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Letter to the Editor

Optimal allocation of limited vaccine to minimize the effective reproduction number☆

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ABSTRACT

We examine the problem of allocating a limited supply of vaccine for controlling an infectious disease with the goal of minimizing the effective reproduction number R_e. We consider an SIR model with two interacting populations and develop an analytical expression that the optimal vaccine allocation must satisfy. With limited vaccine supplies, we find that an all-or-nothing approach is optimal. For certain special cases, we determine the conditions under which the optimal R_e is below 1. We present an example of vaccine allocation for COVID-19 and show that it is optimal to vaccinate younger individuals before older individuals to minimize R_e if less than 59% of the population can be vaccinated. The analytical conditions we develop provide a simple means of determining the optimal allocation of vaccine between two population groups to minimize R_e.

1. Introduction

A natural objective in minimizing the outbreak of an infectious disease is to minimize the effective reproduction number, R_e; this is the average number of secondary cases per infectious case in a population with both susceptible and infected individuals. If a vaccine is available for the disease, vaccination is one means of controlling epidemic spread. However, vaccine supplies may be limited, particularly for newly identified diseases such as COVID-19 [1]. Here we consider the problem of allocating a limited supply of vaccine for controlling an infectious disease with the goal of minimizing R_e.

A number of studies have considered the vaccine allocation problem. Some researchers have proposed a mixed-integer or linear programming formulation to minimize the number or cost of vaccines under the constraint that the reproduction number is below 1 [2–4]. Other researchers use optimal control to determine the allocation of vaccine which minimizes vaccination cost plus the cost of infection [5,6]. Some studies have considered vaccination for seasonal influenza, typically using age-structured compartmental models and numerical simulation of alternative policies [7,8] or numerical optimization to determine the optimal allocation between different groups [9,10]. Recent studies have focused on optimal vaccination policies for COVID-19 using age-structured compartmental models. One study finds that the optimal vaccine allocation should prioritize age-based fatality rates rather than occupation-based infection rates in order to minimize the cost of infections plus economic losses [11]. Other studies find that vaccinating older groups averts more deaths, whereas vaccinating younger groups averts more infections [12–14]. Here we consider the optimal allocation of vaccine between two population groups with the goal of minimizing the effective reproduction number.

2. SIR model with vaccination

We develop an SIR model of a population with two interacting groups in which an infectious disease is spreading (Fig. 1). Individuals in each group i can be susceptible (S_i), infected (I_i), recovered (R_i), or dead (D_i). Individuals in group i can acquire infection from contact with individuals in their own population group (at rate $\beta_{ii} > 0$) or the other population group j (at rate $\beta_{ij} > 0$). Infected individuals in group i either recover (at rate $\gamma_i > 0$) or die (at rate $\mu_i > 0$). We consider a relatively short time horizon and thus do not include births, non-infection-related deaths, or other forms of entry into and exit from the population.

We assume that a preventive vaccine with effectiveness $\eta > 0$ is available and that vaccination of susceptible individuals moves them to a recovered health state. We assume that vaccination takes place at time 0. Vaccination does not affect the transmission rates between infected and susceptible individuals (β_{ij}) nor the recovery rates of infected individuals (γ_i). We denote by P the population size, $v = (v_1, v_2) \in \mathbb{R}^2$ the proportion of individuals vaccinated, $S_i(0)$, $I_i(0)$, $R_i(0)$, $D_i(0)$ the proportion of the entire population in each compartment at time 0 without vaccination, and $S_i(v;t)$, $I_i(v;t)$, $R_i(v;t)$, $D_i(v;t)$ the proportion of individuals in each compartment at time t in the presence of vaccination v. Since v_i is the proportion of the entire population that

