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Preplanned Studies

Association Between COVID-19 Vaccination Coverage and Case Fatality Ratio: a Comparative Study — Hong Kong SAR, China and Singapore, December 2021–March 2022

Guanhao He[1,&]; Sui Zhu[2,&]; Di Fu[1]; Jianpeng Xiao[3]; Jianguo Zhao[3]; Ziqiang Lin[1]; Tao Liu[1]; Xiaofeng Liang[2,#]; Wenjun Ma[1,#]

Summary

What is already known about this topic?

Hong Kong Special Administrative Region (SAR), China and Singapore are both facing considerable Omicron variant epidemic. However, the overwhelmed medical system and high case fatality ratio (CFR) just occurred in Hong Kong SAR, China but not in Singapore.

What is added by this report?

The low vaccination coverage in Hong Kong SAR, China, especially among the older adults, is shown to be a primary reason of its recent high CFR.

What are the implications for public health practice?

Facing the potential epidemic risk, non-vaccinated, non-fully-vaccinated, and non-booster-vaccinated people in China, especially the elderly, should get any type of accessible vaccine, which could save lives when the infection unfortunately befalls.

Hong Kong Special Administrative Region (SAR), China and Singapore have been facing the Omicron epidemic since January 2022. Despite their similar socioeconomic statuses, Hong Kong SAR, China encountered a higher case fatality ratio (CFR) accompanied by an overwhelmed medical system compared to Singapore. This study collected and compared the CFRs, vaccination coverage, infection rate, and medical resources occupancy rates from the two places. The vaccine coverage rates and CFRs in 52 Omicron variant dominated countries and regions were also collected and multiple linear regressions were used to explore associations. The random forest (RF) method was additionally used to estimate the importance of factors contributing to CFRs. The CFR in Hong Kong SAR, China was larger than in Singapore (0.53% *vs.* 0.06%), especially for people ≥70 years (4.46% *vs.* 0.48%). Correspondingly, the vaccine coverage was lower in Hong Kong SAR, China than in Singapore (full vaccine coverage for total population: 76.15% *vs.* 92.00%; for people ≥70 years: 56.82% *vs.* 95.00%). Based on the data from Omicron variant dominated countries and regions, a negative association between vaccine coverage and CFR was observed. The RF model indicated that full vaccination and ≥1 dose vaccination coverages were the top two contributing factors to CFR. These findings call on people without complete coronavirus disease 2019 (COVID-19) vaccinations, especially the elderly, to get any type of accessible vaccine, which could save lives.

Since the emergence of Omicron variant, due to its heightened transmissibility, the whole world has been suffering a new wave of the COVID-19 pandemic (*1*). As finance and trade centers with high international connectivity, Hong Kong SAR, China and Singapore have been experiencing a considerable increase in COVID-19 cases since January 2022. According to the Government of Hong Kong SAR, China, the epidemic was overwhelming the medical system with a relatively high CFR (*2*), while Singapore seemed to manage its epidemic within the capacity of its medical system contributing to a lower CFR (*3*). As we know, Hong Kong SAR, China and Singapore share many similar characteristics, such as developed economy, freeport international trade, and a similar population density. However, it is unclear why there is such a stark difference in CFR between the two locations. This study aims to explore this important issue, which could provide significant implications for China to develop and adjust future COVID-19 prevention strategies.

Hong Kong SAR, China had been applying the zero-COVID policy using strict non-pharmaceutical interventions (NPIs) such as border quarantine, social distancing, and mask wearing, and achieved low cases during the first four waves of epidemic. Unfortunately, several infected flight staff did not obey the quarantine rule and entered the community, which was the suspected origin of the Omicron variant epidemic in Hong Kong SAR, China. Because of the superior transmissibility of Omicron variant, the delayed identification, and the control of all infected people, the epidemic rapidly expanded. Together with low vaccination coverage among the elderly, the imperfect tiered diagnosis, and treatment strategy at the early stage, more severe cases may occur and a few patients with mild symptoms may occupy the hospital beds, which lead to overwhelmed medical systems.

Since the emergence of the first case of COVID-19 in January 2020 in Singapore, its containment strategy had been applied until August 2021, when 78% of its population had been vaccinated with at least one dose. Since then, Singapore has continued to promote COVID-19 vaccination and tried to transition to "co-existence with virus" strategy by gradually lifting NPI restrictions. Singapore has also been optimizing the tiered diagnosis and treatment strategy, which effectively relieved the pressures on the medical system.

CFRs, vaccination coverage, infection rate, medical resources occupancy rates for COVID-19, and other comparative variables, including age structure, the number of swab tests, and prevalence of chronic diseases were obtained and calculated from the Government of the Hong Kong SAR, China and Singapore. The detailed source websites were presented in the footnotes of tables and figures.

To investigate the effects of vaccination coverage after controlling for confounding factors, we collected the data of 52 Omicron dominated countries and regions (Omicron proportion ≥90%) from Our World in Data (https://ourworldindata.org/). Nine explanatory variables, including full vaccination, ≥1 dose, booster vaccination, gross domestic product (GDP) per capita, population density, hospital beds per 1,000 people, human development index, proportion of people aged 70 and older, and cardiovascular mortality per 100,000 people were collected. One dependent variable (CFR) was collected. The detailed definitions of these variables are presented in Supplementary Table S1 (available in http://weekly.chinacdc.cn). Due to the 28-day efficacy assessment period (*4*), the proportion of people with at least one dose, with full vaccination, with booster vaccination before February 7, 2022 were collected and then averaged for analysis.

Multiple linear regression models were employed to explore the effects of vaccination coverage (full vaccination, ≥1 dose, and booster vaccination) on CFR separately, after controlling for potential confounding variables. In addition, a random forest (RF) regression model was used to qualitatively assess the feature importance of nine explanatory variables contributing to CFR. RF regression analysis, a tree-based machine learning algorithm, works well with multicollinearity and nonlinear problems between predictors and makes decisions by constructing a multitude of decision trees (5,000 trees in this study) for training the data included in a model (*5*–*6*). Predictions for each variable are aggregated across all trees and percentage increase in mean square error (%IncMSE) is calculated, which indicates how much the model accuracy decreases if that variable were omitted.

All statistical analyses were performed using R software (version 4.0.5, R Foundation for Statistical Computing, Vienna, Austria). A two-sided *P* value of <0.05 represented statistically significant.

Table 1 shows that from December 31, 2021 to March 22, 2022, the CFR of COVID-19 in Hong Kong SAR, China (0.58%; age standardization: 0.53%) is much larger than in Singapore (0.05%; age standardization: 0.06%). The CFRs increase with the rise of age in both Hong Kong SAR, China and Singapore, and in most age groups, CFRs were higher in Hong Kong SAR, China than in Singapore, especially for people ≥70 years.

As of March 22, 2022, the full vaccination and booster coverage in Hong Kong SAR, China was 76.15% and 34.50%, respectively, which is much lower than in Singapore with 92.00% full vaccination and 71.00% with a booster vaccination. Especially for people aged ≥70 years in Hong Kong SAR, China, the full vaccination rates are far lower (56.82%) than in Singapore (95.00%).

Table 2 presents the CFRs by vaccination status and age groups. The CFRs of cases with full vaccination were far lower than those with partial vaccination, especially for the elderly. In Singapore, the CFR for people ≥70 years ranges 7.20%–16.00% for non-fully vaccinated cases, 0.76%–2.80% for fully vaccinated cases, and 0.08%–0.41% for booster vaccinated cases. The CFRs of fully vaccinated cases were also lower than those without full vaccination in Hong Kong SAR, China.

In order to provide more solid evidence for the effects of vaccination coverage, we further collected data from 52 Omicron variant dominated countries/regions and conducted multiple linear regressions. After adjusting for GDP per capita, proportion of people aged 70 and older, population density, hospital beds per 1,000 people, human

TABLE 1. The comparison of CFR and vaccination coverage in Hong Kong SAR, China and Singapore, by age group — December 31, 2021 to March 22, 2022.

Age group (years)	Hong Kong SAR, China						Singapore*					
	Vaccine coverage (%)			Number of cases	Number of deaths	CFR (%)	Vaccine coverage (%)			Number of cases	Number of deaths	CFR (%)
	≥1 dose	Full vaccination†	Booster vaccination§				≥1 dose	Full vaccination†	Booster vaccination§			
0–19	66.43	34.98	3.97	105,847	11	0.01%	65.00	61.00	–	143,320	0	0.00
20–39	93.77	86.76	31.88	304,771	25	0.01%	98.00	98.00	–	251,281	0	0.00
40–59	98.52	92.67	50.01	353,560	218	0.06%	98.00	98.00	–	199,263	12	0.01
60–69	89.77	81.24	43.97	156,183	521	0.32%	97.00	97.00	–	82,019	38	0.05
≥70	70.93	56.82	24.61	118,570	5,371	4.46%	96.00	95.00	–	63,154	300	0.48
Total	87.61	76.15	34.50	1,038,931	6,146	0.53¶ (0.36–0.70)**	93.00	92.00	71.00	739,037	350	0.06¶ (0.01–0.18)**

Note: CFR, vaccination coverage was obtained and calculated from the Government of the Hong Kong SAR, China (https://www.coronavirus.gov.hk/eng/index.html) and Ministry of Health in Singapore (https://www.moh.gov.sg/).

"–" means data not available.

Abbreviation: CFR=case fatality ratio; SAR=Special Administrative Region.

* The proportion of inactivated vaccination is just 3.52% in Singapore (obtained from: https://www.hsa.gov.sg/COVID19-vaccines-safety-updates).

† Full vaccination in Hong Kong SAR, China refers to people with 2 doses inactivated or mRNA vaccine in this study. Full vaccination in Singapore refers to people with 2/3 doses inactivated vaccine or 2 doses mRNA vaccine.

§ Booster vaccination in Hong Kong SAR, China refers to the people with 3 doses inactivated or mRNA vaccine. Booster vaccination in Singapore refers to the people with "2/3 doses inactivated vaccine + 1 dose mRNA vaccine" or "3 doses mRNA vaccine".

¶ Age standardized CFR (the number of age-specific infections and infected related deaths in Hong Kong SAR, China and Singapore were combined as a reference group).

** 95% confidential interval.

TABLE 2. The CFR with different vaccination statuses in Hong Kong SAR, China and Singapore.

