

ORIGINAL ARTICLE

# Age priority in continuous coronavirus disease 2019 booster doses under China's new policy of free-will nucleic acid test: A dynamic model-based effectiveness and cost-effectiveness analysis

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## ABSTRACT

**Background:** The initial mass vaccination's effectiveness has diminished, necessitating accelerated immunization coverage scaling. China has shifted nucleic acid testing from large-scale to voluntary. This study assesses the effectiveness and cost-effectiveness of different booster vaccination strategies in China. **Methods:** A dynamic transmission model divided the population into three groups: 0-19, 20-59, and 60+ years. We evaluated the effectiveness and cost-effectiveness of three vaccination strategies based on previous studies and public databases. Three scenarios were modeled and compared to no-continuation-vaccination to calculate averted diseases, deaths, and net benefits. One-way sensitivity analysis and probabilistic sensitivity analysis assessed findings' stability. **Results:** COVID-19 vaccination had significant health benefits compared to no continuing vaccination. Strategy II (prioritizing vaccinated 20-59-year-olds, then vaccinated 60+ individuals, and finally 0-19-year-olds) was the most cost-effective. Strategy I (prioritizing unvaccinated 60+ individuals, then 20-59, and finally 0-19) prevented the most deaths. Strategy II was the most cost-effective, with a total cost of 93,995,223,462 USD and the highest net benefit of 3,054,475,908,551,960 USD. Strategy II resulted in the highest number of avoided cases across categories, including infected, asymptomatic, mild/moderate, severe, and critical cases. Each strategy's effects on preventing new cases and critical illness were comparable. Sensitivity analyses confirmed the results' reliability. **Conclusion:** Prioritizing vaccinated 20-59-year-olds, then vaccinated 60+ individuals, and finally 0-19-year-olds was the most effective prevention strategy. The vaccination strategy should be tailored to the pandemic situation and available medical resources for maximum health gains.

**Key words:** coronavirus disease 2019; vaccines; cost-effectiveness analysis; China

## INTRODUCTION

A new coronavirus disease 2019 (COVID-19) emerged at

the end of 2019 and remains a threat to global health, which was announced as a Public Health Emergency of International Concern (PHEIC) on 30 January 2020 and characterized as a pandemic on 11 March 2020 by the

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Received: 19 December 2022; Revised: 11 March 2023; Accepted: 21 April 2023; Published: 26 May 2023

<https://doi.org/10.54844/hd.2022.0294>

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World Health Organization (WHO). As of 29 November 2022, WHO reported approximately 630 million cumulative cases and 6.60 million cumulative deaths worldwide.<sup>[1]</sup> Vaccines against COVID-19 have been developed at an unprecedented rate, and several countries have adopted the vaccines in their efforts to control the pandemic, particularly to avoid symptoms and deaths. The vaccine dose per 100 people in the world has reached 166.26 as of 29 November 2022 according to the report of WHO.<sup>[1]</sup>

As a result of the waning effect of vaccination, evolving variants, and virus breakthroughs, the effect of initial mass vaccination is limited, as evidenced by multiple COVID-19 resurgences worldwide.<sup>[2–5]</sup> The study proved that the vaccine is still effective against the mutant, although the effect did decrease somewhat by 6 months.<sup>[5]</sup> Experts proposed an annual booster dose to control cross-border transmission and local outbreaks.<sup>[2,6]</sup> Since December 2020, China has initiated two rounds of vaccination programs and has been actively promoting the COVID-19 vaccine booster dose. Most people in China have been vaccinated, and there are still a small number, especially the elderly, who have not been vaccinated. Booster vaccination is less than 60% of the total number. There is no doubt that COVID-19 vaccination should be accelerated, but it is worth debating whether to prioritize booster vaccination or coverage of unvaccinated people.

One of the characteristics of COVID-19 is that the susceptibility, infectivity, severity, and mortality of it vary by age, and the current study confirmed that increased age was linked to death in patients with COVID-19.<sup>[7]</sup> While some studies have consistently recommended that prioritizing younger populations with higher contact rate generally exerts a greater effect on reducing morbidity than prioritizing older age groups.<sup>[8]</sup> Thus, not only should the priority of booster vaccination be discussed, but also should the priority of age groups.

China has offered free vaccination to cover the whole population since January 2021. The first step was to cover people aged 18–59, gradually extending to those aged over 60 in April 2021, to adolescents aged 12–17 in July 2021, and to children aged 3–11 in November 2021. In addition, China has transferred test of nucleic acid from large scale to free-will and proposed the plan of continuing to vaccination with booster doses. The priority of vaccination for different age groups needs to be discussed urgently. In this study, we will most likely follow the age groups described above and use a dynamic model to simulate the effectiveness and cost-effectiveness of different vaccination strategies.

## METHODS

### Study design

We conducted an effective and economic evaluation

based on a dynamic transmission model to assess the effectiveness and cost-effectiveness of different vaccination strategies in China. The model was constructed in Microsoft Excel 2019 and the analysis was reported according to the Consolidated Health Economic Evaluation Reporting Standards statement.<sup>[9]</sup>

### Data sources

We collected data (Table 1, Table 2 and Table 3) from a literature search and public databases to parameterize the initial number of people, prevalence data, vaccination data and other model parameters.

