Projecting the impact of the introduction of SARS-CoV-2 Omicron variant in China in the context of waning immunity after vaccination

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Article

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Abstract

After the adoption of a dynamic zero-COVID strategy in China for nearly two years, whether and for how long this policy can remain in place is unclear. The debate has thus shifted towards the identification of mitigation strategies capable to prevent the disruption of the healthcare system, should a nationwide epidemic caused by the SARS-CoV-2 Omicron variant start to unfold. To this aim, we developed a mathematical model of SARS-CoV-2 transmission tailored to the unique immunization and epidemiological situation of China. We find that the level of immunity induced by the current vaccination campaign would be insufficient to prevent overwhelming the healthcare system and major losses of human lives. Instead, a synergistic strategy would be needed and based on 1) a heterologous booster vaccination campaign, 2) treating 50% of symptomatic cases with an antiviral with an 80% efficacy in preventing severe outcomes, and 3) the adoption of non-pharmaceutical interventions (NPIs) capable of reducing R to ≤2. Protecting vulnerable individuals by ensuring accessibility to vaccines and antivirals, and maintaining a certain degree of NPIs should be emphasised in a future mitigation policy, possibly supported by strengthening critical care capacity and the development of highly efficacious vaccines with long-lasting immunity.

Introduction

First discovered in Southern Africa in November 2021¹, the Omicron variant of SARS-CoV-2 has swiftly spread across the world and replaced the Delta variant to become the dominant strain globally². Omicron has demonstrated an increased transmissibility relative to Delta³⁴ and immune escape capability⁷⁸. Together with the progressive waning of the protection against the infection associated with previous infections and/or vaccination⁹¹⁰, these characteristics have led to major Omicron epidemics in most countries¹¹. Despite signs of a possibly lower clinical severity¹²¹³ than Delta, the sheer volume of Omicron infections has strained healthcare systems worldwide, including the US¹⁴ and the UK¹⁵. For instance, in the UK, the Omicron wave has led to higher infection rates than that during the second wave in the winter of 2021, with substantial hospitalizations and deaths, including >1,000 deaths reported per week between January 14 and February 4, 2022²².

After controlling the initial epidemic wave in Hubei in early 2020, China has deployed multilayer non-pharmaceutical intervention (NPI) protocols to contain sporadic COVID-19 outbreaks introduced from international travellers or imported materials. Maintaining a low infection rate in the population throughout the pandemic has bought China time to mass immunize the entire population against SARS-CoV-2. As of February 15, 2022, 90.4% of the population with age ≥3 years has received the full primary schedule of the vaccine, 40.1% among whom have received the booster shot²². However, the vaccine-induced population immunity may be insufficient to prevent COVID-19 outbreaks per se. From March 1 through March 13, 2022, more than 10,000 local Omicron infections have been reported in 27 provinces across China, with growing outbreaks occurring in Jilin, Guangdong, and Shanghai²⁴. To contain the highly infectious and immune evasive Omicron variant, additional NPI measures are required to maintain the dynamic zero-COVID policy²⁵. Whether and for how long these policies can remain in place is debated, and as recommended by the WHO²⁶, every country should be prepared to chart its own path to transit from a pandemic to an endemic phase, accounting for local epidemiology, vaccination levels, population immunity, the strength of health services, etc. In this regard, as of March 2022, two antivirals (BRII-196/BRII-198 combination and Paxlovid) have been approved in China providing a new tool against COVID-19²⁷²⁸. Here we explore the feasibility of a COVID-19 mitigation strategy that could safeguard China’s shift from pandemic containment to mitigation, while minimizing the disease burden and social cost. Specifically, we leverage a mathematical model to simulate a hypothetical Omicron wave in China, project the demand for hospital beds and intensive care units (ICUs), and explore mitigation strategies combining vaccine booster doses, antivirals, and NPIs to reduce COVID-19 burden while preventing the healthcare system being overwhelmed.