Age group (years)	CFR in Hong Kong SAR, China* (%)			CFR in Singapore† (%)		
	Non-full vaccination§	Full vaccination¶	Booster vaccination**	Non-full vaccination§	Full vaccination¶	Booster vaccination**
0–9	0.01	0.00	–	0.00	0.00	0.00
10–19	0.01	0.00	–	0.00	0.00	0.00
20–29	0.03	0.00	–	0.02	0.00	0.00
30–39	0.04	0.00	–	0.04	0.00	0.00
40–49	0.12	0.01	–	0.12	0.01	0.00
50–59	0.44	0.03	–	0.89	0.06	0.00
60–69	0.99	0.08	–	2.90	0.20	0.03
70–79	2.81	0.38	–	7.20	0.76	0.08
≥80	11.25	3.22	–	16.00	2.80	0.41
Total	1.69††,§§	0.10††,§§	–	2.92 (0.26–8.72)††	0.14 (0.01–0.53)††	0.03¶¶

Note: CFR with different vaccination statuses were obtained and calculated from the Government of the Hong Kong SAR, China (https://www.coronavirus.gov.hk/eng/index.html) and Ministry of Health in Singapore (https://www.moh.gov.sg/).
"–" means data not available.
Abbreviation: CFR=case fatality ratio; SAR=Special Administrative Region.
* The CFR in Hong Kong SAR, China from December 31, 2021 to March 22, 2022.
† The CFR in Singapore from May 1, 2021 to February 28, 2022.
§ "Non-full vaccination" refers to people without vaccination and with 1 dose vaccination.
¶ Full vaccination in Hong Kong SAR, China refers to people with 2 doses inactivated or mRNA vaccine in this study. Full vaccination in Singapore refers to people with 2/3 doses inactivated vaccine or 2 doses mRNA vaccine.
** Booster vaccination in Hong Kong SAR refers to the people with 3 doses inactivated or mRNA vaccine. Booster vaccination in Singapore refers to the people with "2/3 doses inactivated vaccine + 1 dose mRNA vaccine" or "3 doses mRNA vaccine.
†† Age standardized CFR (the number of age-specific infections and infected related deaths in Hong Kong SAR, China were used as a reference group; the age-vaccinated status-specific number of infections of Singapore could not be obtained).
§§ The confidence intervals were not presented because the population in Hong Kong SAR, China was used as a reference group.
¶¶ The standardized total CFR of booster vaccinated infectors could not be calculated because the age-specific number of booster vaccinated infectors in Hong Kong SAR, China and Singapore could not be obtained.

development index, and cardiovascular mortality per 100,000 people, we found that a higher coverage of ≥1 dose vaccination, full vaccination, and booster vaccination were all negatively associated with lower CFRs (Supplementary Table S2, available in http://weekly.chinacdc.cn). Moreover, full vaccination and ≥1 dose vaccination coverages were the top two contributing factors to CFR (Figure 1).

DISCUSSION

The CFR in Hong Kong SAR, China during the 5th wave of COVID-19 is much higher than in Singapore, which could be attributed to the relatively low vaccination coverage, especially in elderly populations in Hong Kong SAR, China.

A systematic review indicated that age was the strongest predictor of infection–fatality ratio (IFR) during the pre-vaccine period (*7*). The age-specific IFR during the pre-vaccine period formed a J shape. A series of reasons, like immunosenescence, underlying diseases, and age-related damage could explain the higher IFR in the elderly (*7–8*). Fortunately, vaccination, especially booster vaccination, has been proved effective in reducing COVID-19 related deaths for the elderly (*9*). We also observed that the CFRs in fully vaccinated and booster vaccinated people were lower than in non-fully vaccinated people in Hong Kong SAR, China and Singapore. This difference should also be interpreted with the consideration of the "healthy vaccinee effect." That is people with better health conditions are more likely to adhere to recommended vaccination, which may underestimate the CFR of vaccinated people.

In this study, after adjusting for confounding variables in the countries with a proportion of Omicron variant more than 90%, we also observed that ≥1 dose, full vaccination, and booster vaccination were all effective at reducing CFR. Unexpectedly, the effect and the importance of boosters were lower than the other two vaccination statuses, which may be explained by the low booster vaccine coverage in elderly populations. After the initial booster vaccination, young people could have lower

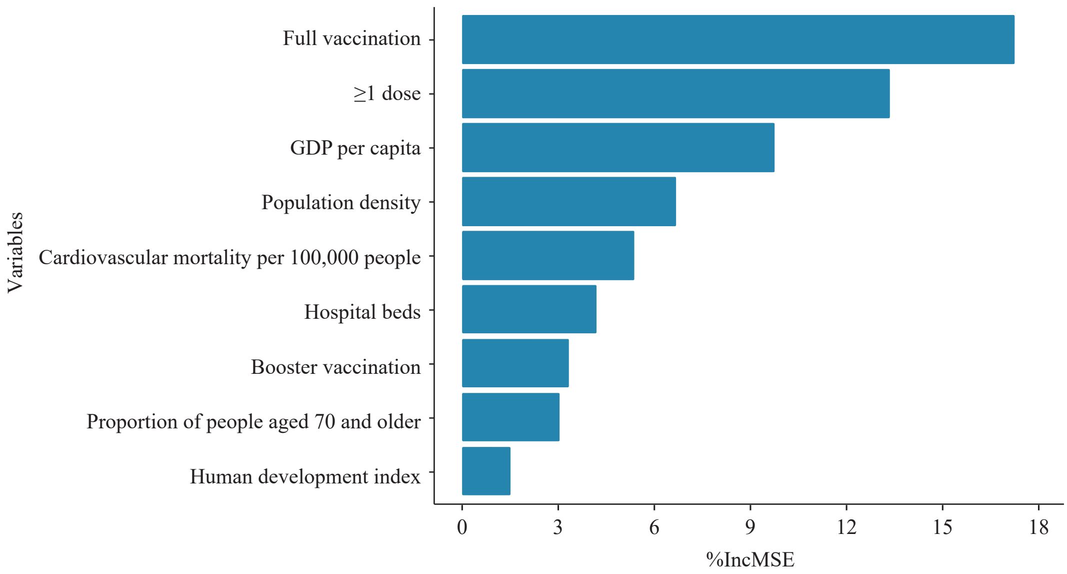

FIGURE 1. The importance rank of contribution variables to CFR using a RF model.

Note: Full vaccination refers to people who received all doses prescribed by the initial vaccination protocol (commonly 2 doses and sometimes 3 doses, depending on the definition by the corresponding countries) per 100 people in the total population of the country or region; ≥1 dose refers to people who received at least 1 dose vaccination per 100 people in the total population of the country or region.

Booster vaccination refers to people with doses administered beyond the number prescribed by the initial vaccination protocol (commonly 3 doses and sometimes 4 doses, depending on the definition by the corresponding countries or regions) per 100 people in the total population of the country or region.

The detailed information of other variables is presented in Supplementary Table S1 (available in http://weekly.chinacdc.cn).

Abbreviation: CFR=case fatality ratio; RF=random forest regression model; %IncMSE=percentage increase in mean square error.

vaccination hesitancy than the older adults and comprise a larger proportion of people vaccinated with a booster dose. Together with the lower mortality risk of young people, the real effect of booster vaccine coverage (normally higher than the coverage of full vaccination) will not emerge until more people, especially older adults, receive booster vaccines. In addition, a large observational study in Hong Kong SAR, China indicated that receiving two doses of mRNA vaccine (vaccine effectiveness: 89.3%) and inactivated vaccine (vaccine effectiveness: 69.9%) could all achieve good effectiveness against COVID-19 related severe diseases and deaths in the elderly (*10*). This study also indicated that receiving three doses of both mRNA and inactivated vaccine could offer superior effectiveness than two doses (*10*). The real-world evidence in Hong Kong SAR, China indicates that the elderly should get any type of accessible vaccine whenever possible.

Outside of vaccination status, the following factors may contribute to a higher CFR in Hong Kong SAR, China than in Singapore. First, Hong Kong SAR, China has a higher proportion of people aged 70 and older (12.10%) than Singapore (7.30%) (Supplementary Figure S1, available in http://weekly.chinacdc.cn). Second, the prevalence of chronic diseases in Hong Kong SAR, China is higher than in Singapore (Supplementary Table S3, available in http://weekly.chinacdc.cn). The prevalence of obesity is 29.9% in Hong Kong SAR, China and only 8.7% in Singapore. The prevalence of hyperlipidaemia and hypertension is also higher in Hong Kong SAR, China than in Singapore (hyperlipidaemia: 49.5% *vs.* 33.6%, hypertension: 27.7% *vs.* 21.5%). Third, in Singapore, a total of 279,450 cases of COVID-19 have been reported as of December 31, 2021. On the contrary, Hong Kong SAR, China has only 12,649 reported cases before 2022, which makes the infection rate in Hong Kong SAR, China (0.20%) before 2022 is lower than that in Singapore (4.80%). Fourth, the number of COVID-19 infections was higher in Singapore than in Hong Kong SAR, China before late February, but the proportion of hospital beds occupied by COVID-19 patients was higher in Hong Kong SAR, China than in Singapore since mid-February (Supplementary Figure S2, available in http://weekly.chinacdc.cn), which could be attributed to the imperfect tiered diagnosis and treatment strategy during the early Omicron epidemic in Hong Kong SAR, China. A few patients without severe symptoms occupied hospital beds, which led to an overwhelmed medical system unable to treat patients with severe illness and contributed to a higher CFR. Finally, the average daily number of swab tests (including polymerase chain reaction and rapid antigen test) of COVID-19 in Hong Kong SAR, China was 22.5 tests per 1,000 people (January to March 2022), while in Singapore it was 37.8 tests per 1,000 people (December 31, 2021 to March 14, 2022) (Supplementary Table S4, available in http://weekly.chinacdc.cn). In conclusion, this comparison between Hong Kong SAR, China and Singapore indicates that vaccination has had good efficacy in preventing deaths from COVID-19. This real-world evidence calls on non-vaccinated, non-fully-vaccinated and non-booster-vaccinated people, especially the elderly, to get any type of accessible vaccine, which could save lives.

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[#] Corresponding authors: Xiaofeng Liang, liangxf@jnu.edu.cn; Wenjun Ma, mawj@gdiph.org.cn.

[1] Department of Public Health and Preventive Medicine, School of Medicine, Jinan University, Guangzhou City, Guangdong Province, China; [2] Disease Control and Prevention Institute, Jinan University, Guangzhou City, Guangdong Province, China; [3] Guangdong Provincial Institute of Public Health, Guangdong Provincial Center for Disease Control and Prevention, Guangzhou City, Guangdong Province, China.

[&] Joint first authors.

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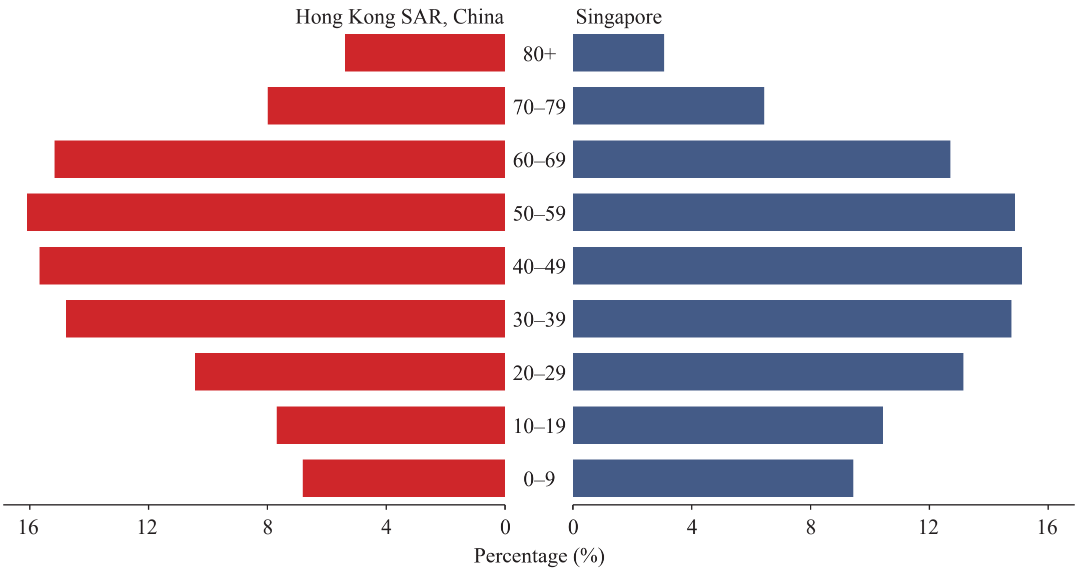
SUPPLYMENTARY MATERIAL

