Optimal adaptation of lockdown measures upon the introduction of a COVID-19 vaccination campaign

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Outline

- Motivations
- Literature analysis
- Our model: Lockdown & Vaccination
- Two-stage optimal control model
- Age dependent optimal control model
- Results
- Conclusions

Motivations

February 2020

- COVID-19 showed up as a pandemic disease
- Additional research was adopted to find vaccines and medications
- Search for efficient tools to overcome the disease (lock-down of non-essential parts of economy, masks, ...)

April 2021

Vaccination seems to be the main instrument to block COVID
A **sufficiently effective** vaccine is still to be found

- Many different vaccines
- Supply problems
- Many variants of the virus
- **In the meantime**, lockdown still remains the most effective tool to contrast this virus.

Lockdown in optimal control literature

In previous literature

- Lockdown as a control: Alvarez et al., Acemoglu et al., Federico et Ferrari, Aspri et al.
- Lockdown as a state variable: e.g. Caulkins et al. [a,b] with controlled variation

In our model

Lockdown is a control function

Vaccine in optimal control literature

In previous literature

- No vaccine
- Availability of a sufficiently effective vaccine
  - expected at (within) a fixed time to justify finite time horizon (Caulkins et al.)
  - discovered at a random time (exponential distribution $\nu = 1/1.5$ Alvarez et al., Federico et Ferrari)

In our model

- Time (τ) of introduction of a sufficiently effective vaccine is not known a-priori.
  It is a random variable (controlled by the research)
- Vaccination doesn't assure an instantaneous coverage of the population, it is a long process, and it is not necessarily organized at a constant rate.
- We assume an exogenous vaccination rate.

Lockdown & Vaccination: 2 stage model

Stage 1: $[0, \tau)$ No effective vaccine available yet.
Lockdown (ℓ) and research effort (r)

Determining the lockdown policy and, at the same time, an optimal research effort towards the discovery of an effective vaccine.

At time τ An effective vaccine becomes available

Stage 2: $t > \tau$ exogenous vaccination rate $\alpha(t)$
Lockdown ℓ

Two-stage optimal control problem
with stochastic switching time

The model: Discovery of an effective vaccine

Random variable

Probability of discovering an effective vaccine after time t remaining in stage 1 until time t

$$\boxed{z_1(t) = Prob\{\tau > t\}}$$

with switching rate

$$\frac{-\dot{z}_1(t)}{z_1(t)} = \eta(x(t), u(t), t)$$

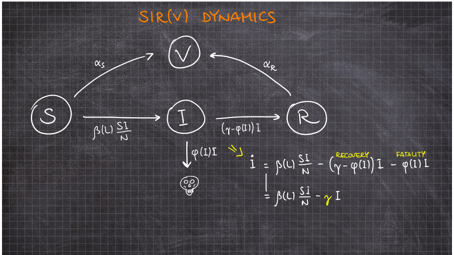
We assume η to be positive, continuous and controlled by the research effort, i.e. $\eta(r) = \eta_0 + \eta_1 r \qquad \eta_0, \eta_1 > 0$

$$\begin{cases} \dot{z}_1(t) = & -\eta(r(t))z_1(t) \\ z_1(0) = 1 \end{cases}$$

The model: SIR(V) N=S+I+R(+V)

$\beta(\ell) = \beta_0(1-\theta\ell)^2$	transmission rate
$\varphi(\mathrm{I}) = \gamma(\bar{\varphi} + \kappa \mathrm{I})$	fatality rate
$\gamma - \varphi(\mathrm{I})$	recovery rate
$\alpha(t) = \dfrac{4t+0.1}{t+1}$	vaccination rate

$$\Longrightarrow \gamma = (\text{recovered} + \text{death}) \quad \dot{\mathrm{I}} = \beta(\ell)\frac{S\mathrm{I}}{N} - \gamma \mathrm{I}$$



