External Supports Are Associated With the COVID-19 Vaccination in Chinese Breast Cancer Patients: A Cross-Sectional Survey

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is a global pandemic. Breast cancer is the most commonly diagnosed malignant cancer in China. Considering the specific national conditions, no evidence is available for factors associated with COVID-19 vaccination in patients with breast cancer.

Methods: This was a cross-sectional survey, fielded from June 21 through June 27, 2021. A total of 944 nationally representative samples of Chinese breast cancer patients participating in the survey were included. Participant surveys included questions addressing who finished COVID-19 vaccination with the question “Have you taken the COVID-19 vaccine?”, and response options were “Yes” and “No”.

Results: Overall, 730 (77.33%) women with breast cancer were unvaccinated, and only 214 (22.67%) were vaccinated with the COVID-19 vaccine. After adjusting for potential confounders, including both sociodemographic and clinical characteristics, we found that external support, including positive doctor suggestions (odds ratio (OR): 5.52; 95% confidence interval (CI): 3.50 - 8.71; P < 0.0001), positive support from surrounding people (OR: 11.65; 95% CI: 7.57 - 17.91; P < 0.0001), and negative initiative from the community (OR: 0.15; 95% CI: 0.06 - 0.35; P < 0.0001), was associated with COVID-19 vaccination rates among breast cancer patients. These results remain stable in subgroup analyses. We found that most participants (82.52%) understood the necessity of COVID-19 vaccinations in China was strong; however, the recognition regarding the COVID-19 vaccine showed different patterns between vaccinated and unvaccinated participants.

Conclusions: Our findings suggest external support, including vaccination suggestions from surgeons or oncologists, vaccination suggestions from associated people, and residents’ committee mandated vaccinations, was associated with the COVID-19 vaccination rates. Interventions regarding these factors and improving publicity as well as education regarding COVID-19 vaccines among breast cancer patients are warranted.

Keywords: Breast cancer patients; COVID-19 vaccination; External supports

Introduction

As of late June 2021, over 178 million patients with coronavirus disease 2019 (COVID-19) have been diagnosed globally, including approximately 3.9 million deaths [1]. The ongoing COVID-19 pandemic poses tremendous hazards to public health and results in devastating medical, economic and social consequences. At present, medications (e.g., remdesivir, hydroxychloroquine, lopinavir, and interferon regimens) have inconsistent effects on overall mortality, initiation of ventilation, and length of stay for inpatients with COVID-19, except for dexamethasone which can help reduce the duration on a ventilator and save the lives of patients with serious and critical disease [2]. The most promising strategy to prevent COVID-19 incidence and mortality is the vaccination of COVID-19 worldwide. To date, over 2.4 billion vaccine doses have been administered, as reported by the World Health Organization (WHO).

Several studies have revealed that patients with malignancy are of the vulnerable population to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and have a higher mortality rate than patients without cancer among in-
patients with COVID-19 [3-6]. Some of these patients have delayed diagnosis and treatment of the disease due to the fear of the COVID-19 pandemic, which in turn affects the survival rate of patients [7]. Data are limited on the safety and efficacy of the COVID-19 vaccine in patients with malignancy because most registration trials include patients without a history of any cancer [8]. Several small studies have shown that the levels of SARS-CoV-2 neutralizing antibodies in patients with cancer treated with immune checkpoint inhibitors are significantly lower than those in healthy volunteers, despite the similar short-term safety of the mRNA vaccines in both groups [9-12].

Female breast cancer has become the most commonly diagnosed malignant tumor worldwide, and the estimated number of Chinese breast cancer incident cases is approximately 416,000 in 2020 [13]. A previous survey shows that 13% of breast cancer patients have been vaccinated and 30% of patients are hesitant to be vaccinated for reasons of mistrust in the health care system, misconception, poor educational attainment, and so on [14].

As most people have been encouraged to receive COVID-19 vaccination and over one billion COVID-19 vaccination doses have now been administered in China, we conducted an online survey to survey the COVID-19 vaccination in Chinese breast cancer patients who have undergone surgery and analyze factors influencing their vaccination. The present study may help health care policy-makers in China and other countries improve patient education and vaccination policies in patients with breast cancer.

Materials and Methods

Study design and participants

This was a cross-sectional study to survey the factors influencing COVID-19 vaccination in Chinese breast cancer patients. The questionnaire was designed using www.sojump.com and could only be submitted upon completion of all questions. Breast cancer patients who visited the WeChat public platform named “Dr. Wang Jing, Cancer Hospital, Chinese Academy of Medical Sciences”, sharing knowledge of breast disease with a total of 32,271 followers from different regions of China, were invited to complete the web-based survey, with only one WeChat ID being submit per person for the questionnaire. First, we pretested 66 patients on June 20, 2021 to assure high standards of data quality. Then, we improved the questions and ran the questionnaire from June 21, 2021 to June 27, 2021. Finally, a total of 4,849 followers received the notice of our questionnaire; of these, 944 breast cancer patients finished the questionnaire. All information of participants was kept anonymous with the understanding that this information could be used for scientific research.

Measures

Participant demographics in our questionnaire included age, employment (yes or no), yearly personal income (≥ 50,000 or < 5,0000), marital status (married or unmarried), region of residency in China (North China, East China, Northeast China, Central China, South China, West China or others), place of residence (urban or rural), education level (higher than high school or high school and lower), influenza vaccination history (never, at least once in 3 years or at least once in 10 years), personal COVID-19 history (yes or no) and COVID-19 vaccination status (yes or no). Medical history information included time after surgery (date of surgery), surgical methods (mastectomy or breast-conserving surgery), neoadjuvant therapy (yes or no), anti-human epidermal growth factor receptor type 2 (HER2) therapy (yes or no), chemotherapy (yes or no), endocrine therapy (yes or no), radiotherapy (yes or no), undergoing treatment (yes or no), current treatment method (no treatment, endocrine therapy, others (chemotherapy, anti-HER2 therapy, radiotherapy, or combined treatment like endocrine therapy with anti-HER2 therapy) or traditional Chinese medicine) and recurrence of breast cancer before vaccination (yes or no).

