Optimal constant picewise vaccination policies for COVID-19

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Abstract

BACKGROUND.
FINDINGS.
IMPLICATIONS.

Keywords: COVID-19, Optimal Control, COVAX, Vaccination, WHO-SAGE, DALYs.

1. Introduction

Main contribution and its relevance.

Background.

Vaccine development.

Problem setup.

Litterature review.

Papaer structure.

2. Covid-19 spread dynamics

Uncontrolled dynamics. We split the the constant population N in a base SEIR structure with segregation infected classes according with manifestation of symptoms. We also postulate the extra state Y_{I_S} to fit commulative symptomatic cases reported in the databases from Mexico city during the exponential grow phase. Our dynamics reads

$$\begin{aligned}
L' &= \theta\mu N^\star - \epsilon\lambda L - \delta_L L - \mu L,\\
S' &= (1-\theta)\mu N^\star + \delta_L L + \delta_R R - (\lambda+\mu)S,\\
E' &= \lambda(\epsilon L + S) - (\kappa+\mu)E,\\
I_S' &= p\kappa E - (\gamma_S + \delta_H + \underline{\mu_{I_S}}^{\text{SDIV}} + \mu)I_S,\\
I_A' &= (1-p)\kappa E - (\gamma_A+\mu)I_A,\\
H' &= \delta_H I_S - (\gamma_H + \mu_H + \mu)H,\\
R' &= \gamma_S I_S + \gamma_A I_A + \gamma_H H - (\delta_R+\mu)R,\\
D' &= \underline{\mu_{I_S} I_S +}^{\text{SDIV}} \mu_H H,\\
\frac{dY_{I_S}}{dt} &= p\kappa E,\\
\lambda &:= \frac{\beta_A I_A + \beta_S I_S}{N^\star},\\
N^\star(t) &= L + S + E + I_S + I_A + H + R.
\end{aligned} \tag{1}$$

See Table 1 for notation and references values.

Hypothesis. We consider that susceptible individuals become infected when they are in contact with asymptomatic individuals and individuals with symptoms, we will propose that a proportion of asymptomatic individuals have a way to get relief and not die. A proportion of individuals infected with symptoms may die from the disease or may be relieved.

We callibrate parameters of our base dynamics in (1) via Multichain Montecarlo (MCMC). To this end, we assume that the comulative incidence of new infected symptomatic cases CI_S follows a Poisson distribution with mean $\lambda_t = IC_s(t)$. Further, following [] we postulate priors for

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Parameter	Description
μ	Death rate
β_S	Infection rate between susceptible and symptomatic infected
β_A	Infection rate between susceptible and asymptomatic infected
λ_V	Vaccination rate
δ_V^{-1}	Vaccine-induced immunity
ε	Vaccine efficacy
κ^{-1}	Average incubation time
p	New asymptomatic generation proportion
θ	Proportion of individuals under lockdown
γ_S^{-1}	Average time of symptomatic recovery
γ_A^{-1}	Recovery average time of asymptomatic individuals
γ_H^{-1}	Recovery average time by hospitalization
δ_R^{-1}	Natural immunity
δ_H	Infected symptomatic hospitalization rate

Table 1: Parameters definition of model in Equation (1).

p and κ

$$\begin{aligned} Y_t &\sim Poisson(\lambda_t), \\ \lambda_t &= \int_0^t p\delta_e E, \\ p &\sim \text{Uniform}(0.3, 0.8), \\ \kappa &\sim \text{Gamma}(10, 50). \end{aligned} \tag{2}$$

Using the reproductive number definition of VanDen-Drishe, we obtain

$$R_0 := \frac{N^*(\beta_S p\kappa + \beta_A\kappa(1-p))}{(\mu-\kappa)(\gamma_S + \mu_{I_s} + \gamma_A + \mu)N^*\mu}$$

Figure 2 displays data of coumulative confirmed cases of COVID-19 of Mexico city, and the fitt of our model in Equations (1) and (2).

