Mixing age and risk groups for accessing COVID-19 vaccines: a modelling study

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ABSTRACT
Objective To characterise the optimal targeting of age and risk groups for COVID-19 vaccines.
Design Motivated by policies in Japan and elsewhere, we consider rollouts that target a mix of age and risk groups when distributing the vaccines. We identify the optimal group mix for three policy objectives: reducing deaths, reducing cases and reducing severe cases.
Setting Japan, a country where the rollout occurred over multiple stages targeting a mix of age and risk groups in each stage.
Primary outcomes We use official statistics on COVID-19 deaths to quantify the virus transmission patterns in Japan. We then search over all possible group mix across rollout stages to identify the optimal strategies under different policy objectives and virus and vaccination conditions.
Results Low-risk young adults can be targeted together with the high-risk population and the elderly to optimally reduce deaths, cases and severe cases under high virus transmissibility. Compared with targeting the elderly or the high-risk population only, applying optimal group mix can further reduce deaths and severe cases by over 60%. High-efficacy vaccines can mitigate the health loss under suboptimal targeting in the rollout.
Conclusions Mixing age and risk groups outperforms targeting individual groups separately, and optimising the group mix can substantially increase the health benefits of vaccines. Additional policy measures boosting vaccine efficacy are necessary under outbreaks of transmissible variants.

INTRODUCTION
On 30 January 2020, the WHO declared that the spread of SARS-CoV-2 (henceforth COVID-19) had led to a 'public health emergency of international concern'. By 31 March 2021, the virus had infected over 128 million people globally, with the death toll reaching 2.9 million. Governments responded by implementing social distancing measures and travel restrictions to control the transmission. As deaths and infections continued to rise, many countries, including China, India and the USA, imposed systematic lockdowns at different points during the pandemic.

While social distancing has slowed down the virus transmission,1 it has also caused disruptions in individuals’ daily lives and well-being. Lockdowns have exacerbated the economic hardships of low-wage workers,2 interrupted learning and worklife,3 and worsened the mental health of younger generations.4 The mounting societal burden of the pandemic has made the development of a COVID-19 vaccine a top priority of the medical science community.

With the approval of the Pfizer-BioNTech vaccine in late 2020, massive rollouts of COVID-19 vaccines took place across the world in 2021. However, the emergence of highly transmissible variants such as Delta and Omicron continued to threaten public safety even in highly vaccinated countries.5 6 Moreover, constrained by vaccine supply and state capacity, rollouts in low/middle-income countries face even greater challenges managing the virus and vaccination conditions on the ground.

The standard approach to distributing the COVID-19 vaccines is through a multistage rollout where individuals become eligible in one of the rollout stages. This gives policymakers two levers to distribute the vaccines. First, the characteristics of eligible individuals...
in each stage are chosen by policy. Second, there is an order of priority regarding which individuals are targeted at different stages. In Japan, for instance, after covering healthcare workers, vaccine access is restricted to the elderly in the first stage, to high-risk young adults with underlying medical conditions in the second, and to low-risk young adults and children in the third. In countries such as the UK and the USA, health authority guidelines recommend targeting the oldest adults in the first stage, the elderly and high-risk young adults in the second, and low-risk young adults and children in the third. In Australia, the rollout targets the oldest adults together with high-risk individuals regardless of age in the first stage, the elderly in the second, and the remaining population in the third. Additional strategies that differ from the national guideline have also been adopted in individual US states.

Despite the differences in design details, a common strategy across countries was to employ both age-based and risk-based criteria when targeting individuals for vaccines, oftentimes mixing different age–risk groups in the same stage. In this study, we take an optimising approach and systematically characterise the optimal targeting strategies across age–risk groups in Japan for three different policy objectives, that is, minimising deaths, minimising severe cases and minimising cases. In Japan, the start date of the rollout was 12 April 2021, by which time the virus had infected over 500 000 individuals. Because the rollout coincided with the outbreak of the Delta variant, we consider optimal targeting under a range of virus and vaccination conditions. We also explore policy measures that can mitigate the health loss due to suboptimal strategies in the rollout.

**METHODS**

**Data sources**

We have obtained data on weekly COVID-19 deaths from Japan’s National Institute of Population and Social Security Research. The data provide detailed death counts by age groups. We use the weekly data to estimate the parameters in the virus transmission model over the period between April 2020 and March 2021. By 29 March 2021, deaths in the 20–59 years age group reached 238 individuals, and deaths in the oldest group (80+ years) reached 5310.