The model: Dynamics

$$\begin{aligned}
\dot{S} &= -\beta(\ell)\frac{S\mathrm{I}}{N} - \alpha(t-\tau)\left(\frac{S}{S+R}\mathbb{1}_{S+R>0}\right) \\
\dot{I} &= \beta(\ell)\frac{S\mathrm{I}}{N} - \gamma\mathrm{I} \\
\dot{N} &= -\varphi(\mathrm{I})\mathrm{I} \qquad N = S + \mathrm{I} + R + V \\
\dot{V} &= \alpha(t-\tau)\mathbb{1}_{S+R>0} \qquad \text{(Stage 2 only)} \\
\dot{z}_1 &= -\eta(r)z_1 \qquad \text{(Stage 1 only)} \\
S(0) &= S_0 \\
\mathrm{I}(0) &= I_0 \\
N(0) &= 1 \\
V(\tau) &= 0 \\
z_1(0) &= 1
\end{aligned}$$

The model: Objectives

Stage 1

- Minimizing death toll, lockdown costs, and research costs

$$g_1(\mathrm{I}, \ell, r) = vsl\ \varphi(\mathrm{I})\mathrm{I} + c_\ell(\ell) + c_r(r)$$

Stage 2

- Minimizing death toll and lockdown costs

$$g_2(\mathrm{I}, \ell) = vsl\ \varphi(\mathrm{I})\mathrm{I} + c_\ell(\ell)$$

vsl : Value of a Statistical Life

$c_\ell(\ell)$: Lockdown costs (In Alvarez et al. linear $c_\ell(\ell) = w\ \ell$)

In our model:

$$c_\ell(\ell) = w\ \ell^2 \qquad c_r(r) = c_0 r^2$$

$$\min_{\ell, r}\ J(\ell, r) = \mathbb{E}\left[\int_0^\tau\ e^{-\rho t} g_1(\mathrm{I}, \ell, r)\ dt + \int_\tau^{+\infty}\ e^{-\rho t} g_2(\mathrm{I}, \ell)\ dt\right]$$

The model: Objective functional

Discounted costs

$$\min_{\ell, r} \mathbb{E} \left[\int_0^{\tau} e^{-\rho t} g_1(\mathrm{I}, \ell, r) \, dt + \int_{\tau}^{+\infty} e^{-\rho t} g_2(\mathrm{I}, \ell) \, dt \right]$$

Feasible controls:

• $\ell(t) \in [0, 0.7]$ lockdown feasible constraint

$\ell(t) = 0$ means no lockdown

$\ell(t) = 0.7$ means most restrictive lockdown

• $r(t) \in [0, 1]$ research effort feasible constraint

Two-stage optimal control problem
with stochastic switching time

Optimal control problems with variable time horizon

(i) optimal control models with random time horizon (models that are deterministic in their state variables but stochastic in the time horizon.)

(ii) multi-stage optimal control models. The time horizon consists of two (or more) stages with different model dynamics and/or objective functions. The switching time is a decision variable, possibly subject to switching costs.
Tomiyama (1985), Tomiyama Rossana (1989), Makris (2001)

(i)+(ii) Two-stage optimal control problems with stochastic switching time. Changes in the dynamics and the objective function at a random switching time, characterized by a known distribution depending on the state and the control variables.

Two-stage optimal control problem with stochastic switching time

These problems can be reformulated as

- **Deterministic OC problems with infinite time horizon**

Boukas and Haurie (1988), Boukas et al. (1990), Sorger (1991), Carlson et al (1991)

- **Deterministic age-structured OC model**

- Transformation method to an age-structured OC model
Wrzaczek et al. (2020)

- Age-structured Maximum Principle
Brokate (1985), Feichtinger et al (2003), Krastev (2013), Skritek and Veliov (2008-2015)

-Advantages

  * Numerical solution with well-established methods
  * Analytical insights: the solution can describe the stage upon the switch expressing explicitly the links between the two stages.