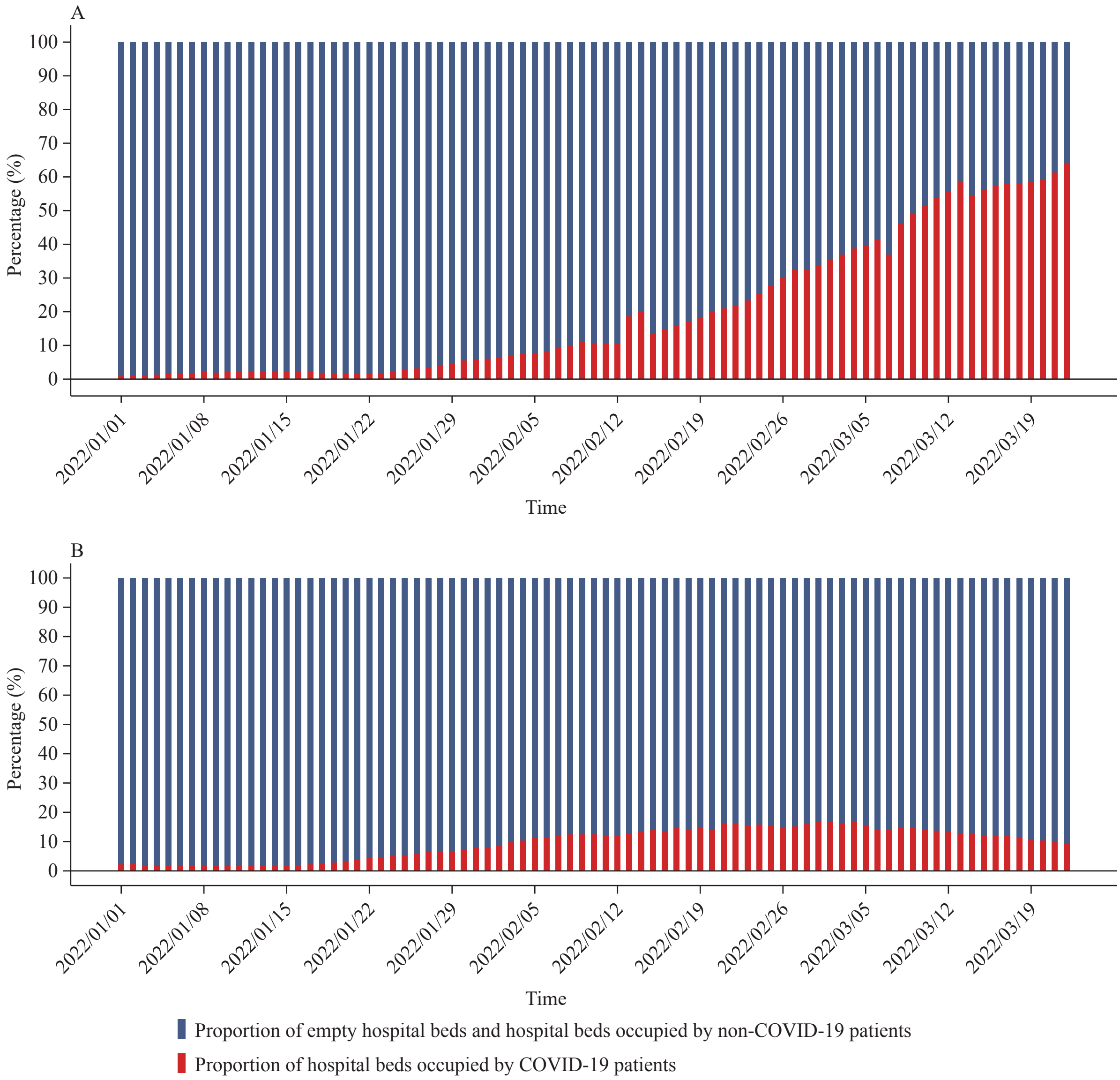


SUPPLEMENTARY FIGURE S1. The age structure of Hong Kong SAR, China and Singapore.
Note: The data for age structure were obtained from census data of Hong Kong SAR, China (https://www.censtatd.gov.hk) and Singapore (https://www.singstat.gov.sg).
Abbreviation: SAR=Special Administrative Region.

SUPPLEMENTARY TABLE S1. Detailed information about 9 explanatory variables in multiple regression models.

Variables	Definition	Values
Full vaccination	People who received all doses prescribed by the initial vaccination protocol (commonly 2 doses and sometimes 3 doses, depending on the definition of the corresponding countries) per 100 people in the total population of the country or region.	Continuous variable
≥1 dose	People who received at least 1 dose vaccination per 100 people in the total population of the country or region.	Continuous variable
Booster vaccination	People with doses administered beyond the number prescribed by the initial vaccination protocol (commonly 3 doses and sometimes 4 doses, depending on the definition of the corresponding countries) per 100 people in the total population of the country or region.	Continuous variable
GDP per capita	Gross domestic product at purchasing power parity (constant 2011 international dollars), most recent year available.	Continuous variable
Population density	Number of people divided by land area, measured in square kilometers, most recent year available.	Continuous variable
Hospital beds per 1,000 people	Hospital beds per 1,000 people, most recent year available since 2010.	Continuous variable
Human development index	A composite index measuring average achievement in three basic dimensions of human development — a long and healthy life, knowledge and a decent standard of living.	Continuous variable
Proportion of people aged 70 and older	Share of the population that is 70 years and older in 2015.	Continuous variable
Cardiovascular mortality per 100,000 people	Death rate from cardiovascular disease in 2017 (annual number of deaths per 100,000 people).	Continuous variable

Note: The data and definition were obtained from https://github.com/owid/covid-19-data/tree/master/public/data.



SUPPLEMENTARY FIGURE S2. The hospital bed occupancy status of Hong Kong SAR, China and Singapore. (A) Proportion of hospital beds occupied by COVID-19 patients in Hong Kong SAR, China; (B) Proportion of hospital beds occupied by COVID-19 patients in Singapore.

Note: The list of 17 designated hospitals for COVID-19 treatment, the number of hospital beds in these hospitals, and the daily number of inpatients in Hong Kong SAR, China were obtained from its Hospital Authority (https://www3.ha.org.hk).

The list of 8 designated hospitals for COVID-19 treatment in Singapore and the daily number of inpatients in Singapore were obtained from its Ministry of Health (https://www.moh.gov.sg). The number of hospital beds in designated hospitals was obtained from their official websites (https://www.ah.com.sg; https://www.cgh.com.sg; https://www.ktph.com.sg; https://www.nuh.com.sg; https://www.ntfgh.com.sg; https://www.skh.com.sg; https://www.sgh.com.sg; https://www.ttsh.com.sg).

Abbreviation: SAR=Special Administrative Region.

SUPPLEMENTARY TABLE S2. The effects of vaccination coverages on the CFR based on multiple linear regression models.

Type of vaccination	Estimate	Std. Error	t value	*P*	R^2
Booster vaccination					
Unadjusted	−0.017	0.010	−1.693	0.098	0.209
Adjusted*	−0.027	0.012	−2.288	0.028	0.274
Non-fully vaccination					
Unadjusted	−0.019	0.011	−1.762	0.084	0.198
Adjusted*	−0.041	0.013	−3.146	0.003	0.324
Fully vaccination					
Unadjusted	−0.022	0.011	−2.042	0.047	0.214
Adjusted*	−0.042	0.012	−3.393	0.001	0.344

* Adjusted for the GDP per capita, population density, hospital beds, human development index, proportion of people aged 70 and older, and cardiovascular mortality.

SUPPLEMENTARY TABLE S3. Prevalence of chronic diseases in Hong Kong SAR, China and Singapore

Chronic disease	Prevalence in Hong Kong	Prevalence in Singapore
Obesity	29.9%	8.7%
Hyperlipidaemia	49.5%	33.6%
Hypertension	27.7%	21.5%
Diabetes	8.4%	8.6%

Note: The data source of the prevalence of chronic diseases in Hong Kong SAR, China was from Center for Health Protection for Hong Kong (https://www.chp.gov.hk), and the data source of Singapore was from the Government of Singapore (https://data.gov.sg).
Abbreviation: SAR=Special Administrative Region.

SUPPLEMENTARY TABLE S4. The number of swab tests in Hong Kong SAR, China and Singapore from January to March 2022.

Place	Time	Average daily number of swabs tested*	Average daily number of swabs tested per 1,000 people*
Hong Kong SAR, China	January	138,860	18.8
	February	241,515	32.6
	March†	124,703	16.8
	January to March†	163,150	22.5
Singapore	January	236,365	41.6
	February	188,825	33.2
	March	89,091	15.7
	January to March	170,847	30.0

Note: The data of swab tests were obtained from the official website of Hong Kong SAR, China (https://www.chp.gov.hk) and Singapore (https://www.moh.gov.sg/covid-19/statistics).
Abbreviation: SAR=Special Administrative Region; PCR=polymerase chain reaction; RAT=rapid antigen test.
* Swab tests included PCR and RAT.
† The data of swabs tested in Hong Kong, SAR, China were as of March 29, 2022.

Outbreak Reports

Response and Assessment of the Effectiveness of the Countermeasures for a COVID-19 Outbreak — Guizhou Province, China, March 2022

Jiao Huang[1,&]; Liying Wang[2,3,&]; Chun Yu[1]; Zhaobing Liu[1]; Guanghong Yang[1]; Ziyao Lan[1]; Zhongfa Tao[1]; Kaike Ping[1]; He Huang[1]; Shijun Li[1]; Yan Huang[1,#]

Summary

What is already known about this topic?

Many regions in China have recently reported outbreaks of the coronavirus disease 2019 (COVID-19) caused by the Omicron variant.

What is added by this report?

Wuchuan County, Guizhou Province reacted quickly and implemented accurate intervention measures to effectively control the outbreak. The susceptible-exposed-infectious-asymptomatic-removed (SEIAR) model was applied to evaluate the effectiveness of intervention measures.

What are the implications for public health practice?

Fast response measures should be taken to prevent the spread of outbreaks caused by the Omicron variant.

Coronavirus disease 2019 (COVID-19) is an acute respiratory infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In China, the Omicron variant was initially detected in the respiratory tract samples of 2 imported cases in Tianjin Municipality, on December 13, 2021 (*1*). The first local transmission case with the Omicron variant BA.2 in China was reported on December 29, 2021, in Guangdong Province (*2*). Subsequently, over 30 provincial-level administrative divisions (PLADs) reported outbreaks caused by the Omicron variant. The Omicron variant BA.2 became the preponderant strain in China in just a few months. An imported case who returned to Wuchuan County, Zunyi City, Guizhou Province from Zhejiang Province was reported on March 11, 2022. The next 11 cases were successively detected from March 12 to 17, 2022 after a series of emergency measures. Wuchuan's outbreak was effectively controlled after the implementation of comprehensive countermeasures, including closing key areas, conducting region-wide and county-wide nucleic acid screening, restricting inbound and outbound traffic, and tracking and isolating close contacts. Once the outbreak was under control, this study used the susceptible-exposed-infectious-asymptomatic-removed (SEIAR) model to evaluate the effectiveness of Wuchuan's prevention and control measures during its March, 2022 COVID-19 outbreak caused by Omicron variant BA.2.

INVESTIGATION AND RESULTS

A total of 12 cases were reported in Wuchuan from March 11 to 17, 2022. Of these cases, 9 were symptomatic and 3 were asymptomatic. Overall, the full course of vaccination was administered to 11 cases, of which 6 were administered with booster injections. The initial case was detected by an individual's nucleic acid test on March 11, 2022, and the other 11 cases were detected through close contact tracking and nucleic acid screening on March 12–15 and 17.