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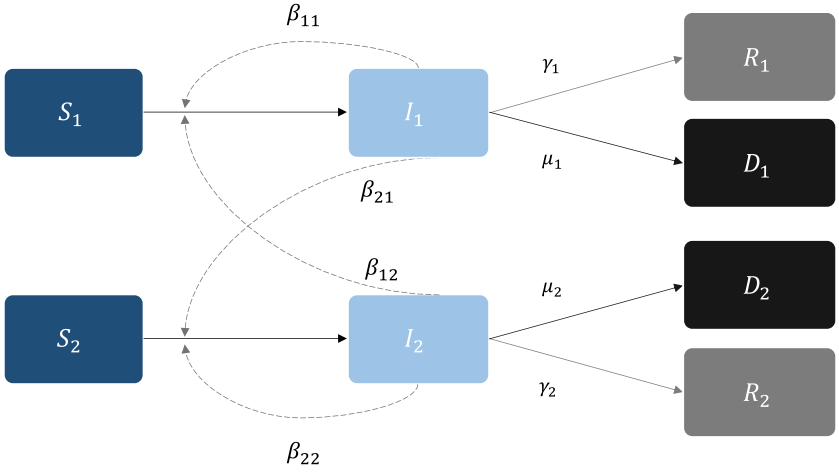

Fig. 1. Dynamic compartmental model.

is vaccinated and belongs to group i, we have the constraints $v_i \le S_i(0)$ for $i = 1, 2$.

Without loss of generality, we assume $S_1(0) > S_2(0)$. We further assume that a limited number of vaccines, N, are available to be distributed at time 0, where $N/P < S_1(0)$ and $v_1 + v_2 \le \frac{N}{P}$. Since vaccination only impacts the initial conditions, we have

$$\begin{aligned} S_i(v;0) &= S_i(0) - \eta v_i \\ I_i(v;0) &= I_i(0) \\ R_i(v;0) &= R_i(0) + \eta v_i \\ D_i(v;0) &= D_i(0) \end{aligned} \tag{1}$$

for $i = 1, 2$.

3. Derivation of the effective reproduction number

We first derive the basic reproduction number R_0 for the epidemic model using the next-generation method [15,16]; R_0 is the average number of secondary cases per infectious case in a fully susceptible population. The model has two infected host compartments, $x = \begin{bmatrix} I_1 & I_2 \end{bmatrix}$. Let $\mathcal{F}_i$ be the rate at which new infected individuals enter compartment i, and let $\mathcal{V}_i$ be the transfer of individuals into and out of compartment i. We define two matrices F and V, where $F_{ij} = \frac{\partial \mathcal{F}_i(x_0)}{\partial x_j}$, $V_{ij} = \frac{\partial \mathcal{V}_i(x_0)}{\partial x_j}$, and x_0 is the disease-free equilibrium. Using this notation, we have $\frac{dx}{dt} = (F - V)x$. For our model, F and V are as follows:

$$F = \begin{bmatrix} \beta_{11}S_1 & \beta_{12}S_1 \\ \beta_{21}S_2 & \beta_{22}S_2 \end{bmatrix}$$

$$V = \begin{bmatrix} \gamma_1 + \mu_1 & 0 \\ 0 & \gamma_2 + \mu_2 \end{bmatrix}$$

R_0 is given by the largest eigenvalue of the next generation operator FV^{-1}, where the entry (i, j) represents the expected number of secondary cases in compartment i caused by an individual in compartment j.

$$\begin{aligned} FV^{-1} &= \begin{bmatrix} \beta_{11}S_1 & \beta_{12}S_1 \\ \beta_{21}S_2 & \beta_{22}S_2 \end{bmatrix} \begin{bmatrix} \frac{1}{\gamma_1+\mu_1} & 0 \\ 0 & \frac{1}{\gamma_2+\mu_2} \end{bmatrix} \\ &= \begin{bmatrix} \frac{\beta_{11}S_1}{\gamma_1+\mu_1} & \frac{\beta_{12}S_1}{\gamma_2+\mu_2} \\ \frac{\beta_{21}S_2}{\gamma_1+\mu_1} & \frac{\beta_{22}S_2}{\gamma_2+\mu_2} \end{bmatrix} \end{aligned}$$

The largest eigenvalue of FV^{-1} is:

$$R_0 = \frac{\beta_{11}S_1}{2(\gamma_1+\mu_1)} + \frac{\beta_{22}S_2}{2(\gamma_2+\mu_2)} + \left| \frac{\beta_{11}S_1}{2(\gamma_1+\mu_1)} - \frac{\beta_{22}S_2}{2(\gamma_2+\mu_2)} \right| + \sqrt{\beta_{12}\beta_{21}S_1S_2} \tag{2}$$