Transformation to an Age-Structured OC Model

- Time horizon is separated into two stages $[0, \tau]$, $[\tau, +\infty]$
- Switching time τ is a positive real random variable
- $F(t)$ cumulative probability $(z_1(t) = Prob\{\tau > t\})$

$$F(t) = P(\tau \leq t) = 1 - z_1(t)$$

The **switching rate** is

$$\frac{F'(t)}{1 - F(t)} = -\frac{z_1'(t)}{z_1(t)} = \eta(x(t), u(t), t)$$

Transformation to an Age-Structured OC Model

dynamics of the model separated into stages 1 and 2

$$\dot{x}(t) = \begin{cases} f_1(x(t), u(t), t) & t < \tau, \quad x(0) = x_0 \\ f_2(x(t), u(t), t, x(\tau), \tau) & t \geq \tau \end{cases}$$

$x(\tau) = \lim_{t \to \tau} \Phi(x(t), t)$, Φ piecewise continuous in (x, t)

In Stage 2: control function $v(t, \tau)$, state function $y(t, \tau)$

$$\begin{aligned} \frac{dy(t,\tau)}{dt} &= f_2(y(t,\tau), v(t,\tau), t, x(\tau), \tau), \quad t \geq \tau \\ y(\tau,\tau) &= \Phi(x(\tau), \tau) \end{aligned}$$

Transformation to an Age-Structured OC Model

Objective functional

$$\mathbb{E}\left[\int_0^{\tau} e^{-\rho t} g_1(x(t), u(t), t)dt + \int_{\tau}^{+\infty} e^{-\rho t} g_2(y(t,\tau), v(t,\tau), t, x(\tau), \tau)dt\right] =$$

recall that $(-\dot{z}_1(t) = \eta(r(t))\ z_1(t))$

$$\begin{aligned} = & \int_0^{+\infty}\int_0^{s} e^{-\rho t} g_1(x(t), u(t), t)dt\ \ (-\dot{z}_1(s))ds + \\ + & \int_0^{+\infty}\int_s^{+\infty} e^{-\rho t} g_2(y(t,s), v(t,s), t, x(s)), s)dt\ \ (\eta(x(s), u(s)s)z_1(s))ds \end{aligned}$$

After Integrating by parts and applying Fubini's Theorem (see Wrzaczek et al. (JOTA 2020)) $\rightarrow$ Age dependent problem

Transformation to an Age-Structured OC Model

$$\int_0^{+\infty} e^{-\rho t}\Bigg[z_1(t) g_1(x(t), u(t), t) +$$

$$\int_0^t \underbrace{\eta(x(s), u(s), s)\ z_1(s)}_{z_2(t,s)}\ g_2(y(t,s), v(t,s), t, \underbrace{x(s)}_{z_3(t,s)}, s) ds \Bigg] dt$$

Auxiliary state variables $z_2(t,s), z_3(t,s)$

$$\frac{dz_i(t,s)}{dt} = 0, \quad i = 2, 3, \qquad \forall t \geq s$$

$z_2(t,s)$ probability density evaluated in s
$z_3(t,s)$ necessary iff g_2 depends on $x(\tau) \rightarrow$ Not in our case

$$\int_0^{+\infty} e^{-\rho t} \left[z_1(t) g_1(x(t), u(t), t) + \int_0^t z_2(t,s) g_2(y(t,s), v(t,s), t, s)\ ds \right] dt$$

Age structure formulation (objective functional)

control functions $v(t,\tau) = (\ell_2)$
state functions $y(t,\tau) = (S_2, I_2, N_2, V)$

$$\min_{\ell_1, r, \ell_2} \int_0^{+\infty} e^{-\rho t} \left[z_1(t) \Big(c_\ell(\ell_1(t)) + vsl\varphi(I_1(t)) I_1(t) + c_r(r(t)) \Big) + Q(t) \right] dt$$

where the aggregate state

$$Q(t) = \int_0^t z_2(t,s) \left(c_\ell(\ell_2(t,s)) + vsl\varphi(I_2(t,s)) I_2(t,s) \right) \, ds$$

sum of all instantaneous objective functionals for all possible switches up to time t, weighted by the probability for their realization at $s \in [0, t]$. (active characteristic lines)
easy representation of the role of duration $t - s$

Age structure formulation (dynamics)