Most vaccines in China have been vaccinated for more than half a year because they were vaccinated earlier. As a result, we assumed that the protection effect of the vaccinated population without booster doses is equivalent to that of the vaccinated population with a single dose. Daily transition rates and utility scores were derived from natural history literature or calculated by differential equations.

All costs were expressed in 2021 USD from the perspective of health system and included direct medical costs as well as the cost of diagnosis and vaccination. The cost of vaccination included vaccines, syringes and safety boxes, cold chain, human resources, and transportation. The cost of contacts included case identification and medical observation. The cost of asymptomatic or mild and moderate included identification and diagnosis, inpatient care, medicines, treatment for pre-existing conditions and follow-up appointment. The cost of severe included identification and diagnosis, inpatient care, medicines, treatment for pre-existing conditions, oxygen therapy and follow-up appointments. The cost of critical included identification and diagnosis, inpatient care, medicines, treatment for pre-existing condition, tracheostomy and tracheal intubation, use of ventilator, extracorporeal membrane oxygenation, artificial kidney, plasma exchange and follow-up appointment.

### Model structure

A dynamic model (Figure 1) was constructed to simulate infection and progression of COVID-19 in China. Since the protection period for COVID-19 vaccination is mostly about half a year, the simulation time of the model is 180 days, with one-day cycle.

The daily transition rates were shown in Figure 1 and some of them were based on the following formulas.

$$\begin{aligned}
 F_1 &= \gamma \left( \frac{E(t)}{N(t)} \beta_1 + \frac{A(t)}{N(t)} \beta_2 + \frac{Ad(t) + As(t)}{N(t)} \beta_3 + \frac{M(t) + I(t) + C(t)}{N(t)} \beta_4 + \frac{M_s(t) + M_r(t) + L_s(t) + L_r(t) + C_s(t) + C_r(t)}{N(t)} \beta_5 \right) \\
 F_2 &= (1 - \varepsilon) F_1 + \varepsilon F_1 (1 - \zeta) \\
 F_3 &= F_2 [\eta_1 (1 - \tau_1) + \eta_2 (1 - \tau_2) + \eta_3 (1 - \tau_3) + (1 - \eta_1 - \eta_2 - \eta_3)] \\
 F_4 &= \sum_{i=1}^n [\eta_i (1 - \lambda_i) + \eta_2 (1 - \lambda_2) + \eta_3 (1 - \lambda_3) + (1 - \eta_1 - \eta_2 - \eta_3)] \\
 F_5 &= \tau_1 [\eta_1 (1 - v_1) + \eta_2 (1 - v_2) + \eta_3 (1 - v_3)]
 \end{aligned}$$

We assumed that treatment would delay the disease

**Table 1: Parameters of initial cohort**

| Parameter  | Base-case value | Deterministic range | PSA distribution | Source  |
|--|-----------------|---------------------|------------------|---|
| Total population   | 1,443,497,378   | -                   | -                | China Population Census Yearbook 2020 <sup>[10]</sup>                                       |
| 0-19 years old   | 347,882,868     | -                   | -                | Tabulation on The 2010 Population Census of The People' S Republic of China <sup>[11]</sup> |
| 20-59 years old  | 903,340,659     | -                   | -                |   |
| 60+ years old  | 192,273,851     | -                   | -                |   |
| Total number of recoveries                                       | 381,286         | -                   | -                | WHO <sup>[12]</sup>   |
| Proportion of recovery with antibody                             | 50.00%          | 20.00%-80.00%       | Beta             | Assumed   |
| The number of people vaccinated with at least one dose           | 1,328,017,588   | -                   | -                | WHO <sup>[12,13]</sup>  |
| The number of people vaccinated with booster dose                | 826,910,000     | -                   | -                |   |
| The number of people infected at the initial stage of simulation | 328,480         | -                   | -                |   |
| The proportion of infection with symptoms                        | 75.00%          | 60.00%-90.00%       | Beta             | Du <i>et al.</i> <sup>[14]</sup>  |

PSA: probabilistic sensitivity analysis; WHO: World Health Organization.

**Table 2: Model parameters**

| Parameter                                 | Base-case value | Deterministic range | PSA distribution | Source   |
|---|-----------------|---------------------|------------------|--|
| Natural mortality/year                    |                 |                     |                  | Tabulation on the 2010 Population Census of the People's Republic of China <sup>[11]</sup> |
| Age category (years)                      |                 |                     |                  |  |
| 0-19                                      | 0.06%           | 0.03%-0.13%         | Beta             |  |
| 20-59                                     | 0.22%           | 0.05%-0.62%         | Beta             |  |
| 60+                                       | 13.14%          | 1.03%-45.44%        | Beta             |  |
| Number of daily contacts ( $\gamma$ )     |                 |                     |                  | Zhao <i>et al.</i> <sup>[15]</sup><br>Dirlikov <i>et al.</i> <sup>[16]</sup>               |
| 0-19 years old                            |                 |                     |                  |  |
| Age category (years)                      |                 |                     |                  |  |
| 0-19                                      | 0.99            | 0.89-1.09           | Gamma            |  |
| 20-59                                     | 0.99            | 0.89-1.09           | Gamma            |  |
| 60+                                       | 4.47            | 4.02-4.91           | Gamma            |  |
| 20-59 years old                           |                 |                     |                  |  |
| Age category (years)                      |                 |                     |                  |  |
| 0-19                                      | 1.07            | 0.96-1.17           | Gamma            |  |
| 20-59                                     | 3.07            | 2.76-3.38           | Gamma            |  |
| 60+                                       | 2.31            | 2.08-2.54           | Gamma            |  |
| 60+ years old                             |                 |                     |                  |  |
| Age category (years)                      |                 |                     |                  |  |
| 0-19                                      | 0.18            | 0.16-0.20           | Gamma            |  |
| 20-59                                     | 1.60            | 1.44 – 1.76         | Gamma            |  |
| 60+                                       | 2.49            | 2.24 – 2.74         | Gamma            |  |
| Proportion of mask wearing( $\epsilon$ )  |                 |                     |                  | Zhang <i>et al.</i> <sup>[17]</sup>  |
| Age category (years)                      |                 |                     |                  |  |
| 0-19                                      | 94.70%          | 85.23%-100.00%      | Beta             |  |
| 20-59                                     | 97.63%          | 87.87%-100.00%      | Beta             |  |
| 60+                                       | 98.60%          | 88.74%-100.00%      | Beta             |  |
| The accuracy of face mask type selection  | 41.61%          | 37.45%-45.77%       | Beta             | Tang <i>et al.</i> <sup>[18]</sup>   |
| Effectiveness of interventions            |                 |                     |                  |  |
| Mask wearing ( $\zeta$ )                  | 50.00%          | 45.00%-55.00%       | Beta             | Ueki <i>et al.</i> <sup>[19]</sup>   |
| Protection rate of two doses AZD vaccines |                 |                     |                  |  |

