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*Research article*

# Prioritizing COVID-19 vaccination. Part 1: Final size comparison between a single dose and double dose

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**Abstract:** In response to the coronavirus disease 2019 (COVID-19) pandemic, Japan conducted mass vaccination. Seventy-two million doses of vaccine (i.e., for 36 million people if a double dose is planned per person) were obtained, with initial vaccination of the older population (≥ 65 years). Because of the limited number of vaccines, the government discussed shifting the plan to administering only a single dose so that younger individuals (< 65 years) could also be vaccinated with one shot. This study aimed to determine the optimal vaccine distribution strategy using a simple mathematical method. After accounting for age-dependent relative susceptibility after single- and double-dose vaccination ($v_s$ and $v_d$, respectively, compared with unvaccinated), we used the age-dependent transmission model to compute the final size for various patterns of vaccine distributions. Depending on the values of $v_s$, the cumulative risk of death would be lower if all 72 million doses were used as a double dose for older people than if a single-dose program was conducted in which half is administered to older people and the other half is administered to adults (i.e., 1,856,000 deaths in the former program and 1,833,000-2,355,000 deaths [depending on the values of $v_s$] in the latter). Even if 90% of older people were vaccinated twice and 100% of adults were vaccinated once, the effective reproduction number would be reduced from 2.50 to1.14. Additionally, the cumulative risk of infection would range from 12.0% to 54.6% and there would be 421,000-1,588,000deaths (depending on the values of $v_s$). If an epidemic appears only after completing vaccination, vaccination coverage using a single-dose program with widespread vaccination among adults will not outperform a double-dose strategy.

**Keywords:** SARS-CoV-2; immunization; mathematical model; epidemic; basic reproduction number; pandemic

## 1. Introduction

In the growing epidemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), effective control measures are required to reduce the final size of infection and mortality. While public health and social measures (PHSMs), especially controlling social mixing or lockdowns, are effective in reducing the final size by 12%–13% [1,2], they impose a considerable economic and social cost. The specific pharmaceutical intervention of mass vaccination is considered useful, especially if it helps to achieve herd immunity level in the population. Various types of vaccines against SARS-CoV-2 have been created in response to the spread of this virus [3]. SARS-CoV-2 has a large basic reproduction number (i.e., the average number of secondary infections due to a single infector in a totally susceptible population) and a relatively high infection fatality risk (IFR) compared with seasonal influenza. Therefore, in 2021, affected countries needed to urgently provide an effective vaccination program.

Amid the growing pandemic worldwide, there was a limited number of vaccine stocks when the program had just begun. Therefore, effective vaccine prioritization became a critical public health issue and was widely debated [4,5]. Some studies show that prioritizing vaccines to people in old age [6–8], essential workers [7,9], or people with disabilities [9,10] would be crucial to minimize the spread of the viral infections. Other studies imply that demographic location [9] and the rollout speed [11–13] are also important factors to expedite the suppression of the epidemic. One study demonstrates that some US states do not prioritize or have no vaccination protocols to incarcerated people and points this out to be a potential risk of future spreading of the virus [14]. We raised an urgent question as to how to prioritize vaccines in order to reduce the cumulative number of coronavirus disease 2019 (COVID-19) cases and deaths by employing two distinct vaccination strategies in Japan more efficiently. One strategy is a severity reduction scheme, which mainly targets older people and people with underlying comorbidities. These hosts have been identified as having particularly high IFRs. Therefore, a reduction in the severity of COVID-19 aimed to protect these vulnerable people by a double dose. The other strategy is a transmission blocking strategy, which targets as many people as possible with only a single dose. The resulting efficacy with a single dose is smaller than that of a double dose. However, if a single dose offers a substantial protection from infection, elevating vaccination coverage would help reduce the reproduction number. Therefore, the herd immunity might be achieved more efficiently than the severity reduction scheme. A previous study showed that mortality and years of life lost were reduced most effectively if adults older than 60 years were prioritized [15]. However, other studies have shown that vaccinating younger essential workers or using transmission blocking strategies is more effective than simply covering older people [4,16].

In February 2021, Japan was successful in importing vaccine stocks that were barely sufficient to cover all adults older than 65 years with the double-dose scheme. Nevertheless, because of forthcoming epidemic risks, policymakers were confronted with the choice to decide on providing a double dose versus a single dose. This decision can sometimes be controversial, especially in a situation where there is a limited number of vaccines available [17]. Therefore, theoretical support using mathematical models is required.

In a series of two studies, we aimed to identify the optimal vaccine distribution strategy using a simple mathematical model. This part 1 study used the final size equation of a heterogeneous epidemic model and addressed the static situation in which an epidemic is expected only after completing the vaccination program.

