Infect Dis Ther (2023) 12:2405–2416
https://doi.org/10.1007/s40121-023-00873-3

ORIGINAL RESEARCH

Distinguishing the Vaccine Effectiveness of Inactivated BBIBP-CorV Vaccine Booster Against the Susceptibility, Infectiousness, and Transmission of Omicron Stains: A Retrospective Cohort Study in Urumqi, China

Ting Zeng · Kailu Wang · Zihao Guo · Shengzhi Sun · Ziyu Zhai · Yaoqin Lu · Zhidong Teng · Daihai He · Kai Wang · Maozai Tian · Shi Zhao

Received: August 15, 2023 / Accepted: September 11, 2023 / Published online: September 28, 2023

ABSTRACT

Introduction: With COVID-19 vaccination rolled out globally, increasing numbers of studies have shown that booster vaccines can enhance an individual's protection against the infection, hospitalization, and death caused by SARS-CoV-2. This study evaluated the effectiveness of COVID-19 vaccine BBIBP-CorV booster against being infected (susceptibility), infecting others (infectiousness), and spreading the disease from one to another (transmission).

Methods: This retrospective cohort study investigated the close contacts of all officially ascertained COVID-19 confirmed cases in Urumqi, China between August 1 and September 7, 2022. Eligible records were divided into four subcohorts based on the vaccination status of both the close contact and their source case: group 2-2, 2-dose contacts seeded by 2-dose source case (as the reference level); group 2-3, 3-dose contacts seeded by 2-dose source case; group 3-2, 2-dose contacts seeded by 3-dose source case; and group 3-3, 3-dose contacts

Ting Zeng, Kailu Wang, and Zihao Guo contributed equally, and they are joint-first authors.

T. Zeng · Y. Lu
School of Public Health, Xinjiang Medical University, Ürümqi 830017, China

K. Wang · Z. Guo
JC School of Public Health and Primary Care, Chinese University of Hong Kong, Hong Kong 999077, China

S. Sun
Department of Epidemiology and Biostatistics, School of Public Health, Capital Medical University, Beijing 100069, China

Z. Zhai · D. He
Department of Applied Mathematics, Hong Kong Polytechnic University, Hong Kong 999077, China

Y. Lu
Urumqi Center for Disease Control and Prevention, Ürümqi 830026, China

Z. Teng · K. Wang (✉) · M. Tian (✉)
Department of Medical Engineering and Technology, Xinjiang Medical University, Ürümqi 830017, China
e-mail: wangkaimath@sina.com

M. Tian
e-mail: mztian@ruc.edu.cn

S. Zhao (✉)
Centre for Health Systems and Policy Research, Chinese University of Hong Kong, Hong Kong 999077, China
e-mail: zhaoshi.cmsa@gmail.com

seeded by 3-dose source case. In the four subcohorts, multivariate logistic regression models were used to examine the vaccine effectiveness (VE) for the BBIBP-CorV booster dose. We adjusted for potential confounding variables, including the sex and age of source cases and close contacts, the calendar week of contact history and contact settings. We evaluated the statistical uncertainty using a 95% confidence interval (CI). In addition, we conducted subgroup analyses to evaluate VE by sex.

Results: The sample sizes of groups 2-2, 2-3, 3-2, and 3-3 were 1184, 3773, 4723, and 27,136 individuals, respectively. Overall VE against susceptibility (group 2-3 vs 2-2) was 42.1% (95% CI 10.6, 62.5), VE against infectiousness (group 3-2 vs 2-2) was 62.0% (95% CI 37.2, 77.0), and VE against transmission (group 3-3 vs 2-2) was 83.7% (95% CI 75.1, 89.4). In the sex-stratified subgroups, male close contacts showed similar VE compared to the overall. However, among female close contacts, while the booster dose improved VE against infectiousness and VE against susceptibility, the VEs were not significantly different from zero.

Conclusion: BBIBP-CorV vaccine booster was associated with mild to moderate levels of protection against Omicron susceptibility, infectiousness, and transmission. Real-world assessment of protective performance of COVID-19 vaccines against the risk of Omicron strains is continuously needed, and may provide information that helps vaccination strategy.

Keywords: COVID-19; Vaccine effectiveness; Cohort study; Contact tracing

Key Summary Points

Why carry out this study?
The vaccines conferred multiple protection against infectious diseases.
By using contact tracing data, we evaluated the vaccine effectiveness of BBIBP-CorV booster against the susceptibility, infectiousness, and transmission of Omicron strains.
What was learned from the study?
BBIBP-CorV vaccine booster was associated with mild to moderate levels of protection against Omicron's susceptibility, infectiousness, and transmission.
Real-world assessment of vaccine performance against the risk of emerging SARS-CoV-2 genetic variants is continuously needed.

