



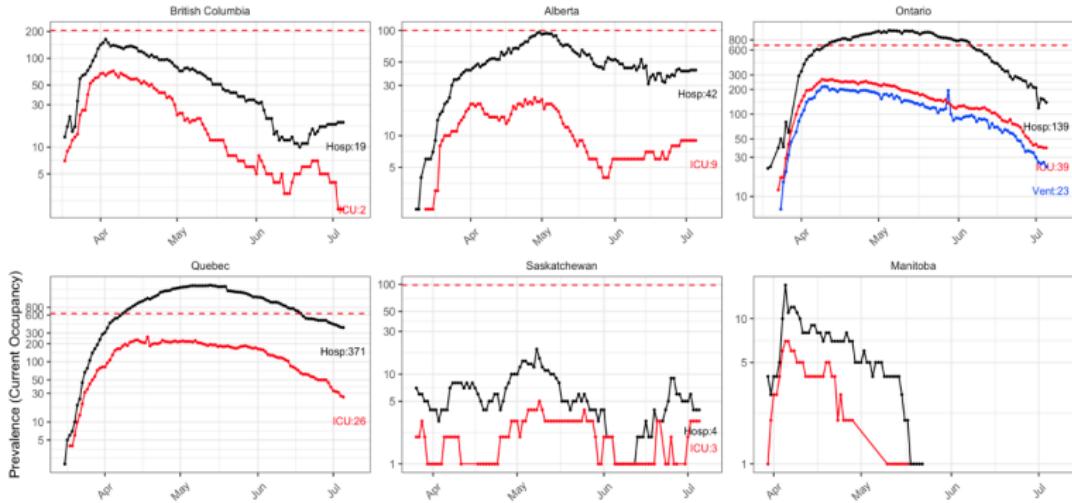
From 1918 to 2020:
analyzing the past and
forecasting the future

David Earn
and
Jonathan Dushoff

McMaster University

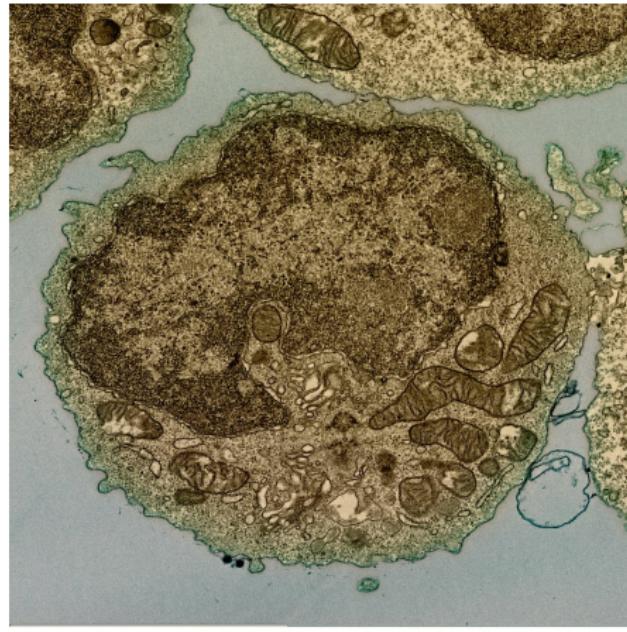


What factors affect spread?



<https://wzml.li.github.io/COVID19-Canada/>

Immunity

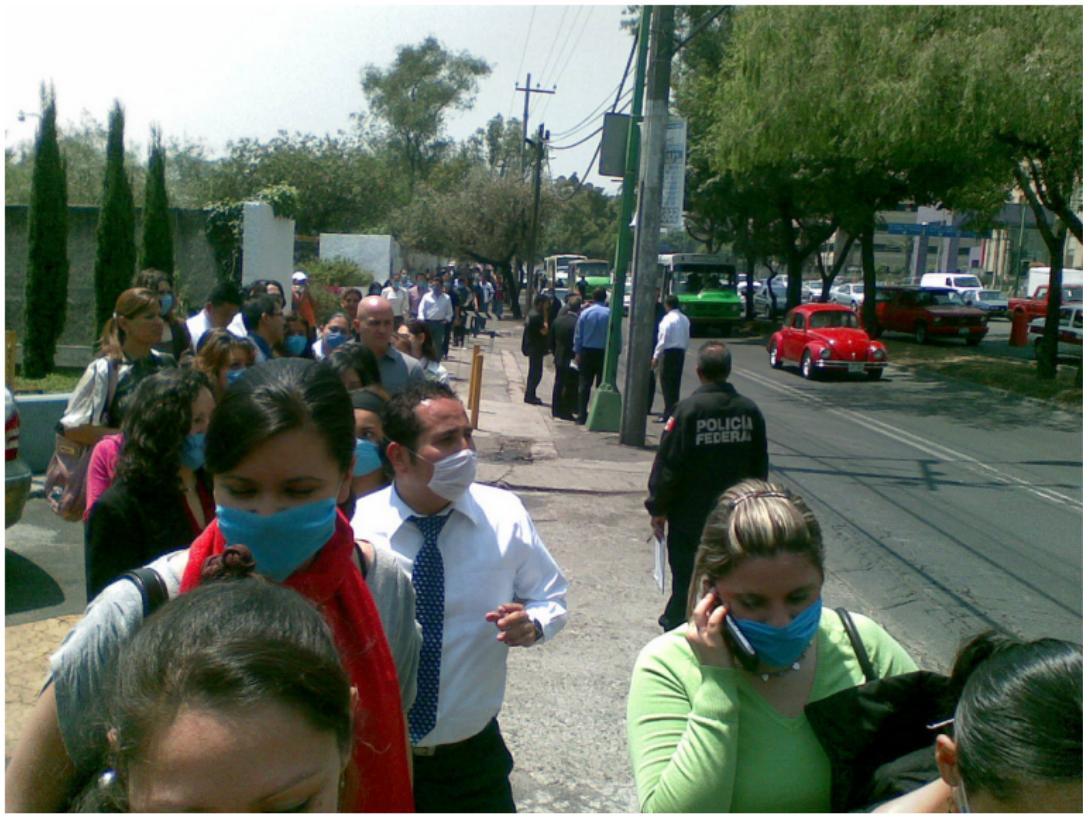


- ▶ How much?
- ▶ How effective?
- ▶ How long?

