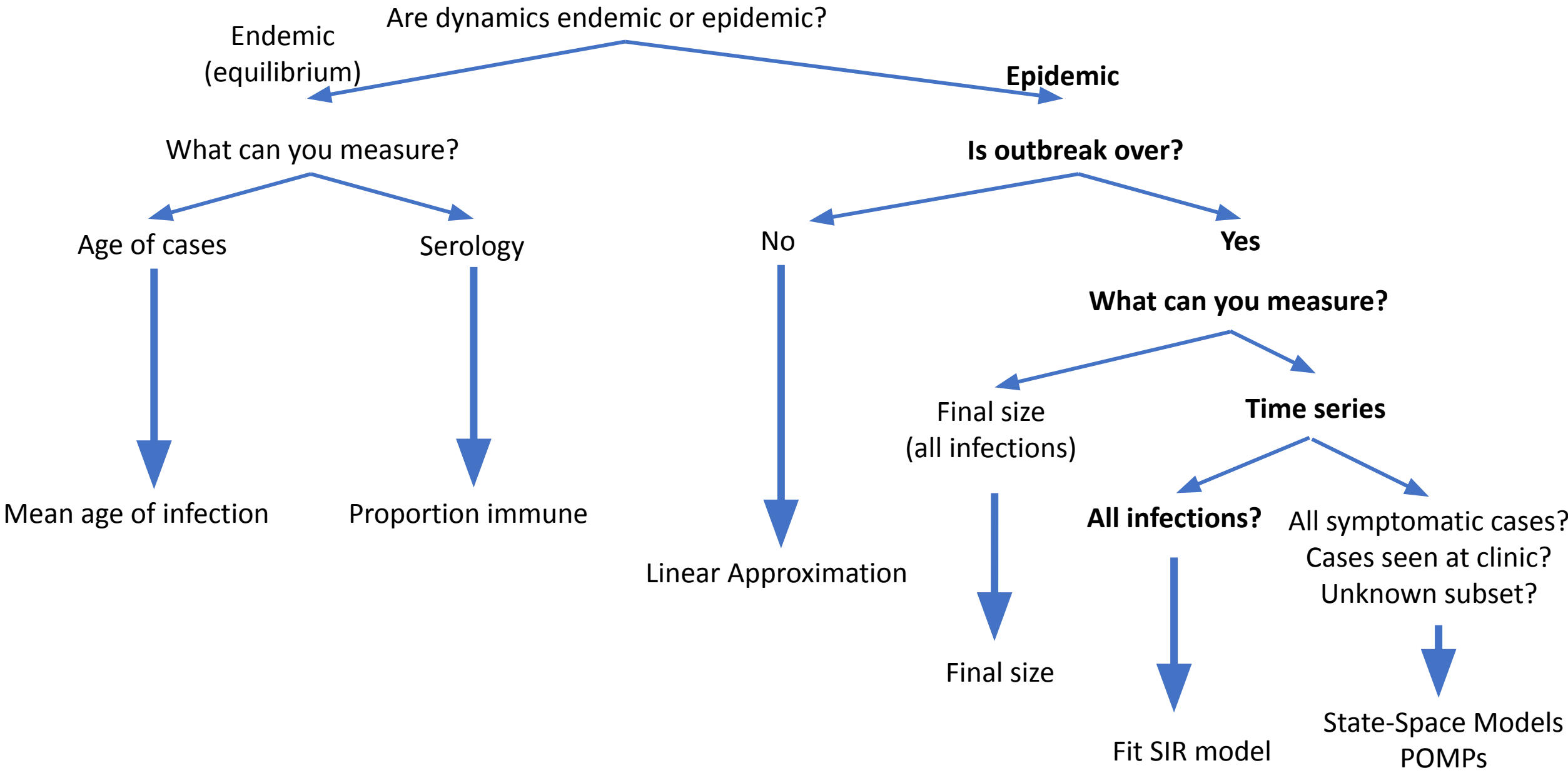
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