Measuring the strength and speed of epidemics

McMaster University Origins Institute Colloquium
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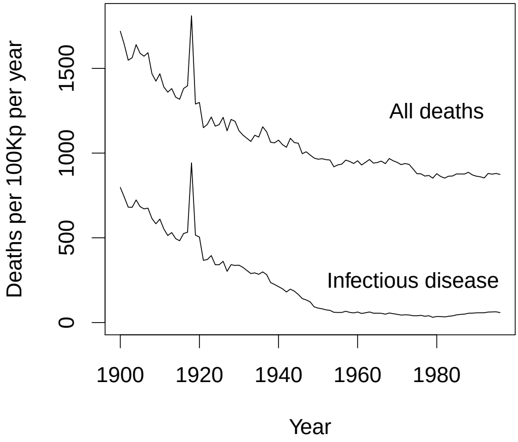
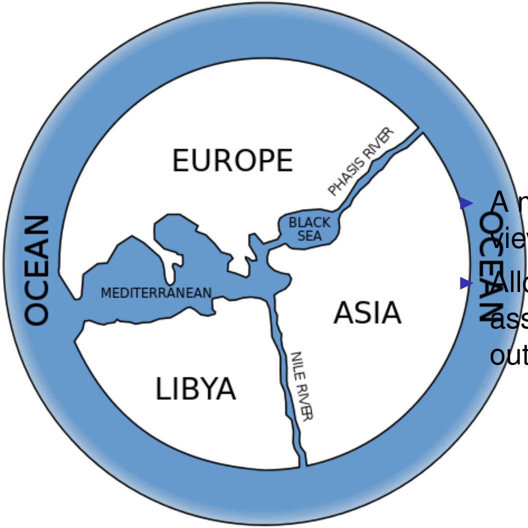
Outline

Infectious diseases

US annual mortality rate (CDC)

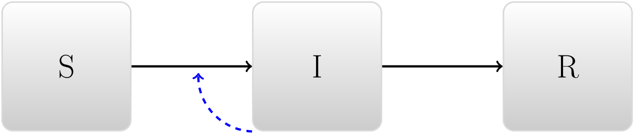


Models



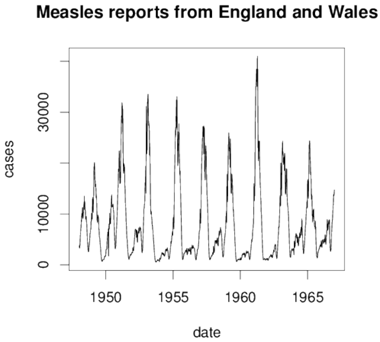
- A model is a simplified view of the world
- Allows linking between assumptions and outcomes

Dynamic models



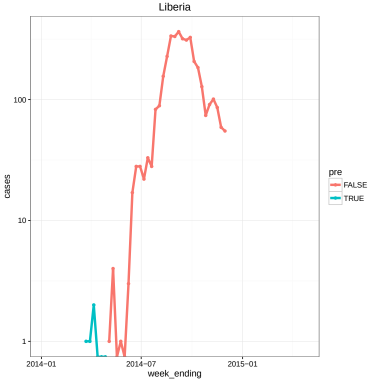
Small-scale events ⇔ Large-scale patterns and outcomes

Dynamic models

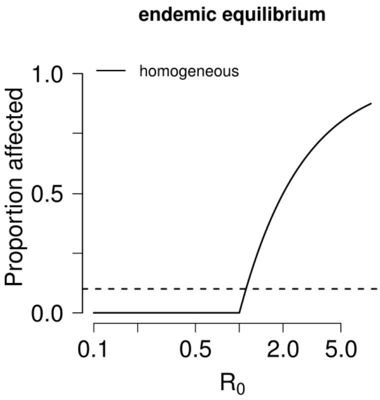


Dynamic modeling

Connects scales

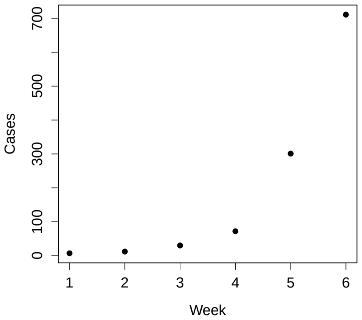


Yellow fever in Panama

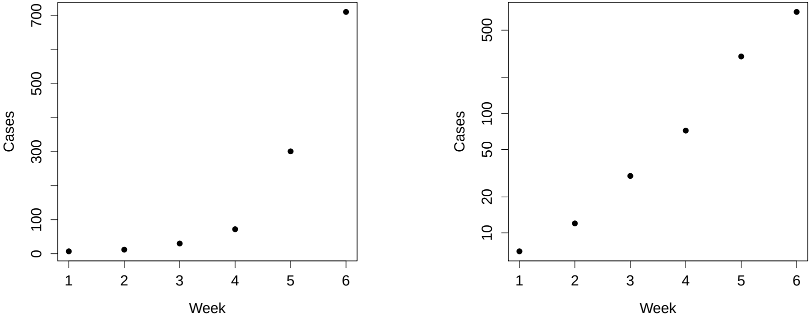


Speed of epidemics

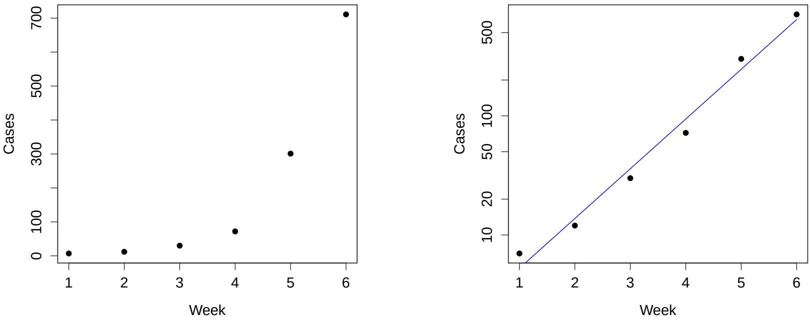
- Exponential growth:
  - Growth proportional to size



Exponential growth



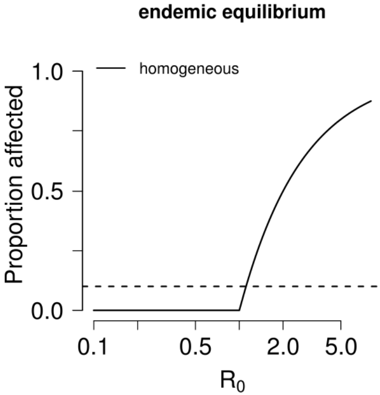
Exponential growth



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, $C \approx 1 month$
  - HIV in SSA, $C \approx 18 month$

