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Impacts of COVID-19 vaccine boosters on clinical outcomes associated with the Omicron variant in China: A cross-sectional survey

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A B S T R A C T

Objective: To investigate the real-world effectiveness of COVID-19 vaccine boosters during China's Omicron wave.
Methods: In January 2023, we surveyed Shenzhen, China residents via online questionnaires to investigate their COVID-19 symptoms and vaccination history. The outcomes of interest included fever, other COVID-19-related symptoms, severity of symptoms, whether early onset (before December 23, 2022) and duration. Respondents were categorized as no booster, one booster 6mo ago, one booster within 6mo, or two boosters based on dose count and vaccination timing. We used multivariable logistic regressions and Tobit models to assess COVID-19 vaccine booster impacts.
Results: Compared to the no booster group, two booster recipients had a lower fever risk (OR = 0.35, 95 %CI = 0.16–0.76) but not lower risks of COVID-19-related symptoms (OR = 0.74, 95 %CI = 0.26–2.06) and self-reported severe symptoms (OR = 0.47, 95 %CI = 0.19–1.15). Nor did the two booster recipients had a shorter illness duration (marginal effect = -0.79 days, 95 %CI = -1.65–0.07) and a lower risk of symptom onset delay (OR = 0.48, 95 %CI = 0.19–1.23). Compared to the no booster group, both one booster within six months (OR = 2.17, 95 %CI = 1.34–3.52) and one booster six months ago (OR = 1.30, 95 %CI = 0.92–1.82) did not reduce the risks of fever and symptoms (one booster within six months: OR = 1.57, 95 %CI = 0.84–2.90; one booster six months ago: OR = 1.23, 95 %CI = 0.79–1.93). Regardless of timing, one booster did not reduce illness duration (within six months: marginal effect = 0.25 days, 95 %CI = -0.20–0.70; six months ago: marginal effect = 0.27 days, 95 %CI = -0.08–0.62). However, receiving one booster within six months delayed symptom onset (OR = 0.54, 95 %CI = 0.34–0.86), while one booster six months ago did not (OR = 1.03, 95 %CI = 0.74–1.44).
Conclusions: Receiving two booster doses reduced the onset of fever during the Omicron outbreak in mainland China.

1. Introduction

Vaccination is among the most effective approaches to reduce the risks of adverse outcomes caused by COVID-19 [1,2]. However, the emergence of new variants causes great uncertainty of vaccine effectiveness (VE) [3,4]. On top of that, the protective effects of vaccines may wane over time [5–8]. Therefore, public health agencies in numerous countries recommended booster shots after completing the primary series of immunizations. In mainland China, the first booster shot program was massively rolled out in September 2021, and the campaign for the second booster was initiated in Dec 2022 but was interrupted by the COVID-19 outbreak in the same month.

A large-scale COVID-19 outbreak occurred in mainland China since December 7, 2022, and caused infections among a sizeable proportion of citizens. To understand the potential effectiveness of booster shots during the outbreak, we conducted a cross-sectional study in Jan 2023 by delivering online surveys to residents in Shenzhen, China, a city with over 17 million residents. The study aimed to evaluate the patterns of COVID-19 vaccination on the incidence of symptomatic infections, the timing of onset, and self-reported severe symptoms.

2. Methods

2.1. Study design and participants

We conducted an anonymous online questionnaire survey on China's largest survey platform. The platform had 6.2 million registered members nationwide, including 115,600 in Shenzhen. We conducted simple random sampling from Shenzhen residents aged 18 and above registered on the platform, distributing questionnaires to 5,832 individuals, and collected a total of 1,367 questionnaires, resulting in a response rate of 23.4 %. The survey was conducted from January 1, 2023, to January 29, 2023. Before the formal survey, a pilot survey was delivered from Dec 26, 2022, to Jan 2, 2023, to test the feasibility of the online survey and the readability of the questionnaire. We collected information about their COVID-19 vaccination status, whether they had experienced

