

Preplanned Studies

Uptake of Heterologous or Homologous COVID-19 Booster Dose and Related Adverse Events Among Diabetic Patients: A Multicenter Cross-Sectional Study — China, 2022

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Summary

What is already known about this topic?

Although a third coronavirus disease 2019 (COVID-19) vaccination (booster) dose is highly recommended for diabetic patients, the vaccination behaviors and related adverse events are unclear among diabetic patients with a COVID-19 booster dose.

What is added by this report?

Diabetic patients with higher postprandial blood glucose, worrying about the safety of the booster dose were less likely to get the vaccine. While having positive attitudes towards COVID-19 booster vaccination, trusting the health professionals' advice on vaccination, diabetic patients were more likely to get the booster vaccine. Furthermore, the prevalence of adverse events was not significantly different between the homologous and heterologous boosting groups.

What are the implications for public health practice?

Effective measures should be taken to promote the COVID-19 booster dose uptake among diabetic patients. Health professionals should educate Chinese diabetic patients about the safety and efficacy of booster doses and continue to increase the COVID-19 booster dose vaccination coverage.

A third coronavirus disease 2019 (COVID-19) vaccination (booster) dose is highly recommended for both the healthy adult population and chronic patients, including diabetic patients. Previous studies have shown that diabetic patients are often hesitant to receive the vaccination due to the vaccination behaviors among diabetic patients to COVID-19 booster doses being unclear. This study aimed to explore the associated factors of COVID-19 booster dose and the prevalence of adverse events in homologous and heterologous boosting groups. A cross-sectional questionnaire survey was conducted

among 457 diabetic inpatients in Shenzhen and Changzhi Cities from April to June 2022, of which 69.6% (318/457) respondents had received a COVID-19 booster dose. About 89.3% (284/318) and 10.7% (34/318) of the participants received homologous boosting and heterologous boosting, respectively. Diabetic patients with higher postprandial blood glucose [adjusted odds ratio (AOR): 0.54; 95% confidence interval (CI): 0.35–0.85], and those worried about the safety of the booster dose (AOR: 0.56; 95% CI: 0.34–0.92) were less likely to get the vaccine. Some factors were significantly and positively associated with COVID-19 booster dose vaccination, including positive attitudes towards COVID-19 booster dose vaccination (AOR: 2.46; 95% CI: 1.06–5.70), agreeing that diabetic patients can get COVID-19 booster dose (AOR: 2.19; 95% CI: 1.29–3.72), and agreeing that COVID-19 booster dose vaccination can effectively reduce the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission risk (AOR: 1.97; 95% CI: 1.13–3.44). Moreover, diabetic patients who were influenced by clinical doctors (AOR: 1.77; 95% CI: 1.07–3.12) and family members (AOR: 1.61; 95% CI: 1.02–2.55) were more likely to get the booster vaccine. Furthermore, the prevalence of adverse events was not significantly different between people vaccinated with COVID-19 booster dose and those not vaccinated with booster [5.3% (17/318) vs. 9.4% (13/139), $\chi^2=2.53$, $P=0.11$], and the prevalence of adverse events was not significantly different between the homologous and heterologous boosting groups [5.6% (16/284) vs. 2.9% (1/34), $\chi^2=0.44$, $P=0.51$]. Health sectors should continue to encourage diabetic patients to receive the booster vaccination based on the study results and relevant guidelines to prevent their acquisition of SARS-CoV-2.

Diabetic patients are more vulnerable to serious illnesses, such as SARS-CoV-2 than people without

diabetes (1), possibly due to systemic inflammatory responses and impaired immune system function. Vaccination can reduce morbidity and mortality caused by SARS-CoV-2. In addition, a third dose (booster) is highly recommended for patients with underlying medical conditions (1–2). Furthermore, China has promoted heterologous vaccines since February 2022 as a prime-boost immunization strategy. Interventions aimed at enhancing COVID-19 booster dose vaccination may reduce SARS-CoV-2 spread among diabetic patients since they are at high risk of severe disease course and mortality. However, previous studies showed that many diabetic patients in Italy (18.3%) and China (56.4%) are hesitant to receive COVID-19 primary vaccination (3–4). It has been noted that vaccination behaviors among diabetic patients to COVID-19 booster doses are unknown. This research aimed to explore COVID-19 booster dose vaccination behavior and its associated factors among diabetic patients, and the prevalence of adverse events between homologous and heterologous boosting groups. This study may facilitate the development of intervention measures for targeted booster vaccination among diabetic patients.