3. Imperfect-preventive Covid-19 vaccination

Preventive vaccines.

Efficacy and vaccine-induced immunity.

Actual vaccine stage development.

Vaccination reproductive number.

Vaccination rate λ_V estimate.

Feasibility regions according to efficacy and vaccination rate.

$$\begin{aligned} L' =& \theta\mu N^\star - (\epsilon\lambda + \delta_L + \mu)L \\ S' =& (1-\theta)\mu N^\star + \delta_L L + \delta_V V + \delta_R R \\ & - (\lambda + \lambda_V + \mu)\, S \\ E' =& \lambda(\epsilon L + (1-\varepsilon)V + S) - (\kappa+\mu)E \\ I_S' =& p\kappa E - (\delta_H + \gamma_S + \mu_{I_S} + \mu)I_S \\ I_A' =& (1-p)\kappa E - (\gamma_A + \mu)I_A \\ H' =& \delta_H I_S - (\gamma_H + \mu_H + \mu)H \\ R' =& \gamma_S I_S + \gamma_A I_A + \gamma_H H - (\delta_R + \mu)R \\ D' =& \mu_{I_S} I_S + \mu_H H \\ V' =& \lambda_V S - [(1-\varepsilon)\lambda + \delta_V + \mu]\, V \end{aligned}$$

$$\begin{aligned} \frac{dX_{vac}}{dt} &= (u_V(t) + \lambda_V)\,[S + E + I_A + R] \\ \frac{dY_{I_S}}{dt} &= p\kappa E \\ \lambda &:= \frac{\beta_A I_A + \beta_S I_S}{N^\star} \end{aligned} \tag{3}$$

$$\begin{aligned} L(0) = L_0,\ S(0) = S_0,\ E(0) = E_0, \\ I_S(0) = I_{S_0}, I_A(0) = I_{A_0}, H(0) = H_0, \\ R(0) = R_0,\ D(0) = D_0, \\ V(0) = 0,\ X_{vac}(0) = 0, \\ X_{vac}(T) = x_{coverage}, \\ N^\star(t) = L + S + E + I_S + I_A + H + R + V. \end{aligned}$$

4. Parameter callibration

Bayesian estimation.

Parameter	Median	Reference
q_r, ϵ	0.4, 0.3, 0.1	this study
β_S	$q_r \times 8.690\,483 \times 10^{-1}$	this study
β_A	$q_r \times 7.738\,431 \times 10^{-1}$	this study
κ	0.196 078 43	*
p	0.1213	*
θ	0.2,	this study
δ_L	0.04	postulated
δ_H	0.2	*
δ_V	0.002 739 726 027 397 260 3	$\delta_V^{-1} = 2$ years CanSinoBIO
δ_R	0.005 555 56	$\delta_R^{-1} \approx 180$ days
μ	$3.913\,894 \times 10^{-5}$	**
μ_{I_S}	0.0	
μ_H	0.016 32	[FENG]
γ_S	0.092 506 94	*
γ_A	0.167 504 19	*
γ_H	$5.079\,869 \times 10^{-1}$	*
λ_V	0.000 611 35	
ε	0.7, 0.80, 0.9, 0.95	[PRESS RELESASES]
N	26 446 435	**
L_0	0.266 260 097 021 127 96	
S_0	0.463 606 046 009 872	
E_0	0.000 670 33	*
I_{S_0}	9.283×10^{-5}	* * *
I_{A_0}	0.001 209 86	*
H_0	$1.341\,579\,69 \times 10^{-4}$	**
R_0	$2.661\,259\,39 \times 10^{-1}$	
D_0	0.001 900 74	**
X^0_{vac}	0.0	
V_0	0.0	
$Y^0_{I_S}$	0.122 581 64	
B	0.000 359 216 658 124 242 5	9500 beds/N
a_{I_S}	0.002 012 775 543 825 648 6	DALY def
a_H	0.001 411 888 738 103 725, or	
	$a_H(x) := 0.001\,411\,888\,738\,103\,725 \log(\frac{1}{B-\kappa I_S})$	DALY def [Jo 2020]
a_D	7.25	DALY def

