Lockdowns in SIR Models

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Useful background readings

Epidemiology references

- Keeling-Rohani "Modeling Infectious Diseases in Humans and Animals"
- Brauer-CastilloChavez "Math Models in Pop Biology and Epidemiology"
- Hethcote "The Mathematics of Infectious Diseases"

Materials from public debate (more at end of slides)

- https://ncase.me/covid-19/
- https://www.nytimes.com/2020/05/01/opinion/sunday/coronavirus-herd-immunity.html
- https://twitter.com/CT Bergstrom/status/1256828517741780992

Large part of notes inspired by recent econ papers:

- 1. Lukasz Rachel "An Analytical Model of Covid-19 Lockdowns"
- 2. Flavio Toxvaerd "Equilibrium Social Distancing"
- 3. Alvarez-Argente-Lippi "A Simple Planning Problem for COVID-19 Lockdown"
- 4. Farboodi-Jarosch-Shimer "Internal and External Effects of Social Distancing"
- 5. Atkeson "What will be the economic impact of COVID-19 in the US?"
 - In contrast to 1.-4., here purely mechanical (no optimality, behavioral feedback)

Main Takeaways on SIR Model

- Even though model is very simple it generates some subtle insights
- Two key quantities that are different
 - 1. herd immunity threshold = after which infections decline
 - 2. final size / burden of disease = cumulative number of infections
- In most cases epidemic "overshoot": final size > herd immunity
- Another two key quantities that sometimes get confused:
 - 1. basic reproduction number
 - 2. effective reproduction number

Main Takeaways on Lockdowns in SIR Model

- 1. Even temporary lockdowns reduce total number of infections, i.e. they don't just postpone the inevitable (+ help with ICU capacity)
- 2. But if temporary lockdowns are only option, total number of infections still > herd immunity threshold
- 3. Best lockdowns-only can do is eliminate epidemic "overshoot"
- 4. If lockdown too short get 2nd wave
- 5. If lockdown too tight get 2nd wave
- 6. Tight lockdown only sensible if switch to alternative strategy after (e.g. test-trace-isolate, "lockdown as reset")
- 7. In absence of such alternatives, if want to save most possible lives, choose intermediate lockdown even if no weight on econ costs
- 8. Some unpleasant arithmetic: for Covid-19 reaching herd immunity with lockdowns only would take a very long time – think 500 days

Simplest SIR Model

- Susceptibles St
- Infectious It
- Recovered or dead R_t

$$\dot{S} = -\beta SI \tag{S}$$

$$\dot{I} = \beta S I - \gamma I \tag{I}$$

$$\dot{R} = \gamma I$$
 (R)

with initial conditions S_0 , I_0 , R_0 satisfying $S_0 + I_0 + R_0 = 1$

• Death: constant death probability out of I state π

$$\dot{D} = \pi \gamma I \quad \Leftrightarrow \quad D = \pi R$$

• Mass preservation: $\dot{S}_t + \dot{I}_t + \dot{R}_t = 0 \Rightarrow S_t + I_t + R_t = 1$, all $t \ge 0$

Simplest SIR Model

Vocabulary

- 1. Basic reproduction number $\mathcal{R}_0 := \beta/\gamma$ (note font to avoid confusion with R_0)
- 2. Effective reproduction number $\mathcal{R}_t^e := \beta/\gamma \times S_t$
- 3. Herd immunity threshold $S^* = 1/\mathcal{R}_0$ or $R^* = 1 1/\mathcal{R}_0$

From (I) we have

$$\dot{I} = (\beta S - \gamma)I = (\mathcal{R}_0 S - 1)\gamma I = (\mathcal{R}^e - 1)\gamma I$$

Therefore

- 1. I > 0 if $\mathbb{R}^e > 1$ and < 0 otherwise
- 2. $\dot{I} > 0$ if $S > S^*$ and < 0 otherwise
- 3. If $\mathcal{R}_0 < 1$ disease never gets off ground: $\dot{I}_0 < 0$ (even when S = 1)
- 4. If $S_0 \leq S^*$ disease never gets off ground: $\dot{I}_0 < 0$ ("herd immunity")

Lockdowns in SIR Model

Simplest way of modeling lockdowns: time-varying, reduced β_t

$$\dot{S}_t = -\beta_t S_t I_t \tag{S}$$

$$\dot{I}_t = \beta_t S_t I_t - \gamma I_t \tag{I}$$

$$\dot{R}_t = \gamma I_t$$
 (R)

with initial conditions S_0 , I_0 , R_0

Some additional vocabulary (I follow Atkeson here)