In this study, a cross-sectional survey was conducted among 502 diabetic inpatients from two hospitals in Shenzhen City, Guangdong Province (Shenzhen Hospital, Peking University, Shenzhen) and Changzhi City, Shanxi Province (Changzhi Heping Hospital). All hospitalized diabetes patients during the study period were continuously invited to attend this study. The participants anonymously filled out an online questionnaire survey between April and June 2022 after informed consent of the study objectives was collected. The questionnaire consisted of three components: 1) demographic and health-related information; 2) perception of booster dose vaccine; and 3) COVID-19 booster dose vaccination history (yes or no), which was a dependent variable. Heterologous boosting was defined as the injection of two doses of inactivated vaccine combined with one dose of adenovirus vaccine or one dose of recombinant protein vaccine. Homologous boosting was defined as the injection of three consecutive doses of inactivated vaccines. An adverse event was defined as an event occurred within 30 days after the last dose of COVID-19 vaccination.

The univariate and multivariable logistic regression model was used to evaluate the association between related variables and COVID-19 booster dose

vaccination behaviors. All variables significant at the $P < 0.05$ level in the univariate model were included in the multivariable logistic regression analysis. The entering procedure was used in the multivariable logistic regression model. The differences in the prevalence of adverse events between the two groups were assessed using Pearson's chi-squared test. $P < 0.05$ was considered statistically significant. SPSS (version 25.0 software for Windows, SPSS, Inc., Chicago, IL, USA) was used for statistical analysis.

A total of 457 of 505 diabetes inpatients completed the survey (response rate; 90.5%), of which 267 were males (58.4%). About 30.2% of the participants had over 10 years of diabetes history, and 318 (69.6%) respondents had received the COVID-19 booster dose, of which 89.3% (284/318) and 10.7% (34/318) had received homologous boosting and heterologous boosting, respectively. Furthermore, two respondents received an adenovirus vaccine, and 32 received a recombinant protein vaccine. Only one health-related factor (baseline postprandial blood glucose) was significantly associated with COVID-19 booster dose vaccination uptake. The associations of demographic and health-related factors with COVID-19 booster dose vaccination behavior are shown in Supplementary Table S1, available in <http://weekly.chinacdc.cn/>.

About 92.8% of the respondents had a positive attitude toward the COVID-19 booster dose. However, only 63.2% of the respondents thought diabetic patients could get the booster dose. 57.3% of the respondents were worried about the side effects of a booster dose. About 80.1% of the participants agreed with the guidance and advice on the COVID-19 booster dose from the clinical doctors. The details of COVID-19 booster dose vaccine perception are shown in Table 1.

The results of the multivariable logistic regression analysis of factors associated with COVID-19 booster dose vaccination behaviors are shown in Table 2. Diabetic patients with higher baseline postprandial blood glucose (AOR: 0.54; 95% CI: 0.35–0.85) and those worried about the safety of booster dose vaccine (AOR: 0.56; 95% CI: 0.34–0.92) were less likely (negatively associated with booster vaccination) to get the booster vaccine. However, five factors were significantly and positively associated with COVID-19 booster vaccination: positive attitudes towards COVID-19 booster dose vaccination (AOR: 2.46; 95% CI: 1.06–5.70), agreeing that diabetic patients can get COVID-19 booster dose vaccine (AOR: 2.19;

TABLE 1. Univariate logistic regression analysis of COVID-19 booster dose vaccine perception with vaccination behavior among Chinese diabetic patients (n=457).

