Supporting Information

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1. Expected Impact of Targeted Interventions

1.1. Objective. In the following section, we present our approach to calculating the expected impact of targeted interventions. Throughout, we assume that the number of new infections per group is observed and that at-risk contacts are reciprocal. We do not require information on the precise contact pattern within and between groups. We relate the magnitude of a targeted intervention measure to the expected change in the effective reproduction number of the infection. We will rely on a more mathematical derivation of our results as compared to the main text, and relegate the detailed derivations to section 3. Table S1 provides a key to the mathematical notation.

1.2. Epidemic Growth in a Structured Host Population. The host population is partitioned into m groups. We use k_{ij} to denote the mean number of individuals in group i that are infected by a single individual in group j during its entire infection period. We will refer to the matrix $\boldsymbol{K}$ with elements k_{ij} as the reproduction matrix. The reproduction matrix provides a fundamental characterization of transmission dynamics in a structured host population. For deterministic models it is known as the "next generation matrix" (1), for stochastic models it is known as the "mean offspring matrix" (2). For individual-based simulation models that exhibit periods of sustained exponential epidemic growth, such as in ref. 3, such a matrix exists implicitly.

We require that an infection, when introduced in an arbitrary group, can spread to every other group in the population within a finite number of generations of infection. For most infections in humans this requirement will be met. This requirement ensures that the reproduction matrix $\boldsymbol{K}$ is primitive, and primitivity of the matrix guarantees the existence of a unique and real positive value of the top eigenvalue R and the existence of a unique real positive value for the elements of the associated right eigenvector $\boldsymbol{w}_1$ and left eigenvector $\boldsymbol{v}_1$ via the so-called "Perron-Frobenius Theorem," see refs 1,4.

For a large class of transmission models, including the standard "Susceptible– Infectious–Recovered" (SIR) model, which will be presented later in section 2.2, Eq. **9**, the reproduction matrix $\boldsymbol{K}$ can be written as

$$\boldsymbol{K} = \boldsymbol{SABC}.$$

The matrices $\boldsymbol{S}$, $\boldsymbol{A}$, $\boldsymbol{B}$, and $\boldsymbol{C}$ have the following epidemiological interpretation.

The matrix $\boldsymbol{S}$ refers to the immunological naiveté of the contacted individuals: it is a matrix with the group-specific number of susceptible individuals at time t as elements $s_1, s_2, \ldots, s_m$ on the diagonal, and zeros elsewhere. These numbers of susceptible individuals will change over time during an epidemic, and therefore the matrices $\boldsymbol{S}$ and $\boldsymbol{K}$ will vary over time. When the dependency on time is obvious from the context, we simplify our notation and denote $s_i(t)$ as s_i, $\boldsymbol{S}(t)$ as $\boldsymbol{S}$ and $\boldsymbol{K}(t)$ as $\boldsymbol{K}$.

The matrix $\boldsymbol{A}$ summarizes the per contact probabilities of acquiring infection during contact: it is a matrix with the group-specific per contact probability of becoming infected $a_1, a_2, \ldots, a_m$ on the diagonal, and zeros elsewhere.

The contact matrix $\boldsymbol{B}$ gives the contact pattern: it is a matrix with elements b_{ij}, the contact parameter of individuals in group j with others in group i. (Using the notation of the standard deterministic SIR transmission model of section 2.2, we have $b_{ij} = \beta_{ij}/\gamma$). The contact parameter b_{ij} is defined such that the total number of contacts from age group j to age group i is given by $p_{ij} = n_i b_{ij} n_j$, where n_i gives the population size of group i and n_j gives the population size of group j. We require the contact matrix $\boldsymbol{B}$ to be symmetric, and this symmetry is guaranteed when infectious agents are transmitted predominantly through direct contact or through small infectious droplets between persons who are present at the same time at the same location.

The matrix $\boldsymbol{C}$ gives the infectivity of the infected individuals: it is a matrix that has the group-specific per contact probability of transmitting infection $c_1, c_2, \ldots, c_m$ on the diagonal and zeros elsewhere.

The top eigenvalue R of the reproduction matrix $\boldsymbol{K}$ is often referred to as the "effective reproduction number," it gives the number of secondary infections produced by a typical infective in the structured population. It is related to the top right eigenvector $\boldsymbol{w}_1$ of the reproduction matrix through the standard characteristic equation (refs. 4 and 5):

$$\boldsymbol{K}\boldsymbol{w}_1 = R\boldsymbol{w}_1. \quad [1]$$

The top eigenvalue R is also related to the top left eigenvector $\boldsymbol{v}_1$ through another characteristic equation (refs. 4 and 5):

$$\boldsymbol{v}_1^{\top}\boldsymbol{K} = R\boldsymbol{v}_1^{\top}. \quad [2]$$

To avoid any ambiguity on the precise values of the eigenvector elements we choose the elements of $\boldsymbol{w}_1$ such that they sum to 1 (that is, $\sum_i w_{i1} = 1$) and the elements of $\boldsymbol{v}_1$ such that the product of left and right eigenvectors equals 1 (that is, $\sum_i v_{i1} w_{i1} = 1$).

We are interested how small changes in the reproduction matrix $\boldsymbol{K}$ will affect its top eigenvalue R. We can write the change in top eigenvalue $\mathrm{d}R$ out in terms of three components: the top left eigenvector $\boldsymbol{v}_1$, the change in the reproduction matrix $\mathrm{d}\boldsymbol{K}$, and the top right eigenvector $\boldsymbol{w}_1$ (refs. 4 and 5):

$$\mathrm{d}R = \boldsymbol{v}_1^{\top}\mathrm{d}\boldsymbol{K}\boldsymbol{w}_1. \quad [3]$$

A detailed derivation is given in section 3.2. This equation shows that we need to know the top eigenvectors $\boldsymbol{v}_1$ and $\boldsymbol{w}_1$. The next sections describe how the top right eigenvector $\boldsymbol{w}_1$ can be related to the group-specific number of new infections, and how the top left eigenvector $\boldsymbol{v}_1$ can be related to the group-specific force of infection.

1.3. Relating the Top Right Eigenvector w_1 to New Infections. We consider an infection that is spreading through a population according to the reproduction matrix $\boldsymbol{K}$. We have an observation interval that covers the period from t to $t + \Delta t$. We count the number of new infections in the ith group during the observation interval, and we denote this number by $x_i(t)$ and the vector with numbers of infections of all groups as $\boldsymbol{x}(t)$. We assume that there have been no interventions or other major perturbations immediately before time t, and that the distribution of number of new infections over groups before time t was close to the distribution of new infections over groups during the observation interval. When we choose the duration of our observation intervals at, say, two generations of infection, and when the distribution of number of infections changes only slightly during the interval, this distribution of number of new infections during the observation interval $\boldsymbol{x}(t)$ is approximately proportional to the right eigenvector $\boldsymbol{w}_1$. We denote this for each element of the vector as

$$w_{i1} \approx f x_i(t), \quad [4]$$

where $f = 1/\sum_i x_i(t)$ is a normalization constant. A detailed derivation is given in section 3.3. This equation enables us to infer the top right eigenvector from the observed number of infections over an observation interval.

