Measuring the strength and speed of epidemics

McMaster University Origins Institute Colloquium
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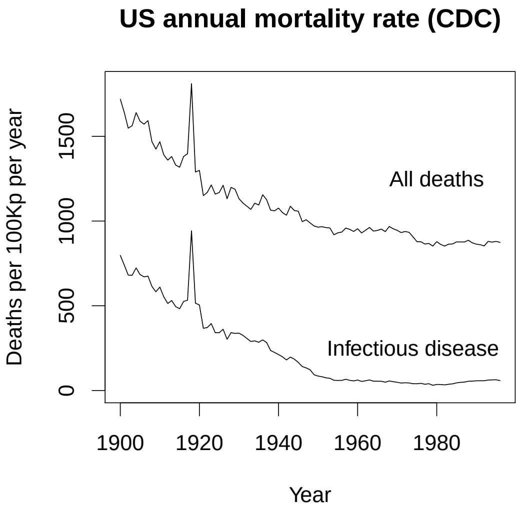
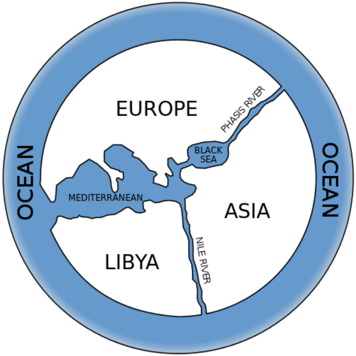
Outline

Infectious diseases

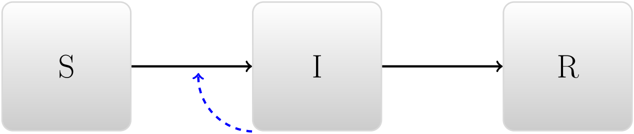

US annual mortality rate (CDC)
All deaths
Infectious disease
Deaths per 100Kp per year
0
500
1000
1500
1900
1920
1940
1960
1980
Year

Models



- A model is a simplified view of the world
- Allows linking between assumptions and outcomes

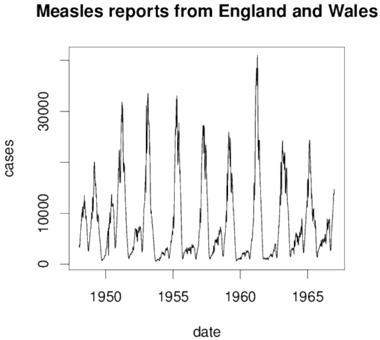
Dynamic models



Small-scale events ⇔ Large-scale patterns and outcomes

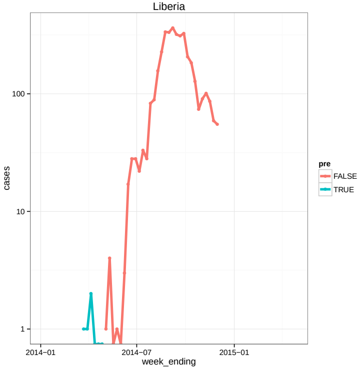
Dynamic modeling

Connects scales

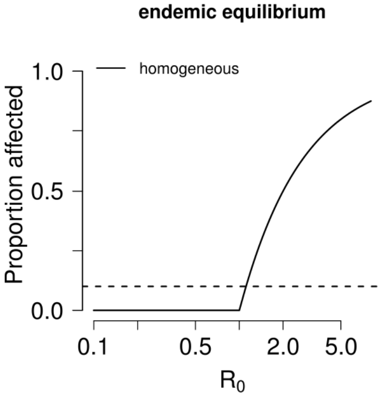


Dynamic modeling

Connects scales

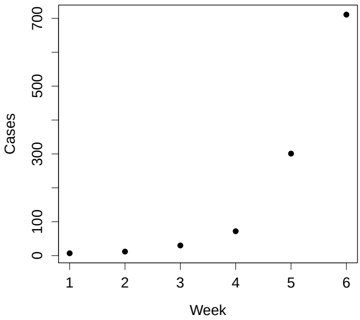


Yellow fever in Panama

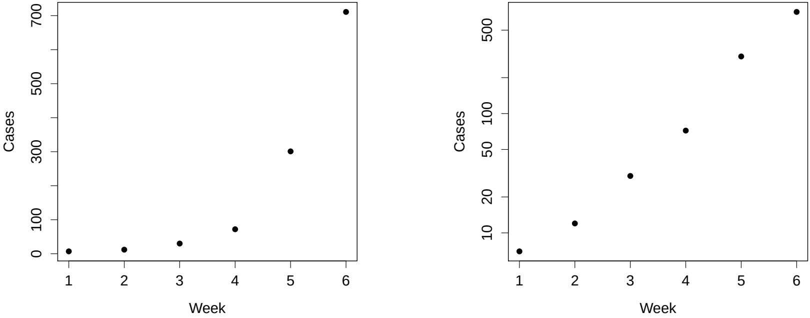


Speed of epidemics

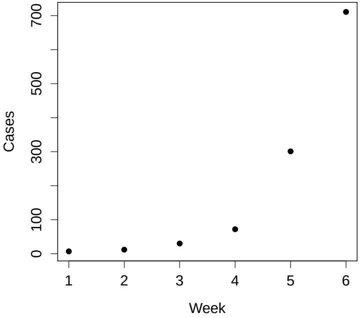
- Exponential growth:
  - Growth proportional to size

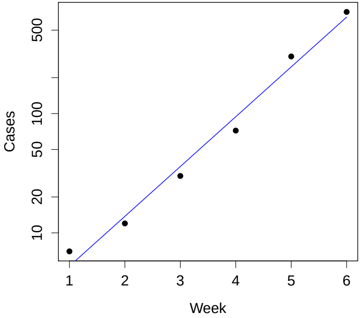


Exponential growth



Exponential growth

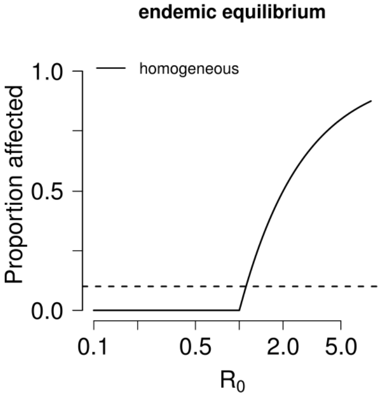




Speed

- 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 $C = 1/r$
  - Ebola, $C \approx 1\mathrm{month}$
  - HIV in SSA, $C \approx 18\mathrm{month}$