Upon the occurrence of the outbreak, Guizhou Province, Zunyi City, and Wuchuan County immediately established three levels of communications linkage to implement coordinated countermeasures. They started the contingency plan and traffic control within 2 hours after confirmation of the first case. Epidemiological investigation, the checking of close contacts and other relevant persons, and the isolation of cases and close contacts were conducted right away. The epidemiological investigation in the field revealed that the first case was a courier who had lived and worked in Yuhang District, Hangzhou City, Zhejiang Province until March 7, 2022. Some key areas were divided into temporary close control areas and management control areas based on the epidemiological investigation's risk evaluation, and one close contact of the first case was detected nucleic acid positive on March 12. The region-wide nucleic acid screening was conducted on

March 13, and 4 additional cases were detected. However, there was no epidemiological correlation among these cases according to the results of the investigation. Wuchuan then extended the scope of nucleic acid screenings on March 14, and 1 case was detected by isolating close contacts and nucleic acid screening. Wuchuan's outbound and inbound traffic were restricted on March 15, and 2 cases were detected in isolation locations on the same day. A county-wide nucleic acid screening was conducted on March 16 because of the rising number of cases, no cases were detected. A second cycle of county-wide nucleic acid screening was then conducted on March 17, and 3 cases were detected. With these additional data points, Wuchuan's response team was able to confirm the epidemiological correlation among the 12 cases by meticulous research. Furthermore, of the 12 cases, the viral genomes of 4 cases were sequenced and all belonged to the Omicron BA.2 branch, which was homologous with the results of a recent outbreak in Zhejiang Province.

During the period of the outbreak, the secondary close contacts were monitored and their nucleic acid results were collected via door-to-door testing; the persons at risk who resided with cases in the same space at the same time were given yellow health codes and conducted their nucleic acid tests under supervision through phone calls; and the list of close contacts in need of testing was checked daily to ensure rigorous adherence to testing requirements. Efficient nucleic acid test administration training helped support this process so that the results of nucleic acid tests were consistently available same-day. In total, 7 cycles of regional nucleic acid screening, 6 cycles of the nucleic acid screening of streets or towns that reported cases, and 4 cycles of the nucleic acid screening of the whole county were completed. In addition, the total number of individual nucleic acid screenings exceeded 1,667,000: there were 628 close contacts tracked and isolated, and 3,180 secondary close contacts were checked and monitored. If no case was detected in 4–5 cycles of nucleic acid screening over the course of 1 week, or if no close contact was added, a close control area would be unlocked after risk evaluation. However, if infections were detected in a close control area, 1–2 cycles of nucleic acid screening would be added for the area. Later, the block of the area would be removed in accordance with the results of the risk evaluation.

The SEIAR model was developed to analyze the transmission dynamics of COVID-19 and to evaluate the effectiveness of countermeasures taken during the COVID-19 outbreak. According to the transmission mechanisms of COVID-19, people who were entered into the SEIAR model were divided into five types: susceptible (S), exposed (E), infectious (I), asymptomatic (A), and removed (R). As presented in Table 1, the parameters of the SEIAR model included β, ω, ω', p, γ, and γ', among which β was obtained by simulating the reported data with the model data; p was calculated in accordance with the reported data of the outbreak and set to 0.33; $1/\omega$ and $1/\omega'$ were set to 3 days on the basis of a previous study (*3*); $1/\gamma$ and $1/\gamma'$ were set to 5 days in accordance with a previous study (*4*); and κ was set to 0.5 in accordance with a previous study (*5*). As illustrated in Figure 1, the SEIAR model was well aligned with the data of reported cases (R^2=0.605, P<0.05). The SEIAR model divided the outbreak into the natural transmission stage (before March 13, 2022), the effective control stage (March 13–15, 2022), and the entire control stage (after March 15, 2022). The effective reproduction numbers (R_{eff}) of the 3 stages were 6.32, 0.83, and 0. After interventions such as the isolation of close contacts or the quarantining of key areas, transmission decreased and the R_{eff} in the second stage declined by 86.87% compared with that of the first stage. Subsequently, after multiple cycles of region-wide and county-wide nucleic acid screenings and traffic restrictions, the R_{eff} declined to 0 by the end of the control stage. As described in Table 2, the simulation results indicated that if any intervening measures were not taken in the first stage, the total number of infected cases would have increased to 1,184 and 19,480 by March 24 and 31, respectively. In stark contrast, only 12 cases were reported during the outbreak. This result indicated that 98.99% and 99.94% of the population avoided COVID-19 infection after the implementation of prevention and control measures in the first stage. Furthermore, if effective measures had not been taken in the second stage, the number of cases would have increased to 39 and 51 by March 24 and 31. After countermeasures were adopted, the actual number of reported cases was reduced by 69.23% and 76.47% relative to those simulated for the second stage. Finally, if countermeasures were not taken during these two early periods of the outbreak, the outbreak is predicted to have continued until April 12. In reality, the outbreak ended on March 17, indicating that the epidemic time was significantly shortened by the series of countermeasures implemented.

TABLE 1. Definition and values of parameters in SEIAR model of COVID-19 in Wuchuan County.

Parameter	Description	Unit	Value	Source
β	The transmission rate	$Person^{-1}×day^{-1}$	–	Model simulating
κ	The transmissibility of A to I	1	0.5	Reference (*6*)
ω	The relative number of incubation period	Day^{-1}	0.33	Reference (*4*)
ω'	The relative number of latent period	Day^{-1}	0.33	Reference (*4*)
p	The proportion of A	1	0.33	Report data
γ	The relative rate of infection period of I	Day^{-1}	0.2	Reference (*5*)
γ'	The relative rate of infection period of A	Day^{-1}	0.2	Reference (*5*)

Note: "–" means not applicable.
Abbreviation: SEIAR=susceptible-exposed-infectious-asymptomatic-removed; COVID-19=coronavirus disease 2019; A=asymptomatic; I=infectious.

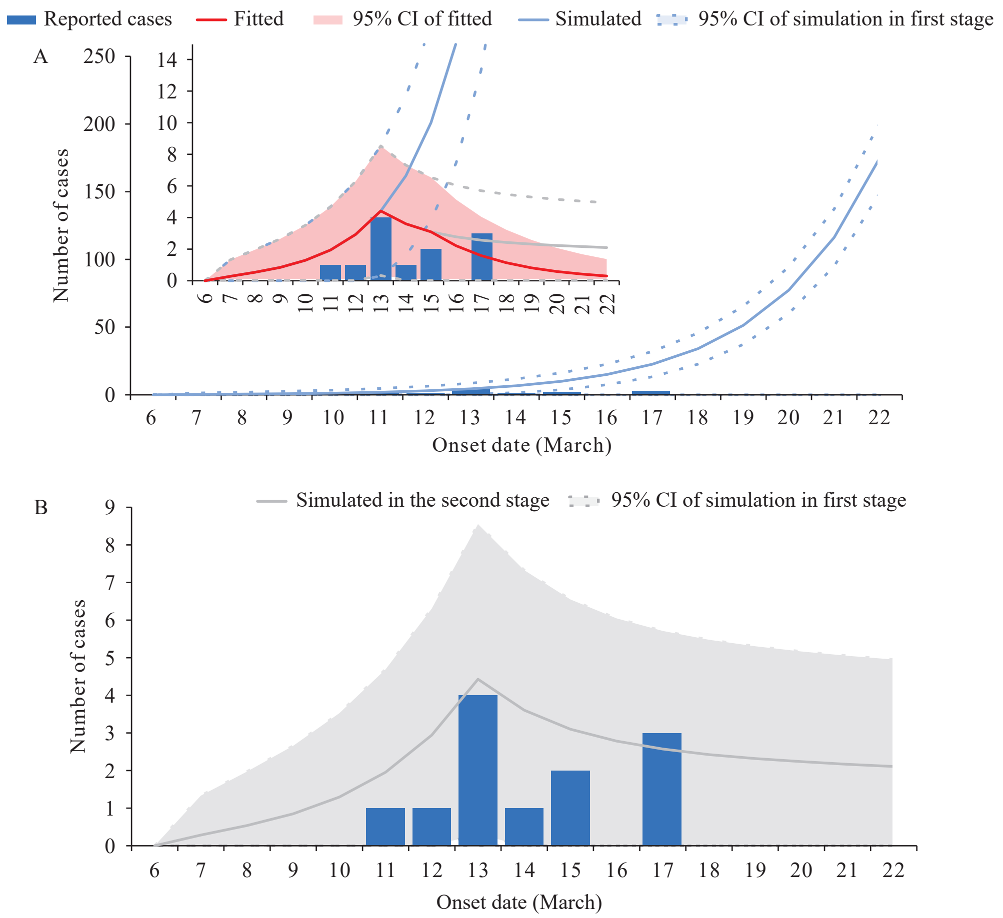


FIGURE 1. The fitting results between SEIAR model and the actual data of COVID-19 cases in Wuchuan County. (A) The result in the first stage without interventions; (B) The result in the second stage with interventions taken in the first stage but not in the second stage.
Abbreviation: SEIAR=susceptible-exposed-infectious-asymptomatic-removed; COVID-19=coronavirus disease 2019; CI=confidence interval.

DISCUSSION

Previous studies predicted the transmission of COVID-19 and assessed the effect of prevention and control measures taken during the COVID-19 pandemic by using the SEIAR model (*6–8*). After implementing prevention and control measures, this study used the SEIAR model; after finding that the model fitted the reported data well, this study divided the outbreak into three stages. The *P* parameter in the

TABLE 2. Comparation of simulated results of the SEIAR model with the reported cases.

Onset date	First stage (No intervention)		Second stage (No intervention)		Report cases	
	New cases	Accumulated cases	New cases	Accumulated cases	New cases	Accumulated cases
March 6	0	0	0	0	0	0
March 7	0	0	0	0	0	0
March 8	1	1	1	1	0	0
March 9	1	2	1	2	0	0
March 10	1	3	1	3	0	0
March 11	2	5	2	5	1	1
March 12	3	8	3	8	1	2
March 13	4	12	4	12	4	6
March 14	7	19	4	16	1	7
March 15	10	29	3	19	2	9
March 16	15	44	3	22	0	9
March 17	23	67	3	24	3	12
March 18	34	101	2	27	0	12
March 19	52	153	2	29	0	12
March 20	78	231	2	31	0	12
March 21	117	347	2	33	0	12
March 22	176	523	2	35	0	12
March 23	264	787	2	37	0	12
March 24	397	1,184	2	39	0	12
March 25	595	1,779	2	41	0	12
March 26	891	2,670	2	43	0	12
March 27	1,332	4,002	2	45	0	12
March 28	1,982	5,984	2	46	0	12
March 29	2,935	8,919	2	48	0	12
March 30	4,309	13,228	2	50	0	12
March 31	6,253	19,480	2	51	0	12
April 1	8,917	28,397	2	53	–	–
April 2	12,407	40,804	2	54	–	–
April 3	16,685	57,488	1	56	–	–
April 4	21,437	78,925	1	57	–	–
April 5	25,986	104,911	1	58	–	–
April 6	29,378	134,289	1	60	–	–
April 7	30,734	165,023	1	61	–	–
April 8	29,702	194,725	1	62	–	–
April 9	26,658	221,383	1	64	–	–
April 10	22,465	243,848	1	65	–	–
April 11	18,018	261,866	1	66	–	–
April 12	13,938	275,804	1	67	–	–
April 13	10,515	286,319	0	0	–	–

Note: "–" means not applicable.
Abbreviation: SEIAR=susceptible-exposed-infectious-asymptomatic-removed.

SEIAR model is the proportion of asymptomatic infections. The *P* value in our study was similar to that obtained for Taiwan, China (*8*), higher than that reported for Anhui Province (*7*), and lower than that found for Zhejiang Province (*6*). The differences among the *P* values of PLADs may be associated with local demography and economics. In this study, the outbreak was transmitted through a breakthrough infection in the first stage. Because the R_{eff} was 6.32, the data from Wuchuan indicates that one case could have infected an average of 6.32 cases even despite high vaccination coverage rates: a value that was similar to values found in outbreaks in South Africa, the United States, and Canada (*9*).