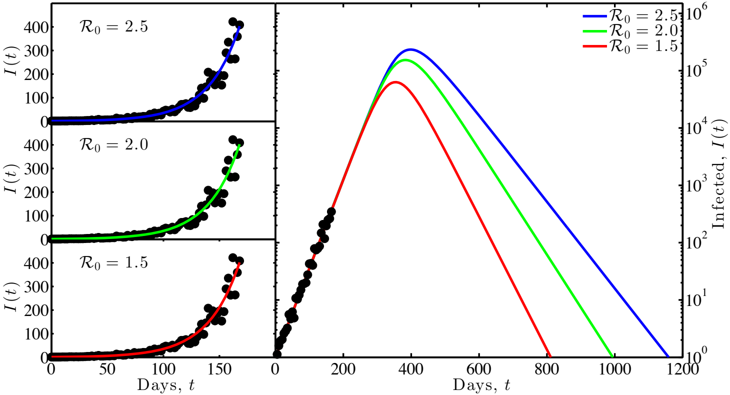
Strength of epidemics



Basic reproductive number

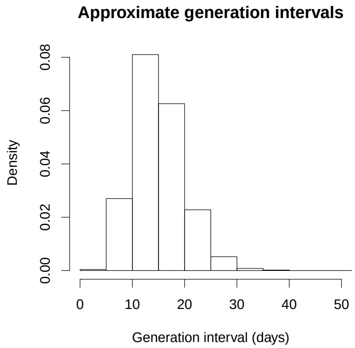
- We describe epidemic strength with big $\mathcal{R}$
- Number of potential new cases per case
- To eliminate disease, we must:
  - Reduce transmission by a factor of $\mathcal{R}$ *or*
  - Reduce number of susceptible people by a factor of $\mathcal{R}$ *or* …
- Examples:
  - Ebola, $\mathcal{R} \approx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

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

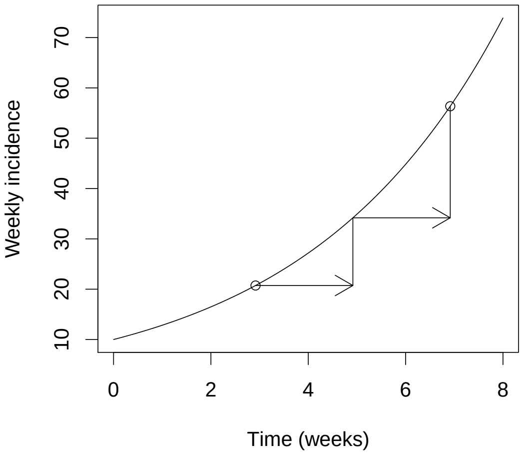


Generation intervals

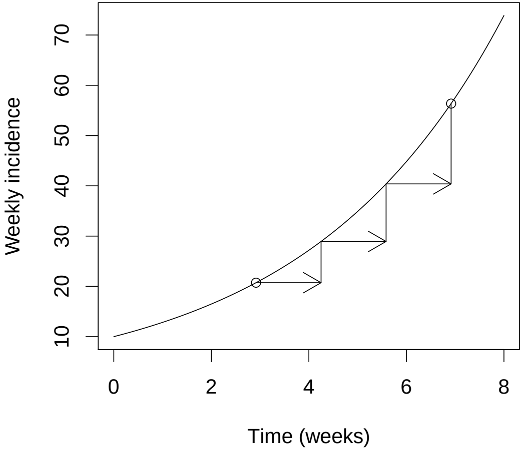
- The generation distribution measures generations of the disease
  - Interval between "index" infection and resulting infection
- What does G tell us about how dangerous the epidemic is?
  - It depends on what else we know!



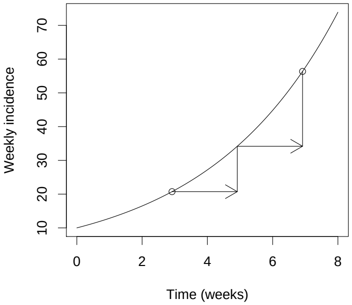
Generations and $\mathcal{R}$

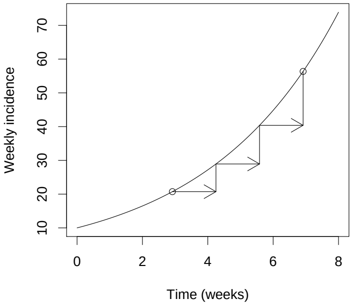


Generations and $\mathcal{R}$



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

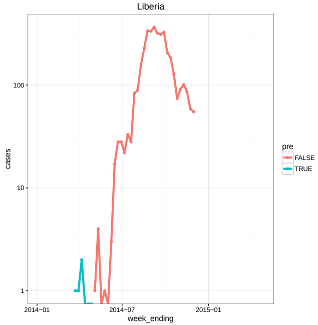
Outline

Generation intervals through time

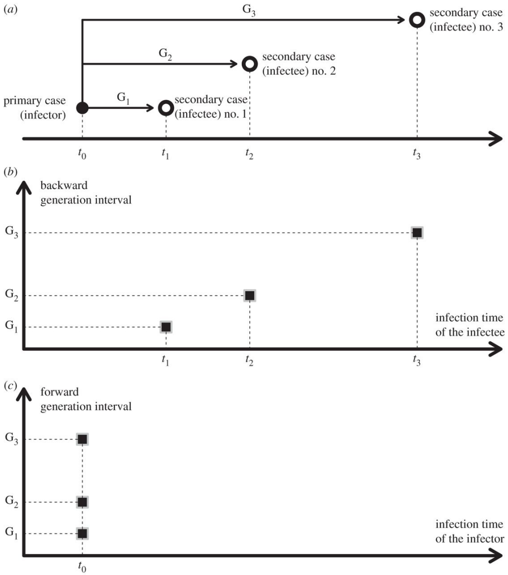
- Generation intervals can be estimated by:
  - Observing patients:
    - How long does it take to become infectious?
    - How long does it take to recover?
    - What is the time profile of infectiousness/activity?
  - Contact tracing
    - Who (probably) infected whom?
    - When did each become ill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