- 1. Normalized transmission rate $\tilde{\mathcal{R}}_t := \beta_t/\gamma$ so that $\mathcal{R}_0 = \tilde{\mathcal{R}}_0$
- 2. Effective reproduction number $\mathcal{R}_t^e := \beta_t/\gamma \times S_t = \tilde{\mathcal{R}}_t \times S_t$

Transition Matrix Formulation

Recall

$$\dot{S} = -\beta SI \tag{S}$$

$$\dot{I} = \beta SI - \gamma I \tag{I}$$

$$\dot{R} = \gamma I$$
 (R)

Can also write this in matrix form (note the transpose)

$$\dot{\mu} = \mathbf{A}(\mu)^{\mathsf{T}}\mu, \qquad \mu = \begin{bmatrix} S \\ I \\ R \end{bmatrix}, \qquad \mathbf{A}(\mu) = \begin{bmatrix} -\beta I & \beta I & 0 \\ 0 & -\gamma & \gamma \\ 0 & 0 & 0 \end{bmatrix}$$

- $\mathbf{A}(\mu)$ = transition matrix across health states (outflows and inflows)
- Useful for numerical solution: I like finite difference method

$$\frac{\mu^{n+1} - \mu^n}{\Lambda t} = \mathbf{A}(\mu^n)^{\mathsf{T}} \mu^n$$

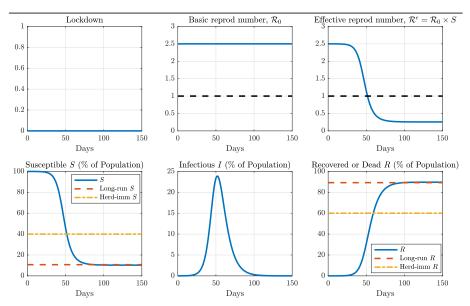
Matlab codes for all simulations, diagrams here:

https://benjaminmoll.com/SIR_no_lockdown/https://benjaminmoll.com/SIR lockdown/

https://benjaminmoll.com/SIR_lockdown_most_lives/

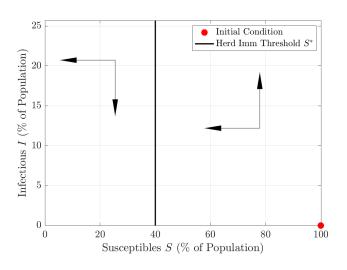
Require arrow3.m at https://uk.mathworks.com/matlabcentral/fileexchange/14056-arrow3

Warmup: dynamics of epidemic with constant β

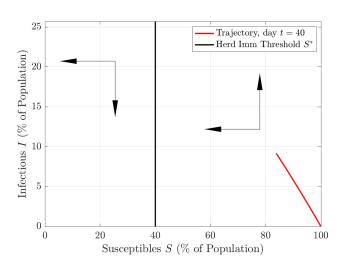


Observations

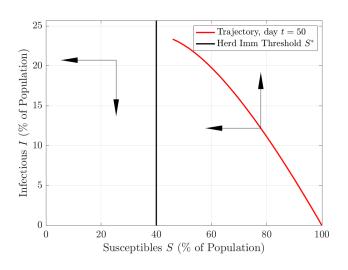
- Long-run $S_{\infty} > 0$, $R_{\infty} < 1$ so not everyone gets disease
- But also long-run $S_{\infty} < S^*$, $R_{\infty} > R^*$, i.e. epidemic "overshoots" herd immunity threshold
- Herd immunity threshold S* coincides with peak I not final I
- After reaching peak $\dot{l} < 0$ but still many more people get infected
- https://www.nytimes.com/2020/05/01/opinion/sunday/coronavirus-herd-immunity.html



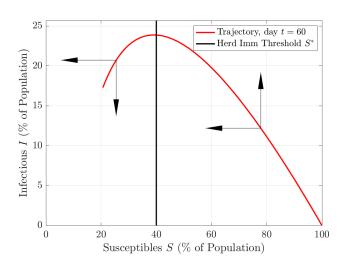
$$\dot{S} = -\beta SI$$
, $\dot{I} = \beta SI - \gamma I$, state space = simplex $S + I \le 1$



