

Epidemic strength and speed: rethinking metrics for infectious disease spread and control.

SMB 2017

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Outline

Introduction

- Speed of epidemics

- Strength of epidemics

Linking strength and speed

- Generation intervals

- The “effective” generation time

- Moment approximations

Generation intervals through time

Strength and Speed of Epidemics

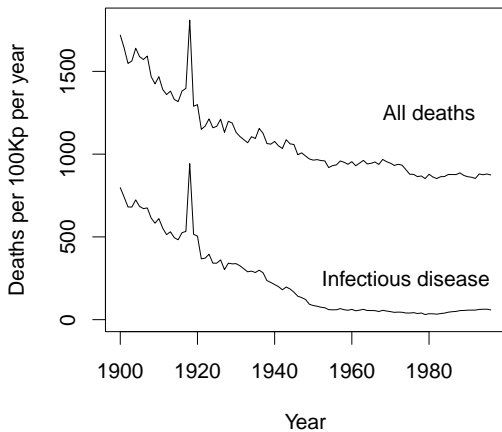
- HIV example

Infectious diseases

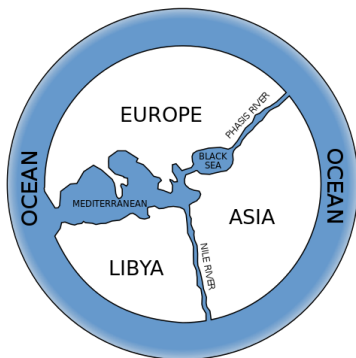




US annual mortality rate (CDC)



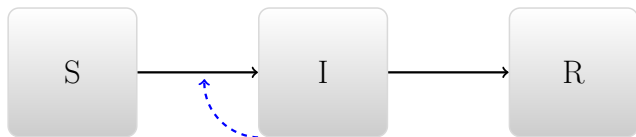
Models



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

Dynamic models

Connect scales



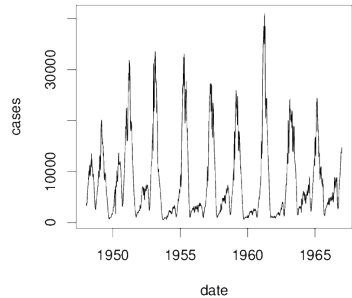
Small-scale events \Leftrightarrow Large-scale patterns and outcomes

Measles

Dynamic modeling connects scales

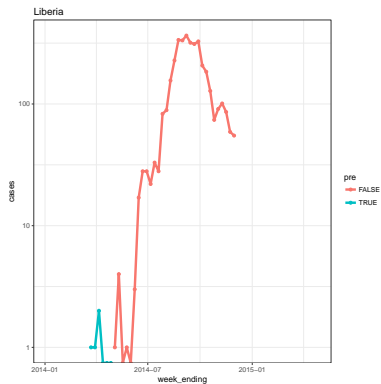


Measles reports from England and Wales



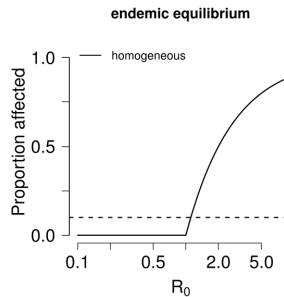
Ebola

Dynamic modeling connects scales



Yellow fever

Dynamic modeling connects scales



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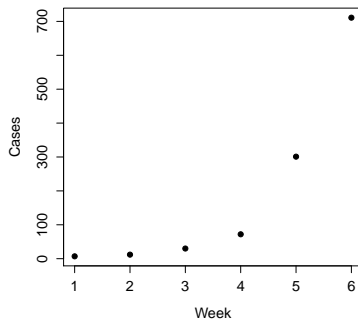
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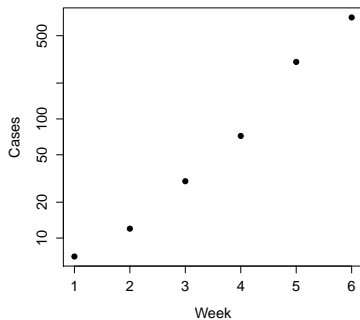
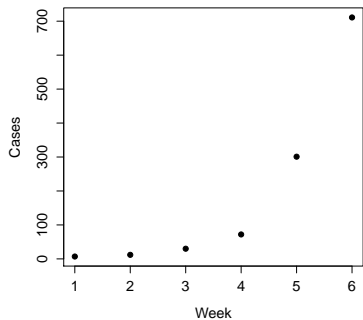
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Speed of epidemics

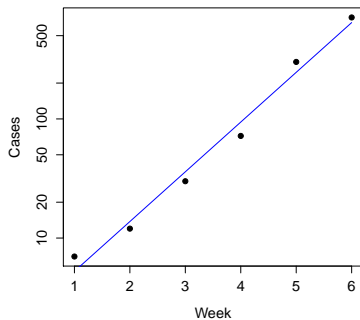
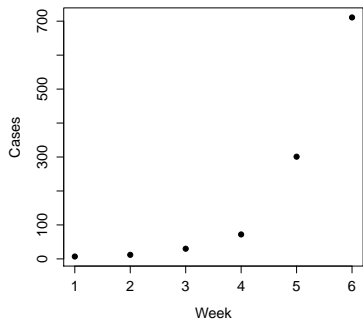
- ▶ Exponential growth:
 - ▶ Growth proportional to size



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, $C \approx 1\text{month}$
 - ▶ HIV in SSA, $C \approx 18\text{month}$
- ▶ ADD Ebola, HIV slides

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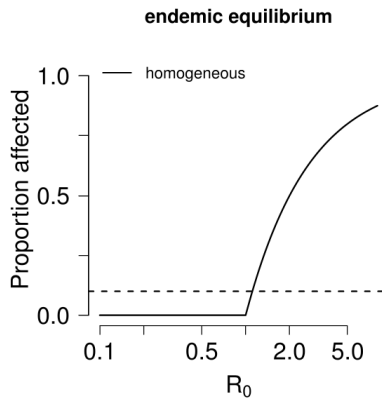
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HIV example