## 2. Materials and methods

As of 8 March 2021, the Japanese government announced that 72 million vaccine shots had been imported to Japan, which could technically cover the population aged 65 years or older. As an alternative, although a single-dose program only provides a partial antibody response compared with that with a double dose, it can virtually double the vaccination coverage if all vaccines are widely distributed. To compare the herd immunity level for these different vaccination strategies, we computed the final size of infection (i.e. the total number of people who experiences infection by the end of epidemic) and cumulative risk of death for each strategy. The cumulative number of confirmed COVID-19 cases in Japan as of 20 April 2021 was 530,000, which is approximately 0.4% of the total population, while the final size ($z$) in a homogenous model was estimated to be 89.3% using the following equation:

$$R_0 = -\frac{\ln(1-z)}{\mathrm{z}} \tag{1}$$

where $R_0$ is the basic reproduction number, which ranges from 1.5 to 3.5 with a representative value of 2.5 in COVID-19 [18]. We assumed that the initial size of infection was negligible and all people who were yet to be vaccinated remained susceptible. The final size equation is known to be extended to multi-host version, and if the type of host corresponds to age group, the age-specific cumulative incidence of age-structured susceptible-infectious-recovered (SIR) model can be conveniently calculated using a single equation in an iterative manner. It should be noted that compartmental extensions to susceptible-exposed-infectious-recovered (SEIR) model or SIR model with realistic infectious period distribution does not alter the final size.

### *2.1. Data*

We categorized the Japanese population into 15 discrete age groups for every 5 years of age, with the oldest age group set at 70 years and older. The population data were retrieved from the census data, which were published by the Statistics Bureau of Japan as of February 2021 (Supplementary Table 1). We used the age-specific IFR that was calculated in a study conducted by Levin et al. [19].

We used the age-dependent transmission model, which required an age-dependent contact matrix. Using a method that was described elsewhere [20,21], we quantified the contact matrix during the spring period of COVID-19 in 2000 before PHSM and used the contact matrix shown in Table 1 [22].

**Table 1.** Contact frequencies between age groups as shown by a contact matrix.

| Age of contactees | Age of contactors | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0–4 | 5–9 | 10–14 | 15–19 | 20–24 | 25–29 | 30–34 | 35–39 | 40–44 | 45–49 | 50–54 | 55–59 | 60–64 | 65–69 | 70– |
| 0–4 | 1.05 | 0.54 | 0.21 | 0.01 | 0.04 | 0.20 | 0.79 | 0.67 | 0.39 | 0.09 | 0.05 | 0.09 | 0.21 | 0.24 | 0.12 |
| 5–9 | 0.56 | 1.03 | 0.59 | 0.21 | 0.01 | 0.07 | 0.24 | 0.49 | 0.57 | 0.36 | 0.07 | 0.03 | 0.08 | 0.14 | 0.05 |
| 10–14 | 0.22 | 0.59 | 1.70 | 0.45 | 0.02 | 0.01 | 0.10 | 0.17 | 0.51 | 0.64 | 0.24 | 0.12 | 0.03 | 0.02 | 0.04 |
| 15–19 | 0.01 | 0.24 | 0.50 | 0.92 | 0.34 | 0.08 | 0.04 | 0.08 | 0.30 | 0.57 | 0.48 | 0.35 | 0.08 | 0.03 | 0.06 |
| 20–24 | 0.06 | 0.02 | 0.04 | 0.45 | 0.47 | 0.48 | 0.24 | 0.13 | 0.22 | 0.33 | 0.77 | 0.84 | 0.35 | 0.10 | 0.13 |
| 25–29 | 0.30 | 0.10 | 0.01 | 0.11 | 0.48 | 0.80 | 0.65 | 0.23 | 0.26 | 0.25 | 0.48 | 0.86 | 0.71 | 0.37 | 0.13 |
| 30–34 | 1.26 | 0.37 | 0.15 | 0.05 | 0.25 | 0.69 | 1.07 | 0.53 | 0.31 | 0.23 | 0.31 | 0.46 | 0.74 | 0.56 | 0.20 |
| 35–39 | 1.17 | 0.84 | 0.29 | 0.12 | 0.15 | 0.27 | 0.58 | 0.88 | 0.57 | 0.33 | 0.22 | 0.28 | 0.56 | 0.48 | 0.26 |
| 40–44 | 0.78 | 1.13 | 1.00 | 0.53 | 0.29 | 0.35 | 0.39 | 0.66 | 1.22 | 0.63 | 0.54 | 0.39 | 0.39 | 0.46 | 0.43 |
| 45–49 | 0.20 | 0.76 | 1.34 | 1.10 | 0.49 | 0.37 | 0.31 | 0.41 | 0.68 | 0.98 | 0.68 | 0.59 | 0.31 | 0.23 | 0.41 |
| 50–54 | 0.08 | 0.13 | 0.43 | 0.78 | 0.95 | 0.61 | 0.36 | 0.24 | 0.50 | 0.58 | 1.08 | 0.64 | 0.41 | 0.20 | 0.31 |
| 55–59 | 0.14 | 0.04 | 0.17 | 0.46 | 0.86 | 0.89 | 0.44 | 0.24 | 0.30 | 0.41 | 0.53 | 1.10 | 0.49 | 0.22 | 0.25 |
| 60–64 | 0.30 | 0.11 | 0.03 | 0.10 | 0.32 | 0.66 | 0.65 | 0.45 | 0.27 | 0.20 | 0.31 | 0.45 | 0.94 | 0.53 | 0.25 |
| 65–69 | 0.41 | 0.23 | 0.04 | 0.05 | 0.11 | 0.42 | 0.59 | 0.47 | 0.39 | 0.18 | 0.18 | 0.24 | 0.65 | 0.62 | 0.43 |
| 70– | 0.57 | 0.25 | 0.21 | 0.26 | 0.42 | 0.41 | 0.60 | 0.71 | 1.02 | 0.90 | 0.79 | 0.77 | 0.87 | 1.22 | 1.46 |