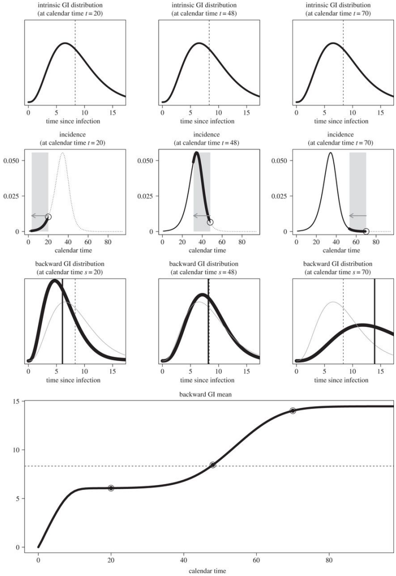


Forward and backward intervals

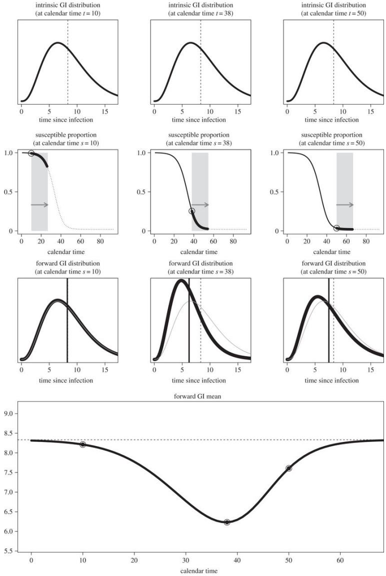


16 Champredon and Dushoff, 2015. DOI:10.1098/rspb.2015.2026

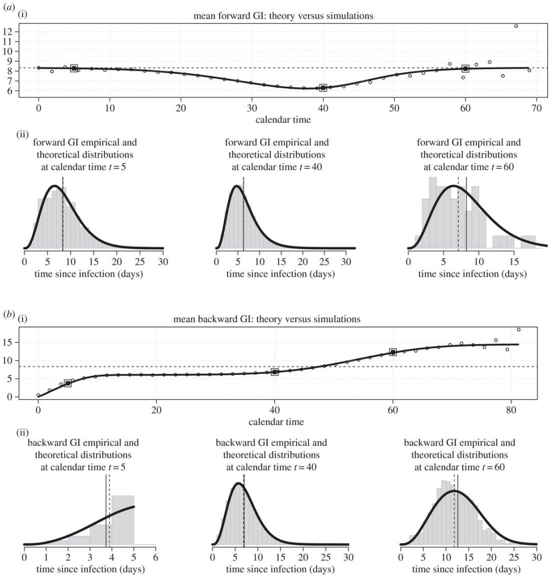
What changes backward intervals?



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

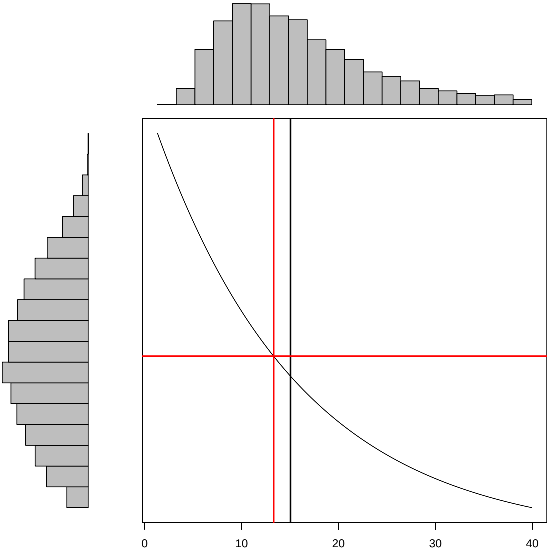
Outline

The "effective" generation time

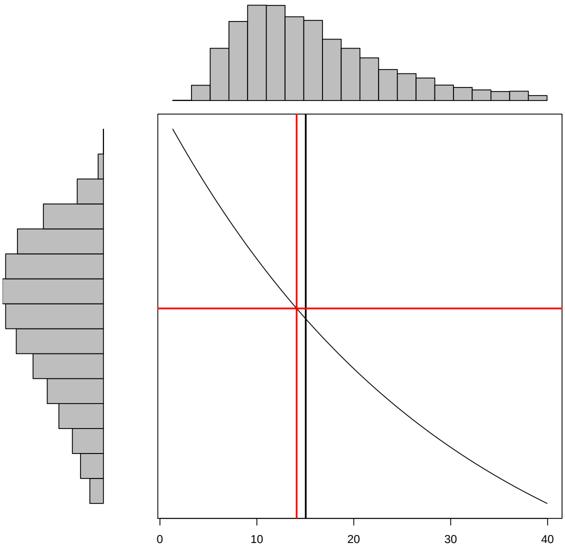
- If the generation interval were absolutely fixed at a time interval of G, then
  - $$\mathcal{R} = \exp(G/C)$$
- *Define* the effective generation time so that this remains true:
  - $$\mathcal{R} = \exp(\hat{G}/C)$$
- We can show $\hat{G}$ is a "filtered mean" of the distribution g:
  - $$\exp(-\hat{G}/C)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

,

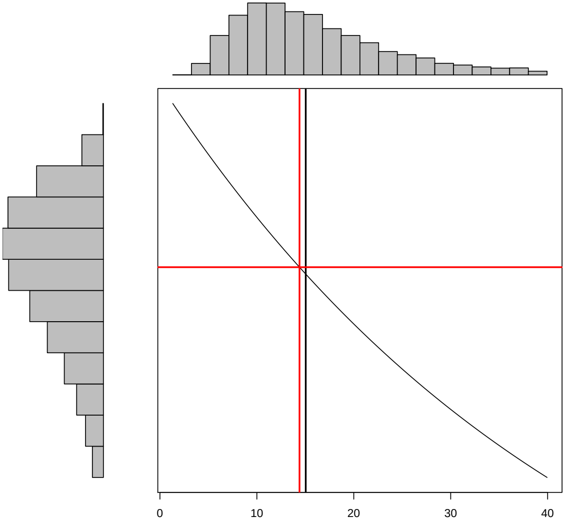
$C = 15d$



$C = 30d$



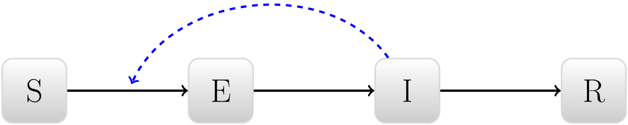
$C = 45d$



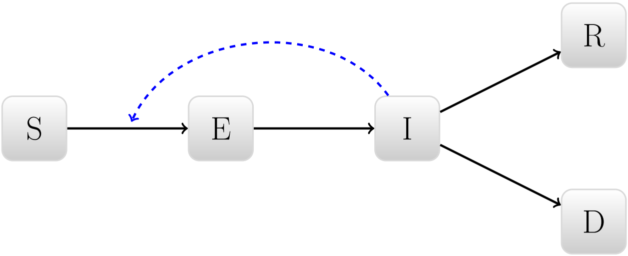
Example: Post-death transmission and safe burial

