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SARS-CoV-2 vaccines in China could reduce COVID-19-related respiratory syndromes and deaths: A retrospective cohort study

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ABSTRACT

Background: Information is limited regarding the effectiveness of the inactivated vaccine for COVID-19 approved in China in preventing infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) when administered in real-world conditions.
Methods: We retrospectively surveyed 1352 patients with a positive SARS-CoV-2 nucleic acid test treated at a major tertiary medical center in Foshan city (Guangdong, China) between November 2022 and February 2023. The exposure group was patients who had previously received the COVID-19 vaccine, which included patients who had received different doses of the vaccine and different vaccine types. The primary outcome of this study was the effectiveness of the vaccine in preventing severe disease and death among SARS-CoV-2-infected patients.
Results: We found a mortality rate of 12.1 % associated with COVID-19. The results showed that an increase in the number of vaccine doses was associated with a reduction in in-hospital mortality. When compared to unvaccinated patients, vaccinated patients had an 8.5 % lower mortality rate. There was also a statistically significant reduction in the risk of death among vaccinated patients compared to unvaccinated patients (OR = 0.521 [95 % CI, 0.366 to 0.741]). Patients who had received the vaccine had a 22.8 % reduction in the risk of severe disease. In addition, the use of antiviral drugs decreased progressively with increasing vaccine doses ($P < 0.05$). Of these, anticoagulation, Paxlovid, and mechanical ventilation were used least frequently in the one-dose group.
Conclusions: The vaccines approved in China mitigated the incidence of severe COVID-19 and reduced mortality. These findings suggest that COVID-19 vaccination can help to control the pandemic.

Introduction

The primary route of infection for the coronavirus disease 2019 (COVID-19) is through the respiratory system, leading to a range of symptoms, including fever, cough, and fatigue. The current global health crisis, known as the COVID-19 pandemic, is attributable to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has resulted in considerable numbers of cases and deaths worldwide. As of 18 December 2022, over 649 million confirmed cases and over 6.6 million deaths have been reported globally. SARS-CoV-2 infection may remain asymptomatic in the early stages until the emergence of severe pneumonia, dyspnea, organ dysfunction, and even death [1]. Although everyone can be affected, the infection has a lower clinical impact on the vaccinated population than on the unvaccinated population. Most infected vaccinated people appear to have a milder course and better clinical outcomes [2–4]. As the COVID-19 pandemic evolved, infections, hospitalizations, vaccines, and deaths varied among and within countries and regions worldwide.

SARS-CoV-2 vaccines may more effectively prevent severe disease and mortality related to infection and transmission [5]. Many studies have evaluated the effectiveness of BNT162b2 mRNA vaccines in preventing severe COVID-19 outcomes. Two recent studies from Israel

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focused on clinical outcomes [6]. The first study reported a 90–96 % reduction in the risk of serious illness on Day 12 after the booster dose. The second study found a 70–84 % reduction in the probability of testing positive for SARS-CoV-2 among vaccinated individuals [6]. Most importantly, the results from an observational study in Israel showed that the BNT162b2 mRNA vaccine was 93 % effective in preventing COVID-19-related hospital admissions, 92 % effective in preventing severe disease, and 81 % effective in preventing COVID-19-related deaths [6]. The study was a large observational study based on nationwide mass vaccination data in Israel, with a broad representation of the population. A large real-world study in Chile showed that a single dose of Ad5-nCoV vaccine provided 95.35 % protection against severe disease after 28 days, which was comparable to the rate of protection against severe disease after 14 days of 2 doses of BNT162b2 vaccine (96.56 %) and higher than the rate of protection against severe disease after 14 days of 2 doses of inactivated vaccine (86.88 %) [7]. Another real-world study in Mexico showed 76 % and 94 % protection rates against hospitalization and death, respectively, with a full course of Ad5-nCoV vaccination [8,9]. The overall effectiveness of the CoronaVac vaccine in a population of over 10 million in Chile was 67 %, with an efficacy of 80 % in preventing death [10].