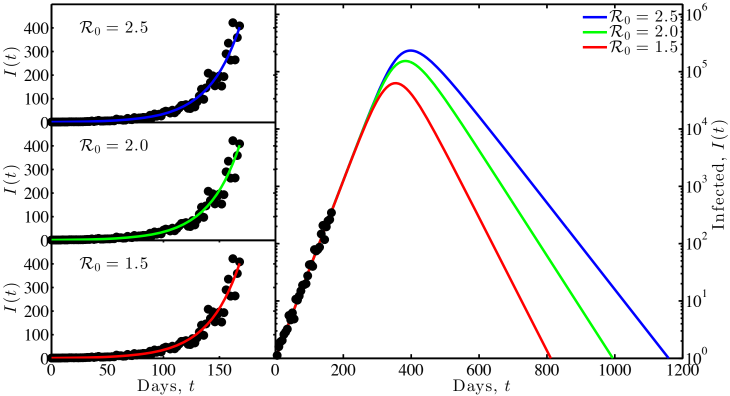
Strength of epidemics



Basic reproductive number

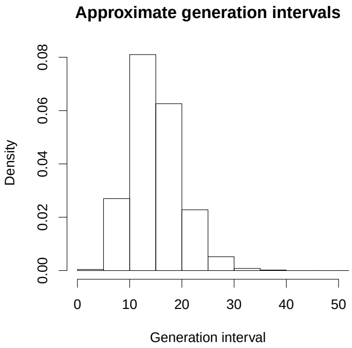
- We describe epidemic strength with big $\mathcal{R}$
- Number of potential new cases per case
- To eliminate disease, we must:
  - Reduce transmission by a factor of $\mathcal{R}$ *or*
  - Reduce number of susceptible people by a factor of $\mathcal{R}$ *or* …
- Examples:
  - Ebola, $\mathcal{R} \approx 2$
  - HIV in SSA, $\mathcal{R} \approx 5$

Linking little r and big $\mathcal{R}$

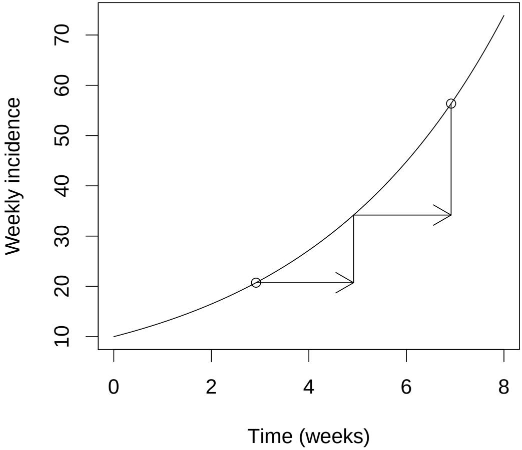


Generation intervals

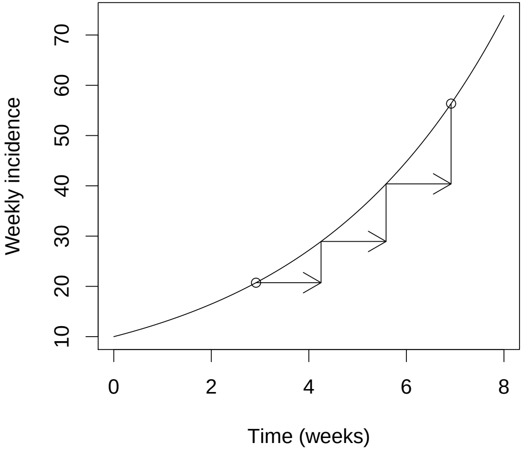
- The generation distribution measures generations of the disease
  - Interval between “index” infection and resulting infection
- What does G tell us about how dangerous the epidemic is?
  - It depends on what else we know!



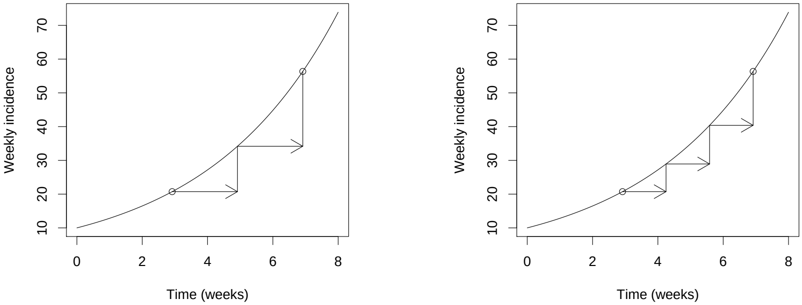
Generations and $\mathcal{R}$



Generations and $\mathcal{R}$



Generations and $\mathcal{R}$



Conditional effect of generation time

- *Given* the reproductive number $\mathcal{R}$
  - faster generation time G means faster spread time C
  - More danger
- *Given* the spread time C
  - faster generation time G means *smaller* $\mathcal{R}$
  - Less danger

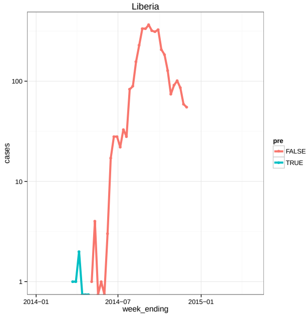
Outline

Generation intervals through time

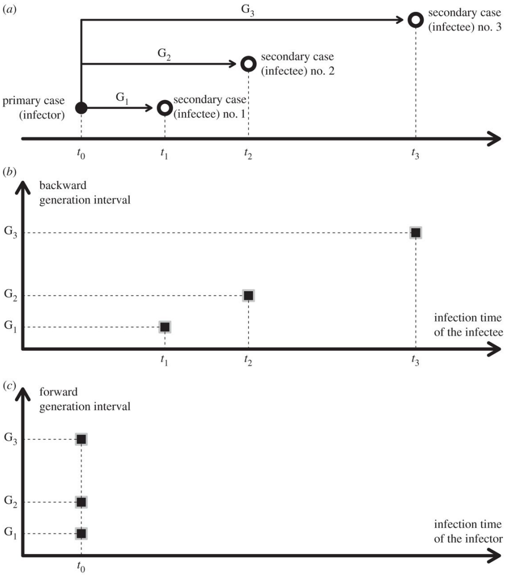
- Generation intervals can be estimated by:
  - Observing patients:
    - How long does it take to become infectious?
    - How long does it take to recover?
    - What is the time profile of infectiousness/activity?
  - Contact tracing
    - Who (probably) infected whom?
    - When did each become ill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

Growing epidemics

- Generation intervals look *faster* 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