Results

Baseline scenario

The baseline scenario assumes that: 1) 20 individuals infected with the Omicron variant are introduced into the Chinese population on March 1, 2022; 2) the basic reproduction number $R_0$ is 7.2 in the absence of NPIs and immunity; 3) the booster vaccination with inactivated vaccines is rolled out at a speed of 5 million doses per day from February 16, 2022, before which the daily vaccination rates were informed by the cumulative doses of COVID-19 vaccines administered in China; 4) 90% of individuals who have completed two-dose primary vaccination for at least 6 months will receive a booster shot²². However, the vaccine-induced population immunity may be insufficient to prevent COVID-19 outbreaks per se. From March 1 through March 13, 2022, more than 10,000 local Omicron infections have been reported in 27 provinces across China, with growing outbreaks occurring in Jilin, Guangdong, and Shanghai²⁴. To contain the highly infectious and immune evasive Omicron variant, additional NPI measures are required to maintain the dynamic zero-COVID policy²⁵. Whether and for how long these policies can remain in place is debated, and as recommended by the WHO²⁶, every country should be prepared to chart its own path to transit from a pandemic to an endemic phase, accounting for local epidemiology, vaccination levels, population immunity, the strength of health services, etc. In this regard, as of March 2022, two antivirals (BRII-196/BRII-198 combination and Paxlovid) have been approved in China providing a new tool against COVID-19²⁷²⁸. Here we explore the feasibility of a COVID-19 mitigation strategy that could safeguard China’s shift from pandemic containment to mitigation, while minimizing the disease burden and social cost. Specifically, we leverage a mathematical model to simulate a hypothetical Omicron wave in China, project the demand for hospital beds and intensive care units (ICUs), and explore mitigation strategies combining vaccine booster doses, antivirals, and NPIs to reduce COVID-19 burden while preventing the healthcare system being overwhelmed.

Our model simulations suggest that, in the absence of NPIs, the introduction of the Omicron variant in March 2022 could have the potential to generate a "tsunami" of COVID-19 cases in China. Over a 6-month simulation period, such an epidemic is projected to cause 476.0 million symptomatic cases (330.7 per 1,000 individuals), 32.0 million hospital admissions (22.3 per 1,000 individuals), 7.9 million ICU admissions (5.5 per 1,000 individuals), and 3.0 million deaths (2.1 per 1,000 individuals), with a major wave between April and June 2022. (Fig. 1 and Supplementary Fig. 11).

According to model simulations, 88.7% of symptomatic infections would occur among vaccinated individuals (36.2% among individuals completing primary doses and 52.5% among those receiving the booster dose); the majority of symptomatic infection is estimated in the adult population (63.9% among individuals aged 18–59 years and 20.4% among aged ≥60 years) (Supplementary Fig. 11b-c). When considering other clinical endpoints, the beneficial effect of vaccination is more evident with 34.9% of deaths estimated to occur among non-vaccinated individuals (despite representing only 10.6% of the population) (Fig. 1). In particular, unvaccinated individuals aged ≥60 years account for 36.6% of the total number of deaths due to the gap in vaccination coverage in this segment of the population. Filling this gap in vaccination coverage among the elderly would lead to a 16.9% decrease in the total number of deaths (Extended Data Fig. 1).
To evaluate the impact of such an epidemic on the national healthcare system, we consider that all COVID-19 hospitalizations require hospital beds for respiratory illness, and critically ill cases require ICU beds (see definitions of clinical outcomes in Sec. 3.5 of Supplementary Information), and then compute the corresponding demands. It is estimated that 10.5 million hospital beds for respiratory illness, and 4.0 million ICU beds would be required at the epidemic peak, which is equivalent to 2.4 times more than the number of existing hospital beds for respiratory illness (3.1 million), and 61.3 times more than the number of existing ICU beds (64,000) in China. The period of hospital and ICU bed shortage is estimated to last 14 and 50 days, respectively. Regardless that all hospital beds in China (9.1 million) would be dedicated for COVID-19, a shortage of 1.4 million beds under the baseline scenario would still occur (Fig. 2). When considering a more conservative scenario on the immune escape of the Omicron variant (referred as to high immune escape, Extended Data Table 1), the health outcomes would increase by 22.3–32.1% (Extended Data Fig. 2).