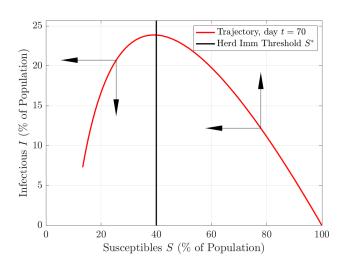
$$\dot{S} = -\beta SI$$
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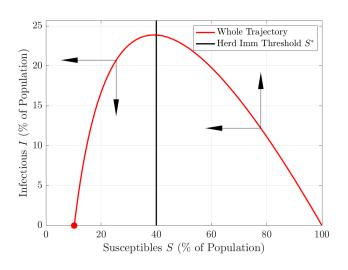
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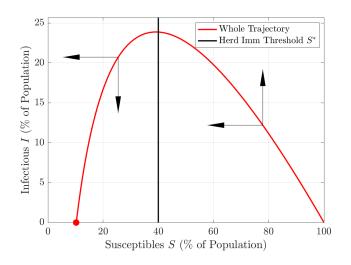
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$$\dot{S} = -\beta SI$$
, $\dot{I} = \beta SI - \gamma I$, state space = simplex $S + I \le 1$



Same diagram as in Hethcote (2000). In econ see Toxvaerd, Rachel,...

Closed-Form Solution for Trajectory

• Claim: trajectory satisfies

$$I_t = 1 - R_0 - S_t + \frac{1}{R_0} \log(S_t/S_0) \tag{*}$$

Derivation: recall

$$\dot{S} = -\beta SI \tag{S}$$

$$\dot{I} = \beta S I - \gamma I \tag{1}$$

$$\dot{R} = \gamma I$$
 (R)

• From (S) and (R)
$$\frac{\dot{S}_t}{S_t} = -\mathcal{R}_0 \dot{R}_t$$
, $\mathcal{R}_0 := \frac{\beta}{\gamma}$

- Interpretation: % decline in S equals \mathcal{R}_0 times level increase in R
- Logic: only way of getting from S to R is via I
- Integrate from 0 to t

$$\log S_t - \log S_0 = -\mathcal{R}_0(R_t - R_0)$$

• Using $S_t + I_t + R_t = 1$ yields (*).

Closed-Form Solution for Trajectory

Recall closed-form solution for trajectory in (S, I) space

$$I_t = 1 - R_0 - S_t + \frac{1}{R_0} \log(S_t/S_0) \tag{*}$$

- This formula is very powerful!
- Next: three immediate implications
 - 1. Final size/burden of disease
 - 2. Peak of infections
 - 3. Trajectories from different initial conditions (lockdown warmup)

Final burden of disease

- In long-run $I_{\infty} = 0$
- Hence S_{∞} satisfies (*) with $I_{\infty} = 0$

$$\log S_{\infty} = \log S_0 - \mathcal{R}_0 (1 - R_0 - S_{\infty})$$
 or $S_{\infty} = S_0 e^{-\mathcal{R}_0 (1 - R_0 - S_{\infty})}$

• Typical initial conditions $S_0 \approx 1$, $I_0 \approx 0$, $R_0 = 0$

$$\log S_{\infty} = -\mathcal{R}_0(1 - S_{\infty}) \quad \text{or} \quad S_{\infty} = e^{-\mathcal{R}_0(1 - S_{\infty})} \tag{**}$$

- This is the formula you will typically find in textbooks
- If $\mathcal{R}_0 > 1$, (**) has two roots $S_\infty = 1$ and $0 < S_\infty < 1$
- Useful to realize: (**) simply says S_{∞} is where trajectory hits x-axis
- Epidemic overshoot immediately obvious from phase diagram

Size of overshoot for different \mathcal{R}_0

- Epidemic overshoot immediately obvious from phase diagram
- But how big is it?
- Overshoot = $|S_{\infty} S^*|$ where $S_{\infty} < 1$ solves (**) and $S^* = 1/\mathcal{R}_0$
- Example 1: $\mathcal{R}_0 = 2.5$ (= in range of \mathcal{R}_0 estimates for Covid-19)

$$S^* = \frac{1}{R_0} = 40\%$$
, $S_{\infty} = 10.7\% \Rightarrow \text{overshoot} = 29.3\%!$

- How does this vary with \mathcal{R}_0 ? Difficulty: no closed-form sol'n to (**)
- Useful approximation: for large R₀ solution to (**) behaves like

$$S_{\infty} \sim e^{-\mathcal{R}_0} =: \tilde{S}_{\infty}$$

(Approximation quality? With $\mathcal{R}_0=$ 2.5: $\tilde{S}_{\infty}=$ 8.2%, true $S_{\infty}=$ 10.7%)