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

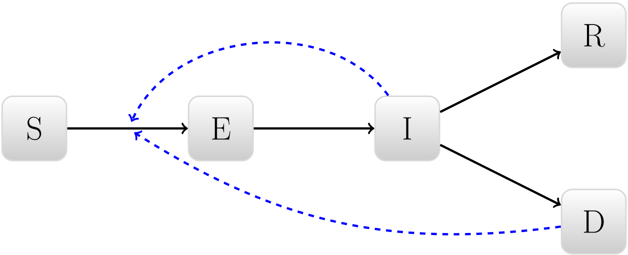
Standard disease model



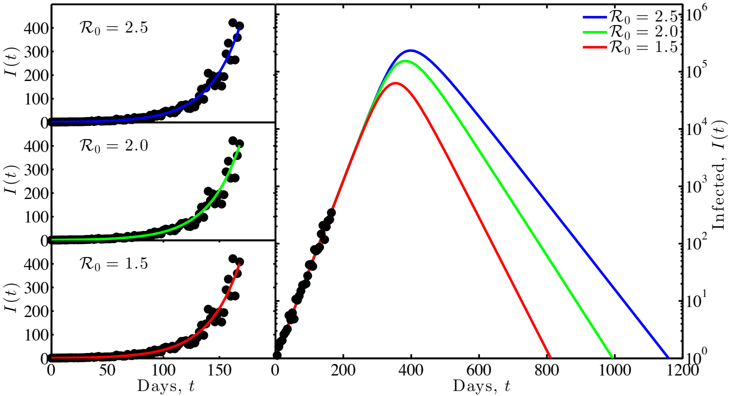
Disease model including post-death transmission



Disease model including post-death transmission



Scenarios



$\mathcal{R}_0 = 2.5$
$\mathcal{R}_0 = 2.0$
$\mathcal{R}_0 = 1.5$
$I(t)$
0
100
200
300
400
0
50
100
150
Days, t
0
200
400
600
800
1000
1200
Days, t
10^0
10^1
10^2
10^3
10^4
10^5
10^6
Infected, $I(t)$

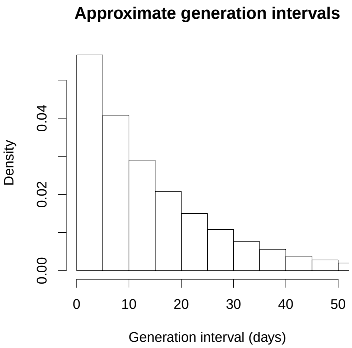
Conclusions

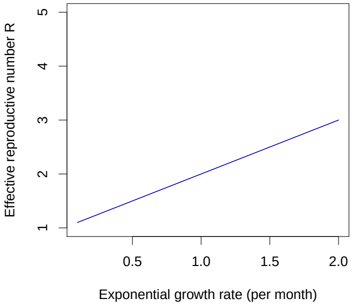
- Different parameters can produce indistinguishable early dynamics
- More after-death transmission implies
  - Higher $\mathcal{R}_0$
  - Larger epidemics
  - Larger importance of safe burials

An approximation

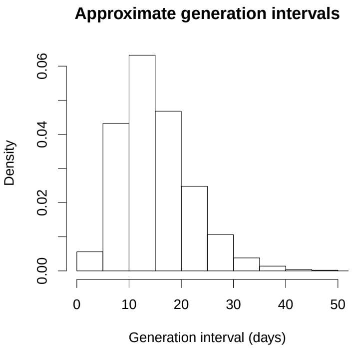
- We connect these quantities with a moment approximation
- Define $\kappa = \sigma_G^2/\mu_G^2$ – the squared coefficient of variation of the generation distribution
- $\mathcal{R} \approx (1 + \kappa\bar{G}/C)^{1/\kappa}$
  - Equal when G has a gamma distribution
  - Simple and straightforward
  -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