We next derive the effective reproduction number R_e. With vaccination $v = (v_1, v_2)$, the starting susceptible population in group i becomes $S_i - \eta v_i$, and the effective reproduction number is:

$$\begin{aligned} f(v) &= R_e(v) \\ &= \frac{\beta_{11}(S_1 - \eta v_1)}{2(\gamma_1+\mu_1)} + \frac{\beta_{22}(S_2 - \eta v_2)}{2(\gamma_2+\mu_2)} + \left| \frac{\beta_{11}(S_1 - \eta v_1)}{2(\gamma_1+\mu_1)} - \frac{\beta_{22}(S_2 - \eta v_2)}{2(\gamma_2+\mu_2)} \right| \\ &\quad + \sqrt{\beta_{12}\beta_{21}(S_1 - \eta v_1)(S_2 - \eta v_2)} \end{aligned} \tag{3}$$

If

$$\frac{\beta_{11}(S_1 - \eta v_1)}{\gamma_1 + \mu_1} \ge \frac{\beta_{22}(S_2 - \eta v_2)}{\gamma_2 + \mu_2}$$

then we have:

$$f(v) = R_e(v) = \frac{\beta_{11}(S_1 - \eta v_1)}{\gamma_1 + \mu_1} + \sqrt{\beta_{12}\beta_{21}(S_1 - \eta v_1)(S_2 - \eta v_2)} \tag{4}$$

where $0 \le v_1 \le S_1, 0 \le v_2 \le S_2$.

4. Minimizing the effective reproduction number

Because (3) provides a closed-form expression for R_e, we can find the optimal solution numerically.

We can also solve the problem analytically for a certain range of N. For notational simplicity, we let $N' = \frac{N}{P}$, $S_1 = S_1(0)$, and $S_2 = S_2(0)$. We want to allocate all available vaccines, so we have $v_1 = N' - v_2$. Defining

$$\phi(N') = \frac{\beta_{22}S_2(\gamma_1+\mu_1) + \beta_{11}(\eta N' - S_1)(\gamma_2+\mu_2)}{\eta[\beta_{22}(\gamma_1+\mu_1) + \beta_{11}(\gamma_2+\mu_2)]}, \tag{5}$$

we can write $R_e(v)$ as a univariate function:

$$\begin{aligned} R_e(v_1, v_2) &= R_e(N' - v_2, v_2) \\ &= \begin{cases} \frac{\beta_{22}(S_2 - \eta v_2)}{\gamma_2+\mu_2} + \sqrt{\beta_{12}\beta_{21}(S_1 - \eta N' + \eta v_2)(S_2 - \eta v_2)}, \\ \qquad v_2 \le \phi(N') \\ \frac{\beta_{11}(S_1 - \eta N' + \eta v_2)}{\gamma_1+\mu_1} + \sqrt{\beta_{12}\beta_{21}(S_1 - \eta N' + \eta v_2)(S_2 - \eta v_2)}, \\ \qquad v_2 > \phi(N') \end{cases} \end{aligned} \tag{6}$$

with $0 \le v_2 \le \min(N', S_2)$.

Proposition 1. *$v \mapsto R_e(N' - v, v)$ is a piecewise concave function, and therefore the minimum is at an extreme point: $v_2^* \in \{0, \phi(N'), \min(N', S_2)\}$.*

Proof. We calculate the first derivative

$$R'_e(N'-v,v)=\begin{cases}-\frac{\beta_{22}\eta}{\gamma_2+\mu_2}+\frac{\sqrt{\beta_{12}\beta_{21}}}{2}\frac{\eta(S_2+\eta N'-S_1-2\eta v)}{\sqrt{(S_1-\eta N'+\eta v)(S_2-\eta v)}}, & v\le\phi(N)\\ \frac{\beta_{11}\eta}{\gamma_1+\mu_1}+\frac{\sqrt{\beta_{12}\beta_{21}}}{2}\frac{\eta(S_2+\eta N'-S_1-2\eta v)}{\sqrt{(S_1-\eta N'+\eta v)(S_2-\eta v)}}, & v>\phi(N)\end{cases} \tag{7}$$