INTRODUCTION

Since the outbreak of the COVID-19, vaccination has been regarded as one of the most effective measures to combat the disease [1–3]. Vaccine developers and manufacturers have conducted large-scale clinical trials worldwide and reported corresponding vaccine efficacy results [4, 5]. Vaccine effectiveness (VE) in real-world studies is a method of assessing a vaccine's ability to prevent infectious diseases in real life [6–9], which is an essential complement to a randomized controlled trial as they involve a broader range of population, and consider various contextual factors beyond experimental conditions.

With the global implementation of COVID-19 vaccination, increasing numbers of studies have shown that booster vaccines can enhance an individual's protection against the virus and improve VE against COVID-19 infection and associated adverse outcomes [10–19]. Booster vaccines are usually administered as a third dose after an individual has received two doses of vaccine. It should be noted that the effectiveness of booster vaccines still depends on various factors, including virus mutations and the individual's immune system status.

The protection levels associated with vaccine in preventing infection and in preventing infecting others are both indicators for evaluating the real-world effectiveness of a vaccine. The most common and fundamental indicator that measures the reduction of infection risk by vaccination is VE in preventing infection. In the

current study, this indicator is specifically defined as VE against susceptibility. VE in preventing infecting others is a new concept that has only received attention in recent years [20–22]. The decrease in transmission risk associated with a specific vaccination in relation to infectiousness after being infected is defined as VE against infectiousness. Furthermore, vaccination can prevent transmission by offering protection against infection and simultaneously reducing the infectiousness of vaccinated individuals who become infected. In this study, VE against transmission is defined as the amalgamation of VE against susceptibility and VE against infectiousness.

Currently, most estimates of VE against Omicron infection focus on various mRNA vaccines, including mRNA-1273 and BNT162b2, or adenovirus vector vaccines such as ChAdOx1-nCoV-19 [6–9]. The COVID-19 vaccines administered in mainland China are predominantly inactivated vaccines, including Sinopharm (BBIBP-CorV) and Sinovac (CoronaVac). Although the VE of inactivated vaccines has been evaluated in phase III clinical trials [11, 23], there is still limited empirical research on the actual effectiveness of inactivated vaccines [4, 5]. Moreover, most studies have only focused on the VE in preventing being infected or severe illness [6, 9].

In 2022, Omicron variants were widely spread globally [24], and Urumqi, China, faced a COVID-19 outbreak caused by Omicron BA.5 variants (nasopharyngeal or oropharyngeal swabs collected from confirmed COVID cases were subjected to whole-genome sequencing; on the basis of the assigned PANGO lineage designation, the samples were classified as SARS-CoV-2 Omicron BA.5.2 sublineage) in August 2022. This study aimed to evaluate the VE of booster inactivated vaccines against the BA.5 in terms of preventing being infected (susceptibility), infecting others (infectiousness), and disease transmission among individuals (transmission) in the real world by comprehensive analysis of contact tracing data during the Omicron outbreak in Urumqi.

METHODS

Study Setting

From the beginning of the COVID-19 pandemic until October 2022 (after the end of our study period), mainland China implemented a "zero-COVID" policy. Therefore, prior to August 2022, there was no large-scale COVID-19 outbreak in Urumqi. This means that most of the 3.8 million people in this region had not been infected by then. Almost all people who received COVID-19 vaccines in mainland China received inactivated BBIBP-CorV vaccines. As of the end of July 2022, before the start of our study period, the coverage rates among mainland China's general population for the primary series and booster dose of inactivated vaccines were greater than 91% and greater than 72% [25], respectively, which were similar to those in Urumqi. Most unvaccinated people (i.e., zero doses) in mainland China are those who are not suitable for vaccination because of medical reasons.

In the context of the Omicron BA.5.2 variant, Urumqi, Xinjiang Uygur Autonomous Region, China, reported the first batch of COVID-19 cases on August 7 and numbers peaked on August 13. In accordance with the "zero-COVID" policy, the local government implemented a series of intensive control measures on August 10, including city lockdowns, large-scale testing, symptom-based monitoring, contact tracing, case isolation, and contact quarantine. This outbreak was brought under control in early September. We selected the period from August 1 to September 7, 2022 as our study period.

All individuals who had epidemiological links with laboratory-confirmed COVID-19 cases were classified as close contacts of COVID-19 [26]. Information on exposure history was collected and recorded through interviews with individuals diagnosed with COVID-19. Contact tracing measures conducted by the local center for disease control and prevention allows for matching the close contacts with their

sourse cases. The epidemiological links were determined for individuals who had contact with COVID-19 cases within 4 days of their test-positive date.

The local government conducted regular real-time reverse transcription polymerase chain reaction (RT-PCR) tests of SARS-CoV-2 infection in a daily basis, using the ORF1ab gene or N gene segment detection kits. All close contacts are subjected to RT-PCR tests (with cycle threshold [Ct] value < 40) using nasal or oral swab samples to achieve laboratory confirmation of SARS-CoV-2 infection.

