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Epidemics models with population structure (subjectively chosen models)

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1. Illustrations of Standard SIR epidemic
2. Optimal prevention
3. Epidemics on fixed (social) networks
4. Epidemics on adaptive (social) networks
5. Back to optimal prevention

Consider a fixed population of size n (assumed large)

The Markovian SIR epidemic model:

- Individuals are classified as *Susceptible*, *Infectious* and *Recovered*
- $S(t), I(t), R(t)$ denote correspondning *numbers* at time t
- $(S(0), I(0), R(0)) = (n-1, 1, 0)$. $S(t) + I(t) + R(t) \equiv n$ for all t
- An infectious individuals has "infectious contacts" at rate β, each time with a uniformly at random selected individual
- Infectious contacts with susceptibles imply infection – other contacts have no effect
- Infectious individuals recover (and become immune) at rate γ
- Model parameters: β and γ ($n =$ population size)

Model properties:

a) As $n \to \infty$: $R(\infty)/n$ (= final fraction getting infected) converges to a 2-point distribution: 0 or, if $R_0 = \beta/\gamma > 1$,
$\tau =$ the positive solution to the equation $1 - x = e^{-R_0 x}$

b) If instead $I(0)/n = \epsilon > 0$ fixed, then $(S(\cdot)/n,\ I(\cdot)/n,\ R(\cdot)/n)$ converges in probability to the deterministic ODE-system

$$
\begin{aligned}
s'(t) &= -\beta s(t) i(t) \\
i'(t) &= \beta s(t) i(t) - \gamma i(t) \\
r'(t) &= \gamma i(t)
\end{aligned}
$$

Illustration of a): $R_0 = 0.8$

Histogram of final sizes from 10 000 simulations in a population with $n = 1000$ individuals

When $R_0 < 1$ no positive solution

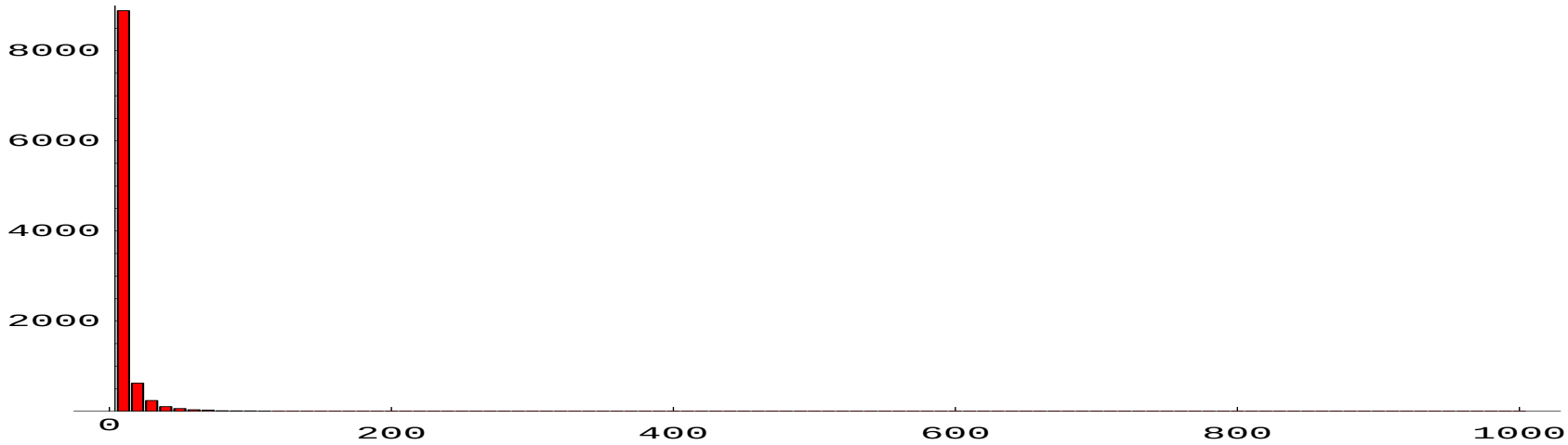

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Illustration of a): $R_0 = 1.5$

Histogram of final sizes from 10 000 simulations in a population with $n = 1000$ individuals

