Human Vaccines & Immunotherapeutics

ISSN: 2164-5515 (Print) 2164-554X (Online) Journal homepage: www.tandfonline.com/journals/khvi20

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To cite this article: Limin Zhang , Dong Liu , Xiaoyu Cao , Hui Zhang , Shasha Li , Ruirui Wang , Yuxian Mu , Mingfeng Han , Yeming Wang & Bin Cao (2025) Long-term effectiveness of COVID-19 vaccination in preventing hospitalization among household contacts: A case–control study from December 2021 to April 2023, Human Vaccines & Immunotherapeutics, 21:1, 2563760, DOI: 10.1080/21645515.2025.2563760

To link to this article: https://doi.org/10.1080/21645515.2025.2563760

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2025, VOL. 21, NO. 1, 2563760
https://doi.org/10.1080/21645515.2025.2563760

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RESEARCH ARTICLE

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Long-term effectiveness of COVID-19 vaccination in preventing hospitalization among household contacts: A case–control study from December 2021 to April 2023

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ABSTRACT

We aimed to assess the long-term effect of Coronavirus disease 2019 (COVID-19) vaccination in improving infection, symptoms and disease severity more than 1 year. Consecutive adult inpatients diagnosed with COVID-19 through clinical criteria from two hospitals with household contacts were included. The exposure was COVID-19 vaccination. The primary outcome was hospitalization, while infection, symptoms, and pneumonia were assessed as exploratory outcomes. Multivariable logistic regression, subgroup and sensitivity analysis were conducted. From December 18, 2022, to April 7, 2023, 1,410 individuals were prospectively screened, and 1,047 individuals were included. The male proportion was 49.24% with the mean age of 66.10 years. A total of 883 (84.34%) participants were vaccinated with a median time of 297.5 (157.0, 389.0) days between the last vaccine and enrollment, and a median time of 446.5 (162.8, 504.8) days was found in fully vaccinated patients. The infection rate among unvaccinated patients was significantly higher (96.72% vs. 88.69%, $p < .001$). Unvaccinated patients reported less symptoms, including sore throat, myalgia and taste disorder. They had a higher hospitalization rate (80.49% vs. 45.07%). In multivariable logistic regression, vaccination was associated with reduced pneumonia risk (aOR: 0.49, 95% CI: 0.32–0.76, $p = .002$). In addition, significant negative association between vaccination and hospitalization risk (aOR: 0.37, 95% CI: 0.26–0.61, $p < .001$) was observed. For vaccination status, the booster vaccination group revealed the aOR of 0.40 (95% CI: 0.24–0.65, $p < .001$), while the fully vaccination group only presented with the aOR of 0.50 (95% CI: 0.28–0.87, $p = .013$). While COVID-19 vaccination may not provide protection against symptoms beyond 1 year, it maintains durable effectiveness in reducing the risk of hospitalization.

ARTICLE HISTORY
Received 22 May 2025
Revised 29 August 2025
Accepted 16 September 2025

KEYWORDS
COVID-19; hospitalization; vaccine effectiveness; long-term protection

Introduction

The coronavirus disease 2019 (COVID-19) continues to exert a profound global impact, presenting significant challenges to healthcare systems worldwide.[1] Vaccination has proven to be a critical intervention in preventing severe outcomes and reducing the burden on healthcare systems.[2] Randomized controlled

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/21645515.2025.2563760.

trials have demonstrated vaccine efficacy against infection and disease severity within 6 months of vaccination.[3–5] Furthermore, real-world test-negative studies have corroborated vaccine effectiveness in population-level datasets, with outcomes including infection, hospitalization, and death, extending protection up to 9 months post-vaccination.[6–13]

Similar to influenza and other respiratory infection vaccines, COVID-19 vaccines may not provide long-lasting protection, necessitating annual vaccination.[14] However, vaccine hesitancy, insufficient supply and vaccination delays have led to missed opportunities for subsequent vaccinations.[15,16] Consequently, it remains unclear whether these individuals retain protective immunity over extended periods following their last dose. Additionally, in certain regions, particularly low- and middle-income countries and areas, access to the latest COVID-19 vaccines is limited.[17] This raises further questions about whether vaccines designed for earlier variants provide adequate protection against currently circulating strains.

Chinese early widespread vaccination was completed prior to Omicron's emergence in 2021,[18] and China followed a "zero-COVID" policy until December 7, 2022,[19] after which non-pharmaceutical interventions were no longer implemented, providing a unique opportunity to assess long-term effectiveness from original strain vaccination without confounding by prior infection. In contrast, studies in other regions were complicated by high rates of prior infection during Omicron waves, obscuring the independent protective effects of vaccination. Household contacts, who share similar behavioral factors and living environments, offer an ideal control group for isolating virus exposure.

This study aimed to conduct a case–control study to clarify whether COVID-19 vaccination provides durable protection against Omicron variant in infection, symptoms, pneumonia and hospitalization. The findings were expected to provide valuable evidence on the continued protection of COVID-19 vaccination after Omicron variant infection and insights into vaccination strategies over time.

Methods

Design

From December 18, 2022, to April 7, 2023, we prospectively included consecutive adult inpatients from the Department of Pulmonary and Critical Care Medicine at China–Japan Friendship Hospital and Fuyang Second Hospital, and their family members living together for more than 2 days were also included. The diagnosis of COVID-19 was defined as a patient with infection symptoms and contact with someone who had a positive nucleic acid or antigen test. All participants provided informed consent. Exclusion criteria included patients under 18 years of age, patients without household members, refusal to participate, missing key variables, and household contacts without COVID-19 diagnosis.