Study Design and Participants

This retrospective cohort study investigated the close contacts of all confirmed COVID-19 cases in Urumqi, China between August 1 and September 7, 2022. We excluded records of those who received fewer than two doses of vaccine or those who had no vaccination information, as we aimed to study the VE of the booster dose. Close contacts without information on their last vaccination before exposure were also excluded. Those who had contact within 14 days after their last vaccination were also excluded [5].

We divided the eligible participants into four subcohorts based on the vaccination status of both the close contact and their source case: 2-dose contacts seeded by 2-dose source case (group 2-2 [reference group]), 3-dose contacts seeded by 2-dose source case (group 2-3), 2-dose contacts seeded by 3-dose source case (group 3-2), and 3-dose contacts seeded by 3-dose source case (group 3-3).

Variables

We extracted individual-level information, including the age and sex of the close contact and their source case, contact setting (i.e., household, community, workplace, and unknown settings), timeline on vaccination and exposure history, the vaccination status, and RT-PCR test results. We deemed RT-PCR positive for SARS-CoV-2 infection as the main outcome variable.

Statistical Analyses

Frequency distribution and measures of central tendency were used to describe the baseline characteristics of the four cohorts, including sex and age of the source cases and contacts, as well as the calendar week of the contact and contact setting. Count data was presented as *n* (%), and the measurement data was presented as the median and interquartile range (IQR). Multivariate logistic regression models adjusting for the baseline characteristics were used to examine the association between the vaccination status (i.e., four subcohorts) and the risk of SARS-CoV-2 infection in terms of odds ratios (OR). We calculated the VE based on the OR, where $VE = (1 - OR) \times 100\%$ when $OR < 1$, and $VE = -(1 - 1/OR) \times 100\%$ when $OR > 1$ [27–29]. Specifically, group 2-2 was considered as the reference level for comparison. VE against infectiousness, susceptibility, and transmission were obtained through group 2-3 versus group 2-2, group 2-3 versus group 2-2, and group 3-3 versus group 2-2 comparisons, respectively. We adjusted for potential confounding variables, including sex and age of source cases and close contacts, as well as the calendar date of contact. We evaluated the statistical uncertainty using a 95% confidence interval (CI). In addition, we conducted subgroup analyses to evaluate VE by sex. All data processing and analysis were performed in R statistical software (version 4.1.1).

RESULTS

From August 1 to September 7, 2022, a total of 51,786 close contacts of confirmed COVID-19 cases were identified. Among them, we excluded 14,051 individuals who received fewer than two doses of the vaccine or had no information about their last vaccination (prior to exposure). Additionally, 919 individuals who were exposed within 14 days after receiving their last vaccine dose were also excluded. The remaining 36,816 eligible contacts were eligible for inclusion in the analysis.

On the basis of the vaccination status of both the contacts and their source cases, we