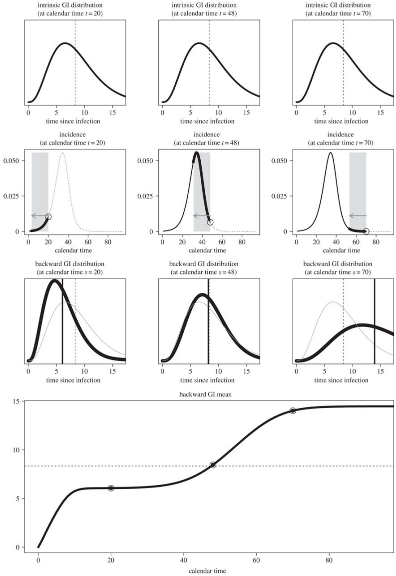


Forward and backward intervals

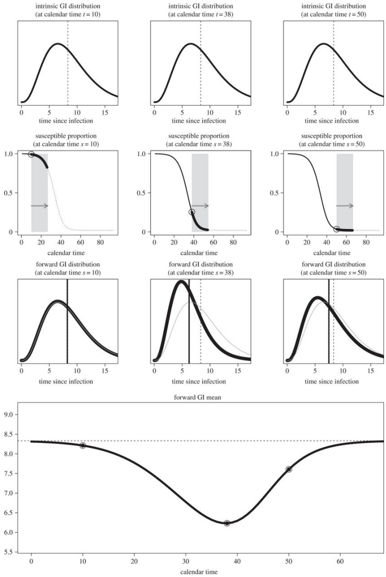


16 Champredon and Dushoff, 2015. DOI:10.1098/rspb.2015.2026

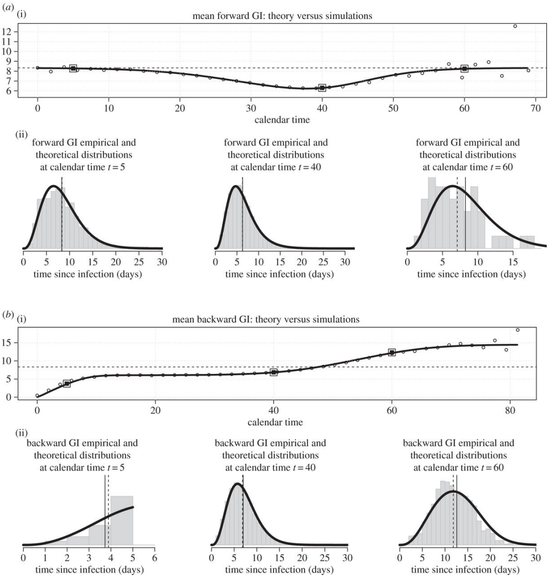
What changes backward intervals?



What changes forward intervals?



Comparison to simulations



Conclusion

- Backward intervals change if the number of infectious individuals is changing as you look back
- Forward intervals change if the number of *susceptible* individuals is changing as you look forward
- Lack of care in defining generation intervals can lead to bias
    - Results also tell us how to correct this bias

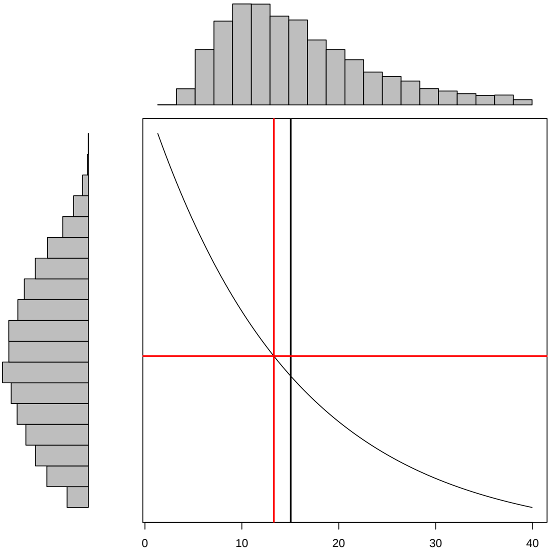
Outline

The “effective” generation time

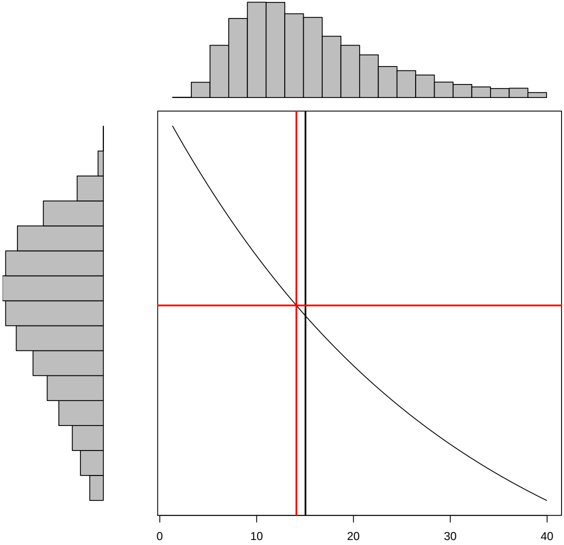
- If the generation interval were absolutely fixed at a time interval of G, then
  - $$\mathcal{R} = \exp(G/C)$$
- *Define* the effective generation time so that this remains true:
  - $$\mathcal{R} = \exp(\hat{G}/C)$$
- We can show $\hat{G}$ is a “filtered mean” of the distribution g:
  - $$\exp(-\hat{G}/C) = \langle \exp(-\tau/C) \rangle_g .$$

,

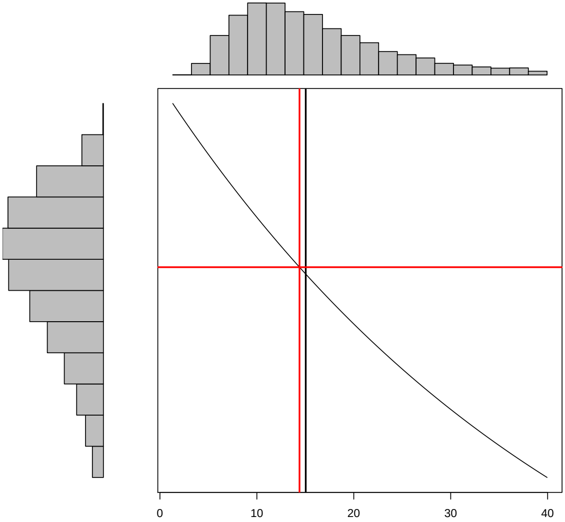
$C = 15d$



$C = 30d$



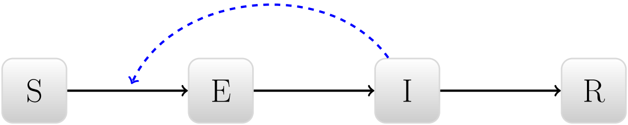
$C = 45d$



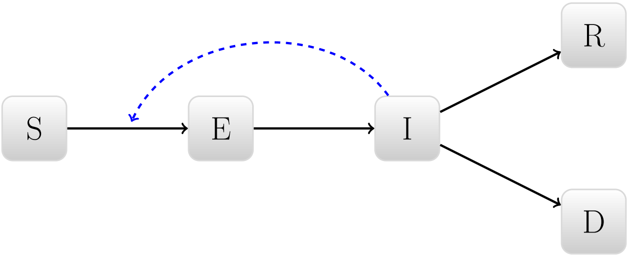
Example: Post-death transmission and safe burial