Unlike China, many countries have already been exposed to past waves of SARS-CoV-2 infection and have, therefore, developed a substantial level of infection-induced immunity from previous variants. To extend the baseline scenario to these countries, we assume that 30% of the population has been exposed to the virus (Delta variant, which may provide better cross-protection against Omicron than inactivated vaccines) before the epidemic onset (see details in Sec. 5.2 of Supplementary Information). Under this scenario, all the health outcomes are estimated to decrease by 26.6–27.2% (Extended Data Fig. 3).

Impact of individual mitigation strategies

We separately investigated the impact of three alternative categories of strategies to mitigate COVID-19 burden: homologous/heterologous booster vaccination with varying rollout speeds, antivirals, and NPIs. Regarding booster vaccination, accelerating the daily vaccine rollout from 5 million to 10 million doses (10 million rollout scenario) would slightly reduce the COVID-19 burden (11.0–11.3%); if we consider the administration of a heterologous booster based on a subunit vaccine (10 million rollout+subunit scenario), a larger decrease of COVID-19 burden (26.5–35.5%) could be achieved (Fig. 3). Whereas, further increasing vaccine rollout to 15 million doses per day, would not provide substantial additional benefits (Supplementary Fig. 12).

In the absence of NPIs, assuming that 50% of symptomatic cases could be treated with the approved Chinese COVID-19 drug BRII-196/BRII-198 combination therapy, which has been reported to be 80% effective in preventing hospitalization and death, a 39.8–40.0% decrease in hospital admissions, ICU admissions and deaths is estimated (50% uptake+80% effect scenario). In the best-case scenario in which all symptomatic cases are treated with the highly efficacious COVID-19 drug Paxlovid (which is 89% effective in preventing hospitalization and death and 31% and has already been approved in China), the number of hospital admissions, ICU admissions, and deaths could be substantially reduced by 88.4–89.0% (100% uptake+89% effect scenario) (Fig. 3).

We then investigated the impact of introducing different levels of NPIs (in the presence of vaccination, but absence of antivirals). First, we tested the extension of the dynamic zero-COVID strategy implemented in China since mid-2020 with the effect of seeding the epidemic in June 2022 (Epi onset: Jun 1 scenario). This scenario would lead to a 10.1–10.6% reduction of COVID-19 burden (Fig. 3). Further delaying the seeding of the epidemic to September 1, 2022 (Epi onset: Sep 1 scenario) may lead to a lower reduction of COVID-19 burden (7.9–8.9% vs. 10.1–10.6%) due to an increased waning of immunity in the population. Second, we tested the implementation of a national-level school closure strategy (School closure scenario); although the number of infections decrease by 1.4%, COVID-19 burden does not, due to a shift in age-distribution of infections towards older ages. Additionally closing all workplaces (School+workplace closure scenario) would lead to a 5.4–5.7% decrease in health outcomes. Third, we considered a scenario where NPIs are able to reduce the risk of infection equally across age groups and we simulated different intensity of NPIs leading to \( R_t \leq 4 \) (similar to values observed in Western countries during the Omicron wave in winter 2021–2022). In this scenario, only NPIs capable of reducing \( R_t \leq 2 \) would lead to a substantial decrease (32.8–39.5% and 95.4–97.8% for \( R_t = 2 \) and \( R_t = 1.5 \), respectively) in health outcomes (Fig. 3).