*2.2. Mathematical models*

We derived the next-generation matrix **K** by calculating the element-wise product of the normalized contact matrix (i.e., contact matrix divided by its eigenvalue) and the vaccination coverage matrix **S**, which was then scaled by the basic reproduction number $R_0$:

$$\mathbf{K} = R_0 \frac{\mathbf{C}}{\rho(\mathbf{C})} \circ \mathbf{S} = \begin{pmatrix} R_{00,00} & \cdots & R_{00,70} \\ \vdots & \ddots & \vdots \\ R_{70,00} & \cdots & R_{70,70} \end{pmatrix} \tag{2}$$

The subscript in the element of the matrix represents the age groups that the infectee and infector belong to (e.g., $R_{25,40}$ represents the average number of secondary cases in the age group of 25–29 years produced by a single primary case in the age group of 40–44 years). The matrix of susceptibility (**S**), including the vaccine effect, was a 15 × 15 matrix, which reflected the relative susceptibility of each age group as determined by vaccination coverage:

$$\mathbf{S} = \begin{pmatrix} (1-p_{00s}-p_{00d})+v_s p_{00s}+v_d p_{00d} & \cdots & (1-p_{00s}-p_{00d})+v_s p_{00s}+v_d p_{00d} \\ (1-p_{05s}-p_{05d})+v_s p_{05s}+v_d p_{05d} & \cdots & (1-p_{05s}-p_{05d})+v_s p_{05s}+v_d p_{05d} \\ \vdots & \ddots & \vdots \\ (1-p_{55s}-p_{55d})+v_s p_{55s}+v_d p_{55d} & \cdots & (1-p_{55s}-p_{55d})+v_s p_{55s}+v_d p_{55d} \\ (1-p_{60s}-p_{60d})+\left(v_s+(1-v_s)(1-w_{60})\right)p_{60s}+\left(v_d+(1-v_d)(1-w_{60})\right)p_{60d} & \cdots & (1-p_{60s}-p_{60d})+\left(v_s+(1-v_s)(1-w_{60})\right)p_{60s}+\left(v_d+(1-v_d)(1-w_{60})\right)p_{60d} \\ (1-p_{65s}-p_{65d})+\left(v_s+(1-v_s)(1-w_{65})\right)p_{65s}+\left(v_d+(1-v_d)(1-w_{65})\right)p_{65d} & \cdots & (1-p_{65s}-p_{65d})+\left(v_s+(1-v_s)(1-w_{65})\right)p_{65s}+\left(v_d+(1-v_d)(1-w_{65})\right)p_{65d} \\ (1-p_{70s}-p_{70d})+\left(v_s+(1-v_s)(1-w_{70})\right)p_{70s}+\left(v_d+(1-v_d)(1-w_{70})\right)p_{70d} & \cdots & (1-p_{70s}-p_{70d})+\left(v_s+(1-v_s)(1-w_{70})\right)p_{70s}+\left(v_d+(1-v_d)(1-w_{70})\right)p_{70d} \end{pmatrix} \tag{3}$$