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

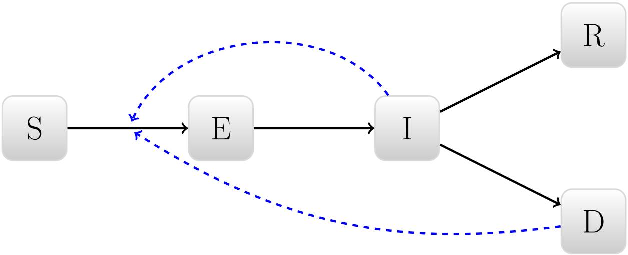
Standard disease model



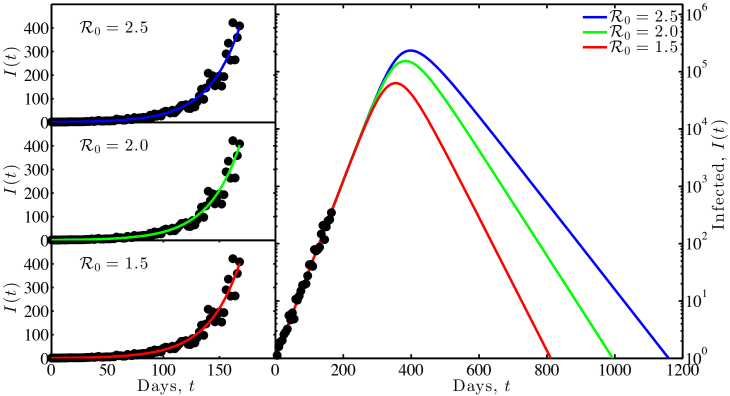
Disease model including post-death transmission



Disease model including post-death transmission



Scenarios



$\mathcal{R}_0 = 2.5$
$\mathcal{R}_0 = 2.0$
$\mathcal{R}_0 = 1.5$
$I(t)$
Days, t
Infected, $I(t)$

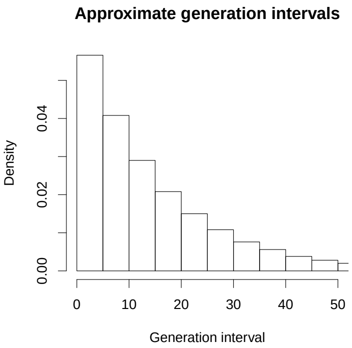
Conclusions

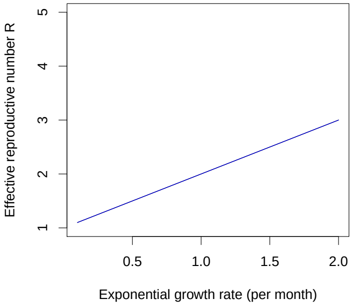
- Different parameters can produce indistinguishable early dynamics
- More after-death transmission implies
  - Higher $\mathcal{R}_0$
  - Larger epidemics
  - Larger importance of safe burials

An approximation

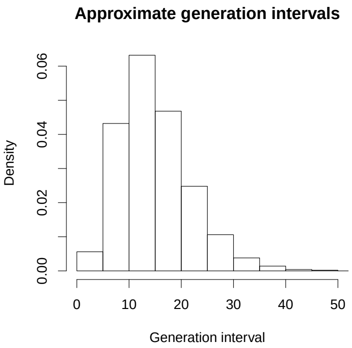
- We connect these quantities with a moment approximation
- Define $\kappa = \sigma_G^2/\mu_G^2$ – the squared coefficient of variation of the generation distribution
- $\mathcal{R} \approx (1 + \kappa\bar{G}/C)^{1/\kappa}$
  - Equal when G has a gamma distribution
  - Simple and straightforward
  - When is it a useful approximation?