• Example 2: $\mathcal{R}_0 = 3 \Rightarrow S^* = 1/3$, $\tilde{S}_{\infty} = e^{-3} = 5\%$ (true $S_{\infty} = 5.9\%$)

$$\Rightarrow$$
 overshoot $\approx 28\%$

Peak of infections

Recall

$$I_t = I(S_t), \quad I(S) := 1 - R_0 - S + \frac{1}{R_0} \log(S/S_0)$$

• From the phase diagram

$$I_{\text{peak}} = \max_{S} I(S) = I(S^*)$$

• Since $S^* = 1/\mathcal{R}_0$

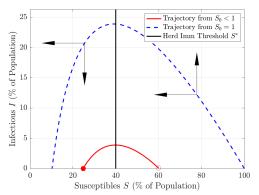
$$I_{\text{peak}} = -\frac{1}{R_0} \log(R_0 S_0) - \frac{1}{R_0} + 1 - R_0$$

Different initial conditions (warmup for lockdowns)

Trajectory also tells us how dynamics depend on initial conditions:

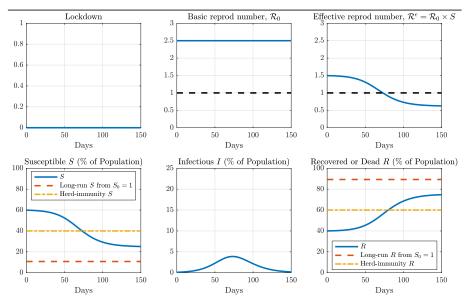
$$I_t = 1 - R_0 - S_t + \frac{1}{R_0} \log(S_t/S_0)$$
 (*)

• Example: S₀ closer to herd immunity but still above



• If $S_0 > S^*$, then for all $I_0 > 0$ (even ≈ 0) epidemic takes off

S_0 closer to herd immunity but still above



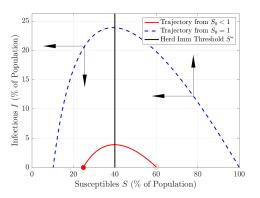
• If $S_0 > S^*$, then for all $I_0 > 0$ (even ≈ 0) epidemic takes off

Epidemic speed slowest at bottom of phase diagram

Follows directly from equations for *S* and *R*:

$$\frac{\dot{S}}{S} = -\beta I, \qquad \dot{R} = \gamma I$$

 \Rightarrow S and R move slowly whenever I is close to zero



Will be relevant for unpleasant lockdown arithmetic later in slides

Analytical solution for entire (S_t, I_t, R_t) time path

- For (complicated) analytical solution to entire time path see
 - Harko et al (2014) "Exact analytical solutions of the SIR epidemic model..."
 - Toda (2020) "SIR Dynamics of COVID-19 and Economic Impact"
- I personally find phase-diagram analysis more intuitive

Lockdowns

Lockdown Scenarios

- 1. Short and tight lockdown
- 2. Loose lockdown
- 3. Lockdown that saves most possible number of lives
- 4. Intermittent lockdowns
- 5. Lockdown that respects an ICU capacity constraint

All results follow directly from phase diagram

Assumptions throughout:

- 1. permanent lockdowns infeasible (i.e. lockdowns until $t = \infty$)
- 2. disease elimination not an option ("atto-fox problem" more later)
- 3. no vaccine or other cures for disease
- 4. lockdown is only policy tool, e.g. rules out test-trace-isolate

Versions of many of these results are in Rachel (2020)

Lockdowns in SIR Model

• Recall: lockdowns = time-varying, reduced β_t

$$\dot{S}_t = -\beta_t S_t I_t \tag{S}$$

$$\dot{I}_t = \beta_t S_t I_t - \gamma I_t \tag{I}$$

$$\dot{R}_t = \gamma I_t$$
 (R)

• Denote β_0 = unmitigated transmission and parameterize

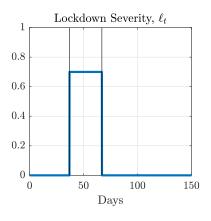
$$\beta_t = (1 - \ell_t)\beta_0, \qquad 0 \le \ell_t \le 1$$

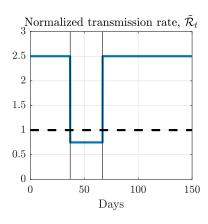
so ℓ_t measures lockdown tightness

Therefore also

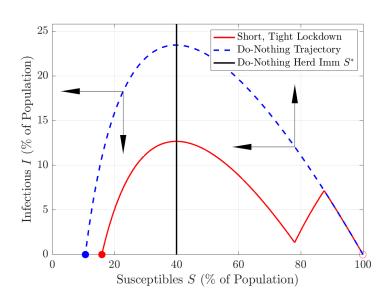
$$\tilde{\mathcal{R}}_t = (1 - \ell_t)\mathcal{R}_0$$