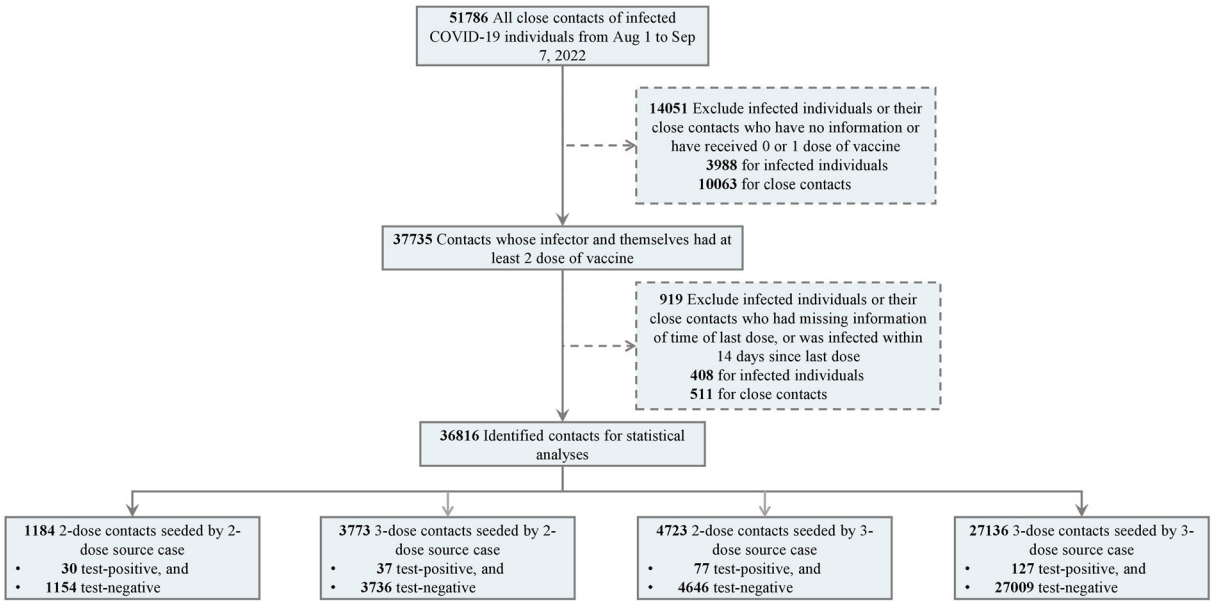

Fig. 1 Flowchart of sample selection and grouping

categorized the study cohort into four subgroups: group 2-2, group 2-3, group 3-2, and group 3-3, as defined earlier. The respective sample sizes of our pre-defined subcohorts were 1184 (group 2-2), 3773 (group 2-3), 4723 (group 3-2), and 27,136 (group 3-3) (Fig. 1). The baseline characteristics of cases and their close contacts were shown in Table 1. The percentages of male and female contacts were similar among different groups of close contacts. However, for source cases, there were more female individuals in group 3-2 (61.7%) and group 3-3 (62.2%) compared to other groups. Among the close contacts, there was a higher percentage of individuals under 18 years old in group 2-2 and group 3-2. In group 2-3 and group 3-3, the majority (over 90%) of the close contacts were 18–59 years old. The majority of the transmission events occurred in August 2022, accounting for over 90% of the total (Table 1).

The overall VE were shown in Table 2. After adjustment for potential confounding variables, the VE against infectiousness was 62.0% (95% CI 37.2–77.0), the VE against susceptibility was 42.1% (95% CI 10.6–62.5), and the VE against transmission was 83.7% (95% CI 75.1–89.4). In the subgroup analyses, male close contacts showed similar VE compared to the overall sample. However, among female close contacts, while the booster dose improved the VE against infectiousness and VE against susceptibility, the VE estimations were not significantly different from zero.

DISCUSSION

Since 2022, the Omicron variant and its genetic subtypes have posed a new threat to global public health. Apart from a shortened incubation period, most Omicron infections are either asymptomatic or present with mild symptoms, leading to relatively low risks of hospitalization and mortality [30, 31]. Consequently, researchers have increasingly focused on assessing the effectiveness of vaccines against the Omicron variant. In Urumqi, when there were no reported local cases, close contacts underwent RT-PCR testing once a week. In the presence of sporadic local transmission chains, testing was conducted every 2–3 days, while daily testing was carried out during local outbreaks. These testing efforts provide an ideal research context allowing us to evaluate, in a real-world scenario, the efficacy of a booster

Table 1 Baseline characteristics of close contacts of COVID-19 who received 2-dose and 3-dose vaccine

Characteristics	Contacts seeded by 2-dose case, *n* (column %)		Contacts seeded by 3-dose case, *n* (column %)	
	Group 2-2: 2-dose contacts	Group 2-3: 3-dose contacts	Group 3-2: 2-dose contacts	Group 3-3: 3-dose contacts
Total	1184 (100%)	3773 (100%)	4723 (100%)	27,136 (100%)
Sex of contacts				
Male	628 (53.0%)	1889 (50.1%)	2263 (47.9%)	12,848 (47.3%)
Female	556 (47.0%)	1884 (49.9%)	2460 (52.1%)	14,288 (52.7%)
Sex of source cases				
Male	62 (50.8%)	75 (52.4%)	161 (38.3%)	189 (37.8%)
Female	60 (49.2%)	68 (47.6%)	259 (61.7%)	311 (62.2%)
Age group of contacts				
Minor: < 18 years	751 (63.4%)	0 (0%)	2033 (43.0%)	0 (0%)
Young adult: 18–39 years	197 (16.6%)	1741 (46.1%)	1522 (32.2%)	13,331 (49.1%)
Middle-age adult: 40–59 years	103 (8.7%)	1700 (45.1%)	655 (13.9%)	11,654 (42.9%)
Old-age adult: 60+ years	133 (11.2%)	332 (8.8%)	513 (10.9%)	2151 (7.9%)
Median age, years [IQR]	15.0 [9.0, 32]	41.0 [31.0, 52.0]	22.0 [12.0, 39.0]	40.0 [30.0, 51.0]
Age group of source cases				
Minor: < 18 years	76 (62.3%)	92 (64.3%)	1 (0.3%)	1 (0.2%)
Young adult: 18–39 years	19 (15.6%)	24 (16.8%)	198 (47.1%)	226 (53.8%)
Middle-age adult: 40–59 years	11 (9.0%)	12 (8.4%)	189 (45.0%)	223 (53.1%)
Old-age adult: 60+ years	16 (13.1%)	15 (10.5%)	32 (7.6%)	50 (11.9%)
Median age, years [IQR]	15.5 [10.0, 33.5]	14.0 [9.0, 29.0]	40.0 [31.0, 50.3]	41.0 [31.0, 51.0]
Epidemiological week of 2022 when contacts were exposed to source cases				
Week 31: Jul 31–Aug 6	282 (23.8%)	936 (24.8%)	955 (20.2%)	5268 (19.4%)
Week 32: Aug 7–Aug 13	299 (25.3%)	1120 (29.7%)	2481 (52.5%)	15,832 (58.3%)
Week 33: Aug 14–Aug 20	155 (13.1%)	416 (11.0%)	680 (14.4%)	3218 (11.9%)
Week 34: Aug 21–Aug 27	331 (28.0%)	1026 (27.2%)	324 (6.9%)	1332 (4.9%)
Week 35: Aug 28–Sep 3	111 (9.4%)	245 (6.5%)	186 (3.9%)	860 (3.2%)
Week 36: Sep 4–Sep 10	6 (0.5%)	30 (0.8%)	97 (2.1%)	626 (2.3%)