In both cases

$$\begin{aligned}R''_e(N'-v,v)&=-\frac{\sqrt{\beta_{12}\beta_{21}}}{2}\eta^2\frac{2}{\sqrt{(S_1-\eta N'+\eta v)(S_2-\eta v)}}\\&\quad-\frac{\sqrt{\beta_{12}\beta_{21}}}{2}\eta^2\frac{(S_2+\eta N'-S_1-2\eta v)^2}{2\big((S_1-\eta N'+\eta v)(S_2-\eta v)\big)^{3/2}}\\&\le 0\end{aligned} \tag{8}$$

Therefore, the function is piecewise concave: the minimum is global and will be at an extreme point: $v_2^*\in\{0,\phi(N'),\min(N',S_2)\}$. □

We can further refine the solution when $\phi(N')<0$ or $\phi(N')>1$. In that case, $v_2^*\in\{0,\min(N',S_2)\}$, since $0\le v_2^*\le 1$. When $\phi(N')<0\le v_2$, we can establish two additional results.

Proposition 2. *If $N'\le S_2$ and $N'\ge\frac{\beta_{12}\beta_{21}}{\eta\beta_{11}^2}(S_1-S_2)(\gamma_1+\mu_1)^2$ or if $N'>S_2$ and $N'\ge\frac{1}{\eta}\Big[S_1-S_2+\eta S_2-\Big(\frac{\beta_{11}}{\gamma_1+\mu_1}\Big)^2\frac{\eta S_2}{\beta_{12}\beta_{21}}\Big]$, then $v_2^*=0$.*

Proof. When $\phi(N')<0$, since $v_2\ge 0$, we have $\phi(N')<v_2$ for all feasible v_2, and from Proposition 1, the optimal solution v_2^* can only be 0 or $\min(N',S_2)$. From (6), we have

$$\begin{aligned}R_e(N'-v_2,v_2)&=\frac{\beta_{11}(S_1-\eta N'+\eta v_2)}{\gamma_1+\mu_1}\\&\quad+\sqrt{\beta_{12}\beta_{21}(S_1-\eta N'+\eta v_2)(S_2-\eta v_2)}\end{aligned}$$

We first consider the case where $N'\le S_2$. We calculate

$$\begin{aligned}&R_e(N',0)-R_e(0,N')\\&=\frac{-\beta_{11}\eta N'}{\gamma_1+\mu_1}+\sqrt{\beta_{12}\beta_{21}}\Big(\sqrt{S_1S_2-\eta N'S_2}-\sqrt{S_1S_2-\eta N'S_1}\Big)\\&\le\frac{-\beta_{11}\eta N'}{\gamma_1+\mu_1}+\sqrt{\beta_{12}\beta_{21}}\Big|\sqrt{S_1S_2-\eta N'S_2}-\sqrt{S_1S_2-\eta N'S_1}\Big|\\&\le\frac{-\beta_{11}\eta N'}{\gamma_1+\mu_1}+\sqrt{\beta_{12}\beta_{21}}\sqrt{|\eta N'(S_2-S_1)|}\\&=\sqrt{\eta N'}\Big(\frac{-\beta_{11}\sqrt{\eta N'}}{\gamma_1+\mu_1}+\sqrt{\beta_{12}\beta_{21}}\sqrt{S_1-S_2}\Big)\end{aligned}$$

where we used $|\sqrt{a}-\sqrt{b}|\le\sqrt{|a-b|}$ in the second inequality. Additionally, we have

$$\frac{-\beta_{11}\sqrt{\eta N'}}{\gamma_1+\mu_1}+\sqrt{\beta_{12}\beta_{21}}\sqrt{S_1-S_2}\le 0\iff N'\ge\frac{\beta_{12}\beta_{21}(S_1-S_2)}{\eta\beta_{11}^2}(\gamma_1+\mu_1)^2$$

Therefore

$$N'\ge\frac{\beta_{12}\beta_{21}}{\eta\beta_{11}^2}(S_1-S_2)(\gamma_1+\mu_1)^2\implies R_e(N',0)-R_e(0,N')\le 0$$

and it is optimal to vaccinate group 1.