After the occurrence of the outbreak, a series of countermeasures were taken, such as the dividing and closing of key areas, the isolation of close contacts, the living at home of secondary close contacts, the conduction of regional nucleic acid screening, the starting of county-wide nucleic acid screening, and the implementation of traffic controls. The R_{eff} value of the COVID-19 outbreak decreased gradually until the outbreak was ultimately controlled. The outbreak involved 12 cases and this number of cases was notably lower than that predicted by the SEIAR model simulation in the absence of intervention, suggesting that the countermeasures taken here were remarkably effective. This is significant because Wuchuan is one of the most important counties in Zunyi; if the implementation of countermeasures was not prompt, the outbreak may have spilled over to the Zunyi, Tongten, and Guiyang cities of Guizhou Province; the Luzhou City of Sichuan Province; or Chongqing Municipality. However, no cases spilled out in this outbreak, further confirming that the response measures enacted were reasonable. Therefore, this study suggests the following measures: 1) dividing key areas as early as possible; 2) tracing and isolating close contacts; 3) conducting county-wide nucleic acid screening; and 4) comprehensive and detailed epidemiological investigation.

This study was subject to some limitations. It had a relatively small sample size, and it did not consider natural births and deaths. This situation might lead to a slight bias between the reality of the Wuchuan outbreak and the results simulated by the SEIAR model.

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Corresponding author: Yan Huang, cdchuangyan@163.com.

[1] Guizhou Center for Disease Control and Prevention, Guiyang City, Guizhou Province, China; [2] National Institute of Parasitic Diseases, Chinese Center for Tropical Diseases Research, Chinese Center for Disease Control and Prevention; NHC Key Laboratory of Parasite and Vector Biology; WHO Collaborating Center for Tropical Diseases; National Center for International Research on Tropical Diseases, Shanghai Municipality, China; [3] Doctorate School of Chemical and Biological Sciences for Health (CBS2), University of Montpellier, Montpellier, France.
& Joint first authors.

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Methods and Applications

Estimating New Cases Among Athletes During the Winter Olympics Based on a Dynamic Model — Beijing, China, February 2022

Zonghao Zhang[1]; Xiaotong Huang[1]; Chuanqing Xu[1,#]; Xiaojing Wang[1]; Songbai Guo[1]

ABSTRACT

Introduction: Since first appearing in late 2021, the Omicron variant has spread rapidly around the world. Nevertheless, the XXIV Winter Olympic Games (WOG) were held in Beijing in February 2022, which undoubtedly posed a huge challenge to domestic epidemic prevention and control.

Methods: To analyze and evaluate the spread of the epidemic within the closed-loop management of the Beijing 2022 WOG, an improved dynamics model was established. Using the known dynamics parameters, the new daily cases and final members of quarantined people were predicted, and the influence of different factors on the change of the number of quarantined people was analyzed.

Results: When the proportion of exposed persons being detected and the degree of admixture between the two populations varied between 0.5 and 0.9, there was little change in the daily predicted number of new cases and the final number of quarantined patients. As the initial value of the exposed among inbound personnel increases, the final size of quarantined patients increased proportionally.

Discussion: From the analysis results, detecting potential virus carriers at the entry stage is the most effective way to control the spread of the epidemic within the closed-loop management of the Beijing 2022 WOG.

INTRODUCTION

Since its first report in South Africa on November 24, 2021, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant has rapidly replaced the Delta variant as the globally predominant variant. The mainland of China also reported the first case of Omicron variant infection on December 14, 2021, which was a closed-loop control entry traveler in Tianjin Municipality. As of January 15, 2022, local outbreaks of Omicron variant have occurred in 6 provincial-level administrative divisions (PLADs) in China, with a total of over 400 infections. The World Health Organization (WHO) briefing on January 15, 2022 reported that 58.5% of the gene sequences uploaded globally in the past 30 days were Omicron variant. Although the disease caused by the Omicron variant is relatively mild, the rapid increase in the number of cases can still put a heavy strain on global health systems.

Existing studies have shown that the Omicron variant has a stronger transmissibility than the Delta variant. Jiahui Chen et al. conducted a comprehensive quantitative analysis using an artificial intelligence model and found that the Omicron variant's infectiousness and immune evasion ability were about twice those of the Delta variant (*1*). Hiroshi Nishiura et al. modeled and analyzed the substitution process of the dominant variant in Gauteng, South Africa, and found that the effective reproduction number of the Omicron variant was about 4.2 times that of the Delta variant, and its transmission was 3.3 times that of the Delta variant (*2*). Li Zhang et al. analyzed the sensitivity of 28 serum samples from coronavirus disease 2019 (COVID-19) convalescent patients infected with the SARS-CoV-2 original strain and found that the Omicron variant had a more significant immune evasion ability against immune protection caused by infection or even by vaccine (*3*).

The XXIV Winter Olympic Games (WOG) were held in Beijing from February 4 to February 20, 2022. At that time, Yanqing District of Beijing and Zhangjiakou of Hebei Province welcomed many foreigners. Although the domestic epidemic has been relatively under control, the Omicron variant has the world. Considering the evasion ability of Omicron variant against existing vaccines, the entry of a large number of foreign personnel undoubtedly posed a huge challenge to the epidemic prevention and control work within the closed-loop management of the

Beijing 2022 WOG.

If the number of secondary cases generated during the Beijing 2022 WOG can be reasonably estimated, preparations for epidemic prevention and control can be made in advance to avoid wider spread of the epidemic. The purpose of this paper is to establish an improved dynamics model of the spread of COVID-19 to analyze the spread of the epidemic within the closed-loop management during the Beijing 2022 WOG.

METHODS

According to the relevant regulations in the "Beijing 2022 Winter Olympics and Paralympic Games Athletes and Accompanying Officials Epidemic Prevention Manual (Second Edition)" (*4*), during the Beijing 2022 WOG, all Olympic-related personnel were under closed-loop management. Closed-loop management implements strict epidemic prevention and control measures, including vaccination, social distancing, daily nucleic acid testing, etc. Based on the closed-loop management policy of the Beijing 2022 WOG, we proposed the following assumptions:

1) We divided all Olympic-related personnel into two subgroups. One part was inbound personnel, including foreign athletes and their entourages, foreign media reporters, foreign referees, and volunteers, etc.; the other part was domestic local personnel, including domestic athletes and their entourage, domestic volunteers, referees and related service personnel, etc.

2) We assumed that there was some degree of admixture between the two populations: a) the spread of the epidemic between the two groups of people was affected by this parameter, and b) the spread within the two groups of people was not affected by this parameter.

3) We assume that a certain percentage of exposed people were not detected, and that all infected people could be detected.

Based on the above assumptions, we established an improved model of the transmission dynamics of COVID-19. The model divides the population of Olympic-related personnel into the following seven compartments: susceptible among inbound personnel (S_1), exposed among inbound personnel (E_1), infected among inbound personnel (I_1), susceptible among domestic natives (S_2), exposed among domestic natives (E_2), infected among domestic natives (I_2), quarantined (Q), recovered (R). Its dynamics flowchart is shown in Figure 1. The red box indicates that the compartment is infectious, and the blue box indicates that the compartment is not infectious.

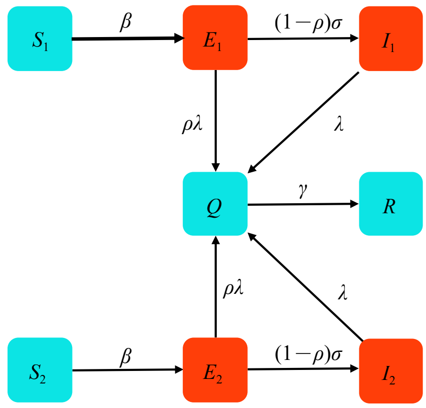

FIGURE 1. Improved COVID-19 transmission flowchart.
Abbreviation: COVID-19=coronavirus disease 2019.

The corresponding transmission dynamics equations were constructed as follows.

$$\begin{cases} \frac{dS_1}{dt} = -\beta S_1 (E_1 + I_1) - \beta S_1 (1-\theta)(E_2 + I_2) \\ \frac{dE_1}{dt} = \beta S_1 (E_1 + I_1) + \beta S_1 (1-\theta)(E_2 + I_2) - \rho\lambda E_1 - (1-\rho)\sigma E_1 \\ \frac{dI_1}{dt} = (1-\rho)\sigma E_1 - \lambda I_1 \\ \frac{dS_2}{dt} = -\beta S_2 (E_2 + I_2) - \beta S_2 (1-\theta)(E_1 + I_1) \\ \frac{dE_2}{dt} = \beta S_2 (E_2 + I_2) + \beta S_2 (1-\theta)(E_1 + I_1) - \rho\lambda E_2 - (1-\rho)\sigma E_2 \\ \frac{dI_2}{dt} = (1-\rho)\sigma E_2 - \lambda I_2 \\ \frac{dQ}{dt} = \rho\lambda (E_1 + E_2) + \lambda (I_1 + I_2) - \gamma Q \\ \frac{dR}{dt} = \gamma Q \end{cases} \quad (1)$$

The explanation of relevant parameters is shown in Table 1.

The disease state compartments in system (1) are E_1, I_1, E_2, I_2, Q. To calculate the control regeneration number of system (1), we take

$$F = \begin{pmatrix} \beta S_1 (E_1 + I_1) + \beta S_1 (1-\theta)(E_2 + I_2) \\ 0 \\ \beta S_2 (E_2 + I_2) + \beta S_2 (1-\theta)(E_1 + I_1) \\ 0 \\ 0 \end{pmatrix}, \quad V = \begin{pmatrix} \rho\lambda E_1 + (1-\rho)\sigma E_1 \\ -(1-\rho)\sigma E_1 + \lambda I_1 \\ \rho\lambda E_2 + (1-\rho)\sigma E_2 \\ -(1-\rho)\sigma E_2 + \lambda I_2 \\ -\rho\lambda (E_1 + E_2) - \lambda (I_1 + I_2) + \gamma Q \end{pmatrix}. \quad (2)$$

The Jacobian matrices of F and V are obtained as

TABLE 1. Explanation of relevant parameters in system (1).