When $R_0 = 1.5$ positive solution equals 0.583

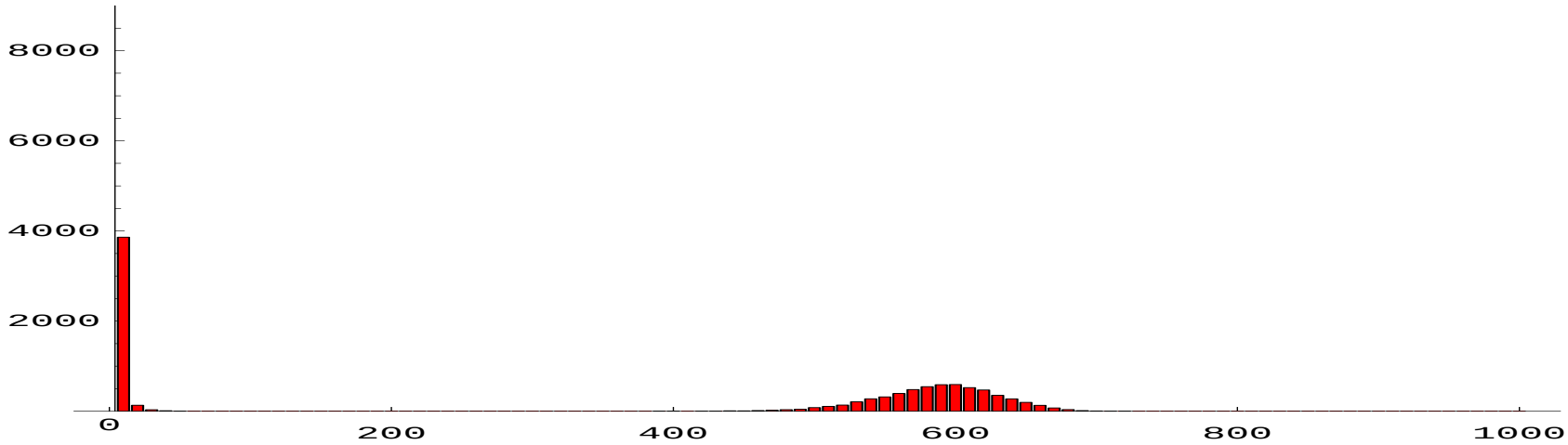

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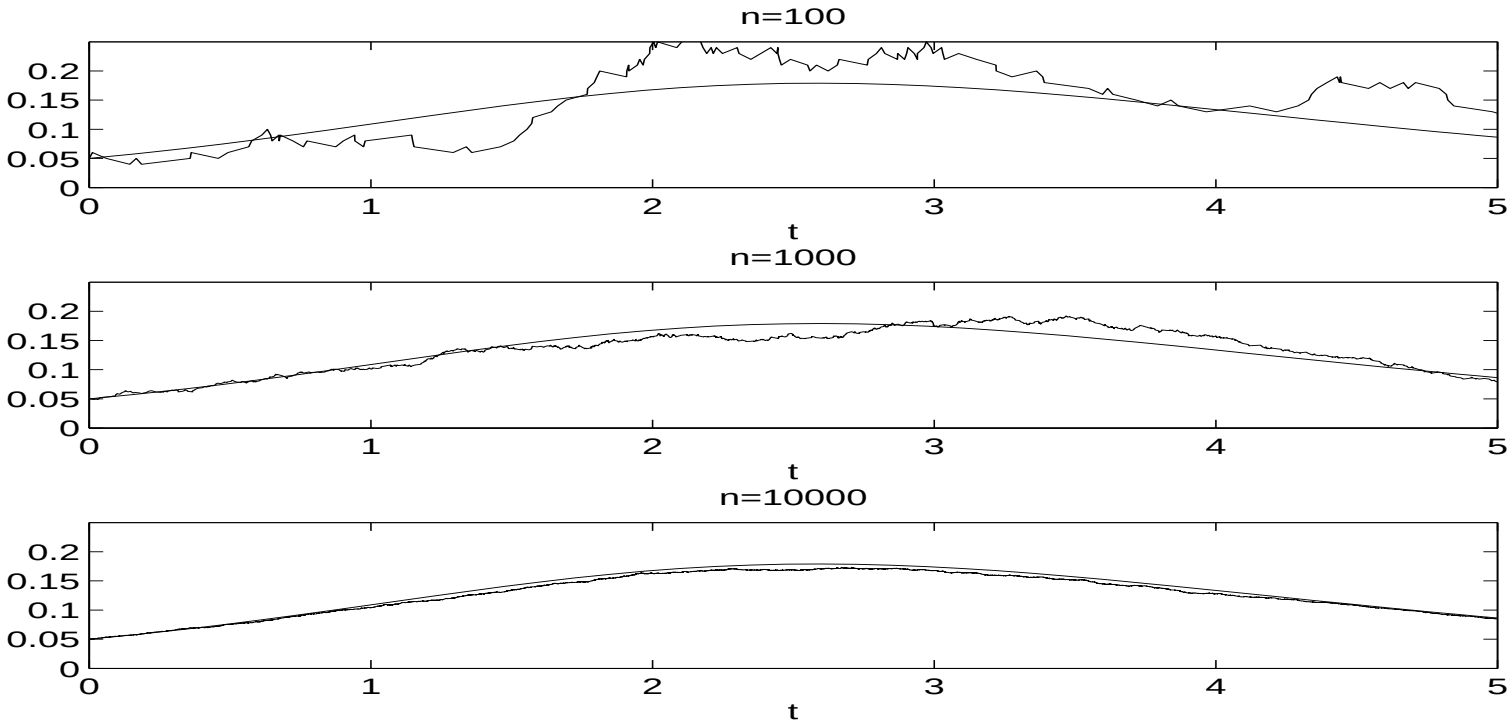
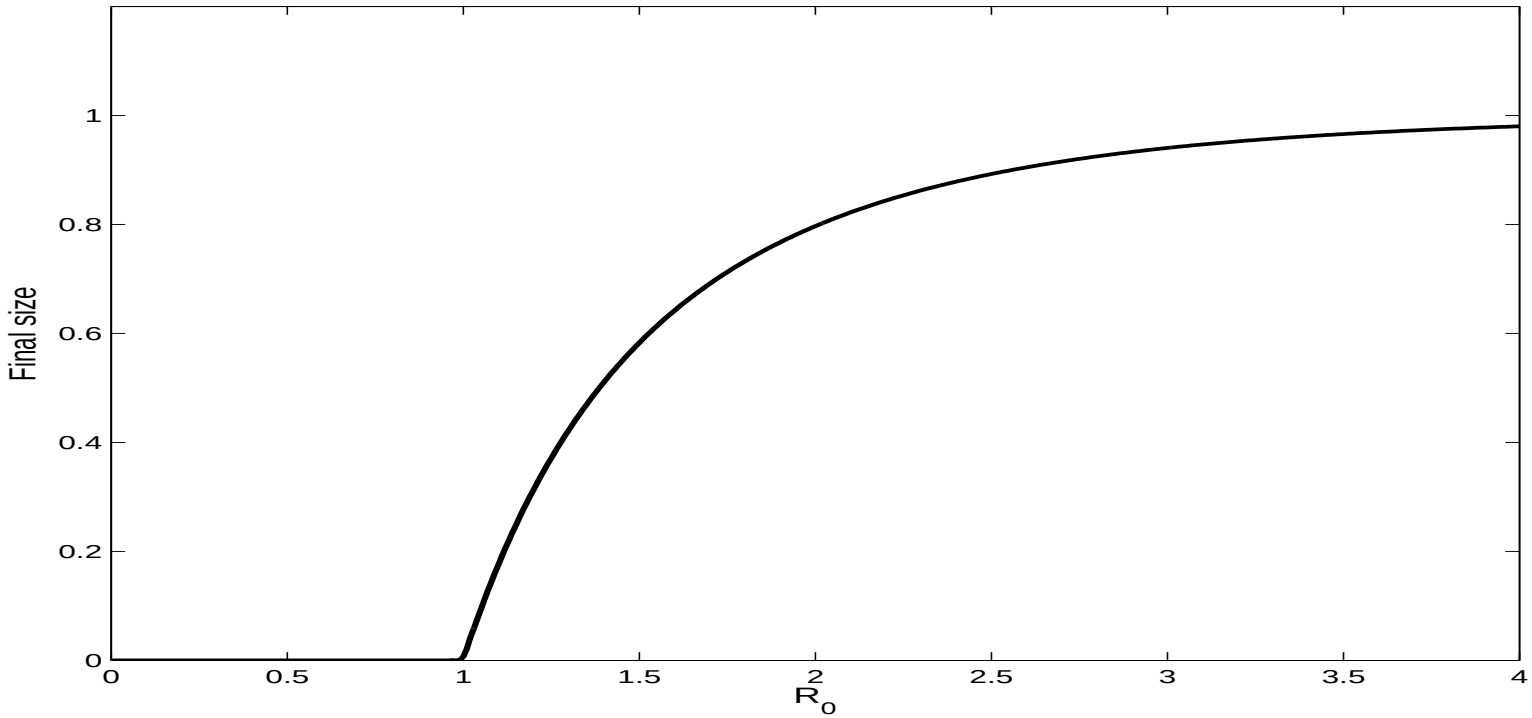
Illustration of b) Plots of deterministic and simulated stochastic curve



Plot of final outbreak size as function of R_0



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Extensions

Many solved *and* open problems for various extentions

- Considering different types of individual (Multitype epidemic)
- Including vaccination and other preventive measures
- Including social structures: network epidemics, household epidemics, ...
- SEIR, SIRS, ,,,
- Dynamic population and dynamic behaviour
- Spatial aspects and mobility
- Effects of preventive measures
- Estimation!!!
- ...

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Vaccination in Standard SIR epidemic

Suppose a fraction v have been vaccinated before disease arrival

Assume vaccine gives 100% immunity

New reproduction number: $R_v = (1 - v)R_0$

$R_v \leq 1$ iff $v \geq 1 - 1/R_0$

Critical vaccination coverage: $v_c = 1 - 1/R_0$

$v \geq v_c$ results in *Herd immunity*)

If $v < v_c$, then $R_v > 1$. Final size τ_v among unvaccinated derived as before but with R_v replacing R_0

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A natural optimizing problem (joint with Lasse Leskelä)

The determinstic SIR epidemic with intervention

Assume no vaccine is available (or expected to arrive)

Introduce a (non-pharamceutical) prevention strategy
$P = \{p(t); 0 \leq t < \infty\}$: contacts reduced by fraction $p(t)$ at t:

$$
\begin{aligned}
s_P'(t) &= -\beta(1-p(t))s_P(t)i_P(t) \\
i_P'(t) &= \beta(1-p(t))s_P(t)i_P(t) - \gamma i_P(t) \\
r_P'(t) &= \gamma i_P(t)
\end{aligned}
$$

Final size: $z_P = r_P(\infty) = 1 - s_P(\infty)$

Total cost of prevention strategy: $\int_0^\infty p(t)dt$

Optimization problem: Which preventive strategy P, with cost satisfying $\int_0^\infty p(t)dt \leq c$, *minimizes* final size z_P?

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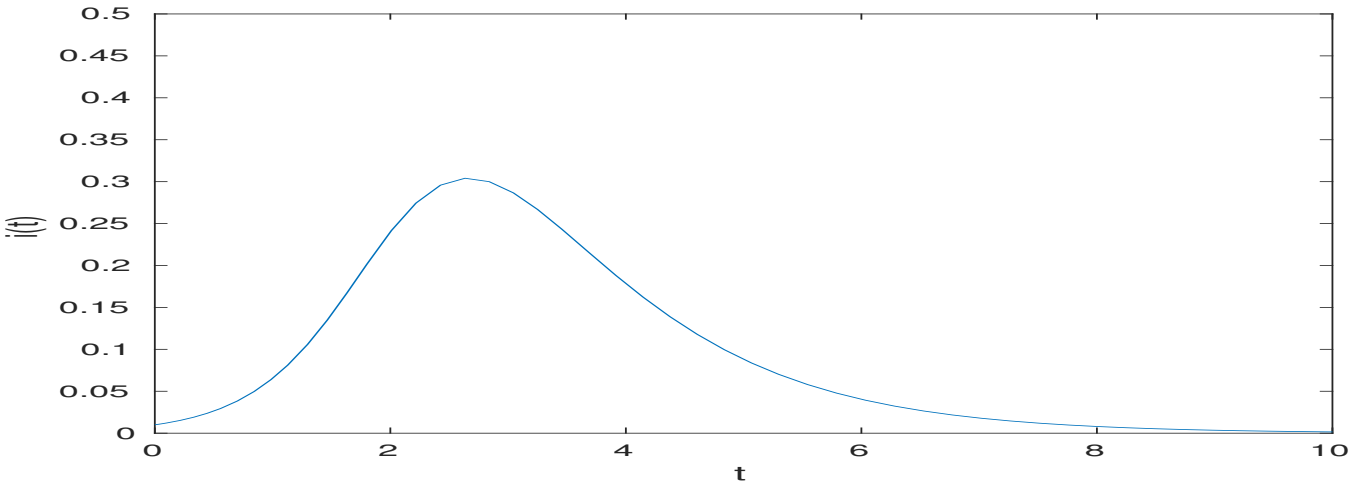
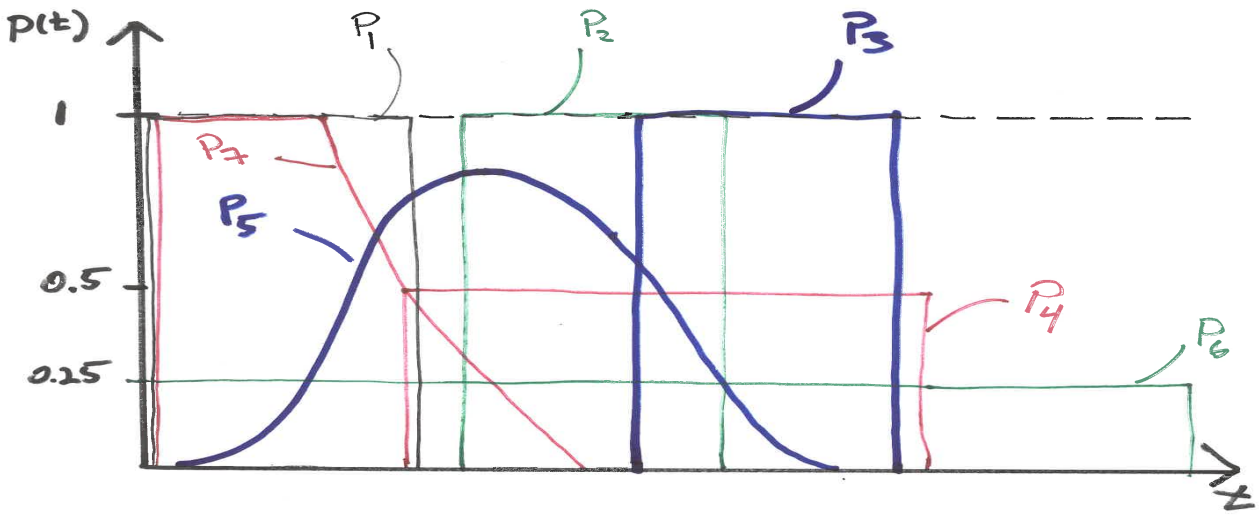
Uncontrolled incidence (top), some preventions (bottom)





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Optimizing prevention in time and size

Solution is presented at end of talk - come up with suggestions during the talk!!

