

Stochastic epidemic models with population structure

Tom Britton

September, 2023

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

⇒ ok for measles (except immunity) but not "valid" for STDs

Many different heterogeneities: individual susceptibility, infectivity and social activity (multitype epidemics), household structure (macro individuals), spatial structure, **social networks**

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

Exercise 21 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 $R_0 = \sum_i \alpha_i \gamma_i \nu \pi_i$

Multitype epidemics

Exercise 22 Interpret α_j and γ_j

Exercise 23 Compute R_0 for the case: $\pi_1 = \pi_2 = 0.5$, $\nu = 1$ and $\beta_{11} = 1$, $\beta_{12} = \beta_{21} = 2$ and $\beta_{22} = 4$ which obeys separable mixing assumption. Is the answer surprising?

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

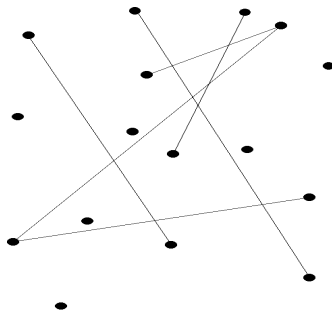
⇒ Important with models allowing for higher transmission within households

Households are small ⇒ randomness important

Networks

For some diseases (e.g. STDs) individuals are not connected in small sub-units

Common representation of social structure: network/graph with **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*)
- $c = P(\text{two friends of an individual are friends})$ (*clustering*)
- $\rho =$ correlation of degrees in a randomly selected friendship (*degree correlation*)

Other features unobserved \implies Random network

Stochastic epidemic model "on" network

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

Simplest model: an infected person infects each susceptible friend independently with prob p and then recovers (one index case)

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

Case study: 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
- Epidemic model: each susc. friend is infected with prob p
- 1 randomly selected index case, $n - 1$ susceptibles

What is R_0 ?

The degree distribution and its effect on R_0

Case study: 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
- Epidemic model: each susc. friend is infected with prob p
- 1 randomly selected index case, $n - 1$ susceptibles

What is R_0 ?

- $R_0 = pE(D)$?

The degree distribution and its effect on R_0

Case study: 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
- Epidemic model: each susc. friend is infected with prob p
- 1 randomly selected index case, $n - 1$ susceptibles

What is R_0 ?

- $R_0 = pE(D)$? – Wrong!

The degree distribution and its effect on R_0

Case study: 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
- Epidemic model: each susc. friend is infected with prob p
- 1 randomly selected index case, $n - 1$ susceptibles

What is R_0 ?

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

The degree distribution and its effect on R_0

Case study: Network epidemic model with arbitrary degree distribution $\{p_k\}$

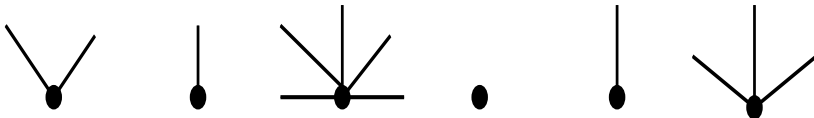
- Social structure: Individuals have degree distribution $D \sim \{p_k\}$ and "friends" are chosen completely at random
- Epidemic model: each susc. friend is infected with prob p
- 1 randomly selected index case, $n - 1$ susceptibles

What is R_0 ?

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

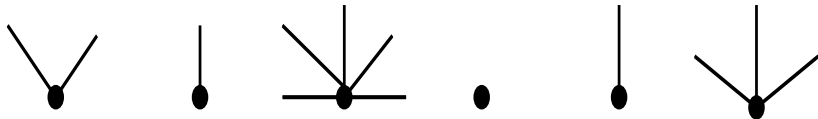
The basic reproduction number

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



The basic reproduction number

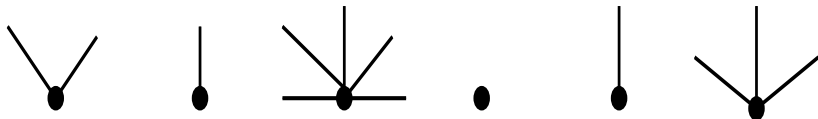
What is the degree distribution of infectives (during early stages)?