where $p_{\mathrm{Xs}}$ and $p_{\mathrm{Xd}}$ represent the fraction of people belonging to age group X who received a single and double dose, respectively (i.e., vaccination coverage), and $v_{\mathrm{s}}$ and $v_{\mathrm{d}}$ denote the relative susceptibility of vaccinated individuals who received a single and double dose, respectively. In the older group of people aged ≥ 60 years, a slightly reduced age-dependent vaccine efficacy compared with younger people was considered [15]. The age-dependent relative vaccine efficacy is denoted by $w_{60}$, $w_{65}$, and $w_{70}$ for the subgroups of 60–64, 65–69, and ≥70 years, respectively. Thus, the relative susceptibility of among vaccinated individuals in these age subgroups, described by $1 - w_{\mathrm{i}}$ ($\mathrm{i} \in \{60, 65, 70\}$), was multiplied to the vaccinated portions of 60–64, 65–69, and ≥ 70 years.

The cumulative proportion of people in each age group who experience infection by the end of epidemic (i.e., the final size) is expressed in the vector form **z**:

$$\boldsymbol{z} = \begin{pmatrix} z_{00} \\ z_{05} \\ \vdots \\ z_{70} \end{pmatrix} = \begin{pmatrix} 1-\exp\left[-\left(R_{00,00}z_{00}+R_{00,05}z_{05}+\cdots+R_{00,70}z_{70}\right)\right] \\ 1-\exp\left[-\left(R_{05,00}z_{00}+R_{05,05}z_{05}+\cdots+R_{05,70}z_{70}\right)\right] \\ \vdots \\ 1-\exp\left[-\left(R_{70,00}z_{00}+R_{70,05}z_{05}+\cdots+R_{70,70}z_{70}\right)\right] \end{pmatrix} \tag{4}$$

Unfortunately, there is no analytical solution for this vector, but the recursive equation (4) can be iteratively solved. The final size of the infection in total ($\mathbf{Z_I}$) was calculated by taking a dot product of **z** and the population fraction vector **p** (i.e., the relative size of the discrete age-specific population):

$$\mathbf{Z_I} = N\boldsymbol{z} \cdot \boldsymbol{p} \tag{5}$$

where $N$ is the total population size of Japan (i.e., 125,620,000 people). Similarly, the final size of death in total ($\mathbf{Z_D}$) was calculated by taking a dot product of **z** and the IFR vector **f**:

$$\mathbf{Z_D} = N\boldsymbol{z} \cdot (\boldsymbol{p} \circ \boldsymbol{f}) \tag{6}$$

As mentioned above, f was retrieved from the literature [19] and is available in the Supplementary

material. Table 2 shows the parameter values and their references that we used. We assumed that the basic reproduction number ($R_0$) was 2.5. On basis of a study conducted by Dagan et al. [23], the relative susceptibility after a single and double dose, denoted by $v_s$ and $v_d$, were fixed at 50% and 5%, respectively. The age-dependent relative vaccine efficacy, $w_{60}$, $w_{65}$, and $w_{70}$, were assumed to be 83.33%, 83.33%, and 66.67%, respectively [15]. To examine the sensitivity of our result (i.e., optimal vaccination target) regarding the age-dependent relative susceptibility, we also conducted the same computation with the relative susceptibility after a single-dose scheme ($v_s$), which was set at 35% and 20% [21,23]. Lastly, we carried out a sensitivity analysis of the cumulative risks of infection and death, varying the relative risk of death to 1%, 5% and 10%, respectively.

**Table 2.** Parameter values used for calculating the final size of infection/death with comparative vaccination strategies against the COVID-19 epidemic in Japan.

| Parameter | Value(s) | Reference |
|---|---|---|
| Basic reproduction number ($R_0$) | 2.5 | [38-40] |
| Relative susceptibility after one dose of vaccination ($v_s$) | 50%, 35%, and 20% | Assumption and [21, 23] |
| Relative susceptibility after two doses of vaccination ($v_d$) | 1%, 5%, and 10% | [23] |
| Age-dependent relative vaccine efficacy in 60–64 ($w_{60}$), 65–69 ($w_{65}$), and 70– ($w_{70}$) | 83.33%, 83.33%, and 66.67% | [15] |

All quantitative analyses as mentioned above were implemented using statistical package R version 4.1.0 (The Comprehensive R Archive Network; https://cran.r-project.org/).