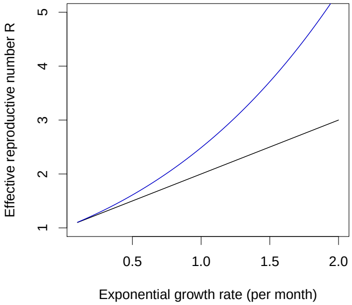
Moment approximation



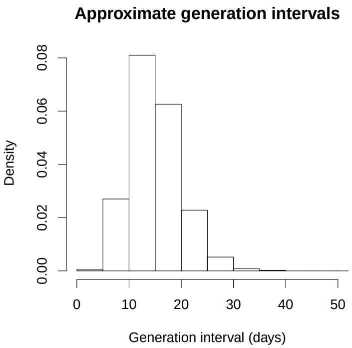


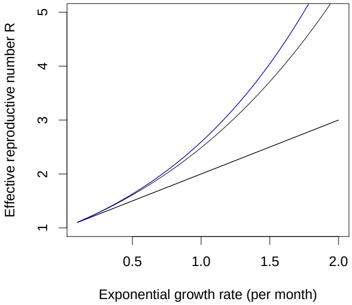
Moment approximation



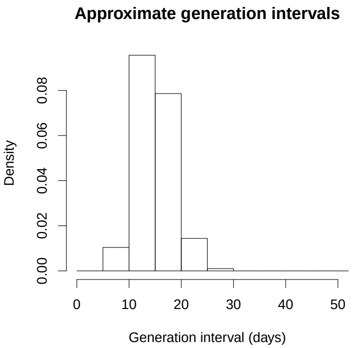


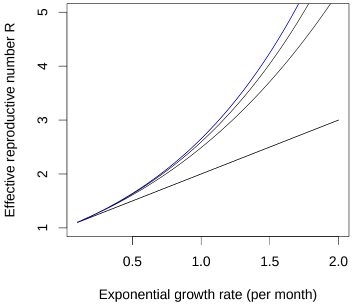
Moment approximation





Moment approximation

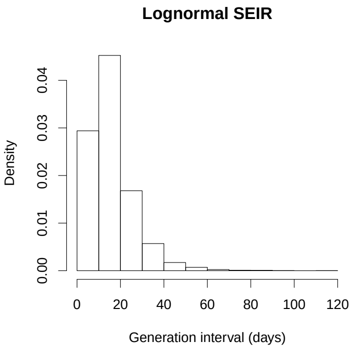




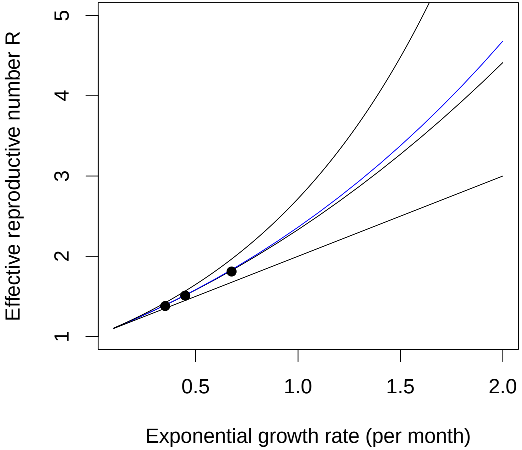
Fitting to Ebola

- 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



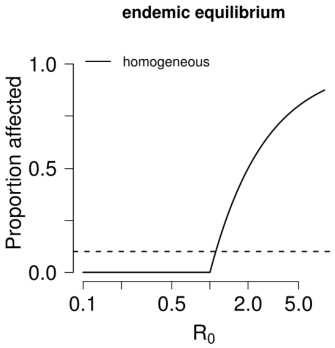
Summary

- 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

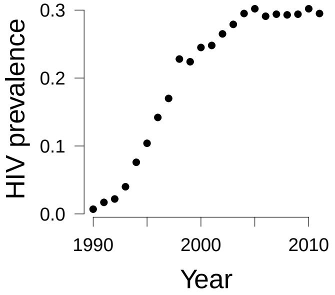
Strength: $\mathcal{R}$ – the reproductive number

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



Speed: r – the growth rate

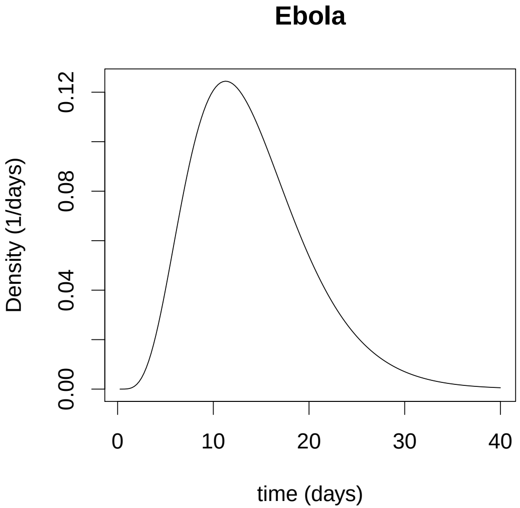
- $i(t) \approx i(0)\exp(rt)$
- $C = 1/r$
- $T_2 = \ln(2)/r$



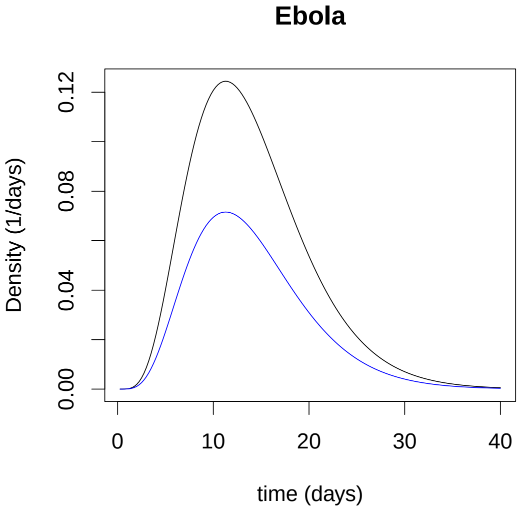
$\mathcal{R}$ and the generation interval

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

$\mathcal{R}$ and the generation interval



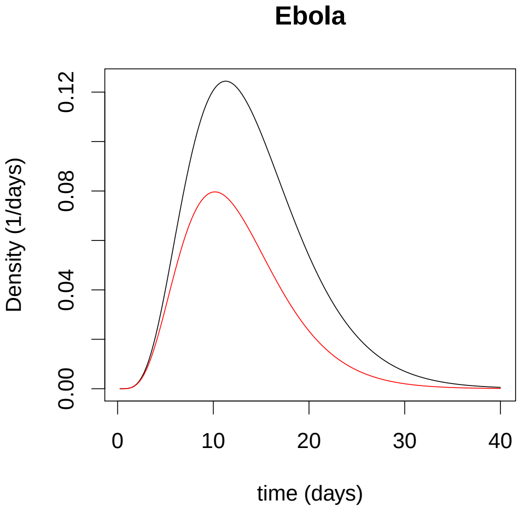
$\mathcal{R}$ and the generation interval