Different heterogeneities

In reality individuals behave differently both

- in terms of susceptibility and infectivity given that a "contact" takes place, and
- in terms of whom they have contact with

Previous results assumed individuals have equal susceptibility and infectivity AND that they "mix" uniformly

Question: Does this simplification make results useless?

Qualitative answer: The more infectious a disease is the less "problematic" is this simplification

$\Longrightarrow$ ok for measles (except immunity) but not "valid" for STDs

Individual heterogeneities

In several situations individuals can be grouped into different *types* of individual

Different types may differ in terms of susceptibility + infectivity

Examples: infants – school children – adults, male – females, partially immune (vaccinated) – fully susceptible

Natural extension: **Multitype epidemic model**

- Let π_j = community fraction of type j, $j = 1, \ldots, k$
- Suppose an i-individual infects a given type-j individual at rate β_{ij}/n and recovers at rate $1/\nu$

Question How many j-individuals does an i-individual on average infect when everyone is susceptible?

Multitype epidemics

Answer: $n_j \frac{\beta_{ij}}{n} \nu$ (=numbers at risk * infection rate * average length of infectious period) $= \beta_{ij} \nu \pi_j$

The matrix with these elements defines the expected number of new infections of various types caused by individuals of various types:

$M = (m_{ij}) = (\beta_{ij} \nu \pi_j)$

Often referred to as *next generation matrix*

R_0 = largest eigenvalue to this matrix (same interpretations as before)

In general no explicit expression, but if $\beta_{ij} = \alpha_i \gamma_j$ ("separable mixing") then $R_0 = \sum_i \alpha_i \gamma_i \nu \pi_i$

Household epidemics

Previous heterogeneity mainly for "individual heterogeneities"

Equally (or more!) important: which individuals people have contact with

For many diseases (influenza, childhood disease, common cold) transmission within *households* is high

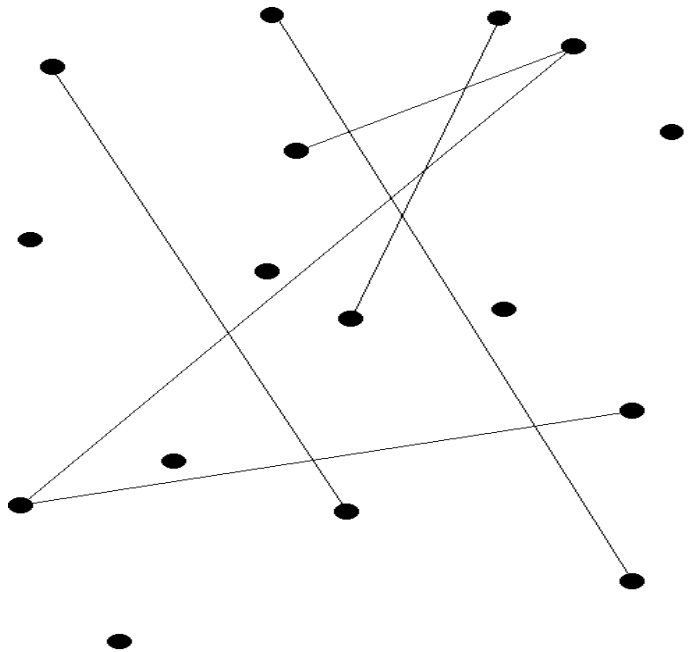
$\Longrightarrow$ Important with models allowing for higher transmission within households

Households are small $\Longrightarrow$ randomness important

Networks

For other diseases (e.g. STDs) individuals are not connected in small cliques

Common representation of social structure: network/graph **nodes** (individuals) and **edges** ("friendship")



Random networks

Social structure only partly known: modelled using random graph/network **with structure**

Some (potentially observed) local structures

- $D = \#$ friends of randomly selected individual (*degree distribution*)
- $c = P$(two friends of an individual are friends) (*clustering*)
- $\rho =$ correlation of degrees in a randomly selected friendship (*degree correlation*)

Other features unobserved $\Longrightarrow$ Random network

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Stochastic epidemic model "on" network

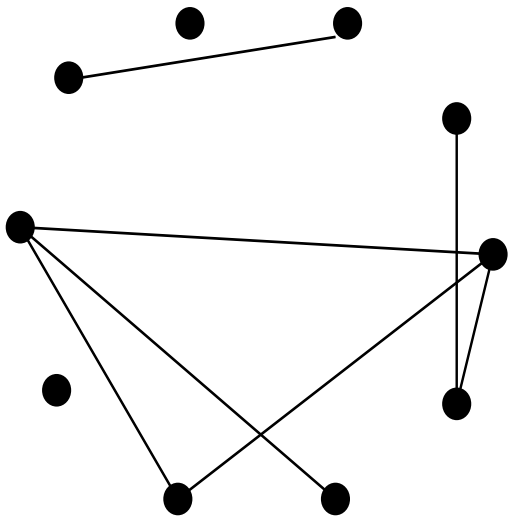
Also spreading is uncertain $\Longrightarrow$ stochastic epidemic model "on" the (random) network

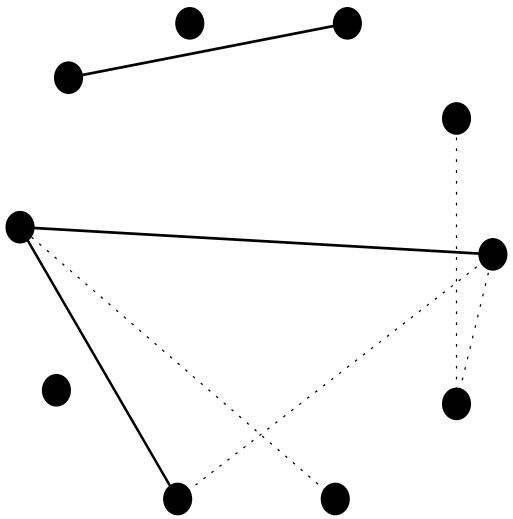
Simplest epidemic model (discrete time): an infected person infects each susceptible friend *independently* with prob p and then recovers (Reed-Frost)

Effect on graph: thinning – each **edge** is removed with prob $1 - p$

Interpretation: remaining edges reflect "potential spreading"

Graph and its thinned version





Those connected to index case make up final outbreak

The degree distribution and its effect on R_0

Focus from now: Network epidemic model with arbitrary degree distribution $\{p_k\}$

- Social structure: Individuals have degree distribution $D \sim \{p_k\}$ and "friends" are chosen completely at random (Configuration model)
- Epidemic model: each susc. friend is infected with prob p
- 1 randomly selected index case, $n-1$ susceptibles

What is R_0?

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- $R_0 = pE(D)$?

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- $R_0 = pE(D)$?– Wrong!
- $R_0 = p(E(D)-1)$?

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The degree distribution and its effect on R_0

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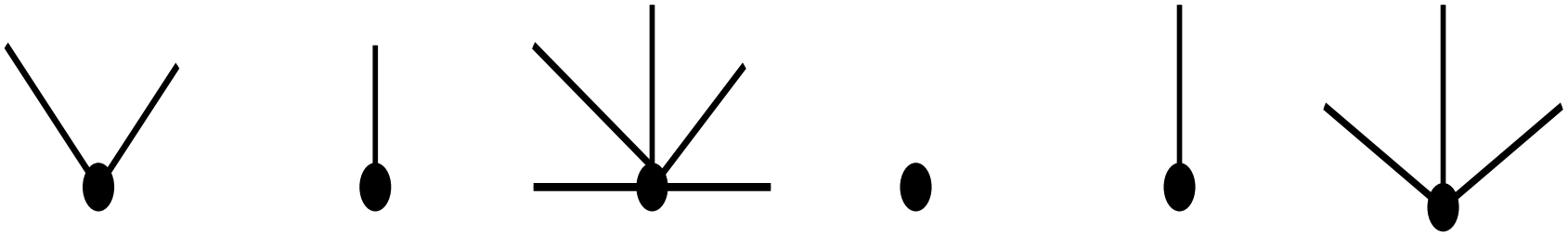
- $R_0 = pE(D)$?– Wrong!
- $R_0 = p(E(D)-1)$?– Wrong!

The basic reproduction number

What is the degree distribution of infectives (during early stages)?