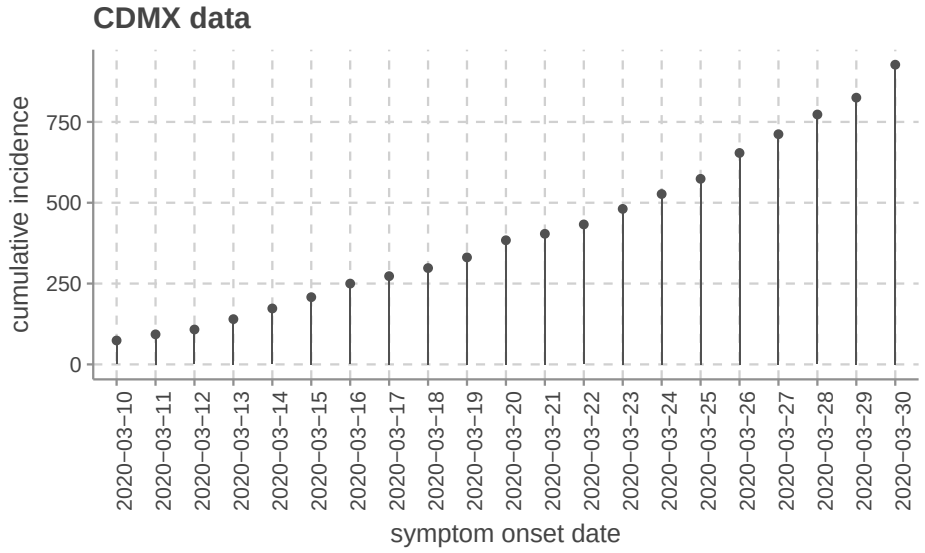

Figure 1: Cummulative new symptomatic and confirmed COVID19 reported cases from Ciudad de Mexico between March, 10, to March 30 of 2020.

5. Vaccination reproductive number

6. Optimal controlled version

Controlled Model. Now wee model vaccination, treatment and lockdown as a optimal control problem. According to dynamics in Equation (1), we modulate the vaccination rate with a time-dependent control signal $u_V(t)$. We add compartment X_{vac} to count all the vaccine applications of susceptible, exposed, asymptomatic and recovered individuals. This process is modeled by

$$X'(t) = (\lambda_V + u_V(t))(S + E + I_A + R) \tag{4}$$

and describes the number of applied vaccines at time t. Consider

$$x(t) := (L, S, E, I_S, I_A, H, R, D, V, X_{vac})^\top(t)$$

and control signal $u_v(\cdot)$. We quantify the cost and reward of a vaccine strategy policy via the penalization functional

$$J(u_V) := \int_0^T a_S I_S + a_d D + \frac{1}{2} c_V u_v^2 ds. \tag{5}$$

In other words, we assume in functional J that pandemic cost is proportional to the symptomatic and death reported cases and that a vaccination policy implies quadratic consumption of resources.

Further, since we aim to simulate vaccination policies at differentcoverage scenarios, we impose the vaccination counter state's final time condition $X(T)$

$$\begin{aligned} x(T) &= (\cdot, \cdot, \cdot, \cdot, \cdot, X_{vac}(T))^\top, \in \Omega \\ X_{vac}(T) &= x_{coverage}, \\ x_{coverage} &\in \{\text{Low}(0.2), \text{Mid}(0.5), \text{High}(0.8)\}. \end{aligned} \tag{6}$$

Thus, given the time horizon T, we impose that the last fraction of vaccinated populations corresponds to 20%, 50% or 80%, and the rest of final states as free. We also impose the path constraint

$$\Phi(x, t) := \kappa I_S(t) \leq B, \qquad \forall t \in [0, T], \tag{7}$$

to ensure that healthcare services will not be overloaded. Here κ denotes hospitalization rate, and B is the load capacity of a health system.