|  |        |                |       |   |
|--|--------|----------------|-------|---|
| Against infection ( $\iota_2$ )  | 65.90% | 65.2%-66.60%   | Beta  | Jara <i>et al.</i> <sup>[20]</sup>  |
| Against symptom ( $\lambda_2$ )  | 87.50% | 86.70%-88.20%  | Beta  |   |
| Against severe ( $\upsilon_2$ )  | 90.30% | 89.10%-91.40%  | Beta  |   |
| Protection rate of one dose AZD vaccines                                   |        |                |       |   |
| Against infection ( $\iota_1$ )  | 15.50% | 14.20%-16.80%  | Beta  |   |
| Against symptom ( $\lambda_1$ )  | 37.40% | 34.90%-39.90%  | Beta  |   |
| Against severe ( $\upsilon_1$ )  | 44.70% | 40.80%-48.30%  | Beta  |   |
| Protection rate of booster dose AZD vaccines                               |        |                |       |   |
| Against infection ( $\iota_b$ )  | 78.80% | 76.80%-80.60%  | Beta  |   |
| Against symptom ( $\lambda_b$ )  | 86.30% | 83.70%-88.50%  | Beta  |   |
| Against severe ( $\upsilon_b$ )  | 92.20% | 88.70%-94.60%  | Beta  |   |
| Infection rate of patients exposed to symptomatic infection ( $\beta_3$ )  | 6.40%  | 5.76%-7.04%    | Beta  | Thron <i>et al.</i> <sup>[21]</sup>   |
| Relative infectiousness of asymptomatic individual                         | 50.00% | 45.00%-55.00%  | Beta  | McEvoy <i>et al.</i> <sup>[22]</sup>  |
| Relative infectiousness of isolation individual ( $\theta$ )               | 66.00% | 59.40%-72.60%  | Beta  | Thron <i>et al.</i> <sup>[21]</sup>   |
| Infection rate of patients exposed to asymptomatic infection ( $\beta_2$ ) | 3.20%  | -              | Beta  | McEvoy <i>et al.</i> <sup>[22]</sup>  |
| Infection rate of patients exposed to infections latent ( $\beta_1$ )      | 15.00% | 13.50%-16.50%  | Beta  | Aleta <i>et al.</i> <sup>[23]</sup>   |
| Recovery time (days)   |        |                |       |   |
| Latency ( $t_1$ )  | 5.20   | 4.68-5.72      | Gamma | Kim <i>et al.</i> <sup>[24]</sup>   |
| Asymptomatic ( $t_2$ )   | 3.50   | 3.15-3.85      | Gamma | Choi <i>et al.</i> <sup>[25]</sup>  |
| Mild or moderate ( $t_3$ )   | 7.00   | 6.30-7.70      | Gamma | Orangi <i>et al.</i> <sup>[26]</sup>  |
| Severe ( $t_4$ )   | 12.00  | 10.80-13.20    | Gamma |   |
| Critical ( $t_5$ )   | 20.00  | 18.00-22.00    | Gamma |   |
| Mortality rate for severe or critical illness                              |        |                |       |   |
| 0-19 years old   | 0.20%  | 0.18%-0.22%    | Beta  | National Health Commission of The People's Republic of China, China <sup>[27]</sup> |
| 20-59 years old  | 0.40%  | 0.44%-0.48%    | Beta  |   |
| 60+ years old  | 0.60%  | 0.54%-0.66%    | Beta  |   |
| Treatment rate   |        |                |       |   |
| Asymptomatic ( $\upsilon_1$ )  | 99.00% | 90.00%-100.00% | Beta  | Assumed   |
| Mild or moderate ( $\upsilon_2$ )  | 99.00% | 90.00%-100.00% | Beta  |   |
| The rate of test for severe or critical people ( $\mu$ )                   | 80.00% | 90.00%-100.00% | Beta  |   |
| Severe ( $\upsilon_3$ )  | 99.00% | 90.00%-100.00% | Beta  |   |
| Critical ( $\upsilon_4$ )  | 99.00% | 90.00%-100.00% | Beta  |   |
| Disease progress rate  |        |                |       |   |
| Mild or moderate→Severe ( $\tau_1$ )                                       | 1.95%  | 1.76%-2.15%    | Beta  | Fu <i>et al.</i> <sup>[28]</sup>  |
| Severe→Critical ( $\tau_2$ )   | 3.29%  | 2.96%-3.61%    | Beta  |   |
| Treatment delays progress ( $\omega$ )                                     | 80.00% | 72.00%-88.00%  | Beta  | Assumed   |

PSA: probabilistic sensitivity analysis; PCR: polymerase chain reaction.