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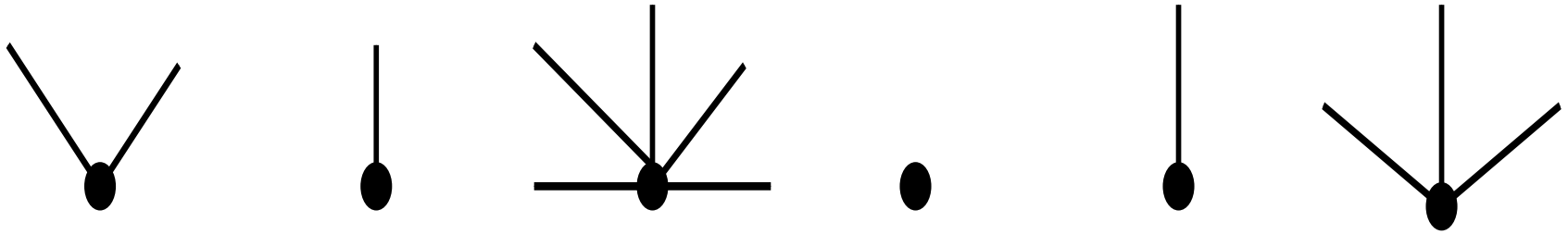

Answer: $\{\tilde{p}_k; k \geq 1\}$, where $\tilde{p}_k = const \cdot kp_k = kp_k/E(D)$

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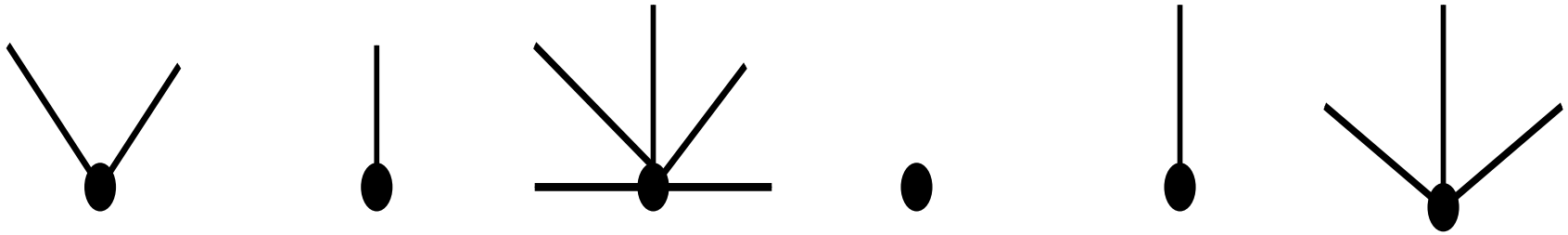

Answer: $\{\tilde{p}_k; k \geq 1\}$, where $\tilde{p}_k = const \cdot kp_k = kp_k/E(D)$

$$\Longrightarrow \; R_0 = p(E(\tilde{D}) - 1) = \cdots = p\left(E(D) + \frac{V(D) - E(D)}{E(D)}\right)$$

Empirical networks have heavy-tailed degree distributions ...

The social network and its thinned version is undirected
$\Longrightarrow P(\text{major outbreak}) = \tau = \text{relative size of outbreak}$

$P(\text{major outbreak})$ derived from Branching Process Approximation

Vaccination (Britton et al. (2007))

Suppose a fraction v are vaccinated prior to outbreak

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Who are vaccinated?

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Suppose a fraction v are vaccinated prior to outbreak

Who are vaccinated?

a) Randomly chosen individuals

$\Longrightarrow R_v = p(1-v)(E(\tilde{D})-1) = (1-v)R_0$

$\Longrightarrow$ if $v \geq 1 - 1/R_0$ then $R_v \leq 1 \Longrightarrow$ no outbreak!

- Critical vaccination coverage: $v_c = 1 - 1/R_0$

Vaccination (Britton et al. (2007))

Suppose a fraction v are vaccinated prior to outbreak

Who are vaccinated?

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$\Longrightarrow R_v = p(1-v)(E(\tilde{D})-1) = (1-v)R_0$

$\Longrightarrow$ if $v \geq 1 - 1/R_0$ then $R_v \leq 1 \Longrightarrow$ no outbreak!

- Critical vaccination coverage: $v_c = 1 - 1/R_0$
- **Problem**: If R_0 large (e.g. due to large $V(D)$), $v_c \approx 1 \quad \Longrightarrow$ impossible!

Vaccination, cont'd

Can we do better than selecting vaccinees randomly?

Vaccination, cont'd

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Yes! Vaccinate social people

But social network usually not observed ...

Vaccination, cont'd

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b) Acquaintance vaccination strategy

- Choose individuals at random

Vaccination, cont'd

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Vaccination, cont'd

Can we do better than selecting vaccinees randomly?

Yes! Vaccinate social people

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b) Acquaintance vaccination strategy

- Choose individuals at random
- vaccinate one of their friends

Vaccinees will have degree distribution $\{\tilde{p}_k\}$ rather than $\{p_k\}$

$\Longrightarrow$ much more efficient

Proportion infected as function of v, $D \sim$ Poisson

$$D \sim Po(6), \quad p = \frac{1}{2} \Rightarrow R_0 = 3$$

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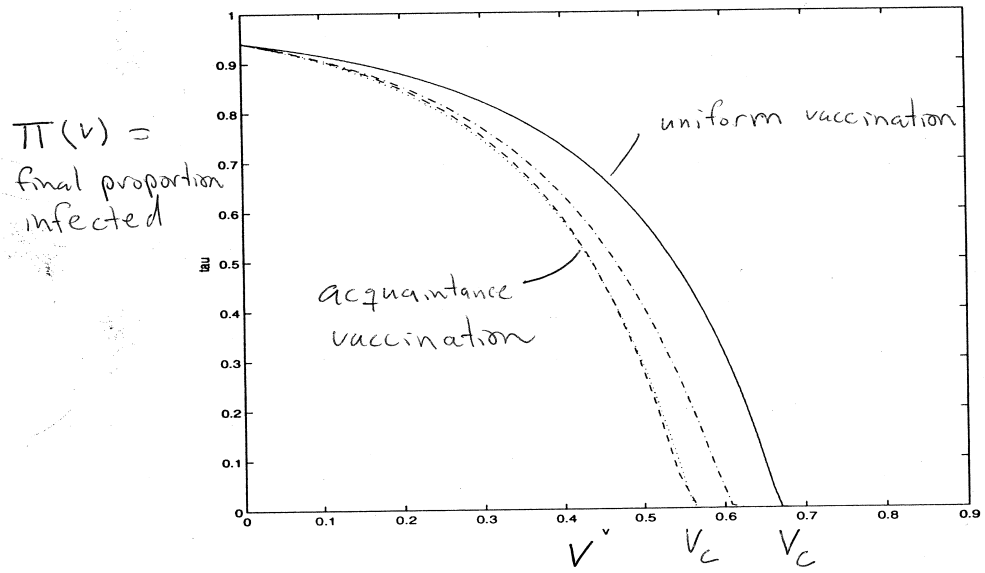

FIGURE 2. Final proportion infected τ as a function of the vaccination coverage v for four vaccination strategies: uni-

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Proportion infected as function of v, $D \sim$ heavy-tailed

$D \sim$ Heavy tail $(E(D)=6)$
$p = 0.5$

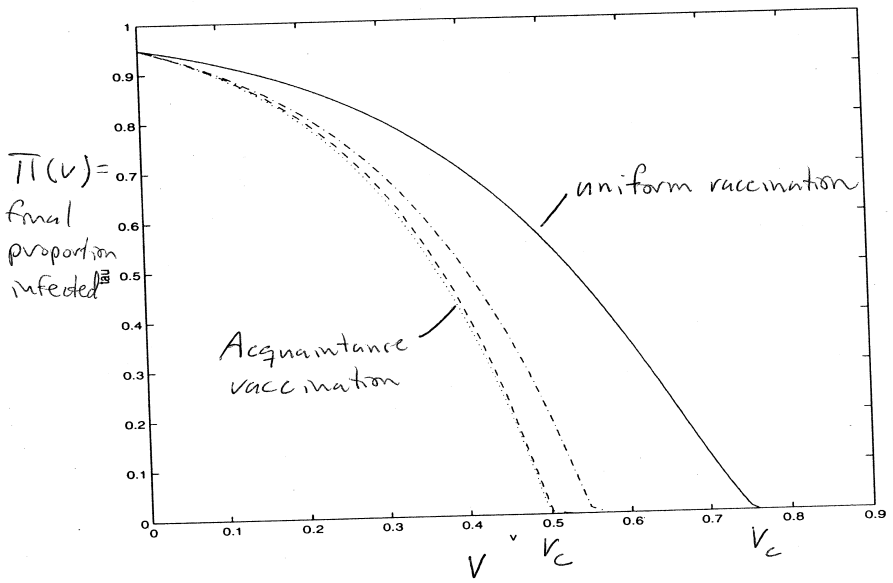

FIGURE 3. Final proportion infected as a function of the vaccination coverage for four vaccination strategies: uniform (—), acquaintance (· · ·), E1 (- - -) and E2 (— · — · —.) The degree distribution is heavy-tailed ($p_d \propto d^{-3.5}$) with mean

Individual prevention – Adaptive dynamics

Without preventive measures modelling predicts that some fraction $\tau(\theta)$ will get infected $\theta =$ model parameters

However, for severe diseases individuals will take precautions even without Public Health: isolation, distancing from infected, improved sanitation, using condom, ...

