Optimal Distribution of Vaccinations (improvement necessary)

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Abstract

Description

Keywords: ...

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1 Introduction

...

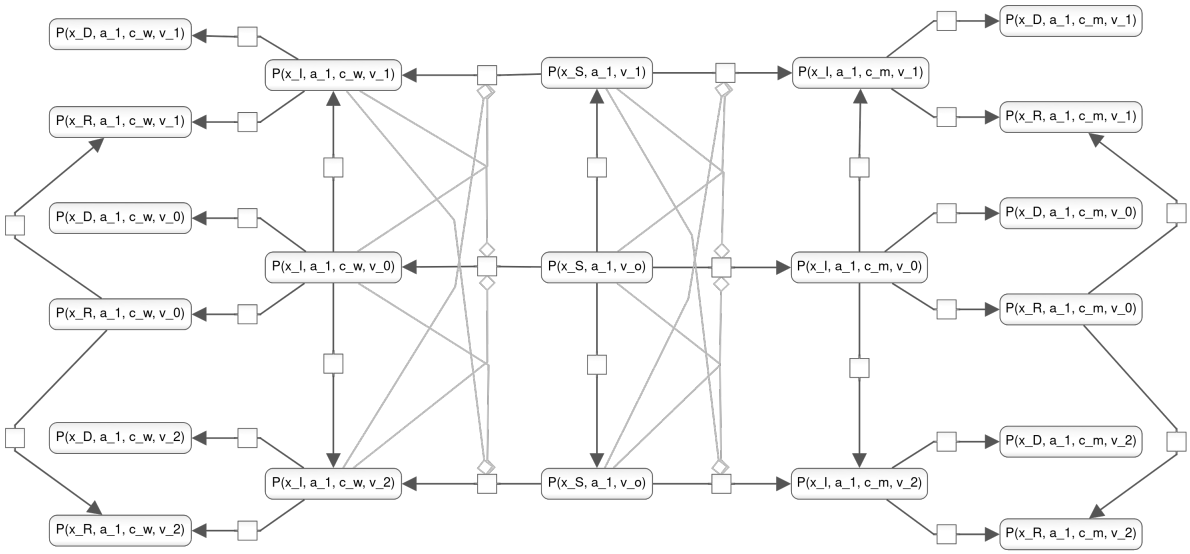
2 Compartments

In the proposed model the compartments are Susceptible (S), Infectious (I), Recovered and Dead (D). Individuals either live in area one (a_1) or area two (a_2). They are non-vaccinated (v_0), vaccinated with vaccine one (v_1) or vaccinated with vaccine two (v_2). Since we are dealing with two virus variants, the wild type w and the mutant m, we account for this by introducing the feature c_j with $j \in \{w, m\}$ that indicates the type of virus we are referring to. For infectious individuals we can distinguish between symptomatic s_y and asymptomatic cases s_n.

We use the set notation of Waites et al. (2021) to address certain subsets of the population. $\mathcal{P}()$ means all individuals. $\mathcal{P}(x_u)$ denotes all individuals from compartment $u \in \{S, I, R, D\}$, $\mathcal{P}(a_l)$ denotes all individuals from area $l \in \{1, 2\}$, $\mathcal{P}(v_i)$ are all individuals with vaccination status $k \in \{0, 1, 2\}$, where zero indicates non-vaccinated, and $\mathcal{P}(c_j)$ are all individuals that currently have or had an infection with virus $j \in \{w, m\}$. With this notation we can pick desired subsets of the population by combining the appropriate features. All individuals from area one that are infected with the wild type are addressed by $\mathcal{P}(x_I, c_m)$. If we only want the unvaccinated individuals of them we use $\mathcal{P}(x_I, c_m, v_0)$. The usual set operators, like $\cup$. Using these operators allows us to address even more specific subsets like the set of all vaccinated individuals $\mathcal{P}(v_1) \cup \mathcal{P}(v_2)$. The set $\mathcal{P}()$ is defined as the whole population. The cardinalty $|\cdot|$ is used to addres the respective number of individuals in a set, e.g. $|\mathcal{P}(x_S, a_1)|$ equals the number of all susceptible individuals in area one.