Policies



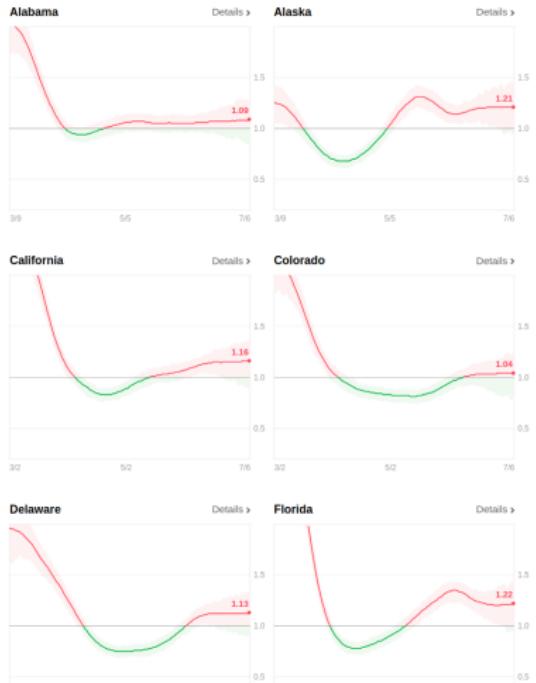
Public response



Weather



\mathcal{R}_t and r_t



<https://coronavirus.jhu.edu> 2020
Jul 08

<https://rt.live> 2020 Jul 08

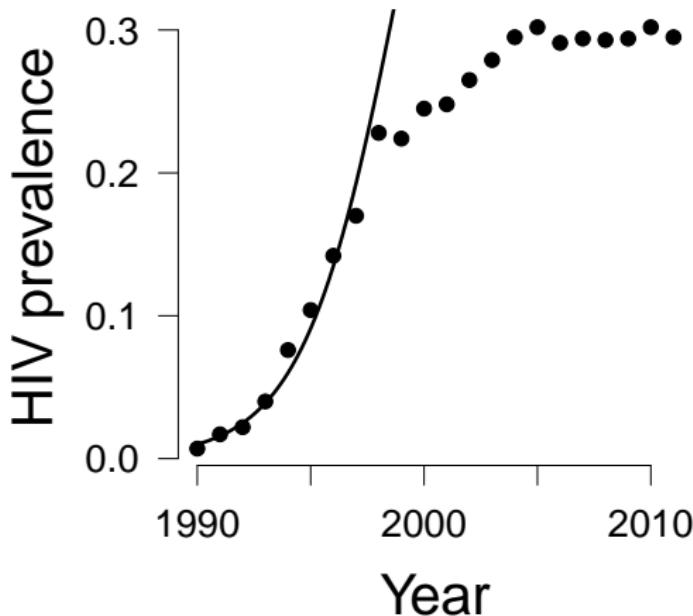
Outline

Foundations

Defining and measuring
Generations in space
Serial intervals

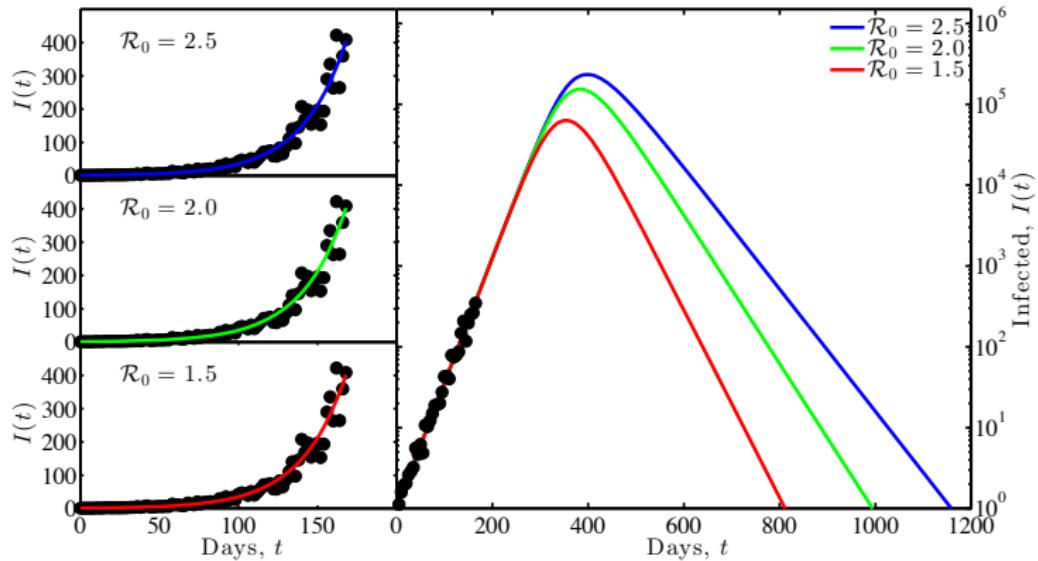
Moving forward

HIV in sub-Saharan Africa



$C = 1/r_0 \approx 18$ month. Horrifyingly fast.

Ebola outbreak



$C = 1/r_0 \approx 1$ month. Not so bad.

Speed

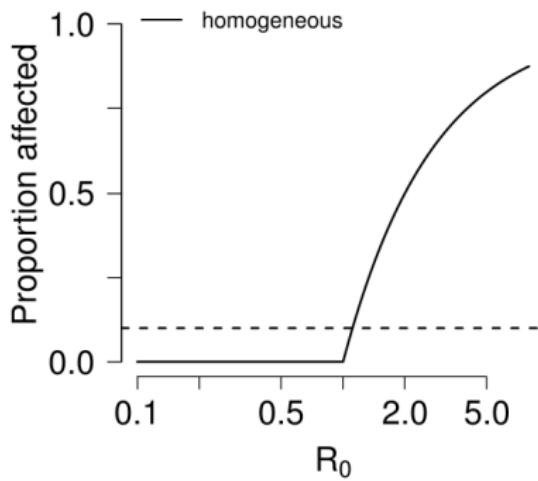
- ▶ We measure epidemic speed using little r :
 - ▶ The ratio of the *change* in disease impact to the *amount* of disease impact
 - ▶ *Units*: [1/time]
 - ▶ Disease increases like e^{rt}
- ▶ Time scale is $C = 1/r$

Strength

- ▶ We describe epidemic strength with big \mathcal{R}
 - ▶ Average number of new cases per case
 - ▶ Unitless
 - ▶ $\mathcal{R} > 1$ for spread

Strength of epidemics

endemic equilibrium

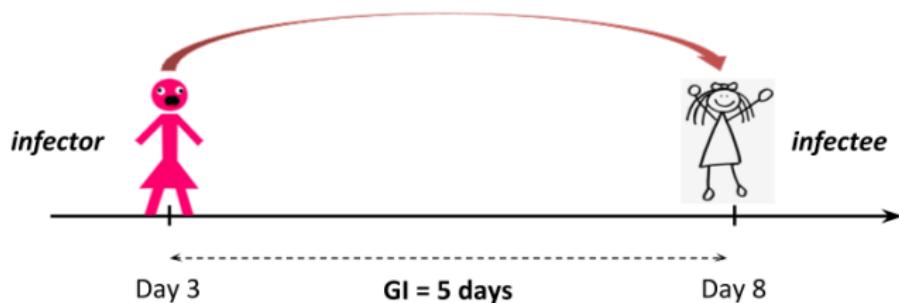


How long is a disease generation? (present)

Definition

Generation Interval:

Interval between the time that an individual is infected by an infector and the time this infector was infected



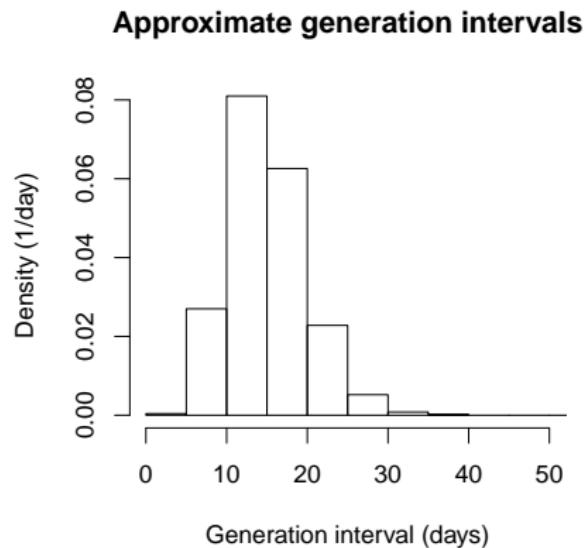
Generation intervals



"I cannot imagine how they will spend half of it."