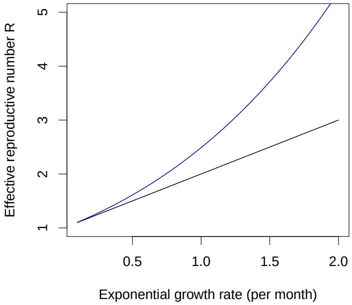
Moment approximation



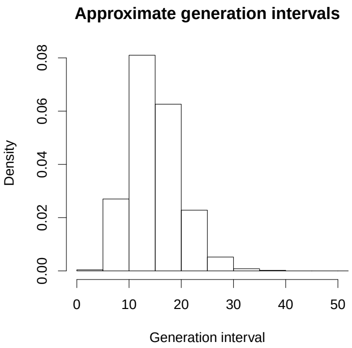


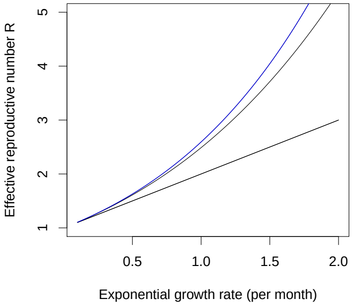
Moment approximation



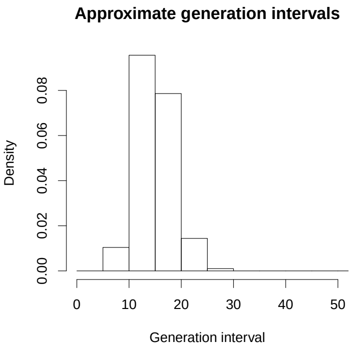


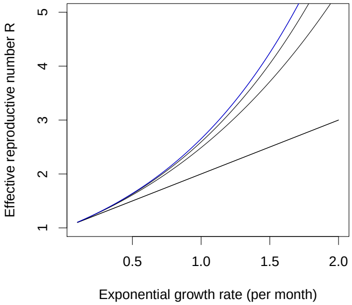
Moment approximation





Moment approximation

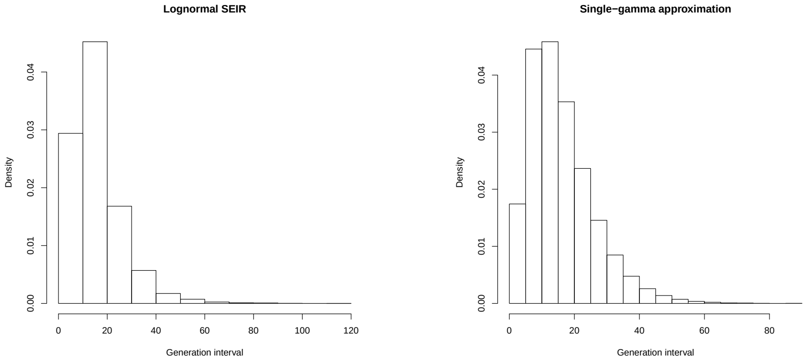




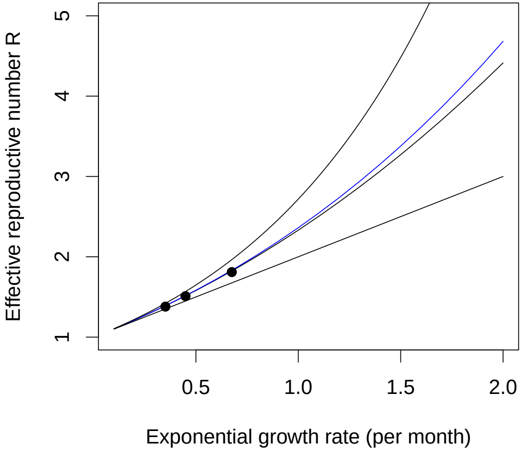
Fitting to Ebola

- Simulate generation intervals based on data and approach from WHO report
- Use both lognormals and gammas
  - WHO used gammas
  - Lognormals should be more challenging

Approximating the distribution



Approximating the curve



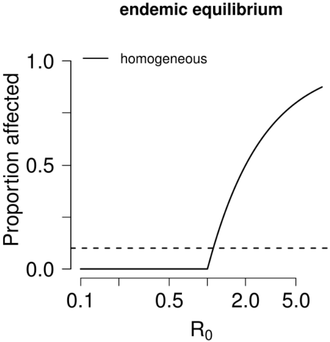
Summary

- Generation intervals are the missing link between r and $\mathcal{R}$
- We need better methods for estimating them, and propagating uncertainty to other parts of the model
- For many practical applications:
  - Knowing the mean generation interval is not enough
  - But knowing the mean and CV may be enough

Outline

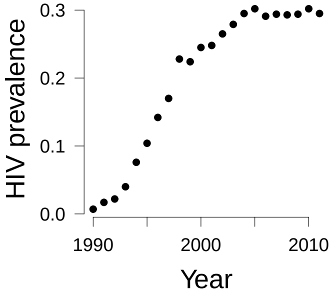
Strength: $\mathcal{R}$ – the reproductive number

- Expected number of new cases per cases
- $\mathcal{R} = \beta DS/N$
  - Disease increases iff $\mathcal{R} > 1$



Speed: r – the growth rate

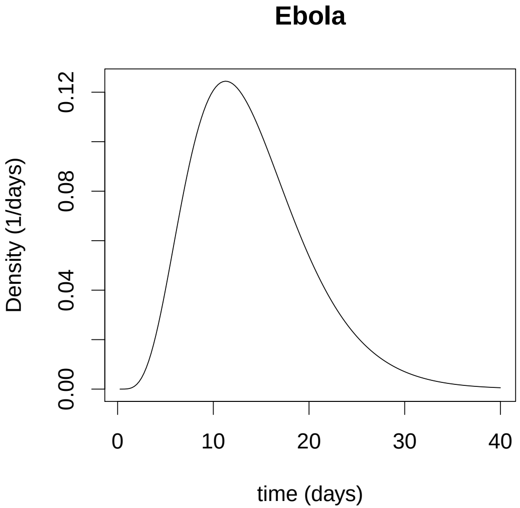
- $i(t) \approx i(0)\exp(rt)$
- $C = 1/r$
- $T_2 = \ln(2)/r$



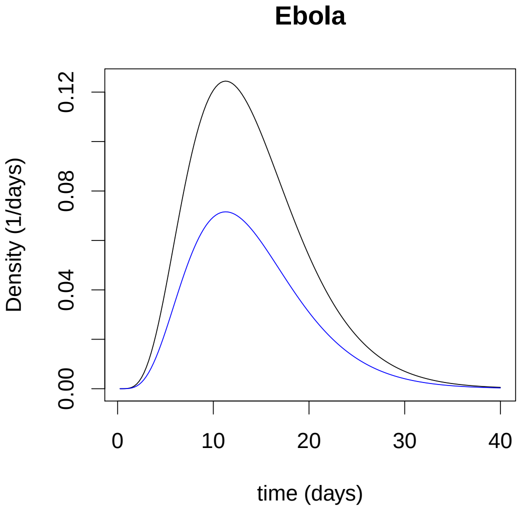
$\mathcal{R}$ and the generation interval

- $i(t) = \displaystyle\int k(\tau) i(t-\tau)\, d\tau$
- $\mathcal{R} = \int k(\tau) d\tau$
- Define the intrinsic generation interval distribution: $k(\tau) = \mathcal{R} g(\tau)$

$\mathcal{R}$ and the generation interval



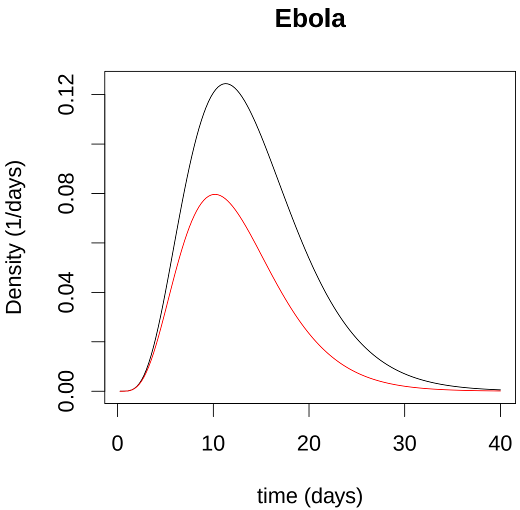
$\mathcal{R}$ and the generation interval