COVID-19 vaccination status, as the exposure, was objectively obtained from verified electronic vaccination information system We also assessed the interval from the last vaccination to infection, with the "long-term" period defined as more than 12 months. Patients were categorized into unvaccinated group and vaccinated group, and vaccinated group included partial vaccination, fully vaccination and booster vaccination subgroups based on vaccination status. Different vaccination statuses were defined as follows: unvaccinated referred to individuals who have received no COVID-19 vaccine doses; fully vaccinated referred to individuals who have completed the recommended primary vaccination course, including two doses of inactivated vaccines, one dose of adenovirus vector vaccines, three doses of recombinant protein vaccines, or two doses of mRNA vaccines. Vaccination status that did not meet the criteria for full vaccination was classified as partial vaccination. Additionally, any dose administered beyond the number required for full vaccination was considered a booster shot. Vaccination status was determined by doses time received, while vaccine type refers to the underlying principles of the vaccine products. Several vaccines were mainly recommended in China, including inactivated vaccines (Sinopharm, Sinovac), adenovirus vector vaccines (CanSinoBIO), and recombinant protein vaccines (Anhui Zhifei Longcom).[20] Based on the vaccine type, the vaccinated group was categorized into three groups: the inactivated vaccine group, the recombinant protein vaccine group, and other type vaccine group.

The outcomes included COVID-19 infection, symptoms, pneumonia (confirmed via self-report among household contacts and CT findings in hospitalized individuals), and COVID-19-related hospitalization.

Our primary aim was to assess vaccine protection against hospitalization, while the analyses of infection, symptom, and pneumonia were conducted as exploratory outcomes. Age, sex, body mass index (BMI), smoking status and comorbidity were considered as potential confounding factors. The Charlson Comorbidity Index (CCI) was calculated based on 19 predefined comorbidities assigned a weighted score. A score of 1 was given for myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, mild liver disease, and diabetes. A score of 2 was assigned for hemiplegia, moderate or severe renal disease, solid tumor (without metastasis), leukemia, and lymphoma. A score of 3 was given for moderate or severe liver disease. A score of 6 was assigned for metastatic solid tumors and acquired immunodeficiency syndrome.

Procedures

Prior to the study commencement, standardized training was conducted for all researchers. Data were collected using standardized questionnaires (Supplementary Material 1) and electronic medical records. The questionnaire employed standardized questions to gather information. When inpatients were admitted to the hospital, household contacts present were guided to fill in the questionnaire on-site, while co-living members unable to be present were provided with an electronic questionnaire. Both questionnaire data and medical record information were entered into an electronic data collection system (REDCap version: 10.x), and data entry was double-checked by two researchers.

Data collection

Data were collected across four domains: (1) Demographic variables included age, sex, height, weight, smoking history, and comorbidities. (2) COVID-19 vaccination data included vaccine status, vaccine time, and vaccine type, including inactivated vaccine, recombinant protein vaccine, adenovirus vector vaccine and inhaled recombinant vaccine. (3) Clinical data included current infection status, the number and timing of previous infections, symptom variations between episodes, and the symptom onset time. Whether participants developed respiratory infection symptoms within 1 week of contact with the infected patients was collected. Symptoms included cough, nasal congestion or rhinorrhea, sore throat, fever, chills, fatigue, myalgia, dyspnea, headache, nausea, vomiting, diarrhea, and smell or taste abnormalities. The most severe symptoms were identified. (4) Treatment information included treatment location, time to symptom resolution.

Statistical analysis

Considering the inactivated vaccine with 88.6% effectiveness in preventing severe cases during the Omicron wave,[13] the sample size was estimated using a two-sided test with α of 0.05 and β of 90%. Given hospitalization cases were enrolled first followed by household contacts, we estimated a baseline hospitalization rate of 30%, and 80% participants were estimated to be vaccinated.[19] Using logistic regression analysis, the required sample size was determined to be 135. Accounting for a 20% refusal rate, 170 participants were calculated using PASS (version 15.0).

All statistical analyses will be conducted using R (version 4.3.3). Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range, IQR). Categorical variables were reported as frequencies and percentages. Differences between groups were assessed using the t-test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables.

Multivariable logistic regression was conducted to evaluate whether vaccination was independently associated with hospitalization and pneumonia after adjusting for potential confounding factors. The CCI was included as an adjustment variable in the regression models to account for underlying comorbidity burden. Analyses by different vaccine type were performed only as exploratory analyses to provide preliminary insights. The results were expressed as adjusted odds ratios (aORs) with corresponding 95% CIs. The vaccine effectiveness was estimated as (1-aOR) × 100%. Subgroup analysis was conducted to explore the effectiveness of subpopulations using univariable logistic regression. Sensitivity analyses were conducted, including multivariable logistic regression after propensity score matching (PSM) regression

excluding booster recipients and regression in all couples. To account for participants from the same household, we applied mixed-effects logistic regression with a household-level random intercept to account for within-household correlation. The intraclass correlation coefficient was calculated from the random intercept variance.

All statistical tests were two-sided, and a p-value of <0.05 was considered statistically significant.

Results

Baseline demographic and baseline characteristics

From December 18, 2022, to April 7, 2023, 1,410 individuals were screened, and 1,047 individuals were included (Figure 1), with the male proportion of 49.24% and a mean age of 66.10 years (SD: 15.38). Two hundred and fourteen patients were excluded due to lack of housemates, and they had higher proportion of females and lower vaccination coverage (Table S1). Two vaccinated participants had a previous history of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection.