1.4. Relating the Top Left Eigenvector v_1 to the Force of Infection. When the contact rate matrix $\boldsymbol{B}$ is symmetric, as described in section 1.2, we can infer an explicit expression of each element of the top left eigenvector $\boldsymbol{v}_1$

$$v_{i1} \approx g \frac{c_i}{a_i} \frac{x_i(t)}{s_i(t)}. \quad [5]$$

Here, $g = \sum_i x_i(t) / \sum_i \frac{c_i}{a_i} \frac{x_i^2(t)}{s_i(t)}$ is a normalization constant. A detailed derivation is provided in section 3.4. This equation allows us to infer the top left eigenvector $\boldsymbol{v}_1$ from the "force of infection", $\frac{x_i(t)}{s_i(t)}$, the per susceptible risk of being infected during a given observation interval.

1.5. Sensitivity of Reproduction Number to Targeted Social Distancing. We are interested in the impact of social distancing measures that aim to reduce the number of at-risk contacts between individuals in the ith group. We denote the total number of contacts within group i as $p_{ii} = {n_i}^2 b_{ii}$. The corresponding perturbation of the reproduction matrix per added or prevented contact within group i is

$$\mathrm{d}k_{ii} = \frac{a_i s_i c_i}{n_i^2} \mathrm{d}p_{ii}, \quad [6]$$

and none of the other elements of the reproduction matrix $\boldsymbol{K}$ changes when the number contacts within group i are altered. A detailed derivation is given in section 3.5.

Now we turn to Eq. **3** for sensitivity of epidemic growth: $\mathrm{d}R = \boldsymbol{v}_1^{\top}(\mathrm{d}\boldsymbol{K})\boldsymbol{w}_1$. We substitute the approximation of the the right eigenvector $\boldsymbol{w}_1$ based on the observed numbers of new infections (Eq. **4**), the perturbation of the reproduction matrix $\mathrm{d}\boldsymbol{K}$ that results from targeted reduction of contacts (Eq. **6**), and the approximation of the left eigenvector $\boldsymbol{v}_1$ based on the observed force of infection (Eq. **5**). This gives an equation for the decrease in reproduction number by preventing a single contact within the group i:

$$\frac{\mathrm{d}R}{\mathrm{d}p_{ii}} \approx -h c_i^2 \left(\frac{x_i(t)}{n_i} \right)^2,$$

where $h = fg = 1/\sum_i \frac{c_i}{a_i} \frac{x_i^2}{s_i}$. The term in brackets, $\frac{x_i(t)}{n_i}$, is the observed incidence of infection in group i over an observation interval that covers the period from t to $t + \Delta t$. This result shows that the expected decrease in reproduction number R by preventing a single contact within the ith group is proportional to the squared incidence in the ith group. The equation allows for quantification of the expected gains of social distancing in absence of information on the precise contact structure of the population.

1.6. Sensitivity of Reproduction Number to Targeted Vaccination. We are interested in the impact of vaccination targeted at unvaccinated susceptible individuals in group i. The number of new vaccines allocated to the ith group is indicated as $\mathrm{d}u_i$. The vaccine efficacy for the ith group is indicated as q_i. The impact of vaccination on the reproduction matrix $\boldsymbol{K}$ depends on the protective effect of the vaccine. Vaccination of a susceptible person can reduce a number of individual outcomes, such as infection or infectivity of infected individuals. In the following sections we assume that vaccination of susceptible individuals renders them completely immune to infection with a probability q_i, and leaves them completely susceptible with a probability $1 - q_i$ (an "all-or-nothing vaccine"). Alternatives are, for example, a vaccine that reduces the probability of infection with a factor q_i during each infectious contact (a "leaky vaccine") or a vaccine that reduces the infectivity of infected individuals by a factor q_i. For each of these alternatives we can derive the resulting change in the reproduction matrix, essentially following ideas as introduced elsewhere (6). The results for these alternatives differ up to a factor a_i or c_i. For brevity, we give only the results for so-called all-or-nothing vaccines. The perturbation of the reproduction matrix that results from vaccination is then

$$\mathrm{d}\boldsymbol{K}\boldsymbol{w}_1 = -\frac{q_i}{s_i} \mathrm{d}u_i R \boldsymbol{w}_i. \quad [7]$$

A detailed derivation of this result is provided in section 3.5. We determine the impact of targeted vaccination by returning to Eq. **3** for sensitivity of epidemic growth: $\mathrm{d}R = \boldsymbol{v}_1^{\top}(\mathrm{d}\boldsymbol{K})\boldsymbol{w}_1$. We substitute the definition of the top left eigenvector in terms of observed force of infection (Eq. **5**) and the perturbation of the reproduction matrix as given above (Eq. **7**). We obtain an equation for the relative change in reproduction number if vaccination is targeted only at susceptible individuals in group i:

$$\frac{1}{R} \frac{\mathrm{d}R}{\mathrm{d}u_i} \approx -h q_i \frac{c_i}{a_i} \left(\frac{x_i(t)}{s_i(t)} \right)^2.$$

The term in brackets, $x_i(t)/s_i(t)$, is the force of infection in group i during the observation interval that covers the period from t to $t + \Delta t$. This result shows that the expected relative decrease in reproduction number R by vaccinating one susceptible individual in group i is proportional to the squared force of infection in group i.

We are also interested in the impact of vaccination targeted at unvaccinated individuals in group i who can be either susceptible or immune due to natural infection. The number of new vaccines allocated to the ith group is indicated as $\mathrm{d}u_i$. The vaccine efficacy for the ith group is indicated as q_i. The perturbation of the reproduction matrix that results from vaccination is now

$$\mathrm{d}\boldsymbol{K}\boldsymbol{w}_1 = -\frac{q_i}{n_i} \mathrm{d}u_i R \boldsymbol{w}_i. \quad [8]$$

A detailed derivation of this result is given in section 3.5. We determine the impact of targeted vaccination by returning to Eq. **3** for sensitivity of epidemic growth: $\mathrm{d}R = \boldsymbol{v}_1^{\top}(\mathrm{d}\boldsymbol{K})\boldsymbol{w}_1$. We substitute the definition of the top left eigenvector in terms of observed force of infection (Eq. **5**) and the perturbation of the reproduction matrix as given above (Eq. **8**). We obtain an equation for the relative change in reproduction number if vaccination is targeted at both susceptible individuals and immune individuals in group i:

$$\frac{1}{R} \frac{\mathrm{d}R}{\mathrm{d}u_i} \approx -h q_i \frac{c_i}{a_i} \frac{x_i(t)}{s_i(t)} \frac{x_i(t)}{n_i}.$$

The term $x_i(t)/s_i(t)$ is the force of infection and the term $x_i(t)/n_i$ is the incidence of infection in group i during the observation interval that covers the period from t to $t + \Delta t$. This result shows that the expected relative decrease in reproduction number R by vaccinating one random individual in group i is proportional to the product of incidence and force of infection in group i. The equation allows for quantification of the expected gains of targeted vaccination in absence of the precise contact structure of the population.