Factor	Total, n (%)	COVID-19 booster dose vaccination, n (%)		COR (95% CI)
		Yes (n=318)	No (n=139)	
Attitudes				
Q1. I support the vaccination of the COVID-19 booster dose.				
No (Strongly disagree or disagree or neutral)	33 (7.2)	13 (4.1)	20 (14.4)	1
Yes (Agree or very agree)	424 (92.8)	305 (95.9)	119 (85.6)	3.94 (1.90–8.18)*
Q2. Diabetic patients can get a COVID-19 booster dose vaccine.				
No (Strongly disagree or disagree or neutral)	168 (36.8)	93 (29.2)	75 (54.0)	1
Yes (Agree or strongly agree)	289 (63.2)	225 (70.8)	64 (46.0)	2.84 (1.88–4.28)*
Perceived efficacy				
Q3. COVID-19 booster dose vaccine can effectively prevent COVID-19.				
No (Strongly disagree or disagree or neutral)	193 (42.2)	119 (37.4)	74 (53.2)	1
Yes (Agree or strongly agree)	264 (57.8)	199 (62.6)	65 (46.8)	1.90 (1.27–2.85)*
Q4. COVID-19 booster dose vaccination can reduce the risk of COVID-19 transmission to other people.				
No (Strongly disagree or disagree or neutral)	92 (20.1)	43 (13.5)	49 (35.3)	1
Yes (Agree or very agree)	365 (79.9)	275 (86.5)	90 (64.7)	3.48 (2.17–5.59)*
Perceived safety				
Q5. COVID-19 booster dose vaccination has side effects.				
Yes (Neutral or agree or strongly agree)	262 (57.3)	166 (52.2)	96 (69.1)	1
No (Strongly disagree or disagree)	195 (42.7)	152 (47.8)	43 (30.9)	2.04 (1.34–3.12)*
Q6. I worry about the safety of the COVID-19 booster dose vaccine				
No (Strongly disagree or disagree or neutral)	334 (73.1)	250 (78.6)	84 (60.4)	1
Yes (Agree or strongly agree)	123 (26.9)	68 (21.4)	55 (39.6)	0.42 (0.27–0.64)*
Social impact				
Q7. I believe in the advice on COVID-19 booster dose vaccination from the doctors.				
No (Strongly disagree or disagree or neutral)	91 (19.9)	43 (13.5)	48 (34.5)	1
Yes (Agree or strongly agree)	366 (80.1)	275 (86.5)	91 (65.5)	3.37 (2.10–5.42)*
Q8. I believe in the advice on COVID-19 booster dose vaccination from the media.				
No (Strongly disagree or disagree or neutral)	179 (39.2)	118 (37.1)	61 (43.9)	1
Yes (Agree or strongly agree)	278 (60.8)	200 (62.9)	78 (56.1)	1.33 (0.88–1.99)
Q9. Family members' COVID-19 booster dose vaccination behavior will affect mine.				
No (Strongly disagree or disagree or neutral)	190 (41.6)	119 (37.4)	71 (51.1)	1
Yes (Agree or strongly agree)	267 (58.4)	199 (62.6)	68 (48.9)	1.75 (1.17–2.61)*

Abbreviation: COVID-19=coronavirus disease 2019; COR=crude odds ratio; CI=confidence interval.

* $P < 0.01$.

95% CI: 1.29–3.72), and agreeing that COVID-19 booster dose vaccination can reduce SARS-CoV-2 transmission risk (AOR: 1.97; 95% CI: 1.13–3.44). Moreover, diabetic patients who could be influenced by doctors (AOR: 1.77; 95% CI: 1.07–3.12) and family members (AOR: 1.61; 95% CI: 1.02–2.55) were more likely to get the booster vaccine.

Adverse events, such as headache, fatigue, fever, and chills occurred in 17 (5.3%) of 318 respondents received booster dose. Furthermore, the prevalence of adverse events was not significantly different between people vaccinated with COVID-19 booster dose and those not vaccinated with booster 9.4% (13/139) ($\chi^2=2.53$, $P=0.11$), and the prevalence of adverse

TABLE 2. Multivariable logistic regression analysis of factors associated with COVID-19 booster dose vaccination behavior among Chinese diabetic patients (*n*=457).