We also obtained data on hospitalised patients from the COVID-19 Registry Study, a national survey of COVID-19 cases in health facilities since March 2020. The survey measures symptoms at admission, outcomes at discharge, as well as patient demographics, drug use and comorbidity. High-risk individuals are those with at least one medical condition listed as a risk factor for COVID-19 in Japan. The list of risk factors is determined by the Ministry of Health, Labour and Welfare, publicised at [https://www.mhlw.go.jp/content/000759274.pdf](https://www.mhlw.go.jp/content/000759274.pdf) (accessed 24 October 2021). Based on the definition, we obtain the share of high-risk individuals by age from the Comprehensive Survey of Living Conditions, a survey of population health and income in Japan.

**Modelling the COVID-19 pandemic in Japan**

We calibrate a susceptible–exposed–infectious–removed (SEIR) model of COVID-19 in Japan as the basis of our analysis. We illustrate the model in online supplemental figure A1. Infectious individuals with severe symptoms are admitted to hospitals and treated under medical quarantine. Both the share of severe cases among infectious individuals and the mortality rate per hospitalisation differ by age and risk status. Infectious individuals with non-severe symptoms are not hospitalised; a fraction of them will self-quarantine, and those not in medical or self-quarantine transmit the virus through contact. The model details are provided in online supplemental appendix A1.

To account for seasonality and contact reductions in multiple state-of-emergency issuances, we adjust the contact matrix by a seasonal factor that differs for each quarter during 2020–2021. The quarterly variation coincides with the onset of two states of emergency in Japan, enabling us to capture the impacts of major policy changes as well as seasonal differences in contact (Japan began the first state of emergency in the second quarter of 2020 (7 April 2020), and imposed a second state of emergency on 7 January 2021, after experiencing surges of infections in the fourth quarter of 2020. A summary of COVID-19 developments in Japan can be found at [https://english.kyodonews.net/news/2021/04/29b154a681ba-chronology-of-major-events-related-to-coronavirus-and-japan.html](https://english.kyodonews.net/news/2021/04/29b154a681ba-chronology-of-major-events-related-to-coronavirus-and-japan.html) (accessed July 2022)). We model the virus outbreak assuming that one individual in each age–risk group was infected on 1 February 2020, and we calibrate virus transmission matching the death count by age groups publicised since April 2020. Online supplemental appendix A2 details the calibration and provides a full list of model parameters in online supplemental table A1. We use the model to predict the state of the pandemic by 12 April 2021, the starting time of the rollout. We then simulate the deaths, severe cases and cases over a 1-year horizon under different rollout strategies in our main analysis.

**Vaccine efficacy**

We consider two protective effects of the COVID-19 vaccines. For infectious individuals, vaccines reduce the probability of developing severe cases by a certain per cent. For susceptible individuals, vaccines reduce infections by simultaneously reducing the infectivity of the virus and the transmissibility from a vaccinated contact by a certain per cent. The protective effects differ by vaccine efficacy. High-efficacy vaccines reduce severe cases by 90% and reduce infections by reducing both infectivity and transmissibility by 90%. Low-efficacy vaccines reduce severe cases and infections both by 60%. We also consider intermediate efficacy vaccines reducing severe cases by 90% and infections by 60%.
Optimal targeting across groups

We analyse the optimal targeting of age-risk groups in an initial rollout of COVID-19 vaccines starting in Japan on 12 April 2021. The rollout occurs over three stages with each stage targeting a different mix of age-risk groups. At a speed of vaccinating a fixed per cent of the population each day, the transition to the next stage is triggered when vaccination in the current stage hits a target coverage rate. Importantly, in addition to the prioritisation across stages, the characteristics of targeted individuals in each stage are explicitly decided by the policymaker. For instance, the government may target the elderly in the first stage and target high-risk individuals in the second stage, or use a more complex group mix in each stage.

Specifically, we consider seven age-risk groups: children (0–19 years), young adults (20–59 years) by risk status, the elderly (60–79 years) by risk status and oldest adults (80+ years) by risk status. We thus consider four broad age categories—children, young adults, the elderly and oldest adults—as well as high-risk and low-risk status for each of the adult groups. Across groups, targeting strategies can replicate those commonly adopted in the rollout of COVID-19 vaccines, and we characterise optimal strategies through an exhaustive search over possible allocations of groups to stages. We also examine how optimal targeting differs by policy objectives minimising deaths, severe cases or cases, and for different vaccine efficacy, vaccination speed, coverage and virus transmissibility. We further assess the robustness of targeting strategies across different scenarios of the initial virus outbreak in January 2020, when reliable surveillance data on COVID-19 cases were still lacking.