In more specific cases it might be more comprehensive to replace the index numbers by meaningful abbreviations.

On the next page you find a graphical representation of the model using tikz. I have omitted the second region and cross-border infections from the graph to increase readability. *no heading and just somewhere*



Assumptions so far:

- distinction between symptomatic and asymptomatic infected cases only at recovered
- mutant can be more infectious but has same mortality. Additional parameter?
- no vaccination during infection see here (US Center for Disease Control)
- no births and other deaths
- no reinfection

- time dependence of parameters
- cross-border with individuals being in the other country
- rate of going somewhere must not be the same as people coming in (modify b function)
- minimize over dead people or integrate of infected

2.1 Dynamics

Susceptible to Infectious

To facilitate notation, we distinguish between individuals that are alive and those that are dead. We exclude all dead individuals by using prime notation to only address all living individuals, e.g. $\mathcal{P}'(a_l) = \mathcal{P}(x_S, a_l) \cup \mathcal{P}(x_I, a_l) \cup \mathcal{P}(x_R, a_l)$. We define $N_l(t) = |\mathcal{P}'(a_l)|$ as the number of living individuals in area l at time t. For specifying the transition rates we need to specify the probabilities that two individuals of a certain type meet. We do so by using the relative frequencies and adjust for cross-area meetings. The probability of an individual

$i \in \mathcal{P}()$ to be in a particular subset is approximated by the relative frequencies. For example, the (time dependent) probability that a randomly drawn living individual is from area l is $\mathbb{P}\left(i \in \mathcal{P}'(a_l)\right) = \frac{N_l(t)}{N_1(t)+N_2(t)}$. To compute the probability that an individual is susceptible, conditioned that it is from area l, we can use Bayes' formula

$$\mathbb{P}\left(i \in \mathcal{P}(x_S)|i \in \mathcal{P}'(a_l)\right) = \frac{\mathbb{P}\left(i \in \mathcal{P}(x_S, a_l)\right)}{\mathbb{P}\left(i \in \mathcal{P}'(a_l)\right)} = \frac{|\mathcal{P}(x_S, a_l)|}{|\mathcal{P}'(a_l)|} = \frac{|\mathcal{P}(x_S, a_l)|}{N_l(t)}. \tag{1}$$

We are interested in how many individuals are on average infected by an infected individual. To facilitate notation we assume that the infected individual lives in area one and is infected with the wild type w. The average number of infected individuals is a composition of the infection rate that is dependent on the virus type, the average number of contacts per infected individual and unit of time and the share of susceptible individuals that can be infected. We start with the baseline case of two unvaccinated individuals and first define the transition for susceptible individuals from area two.

Let $i_1 \in \mathcal{P}(x_I, v_0, c_w, a_1)$ and $i_2 \in \mathcal{P}()$. We fix the location, vaccination status and compartment of individual one and allow individual two to potentially be from both areas and every compartment. We need to define $\mathbb{P}(i_2 \in \mathcal{P}(x_S, v_0, a_2)|i_1 \in \mathcal{P}(x_I, v_0, c_w, a_1))$, the probability that the individual that can be infected is susceptible, unvaccinated and from area two given that individual one is infected with the wild type, unvaccinated and from area one. We assume that only the area has an influence on the probability of meeting an individual. The problem facilitates to finding $\mathbb{P}(i_2 \in \mathcal{P}(x_S, v_0, a_2)|i_1 \in \mathcal{P}(a_1))$ or equivalently $\mathbb{P}(i_2 \in \mathcal{P}(x_S, v_0) \wedge i_2 \in \mathcal{P}(a_2)|i_1 \in \mathcal{P}(a_1))$. Using Bayes' formula we can rewrite this as

$$\begin{aligned}\mathbb{P}(i_2 \in \mathcal{P}(x_S, v_0) \wedge i_2 \in \mathcal{P}(a_2)|i_1 \in \mathcal{P}(a_1)) &= \mathbb{P}(i_2 \in \mathcal{P}(a_2)|i_1 \in \mathcal{P}(a_1)) \\ &\quad \cdot \mathbb{P}(i_2 \in \mathcal{P}(x_S, v_0)|i_1 \in \mathcal{P}(a_1), i_2 \in \mathcal{P}(a_2)) \\ &= \mathbb{P}(i_2 \in \mathcal{P}(a_2)|i_1 \in \mathcal{P}(a_1)) \\ &\quad \cdot \mathbb{P}(i_2 \in \mathcal{P}(x_S, v_0))\end{aligned}$$