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

The basic reproduction number

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



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

$$\Rightarrow R_0 = p(E(\tilde{D}) - 1) = \dots = p \left(E(D) + \frac{V(D) - E(D)}{E(D)} \right)$$

Empirical networks have heavy-tailed degree distributions ...

Vaccination

Suppose a fraction v are vaccinated prior to outbreak

Vaccination

Suppose a fraction v are vaccinated prior to outbreak

Who are vaccinated?

Vaccination

Suppose a fraction v are vaccinated prior to outbreak

Who are vaccinated?

a) Randomly chosen individuals

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

$$\implies \text{if } v \geq 1 - 1/R_0 \text{ then } R_v \leq 1 \implies \text{no outbreak!}$$

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

Vaccination

Suppose a fraction v are vaccinated prior to outbreak

Who are vaccinated?

a) Randomly chosen individuals

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

$$\implies \text{if } v \geq 1 - 1/R_0 \text{ then } R_v \leq 1 \implies \text{no outbreak!}$$

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

Vaccination, cont'd

Can we do better than selecting vaccinees randomly?

Vaccination, cont'd

Can we do better than selecting vaccinees randomly?

Yes! Vaccinate social people

But social network usually not observed ...

Vaccination, cont'd

Can we do better than selecting vaccinees randomly?

Yes! Vaccinate social people

But social network usually not observed ...

b) Acquaintance vaccination strategy

- Choose individuals at random

Vaccination, cont'd

Can we do better than selecting vaccinees randomly?

Yes! Vaccinate social people

But social network usually not observed ...

b) Acquaintance vaccination strategy

- Choose individuals at random
- vaccinate one of their friends

Vaccination, cont'd

Can we do better than selecting vaccinees randomly?

Yes! Vaccinate social people

But social network usually not observed ...

b) Acquaintance vaccination strategy

- Choose individuals at random
- vaccinate one of their friends

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

Britton, Janson & Martin-Löf (2007)

⇒ much more efficient

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

$$\left. \begin{array}{l} D \sim P_0(6) \\ p = \frac{1}{2} \end{array} \right\} \Rightarrow R_0 = 3$$

GRAPHS, EPIDEMICS AND VACCINATION STRATEGIES

17

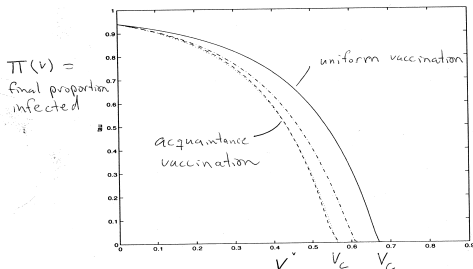


FIGURE 2. Final proportion infected τ as a function of the vaccination coverage v for four vaccination strategies: uni-

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

$$D \sim \text{Heavy tail } (E(D)=6)$$

$$p = 0.5$$

18

TOM BRITTON, SVANTE JANSON AND ANDERS MARTIN-LÖF

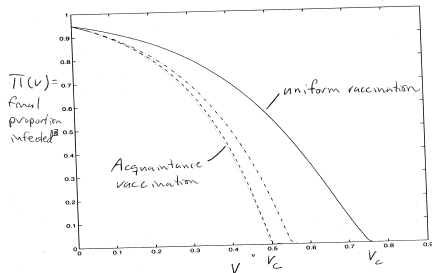


FIGURE 3. Final proportion infected as a function of the vaccination coverage for four vaccination strategies: uniform (—), acquaintance (···), E1 (---) and E2 (-·-·-). The degree distribution is heavy-tailed ($p_d \propto d^{-3.5}$) with mean

Network epidemics: summary and exercise

Main conclusion:

- Not only mean number of partners but also variance important!
- Core-groups play important roll
- Large variance of degree distribution imply large R_0 (but not necessarily large outbreak)

Important extensions: time-dynamic network, clustering, varying/dependent transmission probabilities, degree correlation

Exercise 24. Suppose the mean degree equals $E(D) = 3$ and the transmission probability per relationship equals $p = 0.25$. Compute R_0 and v_c (assuming uniform vaccination) assuming the standard deviation $\sqrt{V(D)}$ of number of partners equal 0, 1, 3, 10.