Table 1 continued

Characteristics	Contacts seeded by 2-dose case, *n* (column %)		Contacts seeded by 3-dose case, *n* (column %)	
	Group 2-2: 2-dose contacts	Group 2-3: 3-dose contacts	Group 3-2: 2-dose contacts	Group 3-3: 3-dose contacts
Contact setting				
Household	91 (7.7%)	149 (3.9%)	218 (4.6%)	629 (2.3%)
Community	37 (3.1%)	97 (2.6%)	130 (2.8%)	894 (3.3%)
Workplace	7 (0.6%)	89 (2.4%)	81 (1.7%)	1156 (4.3%)
Unknown settings	1049 (88.6%)	3438 (91.1%)	4294 (90.9%)	24,457 (90.1%)

dose of inactivated vaccine against Omicron BA.5 infection. This evaluation comprised VE of the booster dose against being infected (susceptibility), infecting others (infectiousness), and spreading the disease from one to another (transmission) combining the VE against being infected and infecting others.

Similar to our findings, a population-based observational study in Hong Kong evaluated the relative VE of three doses versus two doses of CoronaVac during the circulation of the BA.2 variant [6]. The study found that for mild or moderate disease, the third dose increased VE in adults aged 20–59 years (35.7% [95% CI 22.1–47.3]) and adults aged 60 or above (46.9% [95% CI 29.6–60.6]). For severe or fatal disease, the study found that receiving a third dose of the vaccine had additional benefits for adults in all age groups. A systematic review on the real-world effectiveness of inactivated SARS-CoV-2 vaccines reported a pooled booster dose VE of 65.2% (95% CI 48.3–76.6) against the SARS-CoV-2 Delta variant, which decreased to 20.3% (95% CI 10.5-28.0) for the Omicron variant [32] The VE measured in these studies is limited to assessing against susceptibility and is not comprehensive enough.

Our findings indicated that the booster dose of inactivated vaccine provided considerable protection against Omicron infection. Specifically, compared to the reference level group 2-2, group 3-2 achieved a VE against infectiousness, which refers to the extent to which the vaccine reduces infectivity among individuals already infected. The booster dose of inactivated vaccine also conferred a significant reduction in infectivity among the infected individuals. This implied that individuals who received the booster vaccine were likely to have lower transmissibility and therefore transmitted the virus to others at a lower rate. Group 2-3 obtained a VE against susceptibility, which indicated the extent to which the vaccine reduces individual susceptibility. Group 3-3 obtained a VE against transmission, which refers to the vaccine's ability to break the chain of virus transmission and interrupt community spread. The booster vaccine exhibited significant effectiveness in preventing transmission. Our research suggests that individuals who received the booster dose would have an 83.7% reduced risk of transmitting the virus to others compared to those in group 2-2. This contributes to controlling the spread of the pandemic within communities.

The subgroup analysis was conducted on the three-dose inactivated vaccine by sex. It was found that the protective effect was not significant in the female close contact population, which may be attributed to the fact that female are more frequently engaged in social settings such as supermarkets, shopping malls, and social gathering places, which were focal points of disease transmission during the local outbreak. Thus, female residents were likely associated with a higher infection risk than male[33]. Further research is needed to confirm the impact of sex differences on the vaccine's

Table 2 Summary of the effectiveness of 3-dose inactivated vaccine, versus 2-dose (reference level), against SARS-CoV-2 Omicron BA.5 infection