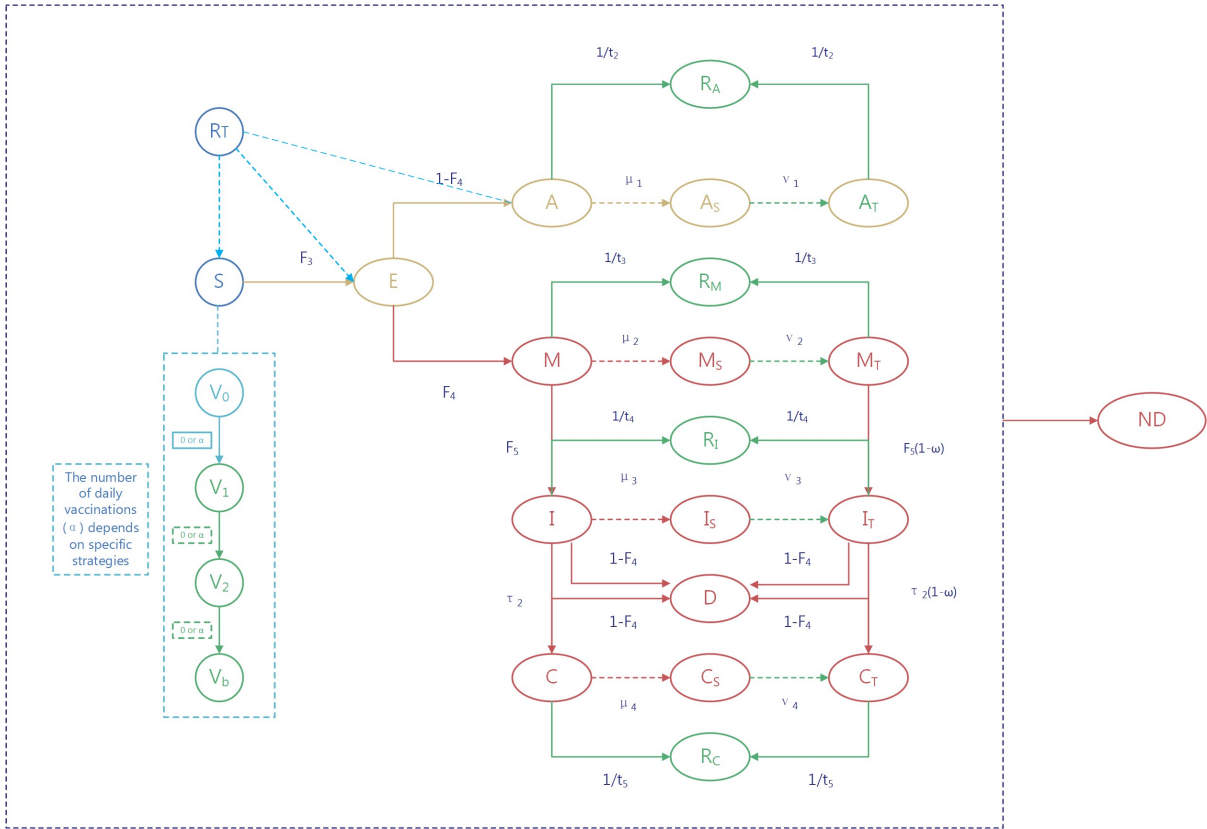
**Table 3: Cost and utility**

| Parameter                         | Base-case value | Deterministic range | PSA distribution | Source                                |
|-----------------------------------|-----------------|---------------------|------------------|---------------------------------------|
| Cost of test and prevention (USD) |                 |                     |                  |                                       |
| Mask/day                          | 0.14            | 0.13-0.15           | Gamma            | Mukerji <i>et al.</i> <sup>[29]</sup> |
| Vaccine/dose                      | 18.60           | 16.74-20.46         | Gamma            | WHO <sup>[12]</sup>                   |
| Syringes and safety boxes/dose    | 0.04            | 0.04-0.04           | Gamma            | Pearson <i>et al.</i> <sup>[30]</sup> |
| Cold chain costs/dose             | 0.13            | 0.12-0.15           | Gamma            |                                       |
| Human resource/dose               | 0.03            | 0.03-0.03           | Gamma            |                                       |