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, $\mathcal{R} \approx 5$

Final size

ADD Content

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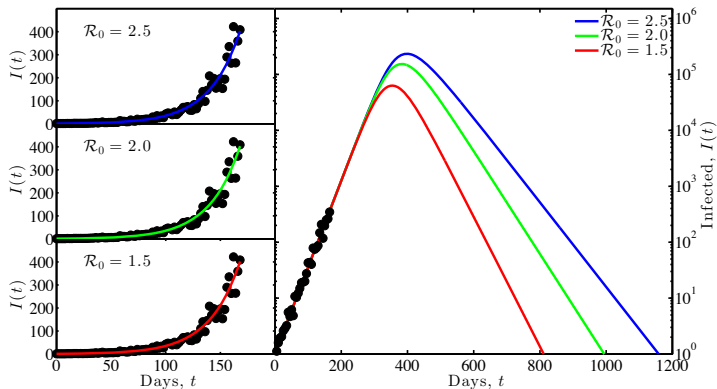
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Linking little r and big \mathcal{R}



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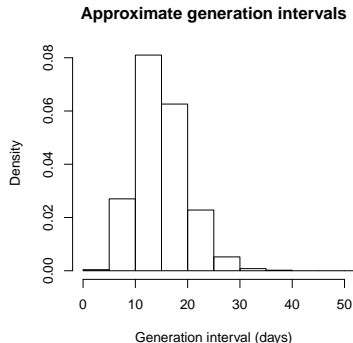
Generation intervals through time

Strength and Speed of Epidemics

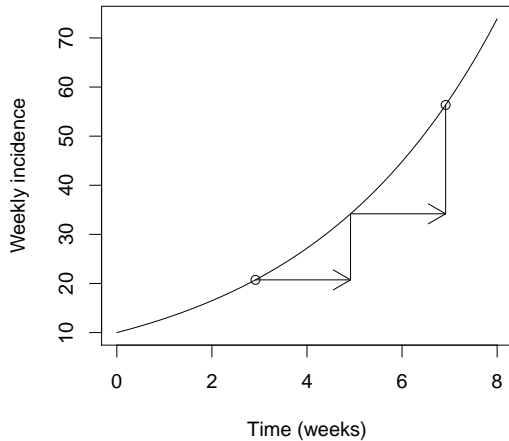
HIV example

Generation intervals

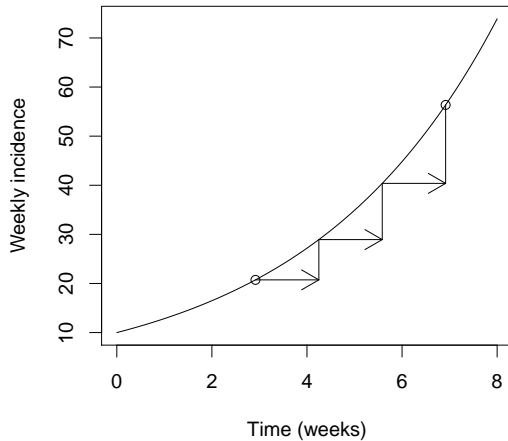
- ▶ The generation distribution measures generations of the disease
 - ▶ Interval between “index” infection and resulting infection
- ▶ What does G tell us about how dangerous the epidemic is?
 - ▶ It depends on what else we know!



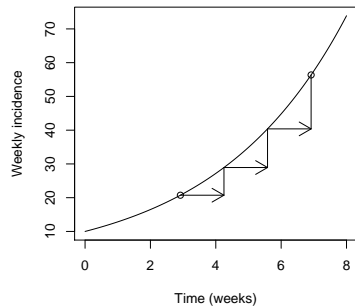
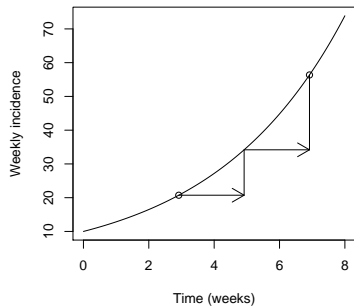
Generations and \mathcal{R}



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

Speed abstraction



Epidemic speed = Epidemic strength \times Generation speed



$$\text{Epidemic strength} = \frac{\text{Epidemic speed}}{\text{Generation speed}}$$

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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:



$$\mathcal{R} = \exp(\hat{G}/C)$$

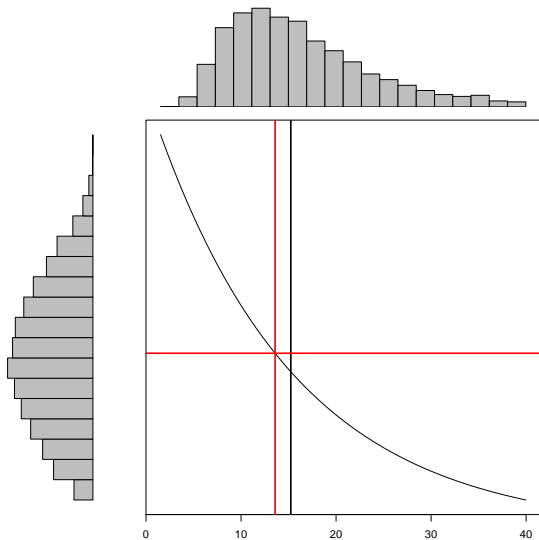
- ▶ We can show \hat{G} is a “filtered mean” of the distribution g :