1.7. Allocation of Stock of Vaccines in Structured Host Population. We are interested in minimizing the reproduction number. From the previous section we know that the expected impact of a single vaccination in group i is determined by the quantity $q_i \frac{c_i}{a_i} \frac{x_i(t)}{s_i(t)} \frac{x_i(t)}{n_i}$.

We can use this quantity to prioritize the groups by their expected impact of a single vaccination. This prioritization remains identical if we rank groups by the square root of this quantity which is $\sqrt{q_i \frac{c_i}{a_i} \frac{n_i}{s_i(t)} \frac{x_i(t)}{n_i}}$. We will refer to this quantity as the "importance weight" of group i, as it scores the importance of group i for their expected impact on transmission if one individual from that group is vaccinated. The importance weight is proportional to the incidence of infection with a "correction factor" that accounts for possible differences in vaccine efficacy, per contact probability of acquiring infection, per contact probability of transmitting infection, and proportion of susceptible individuals. After a single individual has been vaccinated in group i, the importance weight for group i will decrease approximately by a quantity $\frac{q_i}{n_i}\sqrt{q_i \frac{c_i}{a_i} \frac{n_i}{s_i(t)} \frac{x_i(t)}{n_i}}$ whereas the importance weight for other groups in which no one was vaccinated will remain approximately the same (detailed derivation in section 3.6). We can use this information to approximate the optimal allocation of a large stock of vaccines, large enough to vaccinate, say, 50% of the entire population. The main idea is to divide the large stock into small units of one dose and allocate each dose sequentially to the group with the highest importance weight. After allocating each dose we readjust the importance weights and allocate the next dose; and so on, until we run out of vaccines or until all individuals are vaccinated.

This sequential allocation of an entire stock of vaccines is described by the following pseudocode:

(1) Divide the stock of vaccine into units, and label these units as $l = 1, 2, \ldots, z$.
(2) For each of the groups $i = 1, 2, \ldots, m$ assess the numbers of new infections x_i, the numbers of susceptible individuals s_i, and the numbers of individuals n_i.
(3) Calculate the value of the importance weight $y_i(1) = \sqrt{q_i \frac{c_i}{a_i} \frac{n_i}{s_i(t)} \frac{x_i(t)}{n_i}}$ for each of the groups.
(4) For each unit of vaccine $l = 1$ to $l = z$:
(4a) Find the group j with the largest value for its importance weight $y_j(l)$.
(4b) Allocate the lth unit of vaccine to an unvaccinated individual in group j.
(4c) The change in importance weight is obtained as $\frac{dy_i(1)}{du_i} = \frac{q_i}{n_i}\sqrt{q_i \frac{c_i}{a_i} \frac{n_i}{s_i(t)} \frac{x_i(t)}{n_i}}$.
(4d) Update the value of the importance weight for group j, $y_j(l+1) = y_j(l) - \frac{dy_j(1)}{du_j}$, leave the value of the importance weights for all other groups i unchanged: $y_i(l+1) = y_i(l)$ for all $i \neq j$.

The final outcome of this algorithm can be seen at once.

When all vaccines are allocated the last vaccine z was allocated to a group j with a final level for importance weights $r = y_j(z) = \max_i[y_i(z)]$. There is no group with a value for the ranking higher than this final level r, otherwise the last unit of vaccine would have been allocated to that group. For each group i the decrease in the importance weight over the entire allocation process is $y_i(1) - r$. This decrease can be related to the number of vaccines u_i that have been allocated to the ith group by dividing the decrease in importance weight $y_i(1) - r$ by the decrease per vaccination, $\frac{dy_i(1)}{du_i}$. This gives $u_i = \frac{y_i(1)-r}{\frac{dy_i(1)}{du_i}}$. Substiting the definitions for importance weight and its derivative and simplifying gives $u_i = \frac{n_i}{q_i}\left(1 - \frac{r}{\sqrt{q_i \frac{c_i}{a_i} \frac{n_i}{s_i(t)} \frac{x_i(t)}{n_i}}}\right)$. The number of vaccines that are allocated to any group i can now be inferred from the relative decrease in the importance weight:

$$u_i \approx \min\left[n_i(t), \frac{n_i}{q_i}\max\left[0, 1 - \frac{r}{\sqrt{q_i \frac{c_i}{a_i} \frac{n_i}{s_i(t)} \frac{x_i(t)}{n_i}}}\right]\right],$$

subject to a natural constraint of the system: the sum of units of vaccines allocated to each of the groups must equal the size of the stockpile $z = \sum_{i=1}^{i=n} u_i$. The min and max functions serve to guarantee that the number of vaccinations is positive and bounded by the number of individuals in each group. When we drop these obvious bounds, the equation above simplifies to

$$u_i \approx \frac{n_i}{q_i}\left(1 - \frac{r}{\sqrt{q_i \frac{c_i}{a_i} \frac{n_i}{s_i(t)} \frac{x_i(t)}{n_i}}}\right),$$

and the unknown value of the final level of importance weights r is uniquely determined by the constraint that the total amount allocated to all groups should equal the supply $z = \sum_{i=1}^{i=n} u_i$.

An easy way for numerically solving this system with its constraints is to compute a lookup table for stockpile size z and the corresponding allocation $u_1, u_2, \ldots, u_m$. Such a lookup table can be computed by incrementing the final level of importance weights r from 0 in small steps to $max_i(\sqrt{q_i \frac{c_i}{a_i} \frac{n_i}{s_i(t)} \frac{x_i(t)}{n_i}})$, and for each value of r we calculate the number of vaccines to be allocated to the ith group u_i and then the corresponding stockpile size of vaccines $z = \sum_{i=1}^{i=n} u_i$. We use the resulting lookup table to find for a given stockpile size z the corresponding allocation of vaccines u_i.

The allocation algorithm described here works by leveling the importance weights of all groups down to a final level of r, hence we call this algorithm "importance leveling." This algorithm allows us to find an allocation scheme of vaccine units that achieves a near-optimal reduction of the reproduction number during an epidemic. It requires information about the size of the stockpile to be allocated, z, the group-specific proportion of susceptible individuals, $\frac{s_i(t)}{n_i}$, and the group-specific incidence of infection during an observation interval $x_i(t)/n_i$. These variables can be observed in the early phase of the epidemic.

2. Test of Importance Leveling Allocation Against Simulated Data

2.1. Objective. We examine the performance of the importance leveling scheme in minimizing the reproduction number and slowing down epidemic growth using simulated data. We use a deterministic simulation model to generate the number of new cases during an observation interval early on in an emerging epidemic, and we use this simulated number of new infections to calculate the allocation of a limited number of vaccines using importance leveling as explained in section 1.7. We compare the time course of the epidemic when vaccines are allocated according to the importance leveling allocation with two other strategies: allocating vaccines at random and allocating vaccines according to an optimal allocation algorithm that provides the largest possible reduction in the reproduction number. This optimal allocation strategy is calculated with a general optimization algorithm called simulated annealing using knowledge on all contact parameters of the transmission model.