Unlike the large volume of published population-based studies investigating the long-term effectiveness of BNT162b2 mRNA vaccines [11], relatively few large studies have elucidated the effect of the inactivated vaccine on the disease process. Some studies on inactivated vaccines have focused on biological evidence (e.g., antibodies and memory B cells) rather than real-world population data [12–15]. Given the paucity of evidence on the effectiveness of inactivated vaccines in preventing death and reducing symptoms of disease, we decided to investigate the effectiveness of vaccines in the real world.

The inactivated vaccine (Vero cells) was the first and most utilized clinical vaccine in China. As of 23 December 2022, 31 provinces (autonomous regions and municipalities directly under the Central Government) and the Xinjiang Production and Construction Corps reported a cumulative total of 3,469,670,000 doses of SARS-CoV-2 vaccine, with a 90 % vaccination rate across the country [16]. This vaccine is an inactivated vaccine (Vero cells), and several phase III clinical trials have reported that the efficiency of this type of vaccine in preventing severe diseases typically ranges between 60 % and 80 % [17–19].

Based on this, we conducted a retrospective study to compare the incidence and mortality of severe COVID-19 among vaccinated and unvaccinated populations, as well as analyze the protective effect of inactivated vaccines on patients and the changes in treatment modalities across different immunization doses. The goal of this study was to determine the efficacy of inactivated vaccines in preventing severe COVID-19 and death.

Methods

Study design and patients

This was a single-center, retrospective cohort study conducted at a major tertiary medical center in Foshan city (Sanshui District People's Hospital, Guangdong, China).

This study included all SARS-CoV-2 patients between November 5, 2022, and February 27, 2023. The inclusion criteria were as follows: (i) upon admission, patients tested positive for SARS-CoV-2 on the nucleic acid test; (ii) patients included in the study ranged in age from 0 to 100 years. (iii) participants had no previous medical history of respiratory system diseases. (iv) prior to participation, patients signed an informed consent form. The exclusion criteria were as follows: (i) moderate influenza (or high fever) or other pneumonia without SARS-CoV-2 infection; (ii) receipt of a fourth dose of a SARS-CoV-2 vaccine within 7 days before infection; and (iii) receipt of other COVID-19 vaccines outside of China previously. Excluding those two groups ("ii" and "iii") aims to reduce confounding between booster dose side effects and severe illness or death from infection as most of the vaccines received outside China were non-inactived vaccines, and to more accurately assess the effectiveness of the vaccines in preventing severe diseases and death.

The study protocol was reviewed and approved by the Ethics Committee of Foshan Sanshui People's Hospital (Guangdong, China) (SRY-KY-2023046) and conformed to the ethical standards for medical research involving human subjects, as laid out in the 1964 Declaration of Helsinki and its later amendments. Participants provided written informed consent prior to taking part in this study. All the authors had access to the study data and reviewed and approved the final manuscript.

Diagnostic criteria

SARS-CoV-2 infection was defined as nasal swabs or saliva specimens that tested positive for both the ORF1ab gene and N gene by nucleic acid testing. Lung imaging was characterized as follows: (i) by the early presentation of multiple small patchy shadows and interstitial changes that were evident in the outer lung bands; (ii) progression to multiple ground glass and infiltrative shadows in both lungs, and in severe cases, pulmonary solidity and pleural effusion; and (iii) in MIS-C, an enlarged heart shadow and pulmonary edema in patients with cardiac insufficiency. The clinical manifestations included the following: (i) fever and/or respiratory symptoms associated with COVID-19 pneumonia; (ii) imaging features of COVID-19 pneumonia as described above; and (iii) normal or reduced total white blood cell count and normal or reduced lymphocyte count early in the course of the disease.

