On optimally devising a two-shot vaccination rollout through MPC

Parino, Francesco; Zino, Lorenzo; Calafiore, Giuseppe; Rizzo, Alessandro

On optimally devising a two-shot vaccination rollout through MPC

Francesco Parino[1], Lorenzo Zino[2], Giuseppe Carlo Calafiore[1], and Alessandro Rizzo[1,3]

Context - The ongoing COVID-19 vaccination campaign has highlighted the complexity of optimally designing a two-shot vaccination campaign. Mathematical modeling, which has already proved to be key in other aspects of the management of the pandemic [1], can again be utilized to assist public health authorities in the planning of the vaccination rollout [2]. To this aim, we propose a novel epidemic model, which incorporates the effect of nonpharmaceutical interventions (NPIs) and a two-shot vaccination campaign. Then, nonlinear model predictive control (MPC) is used to devise the optimal vaccination rollout (i.e., scheduling first and second shots), taking into account both the healthcare needs and the socio-economic costs associated with the implementation of NPIs. A case study, calibrated on the 2021 COVID-19 vaccination campaign in Italy, is discussed to illustrate the proposed method [3].

Model - We propose a discrete-time deterministic epidemic model that generalizes a standard SIR compartmental model [4] by incorporating a two-shot vaccination campaign, in which the second shot should be administered at least L time-steps after the first one. In our model, the population is partitioned into a set of compartments, which comprises susceptible (S), infectious (I), hospitalized (H), recovered (R), dead (D), and fully vaccinated (V) individuals. A further set of compartments is included to represent people that have already received the first shot since ℓ time-steps (F_ℓ, $\ell = 1,\dots,L-1$), and people that are waiting for the second shot (W).

Susceptible individuals become infected upon interaction with infectious individuals with time-varying rate $\beta(t)$, as detailed below; such a probability is reduced by σ for those who are partially vaccinated (W), while we assume that vaccinated individuals are fully immunized. At each time-step, a fraction μ of the infected individuals recovers, and a fraction γ is hospitalized; among the hospitalized, a fraction ν recovers, while a fraction λ dies. Vaccinations are modeled through two control actions, $u_1(t)$ and $u_2(t)$, which represent the first and second shots that are performed at time t, where $B(t)$ is the total number of vaccines that are available at time t, and $Y(t)$ is the supply at time t, which is assumed to be known. Finally, a parameter α is included, to model the velocity of loss of partial immunity, after the first shot. Hence, the system evolves according to the following recursions:

$$
\begin{aligned}
S(t+1) &= S(t) - \beta(t)S(t)\tfrac{I(t)}{N} + \alpha W(t) - u_1(t)\\
I(t+1) &= (1-\mu-\gamma)I(t) + \beta(t)(S(t) + \textstyle\sum F_\ell(t) + (1-\sigma)W(t))\tfrac{I(t)}{N}\\
H(t+1) &= (1-\nu-\lambda)H(t) + \gamma I(t)\\
R(t+1) &= R(t) + \mu I(t) + \nu H(t)\\
D(t+1) &= D(t) + \lambda H(t)\\
F_1(t+1) &= u_1(t)\\
F_\ell(t+1) &= F_{\ell-1}(t)(1-\beta(t)\tfrac{I(t)}{N}), \qquad \ell = 2,\dots,L-1\\
W(t+1) &= (1-\alpha)W(t) + F_{L-1}(t)(1-\beta(t)\tfrac{I(t)}{N})\\
&\quad -(1-\sigma)\beta(t)W(t)\tfrac{I(t)}{N} - u_2(t)\\
V(t+1) &= V(t) + u_2(t)\\
B(t+1) &= B(t) + Y(t) - u_1(t) - u_2(t),
\end{aligned}
$$

where the time-varying infection rate $\beta(t)$ is designed as a feedback mechanism based on the size of the hospitalized compartment, to mimic the realistic implementation of NPIs during the course of an epidemic. Specifically, we dynamically set

$$\beta(t+1) = \beta_{NPI} + (\beta_0 - \beta_{NPI})\left(1 + \frac{1}{2}\tanh\left(\kappa\frac{H(t)-\bar{H}}{\bar{H}}\right)\right),$$

where $0 < \beta_{NPI} < \beta_0$ are two limit values, corresponding to the maximum level of NPIs and their absence, respectively, $\bar{H}$ is the critical hospitalization threshold, and κ is a parameter that captures the speed of reaction of the population. A schematic of the compartments and the state transitions of the model are illustrated in Fig. 1.