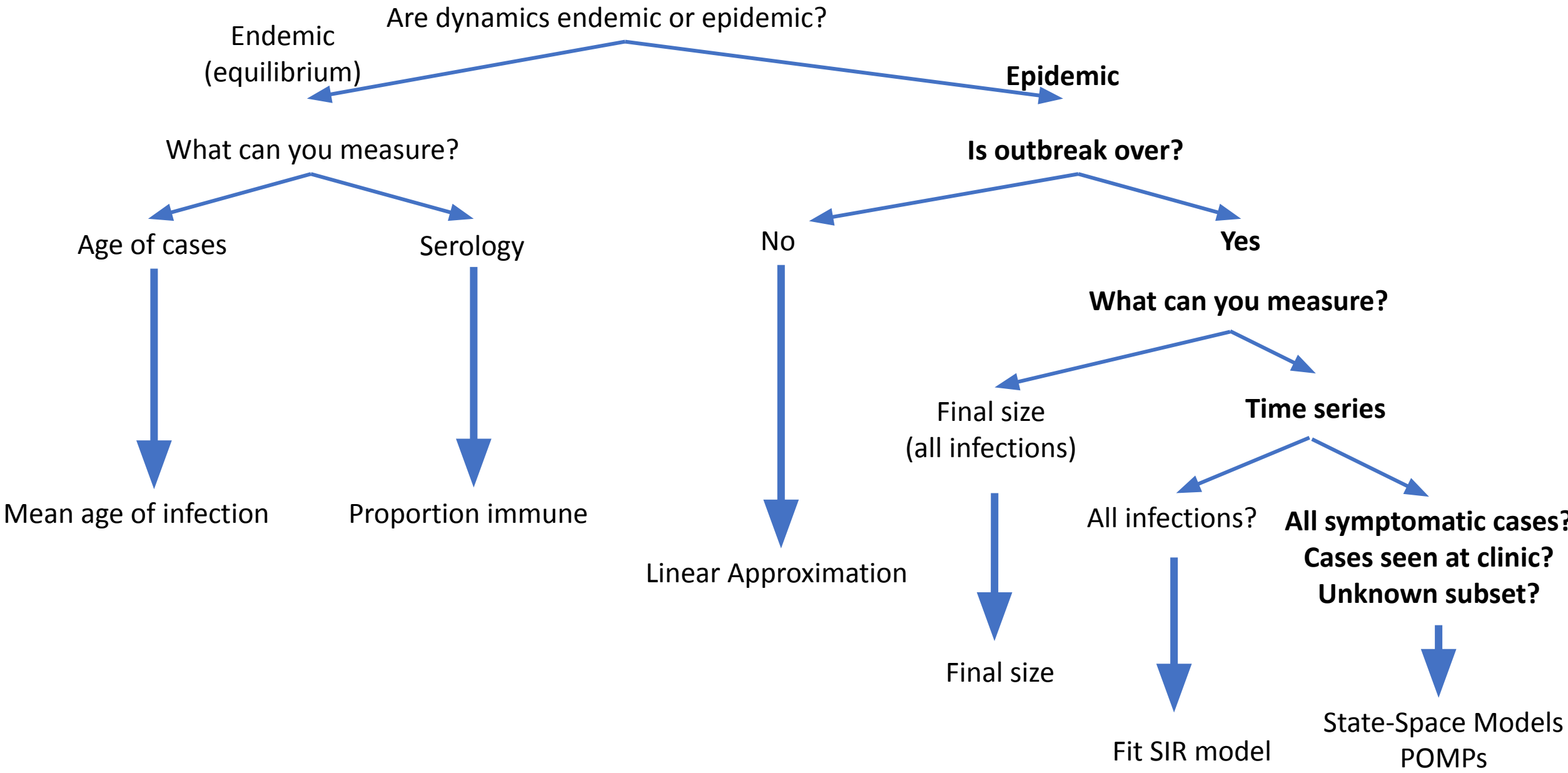
POMPs