Based on the results, we examine the virus and vaccination conditions under which optimally targeting age and risk groups can best improve outcomes. To illustrate the gains from optimisation, we start from simple strategies targeting either the elderly or high-risk individuals and compute the per cent reduction in outcomes if the rollout instead followed optimal targeting across groups. When the health loss from suboptimal targeting is large, we examine whether policy can mitigate the health loss by increasing the vaccination speed, coverage or vaccine efficacy.

Trade-offs between policy objectives

We quantify the extent to which strategies optimised for one policy objective could undermine alternative objectives of interest. For instance, while policymakers may be interested in reducing both deaths and severe cases, strategies optimised for reducing deaths can inadvertently increase severe cases, and we quantify this trade-off using the per cent increase in severe cases under optimal strategies minimising deaths. Comparing across outcomes, we quantify the trade-offs when optimal strategies may not simultaneously improve all outcomes.

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RESULTS

We solved for optimal targeting strategies across age and risk groups based on our calibrated SEIR model for Japan. In light of the uncertainty of variant outbreaks and transmission, we highlight optimal strategies assuming different $R_0$ during the rollout. For an $R_0$ equal to 1.7 or 2.2, optimal strategies minimising deaths would target the high-risk oldest adults in the first stage and target the remaining high-risk elderly as well as low-risk young adults in the second stage (figure 1A,B). For a higher $R_0$ equal to 2.7, however, low-risk young adults are also targeted together with the high-risk oldest adults in the first stage (figure 1C).

Optimal strategies that minimise severe cases would target high-risk young adults in the first stage (figure 2). Compared with strategies minimising deaths, high-risk young adults are targeted more than the low-risk ones, and the elderly overall are less targeted. For a higher $R_0$ equal to 2.7, however, low-risk young adults are targeted together with high-risk young adults under low-efficacy to medium-efficacy vaccines, and the elderly are not targeted under high-efficacy vaccines and high target coverage rates (figure 2C).

In contrast, optimal strategies minimising cases would target low-risk young adults followed by high-risk young adults (figure 3). The low-risk elderly are also targeted when virus transmissibility is high (figure 3B,C). However, across all scenarios we consider, the oldest individuals and the high-risk elderly are not prioritised. This contrasts with strategies targeting the latter groups to minimise deaths but is similar to strategies targeting young adults to minimise cases under high virus transmissibility and high vaccine efficacy (figure 2).

We find similar targeting strategies for alternative $R_0$ ranging from 1.5 to 3.0. As virus transmissibility increases, optimal strategies would target low-risk young adults in the first stage together with the high-risk oldest adults to minimise deaths (online supplemental figure B1), and target low-risk young adults together with high-risk young adults to minimise severe cases (online supplemental figure B2). Targeting young adults ahead of the high-risk elderly also applies to rollouts that minimise cases (online supplemental figure B3), but differs from strategies targeting the high-risk elderly to minimise deaths.

In addition, we find similar strategies across different scenarios of the virus outbreak in early 2020. Assuming that the first case of COVID-19 emerged on 1 January 2020 infecting a low-risk individual aged 20–39 years, optimal strategies under high virus transmissibility would target low-risk young adults together with the high-risk oldest adults to minimise deaths (online supplemental figure B4), target both low-risk and high-risk young adults to minimise severe cases (online supplemental figure B5),
and target young adults followed by the low-risk elderly to minimise cases (online supplemental figure B6). These strategies also apply when the onset of the initial outbreak was delayed to 16 January 2020 (online supplemental figures B7–B9).

Compared with the current policy in Japan (targeting the elderly followed by the high-risk individuals), optimally targeting age and risk groups reduces deaths and severe cases by over 70% and reduces cases by over 80% under the most pessimistic scenario with high virus transmissibility, low vaccination speed and low vaccine efficacy (figure 4). Under low virus transmissibility ($R_0$ below 2.0), optimisation still significantly reduces cases by up to 18% under low-efficacy vaccines but the reductions in deaths and severe cases are smaller (online supplemental figure B10).