Stratification	Number of contacts		Time from last vaccine to contact exposure, days [IQR]		VE (95% CI)	
	Test-positive	Total	For contacts	For source cases	Crude	Adjusted[a]
Overall						
2-dose contacts seeded by 2-dose source case (ref)	30	1184	260.0 [223.0, 343.0]	262.0 [220.5, 356.0]	0% (reference)	0% (reference)
3-dose contacts seeded by 2-dose source case	37	3773	241.0 [212.0, 270.0]	259.0 [206.0, 359.0]	61.9% (38.1, 76.6)	62.0% (37.2, 77.0)
2-dose contacts seeded by 3-dose source case	77	4723	261.0 [193.0, 350.0]	261.0 [223.0, 286.0]	36.2% (2.3, 58.4)	42.1% (10.6, 62.5)
3-dose contacts seeded by 3-dose source case	127	27,136	235.0 [207.0, 267.0]	268.0 [230.0, 287.0]	81.9% (73.0, 87.9)	83.7% (75.1, 89.4)
Among male close contacts						
2-dose contacts seeded by 2-dose source case (ref)	19	628	264.0 [226.5, 345.0]	262.0 [206.0, 353.0]	0% (reference)	0% (reference)
3-dose contacts seeded by 2-dose source case	15	1889	243.0 [217.0, 272.0]	253.0 [206.0, 356.0]	74.3% (49.2, 87.0)	74.4% (47.9, 87.4)
2-dose contacts seeded by 3-dose source case	39	2263	260.0 [172.0, 351.0]	264.0 [228.0, 287.0]	43.8% (2.0, 66.8)	46.7% (5.8, 69.9)
3-dose contacts seeded by 3-dose source case	62	12,848	235.0 [211.0, 267.0]	269.0 [233.0, 287.0]	84.5% (73.8, 90.8)	85.4% (74.4, 91.7)
Among female close contacts						
2-dose contacts seeded by 2-dose source case (ref)	11	556	257.0 [223.0, 341.0]	262.0 [222.0, 356.0]	0% (reference)	0% (reference)
3-dose contacts seeded by 2-dose source case	22	1884	239.0 [206.0, 269.0]	261.0 [222.0, 361.0]	41.5% (− 10.8, 71.8)	42.9% (− 17.2, 73.0)
2-dose contacts seeded by 3-dose source case	38	2460	261.0 [212.0, 349.0]	256.0 [214.0, 284.0]	22.3% (− 34.6, 60.5)	32.9% (− 24.9, 66.2)
3-dose contacts seeded by 3-dose source case	65	14,288	234.0 [204.0, 267.0]	258.0 [224.0, 286.0]	77.4% (56.9, 88.1)	80.7% (62.2, 90.1)

[a]The vaccine effectiveness (VE) was estimated from multivariate logistic regression model adjusted for covariables including sex, age, epidemiological week of 2022, contact setting, and vaccine status of source case

protective effects. Additionally, we observed a VE of over 80% against transmission in both male and female individuals , implying that the effect of vaccination for controlling the spread of the epidemic is insensitive of sex.

Limitations

The study has several limitations. Firstly, there were no participants under the age of 18 in group 3-2 and group 3-3 as a result of different vaccination policies for minors and adults in mainland China. Therefore, there was an imbalance in the distribution of adults and minors used for comparison. Secondly, our dataset did not record information regarding clinical severity, so the findings on vaccine effectiveness cannot be extended to a more severe clinical range of COVID-19. Thirdly, the duration and pattern of exposure (e.g., conversation, shared room) could be potential confounding factors in our study, which were not considered in the analysis as a result of limited data collection. Moreover, among the target population of this study, most of the unvaccinated individuals had existing medical conditions that made them ineligible for vaccination. Thus, we excluded these unvaccinated individuals from the analysis, who accounted for less than 10% of the total population in Urumqi, while participants who received two doses of the vaccine were considered as the reference group for booster analysis. Lastly, the social distancing and personal protection behaviors that may affect the risk of infection were not recorded in the dataset, while the intensive non-pharmaceutical measures made most of these characteristics aligned.

CONCLUSIONS

This retrospective cohort study showed that the booster dose of BBIBP-CorV vaccine was associated with mild to moderate levels of protection against Omicron susceptibility, infectiousness, and transmission. Real-world assessment of protective performance of COVID-19 vaccines against the risk of Omicron strains is continuously needed, and may provide information that helps vaccination strategy.

Author Contributions. Conceptualization: Shi Zhao and Kai Wang. Methodology: Shi Zhao, Ting Zeng, and Yaoqin Lu. Software: Kai Wang and Ting Zeng. Validation: Kailu Wang, Zihao Guo and Shi Zhao. Formal analysis: Kai Wang, Maozai Tian, and Zhidong Teng. Investigation: Kai Wang, Ting Zeng, Yaoqin Lu, and Shi Zhao. Resources: Yaoqin Lu and Kai Wang. Data Curation: Yaoqin Lu and Kai Wang. Writing—Original Draft: Ting Zeng and Kailu Wang. Writing—Review and Editing: Kailu Wang, Zihao Guo, Shengzhi Sun, Ziyu Zhai, Zhidong Teng, Daihai He, Maozai Tian, and Shi Zhao. Visualization: Ting Zeng. Supervision: Kai Wang, Maozai Tian, and Shi Zhao. Project Administration: Kai Wang and Yaoqin Lu. Funding acquisition: Kai Wang and Yaoqin Lu. All authors critically read the manuscript and gave final approval for publication.