We first specify the probability $\mathbb{P}(i_2 \in \mathcal{P}(a_2)|i_1 \in \mathcal{P}(a_1))$, which is to say, the probability that i_2 is from area two. We cannot use the relative frequency of the number of individuals $\frac{N_2(t)}{N_1(t)+N_2(t)}$ as probability since this would not take into account that individuals meet more often within one region. We therefore add a penalty term $b\left(\mathrm{d}(a_1, a_2)\right)$ that accounts for the distance between the areas

$$\mathbb{P}(i_2 \in \mathcal{P}(a_2)|i_1 \in \mathcal{P}(a_1)) = \frac{N_2(t)}{N_1(t) + N_2(t)} \cdot b\left(\mathrm{d}(a_1, a_2)\right).$$

$b(y) \in [0, 1], b\left(0\right) = 1$ and $\lim_{y\to\infty} b\left(y\right) = 0$. *idea for* $b(y) = \frac{1}{1+by}$. Analogously we define the probabilities of $\mathbb{P}(i_1 \in \mathcal{P}(a_1)|i_2 \in \mathcal{P}(a_2))$. Subsequently, we use short-hand notation to

address the conditional location probabilities. Let $m_{u,v}$ be the u-th row and v-th column of the Matrix $\mathbf{M} \in \mathbb{R}^{2\times 2}$.

$$\begin{aligned}\mathbf{M} &= \begin{pmatrix} \mathbb{P}(i_1 \in \mathcal{P}(a_1) | i_1 \in \mathcal{P}(a_1)) & \mathbb{P}(i_1 \in \mathcal{P}(a_1) | i_2 \in \mathcal{P}(a_2)) \\ \mathbb{P}(i_2 \in \mathcal{P}(a_2) | i_1 \in \mathcal{P}(a_1)) & \mathbb{P}(i_2 \in \mathcal{P}(a_2) | i_2 \in \mathcal{P}(a_2)) \end{pmatrix} \\ &= \begin{pmatrix} 1 - \frac{N_2(t)}{N_1(t)+N_2(t)} \cdot b\left(\mathrm{d}(a_1, a_2)\right) & \frac{N_1(t)}{N_1(t)+N_2(t)} \cdot b\left(\mathrm{d}(a_1, a_2)\right) \\ \frac{N_2(t)}{N_1(t)+N_2(t)} \cdot b\left(\mathrm{d}(a_1, a_2)\right) & 1 - \frac{N_1(t)}{N_1(t)+N_2(t)} \cdot b\left(\mathrm{d}(a_1, a_2)\right) \end{pmatrix}\end{aligned}$$

The probability of individual two to be unvaccinated and susceptible, conditioned that it is from area two, is taken to be the relative frequency of unvaccinated, susceptible individuals from area two

$$\mathbb{P}(i_2 \in \mathcal{P}(x_S, v_0)) = \frac{|\mathcal{P}(x_S, v_0, a_2)|}{N_2(t)}$$

Combining both results yields

$$\mathbb{P}(i_2 \in \mathcal{P}(x_S, v_0, a_2) | i_1 \in \mathcal{P}(x_I, v_0, c_w, a_1)) = m_{2,1} \cdot \frac{|\mathcal{P}(x_S, v_0, a_2)|}{N_2(t)}$$