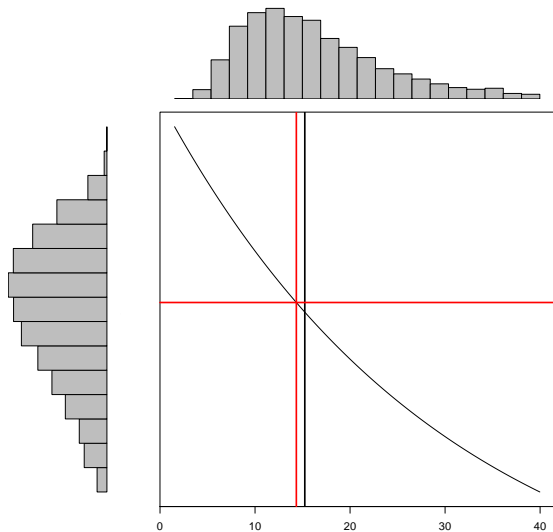
$$\exp(-\hat{G}/C) = \langle \exp(-\tau/C) \rangle_g.$$

,

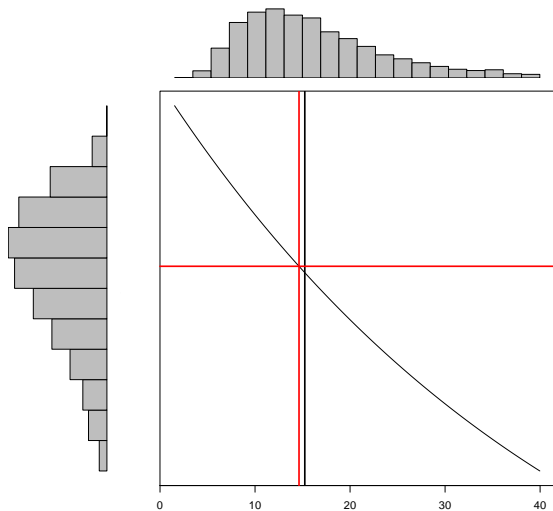
$$C = 15d$$



$$C = 30d$$



$$C = 45d$$

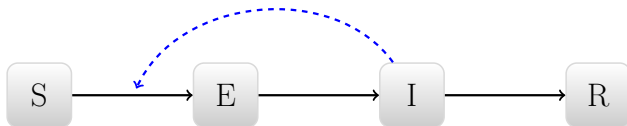


Example: Post-death transmission and safe burial

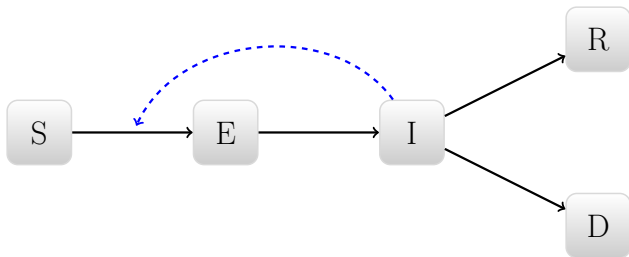
- ▶ How much Ebola spread occurs before vs. after death
- ▶ Highly context dependent
 - ▶ Funeral practices, disease knowledge
- ▶ *Weitz and Dushoff Scientific Reports 5:8751.*



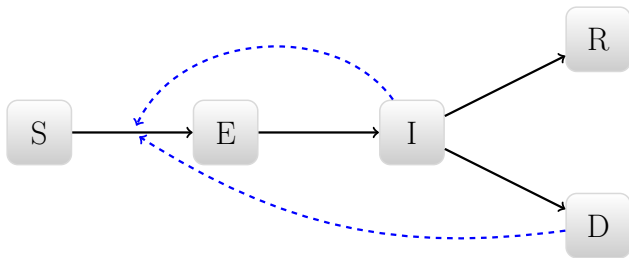
Standard disease model



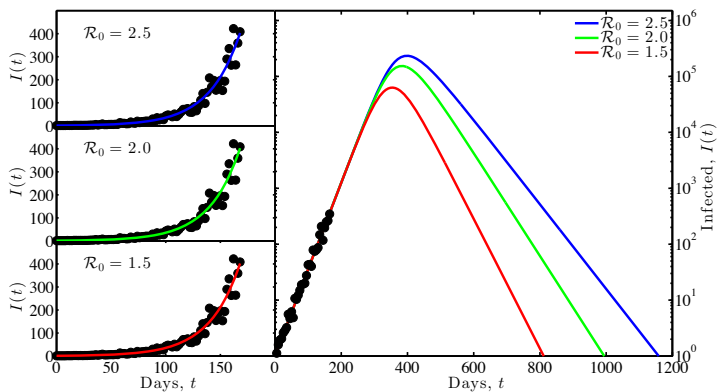
Disease model including post-death transmission



Disease model including post-death transmission



Scenarios



Conclusions

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

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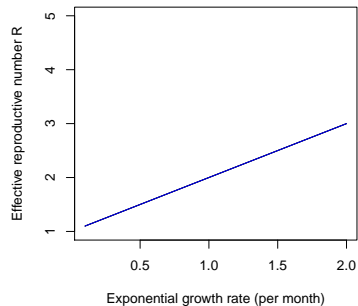
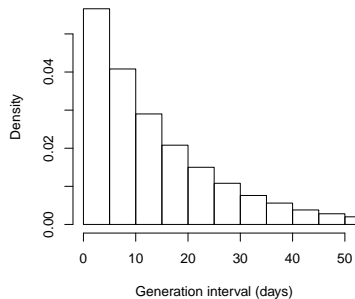
HIV example

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?