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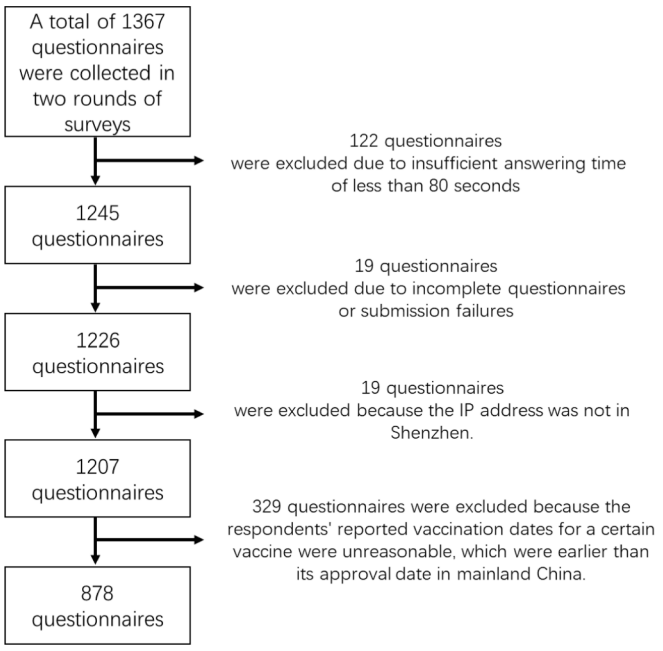

Fig. 1. Questionnaire Screening Process.

symptoms related to COVID-19 in the past two weeks, their self-reported severe symptoms, their time of onset, the duration of their illness, their basic demographic information, and their underlying conditions. We disseminated the questionnaire through a professional survey agency that houses the contact information of general population candidates and provides tailored services to researchers. However, the contact and identifying information of the respondents were kept confidential to the researchers.

The inclusion criteria of the survey were:

(1) adults aged 18 and above in Shenzhen;
(2) had not participated in the pilot survey.

The exclusion criteria were:

(1) time spent on answering the questionnaire was less than 80 s;
(2) did not complete all questions or failed to submit;
(3) the IP address was not in Shenzhen;
(4) the respondents' reported vaccination dates for a certain vaccine were unreasonable, which were earlier than its approval date in mainland China.

According to the results of our pilot survey, respondents took at least 3–5 seconds to answer each multiple-choice question, and answering fill-in-the-blank questions required even more time. The questionnaire had 3 fill-in-the-blank questions and 22 multiple-choice questions. Therefore, we set a threshold of 80 seconds to assess the reasonability of the respondents' completion time for this questionnaire. Questionnaires with excessively short total completion times were considered invalid. This study was approved by the ethical review committee in charge of the study.

2.2. Outcomes and variables

The outcomes of interest in this study pertained to symptoms, self-reported severe symptoms, timing of onset, and duration of illness related to COVID-19 in the past two weeks. The primary outcome was the occurrence of fever (37.3℃ or above) and the secondary outcomes were any COVID-19-related symptoms, self-reported severe symptoms, the time of symptom onset, and the number of days of illness. In addition to fever, we further asked whether they had experienced cough, sore throat, fatigue, eye pain, muscle pain, headache, loss of smell, loss of taste, nasal congestion, runny nose, diarrhea, or other COVID-19-related symptoms. The response was combined with fever to create the outcome of whether one had any symptoms related to COVID-19. When collecting