Hence, i_1 meets on average $m_{2,1} c \frac{|\mathcal{P}(x_S, v_0, a_2)|}{N_2(t)}$ unvaccinated susceptible individuals from area two. At this meetings, α individuals become infected. This probability changes if we condition on the mutant. i_1 infects on average $\alpha m_{2,1} c \frac{|\mathcal{P}(x_S, v_0, a_2)|}{N_2(t)}$ individuals. This is done by $|\mathcal{P}(x_I, v_0, a_1)|$ individuals from area one and therefore we get the transitions $\alpha m_{2,1} c \frac{|\mathcal{P}(x_S, v_0, a_2)|}{N_2(t)} |\mathcal{P}(x_I, v_0, a_1)|$ Using rule-based notation we write this as

$$\mathcal{P}(x_I, v_0, c_w, a_1), \mathcal{P}(x_S, v_0, a_2) \xrightarrow{\frac{\alpha m_{2,1} c}{N_2(t)}} \mathcal{P}(x_I, v_0, c_w, a_1), \mathcal{P}(x_I, v_0, c_w, a_2)$$

Same but for unvaccinated from same area (*we ignore minus one*)

$$\mathcal{P}(x_I, v_0, c_w, a_1), \mathcal{P}(x_S, v_0, a_1) \xrightarrow{\frac{\alpha m_{1,1} c}{N_1(t)}} \mathcal{P}(x_I, v_0, c_w, a_1), \mathcal{P}(x_I, v_0, c_w, a_1)$$

The extension to the mutant and vaccinated individuals is straightforward by multiplying the probability that a meeting of an individual with the base virus type and a susceptible individual results in an infection. We assume that if the infected individual is vaccinated, this reduces the infection probability by the factor $1 - \gamma$ for $\gamma \in [0, 1]$. For $k \in \{1, 2\}$ and $l \in \{1, 2\}$

$$\mathcal{P}(x_I, v_k, c_w, a_1), \mathcal{P}(x_S, v_0, a_l) \xrightarrow{\frac{(1-\gamma)\alpha m_{1,l} c}{N_l(t)}} \mathcal{P}(x_I, v_k, c_w, a_1), \mathcal{P}(x_I, v_0, c_w, a_l).$$

We interpret γ as degree of protection against spreading the virus after being vaccinated.

If the susceptible individual is vaccinated with vaccine $k \in \{1,2\}$ we assume that this reduces the infection probability for virus type $j \in \{w,m\}$ by the factor $1-\delta_{j,k}$ for $\delta_{j,k} \in [0,1]$. For $k \in \{1,2\}$ and $l \in \{1,2\}$

$$\mathcal{P}(x_I, v_0, c_w, a_1), \mathcal{P}(x_S, v_k, a_l) \xrightarrow{\frac{(1-\delta_{w,k})\alpha m_{1,l^c}}{N_l(t)}} \mathcal{P}(x_I, v_0, c_w, a_1), \mathcal{P}(x_I, v_k, c_w, a_l).$$

We can interpret $\delta_{j,k}$ as degree of protection against virus type j we gain from being vaccinated with vaccine k. In the extreme case where $\delta_{j,k} = 1$ vaccine k gives a full protection against virus j and no infections with virus j are possible for individuals vaccinated with k. Analogously, $\delta_{j,k} = 0$ means that there is no additional protection at all.

We allow the mutant to be more or less infectious than the wild type by introducing the additional parameter $\eta \in \left(0, \frac{1}{\alpha}\right]$. $\eta > 1$ means that the mutant is more infectious than the wild type. *maybe restrict to this case?* For $l \in \{1,2\}$

$$\mathcal{P}(x_I, v_0, c_m, a_1), \mathcal{P}(x_S, v_0, a_l) \xrightarrow{\frac{\eta\alpha m_{1,l^c}}{N_l(t)}} \mathcal{P}(x_I, v_0, c_m, a_1), \mathcal{P}(x_I, v_0, c_m, a_l).$$

We can combine the factors for different infection probabilities. For example the transition from the infectious individuals from area one, infected with the mutant, and vaccinated with vaccine one and the susceptible individuals vaccinated with vaccine two is for $l \in \{1,2\}$

$$\mathcal{P}(x_I, v_1, c_m, a_1), \mathcal{P}(x_S, v_2, a_l) \xrightarrow{\frac{\eta\alpha(1-\delta_{m,2})(1-\gamma)m_{1,l^c}}{N_l(t)}} \mathcal{P}(x_I, v_1, c_m, a_1), \mathcal{P}(x_I, v_2, c_m, a_l).$$