Factors	AOR (95% CI)
Attitudes	
Q1. I support the vaccination of the COVID-19 booster dose.	
No (Strongly disagree or disagree or neutral)	1
Yes (Agree or very agree)	2.46 (1.06–5.70)*
Q2. Diabetic patients can get a COVID-19 booster dose vaccine.	
No (Strongly disagree or disagree or neutral)	1
Yes (Agree or strongly agree)	2.19 (1.29–3.72)†
Perceived efficacy	
Q3. COVID-19 booster dose vaccine can effectively prevent COVID-19.	
No (Strongly disagree or disagree or neutral)	1
Yes (Agree or strongly agree)	0.87 (0.52–1.45)
Q4. COVID-19 booster dose vaccination can reduce the risk of COVID-19 transmission to other people effectively.	
No (Strongly disagree or disagree or neutral)	1
Yes (Agree or very agree)	1.97 (1.13–3.44)*
Perceived safety	
Q5. COVID-19 booster dose vaccination has side effects.	
Yes (Neutral or agree or strongly agree)	1
No (Strongly disagree or disagree)	1.42 (0.88–2.30)
Q6. I worry about the safety of the COVID-19 booster dose vaccine	
No (Strongly disagree or disagree or neutral)	1
Yes (Agree or strongly agree)	0.56 (0.34–0.92)*
Social impact	
Q7. I believe in the advice on COVID-19 booster dose vaccination from the doctors.	
No (Strongly disagree or disagree or neutral)	1
Yes (Agree or strongly agree)	1.77 (1.07–3.12)*
Q9. Family members' COVID-19 booster dose vaccination behavior will affect mine.	
No (Strongly disagree or disagree or neutral)	1
Yes (Agree or strongly agree)	1.61 (1.02–2.55)*
Health information	
Postprandial blood glucose	
<10.0 mmol/L	1
≥10.0 mmol/L	0.54 (0.35–0.85)†

Abbreviation: COVID-19=coronavirus disease 2019; AOR=adjusted odds ratio; CI=confidence interval.

* *P*<0.05.

† *P*<0.01.

events was not significantly different between the homologous and heterologous boosting groups [5.6% (16/284) vs. 2.9% (1/34), $\chi^2=0.44$, *P*=0.51].

DISCUSSION

In this study, nearly a third of diabetic patients did not receive the booster dose vaccine. Although a

booster dose is highly recommended for diabetic patients, many diabetic patients are still hesitant to receive a booster dose (3–4). The COVID-19 fatality risk is higher in diabetic patients than in healthy people by about 50% (5). Therefore, evidence-based vaccination strategies should be developed to enhance voluntary booster dose uptake among diabetic patients. Herein, results showed that the perceived safety of

booster dose significantly influences vaccination behaviors. Previous studies conducted in the general adult population also showed that the awareness of vaccine safety is positively related to vaccination willingness (6–7). In addition, Kreps et al. found that a decrease in the incidence of major adverse effects is associated with a higher probability of choosing a vaccine (8). A study also showed that vaccine safety is the top concern for COVID-19 vaccination intentions among children with diabetes (9).

In this study, the perceived efficacy of the booster dose vaccine was positively related to vaccination behavior. Kreps et al. found that the more significant the efficacy of the vaccine, the longer the protection time and the greater the vaccination probability (8). Diabetic patients are susceptible to SARS-CoV-2, which may be more inclined to consider the effectiveness of the COVID-19 vaccine before vaccination. Therefore, the relevant departments should publicize the safety and effectiveness of the COVID-19 booster dose through data and authoritative statements to improve people's perceptions of the booster dose.

Furthermore, results also found that some social factors, such as vaccination suggestions by doctors and family members, were correlated with COVID-19 vaccination uptake, consistent with Duan L's research (3). Social factors have been highlighted in many health behavior theories, such as the Theory of Planned Behavior (TPB) since they change people's health behaviors. Nevertheless, Ai et al. showed that the heterologous booster dose produces higher SARS-CoV-2 neutralizing antibodies and similar adverse events than the homologous booster dose vaccination in healthy adults (10). In this study, heterologous booster dose and homologous booster dose produced similar adverse events in diabetic patients. Considering the safety and immunogenicity of inactivated COVID-19 vaccines (11), and their high effectiveness, especially when boosted (12). Moreover, there are some diabetes patients still cautious about receiving or not the heterologous booster doses, this firsthand real-world evidence may help provide more information to promote heterologous and homologous COVID-19 booster vaccination in China to prevent SARS-CoV-2 in diabetes patients.