Parameter	Definition	Value	Source
β	Base spread rate	7.440×10^{-9}	Estimated
σ	Exposure to infected conversion rate	0.227	(*5*)
λ	Conversion rate from testing positive to being quarantined	2.000	(*4*)
ρ	Proportion of exposed persons detected	0.500–0.900	–*
γ	Recovery rate for quarantined people	0.200	Estimated
θ	Degree of admixture between the two populations	0.500–0.900	–*

* These two parameters need to be adjusted manually in the analysis.

$$F=\begin{pmatrix} \beta S_1 & \beta S_1 & \beta S_1(1-\theta) & \beta S_1(1-\theta) & 0 \\ 0 & 0 & 0 & 0 & 0 \\ \beta S_2 & \beta S_2 & \beta S_2(1-\theta) & \beta S_2(1-\theta) & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V=\begin{pmatrix} \rho\lambda+(1-\rho)\sigma & 0 & 0 & 0 & 0 \\ -(1-\rho)\sigma & \lambda & 0 & 0 & 0 \\ 0 & 0 & \rho\lambda+(1-\rho)\sigma & 0 & 0 \\ 0 & 0 & -(1-\rho)\sigma & \lambda & 0 \\ -\rho\lambda & -\lambda & -\rho\lambda & -\lambda & \gamma \end{pmatrix}. \quad (3)$$

The control reproduction number is the spectral radius of the matrix FV^{-1} at the disease-free equilibrium point $P^*=(S_1^*\ 0\ 0\ S_2^*\ 0\ 0\ 0\ R^*)$. Therefore, the control regeneration number is

$$R_C=\frac{\beta\left(S_1^*+(1-\theta)S_2^*\right)(\lambda+(1-\rho)\sigma)}{\lambda(\rho\lambda+(1-\rho)\sigma)}. \quad (4)$$

RESULTS

Given the dynamics parameters of system (1) and the initial population of all compartments, we predicted the daily increase in the number of quarantined persons (Q). According to the actual situation, we assumed that the initial value of each compartment in system (1) is

$$(S_1(0)\ E_1(0)\ I_1(0)\ S_2(0)\ E_2(0)\ I_2(0)\ Q\ R)= (30000\ 10\ 0\ 37000\ 0\ 0\ 0\ 0). \quad (5)$$

The initial value of the exposed persons among inbound personnel ($E_1(0)$) changed in the subsequent analysis. When the initial value of each compartment was fixed, we analyzed the influence of the proportion of exposed persons being detected (ρ) and the degree of admixture between the two populations (θ) on quarantined persons. As shown in Figure 2, when ρ, θ varied between 0.5 and 0.9, the daily increase of Q hardly changed, and the final size remained between 46 and 47. Fitted data see Supplementary Table S1 (available in https://weekly.chinacdc.cn/). From the predicted results, it can be seen that these two parameters have a certain influence on the daily new number of people and the final size of Q. However, since the magnitude of the total number of people in the closed-loop management of the Beijing 2022 WOG was not high, it has little impact on the absolute number of Q.

When the dynamics parameters of the system (1) were fixed, we analyzed the impact of the initial value of the exposed among inbound personnel ($E_1(0)$) on the quarantined persons. As shown in Figure 3, assuming ρ=0.9 and θ=0.9, when $E_1(0)$ changes between 10, 20, and 30, the daily new number of Q increases significantly. Fitted data see Supplementary Table S2 (available in https://weekly.chinacdc.cn/). According to Figure 3, we can see that when $E_1(0)$ increases by 10 people, the final scale of Q increases by about 50 people, so there is an obvious positive linear relationship between $E_1(0)$ and the final scale of Q.

DISCUSSION

From the predicted results, we can see that compared with the parameters ρ, θ, the initial value of the exposed among inbound personnel ($E_1(0)$) had a more obvious impact on the system (1). This showed that for the epidemic prevention and control within the closed-loop management of the Beijing 2022 WOG, the most effective method was to control the initial number of exposed among inbound personnel. This requires relevant departments to make full preparations for the entry of foreign personnel and try to detect potential virus carriers among inbound personnel at the initial stage as much as possible.

Potential transmission from domestic audiences is not considered in our model. According to press releases from the Beijing Winter Olympics Organizing Committee, the audience policy has been adjusted

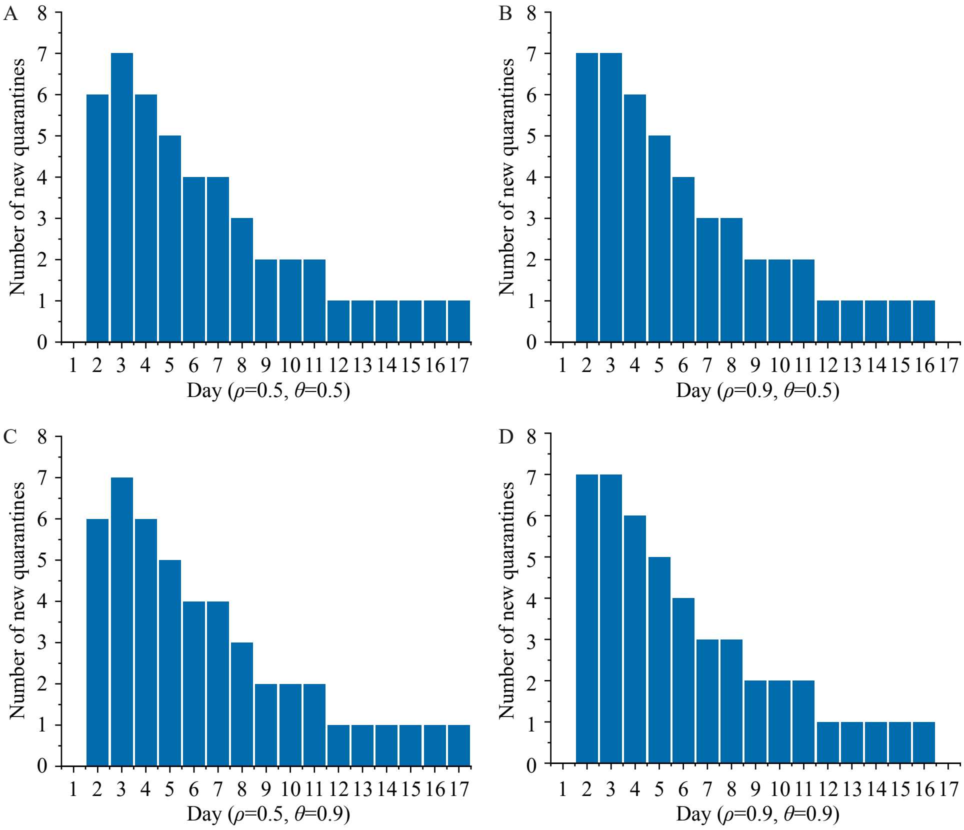

FIGURE 2. The comparison chart of the daily new number of people of quarantined persons (Q) with respect to the changes of the parameters ρ, θ.

from the method of public sales of tickets to the targeted organization of audiences to watch the game on site. Considering the strict epidemic prevention measures during the Beijing 2022 WOG, it is difficult to have significant contact between audiences, athletes, and staff. Therefore, for domestic audience groups, only the spread of the epidemic within the group needs to be considered. In addition, the spread of the epidemic due to the environment is not included in our model. Taking into account the prevention and control measures in closed-loop management, as long as sufficient disinfection work is done, the spread caused by the environment can be effectively limited. Finally, epidemic prevention measures are not as strict outside the closed-loop, so it is necessary to avoid the occurrence of epidemic spillovers from inside the loop to outside.

According to the final actual effect, the epidemic prevention and control of the Beijing Winter Olympics was quite successful. We can make a horizontal comparison with the Tokyo Olympics. During the entire operation cycle of the Tokyo Olympics, outbreaks of epidemics occurred in various regions of Japan. However, during and after the operation cycle of the Beijing Winter Olympics, there was no outbreak of the epidemic in Beijing and related areas, which shows that the closed-loop management policy has a very significant effect on epidemic control.

This study also has some limitations. The Beijing Winter Olympics is a very complex process, so our model can only roughly describe the actual situation and cannot make accurate data predictions. In addition, our research can only stay in the qualitative analysis stage because there is no real data to support it.

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[#] Corresponding author: Chuanqing Xu, xuchuanqing@bucea.edu.cn.

[1] Department of Mathematics and Data Science, Beijing University of Civil Engineering and Architecture, Beijing, China.

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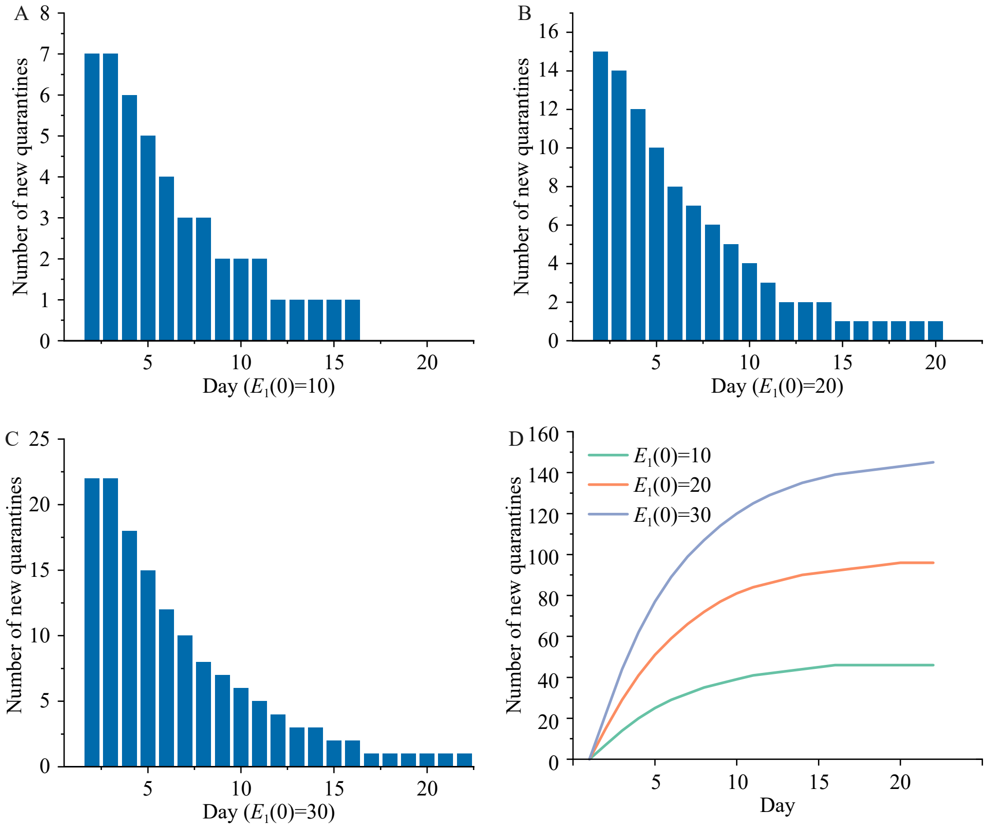

FIGURE 3. The comparison chart of the daily new number of people and the final size of quarantined persons (Q) with respect to the changes of the $E_1(0)$. (A) The daily new prediction results of quarantined persons with $E_1(0)$=10; (B) The daily new prediction results of quarantined persons with $E_1(0)$=20. (C) The daily new prediction results of quarantined persons with $E_1(0)$=30. (D) The change of the cumulative amount of quarantined persons, when $E_1(0)$ takes different values.

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Supplementary Material

SUPPLEMENTARY TABLE S1. The daily new number of people of quarantined persons (Q) with respect to the changes of the parameters ρ, θ.

Days	ρ=0.5, θ=0.5	ρ=0.9, θ=0.5	ρ=0.5, θ=0.9	ρ=0.9, θ=0.9
1	0.000	0.000	0.000	0.000
2	5.772	7.357	5.772	7.356
3	6.809	7.237	6.809	7.237
4	6.285	6.125	6.284	6.124
5	5.382	5.047	5.381	5.047
6	4.484	4.137	4.484	4.137
7	3.697	3.388	3.697	3.388
8	3.035	2.774	3.035	2.773
9	2.487	2.271	2.487	2.270
10	2.037	1.859	2.037	1.859
11	1.668	1.522	1.668	1.522
12	1.366	1.246	1.365	1.246
13	1.118	1.020	1.118	1.020
14	0.915	0.835	0.915	0.835
15	0.749	0.683	0.749	0.683
16	0.613	0.560	0.613	0.559
17	0.502	0.458	0.502	0.458

SUPPLEMENTARY TABLE S2. The daily new number of quarantined persons (Q) with respect to the changes of the $E_1(0)$.