Infectious to Recovered/Death

non-vaccinated. For $l \in \{1,2\}$

$$\begin{aligned} \mathcal{P}(x_I, v_0, c_w, a_l) &\xrightarrow{p\lambda} \mathcal{P}(x_D, v_0, c_w, a_l) \\ \mathcal{P}(x_I, v_0, c_w, a_l) &\xrightarrow{(1-p)\lambda} \mathcal{P}(x_R, v_0, c_w, a_l) \end{aligned} \tag{2}$$

vaccinated. For $k \in \{1,2\}$ and $l \in \{1,2\}$

$$\begin{aligned} \mathcal{P}(x_I, v_k, c_w, a_l) &\xrightarrow{\omega_{k,w}p\lambda} \mathcal{P}(x_D, v_k, c_w, a_l) \\ \mathcal{P}(x_I, v_k, c_w, a_l) &\xrightarrow{(1-\omega_{k,w}p)\lambda} \mathcal{P}(x_R, v_k, c_w, a_l) \end{aligned}$$

Vaccination

For $j \in \{1,2\}$, $l \in \{1,2\}$

$$\begin{aligned}
\mathcal{P}(x_S, v_0, a_l) &\xrightarrow{\nu_{j,l}(\cdot)} \mathcal{P}(x_S, v_j, a_l) \\
\mathcal{P}(x_I, v_0, c_w, a_l) &\xrightarrow{\nu_{j,l}(\cdot)} \mathcal{P}(x_I, v_j, c_w, a_l) \\
\mathcal{P}(x_R, v_0, c_w, a_l) &\xrightarrow{\nu_{j,l}(\cdot)} \mathcal{P}(x_R, v_j, c_w, a_l)
\end{aligned}$$

3 Vaccine allocation

How to determine the vaccination rate? We denote the number of vaccinations of type v_j available at time t in country l by $W_{j,l}(t)$ and the total number number of vaccine j by $W_j(t) = W_{j,A}(t) + W_{j,B}(t)$. We assume that all doses of vaccines are immediately vaccinated. Thus, it must hold that

$$\begin{aligned}
W_{j,A}(t) &= \nu_{j,A} \cdot (|\mathcal{P}(x_S, v_0, a_A)| + |\mathcal{P}(x_R, v_0, a_A, c_w)| + |\mathcal{P}(x_R, v_0, a_A, c_m)|) \\
W_{j,B}(t) &= \nu_{j,B} \cdot (|\mathcal{P}(x_S, v_0, a_B)| + |\mathcal{P}(x_R, v_0, a_B, c_w)| + |\mathcal{P}(x_R, v_0, a_B, c_m)|)\,.
\end{aligned}$$

Which is to say that the total number of vaccines j at t must equal the number of individuals vaccinated with j at t. Let $f_{j,A}(t)$ be the fraction of vaccine j that is allocated to country A. We can write $W_{j,A}(t) = f_{j,A}(t)W_j(t)$ and $W_{j,B}(t) = [1 - f_{j,A}(t)]\, W_j(t)$. Combining both yields for country A and B

$$\begin{aligned}
\nu_{j,A} &= \frac{f_{j,A}(t)W_j(t)}{|\mathcal{P}(x_S, v_0, a_A)| + |\mathcal{P}(x_R, v_0, a_A, c_w)| + |\mathcal{P}(x_R, v_0, a_A, c_m)|} \\
\nu_{j,B} &= \frac{[1 - f_{j,A}(t)]\, W_j(t)}{|\mathcal{P}(x_S, v_0, a_B)| + |\mathcal{P}(x_R, v_0, a_B, c_w)| + |\mathcal{P}(x_R, v_0, a_B, c_m)|}.
\end{aligned}$$

To decide on the vaccination rates we need to specify the trajectory of the fraction $f_{j,A}(t)$. Additional to the time t we use $f_{j,A}(\theta; t, \mathbf{Y}(t))$, with $\theta \in \mathbb{R}^z$, to indicate that the fraction potentially is dependent on an additional parameter vector θ and the compartments $\mathbf{Y}(t)$. In the end we optimize over the parameters θ that parameterizes the fraction. In this paper we examine three different strategies of modeling $f_{j,A}(\theta; t, \mathbf{Y}(t))$. Let $[t_1, t_{z+1}]$ be an interval on the real line and $T_i = [t_i, t_{i+1})$ be a subset of the partition $\cup_{i=1}^{z} = [t_1, t_{z+1}]$ with $t_i < t_{i+1}$ for all $i = 1, 2, \ldots, z$.