Severity typing was confirmed according to the "Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 9) [20]" jointly issued by the General Office of the National Health Commission of the People's Republic of China and the General Office of the State Administration of Traditional Chinese Medicine: (i) asymptomatic; (ii) mild; (iii) moderate; (iv) severe; and (vi) critical. Severe COVID-19 meant that the patient's pneumonia was typed as "severe" or "critical". Pulmonary CT was graded according to the area of typical COVID-19 pneumonia infiltration in the patient's lung images: (i) 0; (ii) < 30 %; (iii) 30 %-50 %; and (iv) > 50 %.

Vaccination status

COVID-19 vaccination status was reported through a survey with identifying information provided by the participant or by their direct upload of an image of their vaccination card. The vaccine information collected included when the participant received the vaccine, the dose of the vaccine, and the type of vaccine. At the time of inclusion in this study, participants were considered fully vaccinated (three doses), partially vaccinated (one dose or two doses), or unvaccinated. All vaccinated individuals had completed their vaccination between 2 January 2021 and 16 January 2023. The vaccine types administered to all study participants were categorized as inactivated vaccines and other types of vaccines. The inactivated vaccines used in this study were manufactured by the Chinese National Pharmaceutical Group, specifically the Beijing Biological Products Institute, the Wuhan Biological Products Institute, and the Beijing Kexing Zhongwei Biotechnology Co., Ltd. Additionally, other vaccine types encompassed adenovirus vector vaccines (CanSino) and recombinant subunit vaccines (Anhui Zhifei Longcom Biopharmaceutical Co., Ltd.).

Outcomes

We retrospectively extracted clinical symptoms, lung imaging information, medical and surgical treatment data, and the clinical outcomes of COVID-19 patients from medical records using a standardized spreadsheet issued to clinicians.

The primary endpoint of this study was the effectiveness of the vaccine in preventing severe disease and death among SARS-CoV-2-

infected patients. Severe disease and mortality rates were assessed between the vaccinated and unvaccinated groups, as well as between the different vaccine dose groups. The secondary endpoints included differences in lung CT and treatment modality between groups.

Covariates

In addition to investigating vaccination information and patient medical records, we also collected information on (i) age; (ii) sex; and (iii) underlying medical conditions, including chronic illnesses such as cardiovascular diseases, hypertension, diabetes, inflammatory bowel disease, chronic kidney disease, chronic obstructive pulmonary disease, immunocompromised status and cancer.

Statistical methods

The effectiveness of inactivated vaccines in preventing mortality and severe COVID-19 was estimated. The means for age and length of stay were compared across groups using one-way ANOVA. Dichotomous variables or unordered multivariate variables for all subjects were analyzed using Pearson's chi-square test or the Wilcoxon rank-sum test. The Pearson chi-square test was used to estimate the difference in mortality between vaccinated participants and unvaccinated participants. The Wilcoxon rank-sum test was used to estimate differences in severe disease rates and lung CT findings in vaccinated versus unvaccinated participants. We assessed the effectiveness of inactivated vaccines against severe COVID-19 using the Wilcoxon rank-sum test by including participants who received an inactivated COVID-19 vaccine as a vaccination group and comparing the results of this group with those of SARS-CoV-2-infected individuals who received other types of vaccines. The effectiveness of the inactivated vaccine in preventing COVID-19 mortality compared to other types of vaccines was assessed using a chi-square test. Binary logistic regression was used to analyze the impact of vaccination on severe disease and mortality. Differences in the means of treatment for patients in different vaccine dose groups were assessed using Pearson's chi-square test. The duration of mechanical ventilation was compared using one-way ANOVA under the assumption of unequal variances. We considered results with P values < 0.05 to be statistically significant. All analyses were performed using SPSS software version 26.0 (Statistical Product and Service Solutions).

Results

Participants' characteristics

Table 1 shows basic information for all participants, who had a mean age of 64.9 years (SD = 20.6) and a roughly balanced ratio of males and females. Among the 1352 participants, most were ≥ 50 years (79.2 %) of age, and 72.6 % had underlying medical conditions. The average age of the vaccinated group was lower than that of the unvaccinated group.