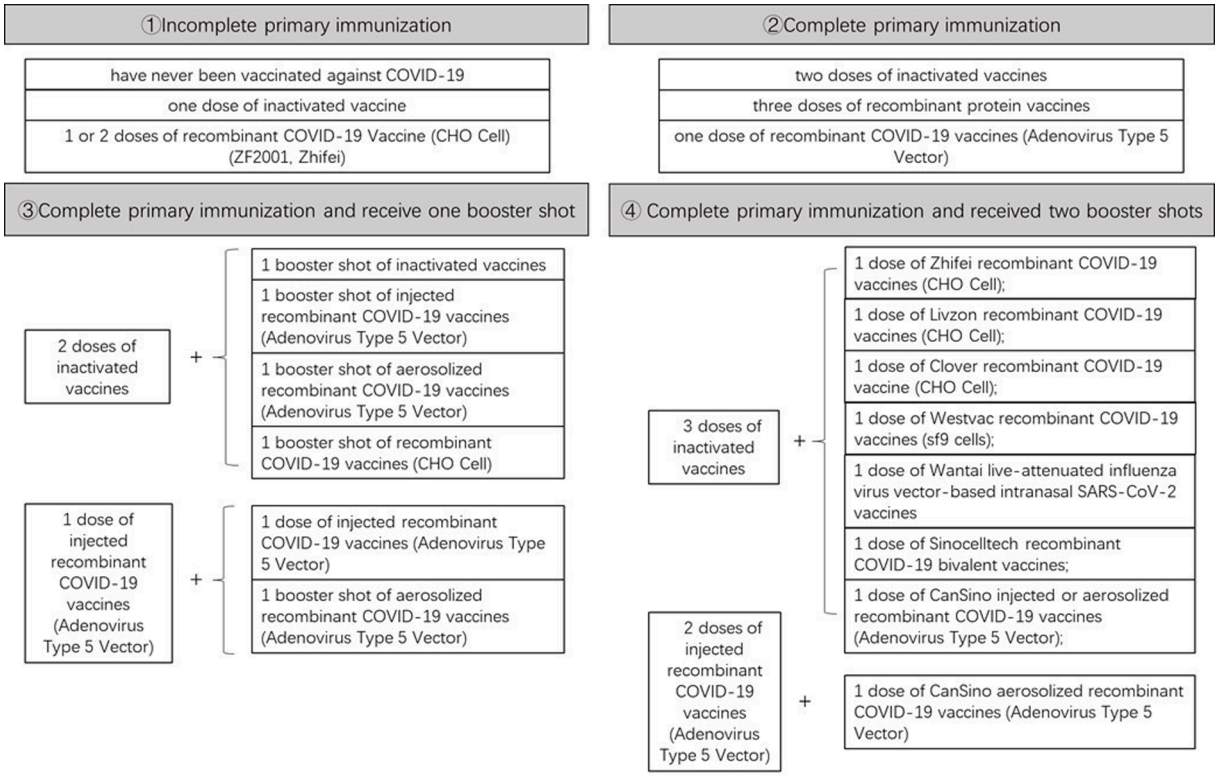

Fig. 2. The description of the types of vaccines included in different vaccination scenarios.

Table 1
Descriptive statistics of baseline characteristics and clinical outcomes.

		COVID-19 vaccine doses and the timing of vaccination				
	Total(%)	No booster (%)	One booster shot(> 6 month)(%)	One booster shot(≤6 month)(%)	Two booster shots(%)	P value
Total	878 (100)	405(46.1)	302(34.4)	141(16.1)	30(3.4)	
Age						0.087
18–34	598(68.1)	284(70.1)	202(66.9)	90(63.8)	22(73.3)	
35–49	157(17.9)	61(15.1)	66(21.9)	24(17.0)	6(20.0)	
≥50	123(14.0)	60(14.8)	34(11.3)	27(19.1)	2(6.7)	
Sex						0.029
Male	385(43.8)	169(41.7)	126(41.7)	78(55.3)	12(40.0)	
Female	493(56.2)	236(58.3)	176(58.3)	63(44.7)	18(60.0)	
Underlying disease						
Hypertension						0.162
No	799r(91.0)	363(89.6)	282(93.4)	125(88.7	29(96.7)	
Yes	79(9.0)	42(10.4)	20(6.6)	16(11.3)	1(3.3)	
Diabetes						0.002
No	850(96.8)	385(95.1)	301(99.7)	134(95.0)	30(100.0)	
Yes	28(3.2)	20(4.9)	1(0.3)	7(5.0)	0(0.0)	
Lower respiratory tract diseases						0.539
No	831(94.6)	382(94.3)	290(96.0)	131(92.9)	28(93.3)	
Yes	47(5.4)	23(5.7)	12(4.0)	10(7.1)	2(6.7)	
Upper respiratory tract diseases						0.205
No	759(86.4)	352(86.9)	262(86.8)	123(87.2)	22(73.3)	
Yes	119(13.6)	53(13.1)	40(13.2)	18(12.8)	8(26.7)	
Cardiovascular and cerebrovascular diseases						0.659
No	846(96.4)	387(95.6)	294(97.4)	136(96.5)	29(96.7)	
Yes	32(3.6)	18(4.4)	8(2.6)	5(3.5)	1(3.3)	
Malignant tumors						0.643
No	869(99.0)	399(98.5)	300(99.3)	140(99.3)	30(100.0)	
Yes	9(1.0)	6(1.5)	2(0.7)	1(0.7)	0(0.0)	
Fever						0.001
No	249(28.4)	126(31.1)	80(26.5)	27(19.1)	16(53.3)	
Yes	629(71.6)	279(68.9)	222(73.5)	114(80.9)	14(46.7)	
COVID-19-related symptoms (include fever)						0.645
No	116(13.2)	58(14.3)	38(12.6)	15(10.6)	5(16.7)	
Yes	762(86.8)	347(85.7)	264(87.4)	126(89.4)	25(83.3)	
Self-reported severe symptoms						0.053
Mild and symptom-free	467(58.3)	225(61.1)	146(53.5)	74(56.5)	22(75.9)	
Moderate and severe	334(41.7)	143(38.9)	127(46.5)	57(43.5)	7(24.1)	
Early vs. late occurrence of illness						0.043
Late onset and symptom-free	525(65.9)	234(63.9)	172(63.0)	96(74.4)	23(79.3)	
Early onset	272(34.1)	132(36.1)	101(37.0)	33(25.6)	6(20.7)	
Duration of symptoms (days)						0.315
0	322(36.7)	159(39.3)	103(34.1)	43(30.5)	17(56.7)	
1	72(8.2)	37(9.1)	23(7.6)	10(7.1)	2(6.7)	
2	120(13.7)	53(13.1)	40(13.2)	25(17.7)	2(6.7)	
3	145(16.5)	57(14.1)	54(17.9)	29(20.6)	5(16.7)	
4	71(8.1)	32(7.9)	24(7.9)	14(9.9)	1(3.3)	
5	61(6.9)	25(6.2)	28(9.3)	7(5.0)	1(3.3)	
6	16(1.8)	7(1.7)	5(1.7)	2(1.4)	2(6.7)	
7	47(5.4)	23(5.7)	15(5.0)	9(6.4)	0(0)	
≥8	24(2.7)	12(3.0)	10(3.3)	2(1.4)	0(0)	