Empirical evidence (e.g. Ebola): spreading drops over time more than predicted by models, and final size often $\ll \tau(\theta)$

Adaptive dynamics: models where individuals change behaviour as an effect of the (epidemic) process

Our focus: Analyse the effect of social distancing from neighbouring infectives in an epidemic model on a social network

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Network SIR Epidemic model with Social Distancing

Leung et al. (2018), Ball et al (2019), Ball & B (2021)

Consider a large fixed community of size n. Continuous time

Network model:
Configuration model: nodes have i.i.d. degrees $D \sim \{p_k\}$ ($\mu := E(D)$) and edge-stubs are connected pairwise at random.

N.B.: network of friendships is static in absence of epidemic!

Transmission model (SIR): infectious individuals transmit to each susceptible neighbour at rate λ, and infectious individuals recover and become immune at rate γ

Social distancing: Susceptibles having infectious neighbours ...
... *rewires* such edges (to a uniformly chosen individual) at rate $\omega\alpha$
... *drops* such edges at rate $\omega(1-\alpha)$

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Comments on model

Model parameters: λ (=transmission rate), γ (=recovery rate), ω (=dropping/rewiring rate), $\alpha = P(\text{rewiring})$, and D degree distribution ($\mu = E(D)$)

Simplifying assumptions: No latent period, constant infectivity during infectious period, Markov assumption, ...

The case $\omega = 0$: well understood (e.g. Ball and others)

Dropping model ($\alpha = 0$) quite hard to analyse,
General model ($\alpha > 0$) very hard to analyse

Complication reason: the probability to get infected from neighbours now changes over course of epidemic

Easy result: **Rewiring/dropping is rational** from individual perspective: the probability to get infected *decreases* with rate at which (s)he drops/rewires!

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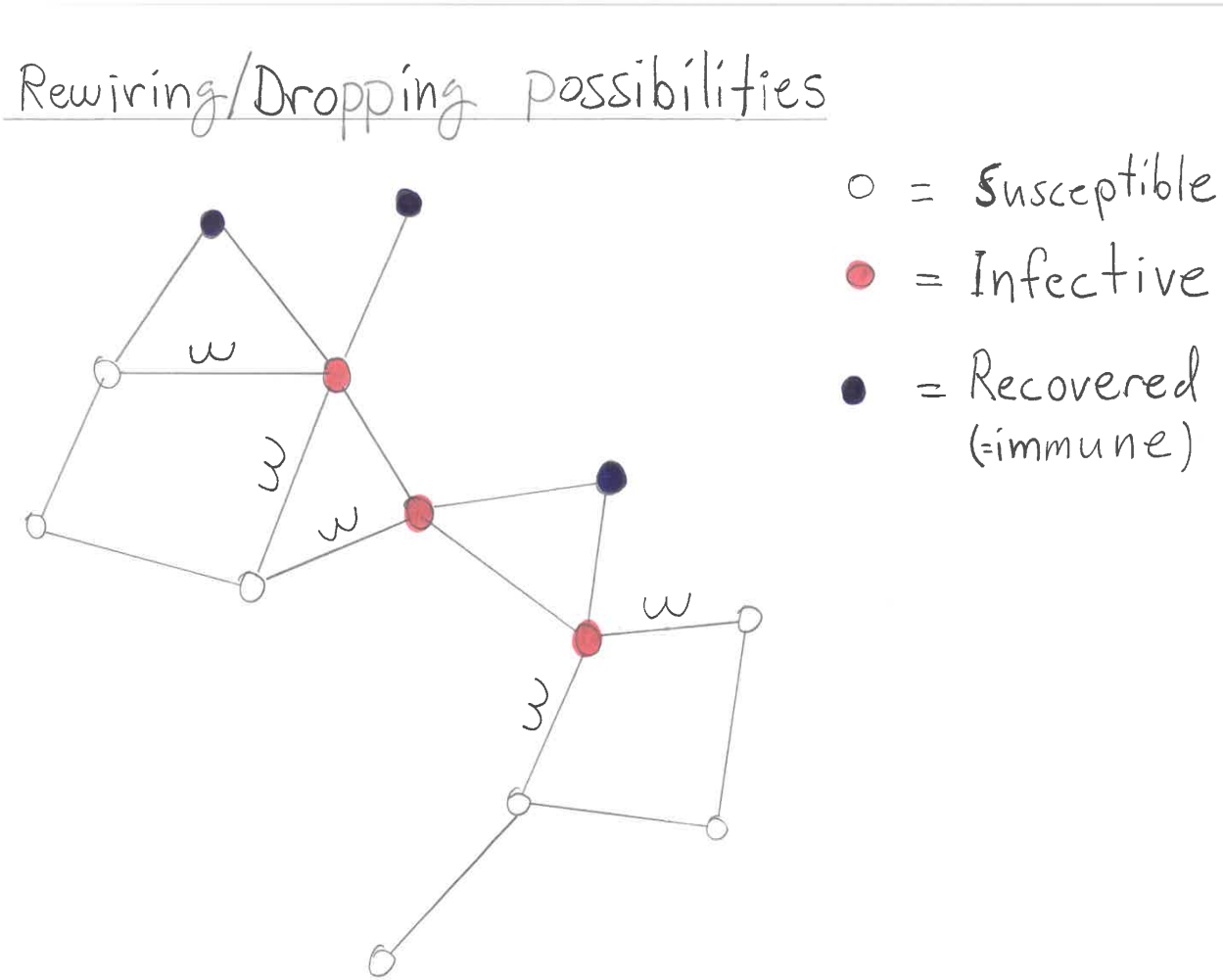
Illustration of dropping/rewiring



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Beginning of epidemic

In beginning of epidemic (when fraction infected still small) the model can be approximated by a branching process

Rewiring or dropping doesn't matter (so α irrelevant): during early stages all rewirings are to susceptibles and have no effect

B-P: An individual who gets infected during early stages has size-biased degree distr $\tilde{D} \sim \{kp_k/\mu\}$ (where $\mu = E(D)$)

Its infector is infected, all other $\tilde{D} - 1$ are susceptible, $\Longrightarrow$

$$R_0 = E(\tilde{D} - 1)P(\text{infect neighbour}) = \left(\frac{E(D^2)}{E(D)} - 1\right)\frac{\lambda}{\lambda + \gamma + \omega}$$

So R_0 **increases** in λ and **decreases** γ and ω (as expected)

No major outbreaks for large ω, ($R_0 = R_0(\omega) < 1$ for large enough ω)

Final size τ: Dropping model ($\alpha = 0$)

Equivalent Def of Dropping model: infectious individuals "inform" each susceptible neighbour, **independently**, at rate ω (when informed, the connection is dropped)

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related Modified model: infectious individual inform **all neighbours at the same time** (still having rate ω)

In Modified model all edges (with transmission potential) from infective are dropped at the same time

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related Modified model: infectious individual inform **all neighbours at the same time** (still having rate ω)

In Modified model all edges (with transmission potential) from infective are dropped at the same time

$\Longrightarrow$ Modified model is equivalent to model without rewiring: $\omega = 0$, and $\gamma \to \gamma + \omega$ for which results are available

$\Longrightarrow \tau = \tau(\omega)$ decreases with ω (as expected)

Result for Dropping model: Initial phase as described above. Final LLN fraction infected τ same as model without dropping but increased recovery rate $\gamma + \omega$ (CLT different but available)

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Final size τ: General model

Much harder to analyse

As a function of rewiring/dropping rate ω

Theorem: There exists degree distribution D and $(\lambda_0, \gamma_0, \alpha_0)$ for which $\tau = \tau(\omega)$ initially **increases**, i.e. $\tau(\omega) > \tau(0)$ for small ω

($\Longrightarrow$ **Bigger** outbreak with social distancing!)

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Heuristic explanation:
– An individual with high degree will most likely get infected even if rewiring at small rate
– After such rewiring events the individual may get connected to individuals who previously had low degree and would likely have avoided infection
$\Longrightarrow$ reduced infection risk *more than* compensated by increased possibility to infect low degree individuals

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$\tau(\omega)$

$\tau(\omega)$ increasing seem to happen when:
– R_0 is large, and
– Many individuals with low degree, and a few with high

Result would be more pronounced if rewiring was focused towards low degree individuals (which is better from an individual's perspective)

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$\tau(\lambda)$: General model

Final size $\tau = \tau(\lambda)$ as a function of transmission rate λ

Consider E-R network ($D \sim Po(\mu)$)

Fix $\mu > 1, \gamma, \omega$ and $\alpha > 0$.