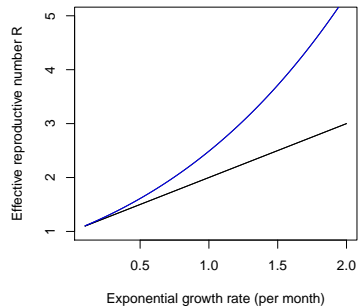
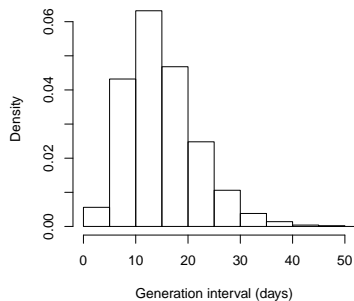
Moment approximation

Approximate generation intervals



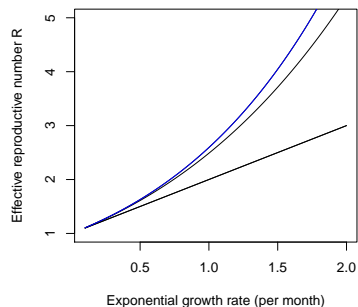
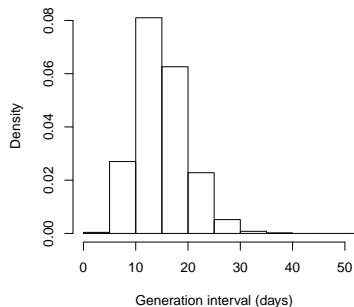
Moment approximation

Approximate generation intervals



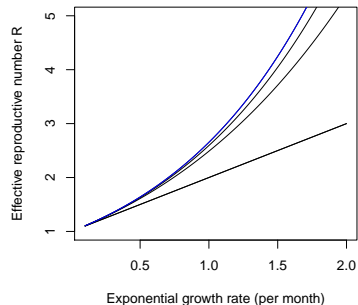
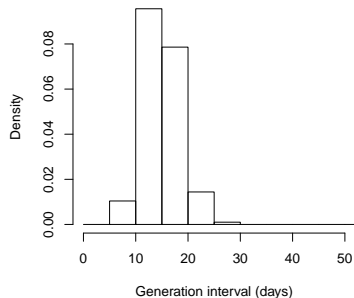
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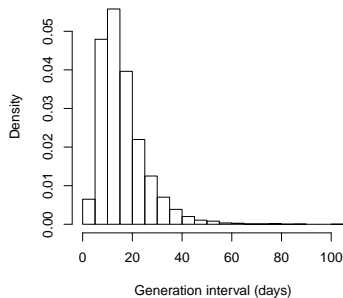


Fitting to Ebola

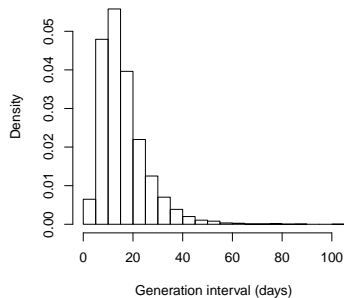
- ▶ Simulate generation intervals based on data and approach from WHO report
- ▶ Use both lognormals and gammas
 - ▶ WHO used gammas
 - ▶ Lognormals should be more challenging

Approximating the distribution

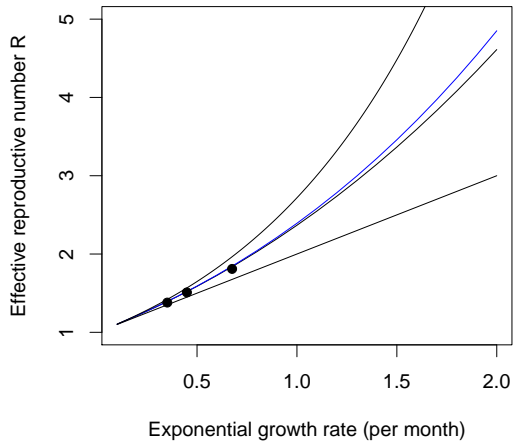
Lognormal SEIR



Single-gamma approximation



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

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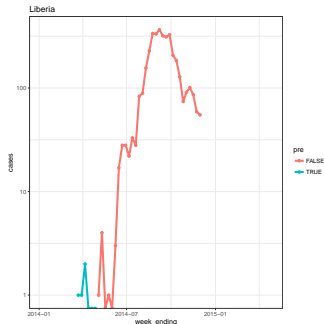
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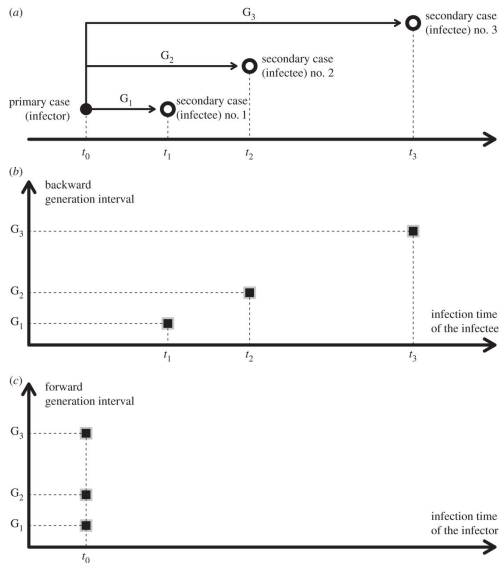
- ▶ Generation intervals can be estimated by:
 - ▶ Observing patients:
 - ▶ How long does it take to become infectious?
 - ▶ How long does it take to recover?
 - ▶ What is the time profile of infectiousness/activity?
 - ▶ Contact tracing
 - ▶ Who (probably) infected whom?
 - ▶ When did each become ill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