Stage 1

$$
\begin{aligned}
\dot{S}_1 &= -\beta(\ell_1)\frac{S_1 \mathrm{I}_1}{N_1} & S_1(0) &= 0.99\\
\dot{\mathrm{I}}_1 &= \beta(\ell_1)\frac{S_1 \mathrm{I}_1}{N_1} - \gamma \mathrm{I}_1 & \mathrm{I}_1(0) &= 0.01\\
\dot{N}_1 &= -\varphi(\mathrm{I}_1)\mathrm{I}_1 & N_1(0) &= 1\\
\dot{z}_1 &= -\eta(r) z_1 & z_1(0) &= 1
\end{aligned}
$$

Stage 2

$$
\begin{aligned}
\partial_t S_2 &= -\beta(\ell_2)\frac{S_2 \mathrm{I}_2}{N_2} - \alpha(t-s)\frac{S_2}{S_2+R_2}\mathbb{1}_{S_2+R_2>0} & S_2(s,s) &= S(s)\\
\partial_t \mathrm{I}_2 &= \beta(\ell_2)\frac{S_2 \mathrm{I}_2}{N_2} - \gamma \mathrm{I}_2 & \mathrm{I}_2(s,s) &= \mathrm{I}(s)\\
\partial_t N_2 &= -\varphi(\mathrm{I}_2)\mathrm{I}_2 & N_2(s,s) &= N(s)\\
\partial_t V &= \alpha(t-s)\mathbb{1}_{S_2+R_2>0} & V(s,s) &= 0\\
\partial_t z_2 &= 0 & z_2(s,s) &= \eta(r(s)) z_1(s)
\end{aligned}
$$

Necessary conditions (PMP age-dependent)

Brokate (1985), Feichtinger et al (2003), Skritek Veliov (2015)

Stage 1

$$\dot{\lambda}_S = \rho\lambda_S + (\lambda_S - \lambda_I)\beta(\ell)\frac{\mathrm{I}}{N} - \xi_S(t,t)$$

$$\dot{\lambda}_{\mathrm{I}} = (\rho+\gamma)\lambda_I + (z_1 vsl + \lambda_N)\frac{d(\varphi(\mathrm{I})\mathrm{I})}{d\mathrm{I}} + (\lambda_S - \lambda_I)\beta(\ell)\frac{S}{N} - \xi_I(t,t)$$

$$\dot{\lambda}_N = \rho\lambda_N - (\lambda_S - \lambda_I)\beta(\ell)\frac{S\mathrm{I}}{N^2} - \xi_N(t,t)$$

$$\dot{\lambda}_{z_1} = \rho\lambda_{z_1} + c_\ell(\ell) + vsl\varphi(\mathrm{I})\mathrm{I} + c_r(r) + (\lambda_{z_1} - \xi_{z_2}(t,t))\eta(r)$$

Stage 2

$$\partial_t\xi_S = \rho\xi_S + (\xi_S - \xi_I)\beta(\ell)\frac{I}{N} + \xi_S\alpha(t-s)\left(\frac{1}{S+R}\mathbb{1}_{S+R>0}\right)$$

$$\partial_t\xi_I = (\rho+\gamma)\xi_I + (z_1 vsl + \xi_N)\frac{d(\varphi(I)I)}{dI} + (\xi_S - \xi_I)\beta(\ell)\frac{S}{N} + \xi_S\alpha(t-s)\frac{S}{(S+R)^2}\mathbb{1}_{S+R>0}$$

$$\partial_t\xi_N = \rho\xi_N - (\xi_S - \xi_I)\beta(\ell)\frac{SI}{N^2} - \xi_S\alpha(t-s)\frac{S}{(S+R)^2}\mathbb{1}_{S+R>0}$$

$$\partial_t\xi_V = \rho\xi_V + \xi_S\alpha(t-s)\frac{S}{(S+R)^2}\mathbb{1}_{S+R>0}$$