## 3. Results

Figure 1 shows the expected cumulative risk of infection as a function of doses consumed using the following two different vaccination strategies: (i) all doses are randomly provided to 36 million people older than 65 years who receive the double-dose scheme; and (ii) 50% of the doses are randomly provided to all people older than 65 years, and the rest are randomly allocated to 69 million adults aged between 20 and 64 years who receive the single-dose scheme. Assuming that the relative susceptibility after a single dose was 50%, in the absence of vaccination, 89.1% of the population were expected to experience infection, leading to 2,652,000 deaths. The cumulative risk of infection gradually decreased as the vaccination coverage increased and changed to 78.2% and 78.3% when all 72 million doses were consumed when following strategies (i) and (ii), respectively (Figure 1A). The cumulative risk of death was expected to change more drastically in strategy (i) than in (ii). The cumulative mortality would decrease from 2,652,000 to 1,856,000 in strategy (i), while strategy (ii) would only decrease to 2,355,000 if all 72 million doses were administered (Figure 1D). However, if we assumed that single-dose vaccination would contribute to yielding a relative susceptibility at 20% (instead of 50%) and that all 72 million doses were consumed, the estimated cumulative risk of infection would be 78.2%, leading to 1856,000 deaths in strategy (i). Additionally, the estimated cumulative risk of infection would be 63.5%, leading to 1833,000 deaths in strategy (ii) (Figure 1F).

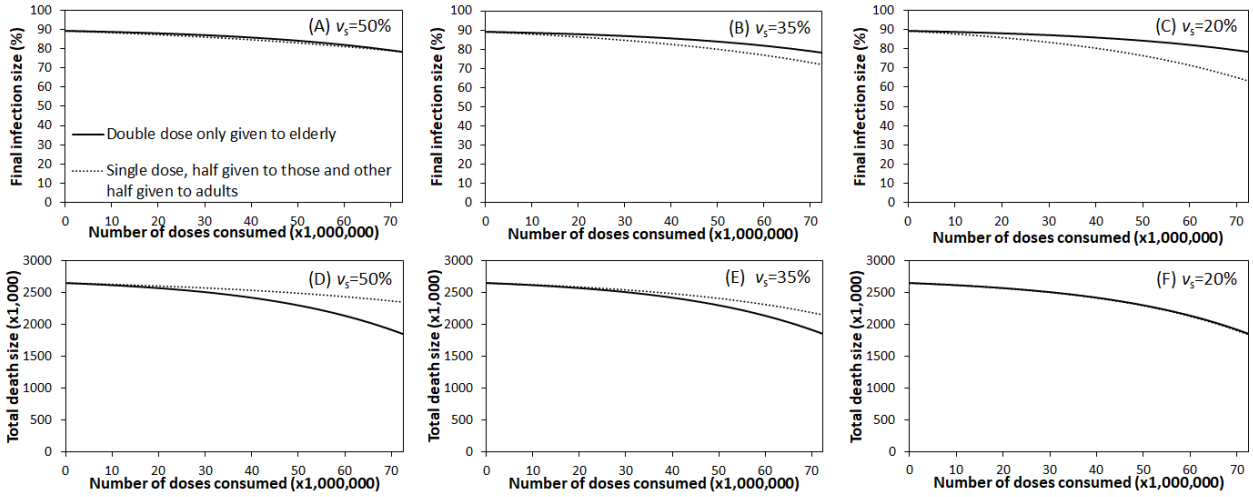


**Figure 1.** Cumulative risk of infection (percentage in relation to the total population of Japan; panels A, B, and C) and the cumulative number of deaths (panels D, E, and F). These data include the total number of doses randomly administered to people older than 65 years receiving the double-dose strategy (solid lines), or half administered to adults aged between 20 and 64 years and the other half administered to people older than 65 years taking the single-dose scheme (dotted lines). The relative susceptibility after a single dose is assumed to be 50% (panels A and D), 35% (panels B and E), and 20% (panels C and F).

Figure 2 shows the cumulative risk of infection and death as a function of single-dose coverage among adults and different double-dose coverage among older people. When $v_s$ was assumed to be 50%, with double-dose coverage of 30% among older people combined with single-dose coverage of 100% among adults, the final size of infection would be 65.3% with 2,317,000 deaths (90.5 million doses are required to achieve these data; Figure 2A and 2D). With the same coverage, if $v_s$ was assumed to be 20% (instead of 50%), the final size of infection would be 23.9% with 1,253,000 deaths (Figure 2C and 2F). However, if double-dose coverage among older people was elevated to 90% (with $v_s$ assumed to be 50%), while single-dose coverage among adults was 100%, the final size of infection would change to 54.6% with 1,588,000 deaths (Figure 2A and 2D). If $v_s$ was assumed to be 20%, the final size of infection would be 12.0% with 421,000 deaths for the same of combination of parameters (134 million doses are required to achieve these data; Figure 2C and 2F). In this scenario, the effective reproduction number was reduced from 2.50 to 1.14, which is still above the herd immunity threshold.