- ▶ Sort of the poor relations of disease-modeling world
- ▶ Ad hoc methods
- ▶ Error often not propagated

Generation intervals link strength and speed

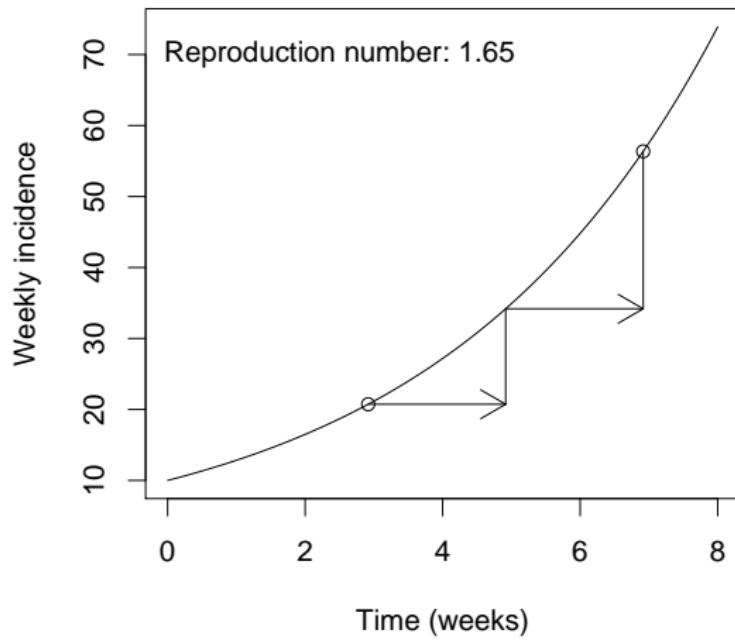


- ▶ Do fast generations mean more danger or less?

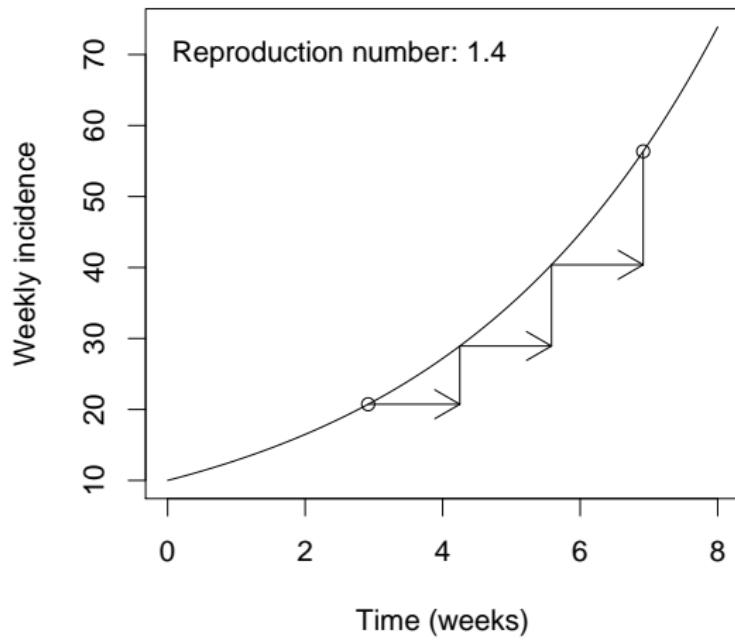
Conditional effect of generation time

- ▶ Given the reproductive number \mathcal{R}
 - ▶ faster generation time G means faster growth rate r
 - ▶ More danger
- ▶ Given the growth rate r
 - ▶ faster generation time G means smaller \mathcal{R}
 - ▶ Less danger

Generations and \mathcal{R}



Generations and \mathcal{R}



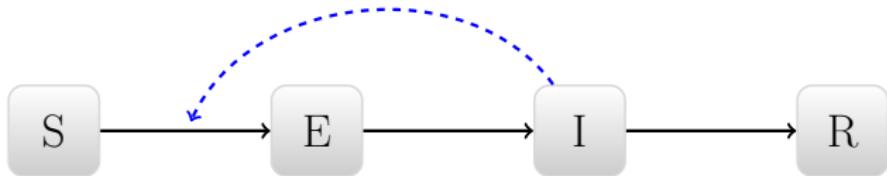
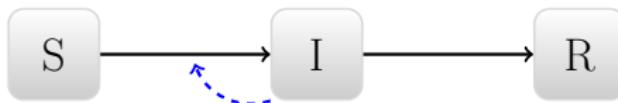
Linking framework

- ▶ Epidemic speed (r) is a *product*:
 - ▶ generation speed ×
 - ▶ epidemic strength
- ▶ WRONG

Linking framework

- ▶ Epidemic speed (r) is a *product*:
 - ▶ (something to do with) generation speed ×
 - ▶ (something to do with) epidemic strength
- ▶ In particular:
 - ▶ $r = (1/\hat{G}) \times \log(\mathcal{R})$
 - ▶ \hat{G} is the effective mean generation time

Box models

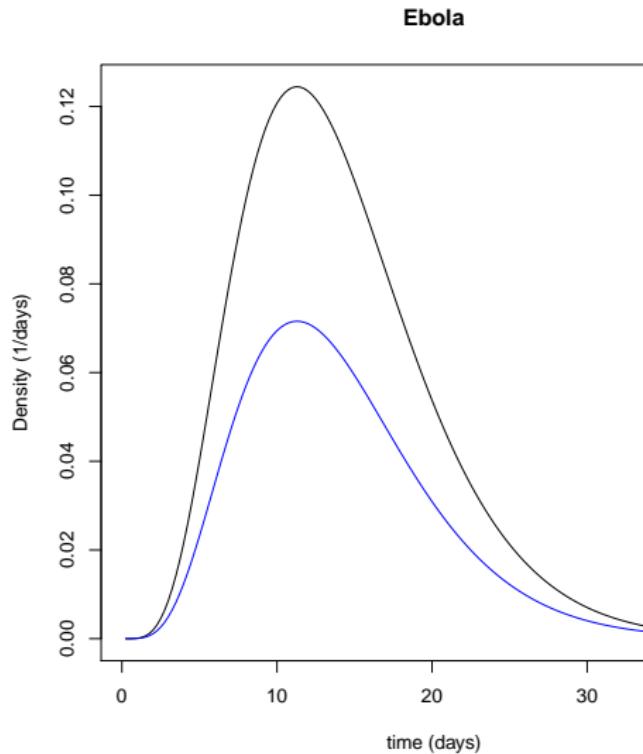


Renewal equation

- ▶ A broad framework that covers a wide range of underlying models
- ▶ $i(t) = \int k(\tau, t)i(t - \tau) d\tau$
 - ▶ $i(t)$ is the *rate* of new infections (per-capita incidence)
 - ▶ $k(\tau)$ measures how infectious a person is (on average) at time τ after becoming infected
- ▶ For invasion, treat k as constant.
- ▶ More generally, we often say $k(t) = \hat{k}(t)S/N$

Infection kernel

- ▶ $k(\tau)$ is the expected rate at which you infect at time τ after being infected
- ▶ $\int_{\tau} k(\tau) d\tau$ is the expected number of people infected:
 - ▶ \mathcal{R} the effective reproductive number
- ▶ $k(\tau)/\mathcal{R}$ is a distribution:
 - ▶ $g(\tau)$, the *intrinsic* generation distribution