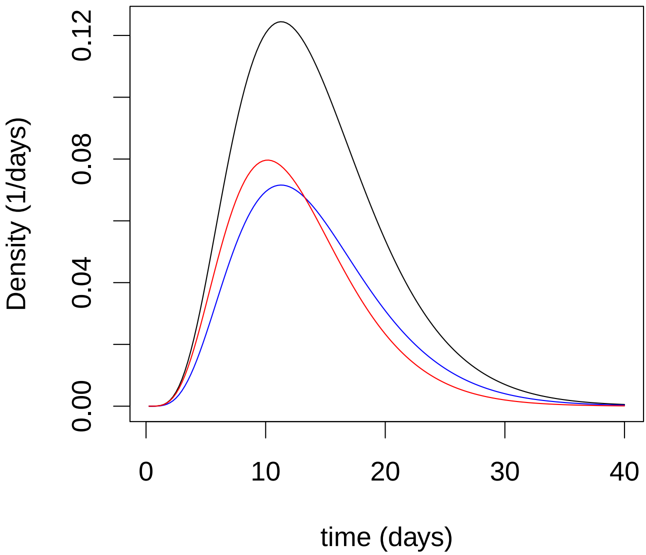
r and the (other) generation interval

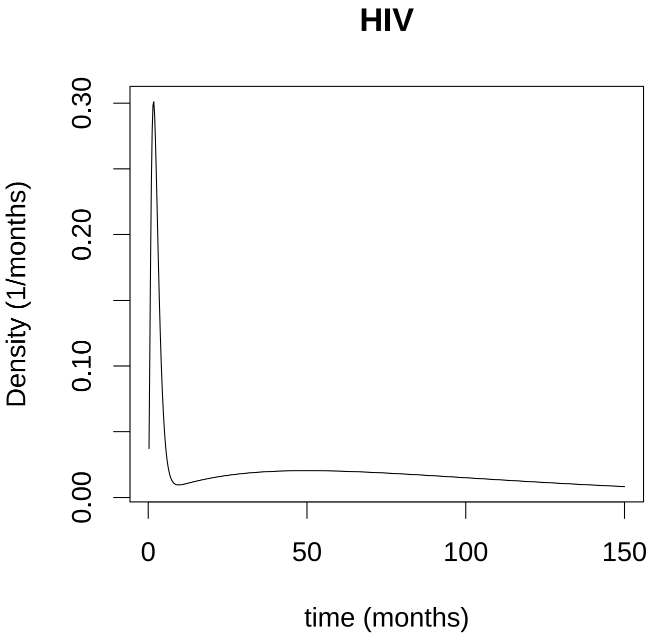
- $i(t) = \int k(\tau) i(t-\tau)\, d\tau$
- if $i(t)$ grows like $\exp(rt)$, then
- $1 = \int k(\tau) \exp(-r\tau)\, d\tau$
- $b_0(\tau) = k(\tau) \exp(-r\tau)$ is the initial *backwards* generation interval

r and the (other) generation interval

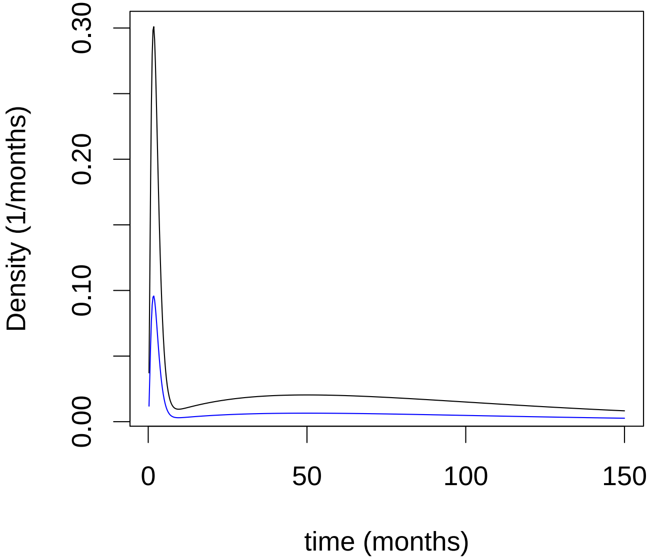


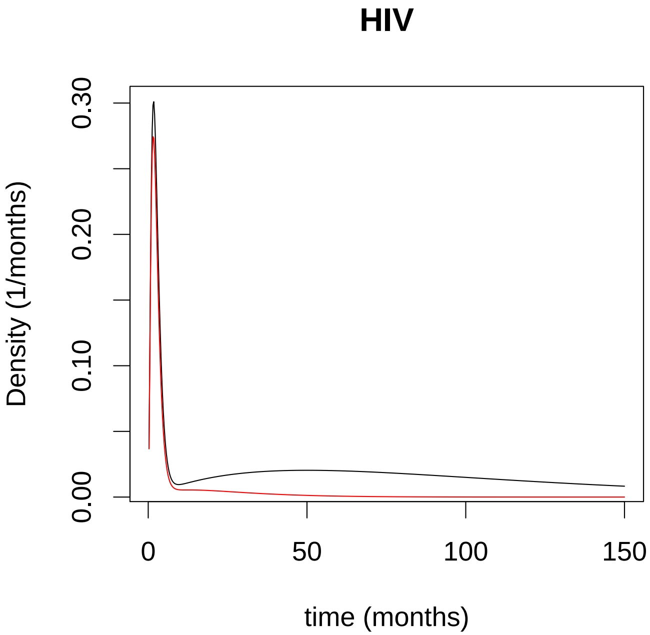
Ebola




HIV
Density (1/months)
0.00
0.10
0.20
0.30
0
50
100
150
time (months)

HIV

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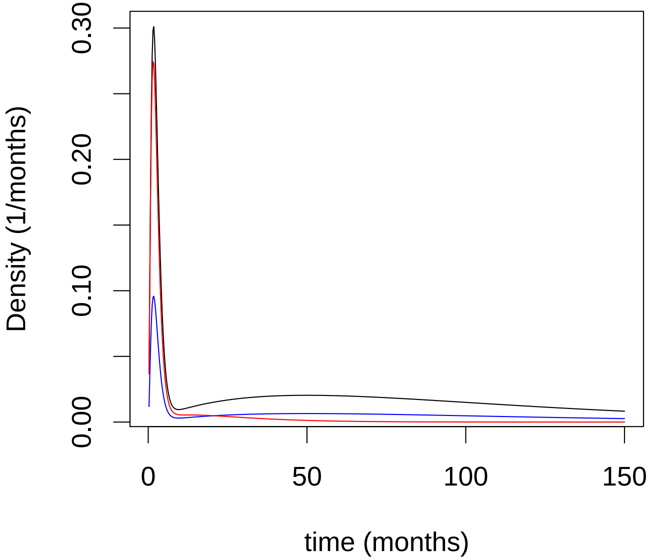