*p < 0.05, **p < 0. 01, ***p < 0.001. Early vs. late occurrence of illness: Late onset was defined as first showing symptoms on or after December 23, 2022.

information on self-reported severe symptoms, patients who had experienced fever or other symptoms rated their symptoms as mild, moderate, or severe. Those who self-reported "severe" were classified into the severe group, and the rest were collectively classified into the mild, moderate, and symptom-free group. In addition, according to official data from the Chinese Center for Disease Control and Prevention [9], the omicron surge in mainland China peaked around December 23, 2022. We chose this date as the cut-off for early and late onset of illness. Those who first showed symptoms before December 23, 2022, were classified into the early onset group, and those who first showed symptoms on or after December 23, 2022, were classified into the late onset and symptom-free group along with those who did not show any symptoms. The study also gathered information on the duration of symptoms among individuals experiencing COVID-19 symptoms, specifically inquiring about the period during which they were unable to work or engage in daily household activities as a result of these symptoms. We requested patients whose symptom duration is less than or equal to 7 days to report the specific number of days, while those with symptoms lasting more than seven days were not required to answer the exact number of days. This is because the duration of symptoms question is a single-choice query. An exhaustive number of options might cause incomplete display on electronic devices, impacting questionnaire readability. Choosing among numerous options may lead to early exits or hasty selections, compromising data accuracy. Furthermore, after an Omicron infection, the average duration of symptoms is approximately 8 days [10]. We considered the duration of symptoms in people who did not have any symptoms to be zero days. Accordingly, this variable can be considered a right-censored continuous variable.

The explanatory variables representing the exposure status in this study were the number of COVID-19 vaccine doses and the timing of vaccination. Those who did not complete the primary immunization series and those who completed the primary immunization series but did not receive a booster shot were classified into the no booster shot group; those who completed the primary immunization series and received one

Table 2
The multiple logistic regression results of the impacts of COVID-19 vaccine doses and the timing of vaccination on COVID-19-related clinical outcomes.