See R Worksheet

- What should be the measure of distance?
  - Trajectory matching?
  - Likelihood?
  - Something else?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Fitting Real Time Series: Measurement Error

- Frequently we can only see a part of the time series, or the time series is obscured:
  - Under-reporting
  - Diagnostic uncertainty

Globally Reported: 147,000 measles cases
Globally Estimated: 7.5 million measles cases

Morbidity and Mortality Weekly Report (*MMWR*)

CDC

Progress Toward Regional Measles Elimination — Worldwide, 2000–2020

Weekly / November 12, 2021 / 70(45);1563–1569

Meredith G. Dixon, MD[1]; Matt Ferrari, PhD[2]; Sebastien Antoni, MPH[3]; Xi Li, MD[1]; Allison Portnoy, ScD[4]; Brian Lambert[2]; Sarah Hauryski[2]; Cynthia Hatcher, MPH[1]; Yoann Nedelec, MPH[3]; Minal Patel, MD[1,3]; James P. Alexander Jr., MD[1]; Claudia Steulet[3]; Marta Gacic-Dobo, MSc[3]; Paul A. Rota, PhD[5]; Mick N. Mulders, PhD[3]; Anindya S. Bose, MD[3]; Alexander Rosewell, PhD[3]; Katrina Kretsinger, MD[1]; Natasha S. Crowcroft, MD[3] (View author affiliations)

Study: US COVID cases, deaths far higher than reported

Filed Under: COVID-19
Mary Van Beusekom | News Writer | CIDRAP News | Jan 05, 2021 Share Tweet LinkedIn Email Print & PDF

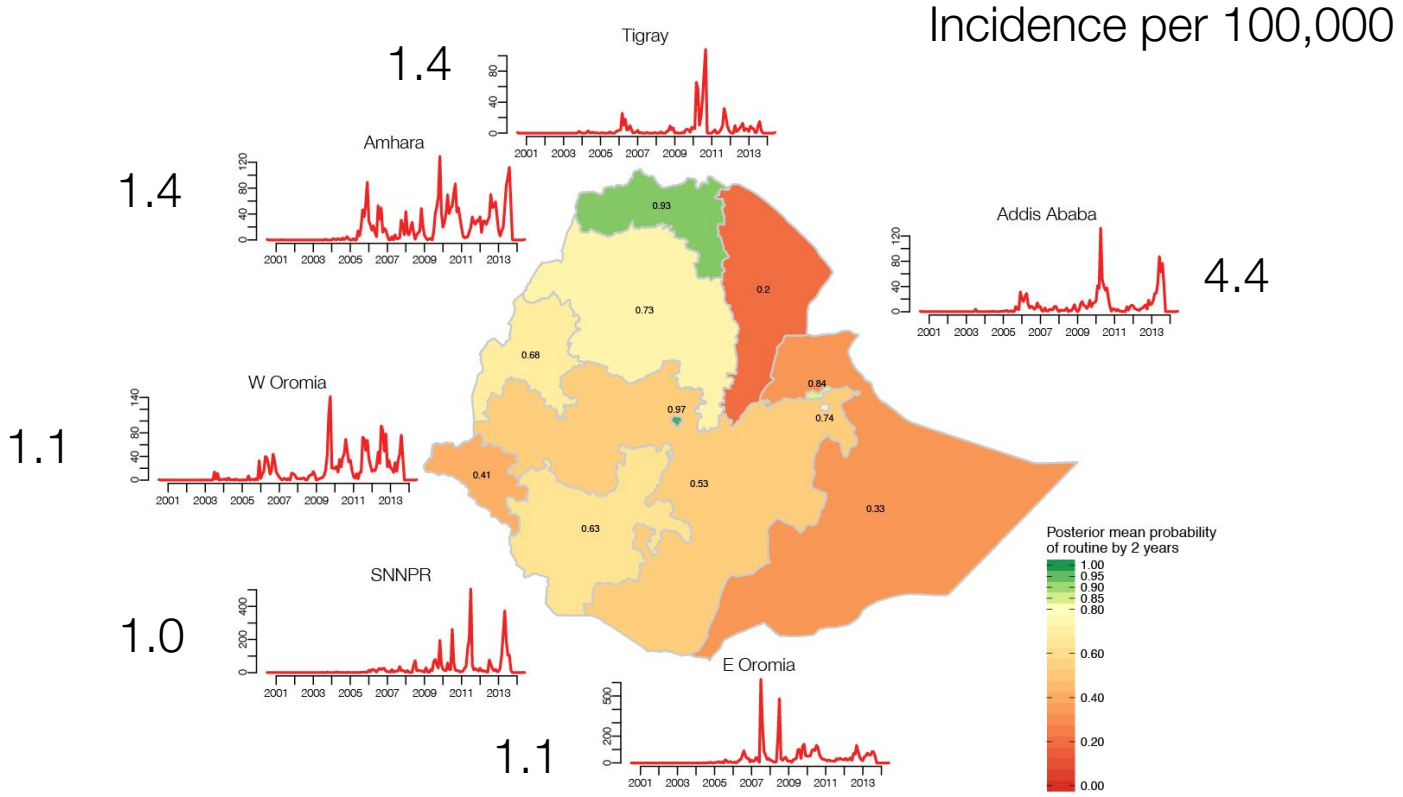
An estimated 14.3% of the US population had antibodies against COVID-19 by mid-November 2020, suggesting that that the virus has infected vastly more people than reported—but still not enough to come close to the proportion needed for herd immunity, according to a study published today in *JAMA Network Open*.