Strength of intervention

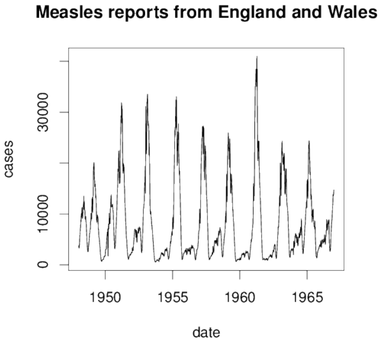
- Imagine we have an intervention that reduces transmission
  - $k(\tau) \to k(\tau)/L(\tau)$
  - Define *strength* $\theta = \mathcal{R}/\hat{\mathcal{R}}$ – the proportional amount by which the intervention reduces transmission.
- We then have:
  - $\theta = 1/\left\langle 1/L(\tau)\right\rangle_{g(\tau)}$
  - θ is *the harmonic mean* of L, weighted by the generation distribution g.
- Outbreak can be controlled if $\theta > \mathcal{R}$

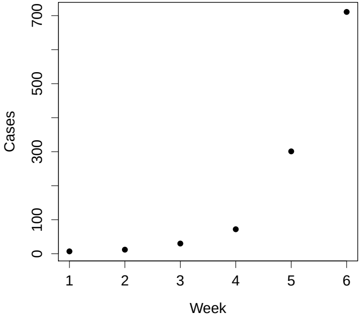
Speed of intervention

- Define the *speed* of an intervention be $\phi = r - \hat{r}$ – the amount by which the intervention slows down spread.
- $1 = \left\langle \dfrac{\exp(\phi\tau)}{L(\tau)} \right\rangle_{b(\tau)}$
- ϕ is *sort of a mean* of the *hazard* associated with L
  - Averaged over the initial *backwards* generation interval
- Outbreak can be controlled if $\phi > r$.

A new way of looking

Measuring the epidemic

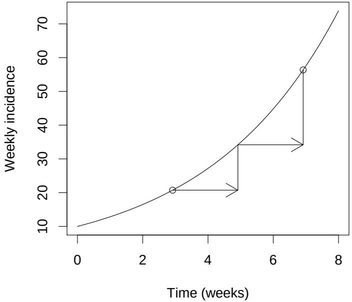




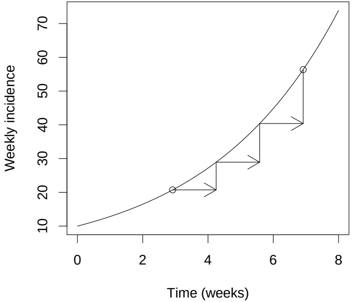
Measuring the intervention

Can treatment stop the HIV epidemic?

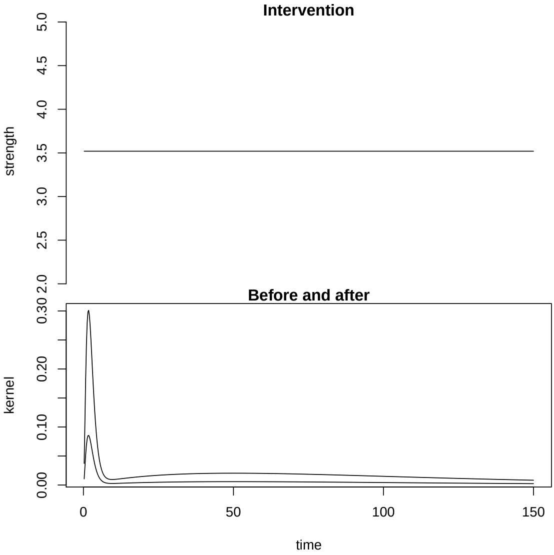
Are HIV generations fast or slow?



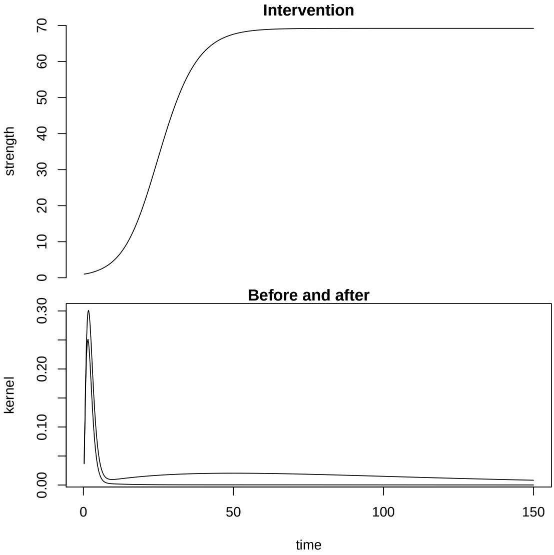
- Fast generations mean:
  - Testing and treating will help less
  - *but* lower epidemic strength