In summary, of all scenarios aforementioned, only in the stringent NPIs (\( R_t = 1.5 \)) scenario, could the number of deaths be reduced to less than the annual influenza-related death toll in China (i.e., 88,000 deaths) (Fig. 3). Regarding the daily requirement for hospital and ICU beds, only in three scenarios, namely 100% uptake+89% effect, \( R_t = 2 \) and \( R_t = 1.5 \), would the number of hospitalised individuals at the epidemic peak not exceed the available capacity of hospital beds for respiratory illness. However even in the best-case scenarios (100% uptake+89% effect and \( R_t = 1.5 \)), the number of ICU patients at the epidemic peak would exceed the number of available ICU beds by 1.3-6.0 times, with a total of 12-28 days of shortage (Fig. 2c–d). In particular, implementing stringent NPIs to reduce \( R_t \) to 1.5 would avoid shortage of ICU beds until mid-August 2022, after which overload of ICU beds will occur due to waning immunity (Fig. 2c).

Impact of combined mitigation strategies

Except for prolonged stringent NPIs (\( R_t \leq 1.5 \)), which come at high socioeconomic cost, any individual mitigation strategy alone is capable of neither reducing the death toll to the level of an influenza season nor preventing overwhelming the healthcare system (Figs. 2 and 3). Here, we assessed the impact of synergetic strategies leveraging homologous/heterologous booster vaccination, distributions of antiviral treatments, and adoption of NPIs at the same time (Fig. 4).

Most combinations of interventions are projected to prevent exceeding hospital bed capacity for respiratory illness. For instance, a practical synergetic strategy is specifically as follows: 1) treating 50% of symptomatic cases aged ≥12 years with a homegrown antiviral of 80% effectiveness in preventing severe outcomes, and 2) administering a heterologous booster vaccination (subunit vaccines) at a daily vaccination rate of 10 million doses. However, a serious shortage of ICU beds and excess death would still occur unless moderate NPIs capable of reducing \( R_t \) to 2 or lower were implemented simultaneously (Fig 4).

Discussion

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Using a stochastic dynamic model of SARS-CoV-2 transmission, our study projects the COVID-19 burden caused by the importation of Omicron infections in mainland China, should the dynamic zero-COVID policy being lifted. In the context of current vaccination strategy (mainly homologous booster vaccination using inactivated vaccines) and booster rollout (5 million doses per day), we estimated that the introduction of the Omicron variant would cause substantial surges in cases, hospitalizations, ICU admissions, and deaths, and would overwhelm hospitals (3.4 times the existing capacity) and ICUs (62.3 times the existing capacity).

Our findings show that should an Omicron variant epidemic be allowed to spread uncontrolled in mainland China, around 35% of the death toll would occur in unvaccinated individuals, with the majority of deaths occurring among unvaccinated individuals aged ≥60 years (40 million people). A similar trend has been observed in the Omicron-driven fifth COVID-19 wave in Hong Kong SAR, China, which began in early 2022. In Hong Kong, the lower vaccine coverage among the vulnerable elderly population (only 31.3% of individuals aged ≥80 years are fully vaccinated as of March 6, 2022) has led to 25.5 deaths per million people. By contrast, other countries like Singapore, the UK, and the US with much higher vaccine coverage in this age group (>90%) had significantly lower death rates (2.1, 4.0, and 7.8 deaths per million people, respectively) during their Omicron wave. Thus, increasing vaccine uptake rate among the elderly is critical and urgent for limiting the COVID-19 burden in a case of a widespread Omicron epidemic in mainland China.

Increasing the rollout speed of booster doses to 10 million doses per day is estimated to be insufficient to prevent overloading the health system. Our results highlight the importance of ramping-up the booster campaign in coordination with the relaxation of NPIs to minimize the waning of immunity around the time of epidemic onset. In addition to booster vaccination, the wide and timely distribution of a highly efficacious antiviral treatment could maintain the peak demand of hospital beds below the available capacity for respiratory illness. However, without relying on NPIs as well, the peak demand for ICUs would largely exceed the current capacity in China (3.6 ICUs per 100,000 individuals — compared to 34.7 per 100,000 individuals in the US). The additional implementation of stringent NPIs could prevent exceeding ICU capacity and reducing the death toll to a level comparable to that of influenza. To lower the dependence on NPIs, it would be critical to timely distribute highly efficacious (≥89%) antivirals to a considerable fraction (≥50%) of symptomatic cases.