Government of Alberta, Chris Schwarz / Flickr cc

In the cross-sectional study, researchers from study sponsors Pfizer and Merck analyzed data from random community seroprevalence surveys and five such regional and national Centers for Disease Control and Prevention (CDC) surveys to estimate infection underreporting multipliers. Seroprevalence surveys reveal the proportion of a population that has antibodies against a certain disease, such as COVID-19.

After adjusting for underreporting using validated multipliers, the analysis revealed an estimated median 46,910,006 infections with SARS-CoV-2, the virus

Measles Incidence in Ethiopia



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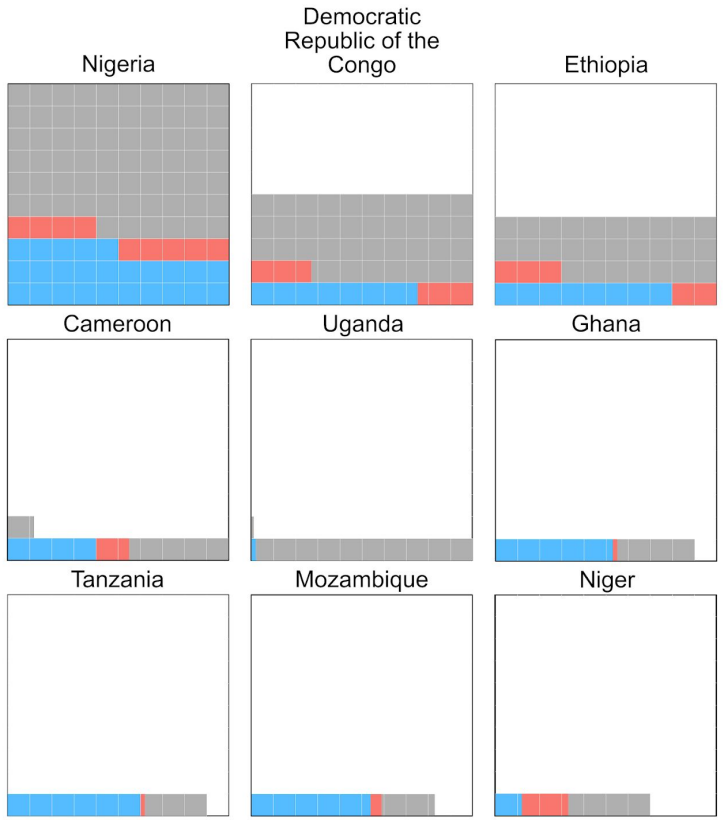
Many infections cause similar syndromes (a collection of clinical symptoms):

Upper respiratory infections	-> influenza, COVID
Fever + rash	-> measles
Acute flaccid paralysis	-> polio
Acute diarrhea	-> cholera
Acute fever	-> malaria



