Optimal intervention policies for an epidemic

Tom Britton, Stockholm University

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Britton T and Leskelä L (2022). Optimal intervention strategies for minimizing total incidence during an epidemic.
https://arxiv.org/abs/2202.07780

The basic SIR epidemic (without prevention)

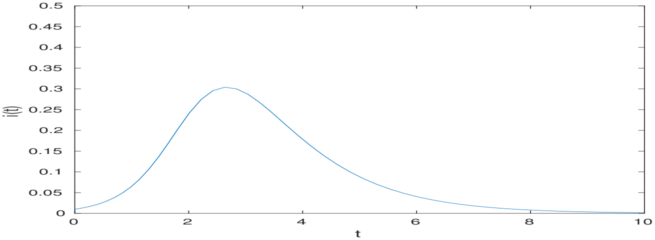
The classic SIR epidemic

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

$R_0 = \beta/\gamma$

Assumptions: homogeneous mixing, homogeneous individuals, no waning of immunity, no seasonality

Plot of $i(t)$ (prevalence) over time



The SIR epidemic with prevention

The basic SIR epidemic **with prevention**

Introduce a (non-pharmaceutical) time-varying prevention strategy $P = \{p(t); 0 \leq t < \infty\}$: contacts reduced by fraction $p(t)$ at t. The *SIR epidemic with prevention*, now depending on P, is defined by

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

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

Total cost of prevention strategy: $||P||_1 = \int_0^\infty p(t)dt$

Optimization problem: Which preventive strategy P, with cost satisfying $\int_0^\infty p(t)dt \leq c_1$, *minimizes* final size $r_P(\infty)$?

Optimal control, alternatives

Note that $r_P(\infty) = \int_0^\infty \gamma i_P(t)dt$, so minimizing final fraction infected (= total incidence) $r_P(\infty)$ is equivalent to minimizing $\int_0^\infty i_P(t)dt$

Disease burden:

- Total incidence $||i_P||_1 = \int_0^\infty i_P(t)\,dt$
- Peak prevalence $||i_P||_\infty = \sup_{t\geq 0} i_P(t)$

Intervention costs (societal and economic):

- Total duration $||P||_0 = \int_0^\infty 1(p(t) > 0)\,dt$
- Total cost $||P||_1 = \int_0^\infty p(t)\,dt$
- Maximum intervention level $||P||_\infty = \sup_{t\geq 0} p(t)$

We focus on minimizing $||i_P||_1$ subject to $||P||_1 \leq c_1$ (no vaccine available or expected to arrive in near future!)

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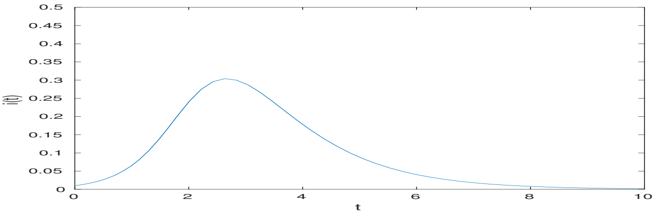
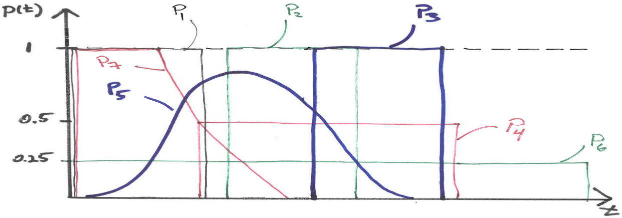
Uncontrolled prevalence (top), some preventions (bottom)





Related problems

Solution is presented at end of talk ...

Other optimality criteria (other than $r_P(\infty) \propto$ ultimate fraction needing hospital care)

- $p(t) > \alpha$ not possible (we consider $\alpha = 75\%$)
- Peak prevalence (temporal burden on hospitals)
- $r_P(t)$: cumulative fraction infected up to some fixed t (e.g. vaccine arrival)
- $r_P(T)$: cumulative fraction infected up to some random T (e.g. vaccine arrival not known exactly)

Other cost functions (other than linear cost $\int_0^\infty p(t)dt$)

- Higher cost for high prevention, e.g. $\int_0^\infty p^2(t)dt$
- Extra price for quick/many changes, e.g. $+\int_0^\infty |p'(t)|dt$

Minimising peak prevalence

Related problem for minimizing peak prevalence (Miclo, Spiro, and Weibull, 2022):

Peak prevalence ($||I_P||_\infty = \sup_{t\geq 0} i_P(t)$), subject to Total cost $||P||_1 \leq c_1$, is minimised by

$$p(t) = \begin{cases} 0, & t \in (0, t_1] \quad \text{(wait)} \\ 1 - \frac{1}{R_0 S(t)}, & t \in (t_1, t_2] \quad \text{(maintain)} \\ 0, & t \in (t_2, \infty) \quad \text{(relax)}. \end{cases}$$

Figure comes later (red curve)