Homogeneous vs Heterogeneous: qualitative results

We now illustrate a general conclusion with an example (from the network model defined earlier)

$$\text{Recall that } R_0 = p \left(E(D) + \frac{V(D) - E(D)}{E(D)} \right)$$

Consider **two networks** with the same mean degree $E(D) = 4$

$$\text{Network 1: } D \equiv 4, \text{ so } V(D) = 0 \text{ and } E(D) + \frac{V(D) - E(D)}{E(D)} = 3$$

$$\text{Network 2: } P(D = 1) = P(D = 7) = 0.5, \text{ so } V(D) = 9 \text{ and } E(D) + \frac{V(D) - E(D)}{E(D)} = 5.25$$

Infectious Disease 1: $p = 0.25$

$$\text{Network 1: } R_0 = 3/4 = 0.75, \text{ Network 2: } R_0 = 5.25/4 = 1.31$$

$\implies R_0$ larger for Network 2. Outbreak not possible in Network 1 but possible for Network 2

Homogeneous vs Heterogeneous: qualitative results, cont'd

Infectious Disease 2: $p=0.75$

$$\text{Network 1: } R_0 = 3 \cdot 0.75 = 2.25,$$

$$\text{Network 2: } R_0 = 5.25 \cdot 0.75 = 3.93$$

$\implies R_0$ larger for Network 2. Outbreak possible in both networks

Which outbreak will be bigger?

Homogeneous vs Heterogeneous: qualitative results, cont'd

Infectious Disease 2: $p=0.75$

Network 1: $R_0 = 3 \cdot 0.75 = 2.25$,

Network 2: $R_0 = 5.25 \cdot 0.75 = 3.93$

$\implies R_0$ larger for Network 2. Outbreak possible in both networks

Which outbreak will be bigger? Outbreak in Network 1 since in Network 2-individuals with deg 1 have a good chance to escape!

General conclusion. (Starting with a homogeneous situation):

- Heterogenizing *always* increases R_0
- If original (=homogeneous case) R_0 is small, then outbreak will be bigger in heterogeneous case
- But if original R_0 is large, then heterogenizing makes outbreak **smaller!!!**

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

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 $\omega(1 - \alpha)$

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)

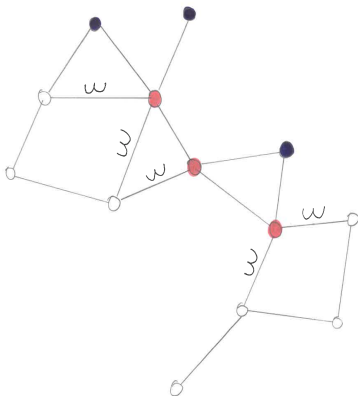
Dropping model ($\alpha = 0$) quite hard to analyse,
General model ($\alpha > 0$) very hard to analyse

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!

Illustration of dropping/rewiring

Rewiring/Dropping possibilities



- = Susceptible
- = Infective
- = Recovered (=immune)

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, \implies

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

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)

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)

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

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)

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

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

$\implies \tau = \tau(\omega)$ 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)

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
(\implies **Bigger** outbreak with social distancing!)

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
 (\implies **Bigger** outbreak with social distancing!)