Cases of fever and rash that match the measles clinical case definition

Untested, clinical cases

Test Positive

Test Negative

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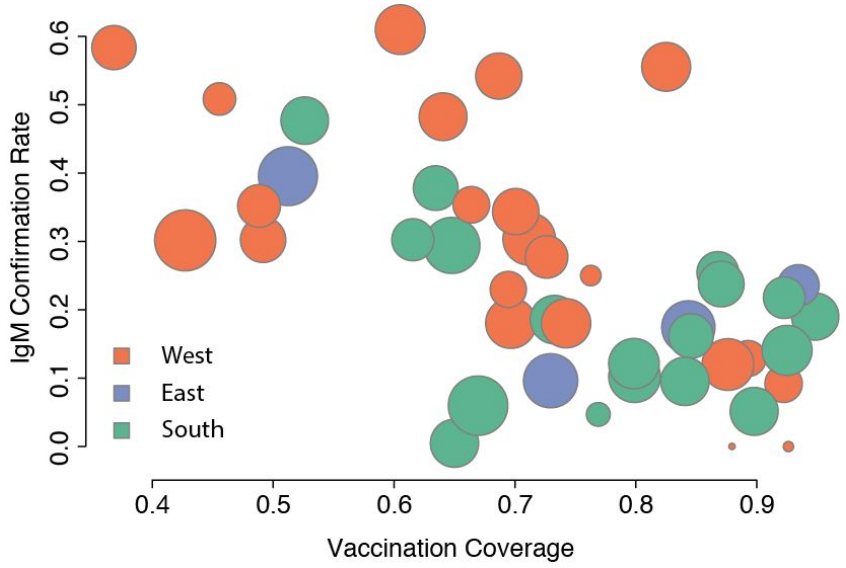
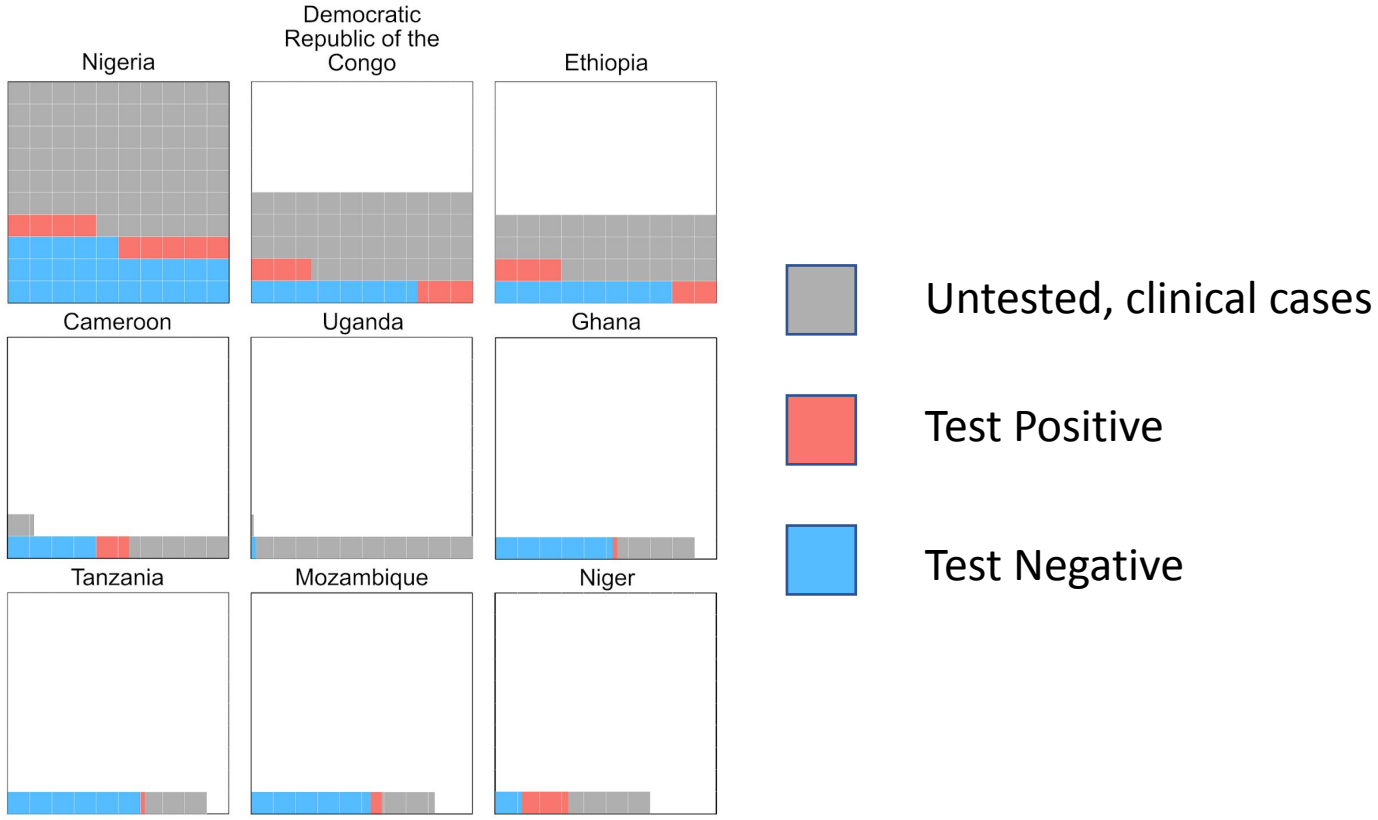
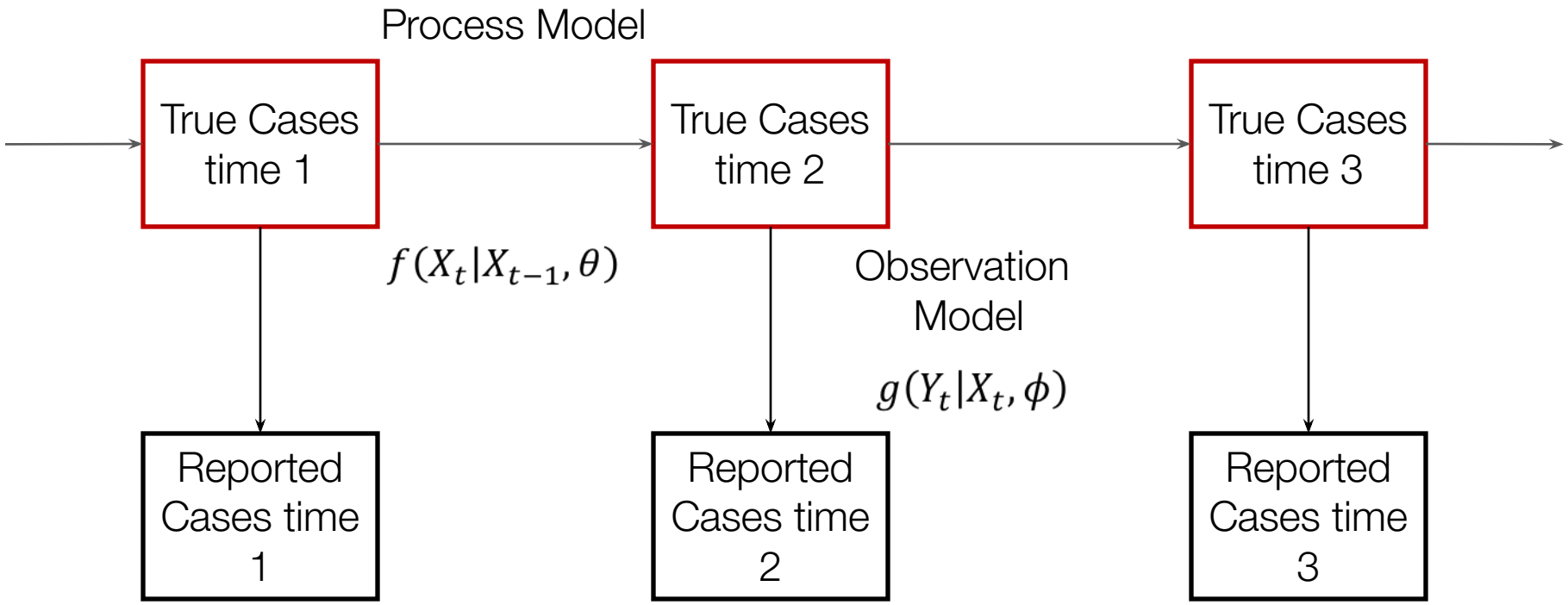