Given a fixed time horizon and vaccine efficiency, we estimate the constant vaccination rate as the solution of

$$x_{coverage} = 1 - \exp(-\lambda_V T). \tag{8}$$

That is, λ_v denotes the constant rate to cover a fraction $x_{coverage}$ in time horizon T. Thus, according to this vaccination rate, we postulate a policy u_v that modulates vaccination rate according to λ_V as a baseline. That is, optimal vaccination amplifies or attenuates the estimated baseline λ_V in a interval $[\lambda_v^{\min}, \lambda_v^{\max}]$ to optimize functional $J(\cdot)$—minimizing symptomatic, death reported cases and optimizing resources.

Our objective is minimize the cost functional (5)—over an appropriated functional space—subject to the dynamics in equations (1) and (4), boundary conditions, and the path constrain in (7). That is, we search for vaccination policies $u_V(\cdot)$, which solve the following optimal control

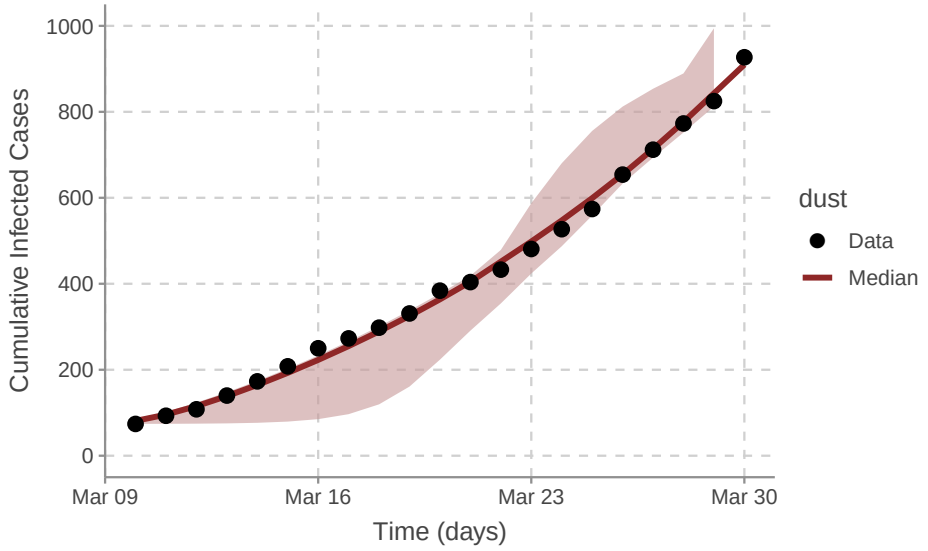

Figure 2: Fit of diary new cases of Mexico city during exponential growth.

problem (OCP).

$$\min_{u\in\mathcal{U}} J(u) := \int_0^T \left[(a_D\mu_s + a_H\delta_H)\, I_S(r) + a_{I_S} p\kappa E(r)\right]\, dr$$

s. t.

$$\begin{aligned}
L' &= \theta\mu N^\star - \epsilon\lambda L - u_L(t)L - \mu L\\
S' &= (1-\theta)\mu N^\star + u_L(t)L + \delta_v V + \delta_R R\\
&\quad - \left[\lambda + (\lambda_V + u_V(t)) + \mu\right] S\\
E' &= \lambda(\epsilon L + (1-\varepsilon)V + S) - (\kappa+\mu)E\\
I_S' &= p\kappa E - (\gamma_S + \mu_{I_S} + \delta_H + \mu) I_S\\
I_A' &= (1-p)\kappa E - (\gamma_A + \mu) I_A\\
H' &= \delta_H I_S - (\gamma_H + \mu_H + \mu) H\\
R' &= \gamma_S I_S + \gamma_A I_A + \gamma_H H - (\delta_R + \mu) R\\
D' &= \mu_{I_S} I_S + \mu_H H\\
V' &= (\lambda_V + u_V(t))S - \left[(1-\varepsilon)\lambda + \delta_V + \mu\right] V
\end{aligned}$$