Attenuation of symptoms and duration of illness with vaccination

First, Table 2 shows that there were 110 COVID-19-related deaths in the unvaccinated group (16.4 %), an 8.5 % higher mortality rate than that in the vaccinated group. We also found that the mortality rate of patients infected with COVID-19 decreased with increasing vaccine doses.

Second, by comparing the vaccinated and unvaccinated groups (Table 2), we found that among patient with COVID-19, up to 36.6 % of patients in the unvaccinated group developed critical COVID-19, while the majority of patients in the vaccinated group were moderately symptomatic (65.3 %), and only 13.9 % developed critical COVID-19, with a severe COVID-19 incidence 22.7 % lower than that in the unvaccinated group ($P < 0.001$). On lung CT, 19.1 % of patients in the unvaccinated group had more than 50 % of the typical infiltrative images of lungs with COVID-19 pneumonia, 11.5 % higher than in the vaccinated group. In contrast, 28.6 % of patients in the vaccinated group had lung CT without associated pneumonia, which was 7.8 % higher than that in the unvaccinated group.

The incidence of severe COVID-19 and symptoms in the lungs was lower in the other three groups of patients who received different doses of a vaccine than in the unvaccinated group; however, the single-dose group (12.9 %, 6.5 %) had fewer patients with severe COVID-19, and presenting with typical lung COVID-19 pneumonia infiltrates was less frequent than in the two-dose group (14.7 %, 7.3 %) and the three-dose group (13.8 %, 8.0 %). Additionally, the incidence of secondary infections decreased with increasing vaccine doses and was significantly lower in the vaccinated group than in the unvaccinated group.

Effectiveness of inactivated vaccines against SARS-CoV-2 infection

By comparing the effect of inactivated vaccines with other vaccines on disease (Table 3), we found that inactivated vaccines provided 93.7 % protection against death. Patients who received inactivated vaccines had a 7.2 % lower mortality rate and 26.7 % fewer cases of severe COVID-19 than those who received other types of vaccines ($P < 0.05$). On lung CT, 30.7 % of patients in the inactivated vaccine group showed no COVID-19-related pneumonia, 9.6 % more than those who received other vaccines.

Vaccination was effective in reducing the risk of COVID-19 mortality (OR = 0.521, 95 % CI 0.365–0.744, adjusted for age and underlying diseases; Table 4). We discovered that receiving two or more doses of a vaccine effectively lowered the chance of death compared to receiving

Table 1
Baseline characteristics of the study cohort.

Variables	Total (n = 1352)	Unvaccinated (n = 669)	Vaccinated(n = 683)				P_1	P_2
			Total(n = 683)	One dose (n = 93)	Two doses (n = 177)	Three doses (n = 413)		
Age, years, mean (SD)	64.9(20.6)	66.1(20.8)	63.7(20.2)	75.0(25.5)	73.0(31.0)	67.0(26.5)	0.030	<0.001
Age group, n (%)							0.007	0.039
<50	281(20.8)	119(17.8)	162(23.7)	18(19.4)	43(24.3)	101(24.5)		
≥50	1071(79.2)	550(82.8)	521(76.3)	75(80.6)	134(75.7)	312(75.5)		
Sex, n (%)							0.207	0.571
Male	694(51.3)	355(53.1)	339(49.6)	44(47.3)	91(51.4)	204(49.4)		
Female	658(48.7)	314(46.9)	344(40.4)	49(52.7)	86(48.6)	209(50.6)		
Underlying diseases, n (%)							<0.001	<0.001
Yes	981(72.6)	574(85.8)	407(59.6)	64(68.8)	109(61.6)	234(56.7)		
No	371(27.4)	95(14.2)	276(40.4)	29(31.2)	68(38.4)	179(43.3)		

*P_1 is used to indicate the significance of the difference in baseline information between the vaccinated and unvaccinated groups. P_2 is used to indicate the significance of the difference in baseline information between the different vaccine dose groups and the unvaccinated group.