The baseline characteristics between vaccinated and unvaccinated patients were shown in Table 1. The mean age in the non-vaccinated group was older (72.15 vs. 62.61, $p < .001$), and the proportion of females in the vaccinated group was significantly higher than males (52.21% vs. 43.29%, $p = .042$). BMI distribution differed significantly, with a higher proportion of underweight individuals (BMI ≤ 18.5) in the non-vaccinated group (8.92% vs. 1.85%, $p < .001$). Non-vaccinated participants were more likely to be current

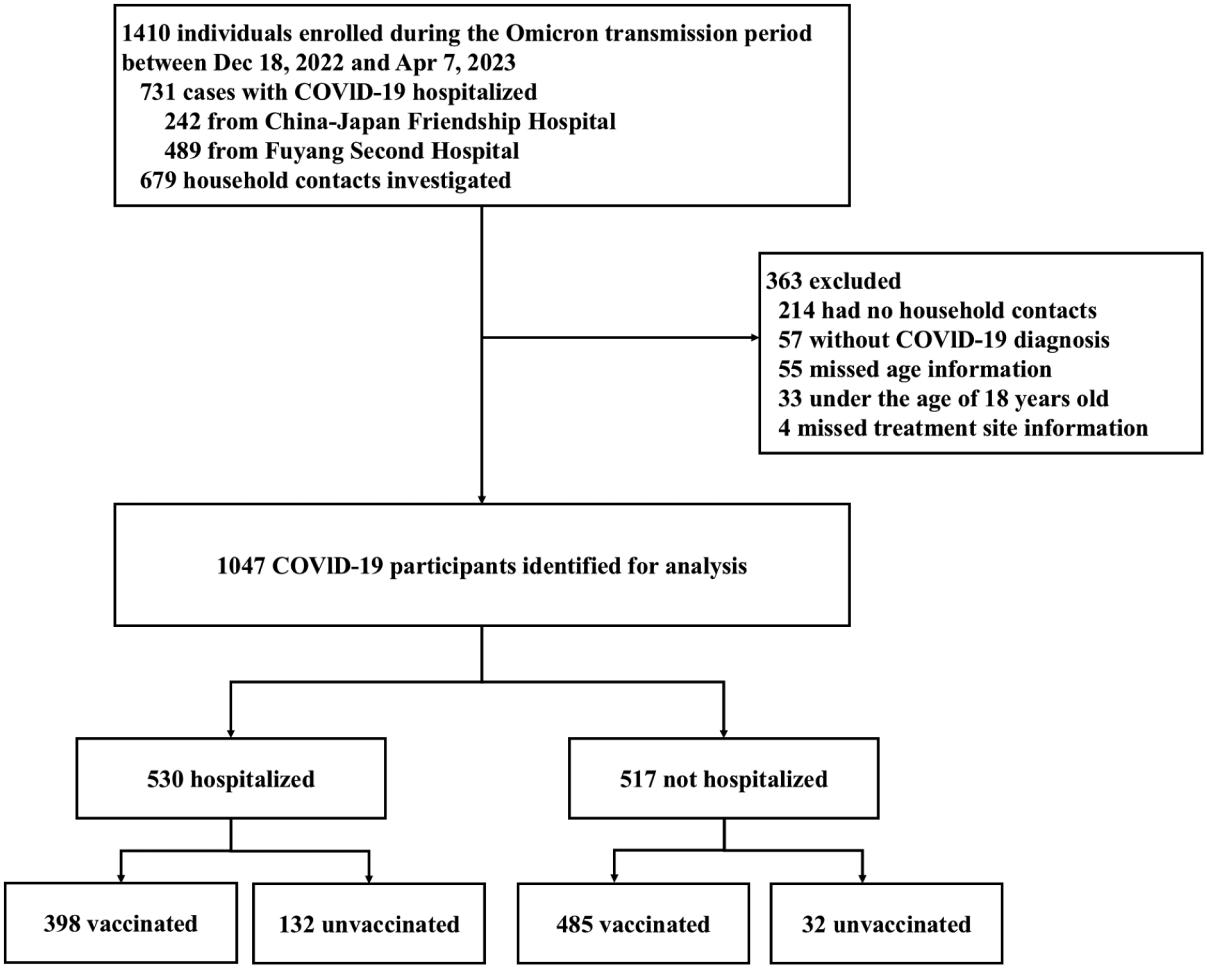

Figure 1. Flow chart of participants included. Note. From December 18, 2022, to April 7, 2023, 1,410 individuals were screened, and 1,047 individuals were included for analysis. A total of 883 participants were vaccinated, and 164 participants were not vaccinated.

Table 1. Comparison of baseline characteristics between vaccinated and unvaccinated patients.