Explanatory variables	OR (95 %CI)				Marginal effects (95 %CI)
	Fever	COVID-19-related symptoms (include fever)	Self-reported severe symptoms	Early vs. late occurrence of illness	Duration of symptoms
COVID-19 vaccine doses and the timing of vaccination					
No booster	–	–	–	–	–
One booster shot (>6 month)	1.30	1.23	1.48*	1.03	0.27
	(0.92,1.82)	(0.79,1.93)	(1.07,2.05)	(0.74,1.44)	(−0.08,0.62)
one booster shot (≤6 month)	2.17**	1.57	1.35	0.54*	0.25
	(1.34,3.52)	(0.84,2.90)	(0.89,2.05)	(0.34,0.86)	(−0.20,0.70)
Two booster shots	0.35**	0.74	0.47	0.48	−0.79
	(0.16,0.76)	(0.26,2.06)	(0.19,1.15)	(0.19,1.23)	(−1.65,0.07)
Age (years)					
18–34	–	–	–	–	–
35–49	0.70	0.75	0.60*	1.13	0.05
	(0.47,1.04)	(0.45,1.24)	(0.40,0.90)	(0.75,1.70)	(−0.79,0.45)
≥50	0.36***	0.74	0.54*	2.67***	−0.54*
	(0.22,0.59)	(0.39,1.42)	(0.33,0.89)	(1.66,4.30)	(−1.80 , -0.23)
Sex					
Male	–	–	–	–	–
Female	1.49*	2.10***	1.53**	0.72*	0.36*
	(1.09,2.02)	(1.39,3.14)	(1.14,2.06)	(0.53,0.98)	(0.15 , 1.09)
Underlying disease					
hypertension	2.14*	1.66	1.68*	0.62	0.50*
	(1.10,4.18)	(0.66,4.17)	(0.92,3.08)	(0.33,1.16)	(−0.11 , 1.84)
diabetes	1.11	3.32	2.35*	0.39*	0.71
	(0.42,2.95)	(0.41,27.11)	(0.97,5.69)	(0.14,1.10)	(−0.41 , 2.44)
lower respiratory tract diseases	1.71	1.50	1.25	1.31	0.15
	(0.75,3.93)	(0.43,5.27)	(0.64,2.45)	(0.65,2.65)	(−0.81 , 1.34)
upper respiratory tract diseases	1.59	3.88**	1.68*	0.72	0.35**
	(0.97,2.63)	(1.52 ~ 9.93)	(1.09,2.5)	(0.45,1.14)	(0.03 , 1.41)
cardiovascular and cerebrovascular diseases	1.10	1.17	0.84	0.95	0.47
	(0.42,2.89)	(0.25,5.56)	(0.36,1.97)	(0.38,2.37)	(−0.74 , 1.94)
malignant tumors	1.23	0.83	1.00	2.43	−0.27
	(0.22,6.92)	(0.09,7.86)	(0.21,4.72)	(0.49,12.05)	(−2.90 , 1.78)

*p < 0.05, **p < 0. 01, ***p < 0.001. Self-reported severe symptoms: 0 = Mild and symptom-free; 1 = Moderate and severe. Early vs. late occurrence of illness: 0 = Late onset and symptom-free, in which late onset was defined as first showing symptoms on or after December 23, 2022; 1 = Early onset.

booster shot were divided into two groups. Namely, they were the 'One Booster Shot Six Months Ago' group and the 'One Booster Shot Within Six Months' group, respectively, depending on whether the last shot was administered after July 1, 2022. Those who completed the primary immunization series and received two booster shots were defined as the two booster shots group.

Fig. 2 displays the types of vaccines included for four scenarios: didn't complete the primary immunization series, completed primary immunization, completed primary immunization and received one booster shot, and completed primary immunization and received two booster shots. We defined inactivated vaccines manufactured by different institutions (CoronaVac [Sinovac], COVILO [Sinopharm, Wuhan], BBIBP-CorV [Sinopharm, Beijing], KCONVAC [Kangtai], ICORNVAC [IMBCAMS]) as the same vaccine type.

The demographic information collected in the survey included age and sex. Age was defined as a categorical variable with three groups: 18–34 years old, 35–49 years old, and 50 years old and above. We also collected information on whether the respondents had the following underlying conditions: hypertension, diabetes, lower respiratory tract diseases, upper respiratory tract diseases, cardiovascular and cerebrovascular diseases, and malignant tumors.

3. Statistical analyses

In the descriptive analysis, we reported the category frequencies and percentages of all characteristics and outcome variables by vaccination exposure status. We used chi-square tests to analyze whether there were differences in the basic characteristics and outcomes across vaccination groups. In addition, we conducted multivariable regressions to estimate the impacts of booster shots on COVID-19-related clinical outcomes. In the multivariable regressions, the covariates were age, sex, and indicators of underlying conditions. In the analysis using the days of illness as the outcome variable, we used a Tobit model and reported the marginal effects. The Tobit model can take into account the censoring nature of the dependent variable[11]. The other outcomes were binary variables and were analyzed using logistic regressions, the effect estimates which were denoted using odds ratios (OR) and Vaccine Effectiveness (VE), VE=(1-OR) *100 %.