We now consider the case $S_2<N'\le S_1$. We have

$$\begin{aligned}&R_e(N',0)-R_e(N'-S_2,S_2)\\&=\frac{-\beta_{11}\eta S_2}{\gamma_1+\mu_1}\\&\quad+\sqrt{\beta_{12}\beta_{21}((S_1-\eta N')S_2-(S_1-\eta N'+\eta S_2)(S_2-\eta S_2))}\\&\le\frac{-\beta_{11}\eta S_2}{\gamma_1+\mu_1}+\sqrt{\beta_{12}\beta_{21}\eta S_2|S_2-\eta S_2-S_1+\eta N'|}\end{aligned}$$

Since $N'\le S_1$, we have $S_2-\eta S_2-S_1+\eta N'\le S_2-\eta S_2-S_1+\eta S_1=(1-\eta)(S_2-S_1)\le 0$. Therefore

$$R_e(N',0)-R_e(N'-S_2,S_2)\le\frac{-\beta_{11}\eta S_2}{\gamma_1+\mu_1}+\sqrt{\beta_{12}\beta_{21}\eta S_2(S_1-\eta N'-S_2+\eta S_2)}$$

Additionally

$$\begin{aligned}&N'\ge\frac{1}{\eta}\left[S_1-S_2+\eta S_2-\Big(\frac{\beta_{11}}{\gamma_1+\mu_1}\Big)^2\frac{\eta S_2}{\beta_{12}\beta_{21}}\right]\\&\implies R_e(N',0)-R_e(N'-S_2,S_2)\le 0\end{aligned}$$

and it is optimal to vaccinate group 1. □

Let R_e^* be the optimal effective reproduction number. We establish conditions under which $R_e^*\le 1$.

Proposition 3. *(i) If $N'\le S_2$ and $v_2^*=\min(N',S_2)=N'$, then $R_e^*\le 1$ if and only if $N'\ge\frac{1}{\eta}\Big(S_2-\frac{\big(1-\frac{\beta_{11}S_1}{\gamma_1+\mu_1}\big)^2}{\beta_{12}\beta_{21}S_1}\Big)$.*
(ii) If $N'>S_2$ and $v_2^*=\min(N',S_2)=S_2$, then $R_e^*\le 1$ if and only if $N'\ge\frac{1}{\eta}\Big(S_1+\eta S_2-\Big(\frac{-\sqrt{\beta_{12}\beta_{21}S_2(1-\eta)}+\sqrt{\Delta_1}}{2\beta_{11}/(\gamma_1+\mu_1)}\Big)^2\Big)$ where $\Delta_1=\beta_{12}\beta_{21}S_2(1-\eta)+4\frac{\beta_{11}}{\gamma_1+\mu_1}$.
(iii) If $v_2^*=0$, then $R_e^*\le 1$ if and only if $N'\ge\frac{1}{\eta}\Big(S_1-\Big(\frac{-\sqrt{\beta_{12}\beta_{21}S_2}+\sqrt{\Delta_2}}{2\beta_{11}/(\gamma_1+\mu_1)}\Big)^2\Big)$ where $\Delta_2=\beta_{12}\beta_{21}S_2+4\frac{\beta_{11}}{\gamma_1+\mu_1}$.

Proof. (i) $v_2^*=N'$: We have $R_e^*(N')=R_e(0,N')=\frac{\beta_{11}S_1}{\gamma_1+\mu_1}+\sqrt{\beta_{12}\beta_{21}S_1(S_2-\eta N')}$. After algebraic manipulation, we find that

$$R_e^*\le 1\iff N'\ge\frac{1}{\eta}\Big(S_2-\frac{\big(1-\frac{\beta_{11}S_1}{\gamma_1+\mu_1}\big)^2}{\beta_{12}\beta_{21}S_1}\Big)$$