	Total (n = 1047)	Non-vaccination (n = 164)	Vaccination (n = 883)	*P*
Age, Mean ± SD	64.10 ± 15.38	72.15 ± 13.54	62.61 ± 15.24	**<.001**
Age group, n (%)				**<.001**
18–59 years old	386 (36.87)	25 (15.24)	355 (40.88)	
60–69 years old	272 (25.98)	44 (26.83)	228 (25.82)	
70–79 years old	222 (21.20)	43 (26.22)	179 (20.27)	
≥80 years old	167 (15.95)	52 (31.71)	115 (13.02)	
Sex, n (%)				**.042**
Female	532 (50.81)	71 (43.29)	461 (52.21)	
Male	515 (49.19)	93 (56.71)	422 (47.79)	
BMI group, n (%)				**<.001**
≤18.5	30 (2.93)	14 (8.92)	16 (1.85)	
18.5–24.0	549 (53.67)	88 (56.05)	461 (53.23)	
24.0–28.0	340 (33.24)	41 (26.11)	299 (34.53)	
≥28	104 (10.17)	14 (8.92)	90 (10.39)	
Cigarette smoking, n (%)				**<.001**
Never smoker	806 (77.95)	113 (70.19)	693 (79.38)	
Current smoker	128 (12.38)	37 (22.98)	91 (10.42)	
Former smoker	100 (9.67)	11 (6.83)	89 (10.19)	
Charlson comorbidity index, Mean ± SD	1.16 ± 1.25	2.14 ± 1.44	0.98 ± 1.12	**<.001**
Comorbidity, n (%)				
Hypertension	394 (37.67)	82 (50.00)	312 (35.37)	**<.001**
Diabetes	176 (16.83)	46 (28.05)	130 (14.74)	**<.001**
Coronary heart diseases	169 (16.16)	42 (25.61)	127 (14.40)	**<.001**
Chronic pulmonary disease	137 (13.10)	48 (29.27)	89 (10.09)	**<.001**
Cerebrovascular diseases	105 (10.04)	32 (19.51)	73 (8.28)	**<.001**
Malignancy	59 (5.64)	26 (15.85)	33 (3.74)	**<.001**
Chronic kidney disease	50 (4.78)	30 (18.29)	20 (2.27)	**<.001**
Chronic liver disease	48 (4.59)	12 (7.32)	36 (4.08)	.069
Long-term use of immunosuppressants	31 (2.96)	18 (10.98)	13 (1.47)	**<.001**
Autoimmune diseases	25 (2.39)	8 (4.88)	17 (1.93)	.050
Prior pulmonary tuberculosis	23 (2.20)	7 (4.27)	16 (1.81)	.093
Clinical management setting, n (%)				<.001
Home quarantine	472 (45.08)	29 (17.68)	443 (50.17)	
Fangcang shelter	5 (0.48)	0	5 (0.57)	
Outpatient clinic or emergency department	40 (3.82)	3 (1.83)	37 (4.19)	
Hospitalization	530 (50.62)	132 (80.49)	398 (45.07)	
Pneumonia	454 (43.65)	112 (69.57)	342 (38.91)	**<.001**

Note. Data were displayed as numbers with percentage and mean ± standard derivation. The comparison between groups was conducted in Chi-square test or Fisher exact test for categorical variables, and t-test was conducted for continuous variables. BMI means body mass index. COVID-19 means Coronavirus disease 2019.

smokers (22.98% vs. 10.42%, $p < .001$). Comorbidities, including hypertension, diabetes, chronic pulmonary disease, coronary heart disease, cerebrovascular diseases chronic kidney disease and malignancy were more frequent in the non-vaccinated group (Table 1).

The overall hospitalization rate was 50.62% (530/1,047), with unvaccinated patients exhibiting a significantly higher hospitalization rate compared to vaccinated patients (80.49% vs. 45.07%, $p < .001$).

Vaccine type distribution

Totally, 883 (84.34%) participants were vaccinated, while 164 (15.67%) participants were not vaccinated. The inactivated vaccines (651, 73.73%) and recombinant protein vaccine (134, 15.29%) were most used, and other types include adenovirus vector vaccine (34, 3.85%), inhaled recombinant vaccine (8, 0.91%), mRNA vaccine (1, 0.11%) and uncertainty about vaccine type (55, 6.23%). In 805 patients with vaccine status, 26 (3.23%) were partially vaccinated, 239 (29.69%) were fully vaccinated, and 540 (67.08%) were received booster shots.

The median time from last vaccine to enrollment was 297.5 (157.0, 389.0) days in overall participants. Notably, patients with fully vaccination presented with longer median time of 446.5 (162.8, 504.8) days.

Household transmission rate

In the overall population, 214 patients without household contact were excluded, resulting in an infection rate of 95.23% (1,139/1,196). About 97.01% (1,134/1,169) patients developed symptoms within 1 week after

contact with infected individuals. The infection rate among vaccinated patients was significantly lower than unvaccinated patients (88.69% vs. 96.72%, $p < .001$).

Symptoms distribution and severity

Diarrhea was reported less among vaccinated patients than unvaccinated patients (17.21% vs. 25.61%, $p = .011$), while sore throat (45.73% vs. 56.29%, $p = .013$), myalgia (45.73% vs. 55.49%, $p = .021$), and taste disorder (31.71% vs. 41.56%, $p = .018$) were reported more frequently among the vaccinated group (Table S2). No significant difference was observed in symptoms severity ($p > 0.05$).

Univariable and multivariable logistic regression for pneumonia

In the multivariable logistic regression for pneumonia, vaccination was associated with pneumonia risk (aOR: 0.49, 95% CI: 0.32–0.76, $p = .002$) (Table S3). Further, reduced risk was observed in the inactivated vaccine group (aOR: 0.51, 95% CI: 0.33–0.79, $p = .003$) and other type vaccine group (aOR: 0.20, 95% CI: 0.10–0.40, $p < .001$) (Table S4). For vaccination status, the booster vaccination group revealed the aOR of 0.50 (95% CI: 0.32–0.78), while no significant differences were noted in other groups (Table S5).