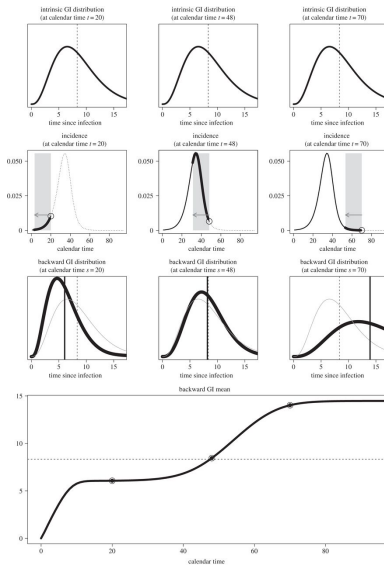


Forward and backward intervals

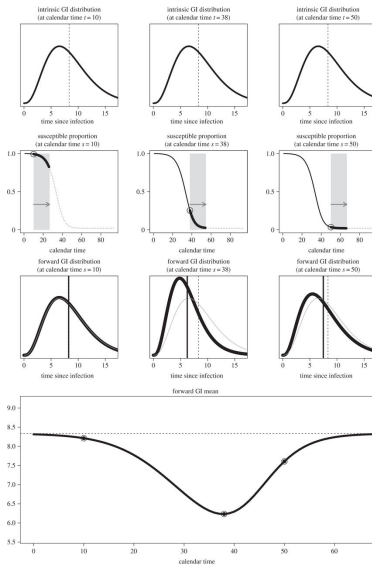


16 Champredon and Dushoff, 2015. DOI:10.1098/rspb.2015.2026

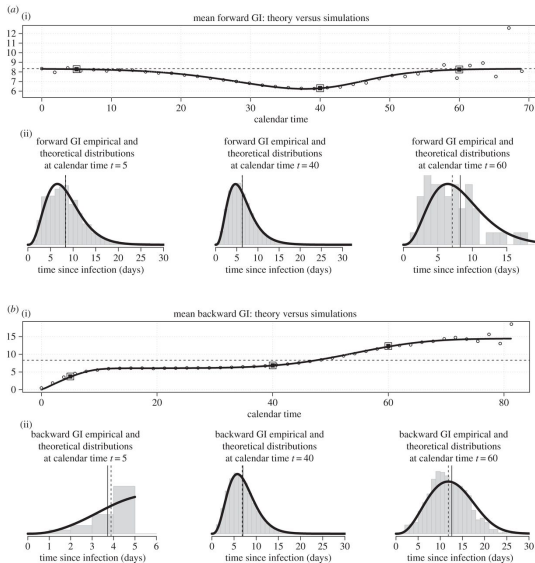
What changes backward intervals?



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

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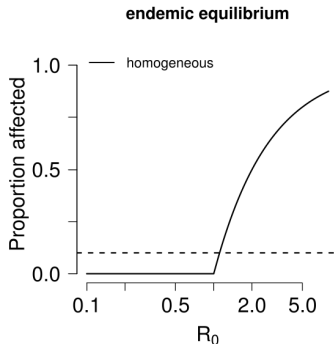
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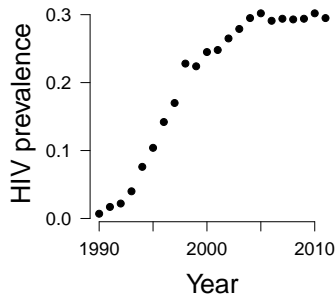
Strength: \mathcal{R} – the reproductive number

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



Speed: r – the growth rate

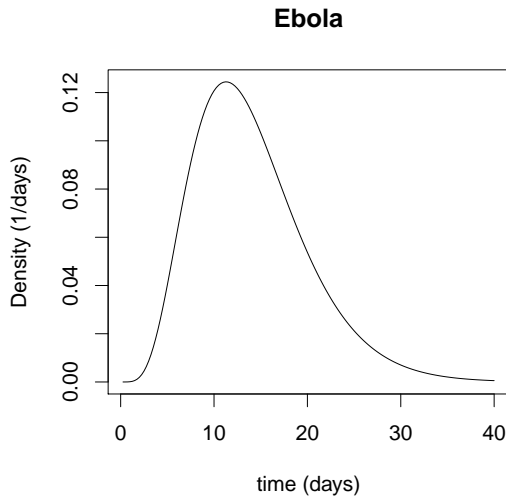
- ▶ $i(t) \approx i(0) \exp(rt)$
- ▶ $C = 1/r$
- ▶ $T_2 = \ln(2)/r$



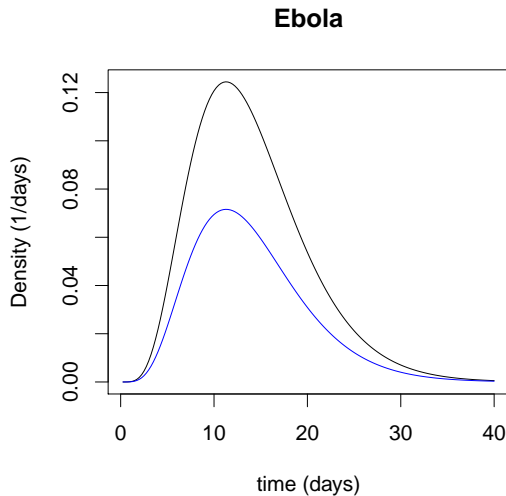
\mathcal{R} and the generation interval

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

\mathcal{R} and the generation interval



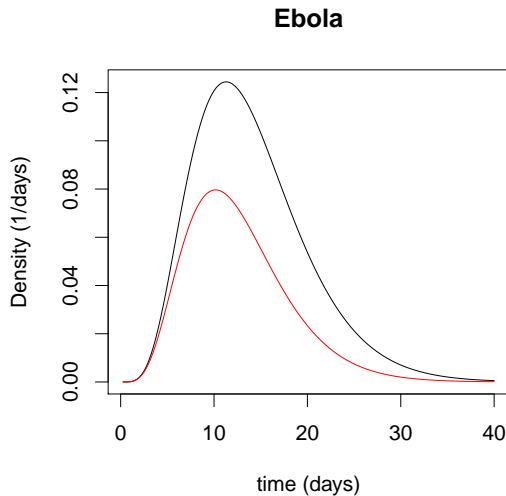
\mathcal{R} and the generation interval



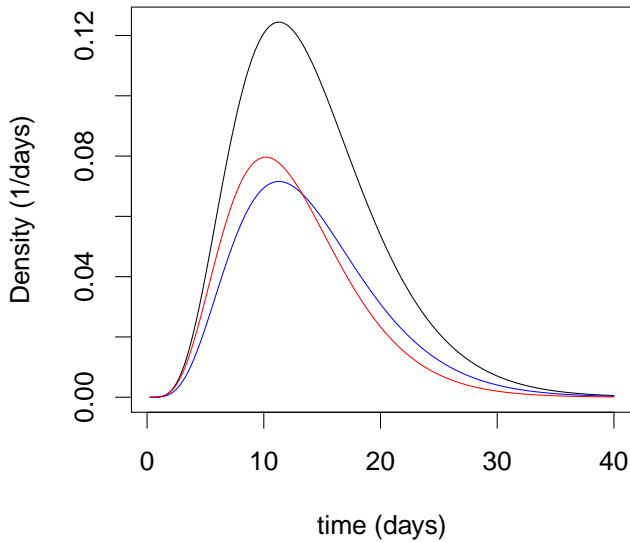
r and the (other) generation interval

- ▶ $i(t) = \int k(\tau) i(t - \tau) d\tau$
- ▶ 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