Compared with simple strategies targeting either the elderly or the high-risk individuals, optimisation substantially improves outcomes in rollouts under the aforementioned most pessimistic scenarios (online supplemental figures B12 and B13). In rollouts targeting high-risk individuals, adopting high-efficacy vaccines and a high vaccination speed greatly reduces the additional number of deaths and severe cases due to suboptimal targeting, and higher target coverage rates do not further improve outcomes (online supplemental figure B12). In rollouts targeting the elderly, even high-efficacy vaccines do not substantially reduce the number of cases under high virus transmissibility (online supplemental figure B12). In contrast, under low virus transmissibility ($R_0$ below 2.0), high-efficacy vaccines are sufficient to control the virus in...
rollouts targeting either the elderly or high-risk individuals (online supplemental figures B13 and B14).

We showcase the trade-offs between policy objectives using the additional number of deaths, cases or severe cases when targeting is optimised for an alternative outcome of interest. Under high virus transmissibility, minimising cases also reduces subsequent severe cases, but minimising either severe cases or cases in general would increase deaths by over 6% once the target coverage rate reaches 90% (figure 5). This is because the high-risk oldest adults are not targeted as much for reducing cases or severe cases, and higher target coverage rates would increase the vaccine delay and deaths in this group. Under low virus transmissibility ($R_0$ below 2.0), minimising either cases or severe cases could increase deaths by over 3%, whereas the trade-off between minimising cases and severe cases is much smaller (online supplemental figure B15).

**CONCLUSION**

This study examines the optimal targeting of age–risk groups in the distribution of COVID-19 vaccines. In an environment with uncertain variant outbreaks and transmission, effectively targeting and prioritising individuals for vaccines is a challenging but important task facing policymakers. Using a modelling approach, we characterise the optimal targeting strategies when the characteristics of eligible individuals are decided by policy. We show that the ability to simultaneously target multiple groups in the rollout is an important policy lever that can substantially improve the health benefits of vaccines.
Strengths

Our modelling approach builds on a sequential rollout framework for COVID-19 vaccines. In our model, the rollout targets multiple age–risk groups in each stage, and the policymaker determines the optimal group mix as well as the prioritisation across stages when designing the rollout. This differs from previous studies that focus on prioritisation without endogenising group choice. Thus, our model is directly applicable to policy settings targeting a mix of population groups for vaccines (as in the USA, UK, Japan and Australia), and we systematically identify optimal strategies for policy.

We find that optimal targeting uses a combination of age-based and risk-based criteria to maximise the health benefit of vaccines, but differs markedly in design across policy objectives: optimal strategies target the high-risk oldest adults to minimise deaths, target high-risk young adults to minimise severe cases and primarily target young adults rather than the elderly to minimise cases. Due to the differences, optimal strategies minimising cases could increase deaths significantly when a high target coverage rate increases the vaccine delay to the high-risk oldest adults, whereas the trade-off between minimising cases and severe cases is much smaller. This differs from the case of influenza vaccination, where strategies are generally in alignment across policy objectives. The trade-offs in the case of COVID-19 should be carefully considered by policymakers. The common practice to target the elderly and high-risk individuals, for instance, is consistent with policymakers tolerating increases in non-lethal infections to better control the deaths from the virus.

Figure 3 Optimal targeting of age–risk groups to minimise cases, vaccination speed=0.3% daily, $R_0$ ranges from 1.7 (A) to 2.2 (B) to 2.7 (C) during the rollout. Each row of the matrix indicates the optimal targeting of age–risk groups across three rollout stages (indicated by colour), given the target coverage rate on the y-axis. The header of the matrix shows the reduction in infection and severe cases conferred by the vaccine. The x-axis indicates the population groups by age (20-year bands) and risk status. For instance, low-risk adults aged 20–59 years are labelled ‘20–59l’ and high-risk young adults are labelled ‘20–59h’.
We also find that optimal strategies vary substantially with virus transmissibility. To reduce deaths, for instance, optimal strategies would target the high-risk oldest adults under low virus transmissibility, but target low-risk young adults together with the high-risk oldest adults when virus transmissibility is high. This is because the non-direct benefits of vaccines become more important under high virus transmissibility, and optimal strategies should consider both direct and non-direct benefits when targeting across groups. As a result, optimal strategies may involve mixing multiple age and risk groups in the same stage in addition to prioritisation over time.