Univariable and multivariable logistic regression for hospitalization

In comparison of vaccinated and non-vaccinated patients, univariate logistic regression revealed that vaccination was associated with significantly reduced risk of hospitalization in each vaccine type. After adjusting for age, sex, BMI, smoking history, and CCI, we still observed a significant negative association between vaccination and hospitalization risk (aOR: 0.37, 95% CI: 0.26–0.61, $p < .001$) (Table 2). In the analysis for different vaccine type, inactivated vaccine (aOR: 0.38, 95% CI: 0.23–0.62, $p < .001$) and other type vaccine (aOR: 0.20, 95% CI: 0.10–0.40, $p < .001$) were associated with lower hospitalization risk (Table S6). For vaccination status, the booster vaccination group revealed the aOR of 0.40 (95% CI: 0.24–0.65, $p < .001$) in multivariable logistic regression, while the fully vaccination group only presented with the aOR of 0.50 (95% CI: 0.28–0.87, $p = .013$) (Table 3). For fully vaccinated patients, we observed that inactivated vaccines (aOR: 0.32, 95% CI: 0.17–0.60, $p < .001$) appeared to provide relatively better protection compared with recombinant protein vaccines (aOR: 0.43, 95% CI: 0.22–0.84, $p = .014$) (Table S7).

The subgroup analysis for hospitalization comparing vaccination and non-vaccination was shown in Figure 2. In age subgroups, the protective effect in hospitalization decreases with age increasing (OR =

Table 2. Univariable and multivariable logistic regression of the effect of COVID-19 vaccine on hospitalization compared with unvaccinated participants.

	OR (95%CI)	*P*	aOR (95%CI)	*P*
Age group				
18–49 years old	Ref		Ref	
50–64 years old	2.30 (1.67 ~ 3.17)	**<.001**	1.36 (0.93 ~ 1.99)	.111
65–79 years old	3.01 (2.14 ~ 4.24)	**<.001**	1.48 (0.98 ~ 2.24)	.060
≥80 years old	5.81 (3.87 ~ 8.73)	**<.001**	3.11 (1.89 ~ 5.11)	**<.001**
Sex				
Female	Ref		Ref	
Male	3.01 (2.34 ~ 3.87)	**<.001**	3.13 (2.25 ~ 4.36)	**<.001**
BMI group				
18.5–24.0	Ref		Ref	
24.0–28.0	1.15 (0.88 ~ 1.51)	.307	1.14 (0.83 ~ 1.58)	.422
≥28.0	1.93 (1.25 ~ 2.98)	**.003**	1.91 (1.15 ~ 3.18)	**.013**
≤18.5	2.59 (1.17 ~ 5.76)	**.019**	2.19 (0.81 ~ 5.96)	.124
Cigarette smoking				
Never smoker	Ref		Ref	
Current smoker	7.36 (4.33 ~ 12.48)	**<.001**	2.31 (1.27 ~ 4.19)	**.006**
Former smoker	0.63 (0.41 ~ 0.98)	**.038**	0.33 (0.19 ~ 0.55)	**<.001**
Vaccination				
No	Ref		Ref	
Yes	0.20 (0.13 ~ 0.30)	**<.001**	0.37 (0.23 ~ 0.61)	**<.001**
Charlson comorbidity index	2.27 (1.98 ~ 2.59)	**<.001**	1.83 (1.58 ~ 2.13)	**<.001**

Table 3. Univariable and multivariable logistic regression of the effect of COVID-19 vaccination status on hospitalization compared with unvaccinated participants.

	OR (95%CI)	*P*	aOR (95%CI)	*P*
Vaccination status				
Non vaccination	Ref		Ref	
Partial vaccination	0.29 (0.12 ~ 0.68)	**.005**	0.40 (0.14 ~ 1.16)	.093
Fully vaccination	0.23 (0.15 ~ 0.36)	**<.001**	0.50 (0.28 ~ 0.87)	**.013**
Booster vaccination	0.23 (0.15 ~ 0.34)	**<.001**	0.40 (0.24 ~ 0.65)	**<.001**
Age group				
18–49 years old	Ref		Ref	
50–64 years old	2.30 (1.67 ~ 3.17)	**<.001**	1.55 (1.04 ~ 2.30)	**.031**
65–79 years old	3.01 (2.14 ~ 4.24)	**<.001**	1.72 (1.12 ~ 2.65)	**.013**
≥80 years old	5.81 (3.87 ~ 8.73)	**<.001**	3.02 (1.82 ~ 5.02)	**<.001**
Sex				
Female	Ref		Ref	
Male	3.01 (2.34 ~ 3.87)	**<.001**	3.18 (2.25 ~ 4.48)	**<.001**
BMI group				
18.5–24.0	Ref		Ref	
24.0–28.0	1.15 (0.88 ~ 1.51)	.307	1.18 (0.84 ~ 1.66)	.338
≥28.0	1.93 (1.25 ~ 2.98)	**.003**	2.06 (1.21 ~ 3.52)	**.008**
≤18.5	2.59 (1.17 ~ 5.76)	**.019**	2.36 (0.84 ~ 6.59)	.102
Cigarette smoking				
Never smoker	Ref		Ref	
Current smoker	7.36 (4.33 ~ 12.48)	**<.001**	2.33 (1.23 ~ 4.44)	**.010**
Former smoker	0.63 (0.41 ~ 0.98)	**.038**	0.32 (0.18 ~ 0.55)	**<.001**
Charlson comorbidity index	2.27 (1.98 ~ 2.59)	**<.001**	1.80 (1.54 ~ 2.10)	**<.001**

Note. Hospitalization was used as the outcome to compare the differences between individuals who received the COVID-19 vaccination and those who did not. Variables with a P-value less than 0.05 in univariate logistic regression were included in the multivariable logistic regression model. 95% CI means the 95% confidence interval for the odds ratio, OR represents the odds ratio, and aOR means adjusted odd ratio. BMI means body mass index. Fully vaccination included inactivated vaccines: 2 doses; adenovirus vector vaccines: 1 dose; recombinant protein vaccines: 3 doses; mRNA vaccines: 2 doses. Vaccination that did not meet the criteria for fully vaccination was classified as partial vaccination. Dose administered in excess of the fully vaccination regimen was considered as booster vaccination.