We need TWO models

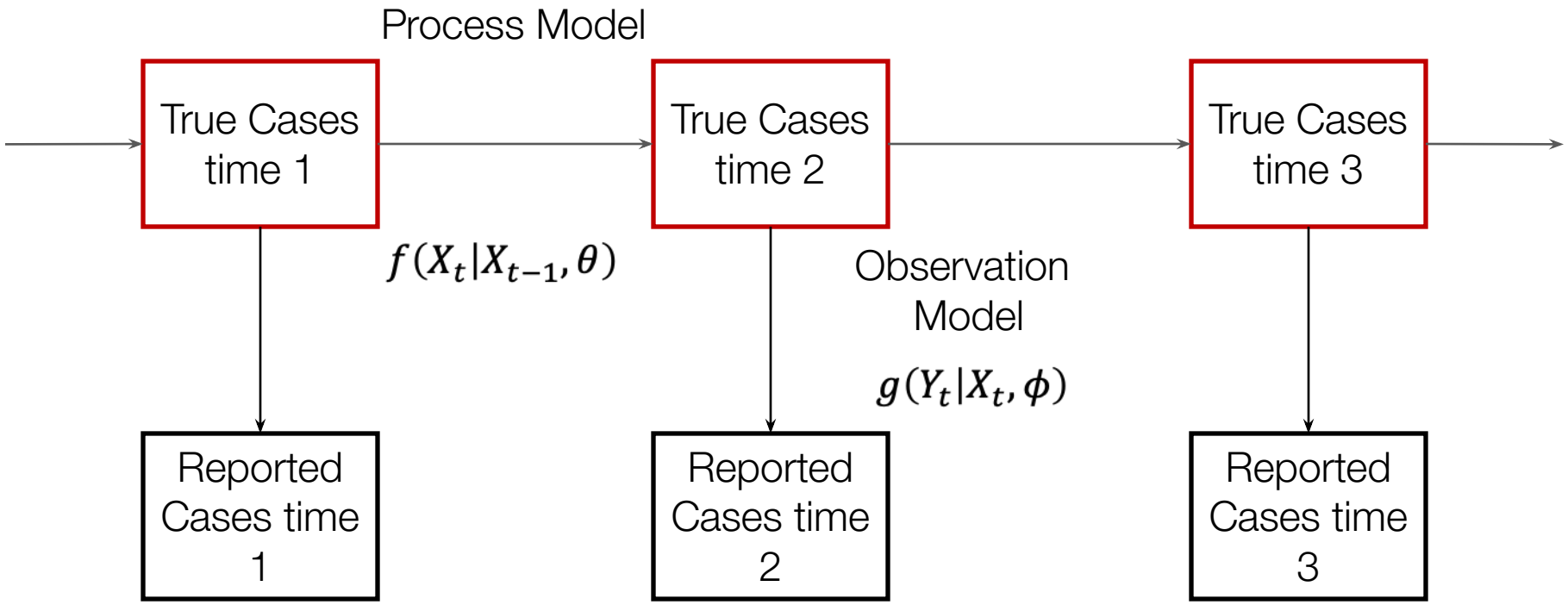


$f(Y_t|Y_{t-1},\theta,\phi)$

- can be stated as a function of these two models, unobserved states are latent variables
- long history in engineering, more recently in population dynamics

We need TWO models

Here we might have the additional goal of estimating the true states; i.e. the true burden of disease among those who were not measured.



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The basic recipe offers a systematic approach to parameter estimation. If you can simulate, you can estimate … even if it isn’t very efficient