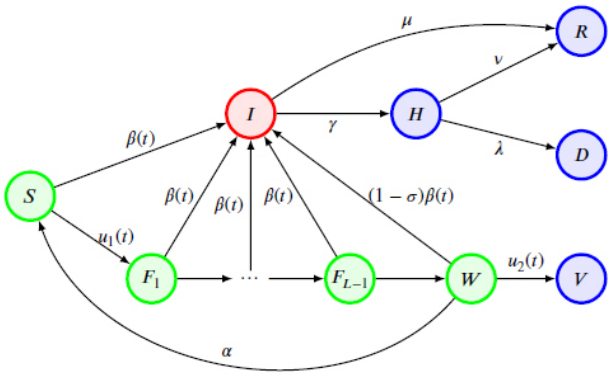

Figure 1: State transitions characterizing the epidemic process.

Optimization problem - Our objective is to optimize the scheduling of the two shots $u_1(t)$ and $u_2(t)$, under some constraints of nonnegativity $u_1(t) \geq 0$, $u_2(t) \geq 0$, maximum capacity ($u_1(t) + u_2(t) \leq C$), and budget ($u_1(t) + u_2(t) \leq B(t)$). The main goal is to reduce the number of hospitalizations and limit the need of adopting NPIs. Hence, fixing a time-horizon T, the control variable is defined as a $2T$-dimensional nonnegative vector $u = (u_1(0),\dots,u_1(T-1),u_2(0),\dots,u_2(T-1))$, and we define the following cost function

$$J = \sum_{t=1}^{T}\left(\frac{H(t)}{H_{max}}\right)^2 + \sum_{t=1}^{T}\left(\frac{\beta_0 - \beta(t)}{\beta_0 - \beta_{NPI}}\right)^2,$$

where the first term represents the *healthcare cost* (with H_{max} being the maximum number of hospitalizations in the absence of any vaccination campaign), and the second one models the *socio-economic cost* associated with the implementation of NPIs.

The cost function J, the constraints, and the dynamical system defined in the above yield a nonlinear optimization problem, which is then leveraged for control purposes in the MPC framework [5]. Specifically, the solution of the nonlinear MPC is based on the iterative, finite-horizon optimization of the cost function. At each time t, the following procedure is implemented: i) the cost-minimizing control strategy is numerically computed for a fixed time-horizon (shorter than T), ii) the first step of the control strategy is executed, iii) the system evolves to a new state at time $t+1$, and the calculations are repeated from item i) from the new current state.

[1]Politecnico di Torino [2]University of Groningen [3]New York University

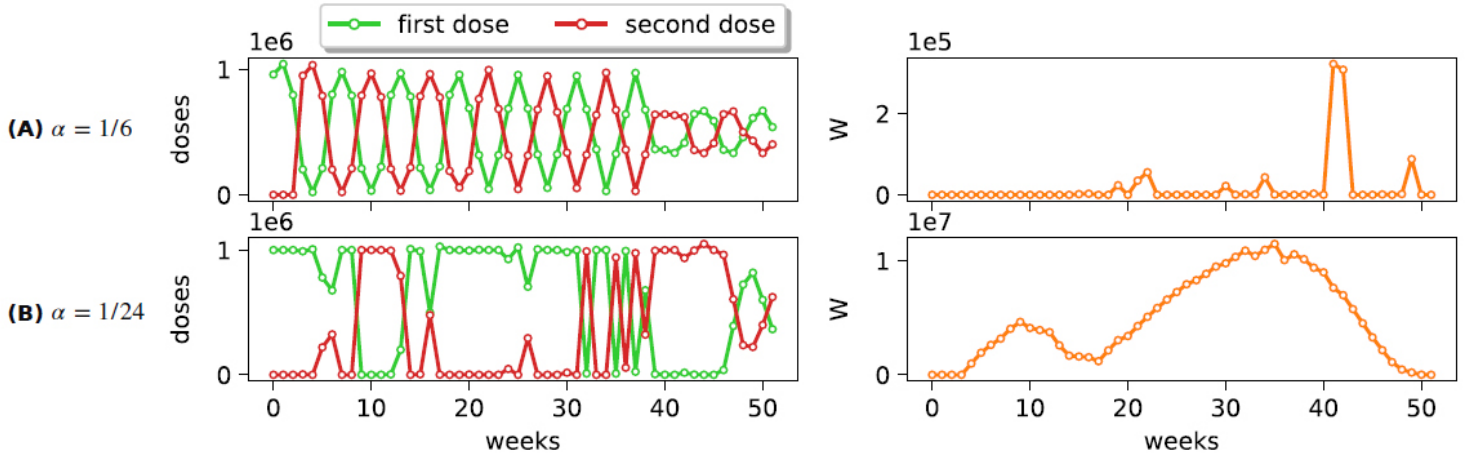

Figure 2: Optimal vaccination rollout for different velocity of loss of partial immunity, α.