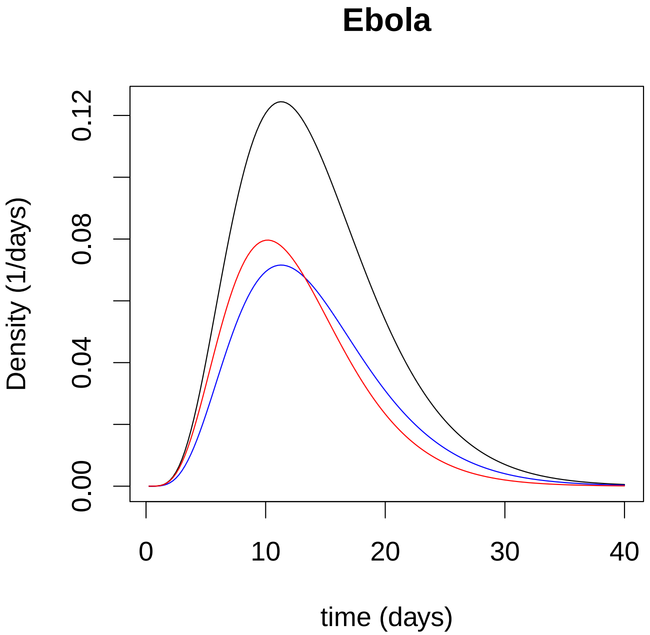


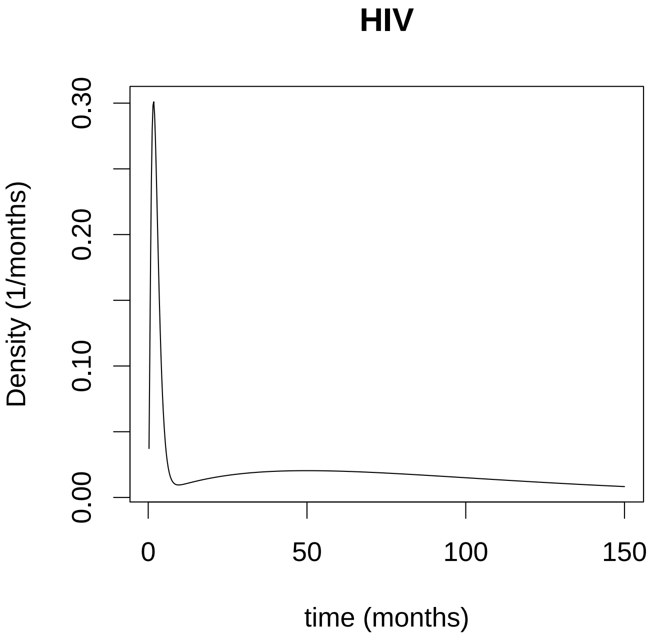
r and the (other) generation interval

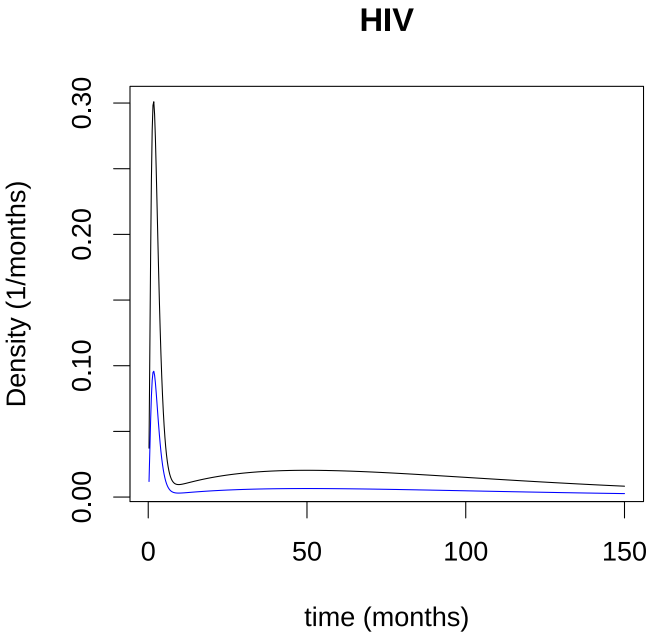
- $i(t) = \int k(\tau) i(t-\tau)\, d\tau$
- if $i(t)$ grows like $\exp(rt)$, then
- $1 = \int k(\tau) \exp(-r\tau)\, d\tau$
- $b_0(\tau) = k(\tau)\exp(-r\tau)$ is the initial *backwards* generation interval

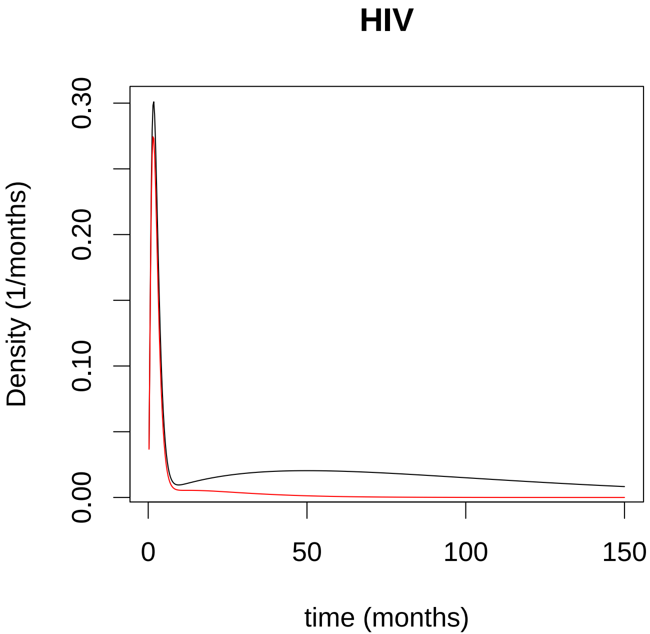
r and the (other) generation interval

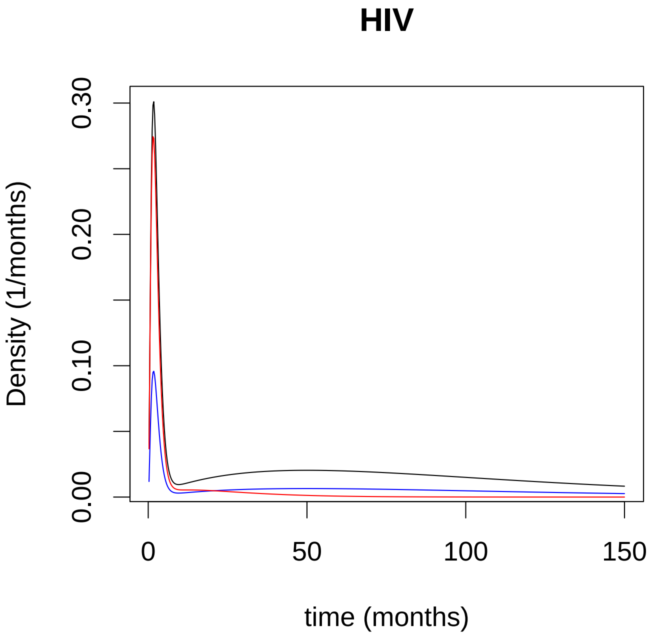



Ebola
Density (1/days)
0.00
0.04
0.08
0.12
0
10
20
30
40
time (days)