Furthermore, we collected some external support information on the COVID-19 vaccination, including vaccination suggestions from surgeons or oncologists (indefinite suggestion, no communication with doctors, recommended, not recommended), vaccination suggestions from around people (no suggestion, recommended or not recommended) and calls for vaccination by the residents’ committees or employers (yes, no, vaccinated notice or no).

To explore potential reasons for unvaccinated participants, we also assessed the subjective factors in unvaccinated participants with questions, “Do you believe COVID-19 vaccination may cause special side effects to breast cancer patients?”, “Do you believe vaccination may lead to recurrence of breast cancer?” and “Do you believe the COVID-19 vaccine is safe?”, followed by the response options “I don’t know”, “Yes” and “No”. We asked, “Do you believe breast cancer patients can be inoculated with COVID-19 vaccine?”; followed by the response options “I don’t know”, “Yes”, “No” and “Depend on current treatment”. We asked, “Do you believe the necessity of COVID-19 vaccination in China is strong or weak?”, followed by the response options “Strong” and “Weak”.

Statistical analysis

Baseline characteristics of participants were summarized by percentages and frequencies. Because the percentage of missing data was minor (0-0.4%), no imputation was performed [15]. The Kruskal-Wallis (for skewed distribution) test, one-way analysis of variance (ANOVA) (for normal distribution), and Chi-square tests (for categorical variables) were used to examine any differences between the proportions and means of the groups. We used a linear regression model to explore potential associations between variables and COVID-19 vaccination among the study population. Following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [16], we simultaneously reported the effect size of exposures in separate models, including a crude model, minimally adjusted model and a fully adjusted model. Confounders were selected based on their associations with the outcomes or a change in effect estimate of more than 10%
[17]. We further used stratified linear regression models to explore the association of exposures and outcomes in subgroup analyses. We examined any modification and interaction of subgroups by the likelihood ratio test. All analyses were performed using the statistical software R (http://www.R-project.org) and EmpowerStats platform (http://www.empowerstats.com). P < 0.05 was considered statistically significant (two-sided).

Ethical considerations

The Research Ethics Committee of National Cancer Center/ National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences approved the study. The study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration. Informed consent was waived because the research was deemed to be of minimal risk and no identifiable data were collected.

Results

Characteristics of participants

All results presented here are based on the 944 participants who responded to the questionnaire. Of these, 730 (77.33%) women with breast cancer were unvaccinated, and less than one-third (22.67%) were vaccinated with the COVID-19 vaccine. The average age of the participants was 49.05 ± 8.84 years old. The baseline characteristics of the participants are listed in Table 1. We found no statistically significant difference in age, previous treatment methods (surgical method, anti-HER2 therapy, breast reconstruction surgery, endocrine therapy, and neoadjuvant therapy), personal COVID-19 history, current therapy, educational level, employment, marital status, region of living in China, and place of residence or recurrence of breast cancer before vaccination between participants who were vaccinated or unvaccinated. Compared with the vaccinated participants, unvaccinated participants had significant differences in time after surgery, axillary lymph node dissection (ALND), chemotherapy, influenza vaccination history, yearly personal income (Chinese Yuan), external support, including vaccination suggestions from surgeons or oncologists, vaccination suggestions from around people, and vaccination suggestions from residents’ committees or employers. Compared with the vaccinated participants, unvaccinated participants had significant differences in time after surgery, axillary lymph node dissection (ALND), chemotherapy, influenza vaccination history, yearly personal income (Chinese Yuan), external support, including vaccination suggestions from surgeons or oncologists, vaccination suggestions from around people, and vaccination suggestions from residents’ committees or employers. Age, previous treatment methods (surgical method, anti-HER2 therapy, breast reconstruction surgery, endocrine therapy, and neoadjuvant therapy), personal COVID-19 history, current therapy, educational level, employment, marital status, region of living in China, and place of residence and recurrence of breast cancer before vaccination were not associated with COVID-19 vaccination. All results are listed in Table 2.

Association between external support and COVID-19 vaccination

To identify potential key factors influencing COVID-19 vaccination among breast cancer patients, we further used a linear regression model to estimate the association between external support and COVID-19 vaccination. The results of the crude model, minimally adjusted model and fully adjusted model are shown in Table 3. Compared with participants receiving indefinite vaccination suggestions from surgeons or oncologists, participants who received recommended suggestions were positively correlated with COVID-19 vaccination (OR: 5.52; 95% CI: 3.50 - 8.71; P < 0.0001), while participants who did not receive recommended suggestions were negatively correlated with COVID-19 vaccination (OR: 0.36; 95% CI: 0.16 - 0.79; P = 0.0107). Compared with participants with no recommended suggestion from around people, participants who received recommended suggestions were positively correlated with COVID-19 vaccination (OR: 11.65; 95% CI: 7.57 - 17.91; P < 0.0001). Compared with participants who were asked to be vaccinated by the residents’ committee or employer, participants who were not asked (OR: 0.15; 95% CI: 0.06 - 0.35; P < 0.0001) or without vaccinal notice (OR: 0.26; 95% CI: 0.16 - 0.42; P < 0.0001) were negatively associated with COVID-19 vaccination. These results remain stable in the crude model, minimally adjusted model and fully adjusted model. We further explored the association between external support and COVID-19 vaccination in subgroup analyses, and we found no interaction between external support and age, time after surgery, ALND, or year personal income (Table 4; P values for interactions were > 0.05).