2.2. Transmission Model. We use a standard deterministic SIR transmission model that categorizes individuals as susceptible (S), infectious (I), or recovered and immune (R) (7). The population is partitioned into m groups. For this transmission model, the dynamics are given by the following system of ordinary differential equations:

$$\frac{dS_i}{dt} = -a_i S_i \sum_{j=1}^{j=n} \beta_{ij} c_j I_j$$

$$\frac{dI_i}{dt} = a_i S_i \sum_{j=1}^{j=n} \beta_{ij} c_j I_j - \gamma I_i$$

$$S_i + I_i + R_i = n_i. \quad [9]$$

Here, S_i is the number of susceptible individuals, I_i is the number of infected individuals, R_i is the number of recovered and immune individuals, and n_i is the total number of individuals in group i. The recovery rate γ gives the proportion of all infected individuals that recover per day; the contact parameters β_{ij} give the proportion of all individuals in group i that are contacted by single individual in group j during a day; the parameters c_j measure the per contact probability of transmitting infection for an infectious individual of group j; and the parameters a_i measure the per contact probability of becoming infected for an individual of group i. The parameters c_i and a_i take values in between 0 and 1, with the value 1 reserved for the group that is most infectious or most likely to be exposed during a contact event.

The effect of vaccination of individuals is implemented in this transmission model as a reduction of the number of susceptible individuals S_i. Vaccination of a small number of du_i susceptible individuals gives a decrease in number of susceptible individuals $dS_i = q_i du_i$ where the vaccine efficacy q_i gives the probability that a susceptible individual in group i becomes immune after vaccination.

A key variable that characterizes the epidemic growth is the reproduction number R, defined as the number of secondary cases produced by a typical infected individual. The value of the reproduction number is completely determined by the parameters of the SIR transmission model (1).

The parameters in Table S2 reflect an infectious agent spreading in a susceptible population with a reproduction number R at the start of the epidemic of 2.0, and a generation interval of 3.5 days. This choice of parameter values is consistent with a doubling time of number of new infections of 2.5 days in the initial phase of an epidemic, and this doubling time is typical for influenza pandemics. The host population is partitioned into six age groups: 0–5 years, 6–12 years, 13–19 years, 20–39 years, 40–59 years, and 60 years and older. The contact rates within and between these age groups are proportional to self-reported conversational contact rates as observed in the Netherlands (8); the population size by age reflects the size of the Dutch population at the time these conversational contacts were observed.

The simulated epidemic starts at day t = 0 with one infection in 40- to 59-year-old group in a population that is otherwise susceptible. In the initial phase of the simulated epidemic, from time $t = 0$ to $t + \Delta t = 14$, we monitor the number of new infections in each group. Over this monitoring period we calculate the group-specific incidence of infection, and use this group-specific incidence of infection to allocate a stock of z vaccine doses using the importance leveling algorithm described in section 1.8. Vaccine-induced immunity sets in 1 month after the end of the monitoring interval at $t = 44$. This allows for the time needed for vaccine delivery and development of an effective immune response.

2.3. Test Results. For the default parameter values and without interventions the epidemic will peak at day $t = 55$, the peak incidence of infection will be 46 new infections per 1000 persons per day, and at the end of the epidemic 75% of the population will have been infected (Fig. S1*A*). The age distribution of proportion infected is 0.65 for the 0- to 5-year-old group, 0.79 for the 6- to 12-year-old group, 0.86 for the 13- to 19-year-old group, 0.82 for the 20- to 39-year-old group, 0.75 for the 40- to 59-year-old group, and 0.58 for the 60-year and older group. If 20% of the population can be vaccinated and the vaccine is allocated at random, the timing of the peak incidence is delayed to day $t = 59$, the peak incidence is lowered to 19 new infections per 1,000 persons per day, and the proportion of the population that is infected is reduced to 49%. Allocating the same amount of vaccines but now allocating them according to the importance leveling scheme results in a further delay of the peak incidence to day $t = 61$. The peak incidence will be lowered further to 14 new infection per 1,000 persons per day, and the proportion of the population that is infected will be reduced further to 44%. At the end of the epidemic the proportion infected is 0.48 for the 0- to 5-year-old group, 0.47 for the 6- to 12-year-old group, 0.38 for the 13- to 19-year-old group, 0.44 for the 20- to 39-year-old group, 0.48 for the 40- to 59-year-old group, and 0.41 for the 60-year and older group. These results for importance leveling are nearly identical to the results obtained by optimal allocation of vaccines such as to minimize the reproduction number.

To investigate the robustness of the test results we conducted sensitivity analyses in which we systematically varied the vaccination coverage in a range from 0 to 50 percent. Fig. S1*B* shows the results for a vaccination coverage of 40%. Whereas random allocation results in increasing incidence after vaccination and leads to a proportion of 21% infected over the epidemic, both the importance leveling and optimal allocation schemes result in a decreasing incidence after vaccination and lead to a proportion of 13% infected for importance leveling and 10% infected for optimal allocation.

We explored adaptations to the simulation model, allowing for more realistic (Erlang) distributed durations of the latent period and infectious period (7). Fig. S1*C* shows the time course of the epidemic for such an adapted model with a different generation interval of 2.85 days. Here we observe a large difference in peak incidence between the alternative allocation strategies. Without vaccination, the peak incidence is 51 new infections per 1,000 persons per day. With random allocation at a coverage of 20% this can be reduced to 35 new infections per 1,000 persons per day. Importance leveling results in a much lower peak incidence of 16 new infections per 1,000 persons per day. Optimal allocation results in a peak incidence of 15 new infections per 1,000 persons per day. The results for the total percentage of the population infected are similar to the simulations for the default parameter setting.

We varied the reproduction number in a range from $R = 1.5$–3.0. Fig. S1*D* shows the time course of the epidemic for a reproduction number of $R = 1.7$. This value for reproduction number results in an epidemic that, without any interventions, will infect 64% of the population. With random allocation at a coverage of 20% the epidemic will infect 35% of the population. With importance leveling at a coverage of 20% the epidemic infects 28% of the population, which is nearly the same as the 27% achieved using optimal allocation. Again we observe a large difference in peak incidence: 28 new infections per 1,000 persons per day in an unchecked epidemic; eight new infections per 1,000 if vaccines are allocated at random; five new infections per 1,000 persons per day if vaccines are allocated according to importance leveling; and four new infections per 1,000 persons per day for optimal allocation.

We repeated the simulations with a different set of contact parameters β_{ij} that are based on self-reported conversational contacts in the Netherlands in 2007 (9). The simulated epidemic without vaccination resulted in a slightly lower peak incidence of 40 new infections per 1,000 persons per day, and at the end of the epidemic 70% of the population was infected. Again, the results for importance leveling at a coverage of 20% were very similar to the results for optimal allocation.

Two results emerge from the simulations. First, in all sensitivity analyses importance leveling and optimal allocation performed better than random allocation. Not only with respect to the

objective of reducing transmission, but also in reducing the peak incidence and reducing the proportion infected over the entire epidemic. We observed in nearly all sensitivity analyses, for nearly all groups, that the numbers of infections per groups were lower for the importance leveling and optimal allocation strategies than they were for random allocation of a given amount of vaccine. Second, the results for importance leveling are nearly identical to those for the optimal allocation for all sensitivity analyses. In other words, the importance leveling algorithm provides a good prediction of a vaccine allocation that minimizes the reproduction number and reduces the further spread of infection.