As in Brazil, Chile, and Argentina, where inactivated vaccines are used for primary vaccination, heterologous booster vaccination using either subunit vaccines or AD5-vectored vaccines was initiated in China in late February 2022. In addition to these two vaccines, which are available in mainland China, our study further assessed the impact of using mRNA vaccines (unavailable at the time of writing — March 8, 2022) in heterologous booster vaccination. We identified that a heterologous boosting would be recommended (Supplementary Fig. 13).

Here, we propose a general framework to simulate the potential impact of Omicron on multiple disease outcomes, project the demand for hospital and ICU beds, and explore potential combinations of vaccination, antivirals, and NPIs. Inactivated COVID-19 vaccines have been used in 108 countries in addition to China. Thus, our results could be valuable for policy-making even for other countries.

Our study has several limitations. First, our baseline scenario without NPIs (using the pre-pandemic mixing patterns) may overestimate health outcomes because human behaviours would likely change spontaneously should an Omicron epidemic start to widely spread in China. Second, we assumed that the mortality rate remains constant over the projection period; however, studies have suggested that the mortality rate may increase during periods of high strain on hospital services. Third, the epidemiological characteristics of Omicron, clinical severity, VEs of primary and booster vaccination and its persistence against different clinical endpoints, as well as the effectiveness of antivirals are not fully understood. Although we conducted a comprehensive literature search and extensive sensitivity analyses to explore the impact of the uncertainty of model parameters (which support the consistency of our findings), our projections should be cautiously interpreted.

In conclusion, despite a primary vaccination coverage of ≥90% and homologous booster vaccination coverage of ≥40%, it is estimated that vaccination alone will not prevent overwhelming the Chinese healthcare system, should an Omicron outbreak be let to unfold. Synergetic strategies (heterologous booster, widespread distribution of antivirals, and NPIs) would be needed to prevent overwhelming the healthcare system. Protecting vulnerable individuals by ensuring access to vaccination and antivirals, as well as maintaining a degree of NPIs (e.g., mask-wearing, enhanced testing, social distancing, and reducing mass gatherings), should be points of emphasis. Moving forward, improving ventilation, strengthening critical care capacity, and the development of new highly efficacious vaccines with long-term immune persistence would be key priorities.

**Methods**

**SARS-CoV-2 transmission model**

We developed an age-structured stochastic compartmental susceptible-latent-infectious-removed-susceptible (SLIRS) model to simulate the transmission of the SARS-CoV-2 Omicron variant in China. The model accounts for primary and booster vaccination, disease progression, antiviral drugs uptake, and waning immunity. Detailed information about the model and its calibration are described in the Supplementary Information.

The model is calibrated to represent the Chinese population and considers the age-mixing patterns quantified prior to the COVID-19 pandemic. Based on the analyses of household transmission of Omicron in Denmark, immune escape and transmissibility of Omicron in South Africa and England, the Omicron variant may possess similar or higher intrinsic transmissibility than the Delta variant, and largely evades immunity from past infection or two vaccine doses. Thus, we considered a 1.2-fold increase of transmissibility of the Omicron variant as compared to the Delta variant, which led to an $R_0 = 7.2$. In the absence of Omicron-specific estimates, the generation time was set to 4.6 days, in line with estimates for the Delta variant. We then considered a longer generation time, in line with previous lineages, of 6.4 days as a sensitivity analysis (Supplementary Table 8 and Supplementary Fig. 18). Baseline simulations were seeded with 20 imported infections on March 1, 2022 and run forward for 6 months. We consider 5 and 10 seeds as sensitivity analyses (Supplementary Fig. 17).
COVID-19 burden model