Set $\lambda_c = (\gamma + \omega)/(\mu - 1)$ ($\Longrightarrow R_0(\lambda_c) = 1$ and $\tau(\lambda_c) = 0$)

Theorem: If $\gamma < \omega(2\alpha - 1)$ and $\mu > 2\alpha\omega/(\omega(2\alpha - 1) - \gamma)$, then

$$\lim_{\lambda \downarrow \lambda_c} \tau(\lambda) > 0$$

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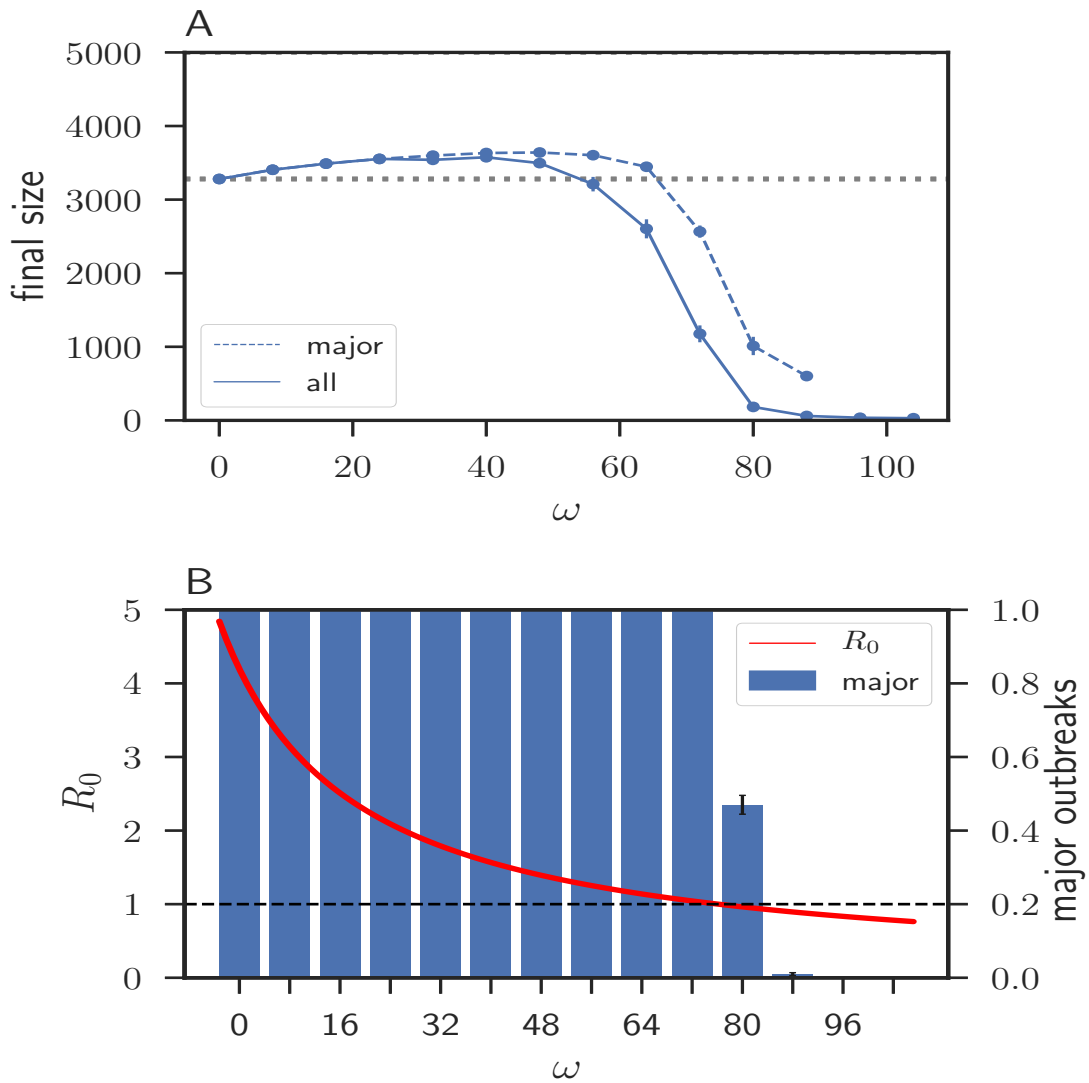
Illustration $\tau(\omega)$: $p_k = c/(k+1), k = 0, .., 10,\ n = 5000$



Simulations and empirical networks

So $\tau(\omega)$ can increase in semi-realistic degree distributions

How about empirical networks?

We simulated our SIR epidemic model with rewiring on 10-15 **empirical networks** in the Stanford network data base

We observed $\tau(\omega)$ initally growing in 2 of them: Social circles on Facebook, and Collaboration network of ArXiv on general relativity

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Empirical networks: Collaboration network