Funding. This work and the journal's rapid service fee were supported by the Youth science and technology innovation talent of Tianshan Talent Training Program in Xinjiang (Grant No. :2022TSYCCX0099) and the Technology Innovation Team (Tianshan Innovation Team) Project (Grant No.: 2022TSYCTD0015).

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest. Ting Zeng, Kailu Wang, Zihao Guo, Shengzhi Sun, Ziyu Zhai, Yaoqin Lu, Zhidong Teng, Daihai He, Kai Wang, Maozai Tan, and Shi Zhao declared no competing interests. The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Ethics approval. The collection of specimens, epidemiological and clinical data for SARS-CoV-2 infected individuals and their close

contacts is a part of a continuing public health investigation of COVID-19 outbreaks, ruled in the Protocol on the Prevention and Control of COVID-19 by the National Health Commission of the People's Republic of China, which was exempt from ethical approval (i.e., institutional review board assessment). This study was approved by the institutional ethics committee of Xinjiang Medical University (IRB No.: XJYKDXR20221001001). Individual verbal consent was obtained from parents or legal guardians of participants when collecting personal information and human samples by governmental healthcare professionals in the field. This study presents no more than minimal risk of harm to all subjects, and involves no procedures for which written consent is normally required outside of the research context. The institutional ethics committee of Xinjiang Medical University waived written informed consent, and approved verbal consent for this study.

REFERENCES

1. Hodgson SH, Mansatta K, Mallett G, Harris V, Emary KRW, Pollard AJ. What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2. Lancet Infect Dis. 2021;21:e26–35.
2. Dagotto G, Yu JY, Barouch DH. Approaches and challenges in SARS-CoV-2 vaccine development. Cell Host Microbe. 2020;28:364–70.
3. Dai LP, Gao GF. Viral targets for vaccines against COVID-19. Nat Rev Immunol. 2021;21:73–82.
4. Al Kaabi N, Zhang Y, Xia S, et al. Effect of 2 inactivated SARS-CoV-2 vaccines on symptomatic COVID-19 infection in adults: a randomized clinical trial. JAMA. 2021;326:35–45.
5. Jara A, Undurraga EA, González C, et al. Effectiveness of an inactivated SARS-CoV-2 vaccine in Chile. N Engl J Med. 2021;385:875–84.
6. McMenamin ME, Nealon J, Lin Y, et al. Vaccine effectiveness of one, two, and three doses of BNT162b2 and CoronaVac against COVID-19 in Hong Kong: a population-based observational study. Lancet Infect Dis. 2022;22:1435–43.
7. Gazit S, Gazit S, Mizrahi B, Kalkstein N, et al. BNT162b2 mRNA vaccine effectiveness given confirmed exposure: analysis of household members of coronavirus disease 2019 patients. Clin Infect Dis. 2022;75:e734–40.
8. Layan M, Gilboa M, Gonen T, et al. Impact of BNT162b2 vaccination and isolation on SARS-CoV-2 transmission in Israeli households: an observational study. Am J Epidemiol. 2022;191:1224–34.
9. Mousa M, Albreiki M, Alshehhi F, et al. Similar effectiveness of the inactivated vaccine BBIBP-CorV (Sinopharm) and the mRNA vaccine BNT162b2 (Pfizer-BioNTech) against COVID-19 related hospitalizations during the Delta outbreak in the UAE. J Travel Med. 2022. https://doi.org/10.1093/jtm/taac036.
10. Liu X, Shaw RH, Stuart ASV, et al. Safety and immunogenicity of heterologous versus homologous prime-boost schedules with an adenoviral vectored and mRNA COVID-19 vaccine (Com-COV): a single-blind, randomised, non-inferiority trial. Lancet. 2021;398:856–69.
11. World Health Organization. Recommendation for an emergency use listing of Covid-19 vaccine (Vero cell), inactivated—submitted by Sinovac. Geneva. https://extranet.who.int/pqweb/sites/default/files/documents/SINOVAC_TAG_PEG_REPORT_EUL-Final28june2021.pdf. Accessed 28 June 2021.
12. Imperial College COVID-19 response team. Growth, population distribution and immune escape of Omicron in England. Report 49. 2022.

https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-49-omicron. Accessed 01 July 2023

13. Sheikh A, Kerr S, Woolhouse M, McMenamin J, Robertson C, EAVE II Collaborators. Severity of omicron variant of concern and effectiveness of vaccine boosters against symptomatic disease in Scotland (EAVE II): a national cohort study with nested test-negative design. Lancet Infect Dis. 2022;22:959–66.