2.4. Uncertainty Cause by Stochastic Fluctuations in Number of Infections. In the initial phase of an outbreak, the numbers of new infections during an observation interval can be small. As a consequence, the estimated group-specific risk of infection might be uncertain. We tested the performance of the importance leveling scheme when the estimated risk of infection is uncertain. We simulated an initial "actual" risk of infection using a model with a contact pattern as presented in Table S2. We used the age-specific risk to calculate the probability p_i that a given infection occurs within age group i; these probabilities specify a multinomial probability distribution. We mimicked observation of the age distribution of a small number of infected cases by drawing a small number from this multinomial probability distribution. The "observed" risk of infection differed from the "actual" risk due to random fluctuations. We used this "observed" risk of infection in the importance leveling scheme to derive the allocation of vaccines, and evaluated the reduction in transmission achieved by this allocation using the same model that was used to generate the "actual" risk of infection. The results are shown in Fig. S2. The performance of importance leveling based on noisy observations is nearly always better than random allocation, and the performance of importance leveling approximates optimal allocation when the observations are based on a larger number of infections.

3. Mathematical Details

3.1. Objective. This sections provides the mathematical derivation of results that are used in section 1.1. For each result, we provide a reference to the subsection where this results supports the line of argument as laid out in section 1.1.

3.2. Epidemic Growth in a Structured Host Population. We decompose the reproduction matrix $\boldsymbol{K}$ into its standard diagonal form as

$$\boldsymbol{K} = \boldsymbol{W}\boldsymbol{\Lambda}\boldsymbol{W}^{-1}. \qquad [10]$$

Here, $\boldsymbol{\Lambda}$ is a diagonal matrix that has as elements the eigenvalues R, λ_2, …, λ_m on the diagonal and zeros elsewhere. The eigenvalues are in order of decreasing magnitude from R to λ_m. The matrix $\boldsymbol{W}$ has as columns the right eigenvectors $\boldsymbol{w}_1, \boldsymbol{w}_2, \ldots, \boldsymbol{w}_m$. The matrix $\boldsymbol{W}^{-1}$ is the inverse of the matrix $\boldsymbol{W}$, such that $\boldsymbol{W}^{-1}\boldsymbol{W} = \boldsymbol{I}$ where $\boldsymbol{I}$ is the identity matrix which has as elements 1 on the diagonal and zeros elsewhere. The matrix $\boldsymbol{W}^{-1}$ has as rows the left eigenvectors $\boldsymbol{v}_1, \boldsymbol{v}_2, \ldots, \boldsymbol{v}_m$. To avoid any ambiguity on the precise values of the elements of matrix $\boldsymbol{W}$ we choose the elements of each right eigenvector such that they are positive and sum to one.

Taking the differential of Eq. **10** and rearranging gives

$$\mathrm{d}\boldsymbol{\Lambda} = \boldsymbol{W}^{-1}\mathrm{d}\boldsymbol{K}\boldsymbol{W}.$$

Here we are interested how small changes in the reproduction matrix $\boldsymbol{K}$ will affect its top eigenvalue R. This change $\mathrm{d}R$ is given by the first element of matrix $\mathrm{d}\boldsymbol{\Lambda}$ and its value is

$$\mathrm{d}R = \boldsymbol{v}_1^{\top}(\mathrm{d}\boldsymbol{K})\boldsymbol{w}_1.$$

This result is used as Eq. **3** in subsection 1.2.

3.3. Relating Top Right Eigenvector w_1 to New Infections. In this section we establish the conditions for which the top right eigenvector $\boldsymbol{w}_1$ is proportional to the group-specific number of infections. We subdivide time into consecutive observation intervals during which the matrix remains approximately constant. The duration of such an observation interval is denoted as Δt. The number of new infections in each group at the start of the observation interval is given by $\boldsymbol{x}_0$. We are interested in the dynamics over successive generations of infection during the observation interval. After t generations of infection we have a number of new infections $\boldsymbol{x}_t$ that is given by

$$\boldsymbol{x}_t = \boldsymbol{K}^t\boldsymbol{x}_0.$$

Writing the reproduction matrix $\boldsymbol{K}$ in its diagonal form yields

$$\boldsymbol{x}_t = \boldsymbol{W}\boldsymbol{\Lambda}^t\boldsymbol{W}^{-1}\boldsymbol{x}_0.$$

We write out the matrix product in terms of eigenvalues and eigenvectors:

$$\boldsymbol{x}_t = (\boldsymbol{v}_1^{\top}\boldsymbol{x}_0)R^t\boldsymbol{w}_1 + (\boldsymbol{v}_2^{\top}\boldsymbol{x}_0)\lambda_2^t\boldsymbol{w}_2 + \ldots + (\boldsymbol{v}_m^{\top}\boldsymbol{x}_0).$$

All but the first term on the right hand side with the lower eigenvalues of the reproduction matrix $\boldsymbol{K}$ are relatively small and we can summarize them as a "correction term" $\boldsymbol{z}_t = (\boldsymbol{v}_2^{\top}\boldsymbol{x}_0)\lambda_2^t\boldsymbol{w}_2 + \ldots + (\boldsymbol{v}_m^{\top}\boldsymbol{x}_0)$. This gives

$$\boldsymbol{x}_t = (\boldsymbol{v}_1^{\top}\boldsymbol{x}_0)R^t\boldsymbol{w}_1 + \boldsymbol{z}_t. \qquad [11]$$

An upper bound for the correction term is $\boldsymbol{z}_t \le (\boldsymbol{x}_0 - \boldsymbol{v}_1^{\top}\boldsymbol{x}_0)|\lambda_2|^t$. The relative contribution of the correction term to x_t is $\frac{(\boldsymbol{x}_0 - \boldsymbol{v}_1^{\top}\boldsymbol{x}_0)}{\boldsymbol{v}_1^{\top}\boldsymbol{x}_0}\left(\frac{|\lambda_2|}{R}\right)^t$ and this contribution will decline exponentially with time because $|\lambda_2| < R$. As stated earlier, we assume that there have been no interventions or other major perturbations immediately before time t, and that the distribution of number of new infections over groups before time t is close to the distribution of new infections over groups during the observation interval, such that the correction term accounts for, say, 10% of the distribution of the distribution of infections at the start of the observation interval. Then we have an explicit criterion for keeping the relative contribution of the correction term below a preset level, of say 5%: as long as we choose the observation interval Δt long enough such that $\frac{(\boldsymbol{x}_0 - \boldsymbol{v}_1^{\top}\boldsymbol{x}_0)|\lambda_2|^{T_I}}{\boldsymbol{v}_1^{\top}\boldsymbol{x}_0 R^{T_I}} \le 0.05$, the correction term $\boldsymbol{z}_t$ can be safely neglected. We can make this argument more precise if we know the ratio of the top eigenvalue R to the second-largest eigenvalue λ_2. For the observed contact pattern as used in the simulation study (section 2 and Table S2) this ratio is 2.2. In that case, a correction term that accounts for 10% of the distribution of infections at the start of the observation interval would decrease exponentially fast to 5% after a single generation and to 2.5% after two generations. This suggests that, at least for contacts patterns similar to the observed pattern as used here, if we set the length of the observation interval to approximately two generations, the approximation error by neglecting the correction term is below the 5% level.