|                             |        |               |       |                               |
|-----------------------------|--------|---------------|-------|-------------------------------|
| Transport/dose              | 0.38   | 0.34-0.42     | Gamma |                               |
| Wastage                     | 15.00% | 13.50%-16.50% | Beta  |                               |
| Cost of treatment (USD)/day |        |               |       | Jin et al. <sup>[31]</sup>    |
| Asymptomatic                | 61.85  | 55.67-68.04   | Gamma |                               |
| Mild or moderate            | 61.85  | 55.67-68.04   | Gamma |                               |
| Severe                      | 383.02 | 344.71-421.32 | Gamma |                               |
| Critical                    | 803.08 | 722.77-883.38 | Gamma |                               |
| Health Utilities            |        |               |       |                               |
| Susceptible person          | 0.95   | 0.90-0.99     | Beta  | Alinia et al. <sup>[32]</sup> |
| Latency                     | 0.95   | 0.90-0.99     | Beta  | Assumed                       |
| Asymptomatic                | 0.95   | 0.90-0.99     | Beta  |                               |
| Mild or moderate            | 0.85   | 0.80-0.89     | Beta  | Alinia et al. <sup>[32]</sup> |
| Severe                      | 0.77   | 0.73-0.80     | Beta  |                               |
| Critical                    | 0.63   | 0.60-0.66     | Beta  |                               |
| Recovery                    | 0.90   | 0.85-0.94     | Beta  |                               |
| Death                       | 0.00   | -             | Beta  |                               |

PSA: probabilistic sensitivity analysis; WHO: World Health Organization.



**Figure 1.** COVID-19 Dynamic Infection Model. S: susceptible; V0: unvaccinated susceptible; V1: 1-dose vaccinated susceptible; V2: 2-dose vaccinated susceptible; Vb: booster vaccinated susceptible; E: incubation period; A: asymptomatic; AS: detected asymptomatic; AT: treated asymptomatic; RA: recovered asymptomatic; M: mild to moderate symptomatic infected; MS: detected symptomatic infected; MT: treated symptomatic infected; RM: recovered mild to moderate symptomatic infected; I: severe infected; IS: detected severe infected; IT: treated severe infected; RI: recovered severe infected; C: critically infected; CS: detected critically infected; CT: treated critically infected; RC: recovered critically infected; D: died from COVID infection; ND: died of natural causes; COVID-19: coronavirus disease 2019.

deterioration. According to China's current pandemic prevention and control policy, we supposed that almost all patients would be treated, with only the elderly suffering from severe and critical illness dying. Furthermore, we assumed that other preventive measures, such as mask wearing rate, are consistent across all strategies except vaccination. Currently, most of the infections have occurred in December. The baseline time for this study was March 1st, with an additional 3 months of protection for recovery after infection. Moreover, the vaccination provides protection for 6 months, meaning that infections would not be expected to occur during the 180 cycles of the new rehabilitated population simulation period.

### ***Vaccination strategies and scenarios***

Three vaccination strategies were investigated. Strategy I was to give priority to people over 60 who had not been vaccinated to two doses, then to people aged 20-59, and finally to people aged 0-19; Strategy II was to give priority to people aged 20-59 who had been vaccinated, then to people aged 60 and above who had been vaccinated, and then to people aged 0-19; Strategy III was to give priority to people aged 20-59 who had not been vaccinated to two doses, then to people aged 60 and above, and finally to people aged 0-19.

Considering the uncertainty of current vaccination and subsequent vaccination mobilization capacity, we assumed scenarios of one million and three million doses of vaccination per day. Combined with three vaccination strategies, six vaccination scenarios were simulated in the model. One million people a day is the base-case analysis.

### ***Effectiveness and cost-effectiveness analysis***

The number of infected, the symptomatic, the severe and deaths was the index of effectiveness. We calculated an incremental cost-effectiveness ratio (ICER, *i.e.*, incremental cost/quality-adjusted life year [QALY] gained) between different vaccination strategies to determine their cost-effectiveness. We used the WHO definition of cost-effectiveness as being less than one-time Chinese Gross Domestic Product (GDP) per capita. The willingness to pay was set as one-time Chinese GDP per capital. The willingness to pay was set as one-time Chinese GDP in 2021 (12,551 USD).

### ***Sensitivity analysis***

One-way sensitivity analysis was used to assess the effect of changing individual model parameters with uncertainty. Based on 1000 Monte Carlo simulation, we also conducted probabilistic sensitivity analysis to

characterize all model parameters' combined uncertainty by using Microsoft Excel 2019. All sensitivity analysis results would be recorded and reported.

## **RESULTS**

### ***Base-case analysis***

Under the base-case analysis (one million people were vaccinated every day), vaccination strategies had significant health benefits compared to not continuing vaccination with booster doses, with fewer infected cases and more Effectiveness.

Assuming the implementation of booster doses for vaccination in China in 2023, it was estimated that strategy I, II, and III could respectively avert a total of 12,577,302, 15,110,392, and 3,055,553 infected cases; 1,783,423, 2,110,488, and 766,994 asymptomatic cases; 10,452,812, 12,653,155, and 2,151,318 mild or moderate cases; 278,632, 331,541, and 119,332 severe cases; and 27,578, 33,172, and 11,721 critical cases compared to the scenario of no ongoing vaccination with booster doses.

Strategy II could obtain more effect compared to other strategies with lower cost, effect and costs for no continuing vaccination and three vaccination strategies were shown in Table 4.

The changes of new and total cases of infections, the asymptomatic, the mild or moderate, the severe, the critical and disease-related deaths were shown in Figure 2 and 3. Although strategy II may have an effect preference, there was no significant difference between strategy I and II. Compared to the scenario of no continuing vaccination with booster doses, Strategy II resulted in the highest number of avoided cases across all categories, including infected, asymptomatic, mild or moderate, severe, and critical cases.