Figure 3 shows the results from the sensitivity analysis with respect to $v_d$. When $v_s$ was fixed at 35% and all 72 million doses were consumed for people aged 65 years and older following strategy (i) 77.2% and 79.5% of the population would eventually experience infection, leading to 1,770 thousand and 1,954 thousand deaths, if the relative susceptibility after a double dose, $v_d$, was 1% and 10%, respectively.

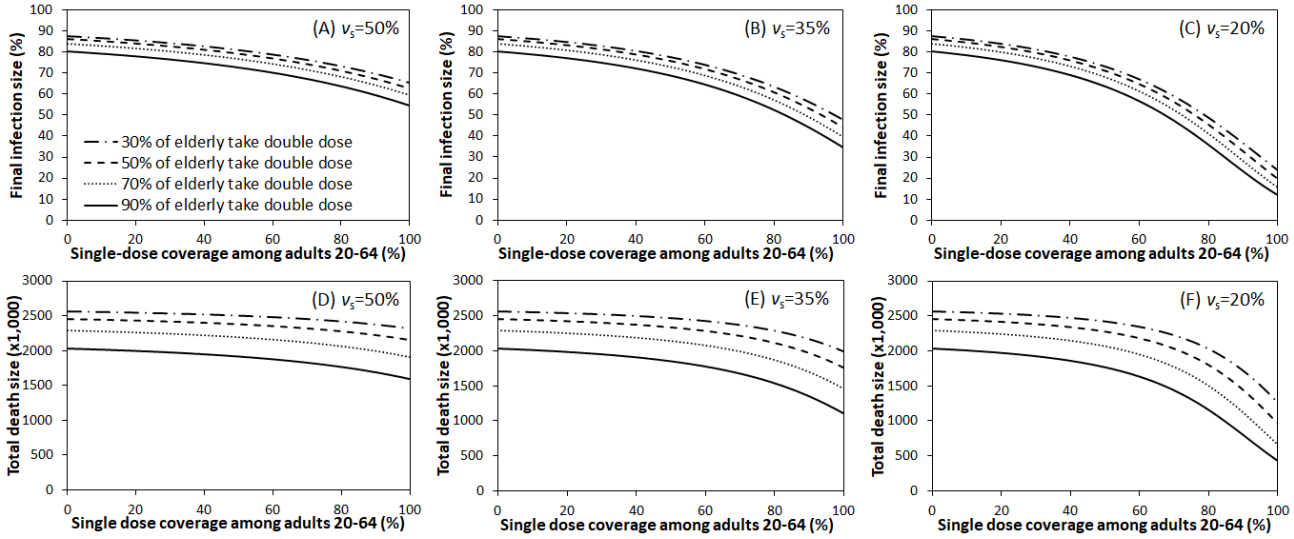


**Figure 2.** Cumulative risk of infection (percentage in relation to the total population of Japan; panels A, B, and C) and the cumulative number of deaths (panels D, E, and F) with single-dose coverage among adults aged between 20 and 64 years, along with different types of double-dose coverage among people aged 65 years and older. The relative susceptibility after a single dose, $v_s$, was assumed to be 50% (A and D), 35% (B and E), and 20% (C and F), while that after a double dose, $v_d$, was fixed at 5%.