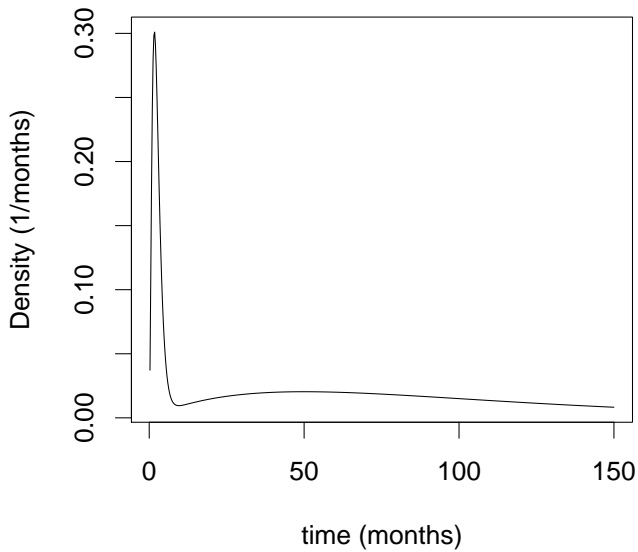
r and the (other) generation interval



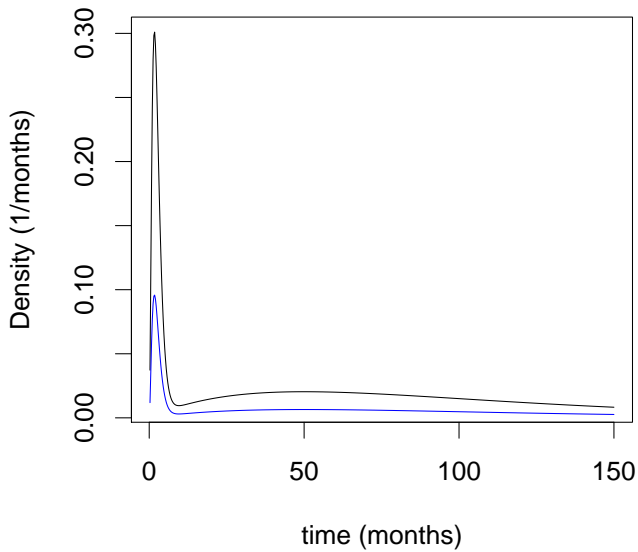
Ebola



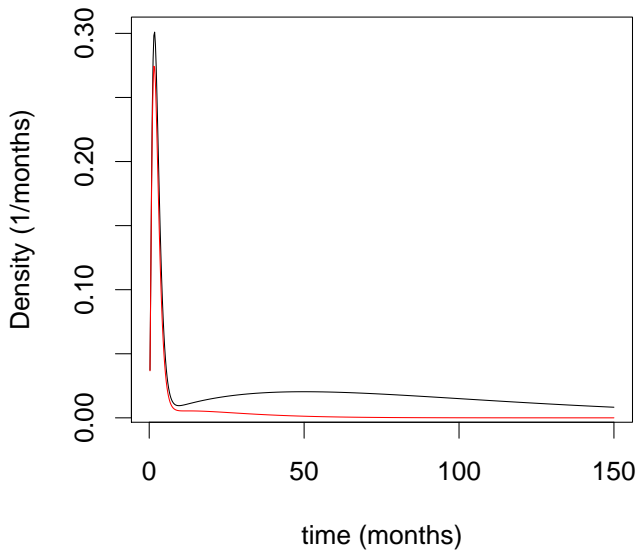
HIV



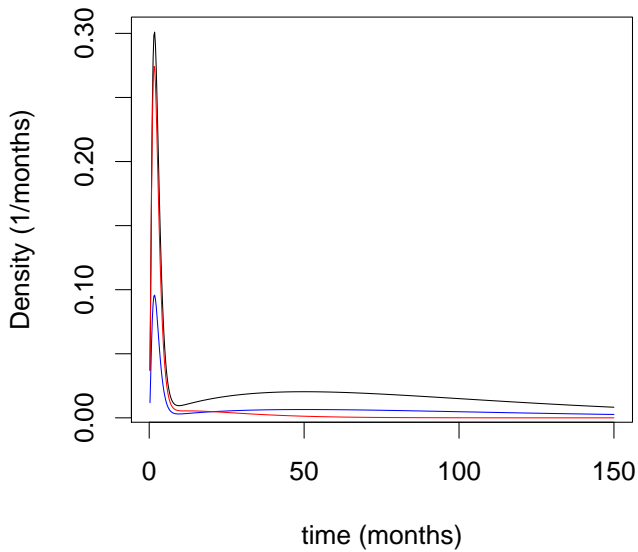
HIV



HIV



HIV



Strength of intervention

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

Speed of intervention

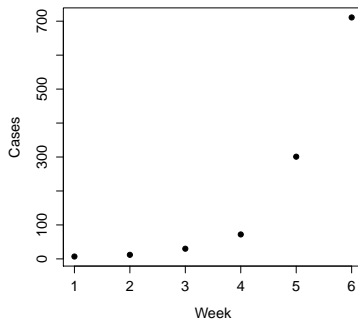
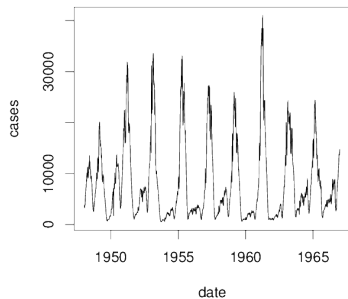
- ▶ Define the *speed* of an intervention be $\phi = r - \hat{r}$ – the amount by which the intervention slows down spread.
- ▶ $1 = \left\langle \frac{\exp(\phi\tau)}{L(\tau)} \right\rangle_{b(\tau)}$
- ▶ ϕ is *sort of a mean* of the *hazard* associated with L
 - ▶ Averaged over the initial *backwards*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