Summarizing, when we choose the duration of our observation intervals from t to Δt at, say, two generations of infection, the correction term can be neglected, and the distribution of new infections during the observation interval $\boldsymbol{x}_t$ is proportional to the right eigenvector $\boldsymbol{w}_1$:

$$\boldsymbol{x}(t) \propto \boldsymbol{w}_1(t) \qquad [12]$$

where the $\propto$ sign denotes "proportional to". This result is Eq. **4** in subsection 1.3.

3.4. Relating Top Left Eigenvector v_1 to Force of Infection. In this section we establish the conditions for which we can take the top left eigenvector as proportional to the observed risk of infection per susceptible—the so-called force of infection. To do this we invoke two arguments.

First, we note that for any reproduction matrix $\boldsymbol{K}$ there exists a nonsingular symmetric matrix $\boldsymbol{M}$ that transforms the reproduction matrix into the transposed reproduction matrix $\boldsymbol{K}^\top$, such that $\boldsymbol{MKM}^{-1} = \boldsymbol{K}^\top$. This transformation matrix $\boldsymbol{M}$ also projects the top left eigenvector along the top right eigenvector:

$$\boldsymbol{v_1} \propto \boldsymbol{Mw_1}.$$

Proof. We verify that the transformation matrix $\boldsymbol{M}$ projects the top left eigenvector along the top right eigenvector. We start out from the standard characteristic Eq. **1**

$$\begin{aligned}\boldsymbol{Kw}_1 &= R\boldsymbol{w}_1\\ \boldsymbol{MKw}_1 &= R\boldsymbol{Mw}_1\\ \boldsymbol{K}^\top(\boldsymbol{Mw_1}) &= R(\boldsymbol{Mw_1})\\ (\boldsymbol{Mw_1})^\top\boldsymbol{K} &= R(\boldsymbol{Mw_1})^\top.\end{aligned}$$

We obtain the second line from the first by premultiplying by $\boldsymbol{M}$, we obtain the third line from the second by using using the property $\boldsymbol{MKM}^{-1} = \boldsymbol{K}^\top$, which can be rewritten as $\boldsymbol{MK} = \boldsymbol{K}^\top\boldsymbol{M}$, and we obtain the fourth line from the third by transposing both sides of the equation.

As we have the characteristic equation $\boldsymbol{v}_1^\top\boldsymbol{K} = R\boldsymbol{v}_1^\top$ (this is Eq. **2**), it follows from the fourth and last line that $\boldsymbol{v_1} \propto \boldsymbol{Mw_1}$□

Second, we note that an explicit expression for the transformation matrix $\boldsymbol{M}$ can be obtained for a large class of transmission models, including the SIR transmission model presented in Eq. **9**. For such transmission models, the reproduction matrix can be expressed as a product of matrices:

$$\boldsymbol{K} = \boldsymbol{SABC}.$$

The constituent matrices $\boldsymbol{S}, \boldsymbol{A}, \boldsymbol{B}, \boldsymbol{C}$ are all symmetric. Taking the transpose of a product of symmetric matrices will reverse the order of the matrices in the product. This gives us an explicit expression for the transposed reproduction matrix:

$$\boldsymbol{K}^\top = \boldsymbol{CBAS}. \qquad [13]$$

The corresponding similarity transformation $\boldsymbol{M}$ that transforms $\boldsymbol{K}$ into its transpose $\boldsymbol{K}^\top$ is

$$\boldsymbol{M} = \boldsymbol{CA}^{-1}\boldsymbol{S}^{-1}.$$

Proof. We verify that this definition of $\boldsymbol{M}$ is correct by substitution:

$$\begin{aligned}\boldsymbol{MKM}^{-1} &= (\boldsymbol{CA}^{-1}\boldsymbol{S}^{-1})(\boldsymbol{SABC})(\boldsymbol{SAC}^{-1})\\ &= (\boldsymbol{CA}^{-1}\boldsymbol{S}^{-1})(\boldsymbol{SABC})(\boldsymbol{C}^{-1}\boldsymbol{AS})\\ &= \boldsymbol{C}(\boldsymbol{A}^{-1}\boldsymbol{S}^{-1}\boldsymbol{SA})\boldsymbol{B}(\boldsymbol{CC}^{-1})\boldsymbol{AS}\\ &= \boldsymbol{CBAS}\\ &= \boldsymbol{K}^\top\square\end{aligned}$$

Taking the two arguments together, we have that for a large class of transmission models there exists a similarity transformation $\boldsymbol{M} = \boldsymbol{CA}^{-1}\boldsymbol{S}^{-1}$ that relates the top right eigenvector $\boldsymbol{w}_1$ to the top left eigenvector $\boldsymbol{v}_1$:

$$\boldsymbol{v}_1 \propto \boldsymbol{CA}^{-1}\boldsymbol{S}^{-1}\boldsymbol{w}_1.$$

Combining this with our earlier finding of Eq. **12**, which says that the top right eigenvector $\boldsymbol{w}_1$ is proportional to the number of new infections in an observations interval, we obtain

$$\boldsymbol{v}_1 \sim \boldsymbol{CA}^{-1}\boldsymbol{S}^{-1}\boldsymbol{x}(t).$$

where the $\sim$ sign denotes "approximately proportional to." We denote this for each element of the vector as

$$v_{i1} \approx g\frac{c_i}{a_i}\frac{x_i(t)}{s_i(t)}$$

The proportionality constant g is obtained by normalizing the vector, that is, we require that the product of left and right eigenvectors equals one. This gives $g = \sum_i x_i(t)/\sum_i \frac{c_i}{a_i}\frac{x_i^2(t)}{s_i(t)}$. This result is Eq. **5** in subsection 1.4.

3.5. Perturbation of Reproduction Matrices. A decrease in contact rate between two groups i and j will result in a change in the reproduction matrix

$$\mathrm{d}\boldsymbol{K} = \mathrm{d}(\boldsymbol{SABC}) = \boldsymbol{SA}(\mathrm{d}\boldsymbol{B})\boldsymbol{C}.$$

First, we focus on the impact of a decrease in the number of contacts between two groups i and j. The total number of contacts from group i to group i is $p_{ij} = n_i b_{ij} n_j$. A change in contact rate $\mathrm{d}\boldsymbol{B}$ for only two groups i and j implies a change in the number of contacts between those groups $\mathrm{d}b_{ij} = \frac{1}{n_i n_j}\mathrm{d}p_{ij}$. The corresponding perturbation of the reproduction matrix is:

$$\mathrm{d}k_{ij} = \frac{1}{n_i n_j} s_i a_i c_j \mathrm{d}p_{ij},$$

and all other elements of the perturbed matrix $\mathrm{d}\boldsymbol{K}$ are zero. This result explains Eq. **6** in subsection 1.5.