Short and Tight Lockdown

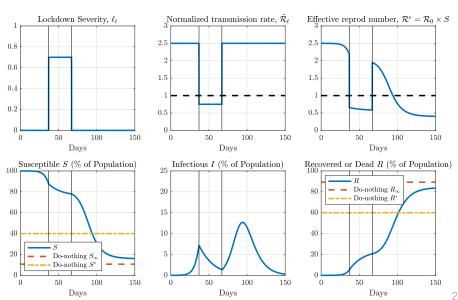




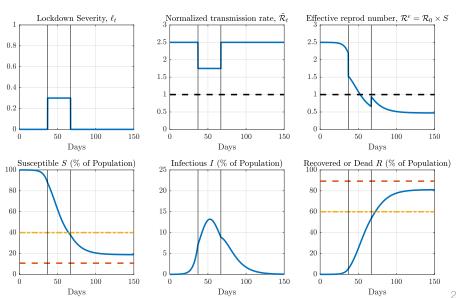
Short and Tight Lockdown



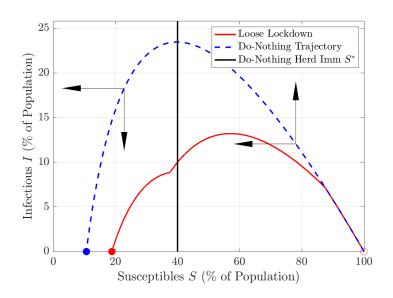
Short and Tight Lockdown



Loose Lockdown



Loose Lockdown

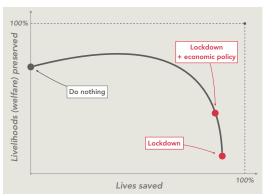


Tight vs Loose Lockdowns?

- In example, loose lockdown saves more lives than tight one
- What's going on?
- Problem with tight lockdown is that it results in 2nd wave
- That's because number of susceptibles S after lockdown similar to that before lockdown & still way above herd immunity threshold S*
- In absence of alternative options reaching herd immunity is only way to avoid 2nd wave – this is by definition of S*
- All lockdown-only strategies are necessarily "herd immunity strategies"

A lockdown that saves the most possible lives

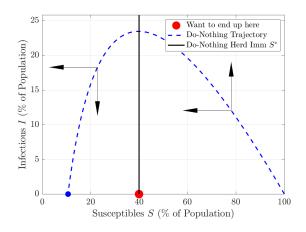
- Suppose objective is to minimize total deaths
- In terms of "Pandemic Possibility Frontier" in paper with Kaplan & Violante, what if only care about lives on x-axis?



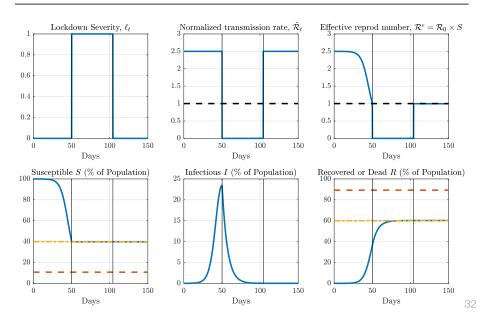
Source: https://benjaminmoll.com/HANK_pandemic/

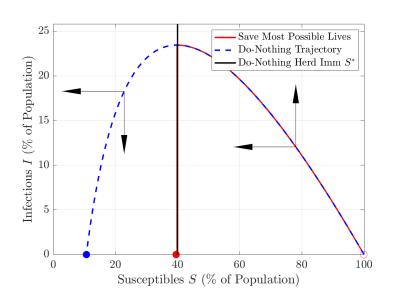
What should lockdown look like? And how well can it do?

- Minimize total deaths $D_{\infty} = \pi R_{\infty}$, equivalently maximize S_{∞}
- Easy to see: best temporary lockdown can do is eliminate overshoot and achieve $S_{\infty} = S^*$

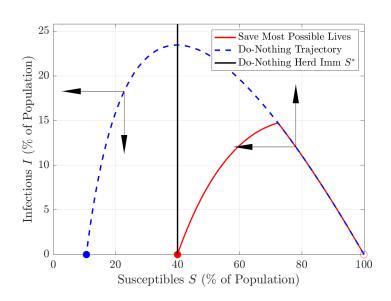


- How to achieve this? Or at least get very close?
- If no constraint on β_t (obviously unrealistic!), one option is:
 - 1. do nothing until reach S^* : $\beta_t = \beta_0$ all t such that $S_t > S^*$
 - 2. once reach S^* , 100% lockdown $\beta_t = 0 \Rightarrow$ no new infections $\dot{S}_t = 0$, current infections decline exponentially γ , $\dot{I}_t = -\gamma I_t$...
 - 3. ... and lift lockdown when $I_t \approx 0$