Recognitions of breast cancer patients regarding COVID-19 vaccine

To identify potential concerns regarding COVID-19 vaccination among unvaccinated breast cancer patients, we further show the recognition of COVID-19 vaccination in Table 5. For the 730 unvaccinated breast cancer patients, most of the participants (81.10%) expressed “I don’t know” regarding whether COVID-19 vaccination may cause special side effects to breast cancer patients, and only a minority of participants (1.51%) believed breast cancer patients could be inoculated with the COVID-19 vaccine. Most of the participants (78.36%) were unsure about whether COVID-19 vaccination may lead to recurrence of breast cancer. More than half of the participants (51.37%) were unsure or concerned about the safety of the COVID-19 vaccine. Interestingly, even for unvaccinated breast cancer patients, most of the participants (79.45%) also
### Table 1. Characteristics of Study Population

|                                    | Unvaccinated | Vaccinated | P-value |
|------------------------------------|--------------|------------|---------|
| No.                                | 730          | 214        |         |
| Age (years)                        | 48.78 ± 8.74 | 50.00 ± 9.12 | 0.075  |
| Time after surgery (days)          | 910.92 ± 681.51 | 1,272.64 ± 883.51 | < 0.001|
| Surgical method                    |              |            | 0.497  |
| Mastectomy                         | 452 (61.92%) | 127 (59.35%) |         |
| Breast conserving surgery          | 278 (38.08%) | 87 (40.65%) |         |
| Axillary lymph node dissection     |              |            | < 0.001|
| Yes                                | 403 (55.21%) | 81 (37.85%) |         |
| No                                 | 327 (44.79%) | 133 (62.15%) |         |
| Breast reconstruction surgery      |              |            | 0.305  |
| No                                 | 659 (90.27%) | 188 (87.85%) |         |
| Yes                                | 71 (9.73%)   | 26 (12.15%) |         |
| Anti-HER2 therapy                  |              |            | 0.081  |
| No                                 | 563 (77.12%) | 177 (82.71%) |         |
| Yes                                | 167 (22.88%) | 37 (17.29%) |         |
| Chemotherapy                       |              |            | < 0.001|
| Yes                                | 503 (68.90%) | 120 (56.07%) |         |
| No                                 | 227 (31.10%) | 94 (43.93%) |         |
| Endocrinotherapy                   |              |            | 0.984  |
| Yes                                | 594 (81.37%) | 174 (81.31%) |         |
| No                                 | 136 (18.63%) | 40 (18.69%) |         |
| Radiotherapy                       |              |            | 0.047  |
| Yes                                | 441 (60.41%) | 113 (52.80%) |         |
| No                                 | 289 (39.59%) | 101 (47.20%) |         |
| Neoadjuvant therapy                |              |            | 0.062  |
| No                                 | 630 (86.30%) | 195 (91.12%) |         |
| Yes                                | 100 (13.70%) | 19 (8.88%)  |         |
| Undergoing treatment               |              |            | 0.085  |
| Yes                                | 480 (65.75%) | 127 (59.35%) |         |
| No                                 | 250 (34.25%) | 87 (40.65%) |         |
| Current treatment method           |              |            | < 0.001|
| No treatment                       | 250 (34.25%) | 87 (40.65%) |         |
| Endocrinotherapy                   | 307 (42.05%) | 109 (50.93%) |         |
| Others                             | 158 (21.64%) | 17 (7.94%)  |         |
| Traditional Chinese medicine       | 15 (2.05%)   | 1 (0.47%)   |         |
| Recurrence of breast cancer before vaccination | 0.282       |            |         |
| No                                 | 706 (96.71%) | 210 (98.13%) |         |
| Yes                                | 24 (3.29%)   | 4 (1.87%)   |         |
| Personal COVID-19 history          |              |            | 0.45   |
| No                                 | 718 (98.36%) | 212 (99.07%) |         |
| Yes                                | 12 (1.64%)   | 2 (0.93%)   |         |
Table 1. Characteristics of Study Population - (continued)