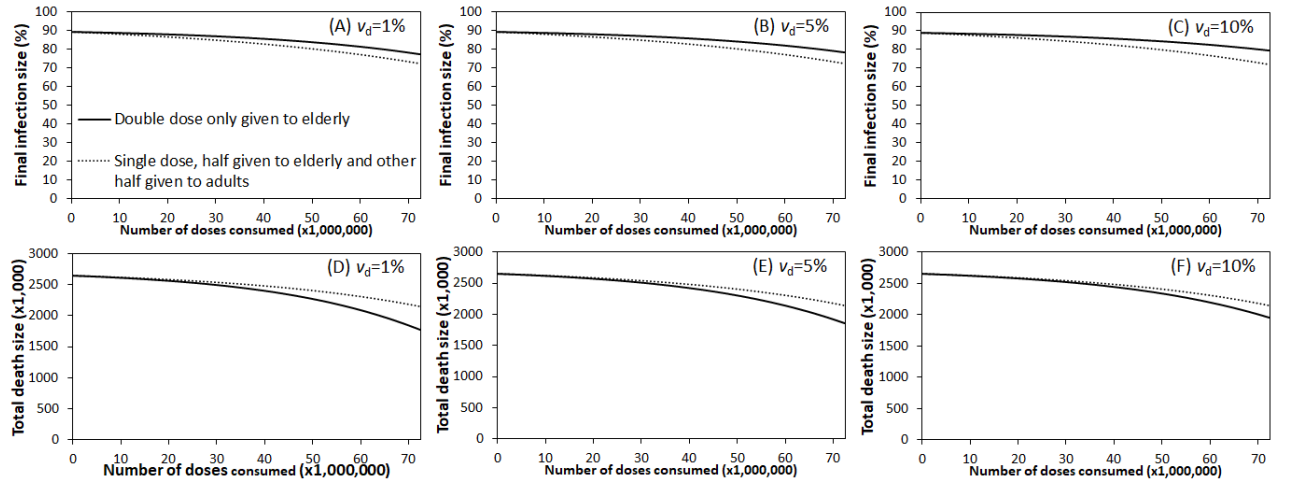


**Figure 3.** Cumulative risk of infection (percentage in relation to the total population of Japan; panels A, B, and C) and the cumulative number of deaths (panels D, E, and F) with single-dose coverage among adults aged between 20 and 64 years, along with different types of double-dose coverage among people aged 65 years and older. The relative susceptibility after a double dose, $v_d$, was assumed to be 1% (A and D), 5% (B and E), and 10% (C and F), while that after a single dose, $v_s$, was fixed at 35%.

## 4. Discussion

To answer a policy question regarding the prioritization of COVID-19 vaccines, we used an age-dependent heterogeneous transmission model and derived a final size equation. We compared the final

sizes in various possible scenarios of the total dose, using either a double-dose or a single-dose (partial) scheme. Our study showed that enlarging the coverage by using a single dose would be beneficial, especially when the reduced susceptibility with one shot was substantial. However, considering that a 50% reduction in susceptibility following one shot was plausible, the single-dose scheme did not outperform the conventional double-dose strategy.

There are two important take-home messages from the present study. First, while the single-dose scheme is expected to contribute to reducing transmission and elevating herd immunity in the population, this strategy is not recommended as an actual policy. Our simulation showed that prioritizing people aged 65 years and older was vital for reducing the death toll. This finding is compatible with a previous study, which showed that vaccine priority for people older than 60 years would reduce mortality and years of life lost [15]. This finding can be explained by the high IFR among older people, especially among those aged 75 years and older [19]. Therefore, the decrease in the relative susceptibility among individuals vaccinated with two doses, especially in older age groups, directly leads to the decrease in the death size (Figure 3D to F). Reducing the incidence of infection was the primary goal of this study, and the single-dose scheme was not substantially inferior to the double-dose scheme. Furthermore, Japan has had intense anti-vaccine campaigns since investigations for adverse effects of human papillomavirus vaccine started in 2014 [24]. However, elevating the vaccination coverage among young adults by the single-dose scheme with insufficient efficacy could be challenging. Second, the vaccine stocks that only covered the older population were not sufficient to contain the epidemic, and a much greater amount was required to anticipate the herd immunity threshold. Because of the limited efficacy, our simulation showed that the minimum double-dose vaccine coverage needed to be 99.4% in those aged 20 years or older to reach the effective reproduction number to fall below 1.0 only using vaccination. Importing vaccines to cover virtually the whole nation has been a formidable task. Therefore, other PHSM, including social distancing and lockdowns, have been required as possible options to concurrently prevent the spread of the epidemic [25].

Another concern of the ongoing epidemic of COVID-19 is that we have repeatedly faced the threat of variants of concern (VOCs), including Alpha, Delta, and Omicron variants. In addition to the elevated transmissibility of these VOCs compared with the wild type (which leads to a higher basic reproduction number), studies have shown slightly lower titers in vaccinated sera against a UK VOC and marked resistance against vaccines in other VOCs (e.g., the Beta variant), even after taking a double dose [3,26–32]. A previous study showed that increasing primary vaccination coverage against the Omicron variant would lead to a reduction in hospitalizations and deaths [33]. Nevertheless, as a practical recommendation to the present status in Japan, the partial effectiveness of vaccinations against these VOCs suggests that rapid implementation of mass vaccination is still urgent to reduce the overwhelming hospital burden. A reduction in the incidence of new COVID-19 cases is required to sustain the socioeconomic burden and to maintain human casualties at the lowest level before new types of vaccines that are effective against VOCs are available.