Figure 4  Improvements in outcomes under optimal targeting of age–risk groups over the current policy, for minimizing deaths (A), minimizing severe cases (B), and minimizing cases (C). $R_0$ ranges from 1.7 to 2.7 during the rollout. Each matrix shows the per cent reduction in outcomes when the rollout optimally targets age–risk groups given the $R_0$ and vaccination speed on the x-axis and the target coverage rate on the y-axis. A fast rollout vaccinates 0.5% of the population daily, and a slow rollout vaccinates 0.3% daily. The denominator of the per cent reduction is the outcome of the current policy in Japan, which targets the elderly in the first stage followed by high-risk individuals in the second stage. The header of the matrix indicates vaccine efficacy in reducing infections and severe cases.
which is an important design feature in the rollout of COVID-19 vaccines that has been overlooked in the literature. This distinction is especially important when the rollout coincides with the outbreak of the Delta variant or Omicron,\textsuperscript{24,25} in which case simple strategies suitable for low virus transmissibility may not effectively contain the virus. Based on the optimal strategies we identify, one could consider shifts in the targeted population in accordance with the nature of the variant and vaccine efficacy against the variant.

Indeed, we find that targeting with optimal group mix substantially improves outcomes under high virus
transmissibility. Compared with the current policy in Japan, optimal targeting can further reduce deaths and severe cases by over 70% and reduce cases by 80%. When simple strategies targeting the elderly or high-risk individuals have already been implemented, additional policy measures such as increasing the vaccination speed and adopting high-efficacy vaccines can mitigate the health loss from suboptimal targeting. Under low virus transmissibility, however, adopting high-efficacy vaccines is sufficient to control the virus even with simple targeting in the rollout. For the ongoing vaccination in low/middle-income countries, these results suggest that high-efficacy vaccines are valuable not only for the health benefits, but also for the protection against suboptimal policy responses due to unforeseen changes in the virus and vaccination conditions.

Limitations
Our study has a number of limitations. While we identify optimal targeting under different vaccination conditions, we do not consider changes in the contact patterns that could vary with vaccination. For instance, increased contact with family members could strengthen the benefit of jointly targeting young and high-risk older groups. In general, responses in the contact rates between groups would further motivate a flexible group mix in the rollout.

We also do not evaluate strategies that delay the second dosing of two-dose vaccines and the interplay with the rollout of a third-dose booster. Delaying the second dose can be optimal for reducing infections in the initial phase of the rollout, whereas reducing the delay of boosters is optimal when vaccine efficacy decreases over time or against new variants. The dynamic concerns could complicate the medium-run strategies responding to changing conditions of the virus.

Our results examine only the health benefits of vaccines. Including the economic losses could increase the targeting of young adults for vaccines. We also do not consider the cost of purchasing the vaccines. While this would be acceptable in the current Japanese context where only mRNA vaccines have been used, balancing the benefits of high-efficacy vaccines against costs could matter in countries with more limited resources and higher opportunity costs of purchase.

Finally, while we simulate the health impacts of vaccines over a 1-year horizon, the long-run impacts on individuals and society should also guide pandemic relief efforts going forward. We leave the study of the long-run impacts of COVID-19 and policy responses to future work.

Policy implications
The targeting of population groups for COVID-19 vaccines should be carefully designed according to the virus and vaccination conditions on the ground. While targeting the most vulnerable individuals can directly reduce deaths and severe cases, simultaneously targeting young or low-risk individuals could further improve outcomes under high virus transmissibility. To maximise the health benefits of vaccines, optimal strategies would flexibly target a mix of age and risk groups in the rollout.

Although policymakers would ideally implement the optimal strategies, the actual transmissibility of the virus and the effectiveness of vaccines and vaccination efforts are often difficult to predict or control. The outbreak of new virus variants is highly uncertain, and the efficacy of current vaccines against variants is less established. Vaccine hesitancy and mistrust can hinder policy efforts increasing uptake and slow down a rollout aimed at high coverage rates.

With these challenges, policy measures that robustly improve outcomes are particularly valuable to policymakers. Due to the complexity of optimal strategies when virus transmissibility is high, social distancing should be maintained if the rollout follows a simple strategy targeting the elderly or the high-risk individuals. In addition, high-efficacy vaccines can greatly reduce the additional deaths and severe cases due to suboptimal targeting. Increasing the vaccination speed is also important for age-based prioritisation targeting the elderly under high virus transmissibility.

To summarise, our results show that targeting a mix of age-risk groups is a powerful policy tool in the distribution of COVID-19 vaccines, and we characterise optimal targeting strategies applicable to the ongoing rollout in low/middle-income countries. While policy objectives ultimately depend on the country’s public health needs, our results highlight the trade-offs between objectives and suggest policy measures that robustly improve outcomes for a range of virus and vaccination conditions.

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