Days	$E_1(0)$=10	$E_1(0)$=20	$E_1(0)$=30
1	0.000	0.000	0.000
2	7.356	14.712	22.069
3	7.237	14.473	21.709
4	6.124	12.248	18.373
5	5.047	10.093	15.140
6	4.137	8.274	12.411
7	3.388	6.776	10.163
8	2.773	5.547	8.321
9	2.270	4.541	6.812
10	1.859	3.718	5.576
11	1.522	3.043	4.565
12	1.246	2.491	3.737
13	1.020	2.040	3.060
14	0.835	1.670	2.505
15	0.683	1.367	2.050
16	0.559	1.119	1.679
17	0.458	0.916	1.374
18	0.375	0.750	1.125
19	0.307	0.614	0.921
20	0.251	0.503	0.754
21	0.206	0.411	0.617
22	0.168	0.337	0.505

Notes from the Field

First Imported Case of SARS-CoV-2 Omicron Subvariant BA.5 — Shanghai Municipality, China, May 13, 2022

Hui Jiang[1,&]; Changcheng Wu[2,&]; Wenbo Xu[2]; Hongyou Chen[1]; Fanghao Fang[1]; Min Chen[1]; Chaonan Wang[1]; Lingyue Yuan[1]; Huanyu Wu[1]; Zheng Teng[1]; Jinyuan Guo[2]; Yaxu Zheng[1]; Xihong Lyu[3]; Xuefei Qiao[3]; Guizhen Wu[2]; Wenjie Tan[2,#]; Xi Zhang[1,#]

On April 27, 2022, an international flight KL857 from Amsterdam, the Netherlands arrived at Pudong International Airport, Shanghai Municipality. Passengers were transferred to the quarantine hotel for a routine 14-day medical observation in Songjiang District and regularly tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). One of the passengers (a 37-year-old Chinese male) was reported positive and diagnosed as a mild case on April 29. The case set out from Uganda (flight KL535) on April 25 and transferred at Amsterdam, the Netherlands on April 26 and Seoul, the Republic of Korea (KL857) on April 27. The patient has been vaccinated in four doses against coronavirus disease 2019 (COVID-19) (Beijing Institute of Biological Products Co., Ltd) in China and Uganda. After diagnosis, he was transferred to Shanghai Public Health Clinical Center for treatment. He recovered after treatment and was discharged on May 12.

A nasopharyngeal swab from the patient was sampled on April 29 and sequenced using MGISEQ-200 (MGI TECH CO., LTD, Wuhan City, Hubei Province, China) on May 13. Genotyping analysis revealed that the patient was infected by SARS-CoV-2 variant of concern (VOC)/Omicron subvariant BA.5. The genome is most closely related to a sequence (GISAID ID: EPI_ISL_12713186) uploaded in South Africa (Figure 1) and 34 nonsynonymous mutations

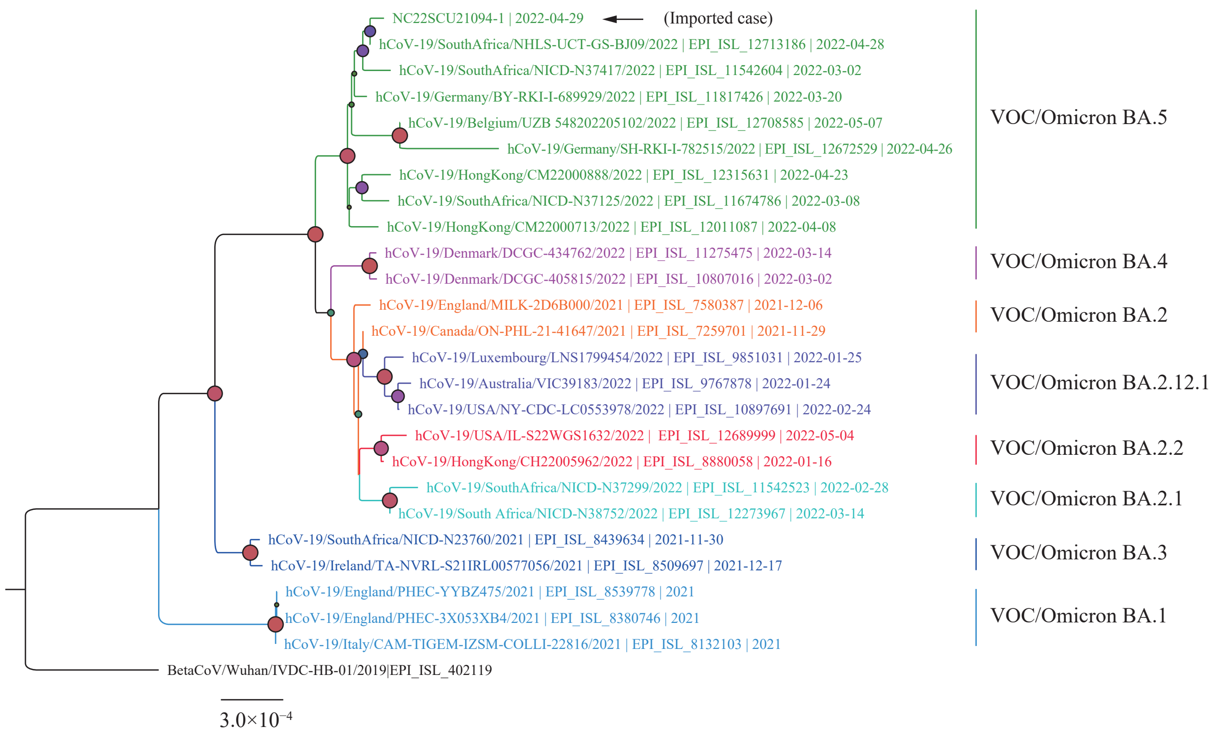

FIGURE 1. Phylogenetic tree of multiple lineages of SARS-CoV-2.
Note: The imported VOC/Omicron (BA.5) is highlighted with an arrow. Other Omicron sublineages in different colors are indicated on the right side.
Abbreviation: SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; VOC=variant of concern.

(T19I, A27S, G142D, V213G, G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, L452R, S477N, T478K, E484A, F486V, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K, and L24del, P25del, P26del, H69del, V70del) occurred in the spike gene matching the signature of the sublineage BA.5.

The sequence of BA.5 was first uploaded to GISAID on March 15, 2022 from a patient's nasopharyngeal and oropharyngeal swab collected on February 25 in South Africa. Together with BA.4, BA.5 has increased in prevalence in South Africa in recent weeks and has already spread to additional 19 countries in 3 months (total of 2,614 sequences submitted to GISAID); BA.5 caused a rise in the number of cases in some countries, such as Portugal, and South Africa has also reported a moderate increase in hospital admissions since late April (*1*). The L452R, F486V, and 69–70del mutations may impact the characteristics of BA.5 and make it appear to have a growth advantage over BA.1 and BA.2, which may mainly be driven by immune evasion (*2–4*). The 69–70del mutation is also responsible for S-gene target failure in polymerase chain reaction (PCR) tests, but PCR assays that include multiple gene targets will maintain accuracy for detecting this lineage (*5–6*). Due to the short duration of the epidemic, studies showed that the extent of vaccination and the high level of BA.2 waves in each country likely influence the emergence of BA.5 (*7*), but ongoing monitoring and assessment are needed to further elucidate the characteristics and impact of this lineage.

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[#] Corresponding authors: Wenjie Tan, tanwj28@163.com; Xi Zhang, zhangxi@scdc.sh.cn.

[1] Shanghai Municipal Center for Disease Control and Prevention, Shanghai, China; [2] National Institute for Viral Disease Control and Prevention, China CDC, Beijing, China; [3] Songjiang District Center for Disease Control and Prevention, Shanghai, China.
[&] Joint first authors.

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Notes from the Field

The First Outbreak of Omicron Subvariant BA.5.2 — Beijing Municipality, China, July 4, 2022

Zhaomin Feng[1,&]; Ying Shen[2,&]; Shuang Li[1]; Jia Li[1]; Shaohua Wang[3]; Zhenquan Zhang[3]; Yunkui Shen[3]; Fu Li[1]; Yang Pan[1]; Quanyi Wang[1]; Da Huo[1,#]

On July 4, 2022, the first case of Omicron subvariant BA.5.2 in Beijing Municipality was discovered in Yanqing District. The case was a 49-year-old Chinese male who had arrived in Shanghai Municipality via international flight DL9927 from North Carolina, U.S. on June 15. He stayed in a hotel for the 14-day arrival quarantine and was discharged on June 30. He arrived in Beijing via domestic flight MU5103 on July 1 and was transferred point-to-point from the airport to his residence community in Yanqing District. On July 3, his sample was collected through community mass screening and reported positive in the next morning. The case had received 3 doses of Moderna's mRNA vaccines in the U.S., with the last shot on May 26, 2022.

The index case caused an outbreak with a total of 16 cases located in 5 districts within 7 days. Among all cases, 12 were males and 4 were females; 12 received a booster shot, whereas 4 were non-vaccinated.

The respiratory samples from 16 cases were sequenced by the Next Generating Sequencing (NGS). A total of 13 full genomes were obtained and all belonged to the same lineage BA.5.2, Variant of Concern (VOC)/Omicron. In particular, 11 genomes shared a nucleotide similarity of 100%, 1 genome carried an additional mutation of T29678C, and 1 carried an additional heterozygous mutation of A6821G with a frequency of 59.39%. Phylogenetic analysis indicated the virus was similar to strains in North America, Europe, and Asia in mid-June, which was different from local clusters in Beijing in the same period (Figure 1).

Omicron subvariant BA.5 had surged dramatically to become dominant in the U.S. (*1*). Research indicated that the Omicron BA.5 subvariant had a growth advantage against other subvariants with a higher ability of immune escape than the BA.1, BA.2, and BA.2.12.1 subvariants (*2*–*5*). Continuous surveillance and assessment need to be implemented to respond Omicron subvariant BA.5 in China.

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[#] Corresponding author: Da Huo, huoda@bjcdc.org.

[1] Institute for Infectious Disease and Endemic Disease Control, Beijing Center for Disease Prevention and Control, Beijing, China; [2] Office of Beijing Center for Global Health, Beijing Center for Disease Prevention and Control, Beijing, China; [3] Yanqing District Center for Disease Prevention and Control, Beijing, China.
[&] Joint first authors.