We determined the age-specific risks of disease progression given Omicron infection from the top to the bottom of the severity pyramid. We first estimate age-specific infection fatality risk (IFR) of Omicron among unvaccinated individuals using the UK COVID-19 vaccine weekly surveillance report\(^44\) and infection survey\(^45\). The estimates of Omicron IFR are well compared with those estimated in a Hong Kong modelling report\(^46\) (Supplementary Table 2). We further calculated age-specific infection hospitalization risk (IHR) by dividing IFR estimates by hospitalization fatality risk (HFR). We assumed that the overall HFR among unvaccinated adults with Omicron is 9.2%, as suggested by a prospective observational study conducted in the US\(^47\). Finally, we estimate the age-specific risk of hospital admission for symptomatic cases (CHR) by dividing the calculated IHR by the probability of developing symptoms for unvaccinated Omicron infection. In the main analyses, we consider that 61% of Omicron infections are asymptomatic\(^48,49\) (a sensitivity analysis on this estimate is reported in Supplementary Fig. 19). Symptomatic individuals are assumed to be equally infectious as asymptomatic individuals\(^50\); we also performed a sensitivity analysis where asymptomatic individuals are assumed to be 65% less infectious than symptomatic ones\(^51\) (Supplementary Fig. 16). Our top–down approach allowed us to estimate the burden matrices (i.e., hospitalizations, ICU admissions, and deaths) and measure the strain for healthcare system regardless of the proportion of symptomatic infections. Details on this approach are reported in Sec. 3.1–3.3 of Supplementary Information and the estimated age-specific risks on disease progression are presented in Supplementary Tables 2 and 9.

We considered that all COVID-19 hospitalizations require hospital beds for respiratory illness and critically ill cases require ICU beds. To determine the demand of hospital and ICU beds, we set the length of stay (LoS) in hospital before being discharged as a pooling mean of 3.1 days\(^16,19,52\); 8 days are considered for non-ICU hospitalizations with fatal outcomes\(^53\). We assumed the ICU LoS to be 8 days, consistent between discharged and deceased individuals\(^53,54\).

In China, a total of 9.1 million hospital beds were available as of 2020, of which 3.14 million could be allocated to respiratory illness (including hospital beds in departments of internal medicine, paediatrics, infectious disease, and ICUs), 64,000 of which are ICUs\(^29\).

Modelling vaccination

A mass vaccination campaign has been launched in China in December 2020\(^55\). On October 3, 2021, a homologous booster vaccination campaign (relying on the same vaccine as the initial inactivated vaccine shots) has been initiated among individuals aged ≥18 years who completed primary vaccination at least 6 months earlier\(^56,57\). As of February 15, 2022, >90% of populations aged ≥3 years have completed primary vaccination and >40% of the populations has received a booster dose\(^23\). Compared to other age groups (86.4%, 100%, and 92.3% fully vaccinated individuals for the age groups 3–11, 12–17, and 18–59 years, respectively), individuals aged ≥60 years have the lowest vaccination coverage (~80%)\(^23\), corresponding to approximately 40 million unvaccinated individuals.

From January 16, 2022 onwards, homologous booster rollout was set at 5 million doses per day in the baseline analysis. Sensitivity analyses considering 2-4 times the baseline rollout capacity as well as heterologous booster vaccination using subunit, mRNA, and vector vaccines were conducted (Supplementary Figs. 12 and 13). In the main heterologous booster vaccination analysis, we assumed the heterologous booster VE to decay at the same rate as the homologous booster VE. Alternatively, we assumed a 50% decreased decay rate for the heterologous booster VE against the homologous booster VE (Supplementary Fig. 13).

We considered different VE against each of the following clinical endpoints: infection, symptomatic illness, hospitalisation, ICU admission, death, and onward transmission (Extended Data Table 1). Both primary and booster vaccination-induced protection, as well as infection-induced immunity, wane over time. Considering the uncertainty surrounding the immune escape of Omicron, we considered two scenarios of immune escape: low immune escape scenario and high immune escape scenario (Supplementary Figs. 4–7). Details on the time-varying VEs are reported in Sec. 4.2–4.4 of Supplementary Information.