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


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


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


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

Strength of intervention

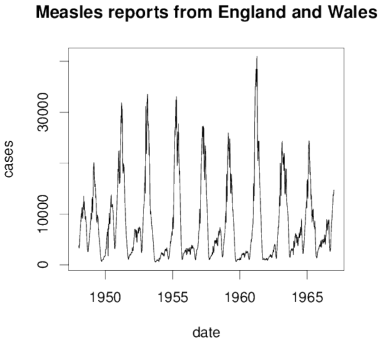
- Imagine we have an intervention that reduces transmission
  - $k(\tau) \to k(\tau)/L(\tau)$
  - Define *strength* $\theta = \mathcal{R}/\hat{\mathcal{R}}$ – the proportional amount by which the intervention reduces transmission.
- We then have:
  - $\theta = 1/\left\langle 1/L(\tau)\right\rangle_{g(\tau)}$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

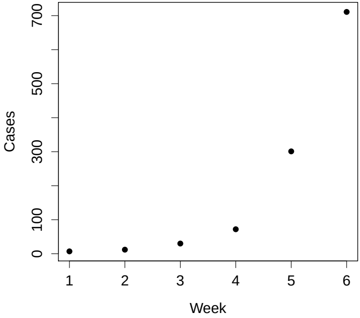
Speed of intervention

- Define the *speed* of an intervention be $\phi = r - \hat{r}$ – the amount by which the intervention slows down spread.
- $1 = \left\langle \frac{\exp(\phi\tau)}{L(\tau)} \right\rangle_{b(\tau)}$
- 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

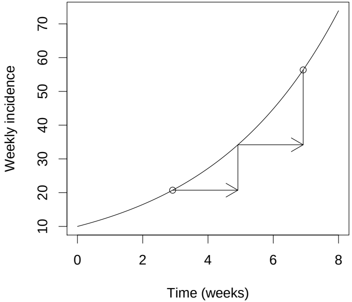




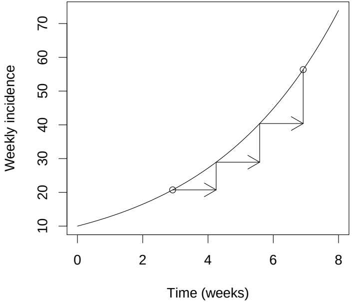
Measuring the intervention

Can treatment stop the HIV epidemic?

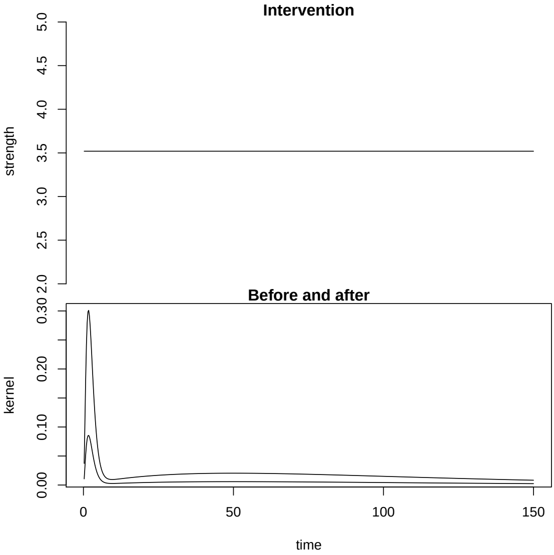
Are HIV generations fast or slow?



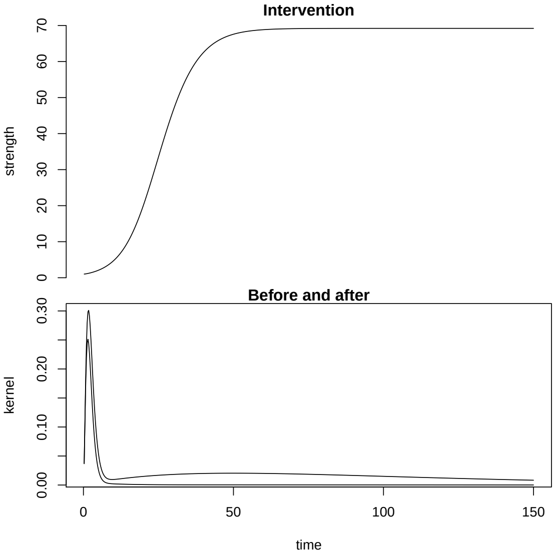
- Fast generations mean:
    - Testing and treating will help less
    - *but* lower epidemic strength