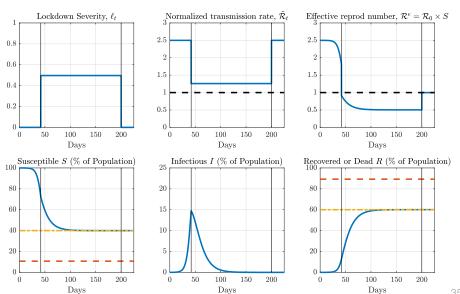




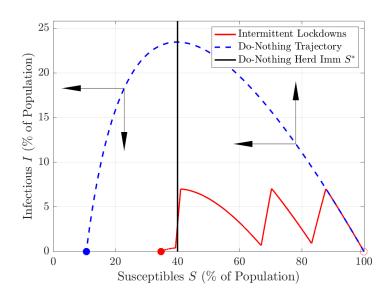
Save most possible lives: more realistic version



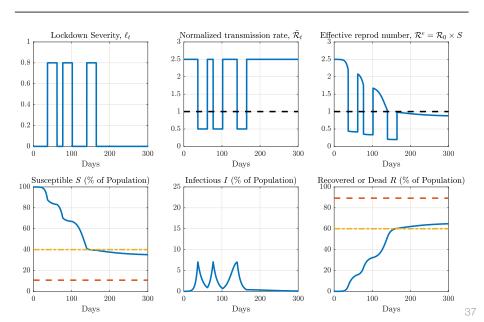
Save most possible lives: more realistic version



Intermittent lockdowns



Intermittent lockdowns

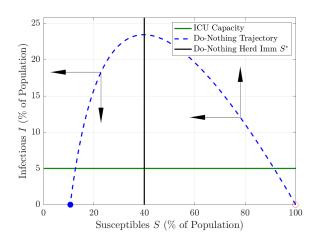


ICU capacity constraint

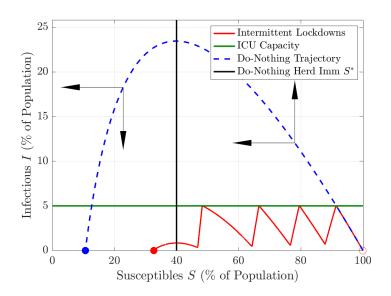
Suppose fixed ICU capacity Θ , death probability much higher if $I > \Theta$:

$$\dot{D} = (\pi_{\ell} \mathbf{1}_{I < \Theta} + \pi_{h} \mathbf{1}_{I > \Theta}) \gamma I, \qquad \pi_{h} >> \pi_{\ell}$$

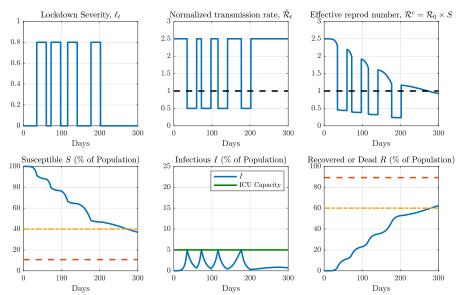
May want to "flatten curve" such that $I_t \leq \Theta$ for all t



Intermittent lockdowns + ICU capacity constraint



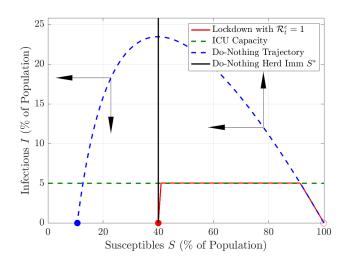
Intermittent lockdowns + ICU capacity constraint



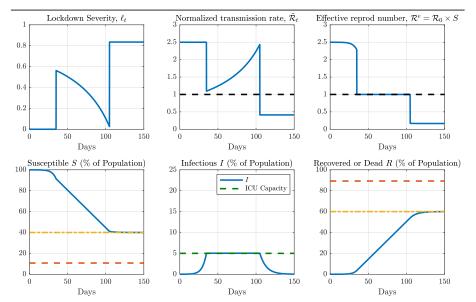
Flatten curve by keeping $\mathcal{R}_t^e = 1$ (roll over infections)

Potentially good strategy: keep effective reproduction number $\mathcal{R}^e_t pprox 1$

$$\dot{S} = -\gamma I$$
, $\dot{I} = 0$ $\Rightarrow I_{t+s} = I_t$, $S_{t+s} = S_t - \gamma I_t s$