A new way of looking



Measuring the epidemic

Measles reports from England and Wales



Measuring the intervention



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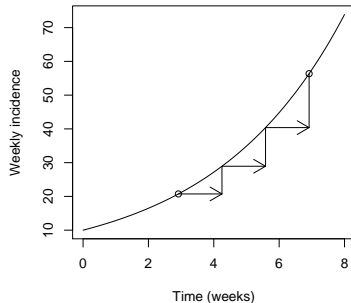
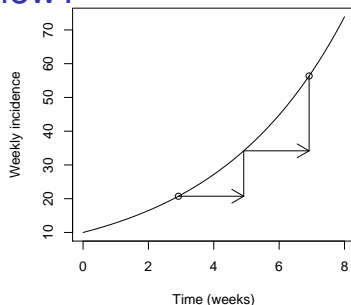
- HIV example

Can treatment stop the HIV epidemic?

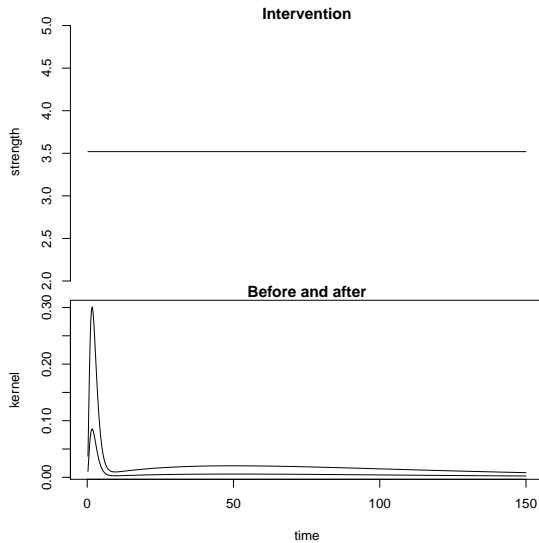


Are HIV generations fast or slow?

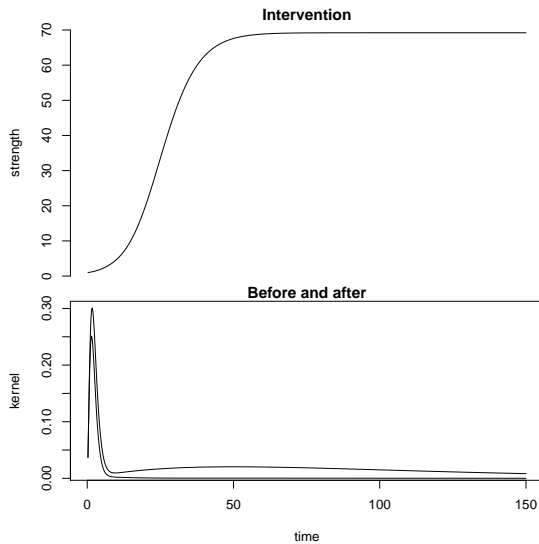
- ▶ Fast generations mean:
 - ▶ Testing and treating will help less
 - ▶ *but* lower epidemic strength