4. Results

By January 29, 2023, we had collected 878 valid questionnaires after excluding 489 questionnaires (Fig. 1). Table 1 presents the results of the descriptive analysis. The majority of the study participants aged between 18–34 years (68.1 %, 598/878), and were predominantly female (56.2 %, 493/878). Among the 878 respondents surveyed, 629 (71.6 %) experienced fever between December 18, 2022, and January 29, 2023, and 762 (86.8 %) experienced any form of COVID-19-related symptoms during this period. Of the symptomatic patients, 334 (41.7 %) respondents considered their symptoms to be moderate or severe. The first onset of symptoms for 272 (34.1 %) respondents was before December 23, 2022. The median number of days that the respondents were unable to work or perform daily household activities due to COVID-19-related symptoms was two days.

Table 2 shows the results of the multivariable logistic regressions using the pre-defined COVID-19-related clinical outcomes as response variables. Compared with no booster shot, one booster shot more than six months ago was not associated with a lower fever risk (OR = 1.30, 95 %CI = 0.92–1.82), whereas one booster shot within six months was significantly associated with a higher risk of fever (OR = 2.17, 95 %CI =

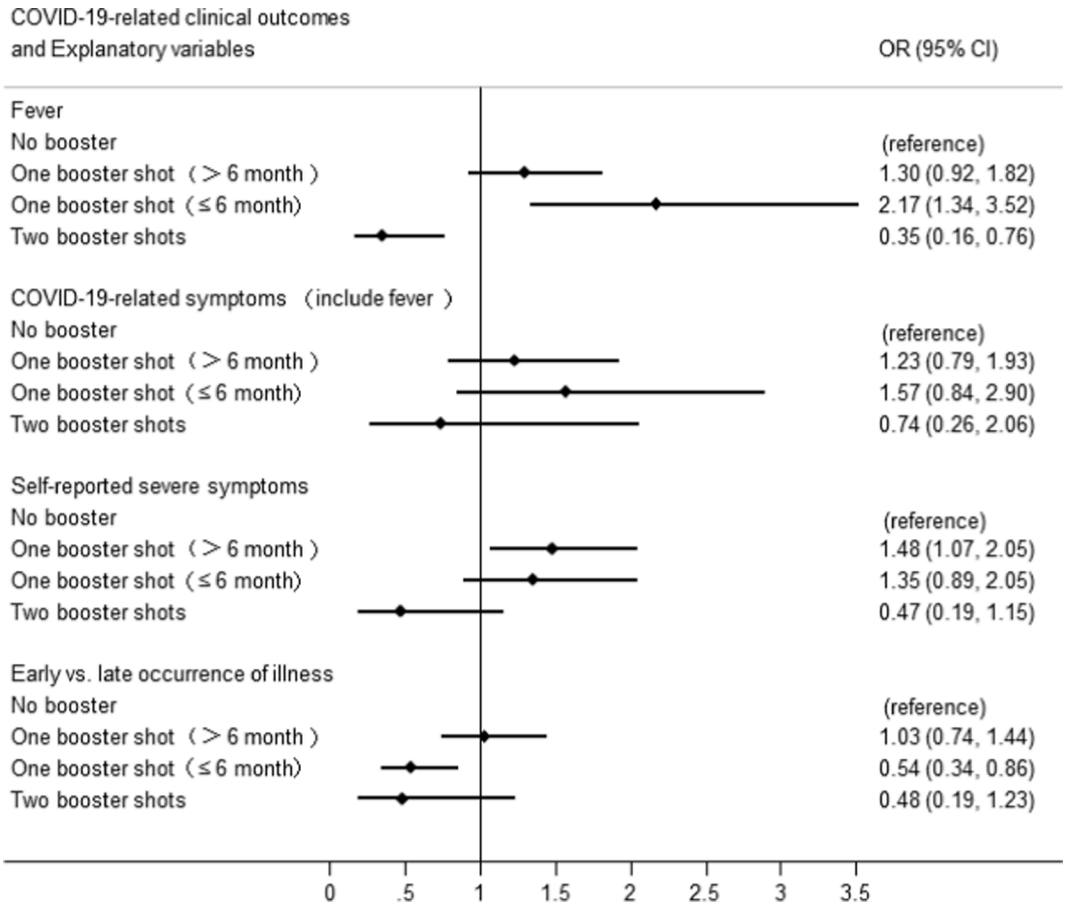

Fig. 3. The forest plot illustrating the impacts of COVID-19 vaccine doses and the timing of vaccination on clinical outcomes.