Results - The model is calibrated on the COVID-19 outbreak in Italy, with a specific focus on the Spring 2021 vaccination campaign. Specifically, we identified the epidemic parameters of the model using reported epidemic data during the second wave (September 2020–April 2021) [6]; then, we calibrate the parameters of the vaccine (minimum delay between first and second shot T, effectiveness of first shot σ, and its duration α) utilizing clinical data for the two vaccines that were mostly adopted in Italy during the Spring 2021 vaccination campaign, that is, Pfizer and AstraZeneca [7, 8], and using officially reported data on vaccinations to determine the constraint C and the supplies $Y(t)$ [9].

Our findings suggest that determining the optimal vaccination strategy is nontrivial, as it is strongly dependent on the efficacy and duration of the first-dose partial immunization. Interestingly, we find that a (partial) herd immunity that is effective in avoiding resurgent waves might be obtained by prioritizing first shots in the early stages of the rollout, for vaccines with a sufficiently efficacious first dose and a long duration of the partial immunity (e.g., AstraZeneca [8]). On the contrary, for vaccines with a shorter minimum delay between the shots, an alternate vaccination strategy that minimizes the delay between the two shots seems to be preferable.

We extend our analysis by investigating the role of the model parameters on the optimal vaccination rollout. In particular, we focus on the role of α, which represent the velocity at which the partial immunity gained with a is lost. Note that, due to the limited amount of clinical data, there is still not an agreement on a reliable estimation for the parameter α in the scientific community. The results of our what/if analysis, illustrated in Fig. 2, show that the parameter α plays a key role in shaping the optimal vaccination rollout. Predictably, if partial immunity has a short duration ($\alpha = 1/6$), alternating solutions are obtained, in which second shots are done as soon as possible. Interestingly, a longer duration of the partial immunity ($\alpha = 1/24$) results in a nontrivial solution, with phases in which first shots are prioritized, thereby delaying the second ones. Such a strategy tends to accumulate individuals in the compartment W (with a reduced infection rate), keeping new contagions under control and avoid resurgent epidemic waves and the need of severe NPIs.

Outlook - Our novel epidemic model and optimization approach provide a tool that can be adopted to help public health authorities in devising the current COVID-19 vaccination campaign. Furthermore, our analysis has highlighted the flexibility of our approach, which enables to test several what/if scenarios, demonstrating its potential use in future stages of the COVID-19 vaccination campaign, and to increase preparedness for future epidemics. In our current research, besides investigating the role of the other model parameters in shaping the optimal vaccination strategy, we are planning to consider further real-world features. Specifically, a key issue that has been observed during the ongoing vaccination campaign concerns the stochasticity of the supply. We are currently working toward incorporating such a source of stochasticity within our optimization framework, and investigate its impact on the device of the optimal vaccination rollout.

Acknowledgment - The work by F.P. and A.R. is partially supported by the Italian Ministry of Foreign Affairs and International Cooperation ("Mac2Mic").

References

[1] E. Estrada, "COVID-19 and SARS-CoV-2. Modeling the present, looking at the future," *Phys. Rep.*, vol. 869, pp. 1–51, 2020.

[2] G. Giordano *et al.*, "Modeling vaccination rollouts, SARS-CoV-2 variants and the requirement for non-pharmaceutical interventions in Italy," *Nat. Med.*, 2021.

[3] F. Parino, L. Zino, C. G. Calafiore, and A. Rizzo, "A model predictive control approach to optimally devise a two-dose vaccination rollout: A case study on COVID-19 in Italy," under review.

[4] W. Mei, S. Mohagheghi, S. Zampieri, and F. Bullo, "On the dynamics of deterministic epidemic propagation over networks," *Ann. Rev. Control*, vol. 44, pp. 116–128, 2017.

[5] S. Gros, M. Zanon, R. Quirynen, A. Bemporad, and M. Diehl, "From linear to nonlinear MPC: bridging the gap via the real-time iteration," *Int. J. Control*, vol. 93, no. 1, pp. 62–80, 2020.

[6] Dipartimento della Protezione Civile, "COVID-19 Italia - Monitoraggio situazione," https://github.com/pcm-dpc/COVID-19, 2020.

[7] N. Dagan *et al.*, "Bnt162b2 mrna covid-19 vaccine in a nationwide mass vaccination setting," *N. Engl. J. Med.*, vol. 384, no. 15, pp. 1412–1423, 2021.

[8] M. Voysey *et al.*, "Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of chadox1 ncov-19 (azd1222) vaccine: a pooled analysis of four randomised trials," *Lancet*, vol. 397, no. 10277, pp. 881–891, 2021.

[9] Struttura Commissariale per l'Emergenza Covid-19, "Covid-19 Opendata Vaccini," https://github.com/italia/covid19-opendata-vaccini, 2021.