0.14 for 18–59 years old; OR = 0.20 for 60–69 years old; OR = 0.28 for 70–79 years old). Notably, the vaccine protection was more obvious in males in reducing hospitalization (OR = 0.09; 95% CI: 0.04–0.22) compared with females (OR = 0.29; 95% CI: 0.17–0.49). In addition, the risk of hospitalization was significantly lower in vaccinated individuals than unvaccinated individuals in multivariable logistic regression with an aOR of 0.20 (95% CI: 0.08–0.51, $p < .001$) (Table S8) in males, which was consistent with subgroup analysis.

Mixed-effects logistic regression for hospitalization

The results were consistent with our primary analysis, revealing vaccination remained significantly associated with a reduced risk of hospitalization (aOR 0.37, 95% CI: 0.23–0.60). Additionally, we computed the intraclass correlation coefficient based on the variance of the random intercept, which approached zero.

Sensitivity analysis

In PSM, 143 vaccinated patients were matched with 143 unvaccinated participants (Figure S1). The baseline characteristics demonstrated balance except for age differences (Table S9). The subsequent multivariable logistic regression confirmed the robust protective effect of vaccination against hospitalization and pneumonia (Table S10, S11), with similar effect estimates with previous analysis.

In the patients excluding booster shots with a longer time from vaccination to infection, multivariate regression analysis still confirmed the protective effect of the vaccination (Table S12, S13). In another analysis of 370 spouses, similar results were also found (Table S14, S15).

Subgroup	n (%)	Non-vaccination	Vaccination	OR(95%CI)	p.value
All patients	1047 (100.00)	132/164	398/883	0.20 (0.13 ~ 0.30)	<.001
Age group					
18-59	386 (36.87)	19/25	109/361	0.14 (0.05 ~ 0.35)	<.001
60-69	272 (25.98)	36/44	109/228	0.20 (0.09 ~ 0.46)	<.001
70-79	222 (21.20)	35/43	98/179	0.28 (0.12 ~ 0.63)	0.002
≥80	167 (15.95)	42/52	82/115	0.59 (0.27 ~ 1.32)	0.198
Sex					
Female	532 (50.81)	45/71	154/461	0.29 (0.17 ~ 0.49)	<.001
Male	515 (49.19)	87/93	244/422	0.09 (0.04 ~ 0.22)	<.001
BMI group					
≤18.5	30 (2.93)	13/14	8/16	0.08 (0.01 ~ 0.74)	0.026
18.5-24.0	549 (53.67)	72/88	188/461	0.15 (0.09 ~ 0.27)	<.001
24.0-28.0	340 (33.24)	32/41	141/299	0.25 (0.12 ~ 0.54)	<.001
≥28	104 (10.17)	11/14	55/90	0.43 (0.11 ~ 1.65)	0.217
Smoking status					
Never smoker	806 (77.95)	84/113	295/693	0.26 (0.16 ~ 0.40)	<.001
Current smoker	128 (12.38)	35/37	76/91	0.29 (0.06 ~ 1.34)	0.112
Former smoker	100 (9.67)	11/11	25/89		
Hypertension					
No	652 (62.33)	63/82	222/570	0.19 (0.11 ~ 0.33)	<.001
Yes	394 (37.67)	69/82	176/312	0.24 (0.13 ~ 0.46)	<.001
Diabetes					
No	870 (83.17)	94/118	311/752	0.18 (0.11 ~ 0.29)	<.001
Yes	176 (16.83)	38/46	87/130	0.43 (0.18 ~ 0.99)	0.048
Chronic pulmonary disease					
No	909 (86.90)	91/116	330/793	0.20 (0.12 ~ 0.31)	<.001
Yes	137 (13.10)	41/48	68/89	0.55 (0.22 ~ 1.41)	0.216
Pulmonary tuberculosis					
No	1023 (97.80)	125/157	384/866	0.20 (0.14 ~ 0.31)	<.001
Yes	23 (2.20)	7/7	14/16		
Coronary heart diseases					
No	877 (83.84)	98/122	316/755	0.18 (0.11 ~ 0.28)	<.001
Yes	169 (16.16)	34/42	82/127	0.43 (0.18 ~ 1.00)	0.051
Cerebrovascular diseases					
No	941 (89.96)	104/132	348/809	0.20 (0.13 ~ 0.32)	<.001
Yes	105 (10.04)	28/32	50/73	0.31 (0.10 ~ 0.99)	0.048
Autoimmune diseases					
No	1021 (97.61)	127/156	384/865	0.18 (0.12 ~ 0.28)	<.001
Yes	25 (2.39)	5/8	14/17	2.80 (0.42 ~ 18.69)	0.288
Malignancy					
No	987 (94.36)	110/138	371/849	0.20 (0.13 ~ 0.31)	<.001
Yes	59 (5.64)	22/26	27/33	0.82 (0.20 ~ 3.27)	0.776
Chronic liver disease					
No	998 (95.41)	121/152	366/846	0.20 (0.13 ~ 0.30)	<.001
Yes	48 (4.59)	11/12	32/36	0.73 (0.07 ~ 7.22)	0.786
Chronic kidney disease					
No	996 (95.22)	104/134	379/862	0.23 (0.15 ~ 0.35)	<.001
Yes	50 (4.78)	28/30	19/20	1.36 (0.11 ~ 16.05)	0.809
Long-term use of immunosuppressants					
No	1015 (97.04)	115/146	387/869	0.22 (0.14 ~ 0.33)	<.001
Yes	31 (2.96)	17/18	11/13	0.32 (0.03 ~ 4.01)	0.380

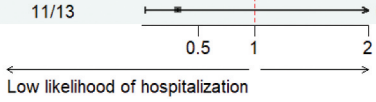

Figure 2. Subgroup analysis of hospitalization comparing patients with and without COVID-19 vaccination. Note. Based on the confounding factors, patients were divided into different subgroups. The univariable logistic regression was conducted to compare the hospitalization rate between vaccinated and unvaccinated patients. 95% CI means the 95% confidence interval, and/OR represents the odds ratio.