Strategy II (giving priority to people aged 20-59 who had been vaccinated, then to people aged 60 and above who had been vaccinated, and then to people aged 0-19) was dominant to other vaccination strategies with more QALYs and lower cost, then followed by Strategy I (giving priority to people over 60 who had not been vaccinated to two doses, then to people aged 20-59, and finally to people aged 0-19) under any threshold of willingness to pay.

### ***Sensitivity analysis***

Some of the data may not reflect actual costs unbiased, but uncertain analysis confirms that cost range fluctuations do not affect the stability of the conclusions. The change of individual model parameters and variations in all parameters did not substantially affect the conclusion that Strategy II was the most cost-effective vaccination strategy for Chinese people.

Table 4: Results of base-case

| Strategy                                      | Cost of vaccination (USD) | Cost of treatment (USD) | Other cost (USD) | Total cost (USD) | Effect (QALYs)  | Net Benefit (USD)     | ICER (USD/QALY) |
|---|---------------------------|-------------------------|------------------|------------------|-----------------|-----------------------|-----------------|
| Not continuing vaccination with booster doses | 0                         | 12,916,627,714          | 85,828,635,850   | 98,745,263,563   | 243,310,045,362 | 3,053,685,634,070,220 | -               |
| Vaccination strategy I                        | 3,970,674,000             | 12,972,375,573          | 78,600,889,112   | 95,543,938,684   | 243,357,951,053 | 3,054,290,099,732,390 | -66.83          |
| Vaccination strategy II                       | 3,970,674,000             | 12,989,565,481          | 77,034,983,981   | 93,995,223,462   | 243,372,631,964 | 3,054,475,908,551,960 | -75.90          |
| Vaccination strategy III                      | 3,970,674,000             | 12,928,849,918          | 83,929,439,780   | 100,828,963,697  | 243,320,604,565 | 3,053,816,078,933,860 | 197.33          |

QALY: quality-adjusted life year.