Table 2
Comparison of clinical characteristics between vaccinated and unvaccinated participants.

Variables	Unvaccinated (n = 669)	Vaccinated(n = 683)				P_1	P_2
		Total (n = 683)	One dose (n = 93)	Two doses (n = 177)	Three doses (n = 413)		
Length of hospitalization, days, mean (SD)	7.0(7.0)	8.2(6.7)	8.0(4.0)	7.0(6.5)	6.0(6.0)	0.277	0.251
Clinical Outcomes, n (%)						<0.001	<0.001
Death	110(16.4)	54(7.9)	11(11.8)	14(7.9)	29(7.0)		
Survival	559(83.6)	629(92.7)	82(88.2)	163(92.1)	384(93.0)		
Pneumonia typology, n (%)						<0.001	<0.001
Asymptomatic	29(4.3)	50(7.3)	4(4.3)	13(7.3)	33(8.0)		
Mild	33(4.9)	22(3.2)	0	9(5.1)	13(3.1)		
Moderate	293(43.8)	446(65.3)	65(69.9)	108(61.0)	273(66.1)		
Severe	69(10.3)	70(10.2)	12(12.9)	21(11.9)	37(9.0)		
Critical	245(36.6)	95(13.9)	12(12.9)	26(14.7)	57(13.8)		
Proportion of infiltrating lung shadows in COVID-19, n (%)						<0.001	<0.001
0	139(20.8)	195(28.6)	21(22.6)	47(26.6)	127(30.8)		
<30 %	322(48.1)	367(53.7)	56(60.2)	92(52.0)	219(53.0)		
30–50 %	39(5.8)	31(4.5)	6(6.5)	12(6.8)	13(3.1)		
>50 %	128(19.1)	52(7.6)	6(6.5)	13(7.3)	33(8.0)		
Other	41(6.1)	38(5.6)	4(4.3)	13(7.3)	21(5.1)		
Secondary infection, n (%)						<0.001	<0.001
Yes	85(12.7)	40(5.9)	10(10.8)	7(4.0)	23(5.6)		
No	584(87.3)	643(94.1)	83(89.2)	170(96.0)	390(94.4)		

*P_1 is used to indicate the significance of the difference in clinical characteristics between the vaccinated and unvaccinated groups. P_2 is used to indicate the significance of the difference in clinical characteristics between the different vaccine dose groups and the unvaccinated group. Severe COVID-19 meant that the patient's pneumonia was typed as "severe" or "critical". If a patient meets any of the following conditions, they would be classified as critical: (a) Respiratory failure requiring mechanical ventilation; (b) Shock; (c) Organ failure requiring ICU-level care.

Table 3
Protectiveness of different vaccine types for vaccinated participants.

Variables	Unvaccinated (n = 669)	Vaccinated(n = 683)		*P1*	*P2*
		Inactivated vaccines (n = 527)	Others (n = 156)		
Age, Years, Mean(SD)	66.1(20.8)	67(32.0)	76.5(15.0)	<0.001	<0.001
Age group, n (%)				<0.001	<0.001
<50 years	119(17.8)	152(28.8)	10(6.4)		
≥50 years	550(82.8)	375(71.2)	146(93.6)		
Sex, n (%)				0.070	0.054
Male	355(53.1)	251(47.6)	88(56.4)		
Female	314(46.9)	276(52.4)	68(43.6)		
Underlying diseases, n(%)				<0.001	<0.001
Yes	574(85.8)	291(55.2)	116(74.4)		
No	95(14.2)	236(44.8)	40(25.6)		
Length of hospitalization, days, Mean (SD)	7.0(7.0)	6.0(6.0)	7.0(5.0)	0.220	0.073
Clinical Outcomes, n (%)				<0.001	0.003
Death	110(16.4)	33(6.3)	21(13.5)		
Survival	559(83.6)	494(93.7)	135(86.5)		
Pneumonia typology, n (%)				<0.001	0.005
Asymptomatic	29(4.3)	34(6.5)	16(10.3)		
Mild	33(4.9)	22(4.2)	0		
Common	293(43.8)	335(67.4)	91(58.3)		
Heavy	69(10.3)	48(9.1)	22(31.4)		
Critical	245(36.6)	68(12.9)	27(17.3)		
Proportion of infiltrating lung shadows in COVID-19, n (%)				<0.001	0.009
0	139(20.8)	162(30.7)	33(21.1)		
<30 %	322(48.1)	266(50.5)	101(64.7)		
30–50 %	39(5.8)	23(4.4)	8(5.1)		
>50 %	128(19.1)	41(7.8)	11(7.1)		
Others	41(6.1)	35(6.6)	3(1.9)		
Secondary infection, n (%)				<0.001	0.737
Yes	85(12.7)	30(5.7)	10(6.4)		
No	584(87.3)	497(94.3)	146(93.6)		