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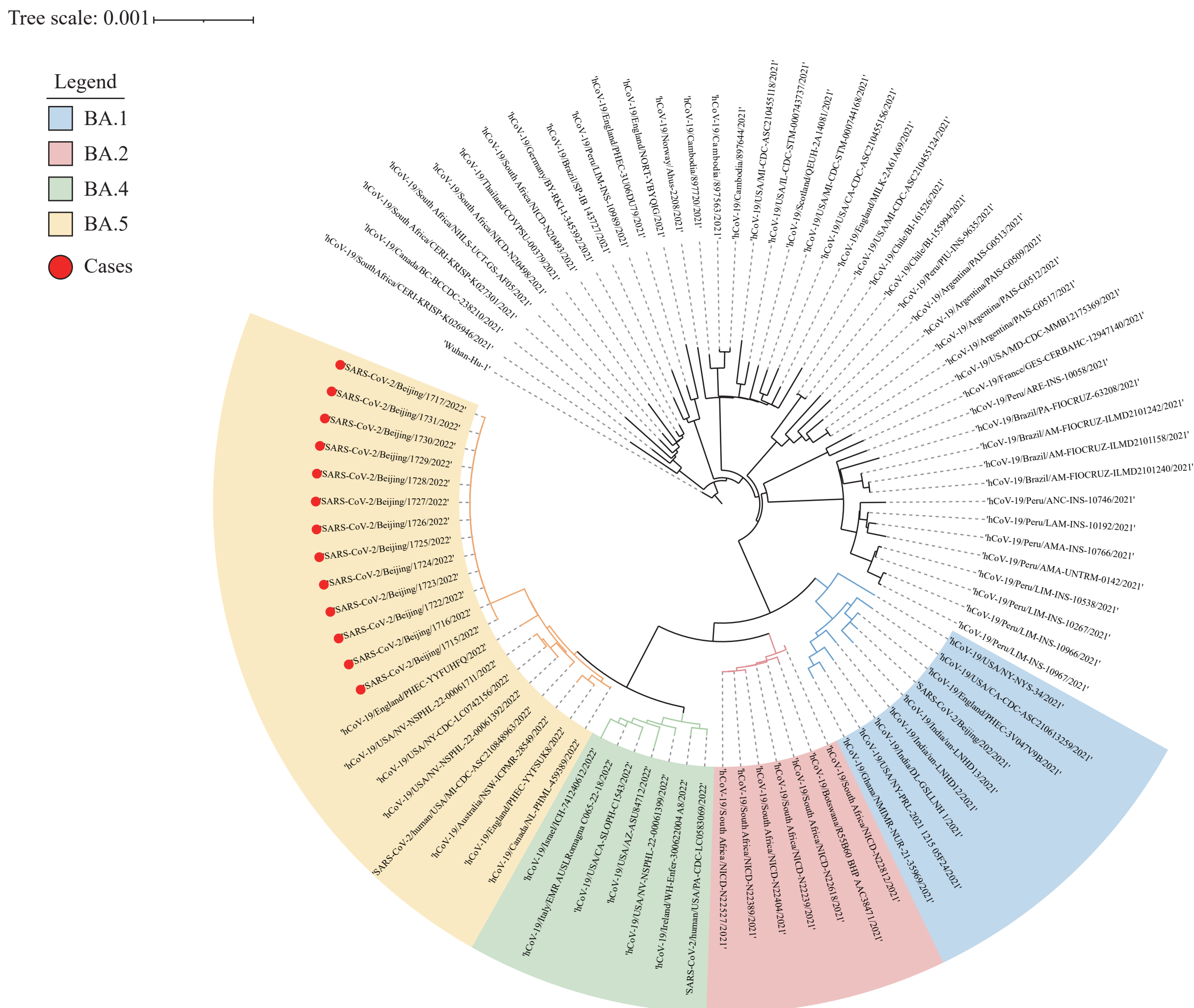

FIGURE 1. Neighbor-joining phylogenetic tree of strains in the outbreak.
Note: The genomes from cases in the outbreak were indicated by red dots. The major VOC/Omicron PANGOLIN lineages were marked and colored on the right. The tree was rooted using strain Wuhan-1 (EPI_ISL_402125).
Abbreviation: VOC=variant of concern.

Notes from the Field

An Outbreak of the SARS-CoV-2 Omicron Variant BA.1 — Zhuhai City, Guangdong Province, China, January 13, 2022

Feng Ruan[1,#]; Xuebao Zhang[1]; Songjian Xiao[1]; Xihe Ni[1]; Xiling Yin[1]; Zhongwen Ye[1]; Guorong Chen[1]; Tingting Zhu[1]; Zeling Chen[1]; Gang Yao[1]; Long Chen[1]; Sichen Huang[1]; Huitao Huang[1]; Yi Zhou[1]; Heyan Wu[1]; Hui Huang[1]; Kejing Zhu[1]; Shanzi Huang[1]; Xiaoou Tang[1]; Min Kang[2]; Bosheng Li[2]; Wenhua Mei[1,#]

On January 13, 2022, Zhuhai CDC received a notification that a coronavirus disease 2019 (COVID-19) case was found in the fever clinic in nearby Zhongshan City. Zhuhai CDC promptly carried out large-scale population screening in three nearby counties. A total of 4 COVID-19 cases were found in Nanping County. 34 cases were screened from close contacts, and 2 cases were reported from close contacts in other cities of Guangdong Province. The 20 cases were sequenced by Guangdong CDC and identified as the variant of concern (VOC)/Omicron variant BA.1. Since January 14, Zhuhai has carried out 8 rounds of nucleic acid screening for COVID-19 in the county where the cases occurred. Four large-scale nucleic acid screening tests for COVID-19 were conducted across the city, and no new community cases were reported after January 15.

In a total of 38 Omicron cases, 76% were mild (26/38) or asymptomatic (3/38) cases and 24% were moderate (9/38) cases; 79% of the mild or asymptomatic (23/29) cases completed more than 2 doses of inactivated COVID-19 vaccine; 83% of cases under the age of 15 were mild (15/18) and 70% of adult cases were mild or asymptomatic (14/20). There was no significant difference between the 2 age groups (P>0.05).The main symptoms were cough (49%, 17/35), fever (29%, 10/35), and dry pharynx (23%, 8/35). Pulmonary inflammation was found on computed tomography in 16% (6/38) of cases, 17% (3/18) in children and 15% (3/20) in adults.

The outbreak occurred in a cluster of work and study places and families (Figure 1A). The first case (a 34 years old female) who worked in Company C developed symptoms on January 8, 2022. Her husband was a yacht harbor driver, her daughter was studying in Primary School B, and her son attended Kindergarten A, all of whom developed symptoms on January 11, 2022.

We identified the outbreak was caused by family cluster cases spreading to kindergartens, elementary schools, and companies, then successively causing 7 families to have cluster cases (Figure 1B). The family secondary attack rate is 15.8%.

This outbreak has produced five generations of cases. The intergenerational time interval was calculated using the time interval of case onset, mean=3.37 days, standard deviations=1.70 days. The basic reproduction number (R_0) from January 8 to 21 was calculated (maximum likelihood method) as 1.3 (95% confidence interval: 0.8, 2.0). On January 13, the effective reproduction number was (R_t)=5.5 at the highest, then decreased rapidly to R_t<1 after January 19 (Figure 1C).

In the mainland of China, the first imported Omicron cases were found in Tianjin in December 2021 (*1*). Zhuhai had had no local COVID-19 cases since February 4, 2020. The first infected case had never left Zhuhai within one month before onset.

Company C mainly undertakes the customized production of foreign dentures and dental membranes. The goods were imported by express delivery from Europe and America. The first case occurred in a customer service employee. She occasionally helped pick up goods in the receiving area without protection (without masks and gloves) from January 1 to 11, 2022.

On January 16, 670 environmental samples were collected from Company C, and 6 single gene positive samples were detected, of which 5 positive samples were from the working area of cases as well as their colleagues without disease, and 1 positive sample was from the inner packaging of imported molds on the first floor.

After cases were found in adjacent cities, Zhuhai rapidly carried out large-scale population screening in three nearby counties. Early detection and isolation has played a key role in containing this Omicron outbreak (*2*). If the outbreak in kindergartens and primary schools had not been blocked in time, it could easily have spread through the community and caused an epidemic.

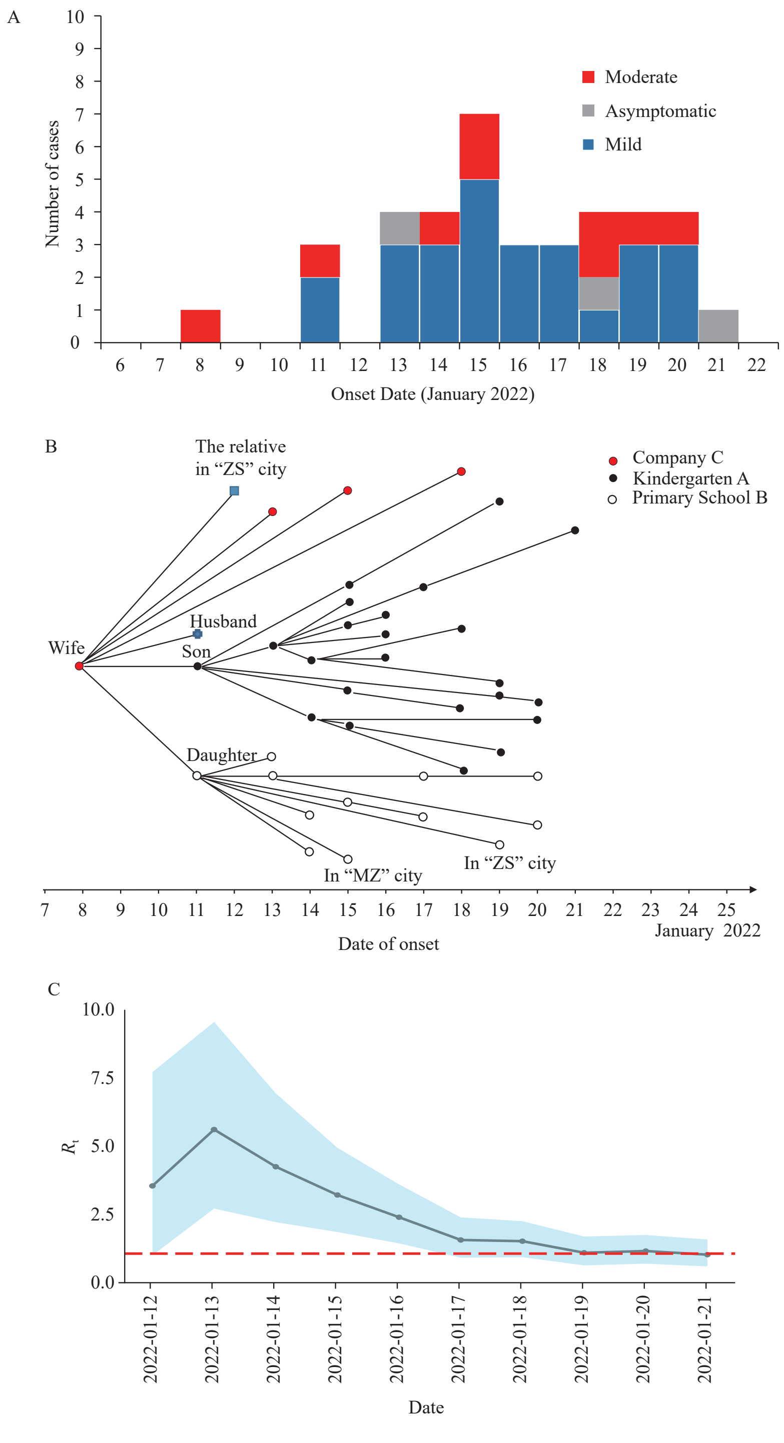

FIGURE 1. The transmission characteristics and transmission chain of an outbreak of the COVID-19 Omicron variant in Zhuhai City, Guangdong Province, China, 2022. (A) The epidemic curve of 38 COVID-19 cases; (B) The transmission chain of 38 COVID-19 cases; (C) The R_t of the ongoing COVID-19 epidemic in Zhuhai City from January 12 to January 21, 2022.

Note: In Figure 1B, each dot represents an infection case, and the connecting line between them represents the transmission relationship. "ZS" City is Zhongshan City of Guangdong Province, "MZ" City is Meizhou City of Guangdong Province. In Figure 1C, the red dotted line indicated R_t=1, below which sustained transmission was unlikely so long as intervention measures were sustained, indicating that the outbreak was under control. The "R0" package of R software (version 3.6.0, R Core Team, Vienna, Austria) was used for the data analysis. Through gamma distribution fitting, the "EpiEstim" package was used to estimate the R_t since January 12. R_0 represents the basic reproduction number; R_t represents the effective reproduction number.

Abbreviation: COVID-19=coronavirus disease 2019.

There was no strong evidence to show that materials other than cold chain food were the infection source (*3*). We suspected foreign dentures and dental membranes were possible sources of infection by epidemiological investigation, and more studies will be conducted in the future.

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Corresponding authors: Feng Ruan, fruan@126.com; Wenhua Mei, 1297648405@qq.com.

[1] Zhuhai Center for Disease Control and Prevention, Zhuhai, Guangdong, China; [2] Guangdong Province Center for Disease Control and Prevention, Guangzhou, Guangdong, China.

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