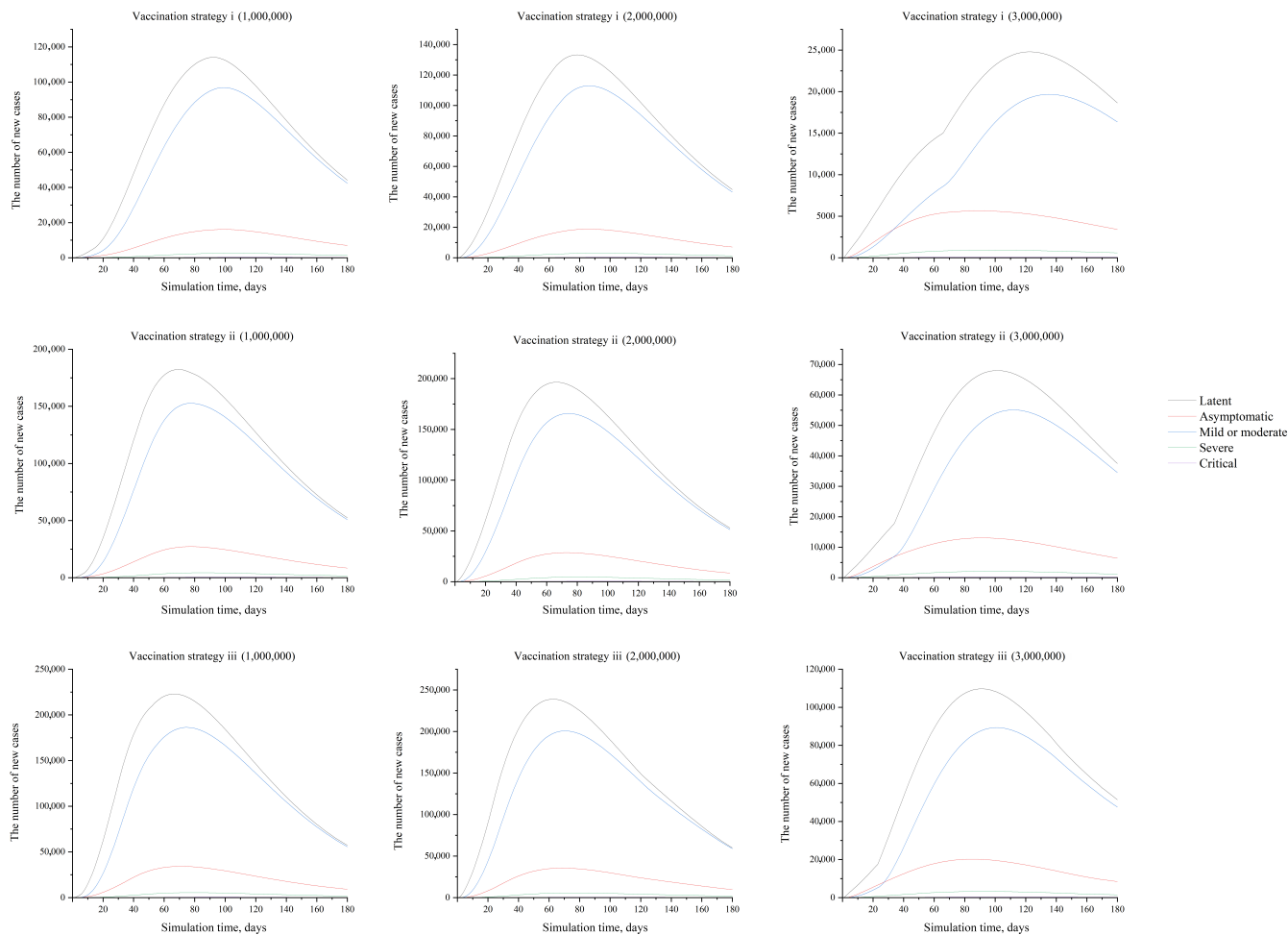


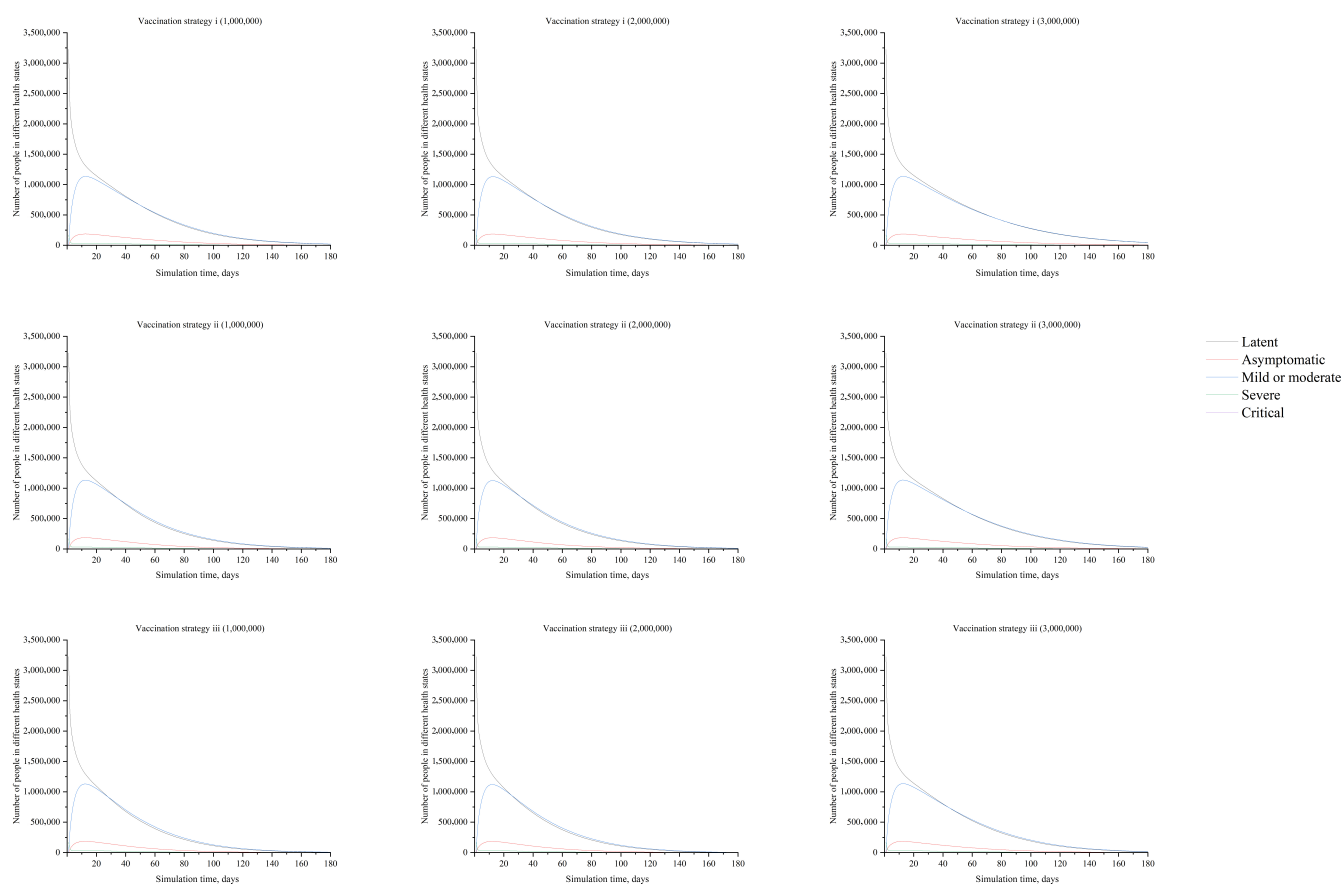
Figure 2. Number of new cases under different strategies.

DISCUSSION

Although the vaccines used may differ, most countries, including low- and middle-income countries, have been vaccinating against COVID-19 for some time. Despite enormous efforts to achieve successful COVID-19 vaccination, vaccine hesitancy towards approved and prospective COVID-19 vaccines is a major impediment.<sup>[33]</sup> COVID-19 vaccines were safe and effective in reducing deaths, severe cases, symptomatic

cases, as well as infections globally,<sup>[34]</sup> and the rapid development of the pandemic may not give us time to delay vaccination.

With the emergence of variant strains like Omicron in recent years, traditional protective measures such as masks appear insufficient to completely contain the pandemic. Although the fact that the protection was limited, COVID-19 vaccination effectively reduced



**Figure 3.** Number of people in each health state under different strategies.

deaths, severe cases, symptomatic cases, and infections even though the virus had mutated.<sup>[35]</sup> Since China has a relatively high vaccination rate in the world, the current vaccination rate of the elderly in China is insufficient, and these people are the most vulnerable to severe or critical illness and death. Although the third dose was initially controversial, real-world evidence demonstrated its relative immunological and clinical efficacy over time. There is a large amount of literature indicating that the neutralization effect of the third dose may be effective against a variety of variants, including Alpha (B. 1.1.7), Beta (B. 1.351), Gamma (P. 1), Delta (B. 1.617.2) and, more recently, Omicron (B. 1.1.529).<sup>[36]</sup> Thus, some countries have begun to consider and provide booster dose of COVID-19 vaccines for preventing infections and deaths.