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
- \implies reduced infection risk *more than* compensated by increased possibility to infect low degree individuals

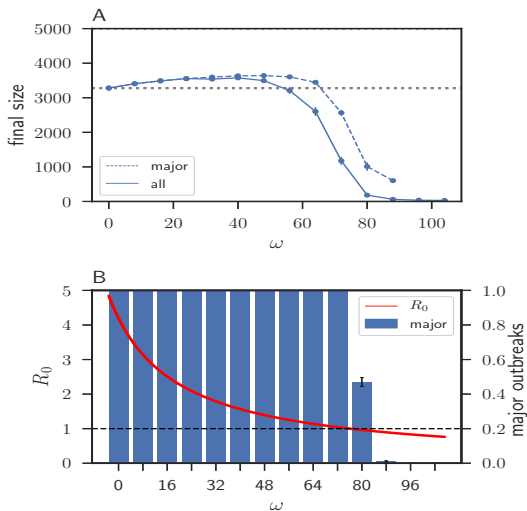
$\tau(\omega)$

$\tau(\omega)$ 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)

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



Simulations and empirical networks

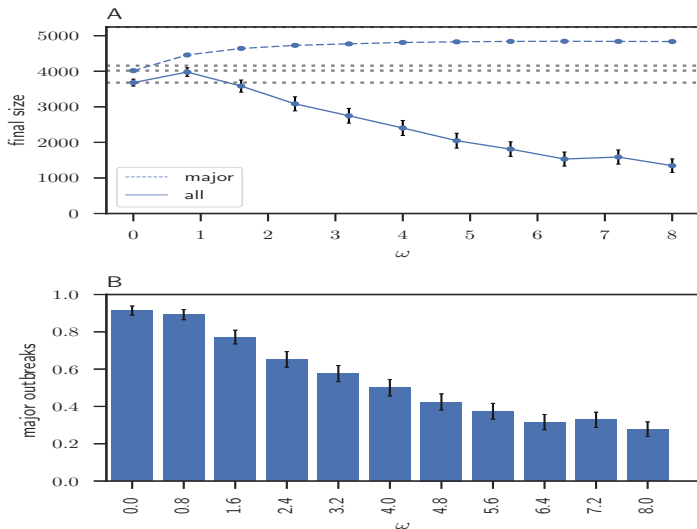
So $\tau(\omega)$ can increase in semi-realistic degree distributions

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

Empirical networks: Collaboration network



$\tau(\lambda)$: General model (Ball & Britton, 2021)

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

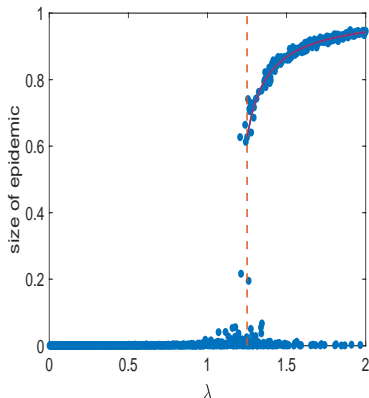
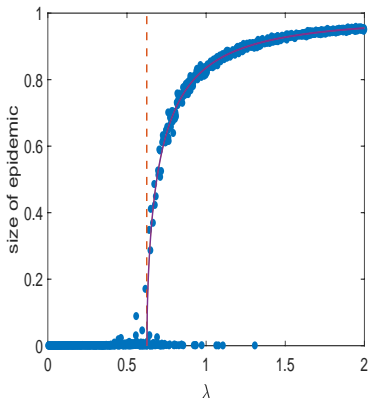
Theorem: If $\gamma < \omega(2\alpha - 1)$ and $\mu > 2\alpha\omega/(\omega(2\alpha - 1) - \gamma)$, then

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

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

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

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



Extensions and Open problems

Many solved as well as open problems for various extensions

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

How to lock down optimally in time and magnitude

T Britton and L Leskelä (2023). Optimal intervention strategies for minimizing total incidence during an epidemic. *SIAM Journal on Applied Mathematics* 83 (2), 354-373