Modelling antiviral uptake

A homegrown monoclonal neutralizing antibody therapy (BRII-196/BRII-198 combination) and an imported antiviral (Paxlovid) have been approved for emergency use in China\(^27,28\). In the baseline scenario, we assumed no symptomatic cases will take COVID-19 drugs. To quantify the mitigating effect of COVID-19 drug uptake, we tested two alternative scenarios: 50% symptomatic cases will take the Chinese COVID-19 drug with 80% effectiveness in preventing hospitalizations or deaths\(^30\) and 100% symptomatic cases will take the imported antiviral with higher effectiveness of 89%\(^31\). Only symptomatic cases aged ≥12 years are eligible to take COVID-19 drugs\(^27\) (see details in Sec. 1.4 of Supplementary Information).

Assessing NPIs

We tested the impact of NPIs in three ways: 1) postponing the time of imported Omicron infections (e.g., through maintaining the dynamic zero-COVID strategy adopted in China since 2020\(^25\)); 2) implementing national school closure or school and workplace closure; 3) reducing effective contacts equally across age groups; that is, a range value of \(R_t = 1.0\sim2.0\) by a step of 0.1 and 2.5~7.0 by a step of 0.5 to represent varying intensities of NPIs (see details in Sec. 6.3 of Supplementary Information).

Data analysis

For each scenario, 200 stochastic simulations were performed. The outcomes of these simulations determined the distribution of the number of symptomatic infections, hospital admissions, ICU admissions, and deaths by age. We defined 95% credible intervals as quantiles 0.025 and 0.975 of the estimated distributions.
Declarations

Author contributions

H.Y. conceived, designed, and supervised the study. J.C. designed the model. X.D. and H.L. developed the model. J.C., X.D., J.Y., X.C., Q.W., J.Z., W.Z., Z.Z., Z.C., W.L., Y.L., and X.Z. collected the data. K.S. and M.A. contributed to the methodology. X.D. and J.C. analysed the model output. J.C., X.D., J.Y., K.S., M.A., and H.Y. interpreted the results. Z.C., X.D., C.P., J.C., and R.S. prepared the figures. J.C., J.Y., X.D., Z.C., and H.L. wrote the first draft of the manuscript. M.A. and K.S. critically revised the content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Competing interests

H.Y. received research funding from Sanofi Pasteur, GlaxoSmithKline, Yichang HEC Changjiang Pharmaceutical Company, Shanghai Roche Pharmaceutical Company, and SINOVAC Biotech Ltd. Except for research funding from SINOVAC Biotech Ltd, which is related to the data analysis of clinical trials of immunogenicity and safety of CoronaVac, the others are not related to COVID-19. M.A. has received research funding from Seqirus; the funding is not related to COVID-19. All the other authors have no competing interests. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US National Institutes of Health.

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Data availability

The data and code that support the findings of this study will be made available on GitHub upon the acceptance of this manuscript.

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Figure 1

Projected COVID-19 burden for baseline scenario. a, Daily hospital (non-ICU) admissions per 10,000 individuals projected for an Omicron epidemic over a 6-month simulation period in China. b, Epidemiological status of hospitalised (non-ICU) patients. c, Age distribution of hospitalised (non-ICU) patients. d, Distribution of hospitalised (non-ICU) patients per 10,000 by age group and epidemiological status. e, As a but for ICU admissions. f, As b but for ICU admissions. g, As c but for ICU admissions. h, As d but for ICU admissions. i, As a but for deaths. j, As b but for deaths. k, As c but for deaths. l, As d but for deaths.
Figure 2