These findings suggest that the perceived safety and efficacy of the COVID-19 booster dose vaccine can increase the vaccination rate among diabetic patients. Suggestions by health professionals and behaviors of

family relatives can also promote booster dose uptake. Therefore, relevant institutions should promote immunization publicity by disseminating information about the safety and efficacy of booster vaccines through health science education by health professionals. Vaccinated diabetic patients can also be invited to conduct peer publicity, eliminating concerns among other patients, and improving their awareness to enhance their willingness to immunize. Furthermore, the results could be generalized to guide booster vaccination promotion in other major chronic comorbidities with COVID-19-like hypertension.

However, this study has some limitations. The enrolled participants were from two cities in China, and thus may limit the generalizability of the findings. In addition, this is a cross-sectional study and prevents the establishment of a causal relationship between vaccination behavior and the associated factors examined. Third, blood specimens were not collected to test COVID-19 immunological reaction items. Lastly, there is a recommendation guideline or consensus for the diabetic patients to get COVID-19 vaccinated, we should follow the instructions when making a recommendation to the patients with diabetes, not just from the result of this study.

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SUPPLEMENTARY TABLE S1. Univariate logistic regression analysis of demographic and health-related factors associated with COVID-19 booster dose vaccination behaviors among Chinese diabetic patients ($n=457$).

Factor	Total, n (%)	COVID-19 booster dose vaccination, n (%)		COR (95% CI)
		Yes ($n=318$)	No ($n=139$)	
Demographics				
Age (years)				
18–39	67 (14.7)	40 (12.6)	27 (19.4)	1
40–49	75 (16.4)	53 (16.7)	22 (15.9)	1.63 (0.81–3.26)
50–59	140 (30.6)	102 (32.0)	38 (27.5)	1.81 (0.98–3.35)
≥60	175 (38.3)	123 (38.7)	52 (37.4)	1.60 (0.89–2.87)
Gender				
Male	267 (58.4)	192 (60.4)	75 (54.0)	1
Female	190 (41.6)	126 (39.6)	64 (46.0)	0.77 (0.51–1.15)
Education level				
Below high school	217 (47.5)	143 (45.0)	74 (53.2)	1
High school	84 (18.4)	60 (18.9)	24 (17.3)	1.29 (0.75–2.24)
College	37 (8.1)	26 (8.2)	11 (7.9)	1.22 (0.57–2.61)
College above	119 (26.0)	89 (28.0)	30 (21.6)	1.54 (0.93–2.53)
Marital status				
Unmarried, divorced, or widowed	60(13.1)	40 (12.6)	20 (14.4)	1
Married	397(86.9)	278 (87.4)	119 (85.6)	1.17 (0.66–2.08)
Residence				
Urban	323(70.7)	224 (70.4)	99 (71.2)	1
Rural	134(29.3)	94 (29.6)	40 (28.8)	1.04 (0.67–1.61)
Monthly income (CNY)				
<2,000	144(31.5)	94 (29.6)	50 (36.0)	1
2,000–4,999	170(37.2)	120 (37.7)	50 (35.9)	1.28 (0.79–2.06)
≥5,000	143(31.3)	104 (32.7)	39 (28.1)	1.42 (0.86–2.35)
Health information				
BMI (kg/m^2)				
<18.5	11 (2.4)	6 (1.9)	5 (3.6)	1
18.5–23.9	209 (45.7)	154 (48.4)	55 (39.6)	2.33 (0.69–7.95)
24.0–27.9	164 (35.9)	112 (35.2)	52 (37.4)	1.80 (0.52–6.15)
≥28	73 (16.0)	46 (14.5)	27 (19.4)	1.42 (0.40–5.10)
Years of diabetes history				
≤10	319 (69.8)	224 (70.4)	95 (68.3)	1
>10	138 (30.2)	94 (29.6)	44 (31.7)	0.91 (0.59–1.39)
Fasting blood glucose (mmol/L)				
<7.0	234 (51.2)	172 (54.1)	62 (44.6)	1
7.0–13.9	203 (44.4)	134 (42.1)	69 (49.6)	0.70 (0.46–1.06)
≥13.9	20 (4.4)	12 (3.8)	8 (5.8)	0.54 (0.21–1.39)
Postprandial blood glucose (mmol/L)				
<10.0	223 (48.8)	165 (51.9)	58 (41.7)	1
≥10.0	234 (51.2)	153 (48.1)	81 (58.3)	0.66 (0.44–0.99)*

Abbreviation: BMI=body mass index, COR=crude odds ratio, CNY=China Yuan.

* $P<0.05$.