Back to our problem: an interesting by-product

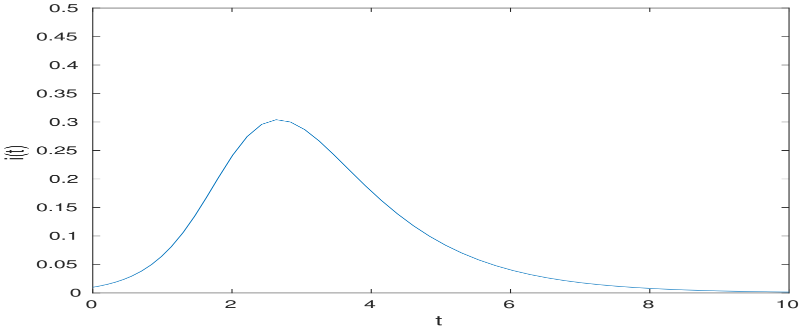
Consider a prevention strategy $P(t)$ consisting of complete lockdowns $(P(t) = 1)$ during n intervals starting at $\{t_i\}$ and lasting for duration $\{\tau_i\}$. Then final size $z_P = r_P(\infty)$ is the positive solution to the following equation

$$1 - z_P = e^{-R_0\left(z_P - \sum_{k=1}^{n} i_P(t_j)(1-e^{-\gamma\tau_j})\right)}$$

The solution is smaller, the *larger* $\sum_{k=1}^{n} i_P(t_j)(1 - e^{-\gamma\tau_j})$ is ...

Back to our problem: Optimal solution

$i(t)$ when no interventions



Which prevention strategy (with $\int p(t)dt \leq c_1$) minimizes final epidemic size?

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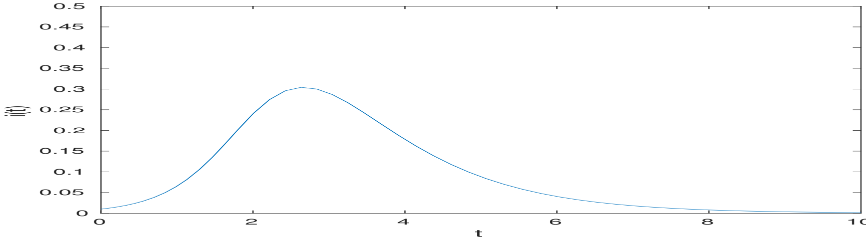
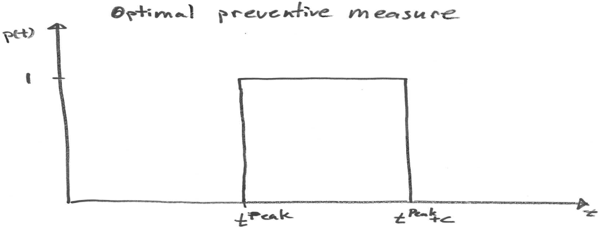
Best strategy: complete lockdown starting at peak





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

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

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.*

Best and worse case bounds

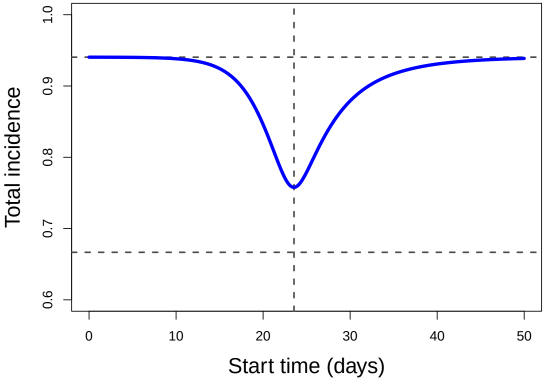
Additional result: *For any intervention strategy with finite cost* $||P||_1 < \infty$*, the total incidence is at least* $1 - 1/(R_0 s(0))$ *(herd immunity level) and at most* $1 - s_0(\infty)/s(0)$ *(total incidence without prevention).*

Illustration: Suppose $R_0 = 3$ and $s(0) \approx 1$ (no initial immunity). Then any intervention with finite cost will result in total incidence between 66.7% and 94.0%.

Figure on next slide Suppose that lockdown up 75% is possible, and that $c_1 = 15$ (full lockdown days). So for instance a 75% lockdown can go on for 20 days, a 50% lockdown can go on for 30 days and a 25% lockdown can go on for 60 days.

Theorem states that a 75% lockdown minimizes total incidence, but when should it start?

Optimal start time



Total incidence with 75% lockdown for 20 days for different starting times. Optimal start time $t_1 = 23.6$ days yields total incidence of 0.758. Universal bounds equal 0.666 and 0.940.

Starting too early is about equally bad as starting too late.