Estimated vaccine effectiveness in hospitalization and pneumonia

The vaccine effectiveness was shown in Figure 3. For different vaccine type, the activated vaccine and other type vaccine groups presented with stable protective effectiveness in reducing the risk of hospitalization and pneumonia. For vaccine status, the booster vaccine group revealed the most obvious protective effect in both hospitalization and pneumonia.

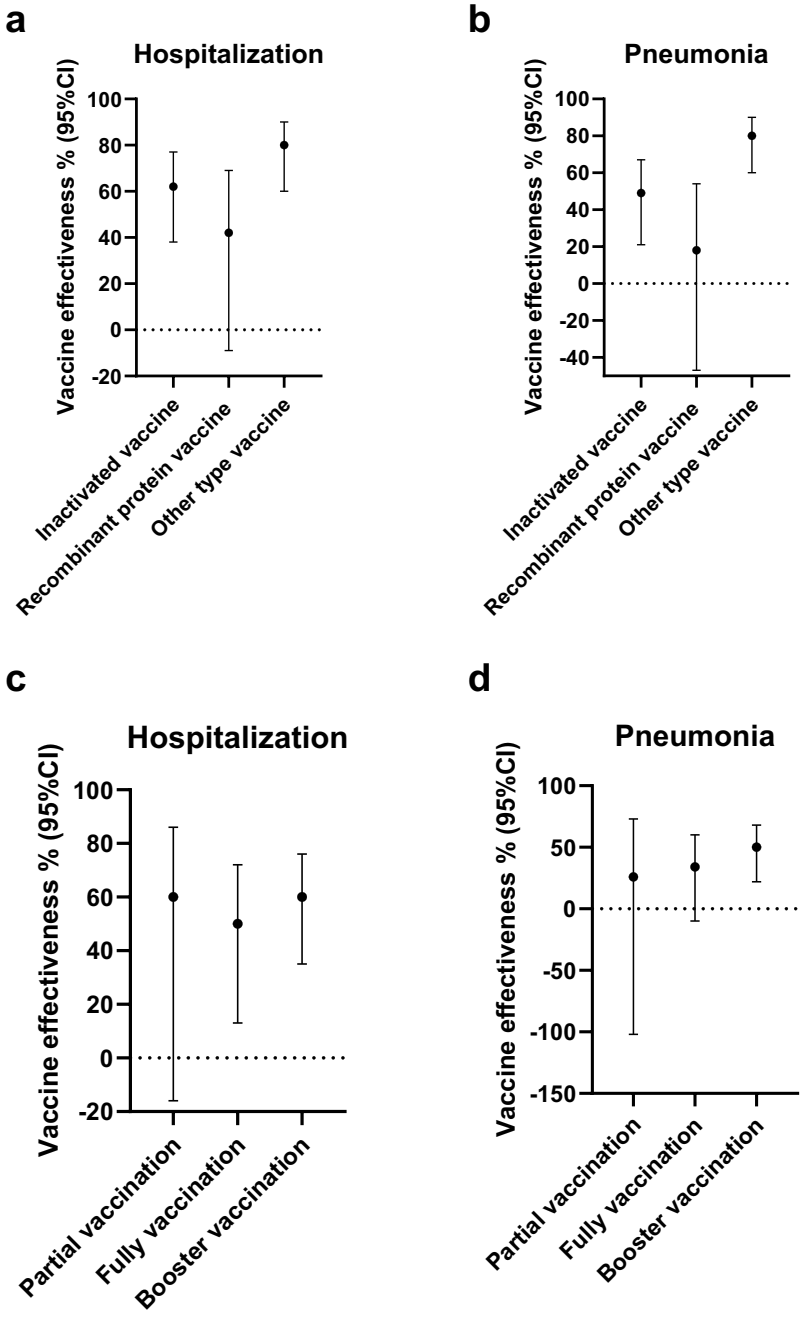

Figure 3. Vaccine effectiveness in different vaccine type and vaccine status. Note.The adjusted odds ratio (aOR) was caclulated with multivariable logistic regression, and the effectiveness was estimated as (1-aOR) * 100%. Other type vaccine included adenovirus vector vaccine, inhaled recombinant vaccine and mRNA vaccine. Fully vaccination included inactivated vaccines: two doses; adenovirus vector vaccines: one dose; recombinant protein vaccines: three doses; mRNA vaccines: two doses. Vaccination that did not meet the criteria for fully vaccination was classified as partial vaccination. A dose administered in excess of the fully vaccination regimen was considered as booster vaccination.

Discussion

This study focuses on the long-term effectiveness of COVID-19 vaccination after infection in household contacts and supports the durable protective effect of vaccination on hospitalization over 1 year. Our research findings indicate that the vaccine formulated for the SARS-CoV-2 original strain exhibited significant protective capabilities against the Omicron variant.