(ii) $v_2^*=S_2$: We have $R_e^*(N')=R_e(N'-S_2,S_2)=\frac{\beta_{11}(S_1-\eta N'+\eta S_2)}{\gamma_1+\mu_1}+\sqrt{\beta_{12}\beta_{21}(S_1-\eta N'+\eta S_2)S_2(1-\eta)}$. Let $x=\sqrt{S_1-\eta N'-\eta S_2}$. Substituting N' by $(S_1+\eta S_2-x^2)/\eta$ yields

$$R_e^*(x)\le 1\iff\frac{\beta_{11}x^2}{\gamma_1+\mu_1}+\sqrt{\beta_{12}\beta_{21}S_2(1-\eta)}x-1\le 0.$$

Solving this quadratic inequality, we have $\Delta_1=\beta_{12}\beta_{21}S_2(1-\eta)+4\frac{\beta_{11}}{\gamma_1+\mu_1}>0$. The two roots are $r_1=\frac{-\sqrt{\beta_{12}\beta_{21}S_2(1-\eta)}-\sqrt{\Delta_1}}{2\beta_{11}/(\gamma_1+\mu_1)}<0$ and $r_2=\frac{-\sqrt{\beta_{12}\beta_{21}S_2(1-\eta)}+\sqrt{\Delta_1}}{2\beta_{11}/(\gamma_1+\mu_1)}>0$. Since $x\ge 0$, we have $R_e^*(x)\le 1\iff 0\le x\le r_2$. Finally,

$$R_e^*(N')\le 1\iff N'\ge\frac{1}{\eta}\left(S_1+\eta S_2-\left(\frac{-\sqrt{\beta_{12}\beta_{21}S_2(1-\eta)}+\sqrt{\Delta_1}}{2\beta_{11}/(\gamma_1+\mu_1)}\right)^2\right).$$

(iii) $v_2^*=0$: We have $R_e^*(N')=R_e(N',0)=\frac{\beta_{11}(S_1-\eta N')}{\gamma_1+\mu_1}+\sqrt{\beta_{12}\beta_{21}(S_1-\eta N')S_2}$. The proof is similar to (ii). Defining $x=\sqrt{S_1-\eta N'}$, we have

$$R_e^*(x)\le 1\iff\frac{\beta_{11}x^2}{\gamma_1+\mu_1}+\sqrt{\beta_{12}\beta_{21}S_2}x-1\le 0.$$

Let $\Delta_2=\beta_{12}\beta_{21}S_2+4\frac{\beta_{11}}{\gamma_1+\mu_1}>0$. The two roots of this quadratic equation are $r_1=\frac{-\sqrt{\beta_{12}\beta_{21}S_2}-\sqrt{\Delta_2}}{2\beta_{11}/(\gamma_1+\mu_1)}<0$ and $r_2=\frac{-\sqrt{\beta_{12}\beta_{21}S_2}+\sqrt{\Delta_2}}{2\beta_{11}/(\gamma_1+\mu_1)}>0$. Therefore

$$R_e^*(N')\le 1\iff N'\ge\frac{1}{\eta}\left(S_1-\left(\frac{-\sqrt{\beta_{12}\beta_{21}S_2}+\sqrt{\Delta_2}}{2\beta_{11}/(\gamma_1+\mu_1)}\right)^2\right).$$ □

5. Example: Minimizing R_e for COVID-19

Similar to Rao and Brandeau [12], we consider the case of COVID-19 spreading in two interacting populations, and use data reflective of the initial COVID-19 outbreak in New York. Group 1 (84% of the population) comprises individuals younger than age 65, and group 2 (16% of the population) comprises individuals age 65 and older. We assume that $S_1=80.9\%, S_2=16.0\%, \gamma_1=0.079, \gamma_2=0.064, \mu_1=0.00012, \mu_2=0.00460, \beta_{11}=0.403, \beta_{12}=0.071, \beta_{21}=0.154, \beta_{22}=0.613, \eta=0.9$ [12]. With these parameter values, the reproduction number with no intervention is 4.31, which is consistent with other studies that aim to estimate R_0 in an initial outbreak while taking into account transmission from unconfirmed cases [17–20].