| Characteristic                              | Unvaccinated | Vaccinated | P-value |
|---------------------------------------------|--------------|------------|---------|
| Educational level                          |              |            |         |
| Higher than high school                    | 504 (69.04%) | 147 (68.69%) | 0.923   |
| High school and lower                      | 226 (30.96%) | 67 (31.31%)  |         |
| Employment status                          |              |            |         |
| Yes                                         | 386 (52.88%) | 125 (58.41%) | 0.153   |
| No                                          | 344 (47.12%) | 89 (41.59%)  |         |
| Influenza vaccination history               |              |            | < 0.001 |
| Never                                       | 617 (84.52%) | 162 (75.70%) |         |
| At least once in 3 years                    | 61 (8.36%)   | 39 (18.22%)  |         |
| At least once in 10 years                   | 52 (7.12%)   | 13 (6.07%)   |         |
| Yearly personal income (Chinese Yuan)       |              |            | 0.012   |
| ≥ 50,000                                    | 397 (54.38%) | 137 (64.02%) |         |
| < 5,000                                     | 333 (45.62%) | 77 (35.98%)  |         |
| Marital status                              |              |            | 0.759   |
| Married                                     | 639 (87.53%) | 189 (88.32%) |         |
| Unmarried                                   | 91 (12.47%)  | 25 (11.68%)  |         |
| Region of living in China                   |              |            | 0.056   |
| North China                                 | 445 (60.96%) | 136 (63.55%) |         |
| East China                                  | 118 (16.16%) | 32 (14.95%)  |         |
| Northeast China                             | 66 (9.04%)   | 19 (8.88%)   |         |
| Central China                               | 37 (5.07%)   | 9 (4.21%)    |         |
| South China                                 | 28 (3.84%)   | 12 (5.61%)   |         |
| West China                                  | 36 (4.93%)   | 4 (1.87%)    |         |
| Others                                      | 0 (0.00%)    | 2 (0.93%)    |         |
| Place of residence                          |              |            | 0.611   |
| Urban area                                  | 653 (89.45%) | 194 (90.65%) |         |
| Rural area                                  | 77 (10.55%)  | 20 (9.35%)   |         |
| Vaccination suggestion from surgeon or oncologist |        |            | < 0.001 |
| Indefinite suggestion                       | 319 (43.70%) | 81 (37.85%)  |         |
| No communication with doctors               | 231 (31.64%) | 40 (18.69%)  |         |
| Recommended                                 | 60 (8.22%)   | 85 (39.72%)  |         |
| Not recommended                             | 120 (16.44%) | 8 (3.74%)    |         |
| Vaccination suggestion from around people   |              |            | < 0.001 |
| No suggestion                               | 398 (54.52%) | 36 (16.82%)  |         |
| Recommended                                 | 161 (22.05%) | 168 (78.50%) |         |
| Not recommended                             | 171 (23.42%) | 10 (4.67%)   |         |
| Calls for vaccination by the residents’ committee or employer |              |            | < 0.001 |
| Yes                                         | 407 (55.75%) | 184 (85.98%) |         |
| No vaccinal notice                          | 213 (29.18%) | 24 (11.21%)  |         |
| No                                          | 110 (15.07%) | 6 (2.80%)    |         |

HER2: human epidermal growth factor receptor type 2; COVID-19: coronavirus disease 2019.
## Table 2. Univariate Analysis of Factors Associated With COVID-19 Vaccination Among Breast Cancer Patients