The standard SIR epidemic

$$s'(t) = -\beta s(t)i(t)$$

$$i'(t) = \beta s(t)i(t) - \gamma i(t)$$

$$r'(t) = \gamma i(t)$$

The SIR epidemic with time-varying prevention

Introduce a (non-pharmaceutical) intervention strategy

$$P = \{p(t); 0 \leq t < \infty\}:$$

Contacts reduced by fraction $p(t)$ at t : $\beta \rightarrow \beta(1 - p(t))$

$$s'_P(t) = -\beta(1 - p(t))s_P(t)i_P(t)$$

$$i'_P(t) = \beta(1 - p(t))s_P(t)i_P(t) - \gamma i_P(t)$$

$$r'_P(t) = \gamma i_P(t)$$

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

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

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

Comments on model

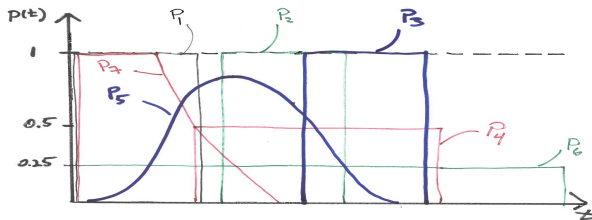
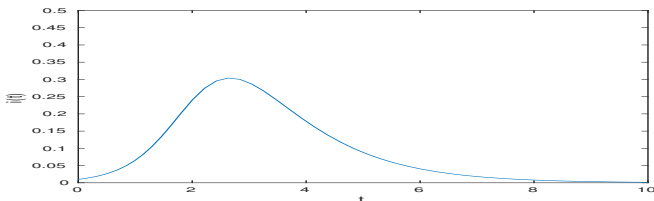
Of course **many simplifications**. Most crucial for conclusions:

- No vaccine available (or expected to arrive in near future)
- No seasonality
- Linear cost function $\int_0^\infty p(t)dt$

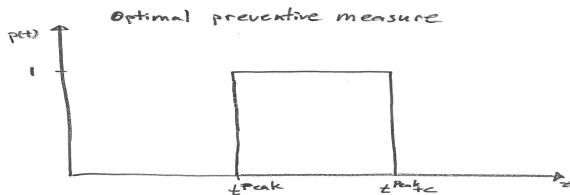
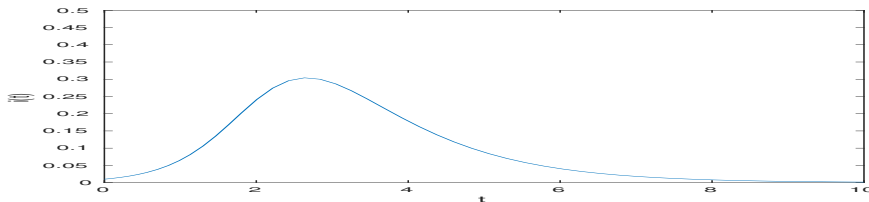
Here Aim is to minimize *total* number of infeced.

Alternative: minimize *peak* prevalence (see later)

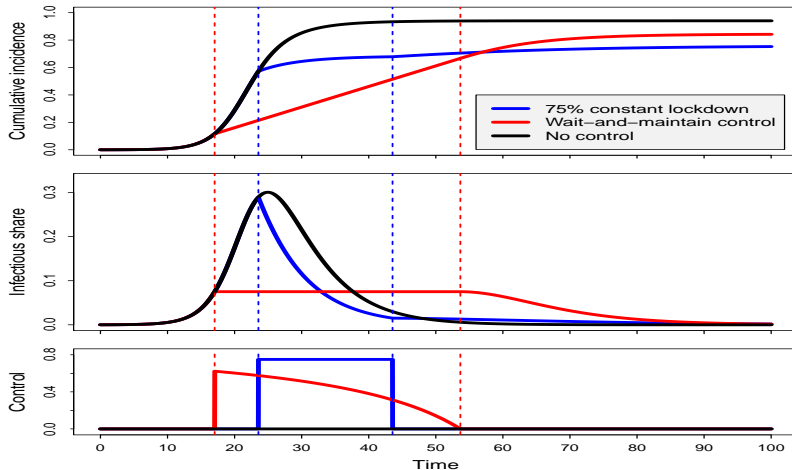
Uncontrolled incidence (top), some preventions (bottom)



Best strategy: complete lockdown starting at peak



Minimizing final size vs minimizing peak



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