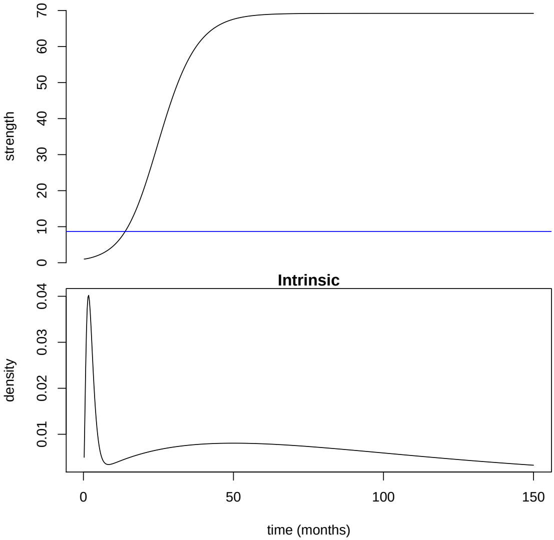
Condom intervention



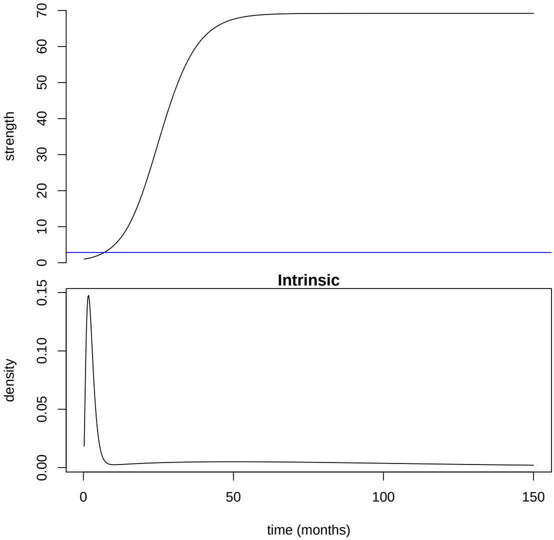
Find and treat



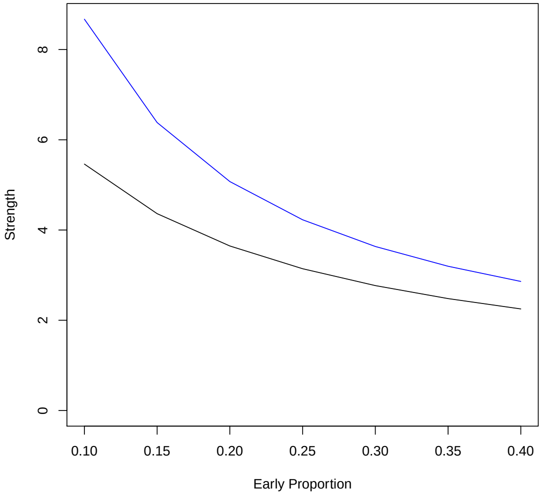
Low early transmission



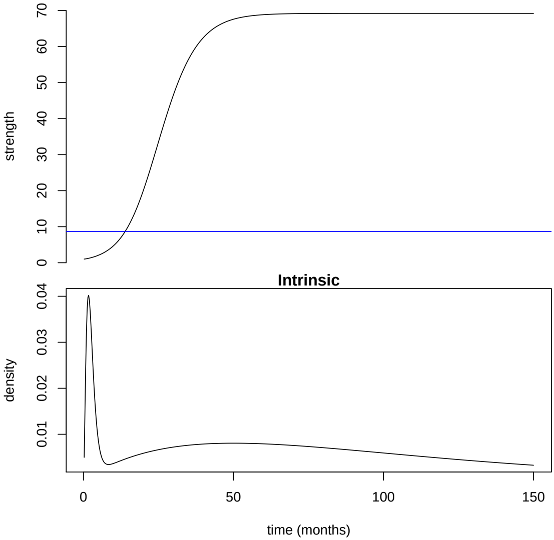
High early transmission



Range of estimates



Find and treat



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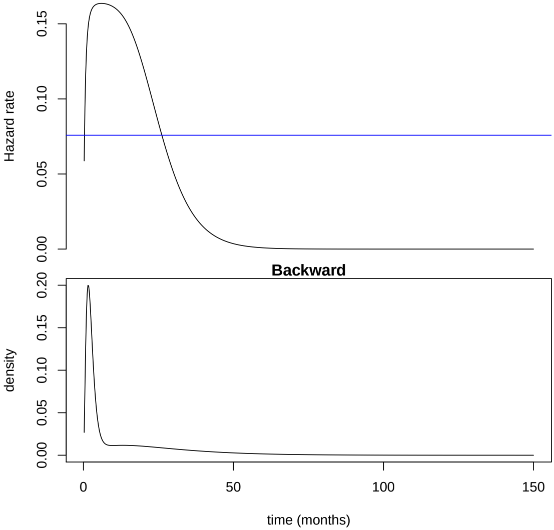
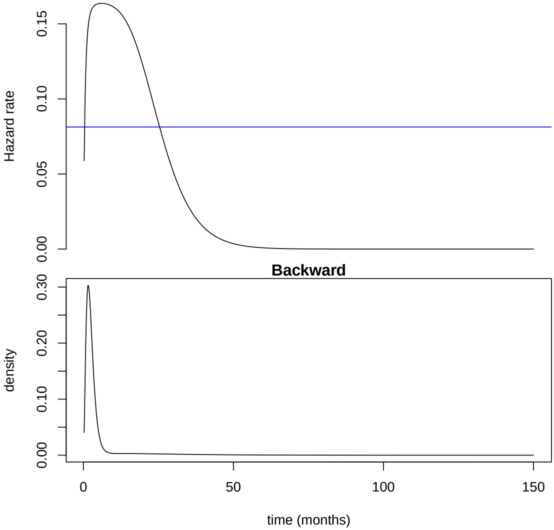
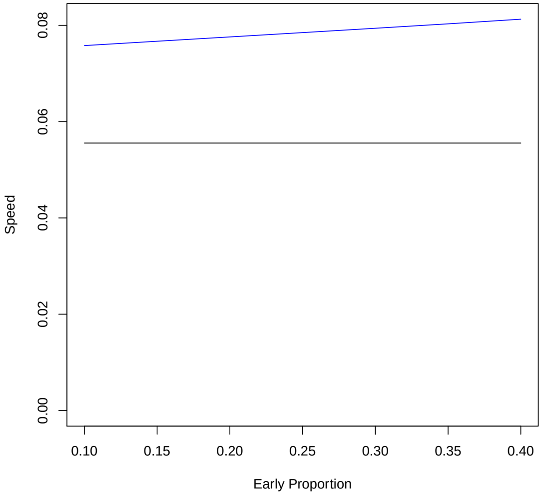


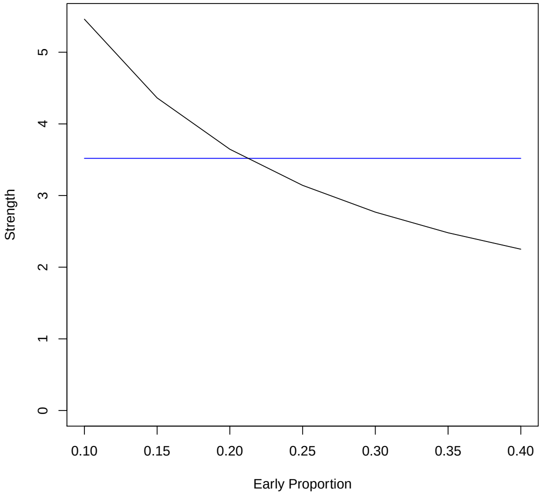
High early transmission



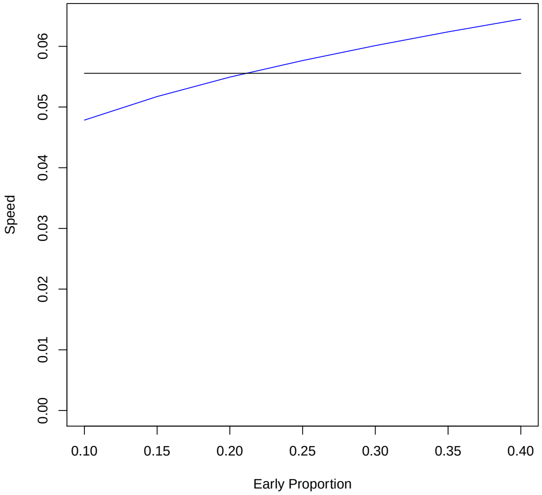
Range of estimates



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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