| Factor                                | Statistics | OR (95% CI)          | P-value |
|---------------------------------------|------------|----------------------|---------|
| **Age (years)**                       | 49.05 ± 8.84 | 1.02 (1.00 - 1.03)   | 0.0751  |
| Time after surgery                    |            |                      |         |
| Q1                                    | 235 (25.00%) | 1                    |         |
| Q2                                    | 233 (24.79%) | 1.35 (0.82 - 2.24)   | 0.2366  |
| Q3                                    | 236 (25.11%) | 2.02 (1.25 - 3.26)   | 0.0039  |
| Q4                                    | 236 (25.11%) | 3.38 (2.13 - 5.35)   | < 0.0001|
| Surgical method                       |            |                      |         |
| Mastectomy                            | 579 (61.33%) | 1                    |         |
| Breast conserving surgery             | 365 (38.67%) | 1.11 (0.82 - 1.52)   | 0.497   |
| Axillary lymph node dissection        |            |                      |         |
| Yes                                   | 484 (51.27%) | 1                    |         |
| No                                    | 460 (48.73%) | 2.02 (1.48 - 2.77)   | < 0.0001|
| Breast reconstruction surgery         |            |                      |         |
| No                                    | 847 (89.72%) | 1                    |         |
| Yes                                   | 97 (10.28%)  | 1.28 (0.80 - 2.07)   | 0.3055  |
| Anti-HER2 therapy                     |            |                      |         |
| No                                    | 740 (78.39%) | 1                    |         |
| Yes                                   | 204 (21.61%) | 0.70 (0.48 - 1.05)   | 0.0818  |
| Chemotherapy                          |            |                      |         |
| Yes                                   | 623 (66.00%) | 1                    |         |
| No                                    | 321 (34.00%) | 1.74 (1.27 - 2.37)   | 0.0005  |
| Endocrinotherapy                      |            |                      |         |
| Yes                                   | 768 (81.36%) | 1                    |         |
| No                                    | 176 (18.64%) | 1.00 (0.68 - 1.48)   | 0.9838  |
| Radiotherapy                          |            |                      |         |
| Yes                                   | 554 (58.69%) | 1                    |         |
| No                                    | 390 (41.31%) | 1.36 (1.00 - 1.85)   | 0.0473  |
| Neoadjuvant therapy                   |            |                      |         |
| No                                    | 825 (87.39%) | 1                    |         |
| Yes                                   | 119 (12.61%) | 0.61 (0.37 - 1.03)   | 0.0639  |
| Current treatment                     |            |                      |         |
| Yes                                   | 607 (64.30%) | 1                    |         |
| No                                    | 337 (35.70%) | 1.32 (0.96 - 1.80)   | 0.0858  |
| Current treatment method              |            |                      |         |
| No treatment                          | 337 (35.70%) | 1                    |         |
| Endocrine                             | 416 (44.07%) | 1.02 (0.74 - 1.42)   | 0.9045  |
| Others                                | 175 (18.54%) | 0.31 (0.18 - 0.54)   | < 0.0001|
| Traditional Chinese medicine          | 16 (1.69%)  | 0.19 (0.02 - 1.47)   | 0.1122  |
| Recurrence of breast cancer before vaccination |        |                     |         |
| No                                    | 916 (97.03%) | 1                    |         |
| Yes                                   | 28 (2.97%)  | 0.56 (0.19 - 1.63)   | 0.2885  |
| Personal COVID-19 history             |            |                      |         |
| No                                    | 930 (98.52%) | 1                    |         |
|                          | Statistics | OR (95% CI)          | P-value   |
|--------------------------|------------|----------------------|-----------|
| **Yes**                  | 14 (1.48%) | 0.56 (0.13 - 2.54)  | 0.4563    |
| **Educational level**    |            |                      |           |
| Higher than high school  | 651 (68.96%) | 1                    |           |
| High school or lower     | 293 (31.04%) | 1.02 (0.73 - 1.41)  | 0.9226    |
| **Employment status**    |            |                      |           |
| Yes                      | 511 (54.13%) | 1                    |           |
| No                       | 433 (45.87%) | 0.80 (0.59 - 1.09)  | 0.1535    |
| **Influenza vaccination history** |      |                      |           |
| Never                    | 779 (82.52%) | 1                    |           |
| At least once in 3 years | 100 (10.59%) | 2.44 (1.57 - 3.77)  | < 0.0001  |
| At least once in 10 years| 65 (6.89%)   | 0.95 (0.51 - 1.79)  | 0.8791    |
| **Yearly personal income (Chinese Yuan)** |      |                      |           |
| ≥ 50,000                 | 534 (56.57%) | 1                    |           |
| < 5,0000                 | 410 (43.43%) | 0.67 (0.49 - 0.92)  | 0.0127    |
| **Marital status**       |            |                      |           |
| Married                  | 828 (87.71%) | 1                    |           |
| Unmarried                | 116 (12.29%) | 0.93 (0.58 - 1.49)  | 0.7589    |
| **Region of living in China** |      |                      |           |
| North China              | 518 (61.55%) | 1                    |           |
| East China               | 150 (15.89%) | 0.89 (0.57 - 1.37)  | 0.5904    |
| Northeast China          | 85 (9.00%)   | 0.94 (0.55 - 1.62)  | 0.8298    |
| Central China            | 46 (4.87%)   | 0.80 (0.37 - 1.69)  | 0.5526    |
| South China              | 40 (4.24%)   | 1.40 (0.69 - 2.83)  | 0.3458    |
| West China               | 40 (4.24%)   | 0.36 (0.13 - 1.04)  | 0.0591    |
| Others                   | 2 (0.21%)    | NA                   | NA        |
| **Place of residence**   |            |                      |           |
| Urban area               | 847 (89.72%) | 1                    |           |
| Rural area               | 97 (10.28%)  | 0.87 (0.52 - 1.47)  | 0.6108    |
| **Vaccination suggestion from surgeon or oncologist** |      |                      |           |
| Indefinite suggestion    | 400 (42.37%) | 1                    |           |
| No communication with doctors | 271 (28.71%) | 0.68 (0.45 - 1.03)  | 0.0706    |
| Recommended              | 145 (15.36%) | 5.58 (3.70 - 8.41)  | < 0.0001  |
| Not recommended          | 128 (13.56%) | 0.26 (0.12 - 0.56)  | 0.0005    |
| **Vaccination suggestion from around people** |      |                      |           |
| No suggestion            | 434 (45.97%) | 1                    |           |
| Recommended              | 329 (34.85%) | 11.54 (7.70 - 17.28)| < 0.0001  |
| Not recommended          | 181 (19.17%) | 0.65 (0.31 - 1.33)  | 0.2372    |
| **Calls for vaccination by the residents’ committee or employer** |      |                      |           |
| Yes                      | 591 (62.61%) | 1                    |           |
| No vaccinal notice       | 237 (25.11%) | 0.25 (0.16 - 0.39)  | < 0.0001  |
| No                       | 116 (12.29%) | 0.12 (0.05 - 0.28)  | < 0.0001  |

HER2: human epidermal growth factor receptor type 2; COVID-19: coronavirus disease 2019; OR: odds ratio; CI: confidence interval.
### Table 3. Relationship Between External Supports and COVID-19 Vaccination in Different Models

| Exposure | Crude model (OR (95% CI), P-value) | Minimally adjusted model (OR (95% CI), P-value) | Fully adjusted model (OR (95% CI), P-value) |
|----------|-----------------------------------|-----------------------------------------------|---------------------------------------------|
|          | Vaccination suggestion from surgeon or oncologist |                                |                                             |
|          | Indefinite suggestion | Ref | Ref | Ref |
|          | No communication with doctors | 0.68 (0.45 - 1.03), 0.0706 | 0.68 (0.45 - 1.04), 0.0757 | 0.80 (0.52 - 1.24), 0.3149 |
|          | Recommended | 5.58 (3.70 - 8.41), < 0.0001 | 5.44 (3.57 - 8.27), < 0.0001 | 5.52 (3.50 - 8.71), < 0.0001 |
|          | Not recommended | 0.26 (0.12 - 0.56), 0.0005 | 0.27 (0.12 - 0.57), 0.0007 | 0.36 (0.16 - 0.79), 0.0107 |
|          | Vaccination suggestion from around people |                                |                                             |
|          | No suggestion | Ref | Ref | Ref |
|          | Recommended | 11.54 (7.70 - 17.28), < 0.0001 | 11.37 (7.58 - 17.06), < 0.0001 | 11.65 (7.57 - 17.91), < 0.0001 |
|          | Not recommended | 0.65 (0.31 - 1.33), 0.2372 | 0.64 (0.31 - 1.32), 0.2262 | 0.66 (0.31 - 1.42), 0.2885 |
|          | Calls for vaccination by the residents’ committee or employer |                                |                                             |
|          | Yes | Ref | Ref | Ref |
|          | No vaccinal notice | 0.25 (0.16 - 0.39), < 0.0001 | 0.25 (0.16 - 0.40), < 0.0001 | 0.26 (0.16 - 0.42), < 0.0001 |
|          | No | 0.12 (0.05 - 0.28), < 0.0001 | 0.12 (0.05 - 0.28), < 0.0001 | 0.15 (0.06 - 0.35), < 0.0001 |

Non-adjusted model adjusted for: none. Minimally adjusted model: we adjusted for age; yearly personal income; educational level; employment status. Fully adjusted model: we adjusted for age; time after surgery; surgical method; axillary lymph node dissection; breast reconstruction surgery; anti-HER2 therapy; chemotherapy; endocrine therapy; radiotherapy; neoadjuvant therapy; undergoing treatment; recurrence of breast cancer before vaccination; personal COVID-19 history; educational level; employment; influenza vaccination history; yearly personal income; marital status; region of living in China; place of residence. OR: odds ratio; CI: confidence interval; Ref: reference.