14. Wang X, Zhao X, Song J, et al. Homologous or heterologous booster of inactivated vaccine reduces SARS-CoV-2 Omicron variant escape from neutralizing antibodies. Emerg Microb Infect. 2022;11:477–81.

15. Pérez-Then E, Lucas C, Monteiro VS, et al. Neutralizing antibodies against the SARS-CoV-2 Delta and Omicron variants following heterologous CoronaVac plus BNT162b2 booster vaccination. Nat Med. 2022;28:481–5.

16. Pajon R, Doria-Rose NA, Shen X, et al. SARS-CoV-2 omicron variant neutralization after mRNA-1273 booster vaccination. N Engl J Med. 2022;386:1088–91.

17. Tuekprakhon A, Nutalai R, Dijokaite-Guraliuc A, et al. Antibody escape of SARS-CoV-2 omicron BA.4 and BA.5 from vaccine and BA1 serum. Cell. 2022;185:2422–2433.e13.

18. Chemaitelly H, Ayoub HH, AlMukdad S, et al. Duration of mRNA vaccine protection against SARS-CoV-2 Omicron BA.1 and BA.2 subvariants in Qatar. Nat Commun. 2022;13:12.

19. Huang Z, Xu S, Liu J, et al. Effectiveness of inactivated and Ad5-nCoV COVID-19 vaccines against SARS-CoV-2 omicron BA 2 variant infection, severe illness, and death. BMC Med. 2022.

20. de Gier B, Andeweg S, Joosten R, et al. Vaccine effectiveness against SARS-CoV-2 transmission and infections among household and other close contacts of confirmed cases, the Netherlands, February to May 2021. Eurosurveillance. 2021;26:7.

21. Madewell ZJ, Yang Y, Longini IM Jr, Halloran ME, Dean NE. Household secondary attack rates of SARS-CoV-2 by variant and vaccination status: an updated systematic review and meta-analysis. JAMA Netw Open. 2022;5:e229317.

22. Lyngse FP, Kirkeby CT, Denwood M, et al. Household transmission of SARS-CoV-2 omicron variant of concern subvariants BA.1 and BA.2 in Denmark. Nat Commun. 2022. https://doi.org/10.1038/s41467-022-33498-0.

23. Tanriover MD, Doğanay HL, Akova M, et al. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. Lancet. 2021;398:213–22.

24. WHO. Weekly epidemiological update on COVID-19–21 September 2022. https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19—21-september-2022. Accessed 21 Sept 2022.

25. Agency TXN. The safety and effectiveness of COVID-19 vaccines in China—the Joint prevention and control mechanism of The State Council answers questions on vaccination. http://www.gov.cn/govweb/xinwen/2022-07/23/content_5702572.htm. Accessed 23 July 2022.

26. Hu S, Wang W, Wang Y, et al. Infectivity, susceptibility, and risk factors associated with SARS-CoV-2 transmission under intensive contact tracing in Hunan, China. Nat Commun. 2021;12:1533.

27. Jackson ML, Nelson JC. The test-negative design for estimating influenza vaccine effectiveness. Vaccine. 2013;31:2165–8.

28. Bond HS, Sullivan SG, Cowling BJ. Regression approaches in the test-negative study design for assessment of influenza vaccine effectiveness. Epidemiol Infect. 2016;144:1601–11.

29. Cowling BJ, Perera RAPM, Fang VJ, et al. Incidence of influenza virus infections in children in Hong Kong in a 3-year randomized placebo-controlled vaccine study, 2009–2012. Clin Infect Dis. 2014;59:517–24.

30. World Health Organization. Coronavirus disease (covid-19): variants of SARS-COV-2. World Health Organization. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/coronavirus-disease-%28covid-19%29-variants-of-sars-cov-2?gclid=CjwKCAiAhqCdBhB0EiwAH8M_GhPGuQ9dTNKI30G41zZGVATx3uZdswb8GBOq4CFvZP02Uk1TJJt_hRoCTMYQAvD_BwE. Accessed 25 Dec 2022.

31. NBC 5 Chicago. Omicron symptoms: here's how they differ from other variants. https://www.nbcchicago.com/news/local/omicron-symptoms-heres-how-they-differ-from-other-variants/2723960. Accessed 7 Jan 2022.

32. Xu S, Li J, Wang H, Wang F, Yin Z, Wang Z. Real-world effectiveness and factors associated with effectiveness of inactivated SARS-CoV-2 vaccines: a systematic review and meta-regression analysis. BMC Med. 2023;21:160.

33. Litwin H, Shiovitz-Ezra S. Social network type and subjective well-being in a national sample of older Americans. Gerontologist. 2011;51:379–88.

Publisher's Note