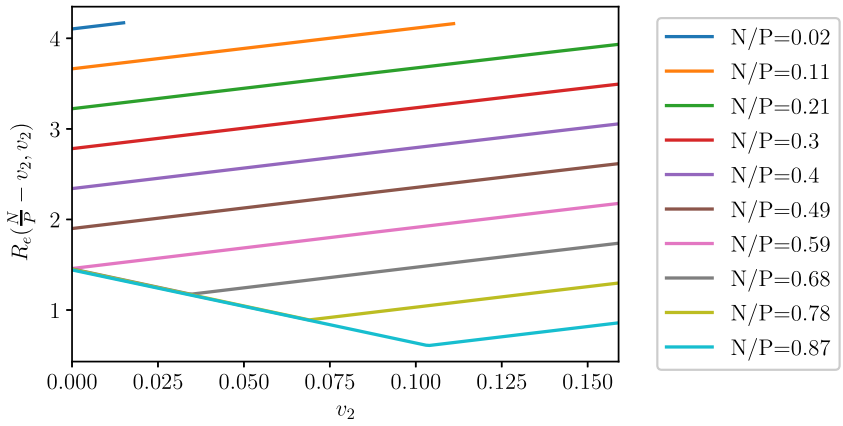

Fig. 2. R_e as a function of vaccination level for different amounts of vaccine available (N/P, colored lines) and different allocations between groups 1 and 2 ($\frac{N}{P} - v_2, v_2$).

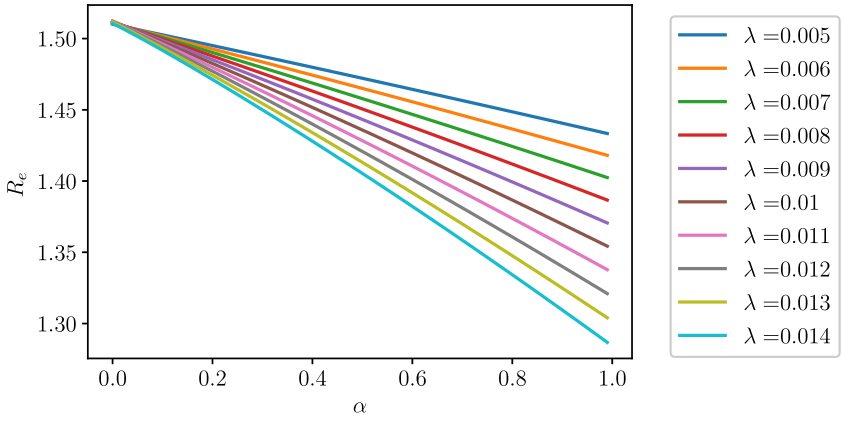

Fig. 3. R_e as a function of constant daily vaccination at different levels (λ, colored lines) and different allocations between groups 1 and 2 ($\alpha\lambda, (1-\alpha)\lambda$).

The optimal allocation can be determined numerically from (6). Plugging in the parameter values, we find that for $N/P \leq 0.59$ we have $\phi(N/P) \leq 0$, and thus

$$R_e(v) = \frac{\beta_{11}(S_1 - \eta v_1)}{\gamma_1 + \mu_1} + \sqrt{\beta_{12}\beta_{21}(S_1 - \eta v_1)(S_2 - \eta v_2)}.$$

Evaluating the conditions from Proposition 2, for $N/P \leq S_2$, we find

$$\frac{\beta_{12}\beta_{21}}{\eta\beta_{11}^2}(S_1 - S_2)(\gamma_1 + \mu_1)^2 = 0.0003 < N/P,$$

and for $S_2 \leq N/P \leq 0.59$, we find

$$\frac{1}{\eta}\left[S_1 - S_2 + \eta S_2 - \left(\frac{\beta_{11}}{\gamma_1 + \mu_1}\right)^2 \frac{\eta S_2}{\beta_{12}\beta_{21}}\right] = -384 < N/P.$$

Thus, from the analytical conditions we find that all vaccine should be allocated to individuals in group 1 for $0.0003 \leq N/P \leq 0.59$. From Proposition 3, we find that $R_e^* \leq 1$ if and only if $N/P \geq 0.85$. Therefore, for $N/P \leq 0.59$, R_e cannot be less than 1.