### Table 4. Effect Size of External Supports on COVID-19 Vaccination in Prespecified and Exploratory Subgroups

| Variables | No. | OR (95% CI), P-value | No. | OR (95% CI), P-value | P for interaction |
|-----------|-----|---------------------|-----|---------------------|-------------------|
|          | Vaccination suggestion from surgeon or oncologist |                                |                                             |
| Age dichotomous | Age = low | Age = high | Age = low | Age = high | 0.922 |
| Indefinite suggestion | 157 | 1 | 243 | 1 | 0.029 |
| No communication with doctors | 142 | 0.76 (0.38 - 1.51), 0.4299 | 129 | 0.86 (0.48 - 1.57), 0.6324 |
| Recommended | 68 | 5.35 (2.58 - 11.10), < 0.0001 | 77 | 6.20 (3.31 - 11.62), < 0.0001 |
| Not recommended | 68 | 0.39 (0.13 - 1.14), 0.0859 | 60 | 0.26 (0.07 - 0.91), 0.0350 |
| Time after surgery = short | 179 | 1 | 218 | 1 | 0.201 |
| Indefinite suggestion | 179 | 1 | 218 | 1 | 0.201 |
| No communication with doctors | 146 | 1.29 (0.61 - 2.73), 0.5077 | 124 | 0.63 (0.35 - 1.14), 0.1289 |
| Recommended | 58 | 12.36 (5.35 - 28.57), < 0.0001 | 87 | 4.56 (2.46 - 8.46), < 0.0001 |
| Not recommended | 85 | 0.67 (0.22 - 2.04), 0.4749 | 43 | 0.21 (0.06 - 0.76), 0.0178 |
| Axillary lymph node dissection = yes | Axillary lymph node dissection = no | 0.762 |
Table 4. Effect Size of External Supports on COVID-19 Vaccination in Prespecified and Exploratory Subgroups - (continued)

| Variables                                      | No.   | OR (95% CI), P-value | No.   | OR (95% CI), P-value | P for interaction |
|------------------------------------------------|-------|----------------------|-------|----------------------|-------------------|
| Indefinite suggestion                          | 209   | 1                    | 191   | 1                    |                   |
| No communication with doctors                   | 146   | 0.89 (0.45 - 1.78), 0.7412 | 125   | 0.74 (0.41 - 1.33), 0.3151 |
| Recommended                                     | 63    | 5.84 (2.81 - 12.14), < 0.0001 | 82    | 5.89 (3.17 - 10.95), < 0.0001 |
| Not recommended                                 | 66    | 0.54 (0.17 - 1.68), 0.2867 | 62    | 0.23 (0.07 - 0.71), 0.0104 |
| Chemotherapy = yes                              |       |                      | Chemotherapy = no |                      | 0.331             |
| Indefinite suggestion                           | 246   | 1                    | 154   | 1                    |                   |
| No communication with doctors                   | 188   | 0.69 (0.37 - 1.27), 0.2288 | 83    | 0.81 (0.41 - 1.60), 0.5405 |
| Recommended                                     | 94    | 6.79 (3.62 - 12.74), < 0.0001 | 51    | 3.19 (1.51 - 6.73), 0.0024 |
| Not recommended                                 | 95    | 0.41 (0.15 - 1.16), 0.0927 | 33    | 0.23 (0.06 - 0.88), 0.0320 |
| Yearly personal income ≥ 50,000                 |       |                      | Yearly personal income < 50,000 |                      | 0.927             |
| Indefinite suggestion                           | 216   | 1                    | 184   | 1                    |                   |
| No communication with doctors                   | 152   | 0.72 (0.41 - 1.29), 0.2750 | 119   | 0.88 (0.43 - 1.80), 0.7174 |
| Recommended                                     | 100   | 5.68 (3.21 - 10.05), < 0.0001 | 45    | 5.66 (2.44 - 13.14), < 0.0001 |
| Not recommended                                 | 66    | 0.28 (0.09 - 0.84), 0.0234 | 62    | 0.45 (0.13 - 1.48), 0.1868 |
| Vaccination suggestion from around people       |       |                      |                   |                      |                   |
| Age dichotomous                                 |       |                      |                   |                      | 0.600             |
| No suggestion                                   | 205   | 1                    | 229   | 1                    |                   |
| Recommended                                     | 141   | 12.58 (6.36 - 24.88), < 0.0001 | 188   | 12.85 (7.01 - 23.56), < 0.0001 |
| Not recommended                                 | 89    | 0.90 (0.32 - 2.55), 0.8409 | 92    | 0.41 (0.12 - 1.46), 0.1687 |
| Time after surgery = short                      |       |                      | Time after surgery = long |                      | 0.853             |
| No suggestion                                   | 217   | 1                    | 216   | 1                    |                   |
| Recommended                                     | 149   | 13.90 (6.30 - 30.67), < 0.0001 | 179   | 11.78 (6.72 - 20.65), < 0.0001 |
| Not recommended                                 | 102   | 0.56 (0.14 - 2.21), 0.4052 | 77    | 0.68 (0.26 - 1.79), 0.4343 |
| Axillary lymph node dissection = yes            |       |                      | Axillary lymph node dissection = no |                      | 0.241             |
| No suggestion                                   | 235   | 1                    | 199   | 1                    |                   |
| Recommended                                     | 142   | 8.27 (4.38 - 15.64), < 0.0001 | 187   | 17.19 (9.15 - 32.30), < 0.0001 |
| Not recommended                                 | 107   | 0.40 (0.11 - 1.44), 0.1607 | 74    | 0.97 (0.36 - 2.63), 0.9491 |
| Chemotherapy = yes                              |       |                      | Chemotherapy = no |                      | 0.907             |
| No suggestion                                   | 302   | 1                    | 132   | 1                    |                   |
| Recommended                                     | 191   | 12.16 (6.72 - 22.02), < 0.0001 | 138   | 12.77 (6.09 - 26.80), < 0.0001 |
| Not recommended                                 | 130   | 0.59 (0.21 - 1.66), 0.3166 | 51    | 0.84 (0.25 - 2.84), 0.7794 |
Table 4. Effect Size of External Supports on COVID-19 Vaccination in Prespecified and Exploratory Subgroups - (continued)