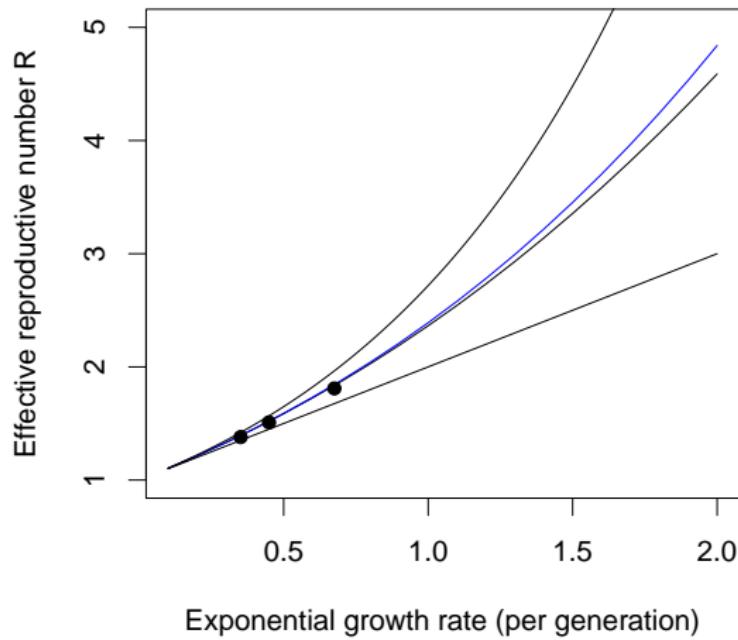
Inverting

- ▶ $\mathcal{R} = 1 + r\bar{G}$
- ▶ $\mathcal{R} = \exp(r\bar{G})$
- ▶ $1/\mathcal{R} = \int g(\tau) \exp(-r\tau) d\tau$ (Euler-Lotka)
- ▶ $\mathcal{R} = 1/M(-r\bar{G})$
 - ▶ *J Wallinga, M Lipsitch; DOI: 10.1098/rspb.2006.3754*

Compound-interest interpretation

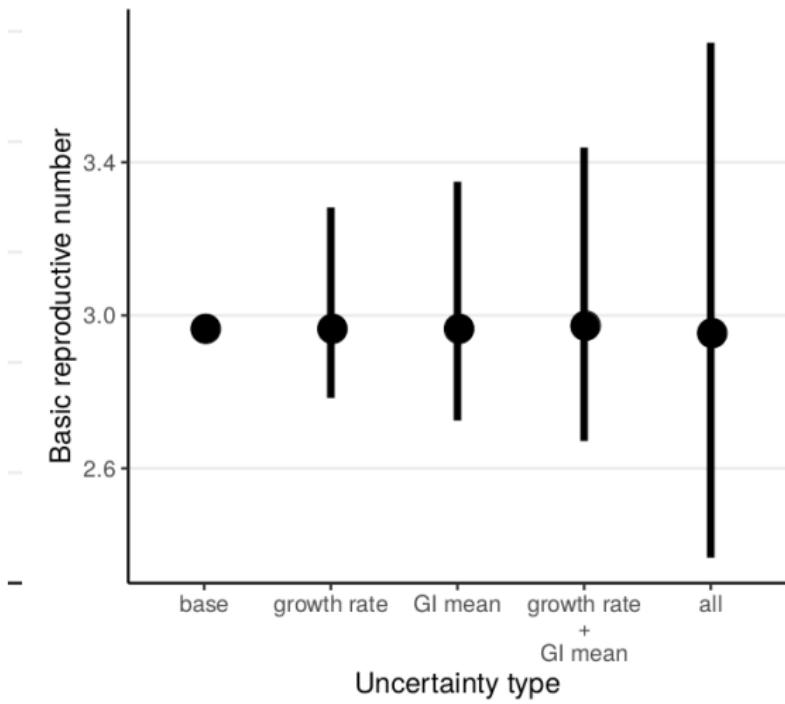
- ▶ Define the *effective dispersion* $\hat{\kappa}$ so that
- ▶ $\mathcal{R} = (1 + r\hat{\kappa}\bar{G})^{1/\hat{\kappa}} \equiv X(r\bar{G}; 1/\hat{\kappa})$
- ▶ $\hat{\kappa}$ is in fact a measure of variation (if g is gamma distributed, $\hat{\kappa}$ is exactly the CV^2)
- ▶ X is the compound-interest approximation to the exponential
 - ▶ Linear when $\hat{\kappa} = 1$ (i.e., when g is exponential)
 - ▶ Approaches exponential as $\hat{\kappa} \rightarrow 0$

Ebola example



Propagating error for coronavirus

B. Reduced uncertainty in the growth rate



Park et al., DOI: 10.1101/2020.01.30.20019877 (in press, JRSI)

Outline

Foundations

Defining and measuring
Generations in space
Serial intervals

Moving forward

Generations through time

- ▶ Generation intervals can be estimated by:
 - ▶ Observing patients:
 - ▶ How long does it take to become infectious?
 - ▶ How long does it take to recover?
 - ▶ What is the time profile of infectiousness/activity?
 - ▶ Contact tracing
 - ▶ Who (probably) infected whom?
 - ▶ When did each become infected?
 - ▶ — or ill (serial interval)?

Which is the real interval?

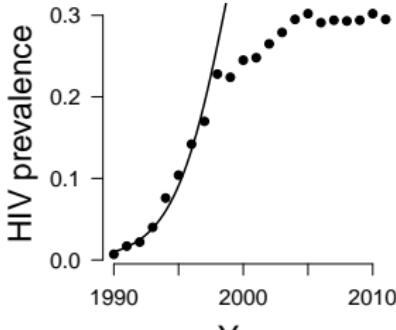
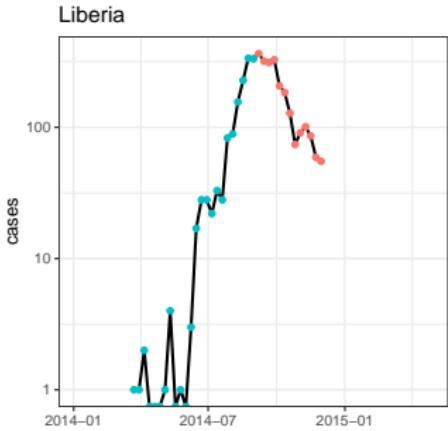
- ▶ Contact-tracing intervals look systematically different, depending on when you observe them.
- ▶ Observed in:
 - ▶ Real data, detailed simulations, simple model
- ▶ Also differ from intrinsic (infector centered) estimates