In the present study, we addressed the vaccine prioritization issue in a static parameter setting; the cumulative number of cases and deaths can be calculated by simply solving a set of mathematical equations. Using this model, vaccination was assumed to be completed in advance of the epidemic, and key parameters, including the basic reproduction number, were not assumed to vary over the course of the epidemic. While the final size did not differ substantially with varying relative susceptibility after single- or double-doses of vaccines (Figure 1 and 3), the equation allowed us to solve the policy question in a simple manner. However, the use of a final size equation was based on the assumption

that the dynamics of the entire epidemic were sufficiently captured by the assumed model. If the epidemic starts during the course of vaccination, and if several epidemiological parameters, including transmissibility, vary over the course of time, other approaches accounting for such dynamic process are required. Partly because of this technical issue, and also because modelling study was not necessarily considered during decision making process by all countries, policy decisions on this matter across the world were highly variable. From ethical point of view, it was reasonable to choose double dose strategy as a convention, but some dynamic modelling studies indicated that single dose would outperform [4,16]. As a consequence, it was evident in real time that modelling studies yield diverse policy recommendations depending on varying assumptions and methodologies, and in practice, it was difficult to make a proper conclusive judgement in real time. In fact, a published study emphasized an importance of sociocultural factors that change the transmission dynamics, such as cultural difference from region to region, attitude changes, educational backgrounds, and people's adherence to prevention activity [34]. This point remained to be a future subject for policy science to resolve possibly in advance of pandemic event.

There are several limitations to this study. First, the vaccine rollout rate was not taken into consideration. We only computed the cumulative risk of infection from the final size and the cumulative number of deaths as a weighted average, and these are what we expect to observe in a long span. The time gap between vaccination and the titers to reach a protective level was also disregarded, but they did not matter during the process of final size computation [35]. Second, the initial infection size was disregarded. As of 30 April 2021, Japan has experienced 590,000 reported cases with > 10,000 deaths, accounting for 0.5% and 0.01% of the whole population, respectively [36]. Even though these numbers are negligible, the computed infection size and death toll might differ if the initial infection size was considered, especially if using a similar approach at a later stage of the pandemic. Third, VOCs were ignored in this analysis, but Japan has continuously experienced a series of epidemics induced by VOCs [37]. As mentioned above, VOCs induced altered susceptibility against vaccines, and the cumulative risks could have been larger than what was computed in the present study. Fourth, heterogeneities other than age were not explicitly considered. Vaccine priority in Japan was given to medical professionals who are at a particularly elevated risk of infection.

## 5. Conclusions

We believe that our simple method will be useful in public health decision-making in determining vaccine dosage and distribution. When the vaccine stock is limited, enlarging vaccination coverage by using a single-dose regimen would not substantially outperform a double-dose scheme in avoiding mortality.

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## Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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## Supplementary material

**S1.** Age-specific population fraction

| Age group | Fraction |
|---|---|
| 0–4 ($p_{00}$) | 0.037 |
| 5–9 ($p_{05}$) | 0.040 |
| 10–14 ($p_{10}$) | 0.043 |
| 15–19 ($p_{15}$) | 0.045 |
| 20–24 ($p_{20}$) | 0.051 |
| 25–29 ($p_{25}$) | 0.050 |
| 30–34 ($p_{30}$) | 0.052 |
| 35–39 ($p_{35}$) | 0.059 |
| 40–44 ($p_{40}$) | 0.066 |
| 45–49 ($p_{45}$) | 0.078 |
| 50–54 ($p_{50}$) | 0.070 |
| 55–59 ($p_{55}$) | 0.063 |
| 60–64 ($p_{60}$) | 0.059 |
| 65–69 ($p_{65}$) | 0.064 |
| 70– ($p_{70}$) | 0.224 |

**S2.** Age-specific IFR

| Age group | IFR |
|---|---|
| 0–4 ($f_{00}$) | 0.00004 |
| 5–9 ($f_{05}$) | 0.00004 |
| 10–14 ($f_{10}$) | 0.00004 |
| 15–19 ($f_{15}$) | 0.00004 |
| 20–24 ($f_{20}$) | 0.00004 |
| 25–29 ($f_{25}$) | 0.00004 |
| 30–34 ($f_{30}$) | 0.00004 |
| 35–39 ($f_{35}$) | 0.00068 |
| 40–44 ($f_{40}$) | 0.00068 |
| 45–49 ($f_{45}$) | 0.0023 |
| 50–54 ($f_{50}$) | 0.0023 |
| 55–59 ($f_{55}$) | 0.0075 |
| 60–64 ($f_{60}$) | 0.0075 |
| 65–69 ($f_{65}$) | 0.025 |
| 70– ($f_{70}$) | 0.085 |

IFR, infection fatality risk. Retrieved from [19].