| Variables | No. | OR (95% CI), P-value | No. | OR (95% CI), P-value | P for interaction |
|-----------|-----|----------------------|-----|----------------------|------------------|
| Yearly personal income ≥ 50,000 | Yearly personal income < 50,000 | | | | 0.736 |
| No suggestion | 235 | 1 | 199 | 1 | |
| Recommended | 202 | 13.78 (7.73 - 24.57), < 0.0001 | 127 | 10.47 (5.20 - 21.08), < 0.0001 | |
| Not recommended | 97 | 0.79 (0.30 - 2.10), 0.6396 | 84 | 0.45 (0.12 - 1.70), 0.2375 | |

Calls for vaccination by the residents' committee or employer

| Age dichotomous | Age = low | Age = high | 0.421 |
|----------------|-----------|------------|-------|
| Yes | 293 | 1 | 298 | 1 | |
| No vaccinal notice | 87 | 0.37 (0.18 - 0.79), 0.0104 | 150 | 0.19 (0.10 - 0.38), < 0.0001 | |
| No | 55 | 0.12 (0.03 - 0.53), 0.0050 | 61 | 0.16 (0.05 - 0.46), 0.0008 | |
| Time after surgery = short | Time after surgery = long | | | 0.283 |
| Yes | 282 | 1 | 308 | 1 | |
| No vaccinal notice | 115 | 0.18 (0.07 - 0.44), 0.0002 | 120 | 0.26 (0.14 - 0.48), < 0.0001 | |
| No | 71 | 0.05 (0.01 - 0.36), 0.0034 | 44 | 0.22 (0.08 - 0.61), 0.0036 | |
| Axillary lymph node dissection = yes | Axillary lymph node dissection = no | | | 0.331 |
| Yes | 274 | 1 | 317 | 1 | |
| No vaccinal notice | 140 | 0.28 (0.13 - 0.58), 0.0006 | 97 | 0.18 (0.08 - 0.37), < 0.0001 | |
| No | 70 | 0.23 (0.08 - 0.69), 0.0090 | 46 | 0.07 (0.01 - 0.29), 0.0004 | |
| Chemotherapy = yes | Chemotherapy = no | | | 0.801 |
| Yes | 370 | 1 | 221 | 1 | |
| No vaccinal notice | 165 | 0.30 (0.16 - 0.58), 0.0004 | 72 | 0.21 (0.09 - 0.49), 0.0003 | |
| No | 88 | 0.15 (0.05 - 0.45), 0.0007 | 28 | 0.15 (0.03 - 0.69), 0.0150 | |
| Yearly personal income ≥ 50,000 | Yearly personal income < 50,000 | | | 0.932 |
| Yes | 367 | 1 | 224 | 1 | |
| No vaccinal notice | 107 | 0.23 (0.12 - 0.46), < 0.0001 | 130 | 0.25 (0.12 - 0.54), 0.0004 | |
| No | 60 | 0.12 (0.04 - 0.40), 0.0006 | 56 | 0.17 (0.05 - 0.60), 0.0059 | |

Above model adjusted for age; time after surgery; surgical method; axillary lymph node dissection; breast reconstruction surgery; anti-HER2 therapy; chemotherapy; endocrinotherapy; radiotherapy; neoadjuvant therapy; undergoing treatment; recurrence of breast cancer before vaccination; personal COVID-19 history; educational level; employment; influenza vaccination history; yearly personal income; marital status; region of living in China; place of residence. In each case, the model is not adjusted for the stratification variable. OR: odds ratio; CI: confidence interval; HER2: human epidermal growth factor receptor type 2.
Table 5. Recognitions of Breast Cancer Patients Regarding COVID-19 Vaccination