Types of interval

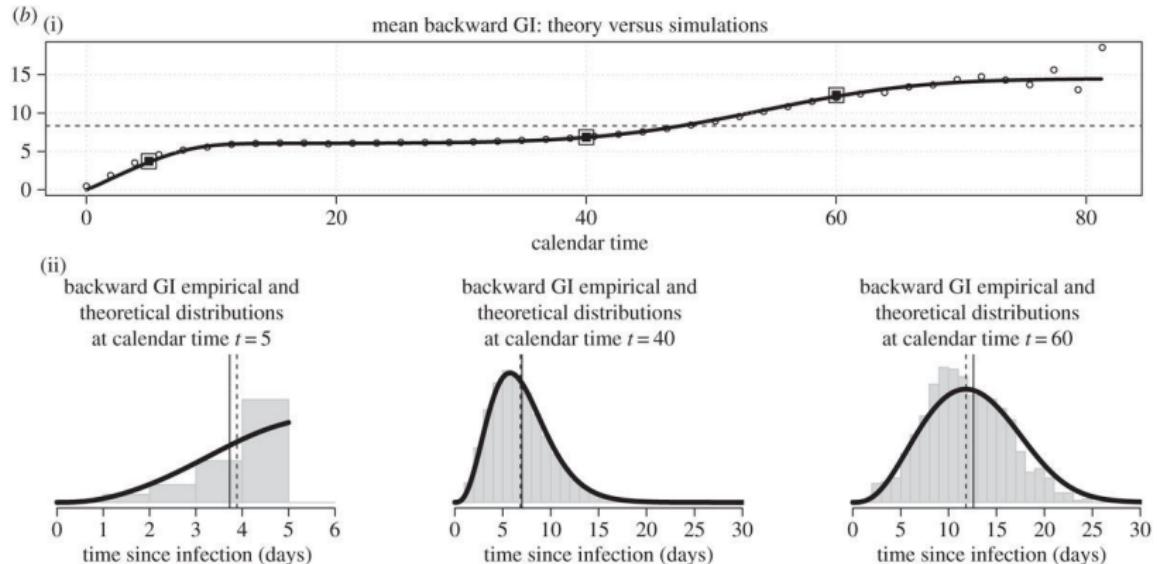
- ▶ Define:
 - ▶ *Intrinsic interval*: How infectious is a patient at time τ after infection?
 - ▶ *Forward interval*: When will the people infected today infect others?
 - ▶ *Backward interval*: When did the people who infected people today themselves become infected?
 - ▶ *Censored interval*: What do all the intervals observed up until a particular time look like?
 - ▶ Like backward intervals, if it's early in the epidemic

Growing epidemics

- ▶ Generation intervals look *shorter* at the beginning of an epidemic
 - ▶ A disproportionate number of people are infectious right now
 - ▶ They haven't finished all of their transmitting
 - ▶ We are biased towards observing faster events



Backward intervals



Champredon and Dushoff, 2015. DOI:10.1098/rspb.2015.2026

Outline

Foundations

Defining and measuring
Generations in space
Serial intervals

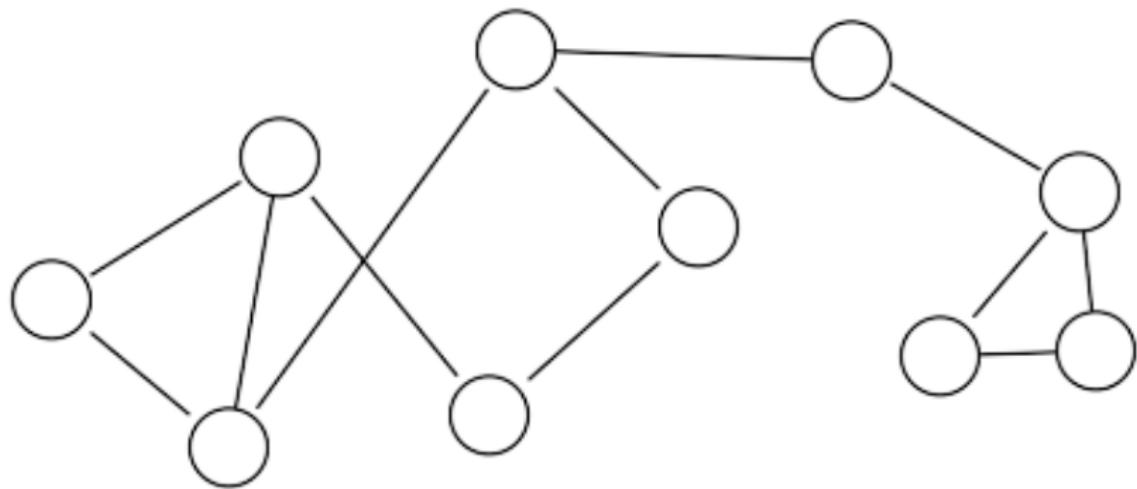
Moving forward

Generations in space

- ▶ How do local interactions affect realized generation intervals?



Individual



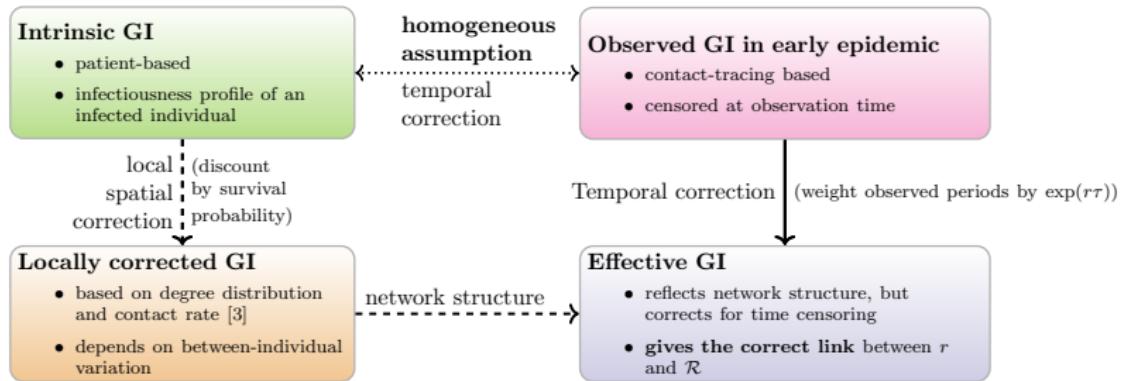
Surprising results

- ▶ We tend to think that heterogeneity leads to underestimates of \mathcal{R} , which can be dangerous.
- ▶ \mathcal{R} on networks generally *smaller* than values estimated using r .
 - ▶ Trapman et al., 2016. *JRS Interface*
DOI:10.1098/rsif.2016.0288

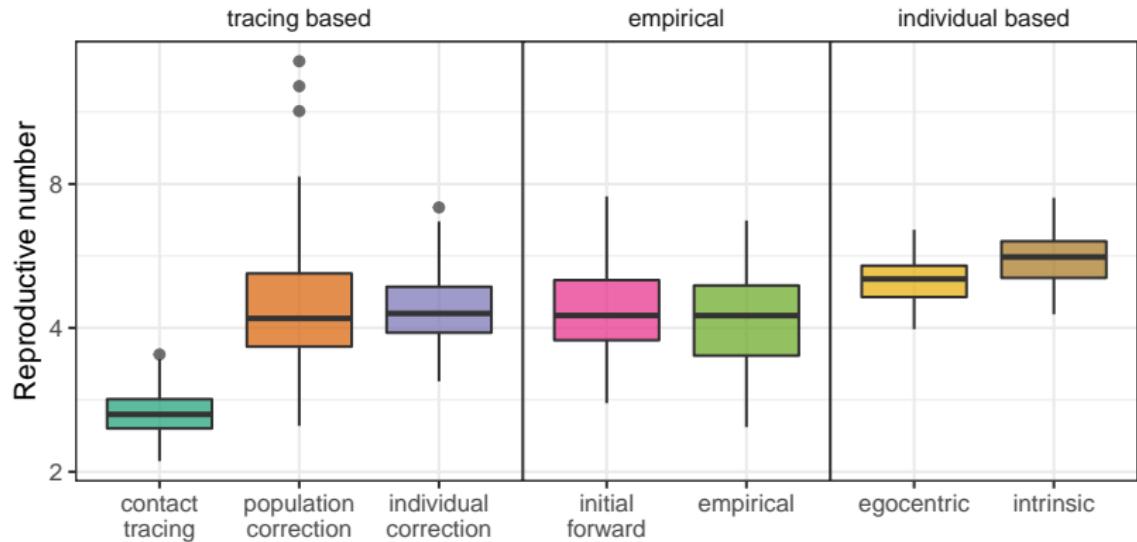
Generation-interval perspective

- ▶ Modelers don't usually question the intrinsic generation interval
- ▶ But spatial network structure does change generation intervals:
 - ▶ Local interactions
 - ▶ \implies wasted contacts
 - ▶ \implies shorter generation intervals
 - ▶ \implies smaller estimates of \mathcal{R} .