We can show numerically that for any amount of vaccine up to $N/P \leq 0.59$ (including $0 \leq N/P \leq 0.0003$), it is optimal to vaccinate group 1 only (Fig. 2). For $N/P > 0.59$, allocating a portion of the vaccines to individuals in group 2 is optimal: for example, $(v_1^*, v_2^*) = (0.65, 0.03)$ for $N/P = 0.68$ and $(v_1^*, v_2^*) = (0.69, 0.09)$ for $N/P = 0.78$. In these cases, we find that $v_2^* = \phi(N/P)$.

We compare the values of the effective reproduction number under optimal allocation, R_e^*, and equal allocation, $R_e^{eq} = R_e(\frac{N}{P}\frac{S_1(0)}{S_1(0)+S_2(0)}, \frac{N}{P}\frac{S_2(0)}{S_1(0)+S_2(0)})$ (Table 1). We find that R_e^* is up to 23% lower than R_e^{eq}.

Our analysis assumes that all vaccination occurs at time 0, but in practice vaccination campaigns take place over time. We perform numerical simulations in which vaccination occurs over 10 days, with $\lambda = 0.5\%$ to 1.4% of the population being vaccinated each day (thus, $N/P \leq 0.14$), and calculate R_e after 10 days. We find that it is optimal to vaccinate only younger individuals (Fig. 3), which is consistent with our analytical findings for a one-time vaccine allocation.

Table 1
R_e^{eq}, R_e^*, and percentage decrease for different amounts of vaccine available (N/P).

N/P	R_e^{eq}	R_e^*	$\frac{R_e^{eq} - R_e^*}{R_e^{eq}}$
0.02	4.12	4.10	0.3%
0.11	3.75	3.66	2.2%
0.21	3.38	3.22	4.6%
0.30	3.01	2.78	7.5%
0.40	2.64	2.34	11.2%
0.49	2.27	1.90	16.2%
0.59	1.90	1.46	23.2%
0.68	1.53	1.18	23.1%
0.78	1.16	0.89	23.2%
0.87	0.79	0.61	22.9%

6. Conclusion

The analytical conditions we develop provide a simple means of determining the optimal allocation of vaccine between two population groups to minimize R_e. Our analysis shows that the optimal vaccination strategy depends on the number of vaccines available: an all-or-nothing approach is only optimal when vaccine supplies are limited. Therefore, before determining the vaccine allocation, policy makers must first estimate the proportion of the population that can be vaccinated, taking into account not only vaccine supply but also other limiting factors such as operational constraints and vaccine hesitancy. For instance, recent

polls suggest that approximately 30% of the U.S. population is hesitant about COVID-19 vaccination, suggesting that $N/P \leq .70$ for COVID-19 vaccination [21,22].

We assumed that $N/P \leq S_1(0)$ in order to simplify calculations. It is straightforward to extend the analysis to the case $N/P \leq S_1(0) + S_2(0)$, a less limited vaccine supply. To do so, one must separately consider the case $N/P \geq S_1(0)$, and add the constraint $v_2 \geq N' - S_1(0)$ to the univariate problem (6); otherwise $R_e(N' - v_2, v_2)$ would not be well defined. The minimum will again be at an extreme point: $v_2^* \in \{N' - S_1(0), \phi(N'), S_2(0)\}$.

Our analysis is based on a relatively simple SIR model. We illustrate the model with an example of COVID-19. Although COVID-19 may be more accurately modeled with an SEIR model, several studies have used an SIR model for COVID-19 and have obtained a good fit to the data [12,23–25]. Further work is needed to extend our analytical approach to more complex compartmental models that can capture more details of disease transmission and progression.

Finally, we consider a static policy with a single allocation of vaccine at time 0. In numerical simulations, we consider a constant daily vaccination rate and find that the same solution as for one-time allocation is still optimal. In practice, because vaccination efforts will occur over time, the vaccination policy can evolve. A heuristic dynamic solution would be to recalculate R_e at certain points in time and then adjust the vaccine allocation using the optimization criteria we provide. Further work is needed to extend our analysis to a multi-period setting.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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