Projected demand and shortage of hospital beds and ICUs for scenarios adopting single measures. **a**, Projected daily demand of hospital beds over a 6-month simulation period for scenarios adopting single measures compared with the capacity of hospital beds in China. The green and red horizontal dashed lines indicate the number of hospital beds for respiratory illness and all hospital beds available in China, respectively. **b**, Days of shortage of hospital beds as a function of the number of insufficient hospital beds compared with the capacity of hospital beds for respiratory illness. The curves are smoothed by B-spline with 5 degrees of freedom. **c**, As **a** but for ICUs. **d**, As **b** but for ICUs with 8 degrees of freedom. The scenarios included in legend are as follows: **10 million rollout + subunit** refers to using protein subunit vaccine as booster dose and increasing the rollout speed of booster doses from 5 million doses per day in baseline scenario to 10 million doses per day. **100% uptake + 89% effect** corresponds to a scenario where all symptomatic cases are treated with a COVID-19 drug with 89% effectiveness. **Epi onset: Sep 1** correspond to a scenario where the epidemic onset is delayed until September 1, 2022. **School + workplace closure** corresponds to a scenario where, on the top of baseline strategy, all schools and workplaces remain closed for the duration of the epidemic. **Rt: 2.0** and **1.5** correspond to scenarios assuming different levels of NPIs leading to reduced values of the reproduction number. Note that no NPIs is implemented in the baseline scenario.
Figure 3

Projected impact of adopting single measure on COVID-19 burden. a, Total number of hospital admissions projected for an Omicron epidemic over a 6-month simulation period in China when adopting a single measure among booster vaccination, antiviral drugs, and NPIs. The scenarios indicated on y-axis are as follows: 10 million rollout corresponds to increasing the rollout speed of booster doses from 5 million doses per day in baseline scenario to 10 million doses per day. 10 million rollout + subunit refers to using protein subunit vaccine as booster dose and increasing the speed of booster dose rollout to 10 million doses per day. 50% uptake + 80% effect corresponds to a scenario where 50% of symptomatic cases are treated with a COVID-19 drug with 80% effectiveness. 100% uptake + 85% effect corresponds to a scenario where all symptomatic cases are treated with a COVID-19 drug with 89% effectiveness. Epi onset: Jun 1 and Sep 1 correspond to two scenarios where the epidemic onset is delayed until June 1 and September 1, 2022, respectively. School closure corresponds to a scenario where, on the top of baseline strategy, all schools remain closed for the duration of the epidemic. Similarly, School + workplace closure corresponds to a scenario, where on the top of baseline strategy, all schools and workplaces remain closed for the duration of the epidemic. RT: 4.0, 2.0, and 1.5 correspond to scenarios assuming different levels of NPIs leading to reduced values of the reproduction number. Note that no NPIs is implemented in the baseline scenario. b, As a but for the total number of ICU admissions. c, As a but for the total number of deaths.
Figure 4

Projected healthcare demand and number of deaths for scenarios combining multiple measures. **a**, Projected peak hospital bed occupancy during a 6-month simulation period when adopting multiple measures combining booster vaccination, antivirals, and NPIs under a scenario where the vaccination gap among individuals aged ≥60 years is filled. The Luopan from the innermost concentric circle to the outermost concentric circle indicates the combination of adopting different intervention measures: homologous (inactivated) or heterologous (subunit) booster regimen; low (5 million) or high (10 million) booster rollout capacity per day; 80% or 89% COVID-19 drug effectiveness; 50% or 100% COVID-19 drug uptake among symptomatic cases; $R_t$, representing varying intensity of NPIs. $R_t = 7.2$ corresponds to the scenario with no NPIs. The numbers on top of bars represent the numbers of peak hospital bed occupancy; when the number is reported in red, it indicates that the projected number of hospital beds does not exceed the number of beds dedicated to respiratory illness available in China. **b**, As **a**, but for peak ICU occupancy. The numbers on top of bars in red indicate that the peak ICU occupancy when it is lower than the number of ICUs available in China. **c**, As **a**, but for total number of deaths over a 6-month simulation period. The numbers on top of bars in red indicate that the projected number of total deaths does not exceed the annual influenza-related death toll in China (i.e., 88,000 deaths)\textsuperscript{32}.

Supplementary Files

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