*P_1 is used to indicate the significance of the difference in Protectiveness between the unvaccinated group and different types of vaccine group. P_2 is used to indicate the significance of the difference in Protectiveness between the different types of vaccine group.

only one dose ($P < 0.05$). Notably, inactivated vaccines significantly reduced the risk of death from COVID-19 compared with other vaccines (adjusted OR = 0.444, 95 % 0.292 to 0.675). Notably, vaccination was effective in preventing severe COVID-19, and the risk-adjusted OR for severe disease was 0.332 (95 % CI 0.256–0.429).

Differences in the treatment of patients with different vaccine doses

Table 5 compares the differences in COVID-19 treatment modalities between the unvaccinated and vaccinated groups for different doses. The results showed that patients in the vaccine group utilized medication and physical therapy (mechanical ventilation and prone position)

Table 4
Multivariate logistic regression analysis of risk factors for death and severe disease in COVID-19 patients.

Variable	Risk of death				Risk of severe disease			
	Crude OR (95 % CI)	P_1	Adjusted OR (95 % CI)	P_2	Crude OR (95 % CI)	P_3	Adjusted OR (95 % CI)	P_4
Vaccination (Reference: Unvaccinated group)								
Vaccinated	0.436 (0.309–0.616)	<0.001	0.521 (0.365–0.744)	<0.001	0.291 (0.226–0.374)	<0.001	0.332 (0.256–0.429)	<0.001
Vaccine doses (Reference: Unvaccinated group)								
One	0.682 (0.352–1.321)	0.256	0.656 (0.332–1.298)	0.226	0.208 (0.111–0.389)	<0.001	0.225 (0.119–0.423)	<0.001
Two	0.436 (0.244–0.782)	0.005	0.458 (0.251–0.833)	0.011	0.347 (0.232–0.517)	<0.001	0.399 (0.265–0.600)	<0.001
Three	0.384 (0.250–0.590)	<0.001	0.516 (0.332–0.803)	0.003	0.287 (0.213–0.387)	<0.001	0.331 (0.243–0.450)	<0.001
Vaccine type (Reference: Unvaccinated group)								
Inactivated vaccine	0.339 (0.226–0.510)	<0.001	0.444 (0.292–0.675)	<0.001	0.290 (0.220–0.381)	<0.001	0.338 (0.255–0.448)	<0.001
Others	0.791 (0.478–1.307)	0.360	0.720 (0.430–1.205)	0.211	0.294 (0.189–0.458)	<0.001	0.312 (0.199–0.490)	<0.001

*Adjusted for age and underlying diseases.

Table 5
Comparison of treatments for vaccinated and unvaccinated participants.