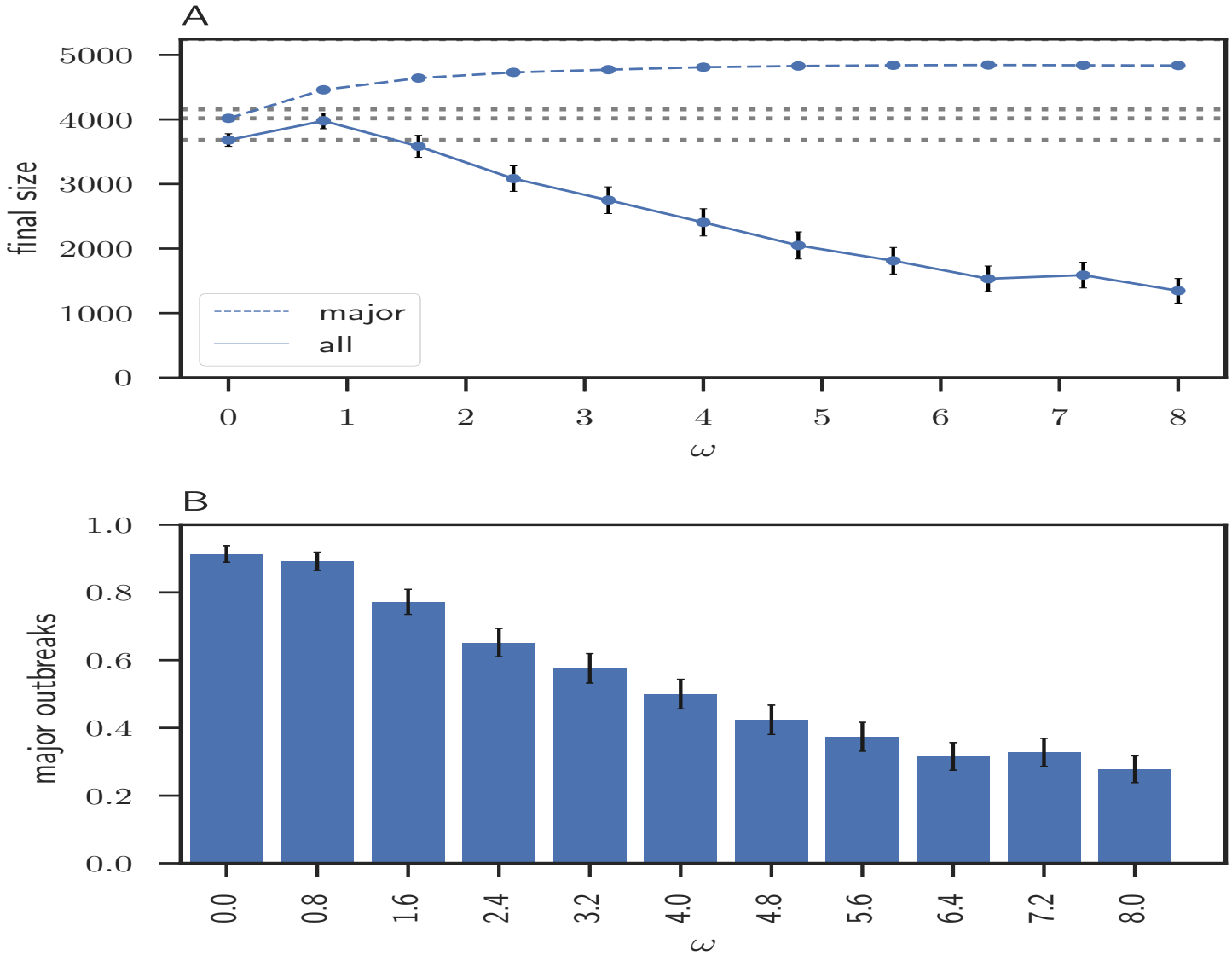

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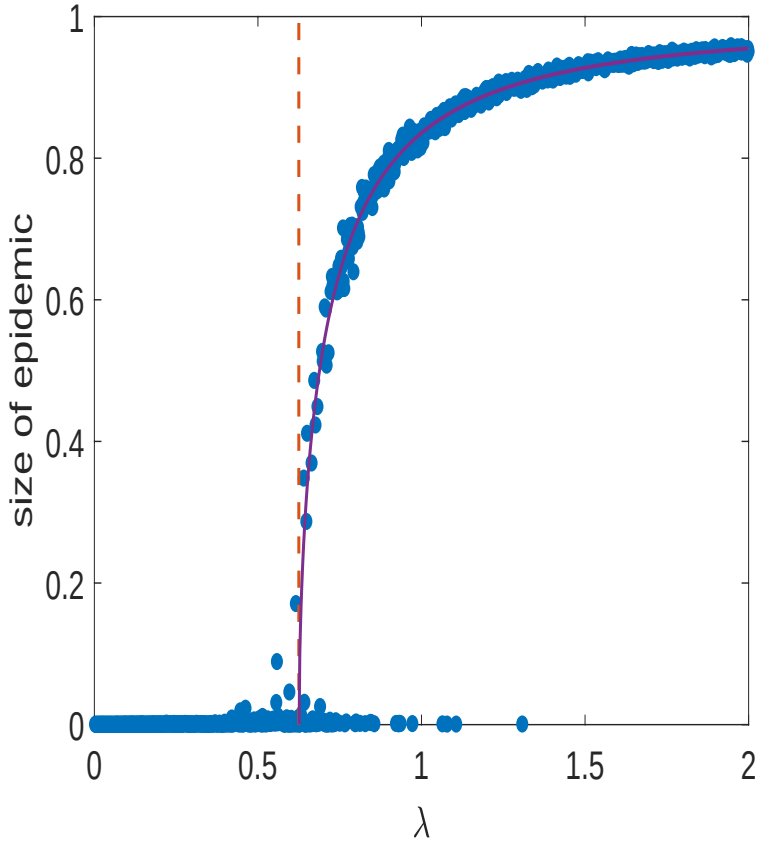
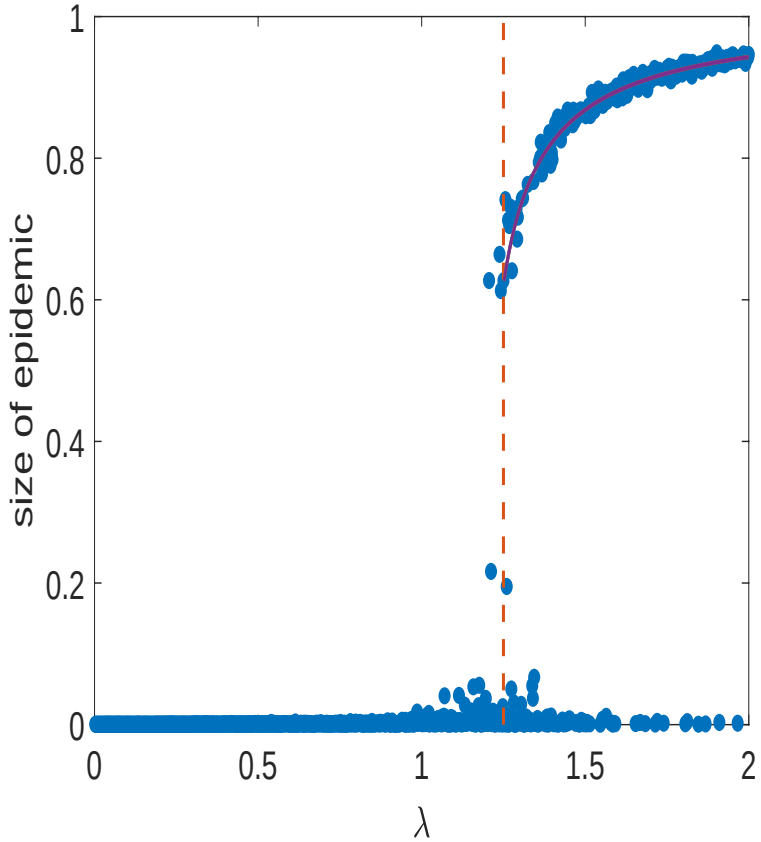
Illustration $\tau(\lambda)$: $\mu = 5,\ \gamma = 1,\ \alpha = 1,\ n = 10000$

Left panel: $\omega = 1.5$ (continuous)

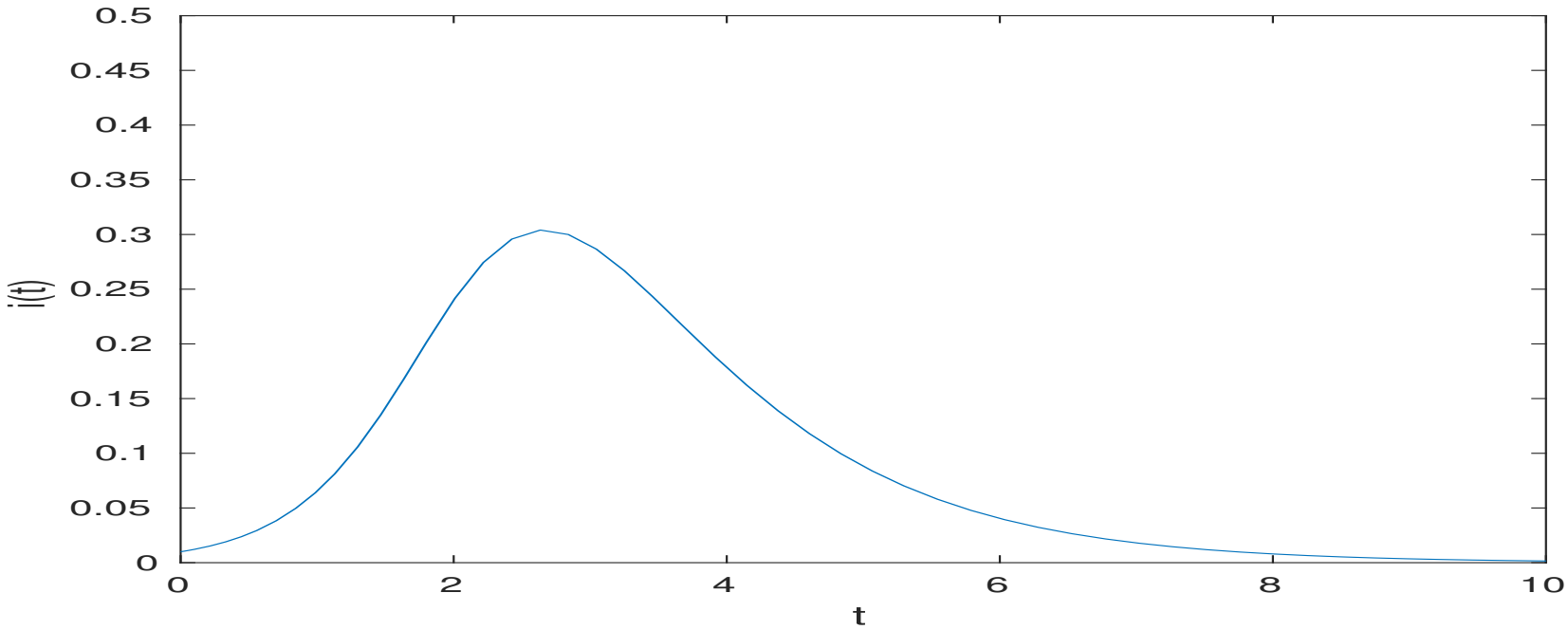


Right panel: $\omega = 4$ (discont)



Back to: Optimizing preventions (with Lasse Leskelä)

$i(t)$ when no interventions



Which prevention strategy (with $\int p(t)dt \leq c$) minimizes final epidemic size?

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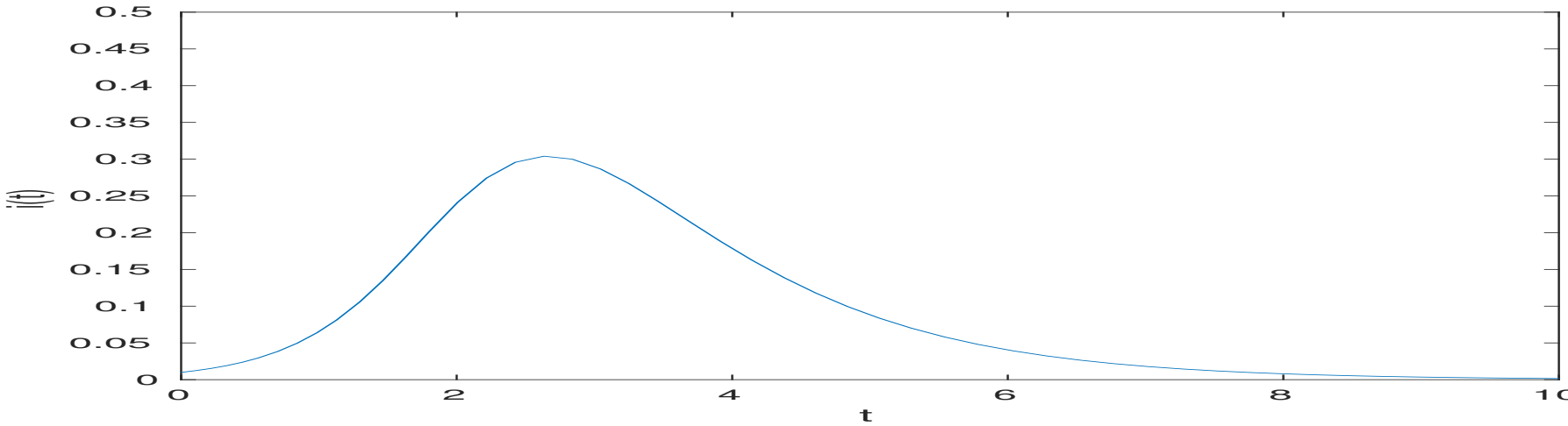
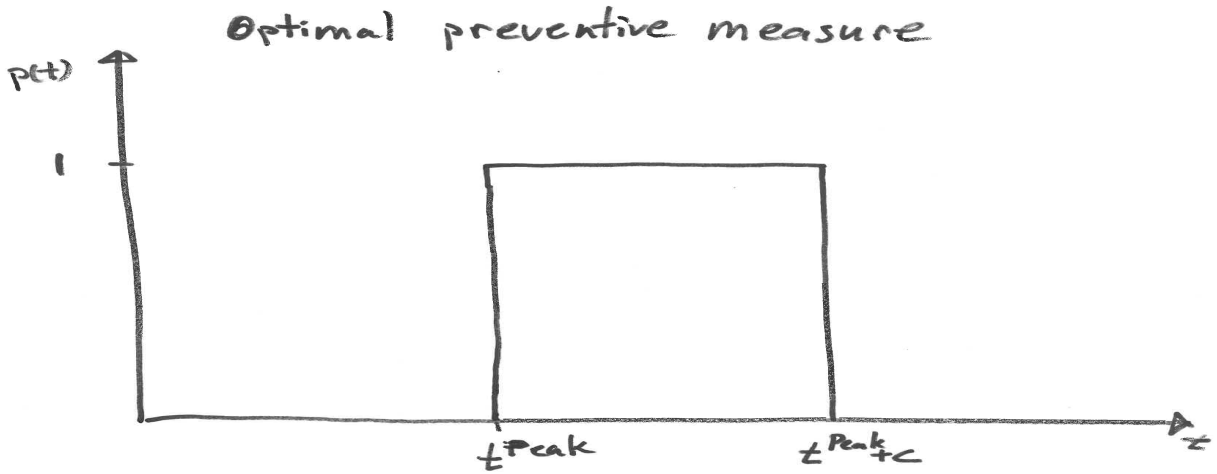
Best strategy: complete lockdown starting at peak





Minimising total incidence (main result)

Theorem

For any initial state with $S(0), I(0) > 0$, the total incidence $||i_P||_1$ among all piecewise continuous intervention strategies such that $||P||_1 \leq c_1$ and $||P||_\infty \leq c_\infty$ is minimised by an intervention of form

$$p(t) = \begin{cases} 0, & t \in (0, t_1] \quad \textit{(wait)} \\ c_\infty, & t \in (t_1, t_1 + c_1/c_\infty] \quad \textit{(suppress)} \\ 0, & t \in (t_2, \infty) \quad \textit{(relax)} \end{cases}$$

for a uniquely determined start time t_1.