1. The fraction is stepwise defined according to the time t. No additional compartments are used. In this setup we associate z parameters $\theta_i \in [0, 1]$ to the z intervals T_i. We assume in our model that we start with the vaccination from the very beginning and therefore set $t_1 = 0$. At each time t_i the policy maker decide which fraction of the

vaccine is assigned to country A up to time t_{i+1}. The resulting function is a stepwise function that takes the the value θ_i in the interval $[t_i, t_{i+1})$ such that

$$f_{j,A}(\theta; t) = \theta_i \quad \forall t \in T_i$$

We can interpret this approach as follows: Policy makers determine a fraction that is

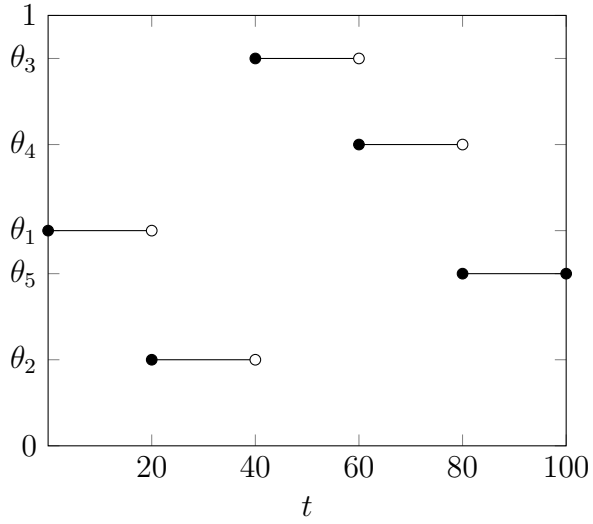
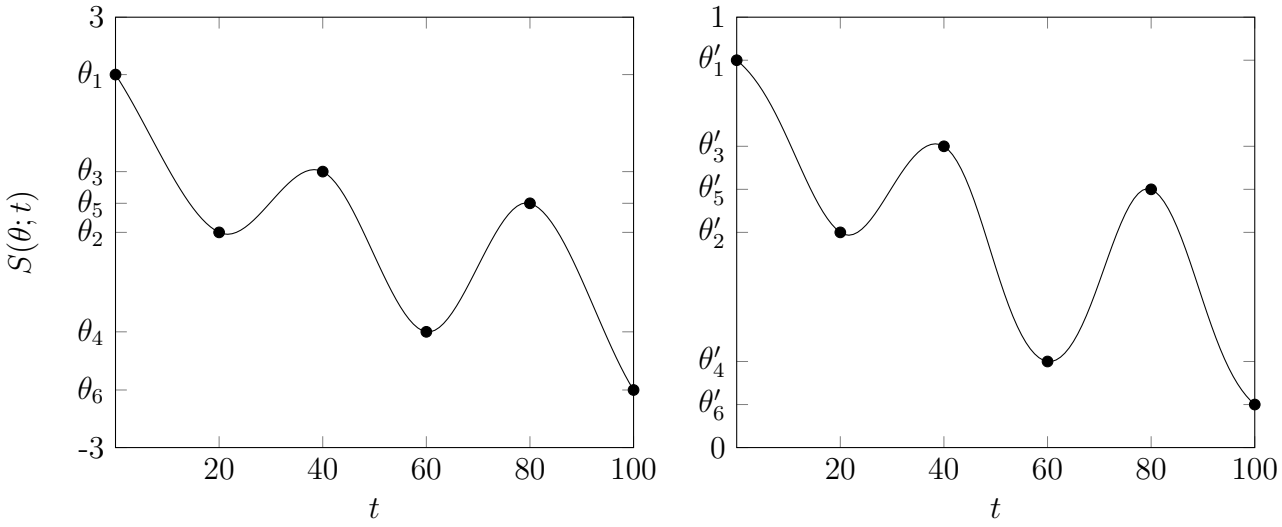


Figure 1: Example for stepwise $f_{j,A}(\theta; t)$

allocated to country A for a fixed decision period, evaluate, and then adjust before the next decision period begins.