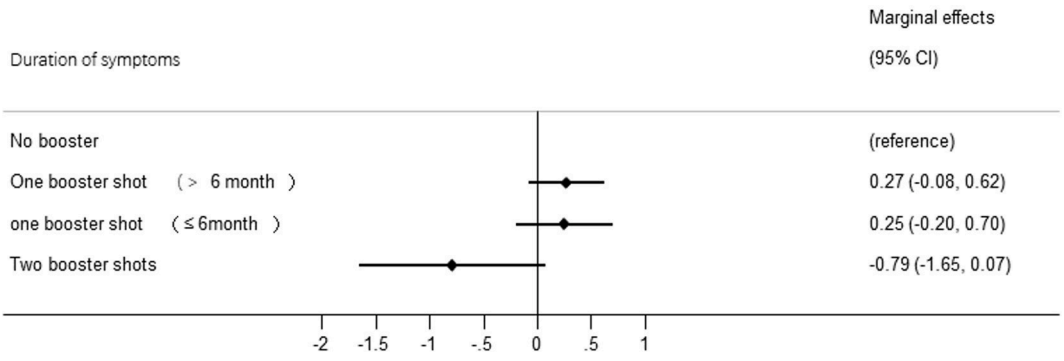

Fig. 4. The forest plot of the impacts of COVID-19 vaccine doses and the timing of vaccination on the duration of symptoms.

1.34–3.52). In contrast, the group receiving two booster shots had a significantly lower fever risk than those without any boosters. (OR = 0.35, 95 %CI = 0.16–0.76).

When using the occurrence of any COVID-19-related symptoms as the outcome, one booster shot more than six months ago (OR = 1.23, 95 %CI = 0.79–1.93), one booster shot within six months (OR = 1.57, 95 % CI = 0.84–2.90), and receiving two booster shots (OR = 0.74, 95 %CI = 0.26–2.06) were not associated with differential risks compared with no booster shot.

More, compared with no booster shot, one booster shot over six months ago was associated with a higher risk of self-reported severe diseases (OR = 1.48, 95 %CI = 1.07–2.05), whereas one booster shot within six months (OR = 1.35, 95 %CI = 0.89–2.05) and two booster shots (OR = 0.47, 95 %CI = 0.19–1.15) were not associated with self-reported severe symptoms.

Furthermore, one booster shot more than six months ago had no effects on delaying the onset of illness (OR = 1.03, 95 %CI = 0.74–1.44), while one booster shot within six months (OR = 0.54, 95 %CI = 0.34–0.86) had a statistically significant effect on delaying the onset of illness. The effect size of two booster shots on delaying the onset of illness was comparable to that of one booster shot within six months (OR = 0.48, 95 %CI = 0.19–1.23) but not statistically significant.

Finally, neither one booster shot more than six months ago (marginal effect = 0.25 days, 95 %CI = -0.20–0.70) nor within six months (marginal effect = 0.27 days, 95 %CI = -0.08–0.62) had effects on reducing the duration of sick days compared with no booster shot. Similarly, two booster shots insignificantly reduced the number of sick days (marginal effect = -0.79 days, 95 %CI = -1.65–0.07). The forest plots depicting the

Table 3
The vaccine effectiveness estimates of COVID-19 vaccine doses and the timing of vaccination on COVID-19-related clinical outcomes.

COVID-19 vaccine doses and the timing of vaccination	VE%(95CI%)			
	Fever	COVID-19-related symptoms (include fever)	Self-reported severe symptoms	Early vs. late occurrence of illness
No booster	–	–	–	–
One booster shot (> 6 month)	−30 (−82,8)	−23(−93,21)	−48(−105,-7)	−3(−44,26)
One booster shot (≤6 month)	−117 (−252,-34)	−57(−190,16)	−35(−105, 11)	46(14,66)
Two booster shots	65 (24,84)	26(−106,74)	53(−15, 81)	52(−23,81)

Self-reported severe symptoms: 0 = Mild and symptom-free; 1 = Moderate and severe. Early vs. late occurrence of illness: 0 = Late onset and symptom-free, in which late onset was defined as first showing symptoms on or after December 23, 2022; 1 = Early onset.

impacts of COVID-19 vaccine doses and the timing of vaccination on COVID-19-related clinical outcomes are depicted in Figs. 3 and 4.