Variables	Unvaccinated (n = 669)	Vaccinated(n = 683)				*P1*	*P2*
		Total(n = 683)	One dose (n = 93)	Two doses (n = 177)	Three doses (n = 413)		
Antiviral, n (%)						<0.001	<0.001
Azulfidine	211(31.5)	218(31.9)	41(44.1)	60(33.9)	120(29.0)		
Paxlovid	6(0.9)	12(1.8)	1(1.1)	4(2.3)	9(2.2)		
Others	113(16.9)	43(6.3)	3(3.2)	14(7.9)	25(6.1)		
No	339(50.7)	410(60.0)	48(51.6)	99(55.9)	259(62.7)		
Hormones, n (%)						<0.001	<0.001
DXM	229(34.2)	149(21.8)	18(19.4)	41(23.2)	90(21.8)		
GEM-P	119(17.8)	123(18.0)	24(25.8)	38(21.5)	61(14.8)		
Others	19(2.8)	259(37.9)	2(2.2)	2(1.1)	7(1.7)		
No	302(45.1)	152(22.3)	49(52.7)	96(54.2)	255(61.7)		
Anticoagulation, n (%)						<0.001	<0.001
Yes	232(34.7)	189(27.7)	27(29.0)	51(28.8)	111(26.9)		
With concurrent bleeding	72(10.8)	26(3.8)	1(1.1)	9(5.1)	16(3.9)		
No	365(54.6)	468(68.5)	65(69.9)	117(66.1)	286(69.2)		
Prone positioning, n (%)						0.833	0.128
Yes	37(5.5)	36(5.3)	1(1.1)	7(4.0)	28(6.8)		
No	632(94.5)	647(94.7)	92(98.9)	170(96.0)	385(93.2)		
Mechanical Ventilation, n (%)						<0.001	<0.001
Yes	263(39.3)	119(17.4)	15(16.1)	33(18.6)	71(17.2)		
None	406(60.7)	564(82.6)	78(83.9)	144(81.4)	342(82.8)		
Antibiotics, n (%)						<0.001	<0.001
Yes	507(75.8)	406(59.4)	61(65.6)	109(61.6)	236(57.1)		
No	162(24.2)	277(40.6)	32(34.4)	68(38.4)	177(42.9)		
Paxlovid, n (%)						<0.001	<0.001
Yes	170(25.4)	70(10.2)	6(6.5)	22(12.4)	42(10.2)		
No	499(74.6)	613(89.8)	87(93.5)	155(87.6)	371(89.8)		
Blood plasma, n (%)						0.015	0.091
Yes	32(4.8)	16(2.3)	3(3.2)	5(2.8)	8(1.9)		
No	637(95.5)	667(97.7)	90(96.8)	172(97.2)	405(98.1)		

*P_1 is used to indicate the significance of the difference in treatments between the vaccinated and unvaccinated groups. P_2 is used to indicate the significance of the difference in treatments between the different vaccine dose groups and the unvaccinated group.

less frequently than patients in the unvaccinated group and that the use of antiviral medications gradually decreased as the number of vaccine doses increased ($P < 0.05$). The frequency of hormone and antibiotic use gradually decreased in the three-dose group compared to the non-vaccinated group ($P < 0.05$), as did the use of mechanical ventilation ($P < 0.05$). Notably, the one-dose group had the lowest frequency of Paxlovid use (6.5 %), as well as the lowest number of patients requiring mechanical ventilation (16.1 %) and prone positioning (1.1 %), with a significant difference ($P < 0.05$).

Discussion

This was a real-world observational study that compared vaccine-induced immunity following SARS-CoV-2 infection by different doses of inactivated vaccines and other vaccine types. Although there was no difference in the length of hospital stay between the two groups, we

discovered that mortality and severe disease rates were lower in the vaccinated group than in the unvaccinated group. After adjusting for confounding effects of age and underlying diseases conditions, the results showed that the inactivated vaccine in China was 93.7 % effective in preventing death and 78 % effective in preventing severe COVID-19. We also found that as the number of vaccine doses increased, the number of anti-infective drugs used gradually decreased.