Observed and estimated intervals



Outbreak estimation



Park et al. DOI: 10.1101/683326 (preprint)

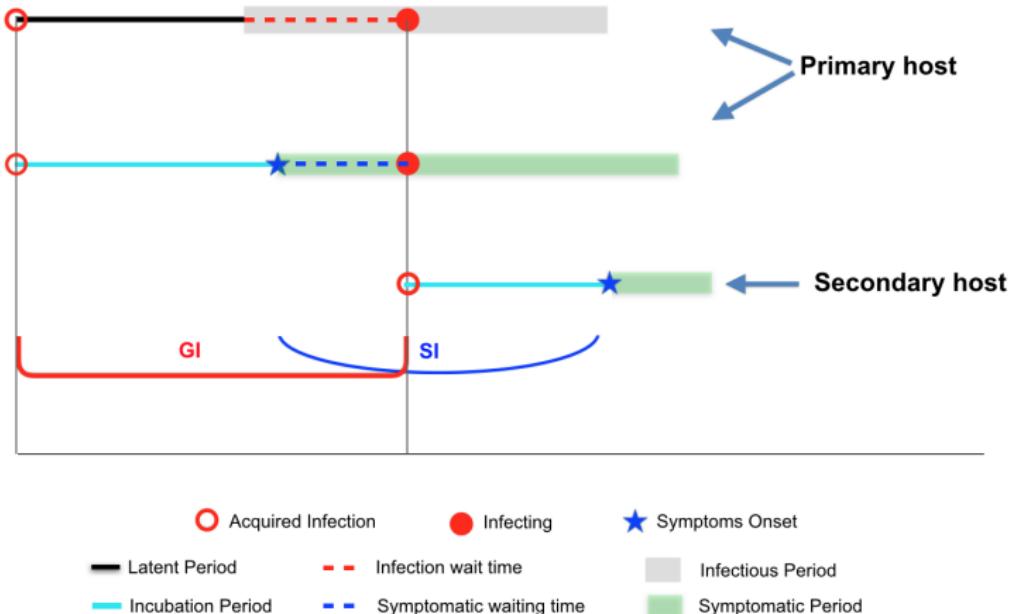
Outline

Foundations

Defining and measuring
Generations in space
Serial intervals

Moving forward

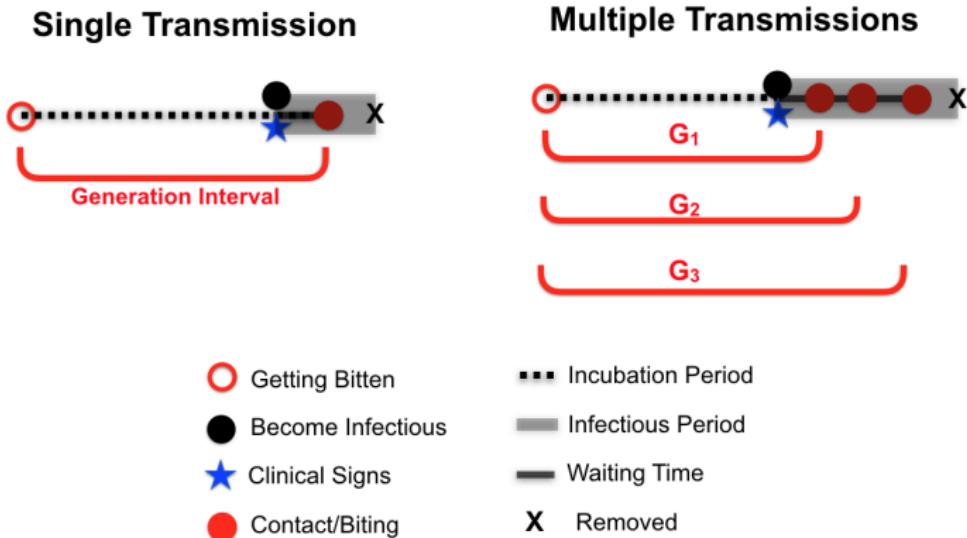
Serial intervals



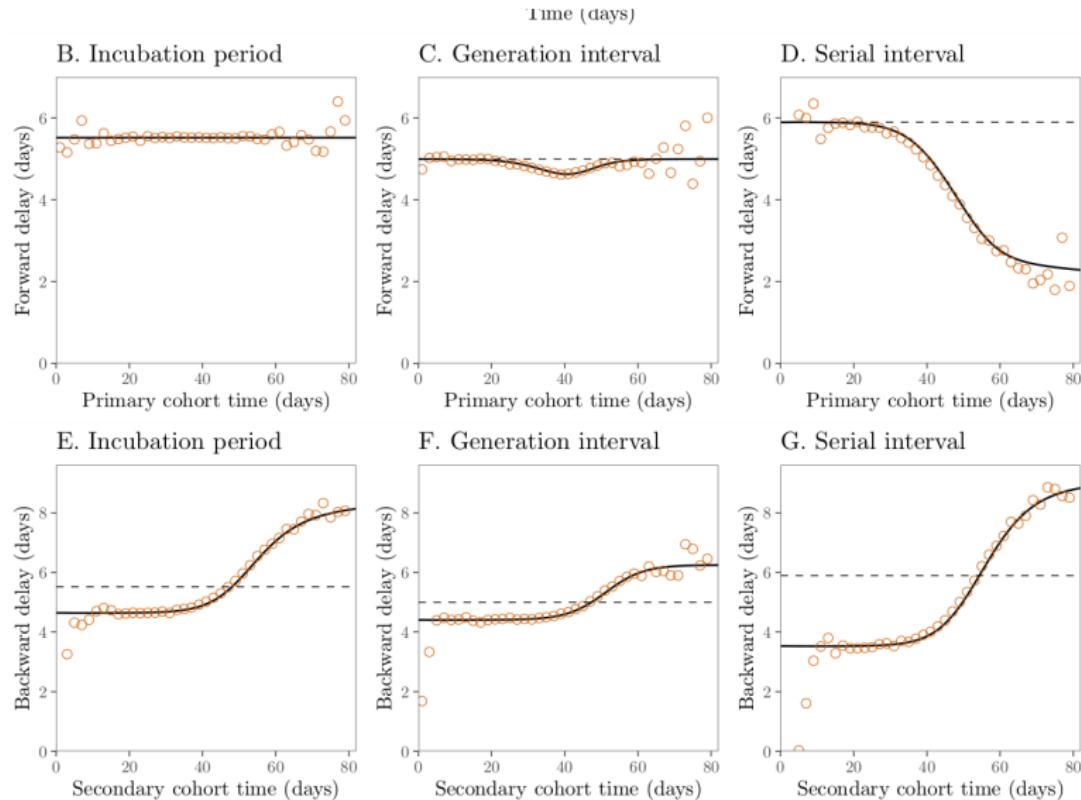
Serial intervals

- ▶ Do serial intervals and generation intervals have the same distribution?
- ▶ It seems that they should: they describe generations of the same process
 - ▶ But serial intervals can even be very different
 - ▶ Even negative! You might report to the clinic with flu before me, even though I infected you