Table 3 presents the VE estimates of different COVID-19 vaccine booster doses and the timing of vaccination on clinical symptoms, which were calculated from the OR estimates as stated in the methods section.

5. Discussion

Understanding the effectiveness of COVID-19 vaccines against the onsets of clinical symptoms and the exacerbation of illness during a pandemic is crucial for population health and society, especially when vaccination programs are deployed with massive resources. Aside from the prevention of infection, the effectiveness of COVID-19 vaccines can be reflected using several other indicators such as the prevention of disease onset, the severity of the disease, and the duration of the disease [12,13]. Previous studies documented that COVID-19 vaccines can reduce infection, hospitalization, and mortality associated with SARS-Cov-2[1,12]. In this study, we provided preliminary evidence that receiving two booster shots reduced the risk of fever during the omicron surge. Also, our results suggest that having a booster shot within six months may delay the time of infection when weathering an outbreak, which is important for both individuals receiving the vaccines and society in the early stages of the outbreak. For individuals, delayed illness means potentially avoiding the peak of healthcare system pressure, thereby having greater chances of accessing necessary resources. For the healthcare system, delaying the development of epidemics allows a relatively flat curve of healthcare needs at the population level.

A *meta*-analysis has also found that, during the Omicron surge, receiving two booster shots provided better protection compared to not receiving a booster shot[14]. Additionally, a study from Hungary[15] reported that receiving two booster shots had additional benefits in reducing Omicron infection and mortality compared to receiving a single booster shot. But what differs from our results is that, according to previous studies in China, receiving one booster shot should reduce the risks of infection and severe illness, even against the Omicron variant [16–19]. The findings on the absence of effects associated with one booster in the current analysis are likely attributable to confounding factors such as occupation and willingness to vaccinate. For example, healthcare workers are more likely to get vaccinated[20], but their risk of infection is also among the highest [21]. From another perspective, people with a low willingness to vaccinate are likely to receive the first booster relatively late (therefore being in the "one booster within six months" group), yet they are also likely to engage in other behaviors that engender them vulnerable to infection and severe diseases due to relatively low health literacy. These confounding factors would bias our estimates against the protective effects of more frequent and more recent vaccination. If that's the case, then the effect of the second booster shot should theoretically be stronger than what was observed in this study even under the assumption that one booster shot had null protective effects. Several caveats must be noted when interpreting the results. First, because this study was conducted online, the authenticity of the answers cannot be fully guaranteed due to recall bias. For example, verifying the participants' actual vaccination status or confirming whether respondents experienced COVID-19-related clinical symptoms proved unfeasible. But the inaccuracies in reporting on these two aspects were likely random; thus, systematic differences between various vaccination groups appeared to be unlikely and bias rising from this might be minimal. Second, respondents were not required to provide information on whether they were diagnosed with a COVID-19 infection. Therefore, symptomatic respondents might not have been infected with the COVID-19 virus or might have been infected with other viruses, while asymptomatic respondents could have been carriers of either the COVID-19 virus or alternative pathogens, potentially introducing a degree of bias into the findings, resulting in ascertainment bias in the results. However, according to official data[22], during the initial outbreak of Omicron from December 2022 to January 2023, COVID-19 infections predominantly accounted for cases of influenza-like illness. Thus, ascertainment bias is not expected to impact the study results substantially. Third, the second booster shot program only started to roll out in December 2022. Therefore, the sample size of those who got the second booster shot was extremely limited, which might have led to statistically insignificant protective effect estimates for some of the outcomes. However, this is also a potential signal that the timing of booster shots is important in shaping immunity. Future research should focus on ascertaining the occurrence of outcomes specific and non-specific to COVID-19 and verifying vaccination statuses.

6. Conclusion

Two booster shots of COVID-19 vaccines on top of the primary series vaccination in China may have reduced the onsets of fever during late 2022 and early 2023. To protect the most vulnerable population, booster shot programs should be planned based on the predicted timing of epidemics.

CRediT authorship contribution statement

Haisu Feng: Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Jiayue Chen:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Jiatong Sun:** Writing – review & editing, Formal analysis, Data curation, Conceptualization. **Yawen Jiang:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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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Ethical Approval.

This study was approved by the Human Studies Committee of Sun Yat-sen University School of Public Health (Shenzhen) [no. 2023(10)].

Data Availability.

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

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