### Main findings

Our study proved the effectiveness of different COVID-19 vaccination strategies in China and the most cost-effective was Strategy II, giving priority to people aged 20-59 who had been vaccinated, then to people aged 60 and above who had been vaccinated, and then to people aged 0-19.

Individual or all parameter changes had no effect on the conclusion that Strategy II was the most cost-effective.

Although the model simulation data showed that Strategy II had a weak effect advantage, we did not see a significant effect gap from Figure 2 and Figure 3 when compared to others, which benefited primarily from China's personal protection and previous high vaccination rate.

Wearing masks was effective in reducing the risk of transmission,<sup>[36]</sup> which not only China but many other countries were trying to do.<sup>[37,38]</sup> A high rate of wearing masks could almost prevent most infections from occurring before the incidence of variant strains like Omicron with high infectivity. Non-pharmacological prevention may be insufficient to minimize the health impact of COVID-19 after the incidence of the highly infectious mutant. Vaccination was a global trend and almost no country did not implement COVID-19 vaccination, which also proved significant health benefits compared to no continuing vaccination with booster doses, so we did not adopt unrealistic cost-effective comparisons between no continuing vaccination and vaccination strategies.

Although aging was a significant risk factor for severe disease and death from COVID-19 due to self-resistance and underlying diseases, Strategy II appeared to be the most cost-effective strategy. With COVID-19 non-

pharmacological prevention such as wearing masks, the probability of infection and transmission was not severe for the elderly even though there was no priority for their vaccination due to small social distance and contacts.

Notably, the younger age group (20-59) would benefit more from vaccination because of better booster dose protection, which would bring greater QALYs gained. The effect of the booster dose was relatively greater than that of one dose of vaccination and no-vaccination. Strategy II was the most cost-effective. However, there was no doubt that the elderly should be prioritized in the decision to prioritize non-vaccine coverage. The results were similar to Buckner's "dynamic prioritization" strategy,<sup>[39]</sup> which was a vaccination plan that first targeted people at high risk of infection and then switched to targeting groups with high fatality rates. However, there was no doubt that priority should be given to the elderly for the purpose of avoiding deaths which is also proved by our model.

Given the outbreak situation, our study was based on current public health interventions to demonstrate the need to prioritize vaccination with booster needles. This study added significantly to the growing body of literature on vaccine prioritization, but the findings and conclusions cannot be generalized to most countries due to differences in vaccination coverage and mask wearing, and it was difficult for most countries to achieve the same high treatment rate as China, regardless of budget or number of infected people.

### **Strength and limitations**

Compared with other kinds of studies on COVID-19, studies on vaccine prioritization were quite sparse. To our knowledge, this study appeared to be the first economic evaluation study of different vaccination strategies combined with age and booster dose for COVID-19 in China. We took many public health interventions, such as masks, in account and constructed a dynamic model that can simulate transmission and indirect protection. The study was of great significance in terms of both study design and display of results.

Despite a reasonable design, this study had several limitations. Firstly, due to a lack of parameters, we did not consider the various professions of the population, though front-line workers may be important to target. Secondly, the model parameters were not collected from the same group at the same time, so they may not be representative of all regions of China. Furthermore, with the brief appearance of the Omicron virus, some data were still from other strains. Thirdly, we assumed that the efficacy of COVID-19 vaccines could maintain within six months after vaccination, but vaccine efficacy was more likely to decline gradually in reality—that

means this assumption may lead to an overestimation of vaccine efficacy in the short term and an underestimation in the long term. Finally, some factors included logistic hurdles—delay of vaccine supplies, budget burden, vaccine hesitancy were not considered in the study due to lack of parameters.

## **CONCLUSION**

Strategy II that giving priority to people aged 20-59 who had been vaccinated, then to people aged 60 and above who had been vaccinated, and then to people aged 0-19 was effective and cost-effective. To maximize health gains, the vaccination strategy should be tailored to the pandemic situation and available medical resources.

## **DECLARATION**

### **Author contributions**

Tang W and Malone DC designed the study and interpreted findings. Zhou D and Shao H wrote initial drafts of the manuscript, developed the model and did all model analyses. Shao H and Tu Y search the parameters and data for the model. Zhou D and Shao T analysed the epidemic data to parameterise the model. Zhou D visualised the data. Malone DC, Xing Y and Tang W revised and polished the initial drafts. All authors reviewed the manuscript. All authors had full access to all the data in the study and the corresponding author had final responsibility for the decision to submit for publication.

### **Source of funding**

The National Natural Science Foundation of China (Grant No. 72174207).

### **Ethics approval and consent to participate**

Ethics approval was not required for this modelling study, as no patient-related individual data were used.

### **Conflict of interest**

Daniel C. Malone is the Co-Editor-in-Chief of the journal. Wenxi Tang and Taihang Shao are the editors of the journal. The article was subject to the journal's standard procedures, with peer review handled independently of this member and his research group.

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