$$\partial_t\xi_{z_2} = \rho\xi_{z_2} + c_\ell(\ell) + vsl\varphi(I)$$

Simulations

Parameters' values

- $S_0 = 0.99$ Initial n. of Susceptible
- $\mathrm{I}_0 = 0.01$ Initial n. of Infected
- $\rho = 0.05$ discount rate
- $\overline{\varphi} = 0.0068$ historical fatality rate
- $k = 0.034$ Covid fatality coefficient
- $\gamma = 1/18(365) \quad \Longrightarrow \gamma - \varphi =$ recovery rate
- $\beta_0 = 0.13(365)$ transmission rate without lockdown
- $\theta = 0.5$ reducing transmission coefficient of lockdown
- $vsl = 40$ value of statistical life
- $\eta_0 = 1/1.5$ switching rate without research
- $\eta_1 = 4 - \eta_0$ switching rate coefficient
- $c_0 = 0.05$ cost coefficient

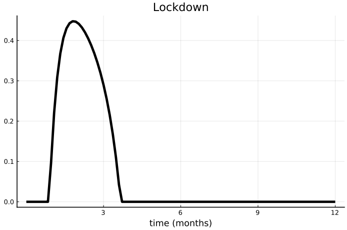
Julia programming Language for ODEs and PDEs resolution

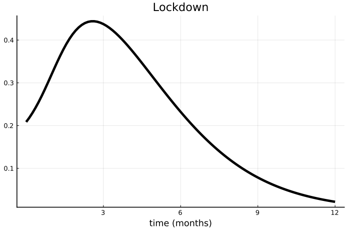
Benchmark case Alvarez et al.

Stage 1 without vaccine and without reasearch effort

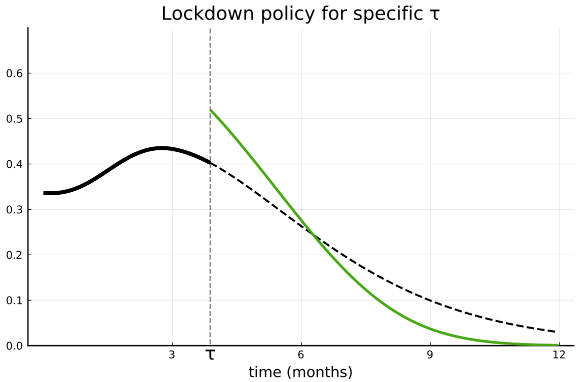
Lockdown costs

Linear (Alvarez et al.) vs Quadratic



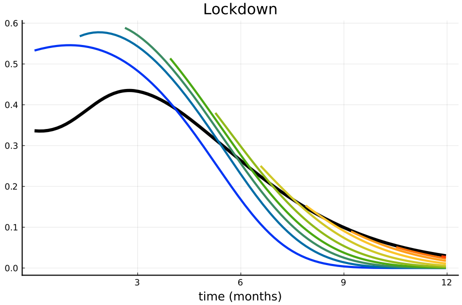


Graphics interpretation with 2 stages



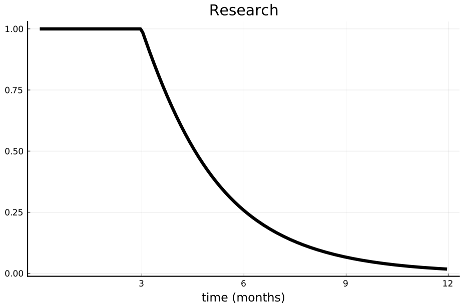
- Upon the vaccine introduction the lockdown is initially more intense, and then it drastically plunges
- It goes to zero (end of the lockdown)

Optimal Lockdown policies

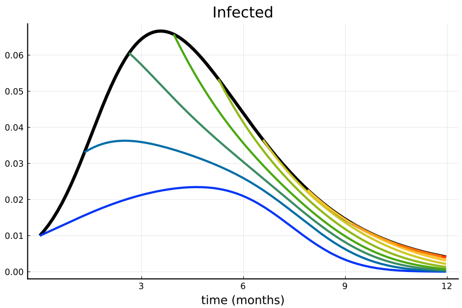


- the lighter the color the later the vaccine introduction
- blue line = immediate vaccine introduction
- all lines go to zero faster than the non-vaccination one
- early vaccine introduction $\Longrightarrow$ early lockdown end