Starting time t_1: If $c_\infty = 1$ (complete lockdown possible) then $t_1 =$ peak-prevalence time of unrestricted epidemic. If $c_\infty < 1$ then t_1 earlier

Take home message: *Heavy lockdowns of short duration outperform light lockdowns of longer duration.*

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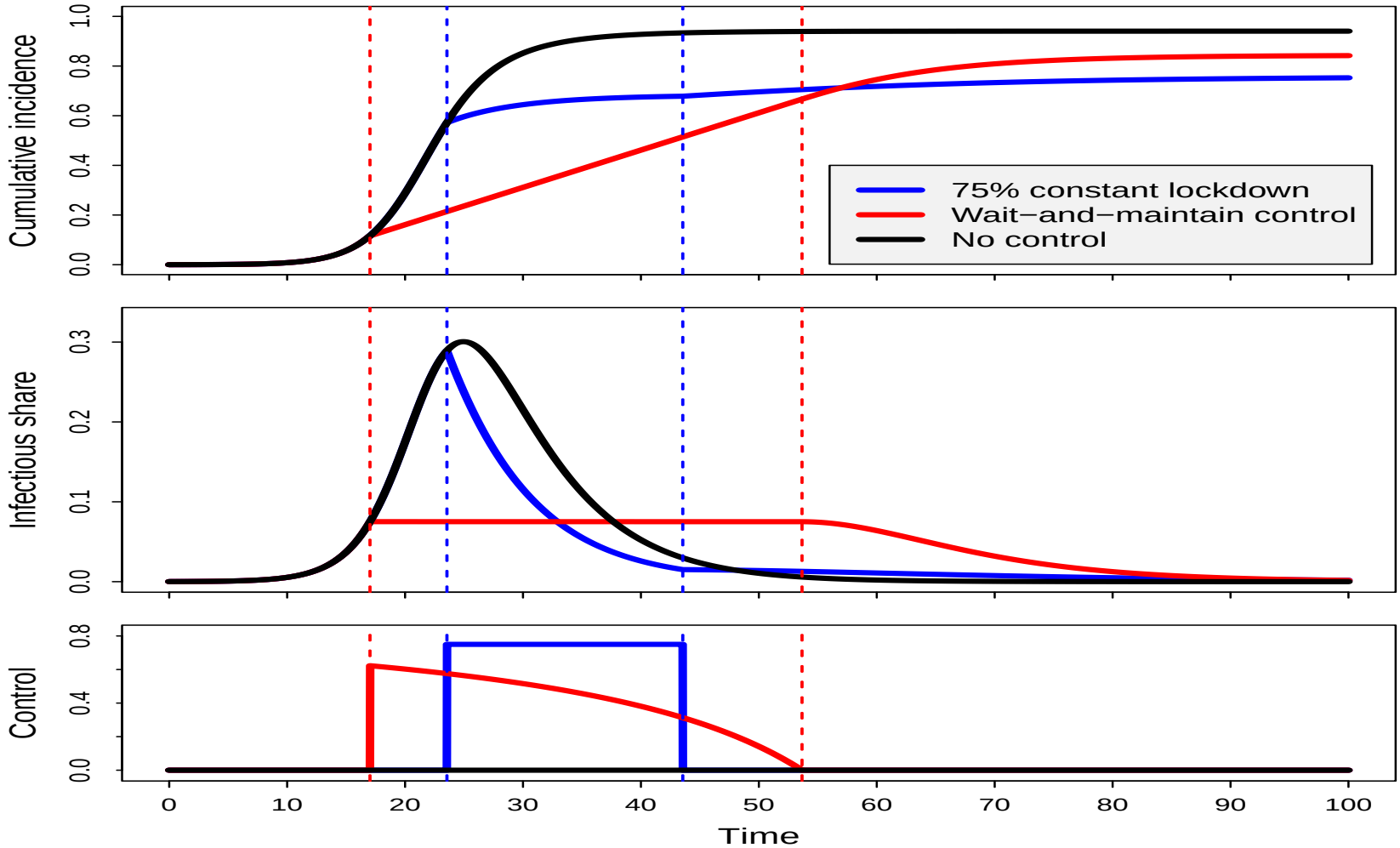
Minimizing final size vs minimizing maximum peak



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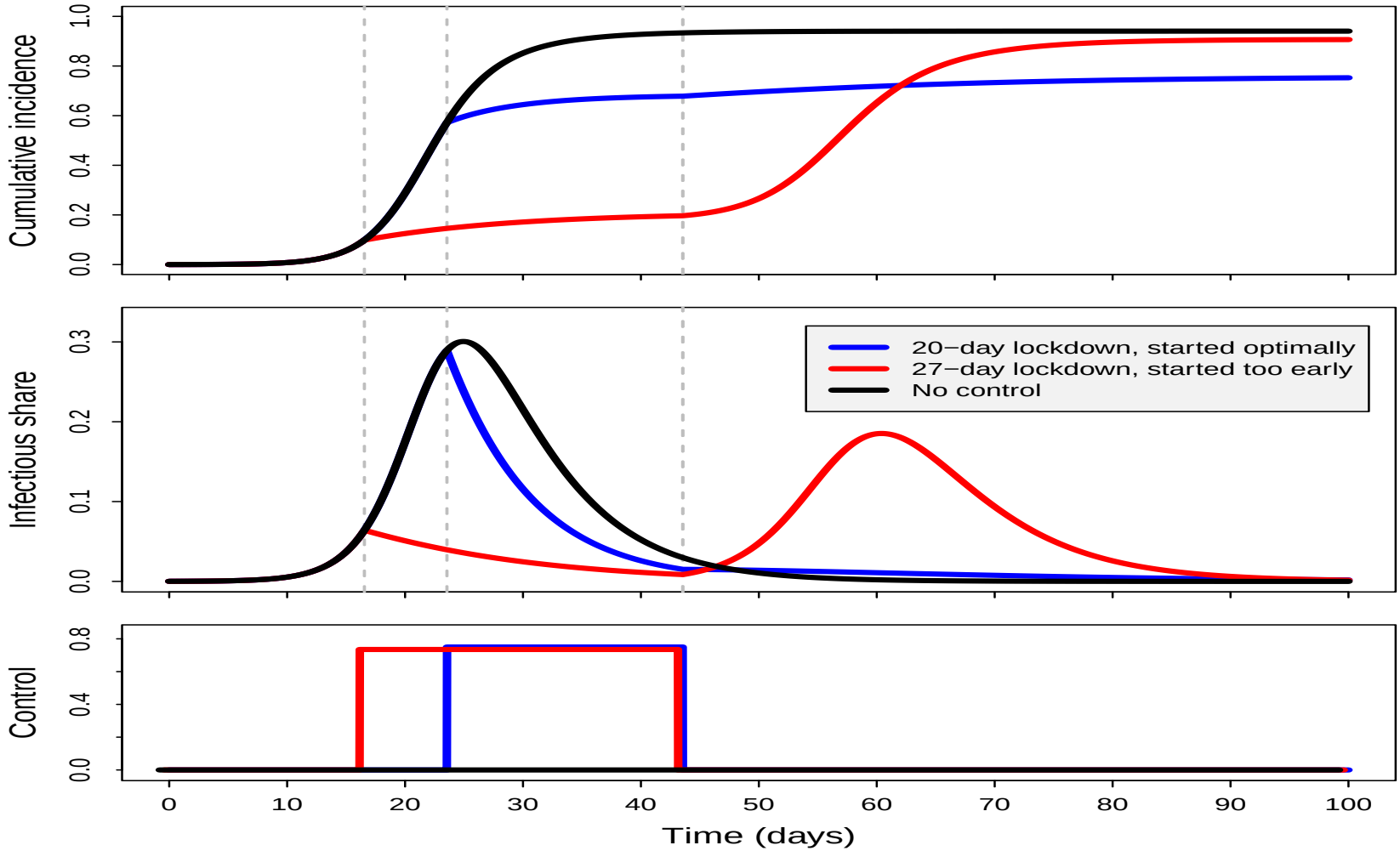
Adding prevention before optimal may **increase** final size!



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Thanks for your attention!

References

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