$$\begin{aligned}
\frac{dX_{vac}}{dt} &= (u_V(t) + \lambda_V)\left[L + S + E + I_A + R\right]\\
\frac{dY_{I_S}}{dt} &= p\kappa E\\
\lambda &:= \frac{\beta_A I_A + \beta_S I_S}{N^\star}
\end{aligned}$$

$$\begin{aligned}
L(0) = L_0,\ S(0) = S_0,\ E(0) = E_0,\ I_S(0) = I_{S_0},&\\
I_A(0) = I_{A_0}, H(0) = H_0,\quad R(0) = R_0,\ D(0) = D_0,&\\
V(0) = 0,\ X_{vac}(0) = 0,\quad u_V(.) \in [u_{\min}, u^{\max}],&\\
X_{vac}(T) = x_{coverage},\quad \kappa I_S(t) \le B,\qquad \forall t \in [0,T],&\\
N^\star(t) = L + S + E + I_S + I_A + H + R + V&
\end{aligned} \tag{9}$$

7. Optimal control problem

8. Numerical Results

Appendix A. Appendix

Consider the following cost functional that we want to minimize

$$\int_0^T C(t, X(t), u(t))dt \tag{A.1}$$

subject to the dynamics

$$\dot{X}(t) = f(t, X(t), u(t)), \qquad 0 \le t \le T, \tag{A.2}$$

and the initial state $X(0) = x_0$. Let $t_0 < t_1 < \ldots < t_n$, with $t_0 = 0$ and $t_n = T$, be a partition of the interval $[0, T]$. We consider *piecewise constant controls* $\tilde{u}$ of the form

$$\tilde{u}(t) = a_j \qquad t_j \le t < t_{j+1} \tag{A.3}$$

for $j = 0, \ldots, n-1$. Assumption 1. Assumption 2. By Assumption 1, the system

$$\dot{X}(t) = f(t, X(t), a_0), \quad X(0) = x_0, \qquad 0 \le t \le t_1,$$

has a unique solution $\tilde{X}_0(t; x_0, a_0)$ which is continuous in (x_0, a_0). Next, put $x_1 := \tilde{X}_0(t_1; x_0, a_0)$ and consider the system

$$\dot{X}(t) = f(t, X(t), a_1), \quad X(t_1) = x_1, \qquad t_1 \le t \le t_2,$$

which, again by Assumption 1, has a unique solution $\tilde{X}_1(t; x_1, a_1)$ continuous in (x_1, a_1). By following this procedure, we end up having a recursive solution

$$\begin{aligned}
&\tilde{X}_{n-1}(t; x_{n-1}, a_{n-1}),\\
&x_{n-1} := \tilde{X}_{n-2}(t_{n-1}; x_{n-2}, a_{n-1}), \quad t_{n-1} \le t \le T.
\end{aligned}$$

Thus, for a control $\tilde{u}$ of the form (A.3) and the corresponding solution path $\tilde{X}$, we have

$$\int_0^T C(t, \tilde{X}(t), \tilde{u}(t))dt = \sum_{j=0}^{n-1} \int_{t_j}^{t_{j+1}} C(t, \tilde{X}_j(t), a_j)dt.$$

Notice that each $\tilde{X}_j$ is a continuous function of $(a_0, \ldots, a_j)$ and x_0. Therefore, by Assumption 2, the mapping

$$(a_0, \ldots, a_{n-1}) \mapsto \sum_{j=0}^{n-1} \int_{t_j}^{t_{j+1}} C(t, \tilde{X}_j(t), a_j)dt$$

is continuous.

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