Flatten curve by keeping $\mathcal{R}_t^e = 1$ (roll over infections)



Similar to Farboodi-Jarosch-Shimer optimal strategy: $\mathcal{R}_t^e \approx 1 \ \& \ \mathcal{R}_t^e > S_t >> 0$

"Flatten curve" vs "herd immunity" strategies

Previous four slides show: if disease elimination or alternative strategies (slide 45) infeasible, also "flatten curve" only stops at herd immunity

https://ncase.me/covid-19/ make point that "flatten curve strategy" may not be so dissimilar from "herd immunity strategy"

But important difference: hope of "flatten curve" advocates was/is elimination, switch to test-trace-isolate, emphasis on ICU capacity

• See e.g. https://twitter.com/CT_Bergstrom/status/1239805584188137472

Easy extensions

- 1. $\tilde{\mathcal{R}}_t$ declining over time due to other reasons than lockdowns, e.g. better hygiene, masks \Rightarrow lower herd imm threshold R^* (higher S^*)
- 2. Expanding ICU capacity
- 3. Stochastic arrival of vaccine
- 4. Other forms of learning, e.g. about better disease treatments, better policies
- All of these obviously make lockdowns look better "buy time"

Disease Elimination ("#ZeroCovid")?

Feature of SIR models:

- continuum of individuals ⇔ individuals are "divisible"
- e.g can have infections = $I_t = 1/3$ of a person

This can lead to counterintuitive implications

Important example: standard SIR model ⇒ elimination is impossible

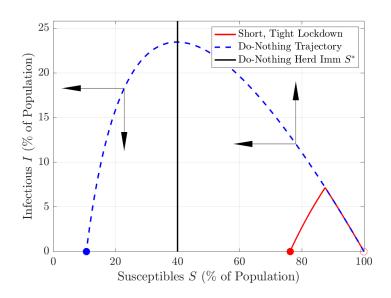
- Can use lockdowns to reduce I_t to very low levels, e.g. $I_t = 10^{-18}$
- ... but since $I_t > 0$, if lift lockdown before reaching herd immunity threshold, will always get 2nd wave
- This undesirable model feature has name: "atto-fox problem" https://en.wikipedia.org/wiki/Lotka-Volterra_equations#A_simple_example
 - "atto" = 10^{-18} (like "milli" = 10^{-3}), "atto-fox" = 10^{-18} th of a fox

Solution: assume that disease is eliminated whenever $I_t < 1/pop$ size

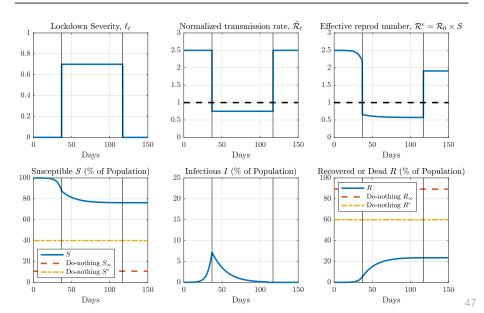
For good discussion see Section 6.1 of Rachel (2020)

If elimination feasible = good potential option (New Zealand)

Disease Elimination ("#ZeroCovid")?



Disease Elimination ("#ZeroCovid")?



Some Unpleasant Lockdown Arithmetic

- If lockdowns only option, how long do effective ones need to last?
- Key: need to reach herd immunity. So: how long to reach that?
- Optimistically assume perm immunity, $\mathcal{R}_0\downarrow$ to 2 (better hygiene...) herd immunity threshold = $1-1/\mathcal{R}_0=50\%$
- Simple back of envelope calculation for U.S. Assumptions:
 - 1. 10% have had disease \Rightarrow need additional 40% \approx 100 million
 - 2. lockdown suppresses \mathcal{R}_t^e to 1, infections rolled over (sl 40-41) $(\mathcal{R}_t^e = 1 \text{ close to current US estimate})$
 - 3. 200,000 new infections per day (current official count ≈ 30,000)
- ⇒ need some sort of lockdown / control for

$$\frac{100 \text{ million}}{200,000} = 500 \text{ days}$$

ullet Note: optimistic calculation assuming low \mathcal{R}_0 , permanent immunity