Optimal research effort

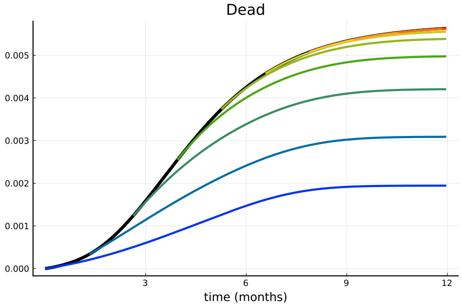


Infected



- all lines lay below the non-vaccination one
- the sooner the vaccine introduction the smaller the peek (Crucial for ICU)
- early vaccine introduction $\Longrightarrow$ early Covid overcome

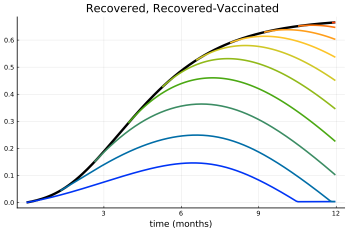
Deaths

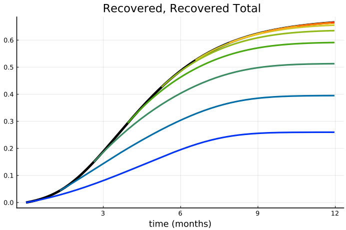


- all lines lay below the non-vaccination one
- the sooner the vaccine introduction the smaller the number of deaths

Unvaccinated Recovered & Total Recovered

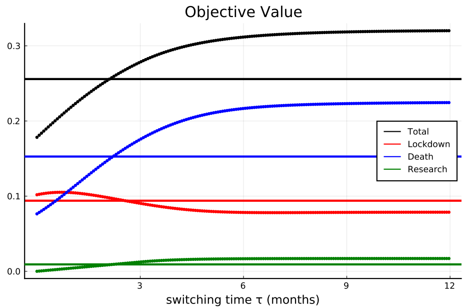
Unvaccinated Recovered (R)
Total Recovered (included the vaccinated ones)





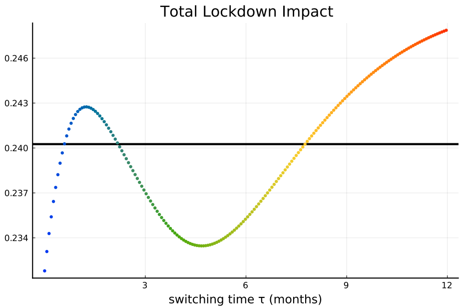
- all lines lay below the non-vaccination one
- the sooner the vaccine introduction the smaller the number of recovered

Optimal costs



- Horizontal lines: Mean value - Expected cost
- Dotted lines: cost depending on the switching time
- the later the vaccine introduction the higher the total cost
- major contribution given by deaths
- lockdown costs are higher for early switching time (?!)

Total Lockdown Impact

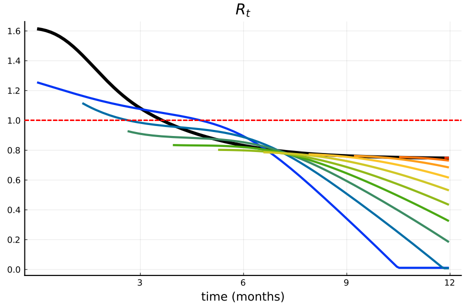


- $TLI(\tau) = \int_0^{\tau} \ell(t)dt + \int_{\tau}^{+\infty} \ell(t)dt$
- horizontal line: expectation of $TLI(\tau)$

Any comments on it?

R_t coefficient

$$R_t = \frac{\beta(\ell) S/N}{\gamma - \varphi(\mathrm{I})}$$



There are two effects that diminish the R_t over time:

- as the pandemic evolves the S decreases
- after τ the R_t is reduced by vaccination

Future developments

- vaccines not 100% effective
- virus mutation
- lockdown fatigue (Caulkins et al)
- age sensitive lockdown
- test tracing quarantine (TTQ)

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THANKS

Keep safe!

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