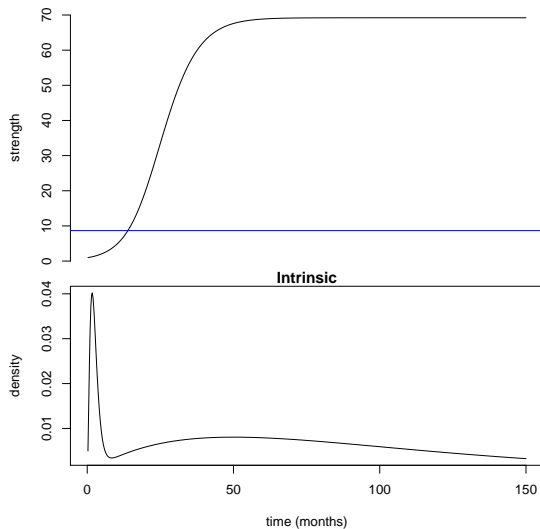
Condom intervention



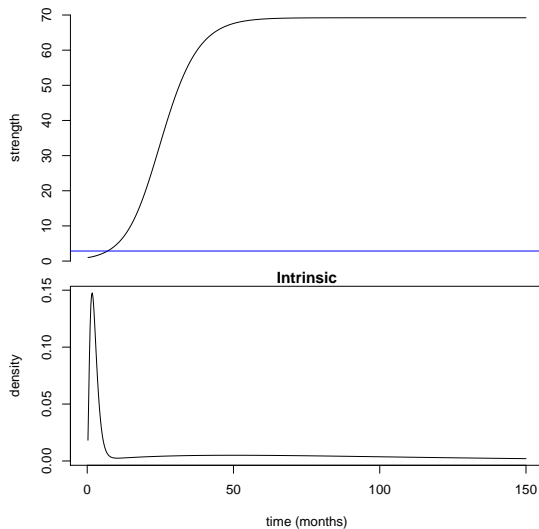
Find and treat



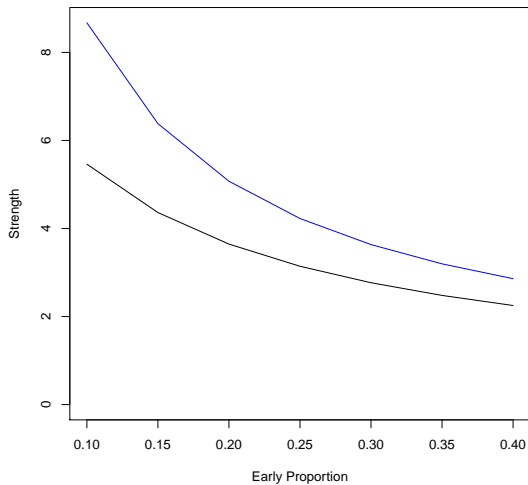
Low early transmission



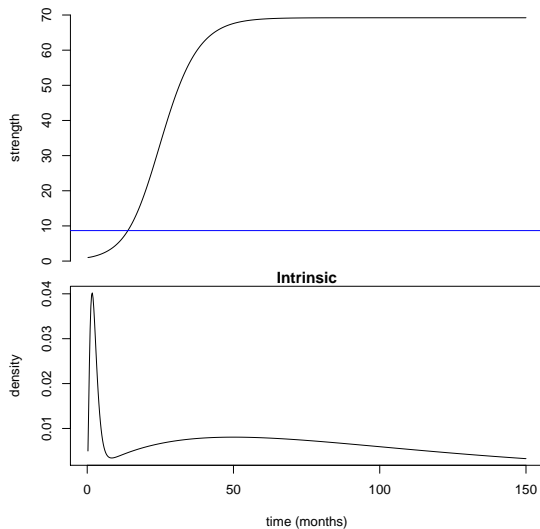
High early transmission



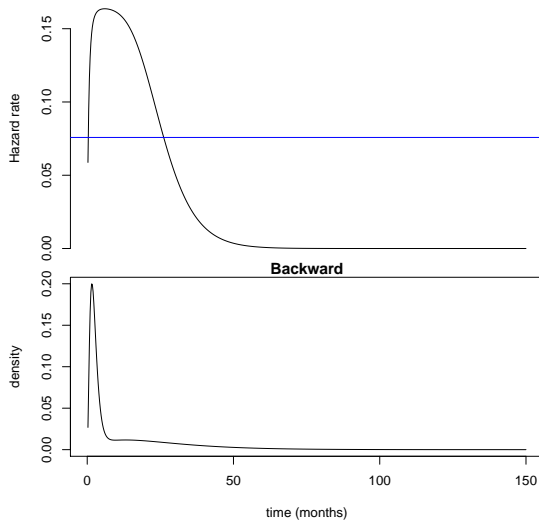
Range of estimates



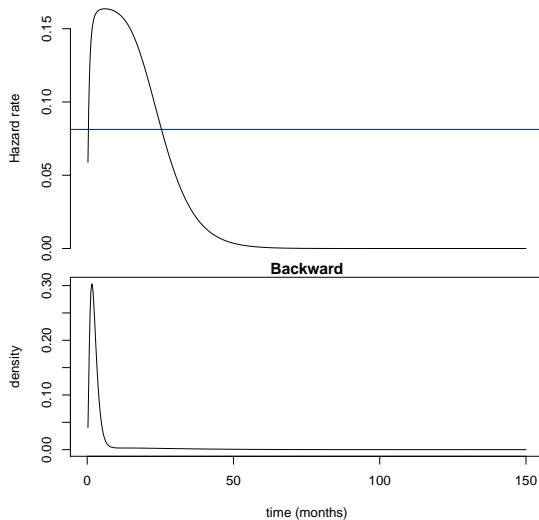
Find and treat



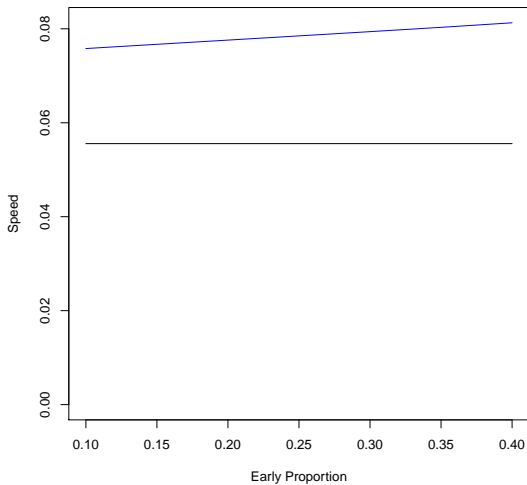
Low early transmission



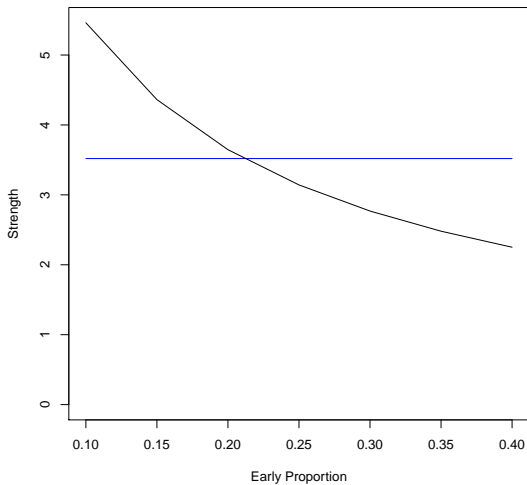
High early transmission



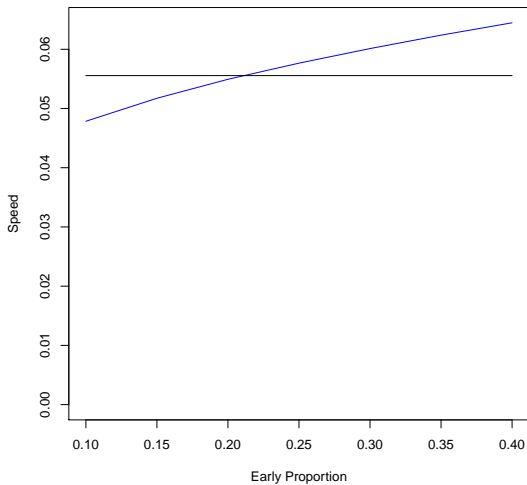
Range of estimates



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
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