We discovered that vaccination decreased mortality by 8.5 % and that as the number of vaccine doses increased, the mortality rate of patients with COVID-19 gradually decreased. The rate of serious disease was also decreased by vaccination by 22.7 %. Vaccination not only decreased mortality and morbidity but also decreased the occurrence of pneumonia infiltrates on CT. Notably, the inactivated vaccine in China offered 14 % less protection against severe COVID-19 and, conversely, 12 % more protection against mortality than the mRNA vaccine. Compared to data from previous studies of the CoronaVac vaccine [21], Our results demonstrate that in the context of the COVID-19 epidemic in China, inactivated vaccines are more effective in preventing mortality.

The data showed that immunity induced by inactivated vaccines was more effective in preventing mortality and less effective in preventing severe COVID-19. A theoretical advantage of inactivated vaccines is that they contain additional viral proteins, including nucleoproteins, which have the potential to extend protection beyond the anti-spike protein response and to reduce immune evasion by variants. Inactivated vaccines have lower rates of local and systemic adverse reactions than other types of vaccines. Most importantly, developing countries have very limited procurement and payment capacity and vaccine storage and transportation facilities compared to developed countries. Inactivated vaccines have a clear advantage in cold chain transport, with storage and transport conditions ranging from 2 °C to 8 °C, which is in line with the existing level of vaccine storage and transport in many countries, without the need to reconfigure cold chain system facilities and with greater accessibility [22].

In addition, by comparing the treatment modalities of the three groups of patients who received different vaccine doses, we found that the frequency of hormone and antibiotic use gradually decreased as the number of vaccine doses increased ($P < 0.05$). Few patients in each group required mechanical ventilation (16.1 % for the first dose, 18.6 % for the second dose, and 17.2 % for the third dose). Notably, the single-dose group had the lowest frequency of Paxlovid use (6.5 %) and the lowest number of patients requiring mechanical ventilation (16.1 %) and prone positioning (1.1 %). This suggests that immunity induced by the single-dose vaccine was more effective, which may be due to the higher antibody concentration in patients in the single-dose group due to the shorter mean duration of vaccination. This may also be because most of the patients in the one-dose group were vaccinated with an adenovirus vector vaccine, which is more potent in protecting against severe disease, so the treatment is simpler.

The real-world efficacy of COVID-19 vaccines will play a crucial role in driving higher vaccination rates among individuals. By promoting higher vaccination rates, there is the potential for a substantial reduction in both severe cases and mortality rates throughout the entire population. The establishment of population immunity would progressively alleviate the strain on healthcare systems, thereby guaranteeing that critically ill individuals receive prompt and comprehensive care. Furthermore, effective epidemic control and reduced public health risks can play a facilitating role in the restoration of regular societal, economic, and educational functioning.

This study has limitations. As this was an observational study, the investigated cohort was not masked or randomized, and therefore, unmeasured or uncontrolled confounders could not be excluded. Second, this was a single-center study with a small sample size. Most importantly, the viral strains of COVID-19 are always changing, and the vaccine may have different effects for different viral variants. Our study did not address the long-term efficacy of the vaccines used in China. Therefore, more research especially well designed prospective studies are needed to further evaluate the duration of the vaccine's protective effect.

Nevertheless, this is one of the few studies currently available to assess the impact of vaccines on the severity, clinical manifestations, and clinical outcomes of COVID-19 infection.

In conclusion, this study showed that vaccination remains the safest and best tool for protecting against infection and COVID-19-related hospitalization and death, irrespective of infection status. In China, inactivated vaccines may be more effective in reducing severe disease than other types of vaccines.

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CRediT authorship contribution statement

Weiping Yao: Writing – original draft, Writing – review & editing. **Yunhui Chen:** Formal analysis, Investigation, Writing – original draft. **Qiyu Huang:** Methodology, Visualization, Writing – review & editing. **Wanxia Luo:** Data curation, Resources. **Yueming Chen:** Data curation, Investigation. **Chuanbo Xie:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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