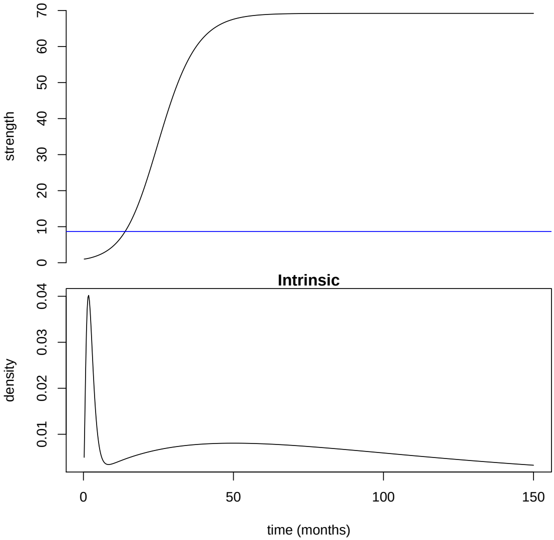
Condom intervention



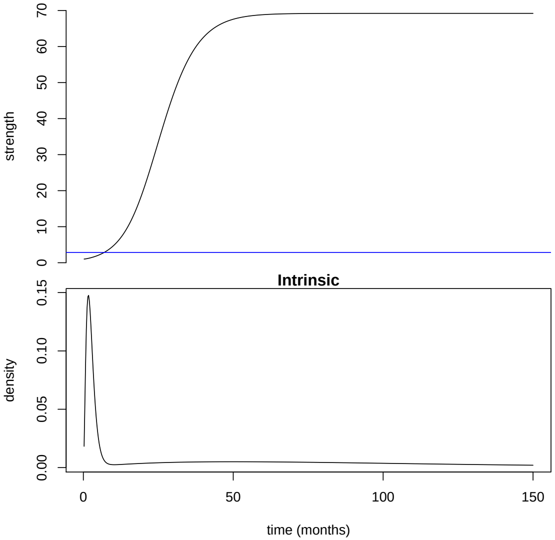
Find and treat



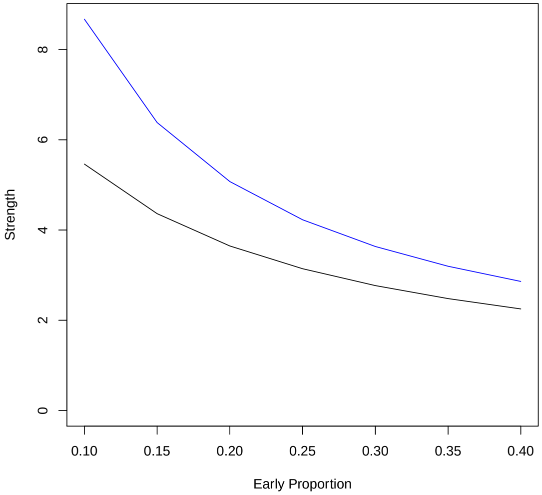
Low early transmission



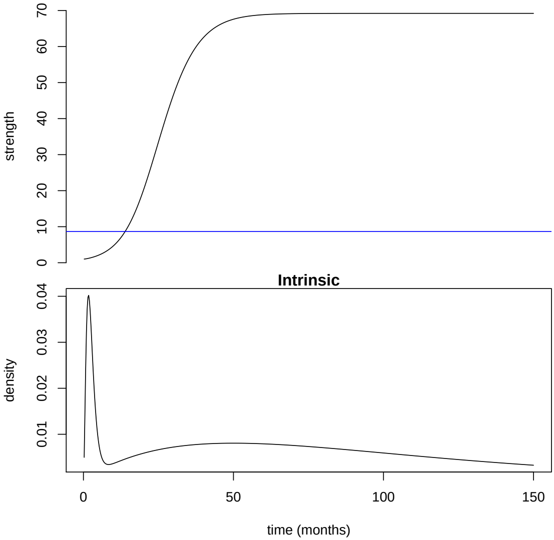
High early transmission



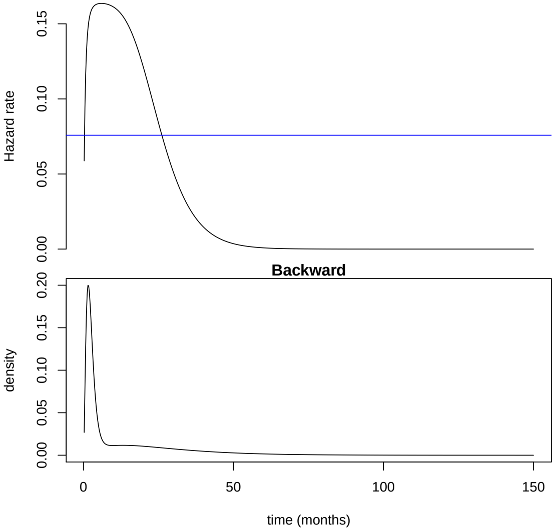
Range of estimates



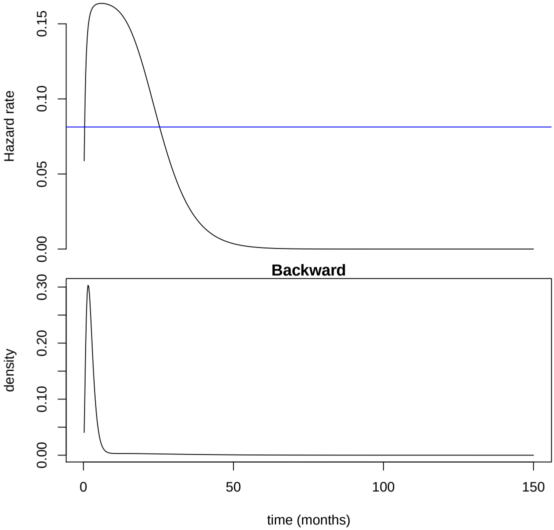
Find and treat



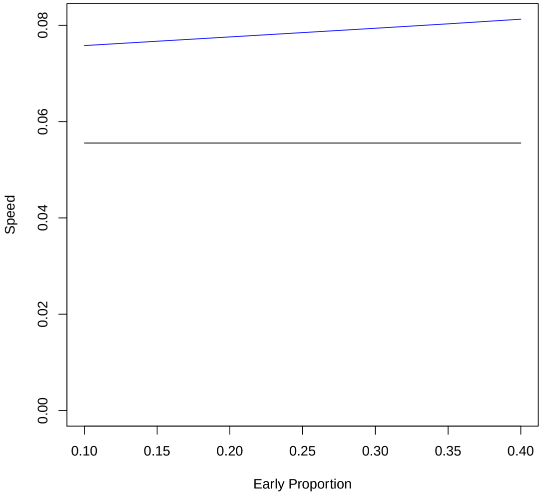
Low early transmission



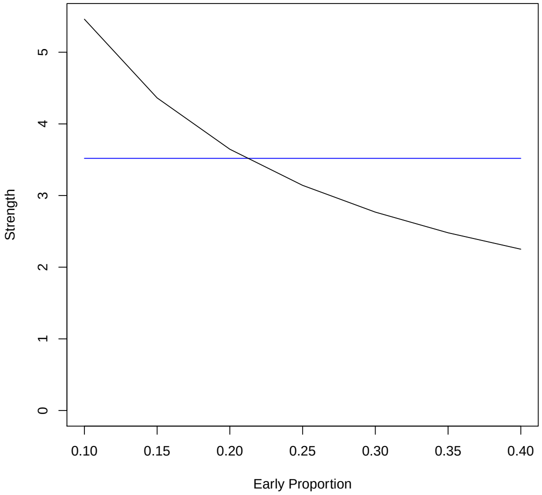
High early transmission



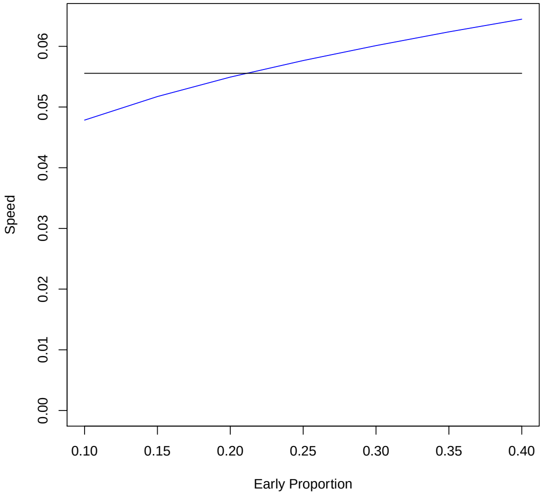
Range of estimates



Condom intervention



Condom intervention



Conclusion

- This perspective helps us understand why find and treat predictions are robust to assumptions about transmission
- Sometimes “strength” and sometimes “speed” can help us see epidemic control questions more clearly

Thanks

- Organizers
- Audience
- Collaborators
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