2. The fraction follows a cubic hermite spline $S(\theta; t)$ of order three that is transformed via a sigmoid function to obtain values between zero and one. No additional compartments are used. Following this approach we associate each Polynomial $P_i(\theta; t)$ with the subset T_i. On the contrary to the previous approach, the rate of vaccine is not determined in each subinterval by a fixed constant value but by a polynomial of order three. For the cubic hermite splines each polynomial $P_i(\theta; t)$ is of degree three and can be defined by the basis polynomials $b_1(t) = 2t^3 - 3t^2 + 1, b_2(t) = t^3 - 2t^2 + t, b_3(t) = -2t^3 + 3t^2$ and $b_4(t) = t^3 - t^2$, the infimum (t_i) and supremum (t_{i+1}) of T_i and specified values of $P_i(\theta; t_i) = \theta_i$, $P_{i+1}(\theta; t_{i+1}) = \theta_{i+1}$ and its derivatives $P_i'(\theta; t_i)$, $P_i'(\theta; t_{i+1})$.
To compute the derivatives we use finite differences with one-sided approximations at



(a) Cubic hermite spline $S(\theta;t)$

(b) Fraction $f_{j,A}(\theta;t) = \sigma\left(S(\theta;t)\right)$

the boundaries t_1 and t_{z+1}

$$
\begin{aligned}
P'_1(\theta;t_1) &= \frac{P_2(\theta;t_2) - P_1(\theta;t_1)}{t_2 - t_1} \\
P'_i(\theta;t_i) &= \frac{1}{2}\left[\frac{P_{i+1}(\theta;t_{i+1}) - P_i(\theta;t_i)}{t_{i+1} - t_i} + \frac{P_i(\theta;t_i) - P_{i-1}(\theta;t_{i-1})}{t_i - t_{i-1}}\right] \\
P'_z(\theta;t_{z+1}) &= \frac{P_{z+1}(\theta;t_{z+1}) - P_z(\theta;t_z)}{t_{z+1} - t_z}
\end{aligned}
$$

For $t \in T_i$ let $t' = (t - t_i)/(t_{i+1} - t_i)$. Then the polynomial $P_i(\theta;t)$ is given by

$$
\begin{aligned}
P_i(\theta;t) = b_1(t')\overbrace{P_i(\theta;t_i)}^{\theta_i} &+ b_2(t')(t_{i+1} - t_i)P'_i(\theta;t_i) \\
&+ b_3(t')\underbrace{P_{i+1}(\theta;t_{i+1})}_{\theta_{i+1}} + b_4(t')(t_{i+1} - t_i)P'_i(\theta;t_{i+1})
\end{aligned}
$$

$P_i(\theta;t)$ depends on θ_i and θ_{i+1} through the functional values and the derivatives at the boundaries.

To ensure that the fractions stay between zero and one, we apply a sigmoid transformation of the polynomials such that the fraction of vaccine j that is allocated to country A can be written as

$$
f_{j,A}(\theta;t) = \frac{1}{1 + \exp\left(-P_i(\theta_i;t)\right)} \quad \forall t \in T_i. \tag{3}
$$

Note that $S(\theta;t)$ is continuous by construction, the sigmoid function $\sigma(\cdot)$ is continuous and thus the composition $\sigma(S(\theta;t))$ is also continuous.

3. The fraction is determined by a neural network.

References

Waites, W., Cavaliere, M., Manheim, D., Panovska-Griffiths, J., and Danos, V. (2021). Rule-based epidemic models. *arXiv Working Paper*.