Serial intervals with no asymptomatic spread



Serial intervals with asymptomatic spread



Outline

Foundations

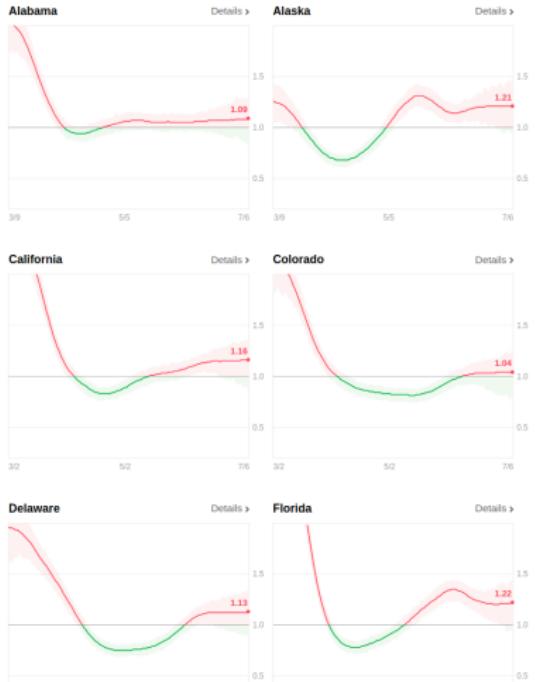
Defining and measuring
Generations in space
Serial intervals

Moving forward

What about R_t ?

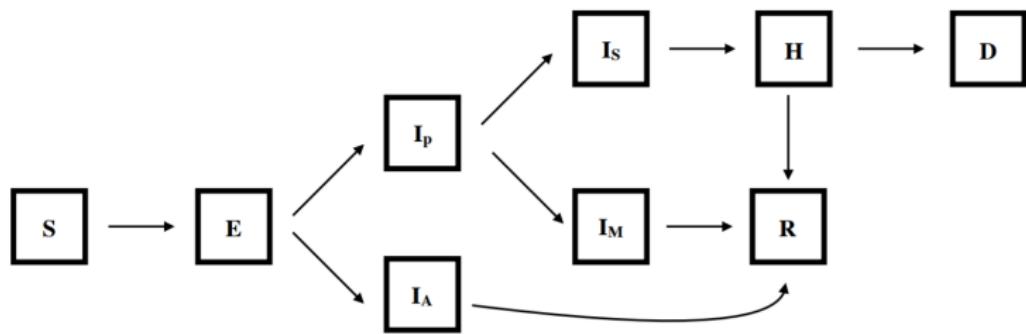


<https://coronavirus.jhu.edu> 2020
Jul 08



<https://rt.live> 2020 Jul 08

Mechanistic modeling



S = susceptible

E = exposed

I_p = pre-symptomatic

I_a = asymptomatic

I_s = symptomatic, severe case

I_m = symptomatic, minor case

H = hospitalized

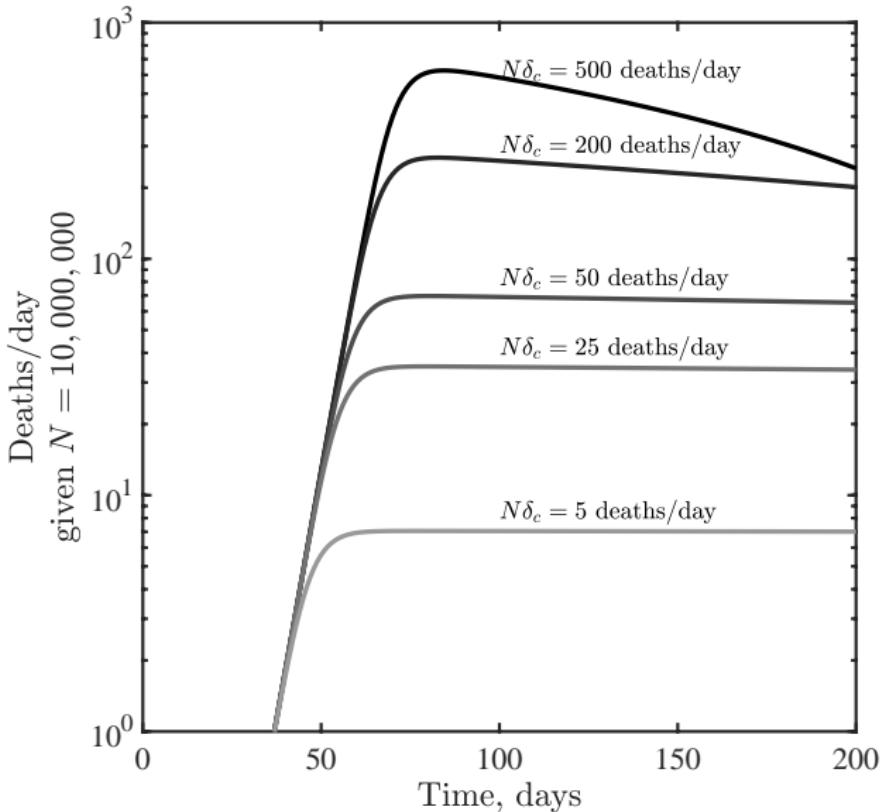
R = recovered

D = dead

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

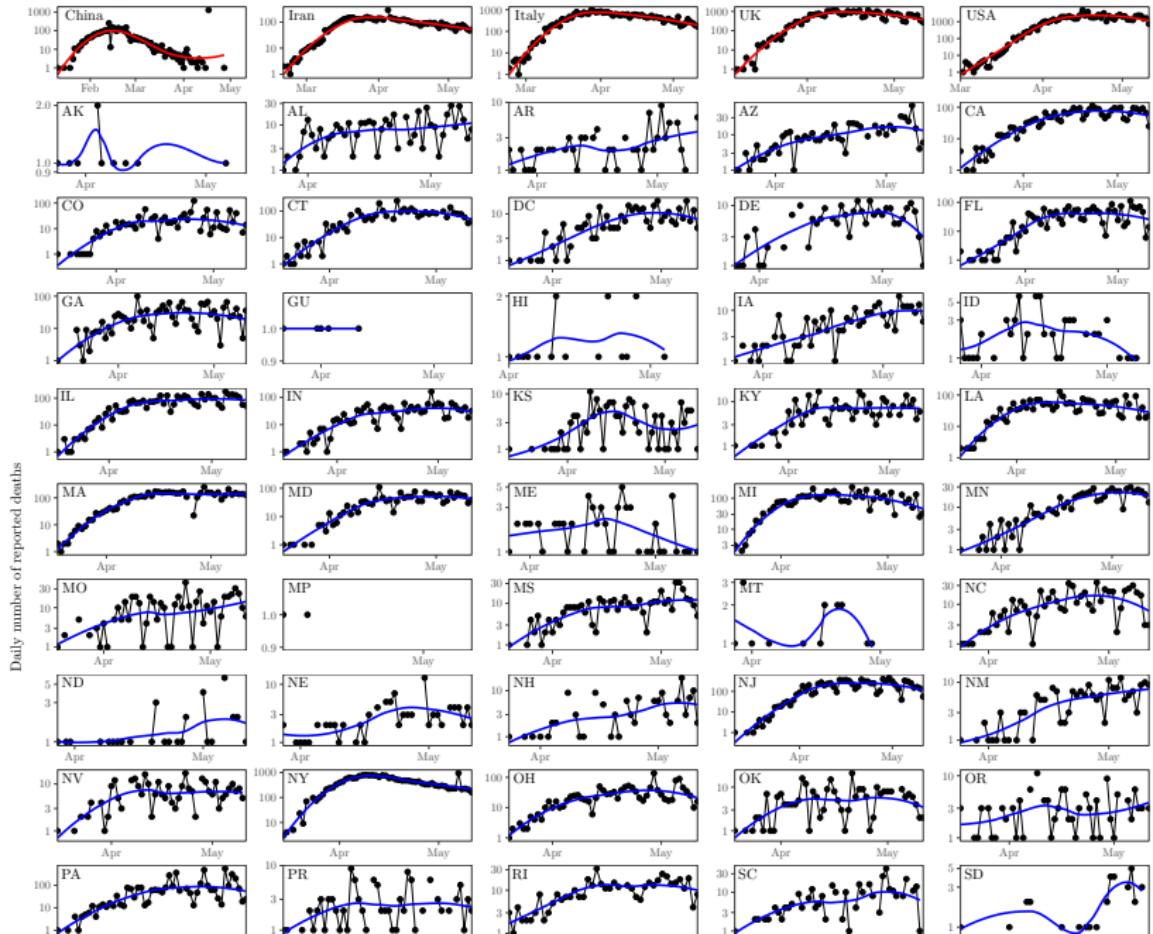
Macpan: <https://github.com/bbolker/McMasterPandemic>