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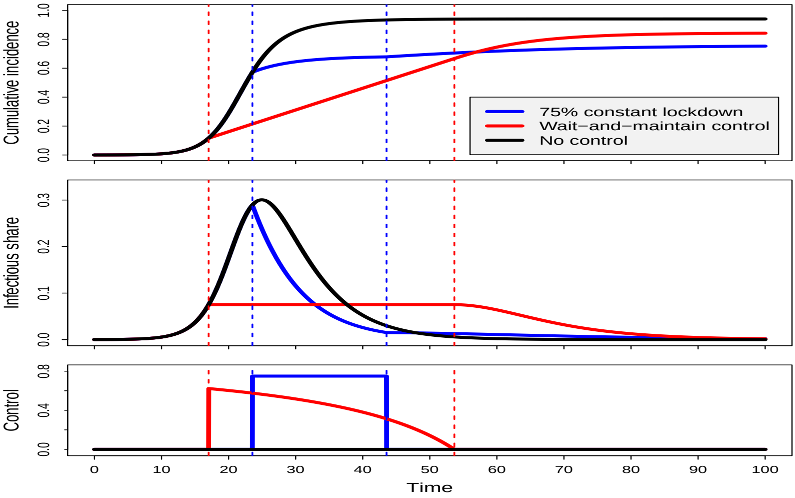
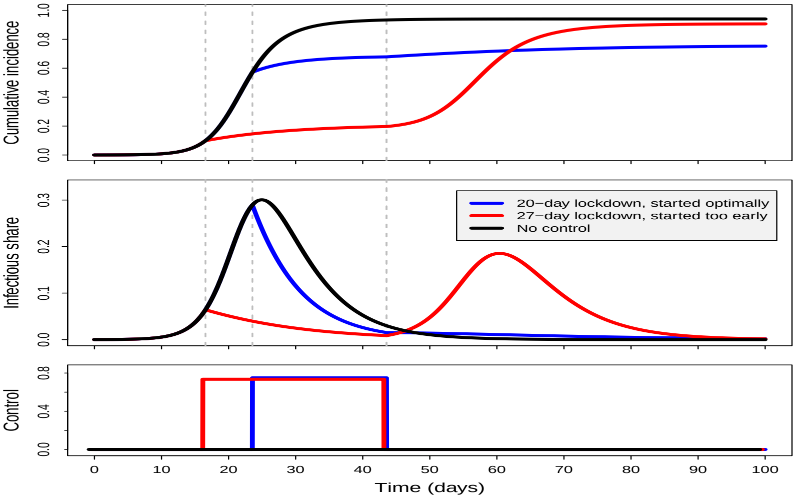
Minimizing final size vs minimizing peak prevalence



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



Sketch of Proof

We reduce the problem to finite horizon and on–off controls, and then apply the on–off control theory result in Feng, Iyer, and Li (2021).

Four steps steps:

1. Truncation
2. Quantisation (Lipschitz interpolation lemma + Gronwall's inequality)
3. Prolongation
4. Feng et al (2021): Many constant level prevention periods minimize total incidence if they are merged into one long prevention period

Step 1: Truncation

Lemma (Time to herd immunity)

For any piecewise continuous control such that $||P||_1 < \infty$, the time to reach herd immunity is finite and bounded by

$$t_H(P) \ \leq \ ||P||_1 + \frac{\log(\frac{\beta}{\gamma} s(0))}{\beta i(0)} e^{\gamma ||P||_1}.$$

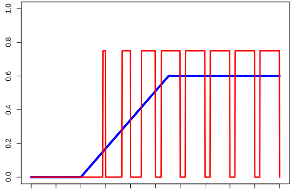
Lemma (Uniform integrability)

For any $c_1 \geq 0$, there exist constants $\alpha, C, T_* > 0$ such that

$$\sup_{||P||_1 \leq c_1} \int_T^\infty i_P(t)\, dt \ \leq \ Ce^{-\alpha T} \qquad \text{for all } T \geq T_*.$$

Step 2: Quantisation

Quantisation of a function P by frequency modulated function $\hat{P}$ with amplitude 0.75.



Lemma (Approximation by on-off controls)

For any $b, h > 0$, the approximation $\hat{P} = Q_{b,h}P$ satisfies $||\hat{P}||_1 = ||P||_1$, and

$$\left| \int_0^t \left(\hat{P}(s) - P(s)\right)\phi(s)\, ds \right| \;\leq\; bh\left(||\phi||_{\infty,t} + t||\phi||_{\mathrm{Lip},t}\right)$$

for all $t \geq 0$ and all locally bounded and locally Lipschitz continuous ϕ.

Step 3: Prolongation

Lemma (Monotonicity)

Let (s_1, i_1, r_1) be an epidemic trajectory controlled by P_1 such that $P_1 = 0$ outside $[0, T]$. Let (s_2, i_2, r_2) be an epidemic trajectory with the same initial state but a modified control $P_2 = P_1 + c1_{[t_1, t_2]}$ with $T \leq t_1 \leq t_2$. Then $r_2(\infty) \leq r_1(\infty)$.

Prolonged interventions (extended at the end) imply less infections.

Step 1-3 + result by Feng et al (merge multiple constant level prevention periods) gives the desired result

Discussion

Main conclusion (given assumptions and minimzation criteria):

It is best to wait (a surprisingly long time) and then impose as much lockdown as possible until the intervention cost is used up.

However

- Is there a maximal total cost $c_1 < \infty$ or a maximal cost per month/quarter of year/year?
- No vaccine (or expected to arrive)
- Immunity waning not considered
- No seasonality
- Homogeneous mixing, homogeneous individuals