Optimal control of the COVID-19 epidemic before setting up pharmaceutical interventions

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susceptible ($S$) 
infected but asymptomatic and not infectious ($E$) 
asymptomatic infectious ($A$) 
symptomatic infectious ($I$) 
recovered ($R$) 
dead ($D$).
Some models incorporate the bifurcation between mild and severe cases after stage E or stage A (or even stage I). This is problematic:

- For high proportions of mild cases (i.e., $1 - p$ is a rare event), one finds very low transition rates to severe cases.
- The fact that an event is rare, does not mean that it occurs very late in the course of the infection.
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- The fact that an event is rare, does not mean that it occurs very late in the course of the infection.
Differential severity.

• To solve this problem, we have made the waiting time refer to an infection event (change from S to E).

• Indeed, it is possible that "by chance" a susceptible person is infected very quickly (the next day) or very late (in two months) whereas for a duration of infection it is biologically unrealistic (you don’t get better in 1 day or 2 months).
Mortality rates.

$I^*$ : the total number of infected hosts the health care system (especially the intensive care units, ICU) can sustain.

- Disease induced mortality

$$\alpha [l_s] = \begin{cases} 
\alpha_{\text{min}} & \text{if } l_s < I^* \\
\alpha_{\text{max}} & \text{if } l_s \geq I^*
\end{cases}$$

- Natural mortality increases because of hospital saturation:

$$\mu [l_s] = \begin{cases} 
0 & \text{if } l_s < I^* \\
\mu & \text{if } l_s \geq I^*
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- **Disease induced mortality**

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- **Natural mortality increases because of hospital saturation:**

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Model overview

The SEAIR model ...

\[
\begin{align*}
\dot{S} &= - S \left( \beta, (A, I)^T \right), \\
\dot{E} &= S \mathcal{P} \beta (A, I)^T - (\varepsilon + \mu[I]) E + \nu \mathcal{P}, \\
\dot{A} &= \varepsilon E - (\sigma + \mu[I]) A, \\
\dot{I} &= \sigma A - (\gamma + \mu[I] \mathbb{I} + d(I)) I,
\end{align*}
\]

R. Djidjou-Demasse et al., medRxiv, 2020
Objective function

Deaths directly attributable to COVID-19 ($D_{\text{COVID}} = \alpha [I_s] I_s$).
Deaths indirectly linked to COVID-19 infection but due to the saturation of the hospital system ($D_{\text{SAT}} = \mu [I_s] N$).

The control scheme is optimal if it minimizes the objective function

$$M[c] = \int_0^T (D_{\text{COVID}}(t) + D_{\text{SAT}}(t)) \, dt + B \int_0^T c^2(t) \, dt,$$

$B$ is a coefficient allowing to weight the "cost" associated to the control implementation ($c(t)$) relative to the cost due to deaths.
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$$M[c] = \int_0^T (D_{\text{COVID}}(t) + D_{\text{SAT}}(t)) \, dt + B \int_0^T c^2(t) \, dt,$$

Find the function $c^*$ satisfying

$$M(c^*) = \min_{c \in \mathcal{U}} M(c),$$

on the set $\mathcal{U} = \{c \in L^\infty(0, \infty) : 0 \leq c(\cdot) \leq c_{\text{max}}\}$, where $c_{\text{max}} \leq 1$, where

...
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the hospital system ($D_{SAT} = \mu [l_s] \ N$).

$$M[c] = \int_0^T (D_{COVID}(t) + D_{SAT}(t)) \, dt + B \int_0^T c^2(t) \, dt,$$

$$M(c^*) = \min_{c \in U} M(c),$$

Time ($T$) required for pharmaceutical intervention:

- Treatment: generally few months
- Vaccine: at least 18 to 24 months
Pontryagin’s maximum principle and introduce the following Hamiltonian

\[ H(c) = \alpha [I_s] I_s + \mu [I_s] N + Bc^2 + \sum_{v \in V} z_v f_v, \]

where \( V = \{S, E_m, E_s, A_m, A_s, I_m, I_s, R_m, R_s\} \) and \((z_v)_{v \in V}\) are adjoint functions.

The necessary conditions for the existence of the solution:

\[ \dot{z}_v = -\frac{\partial H}{\partial v}, \quad \text{for, } v \in V, \]
\[ \frac{\partial H}{\partial c} = 0. \]

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Optimal control scenario

(a) The graph shows the function c over time (weeks) with three different control scenarios: Do nothing, Optimal, and Constant control. The Optimal control shows a rapid decline in c, while the Do nothing control shows a gradual increase.

(b) The graph plots \log_{10}(I_s) over time (weeks) with three different control scenarios: Do nothing, Optimal, and Constant control. The Optimal control keeps I_s at a lower level compared to the other two.

(c) The graph shows \log_{10}(D_{COVID}) over time (weeks) with three different control scenarios: Do nothing, Optimal, and Constant control. The Optimal control keeps D_{COVID} at a lower level compared to the other two.

(d) The graph plots \log_{10}(D_{SAT}) over time (weeks) with three different control scenarios: Do nothing, Optimal, and Constant control. The Optimal control keeps D_{SAT} at a lower level compared to the other two.
Such a solution leads to an increasing level of control with a maximum reached near the fourth month of the epidemics and a steady decrease until vaccine deployment.
Constant control scenario

(a) Time (weeks)

(b) log_{10}(I_s)

(c) log_{10}(D_COVID)

(d) log_{10}(D_{SAT})

- Do nothing
- Optimal
- Constant control
Effect of the cost of control $B$

(a) $C$ vs. Time (weeks)
(b) $\log_{10}(I_s)$ vs. Time (weeks)
(c) $\log_{10}(D)$ vs. Time (weeks)

- Do nothing
- $B=0.1$
- $B=1$
- $B=10$
- $B=50$
- $B=800$
Effect of the initial epidemics size

(a) C vs. Time (weeks)
(b) $\log_{10}(I_s)$ vs. Time (weeks)
(c) $\log_{10}(D)$ vs. Time (weeks)

- Do nothing
- $I_0 = 10 \, I^*$
- $I_0 = I^*$
- $I_0 = 0.01 \, I^*$
Full lock-down vs Optimal strategy

(a) 

(b) 

(c) 

- Do nothing
- 12–weeks
- 50–weeks
- Optimal
team work on COVID-19

available reports

• basic and effective reproduction number estimation for France
• herd immunity threshold vs final size proportion
• phylodynamics

COVID work in progress Age-structure model, non-markovian simulations


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