Our study confirmed the protective effect of the ancestral strain SARS-CoV-2 against Omicron infection over 1 year on hospitalization, and we found the more pronounced protective effect of booster shots than fully vaccination. Previous study has reported similar results, confirming the potential for cross-protection from vaccination.[21] One cohort study conducted in China through phone interviews also confirmed inactivated COVID-19 vaccines are still effective in preventing COVID-19-related hospitalizations in December 2022.[22] But another study conducted found that vaccine effectiveness decreased over time. In the 12–59 years age group, vaccine effectiveness against COVID-19 hospitalization following Omicron infection was 96.2% (95% CI: 72.9–99.5) at 14–30 days post-vaccination and 77.6% (95% CI: 72.6–81.6) beyond 120 days post-vaccination.[9] Further studies are needed to fully understand the mechanisms underlying these differences and to explore the long-term dynamics of vaccine protection against emerging variants. Collectively, these findings reinforce vaccination's critical role in reducing severe COVID-19 outcomes and underscore the necessity of booster doses to sustain immunity.

Subgroup analyses revealed decreased vaccine effectiveness with increasing age range and obvious protection from vaccination in males. One study in 2022 found that the effectiveness of inactivated vaccines tended to decrease with age increasing, which contrasts with our findings.[13] This discrepancy may be due to differences in the trends of immune status changes over time.[23] These results highlight the importance of studying the dynamic immune profiles of people of different ages. Despite males' higher risk of severe prognosis,[24] a pronounced benefit from vaccination in reducing hospitalization and pneumonia risk was found in our study. A meta-analysis found vaccination efficacy was significantly higher in males than females (OR = 0.67, 95% CI: 0.48–0.94), which supports our findings.[25] After SARS-CoV-2 infection, adaptive immunity, innate immunity, and hormonal levels may contribute to the poor prognosis observed in males.[26] While biological mechanisms such as hormonal influences and heightened female immune responses to vaccines[27–29] may explain sex-specific outcomes, they fail to account for the observed paradox of higher male benefit despite poorer prognosis. These discrepancies underscore the need for deeper investigation into sex-specific immune profiles and sex as a variable in clinical trials and public health strategies.

The findings suggest vaccination reduces the long-term risk of infection but appears to have no effect on alleviating acute symptoms. While numerous studies assessed the association between vaccination and long-term health outcomes,[30] such as long-COVID, research addressing infection and acute infectious symptoms in extended phase remains limited. This further underscores the importance of booster vaccinations, while highlighting the need for strategies that continuously reduce infections and alleviate symptoms.

The study advantage lies in revealing the durable protective effect vaccination in household contacts with shared exposure risk, transmission and similar behavior factors. Almost no previous SARS-CoV-2 infection was reported. However, the use of hospitalized patients as cases and their household contacts as controls may introduce selection bias, and patients without household contacts were excluded but with different characteristics, affecting generalizability. Infection and pneumonia outcomes could not be fully assessed due to control selection, and these results should be considered exploratory and interpreted with caution. Small sample size may limit the direct comparison in protective effectiveness between different vaccine types. While confounders were adjusted, unmeasured variables such as antiviral drug could have influenced the results. During the research period, the availability of antiviral drugs in China was still limited, posing little impact on the findings.

While COVID-19 vaccination may not provide long-term protection against symptoms, it maintains sustained effectiveness in reducing the risk of hospitalization even beyond 1-year post-vaccination. Future research should focus on identifying populations deriving clinical benefits from vaccination and revealing dynamic immune characteristic, while enhancing transparency in vaccine-related information dissemination and developing targeted strategies to mitigate vaccine hesitancy.

Author contributions

CRediT: **Limin Zhang:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Writing – original draft, Writing – review & editing; **Dong Liu:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing; **Xiaoyu Cao:** Data curation, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft; **Hui Zhang:** Formal analysis, Investigation, Methodology, Project administration, Validation, Writing – original draft; **Shasha Li:** Investigation, Methodology, Project administration, Supervision; **Ruirui Wang:** Investigation, Project administration, Resources, Supervision; **Yuxian Mu:** Investigation, Project administration, Visualization; **Mingfeng Han:** Conceptualization, Investigation, Methodology, Resources, Supervision, Validation, Writing – review & editing; **Yeming Wang:** Conceptualization, Formal analysis, Investigation, Methodology, Resources, Supervision, Validation, Writing – review & editing; **Bin Cao:** Conceptualization, Funding acquisition, Methodology, Supervision, Validation, Writing – review & editing.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work was supported by the Chinese Academy of Medical Sciences Innovation Fund for Medical Sciences [No.2021-I2M-1-048], New Cornerstone Science Foundation [grant number NCI202231], National Key Research and Development Program of China [No.2022YFF1203001] and Elite Medical Professionals Project of China–Japan Friendship Hospital [No. ZRJY2023-GG18], in the study design and investigation.

Notes on contributors

Mingfeng Han, M.D., Pro. Mingfeng Han has dedicated his career mainly to respiratory infection research. Specializing in clinical epidemiology and chronic infectious diseases, he has authored or co-authored over 10 SCI publications as a first or corresponding author in leading journals, including *BMJ*, *Journal of Infection*, and *International Journal of Infectious Diseases*.

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Data availability statement

Anonymized research data will be made available on reasonable requests directed to the corresponding author (Bin Cao: caobin_ben@163.com). Study proposals will be reviewed and approved by the ethics committee, investigators, and collaborators.

Ethics statement

Every patient's written consent was obtained. This study was conducted in accordance with the Declaration of Helsinki and received approval from the China–Japan Friendship Hospital Institutional Review Board (2022-KY-052).

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