Second, we focus on the impact of vaccinating group i when all individuals in that group are susceptible. A change in numbers of susceptible individuals $\mathrm{d}\boldsymbol{S}$ will result in a perturbation of the reproduction matrix:

$$\mathrm{d}\boldsymbol{K} = (\mathrm{d}\boldsymbol{S})(\boldsymbol{ABC}) = (\mathrm{d}\boldsymbol{S})(\boldsymbol{S}^{-1}\boldsymbol{K}).$$

The number of new vaccinations allocated to the ith group is indicated as $\mathrm{d}u_i$ and the matrix $\mathrm{d}\boldsymbol{U}$ is a diagonal matrix with elements $\mathrm{d}u_i$ on the diagonal and zeros elsewhere. The vaccine efficacy for the ith group is indicated as q_i, and the matrix $\boldsymbol{Q}$ is a diagonal matrix with elements q_i on the diagonal and zeros elsewhere. The change in number of susceptible individuals due to vaccination is

$$\mathrm{d}\boldsymbol{S} = -\boldsymbol{Q}\mathrm{d}\boldsymbol{U}.$$

Combining these two equations gives the perturbation of the reproduction matrix

$$\mathrm{d}\boldsymbol{K} = (-\boldsymbol{Q}\mathrm{d}\boldsymbol{U})(\boldsymbol{S}^{-1}\boldsymbol{K}).$$

Right multiplication of both sides of the equation by the top right eigenvector $\boldsymbol{w}_1$ yields

$$\mathrm{d}\boldsymbol{K}\boldsymbol{w}_1 = -\boldsymbol{Q}\mathrm{d}\boldsymbol{U}\boldsymbol{S}^{-1}R\boldsymbol{w}_1.$$

When vaccination is targeted only at group i this gives

$$\mathrm{d}k_{ij}w_{i1} = -\frac{q_i \mathrm{d}u_i}{s_i} R w_{i1}.$$

This result explains Eq. **7** in subsection 1.6.

Third, we focus on the impact of vaccinating group i when individuals in that group can be immune or susceptible. This is relevant when we cannot distinguish individuals who have natural immunity from individuals who are susceptible to infection at the time of vaccination. We need to know the proportion of susceptible individuals at time t before vaccination, which we denote by $\boldsymbol{S}\boldsymbol{N}^{-1}$. The change in number of susceptible individuals due to vaccination is now

$$\mathrm{d}\boldsymbol{S} = -\boldsymbol{Q}\boldsymbol{S}\boldsymbol{N}^{-1}\mathrm{d}\boldsymbol{U}.$$

The perturbation of the reproduction matrix is now

$$\mathrm{d}\boldsymbol{K} = (-\boldsymbol{Q}\boldsymbol{S}\boldsymbol{N}^{-1}\mathrm{d}\boldsymbol{U})(\boldsymbol{S}^{-1}\boldsymbol{K}).$$

Right multiplication of both sides of the equation by the top right eigenvector $\boldsymbol{w}_1$ yields

$$\mathrm{d}\boldsymbol{K}\boldsymbol{w}_1 = -\boldsymbol{Q}\boldsymbol{N}^{-1}\mathrm{d}\boldsymbol{U}R\boldsymbol{w}_1.$$

When vaccination is targeted only at group i this gives

$$\mathrm{d}k_{ij}w_{i1} = -\frac{q_i \mathrm{d}u_i}{n_i} R w_{i1}.$$

This result explains Eq. **8** in subsection 1.6.

3.6. Eigenvector Sensitivity to Changes in Reproduction Matrix. The sensitivity of eigenvectors to a small change of $\mathrm{d}\boldsymbol{K}$ to the reproduction matrix $\boldsymbol{K}$ can be approximated using power iteration with the new matrix $\boldsymbol{K} + \mathrm{d}\boldsymbol{K}$ (see ref. 5, p351). After changing the matrix $\boldsymbol{K}$ to a new matrix $\boldsymbol{K} + \mathrm{d}\boldsymbol{K}$ we have after one generation:

$$\begin{aligned}\boldsymbol{w}_1 + \mathrm{d}\boldsymbol{w}_1 &\sim (\boldsymbol{K} + \mathrm{d}\boldsymbol{K})\boldsymbol{w}_1 \\ &\propto \boldsymbol{K}\boldsymbol{w}_1 + \mathrm{d}\boldsymbol{K}\boldsymbol{w}_1 \\ &\propto R\boldsymbol{w}_1 - \boldsymbol{Q}\boldsymbol{N}^{-1}\mathrm{d}\boldsymbol{U}R\boldsymbol{w}_1\end{aligned}$$

Here, we use the $\propto$ sign to mean "proportional to" and the $\sim$ sign to mean "approximately proportional to." If group i is targeted with one vaccination, this means that the ith element of the top right eigenvector changes as

$$w_{i1} + \mathrm{d}w_{i1} \sim w_{i1} - \frac{q_i}{n_i} w_{i1}$$

and all other elements of the top left eigenvector remain unchanged.

We use the above equation to find out how importance weights change after targeting one group with one vaccination. We multiply both sides by the factor $\frac{1}{f}\sqrt{q_i \frac{c_i}{a_i} \frac{n_i}{s_i(t)}} \frac{1}{n_i}$, and simplify using first $x_i(t) \approx \frac{1}{f} w_{i1}$ and then $y_i = \sqrt{q_i \frac{c_i}{a_i} \frac{n_i}{s_i(t)}} \frac{x_i(t)}{n_i}$. We obtain an equation for the change in importance weight after group i is targeted with one vaccination:

$$y_i + \mathrm{d}y_i \sim y_i - \frac{q_i}{n_i} y_i.$$

The value for the importance weight for other groups remains unchanged. This result explains the change in importance value as used in subsection 1.7.

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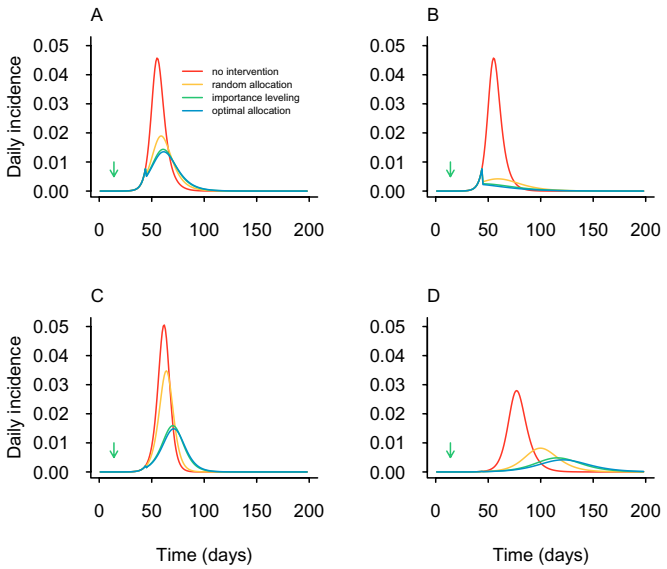

Fig. S1. Testing the importance leveling scheme. We use a standard deterministic SIR transmission model where the population is partitioned into six age strata. The time course of incidence, as new infections per day, is shown when there is only a limited number of vaccine doses that suffice to vaccinate 20% (*A*) and 40% (*B*) of the entire population. We explored the use of a different transmission model with more realistic distributions for the latent and the infectious period (*C*) and a lower value of the reproduction number *R* (*D*). The time course of incidence is shown without interventions (red line), with vaccinated allocated at random (yellow line), with vaccines allocated according to the importance leveling scheme (green line), and with vaccines allocated according to an allocation schedule that minimizes the reproduction number *R* (blue line). The time course of the epidemic after allocating vaccines according to the importance leveling algorithm closely follows the time course of the epidemic after optimal allocation, even though the importance leveling algorithm only requires information on the (observable) incidence of infection at time $t = 14$ (indicated by green arrow) whereas the optimal allocation requires full information on all (unobservable) transmission parameters. Both allocations do considerably better than random allocation.