Ways Out? Candidates for Alternative Strategies

1. Test-trace-isolate

- Good discussion https://ncase.me/covid-19/, Keeling-Rohani 8.2-8.3
- Some studies suggest large potential decreases in \(\tilde{\mathcal{K}}_t\), e.g.
 Ferretti et al. https://science.sciencemag.org/content/368/6491/eabb6936
 Kucharski et al. https://www.medrxiv.org/content/10.1101/2020.04.23.20077024v1.full.pdf
- Econ analysis of some of these issues: Alvarez-Argente-Lippi (2020),
 Berger-Herkenhoff-Mongey "An SEIR Model with Testing and Conditional Quarantine"
- 2. Disease elimination: aggressive lockdown + border closures,... (NZ)
- 3. Routine testing of asymptomatic cases
 - Universal or targeted, e.g. at high-risk populations? Practicality?
 - Group/batch testing potentially promising (old idea due to Robert Dorfman)
- 4. Targeted lockdowns, e.g. by age: for econ analyses see
 - Glover-Heathcote-Krueger-RiosRull, "Health versus Wealth"
 - Acemoglu-Chernozhukov-Werning-Whinston "A Multi-Risk SIR Model with Optimally Targeted Lockdown"
 - Other dimensions, e.g. occupation, geography?
 - Ethical and political economy considerations?

Ways Out? Candidates for Alternative Strategies

5. Staggering and clusters

- staggered work week, school week (Uri Alon, Eran Yashiv, ...)
 e.g. https://www.medrxiv.org/content/10.1101/2020.04.04.20053579v4
- "contact clustering" or "pods" (Stefan Flasche, ...)
- general idea = reduce movements between networks

6. Better options for self isolation

- e.g. offer hotel rooms to infected living in crowded homes
- could help with household transmission (= frequent)

7. ... and of course various pharmaceutical interventions

- pre-exposure prophylaxis: low-dose antivirals may be able to prevent infection or symptomatic disease (a bit like vaccines)
- could be targeted at particular occupations (e.g. health care)
- post-exposure prophylaxis
- monoclonal antibodies

8. What else?!?

(Thanks to Natalie Dean and Carl Bergstrom for suggesting a number of these!)₅₀

Other Models of Epidemics: SEIR Model

Additional state: E = "exposed" = infected but not yet infectious

$$\dot{S} = -\beta SI \tag{S}$$

$$\dot{E} = \beta SI - \sigma E \tag{E}$$

$$\dot{I} = \sigma E - \gamma I \tag{1}$$

$$\dot{R} = \gamma I$$
 (R)

- Same qualitative properties as SIR model but quantitative diff's
- Previous analysis goes through with X := E + I, e.g.

$$\dot{X} = \beta SI - \gamma I = (\mathcal{R}_0 S - 1)\gamma I, \quad \mathcal{R}_0 := \beta/\gamma$$

so same herd immunity threshold $S^* = 1/\mathcal{R}_0$ as SIR model

Also (S)+(R) ⇒

$$\frac{\dot{S}}{S} = -\mathcal{R}_0 \dot{R}$$

so same final size of epidemic S_{∞} , R_{∞} as SIR model

Other Models of Epidemics

Models that have been influential for policy:

- Imperial College model https://github.com/ImperialCollegeLondon/covid19model
- IMHE model https://github.com/ihmeuw-msca/CurveFit

But see criticisms of IMHE model

- Jewell-Lewnard-Jewell "Caution Warranted: Using the Institute for Health Metrics and Evaluation Model for Predicting the Course of the COVID-19 Pandemic"
- https://qz.com/1840186/what-the-ihme-covid-19-model-can-and-cant-tell-the-us/

Other models: richer heterogeneity, networks etc

Heterogeneity and network effects raise possibility that herd immunity can be achieved with $S^* > 1/\mathcal{R}_0$

- Gomes et al. https://www.medrxiv.org/content/10.1101/2020.04.27.20081893v1
- Britton-Ball-Trapman https://arxiv.org/abs/2005.03085
- Hébert-Dufresne et al. https://arxiv.org/abs/2002.04004
- and summary here https://twitter.com/mlipsitch/status/1258827506930667523

How much of a difference these effects can make = open question, e.g.

- https://twitter.com/CT_Bergstrom/status/1256828517741780992
 "The model includes age structure, age-specific interactions (workplaces, schools, etc.), multiple network layers of hierarchically structured contacts, family structure, and heterogeneity in individual social and biological parameters. I've found it remarkable how little the heterogeneity and network structure impact basic epi dynamics. Hence my confidence in using a simple SIR model to illustrate concepts such as herd immunity and overshoot."
- https://twitter.com/CT_Bergstrom/status/1258882015203430400
 "The bottom line seems to be that all these calculations around herd immunity levels and total epidemic sizes depending complicated ways on population structure and network structure."
- https://twitter.com/nataliexdean/status/1259248274625761282