Modeling responses

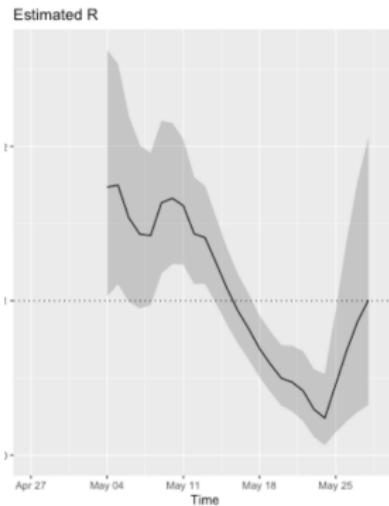


Weitz et al., <https://github.com/jsweitz/covid19-git-plateaus>

Modeling responses



Direct calculation



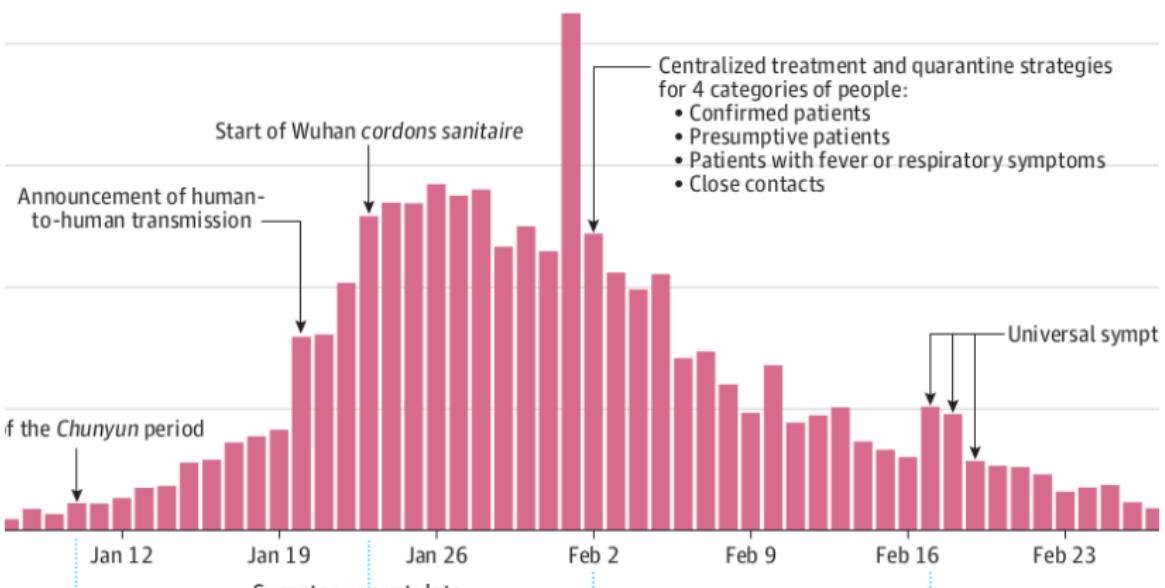
EpiEstim,

<https://cran.r-project.org/web/packages/EpiEstim/vignettes/demo.html>

Wallinga and Teunis, <https://doi.org/10.1098/rsif.2010.0679>

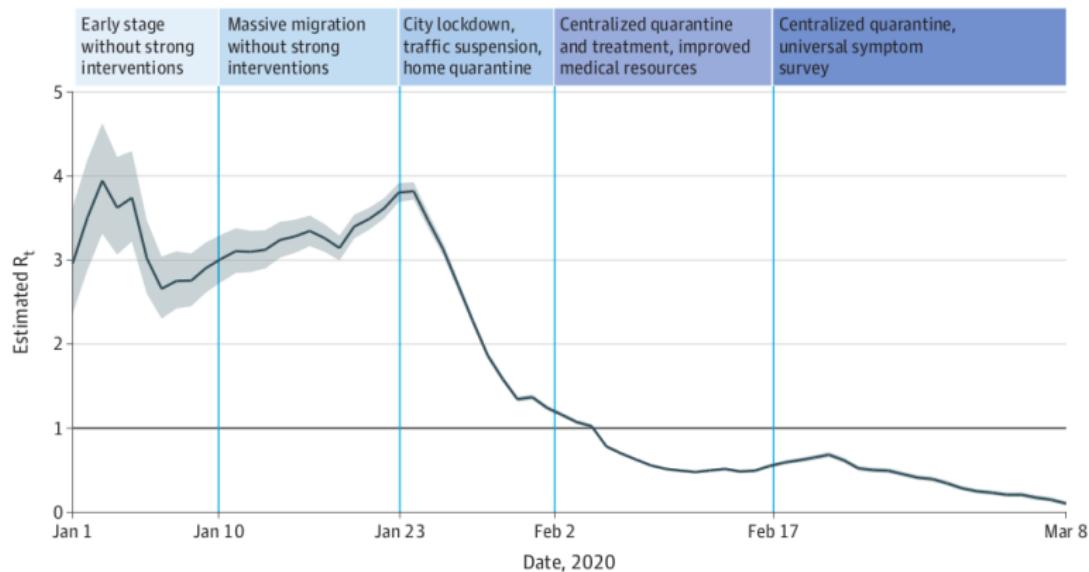
Goldstein et al., <https://doi.org/10.1073/pnas.0902958106>

Wuhan control measures



<https://jamanetwork.com/journals/jama/fullarticle/2764658>

Wuhan control measures



<https://jamanetwork.com/journals/jama/fullarticle/2764658>

How important is interval estimation?

- ▶ It's all averaging
- ▶ Simulation-based validation

Thanks

- ▶ UBC and the organizers
- ▶ Collaborators:
 - ▶ Li, Park, Weitz, Bolker, Earn, Champredon ...
- ▶ Funders: NSERC, CIHR, PHAC, WHO