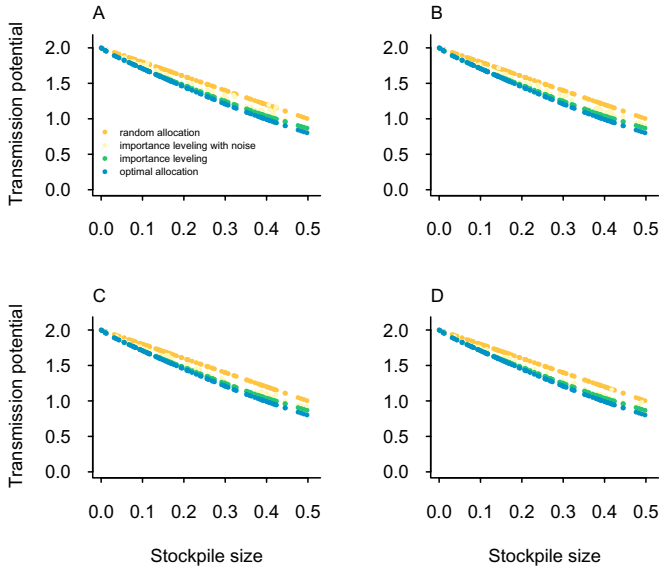

Fig. S2. Sensitivity analysis of the reduction in transmission potential to stochastic variations in the risk of infection. We simulate initial risk of infection using a contact pattern as in Fig. 2*A* and Table S2. We randomly sampled 100 possible values for the stockpile size on the interval 0–0.5 times the size of the entire population. We generated noisy observations of the incidence of infection by sampling a small number of infections from a multinomial distribution specified by the exact probability that an infection occurs in each of the six age classes. Importance leveling was applied based on noisy observations while ignoring the uncertainty (yellow dots). For each stockpile size, we repeated the simulations of noisy age distributions with an increasing number of infections: 100 for *A*, 150 for *B*, 200 for *C*, and 250 for *D*. For comparison, we indicated the reduction in reproduction number if the same amount of vaccine was allocated at random (orange dots), if importance leveling was based on the exact risk of infection (green dots), and if the same amount of vaccine was optimally allocated (blue dots). The results show that the performance of the importance leveling scheme, even when based on uncertain risks of infection, is considerably better than random allocation. The size of the stockpile is expressed relative to total population size; the transmission potential is scaled such that it equals 2.0 when the stockpile size is 0.

Table S1. Notation and Meaning of Variables

Symbol	Meaning
a_i	Per contact probability of acquiring infection for stratum i
b_{ij}	Contact parameter, proportion of stratum i contacted by an infective in stratum j
β_{ij}	Contact rates, proportion of stratum i contacted by an infective in stratum j per unit of time
c_i	Per contact probability of transmitting infection for stratum i
$1/\gamma$	Duration of infectious period
f, g, h	Normalization constants
i, j	Indices for strata, running from 1 to m
k_{ij}	Number of secondary infections in stratum i due to a single infective in stratum j
R	Top eigenvalue of the reproduction matrix $\boldsymbol{K}$
l	Index for vaccination
m	Number of strata into which the population is partitioned
n_i	Population size of stratum i
p_{ij}	Number of contacts with stratum i by stratum j
q_i	Vaccine efficacy for stratum i
r	Final level for importance weights
$s_i(t)$	Stratum-specific number of susceptible individuals in stratum i at time t
t	Time in days
Δt	Duration of the observation interval
u_i	Number of vaccinations given to stratum i
v_{i1}	i^{th}Element of the top left eigenvector of the reproduction matrix $\boldsymbol{K}$
w_{i1}	i^{th}Element of the top right eigenvector of the reproduction matrix $\boldsymbol{K}$
$x_i(t)$	Number of new infections during the observation interval starting at time t in stratum i
$y_i(l)$	Importance weight for prioritization of vaccination in stratum i
z	Number of vaccine units
$\boldsymbol{A}$	Matrix with stratum-specific per contact probability of acquiring infection a_i on the diagonal
$\boldsymbol{B}$	Contact matrix with elements b_{ij}
$\boldsymbol{C}$	Matrix with stratum-specific per contact probability of transmitting infection c_i on the diagonal
$\boldsymbol{K}$	Reproduction matrix with elements k_{ij}
$\boldsymbol{\Lambda}$	Matrix with eigenvalues of the reproduction matrix $\boldsymbol{K}$ on the diagonal
$\boldsymbol{N}$	Matrix with stratum-specific population size on the diagonal
$\boldsymbol{M}$	Similarity transformation of reproduction matrix $\boldsymbol{K}$ to its transpose K^{T}
$\boldsymbol{Q}$	Matrix with stratum-specific vaccine efficacy on the diagonal
$\boldsymbol{S}$	Matrix with stratum-specific number of susceptible individuals on the diagonal
$\boldsymbol{U}$	Matrix with stratum-specific number of targeted vaccinations
$\boldsymbol{v}_1$	Normalized top left eigenvector of the reproduction matrix $\boldsymbol{K}$
$\boldsymbol{w}_1$	Normalized top right eigenvector of the reproduction matrix $\boldsymbol{K}$
$\boldsymbol{W}$	Matrix with right eigenvectors as columns
$\boldsymbol{W}^{-1}$	Matrix with left eigenvectors as rows
$\boldsymbol{x}(t)$	Vector with stratum-specific number of new infections
$z(t)$	Correction term that accounts for the lesser eigenvalues and corresponding normalized eigenvectors of $\boldsymbol{K}$

Table S2. Default parameter values and initial conditions

Variable	Symbol		Value						Unit
Recovery rate	γ		0.286						day^{-1}
Generation interval			3.5						day
Reproduction number	R		2.0						
		Age	0–5	6–12	13–19	20–39	40–59	60+	
Contact parameters	β_{ij}	0–5	1.393	0.259	0.146	0.284	0.130	0.094	$10^{-7}day^{-1}$
		6–12	0.259	2.261	0.266	0.287	0.170	0.095	
		13–19	0.146	0.266	1.847	0.418	0.309	0.123	
		20–39	0.284	0.287	0.418	0.623	0.407	0.207	
		40–59	0.130	0.170	0.309	0.407	0.504	0.272	
		60+	0.094	0.095	0.123	0.207	0.272	0.447	
Population size	n_i		1060	1265	1642	4857	3312	2477	10^3
Number of susceptible individuals	$S_i(0)$		1060	1265	1642	4857	3312	2477	10^3
Number of infected individuals	$I_i(0)$		0	0	0	0	1	0	
Per contact probability of acquiring infection	a_i		1	1	1	1	1	1	
Per contact probability of transmitting infection	c_i		1	1	1	1	1	1	