| Query                                                                 | Unvaccinated | Vaccinated | OR (95% CI)       | P-value |
|-----------------------------------------------------------------------|--------------|------------|-------------------|---------|
| Do you believe COVID-19 vaccination may cause special side effect to breast cancer patients? | 730          | 214        | 1.17 (1.01 - 1.33) | < 0.001 |
| I don’t know                                                          | 592 (81.10%) | 98 (45.79%)|                   |         |
| No                                                                    | 53 (7.26%)   | 112 (52.34%)|                   |         |
| Yes                                                                   | 85 (11.64%)  | 4 (1.87%)  |                   |         |
| Do you believe breast cancer patients can be inoculated with COVID-19 vaccine? |              |            | 0.73 (0.57 - 0.89) | < 0.001 |
| No                                                                    | 284 (38.90%) | 53 (24.77%)|                   |         |
| Depend on current treatment                                           | 189 (25.89%) | 108 (50.47%)|                   |         |
| I don’t know                                                          | 246 (33.70%) | 33 (15.42%)|                   |         |
| Yes                                                                   | 11 (1.51%)   | 20 (9.35%) |                   |         |
| Do you believe the necessity of COVID-19 vaccination in China is strong or weak? |              |            | 0.40 (0.25 - 0.55) | < 0.001 |
| Strong                                                                | 580 (79.45%) | 199 (92.99%)|                   |         |
| Weak                                                                  | 150 (20.55%) | 15 (7.01%)  |                   |         |
| Do you believe vaccination may lead to recurrence of breast cancer?   |              |            | 1.02 (0.86 - 1.18) | < 0.001 |
| I don’t know                                                          | 572 (78.36%) | 74 (34.58%) |                   |         |
| No                                                                    | 147 (20.14%) | 139 (64.95%)|                   |         |
| Yes                                                                   | 11 (1.51%)   | 1 (0.47%)  |                   |         |
| Do you believe the COVID-19 vaccine is safe?                          |              |            | 0.74 (0.59 - 0.90) | < 0.001 |
| Yes                                                                   | 355 (48.63%) | 175 (81.78%)|                   |         |
| No or I don’t know                                                    | 375 (51.37%) | 39 (18.22%) |                   |         |

COVID-19: coronavirus disease 2019; OR: odds ratio; CI: confidence interval.
believed in the need for vaccinations against COVID-19 in China to be strong. We found recognitions regarding the COVID-19 vaccine showed different patterns between vaccinated and unvaccinated participants (Table 5).

**Discussion**

Previous surveys studied factors influencing attitudes on COVID-19 vaccination among the general populations and showed that 71.5% of participants would be likely to take the COVID-19 vaccine [18]. Only two studies have reported attitudes and factors associated with COVID-19 vaccine hesitancy in the special population of those who are patients with malignancy. One study from Mexico reported that 12.76% of breast cancer patients had received COVID-19 vaccination, 57.67% were willing to be vaccinated immediately [14], and another study determined the rate of willingness to get vaccinated was 60.3% [19]. However, people’s willingness to receive the COVID-19 vaccine might not be a good predictor of acceptance, while decisions regarding COVID-19 vaccination are multifactorial and can shift over time. In the present study, only 26.87% of patients who received notice of COVID-19 vaccination were vaccinated.

Chinese cases of breast cancer account for nearly 20% of the world cases in 2020 according to the WHO. Considering the national conditions of COVID-19 prevention and control in China, we evaluated the relationship between external support and COVID-19 vaccination among breast cancer patients. As shown in the fully adjusted model, the present study is the first to suggest a strong association between external support (vaccination suggestions from surgeons or oncologists, vaccination suggestions from associated people, and calls for vaccination by the residents’ committees or employers) and COVID-19 vaccination in patients with malignancy, with these results remaining stable in subgroup analyses. Furthermore, two out of these three factors can be easy to intervene. Positive vaccination suggestions from surgeons or oncologists and more appeals by the residents’ committees or employers would contribute to increased COVID-19 vaccination rates in patients with breast cancer.

Similar to previous studies [14, 18, 20, 21], the present study shows that patients with higher personal income and higher previous influenza vaccinations prefer to take the COVID-19 vaccine. In addition, this is the first study to adjust for potential confounding factors of patient treatment methods. We found that there was a lower vaccination rate in patients with a shorter period after surgery who underwent ALND, chemotherapy and radiotherapy. More patients undergoing only endocrine therapy and no adjuvant treatment are vaccinated than patients undergoing other treatments and/or combined treatments.

Additionally, patient education is another factor associated with vaccination. Our findings suggest that even if most participants agree that it is necessary for COVID-19 vaccination, concerns including side effects specific to breast cancer patients, safety of the COVID-19 vaccine, and potential for recurrence of breast cancer may be potential factors that hinder them from COVID-19 vaccination.

The present study has several strengths. First, this is the first study reporting that external support is associated with COVID-19 vaccination in breast cancer patients. Second, we used a large nationally representative sample of breast cancer patients in China, therefore allowing the generation of our findings in China. Third, one important feature of these external supports is that these factors are intervenable, thus improving their clinical value. Fourth, strict statistical adjustment was used to minimize potential confounding factors, including both sociodemographic and clinical characteristics, while previous studies only considered sociodemographic factors. Despite the cross-sectional nature of this study, we provide needed evidence to understand factors associated with COVID-19 vaccination among breast cancer patients in China.

**Conclusions**

Overall, we found that most of the breast cancer patients had not completed their COVID-19 vaccinations. We identified strong associations between external support (vaccination suggestions from surgeon/oncologist and associated people and calls for vaccinations by the residents’ committees or employers) and COVID-19 vaccination. Even if most participants agree that it is necessary to finish COVID-19 vaccination, personal concerns and insufficient recognition regarding COVID-19 vaccination remain as obstacles for breast cancer patients. Future interventions regarding these factors and improving publicity and patient education regarding the COVID-19 vaccine might prove helpful.

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**Conflict of Interest**

The authors declare no conflict of interest.

**Author Contributions**

XYW, QL, WXZ, KXY, YF, and JW were involved in the conception, design, or planning of the study. TW and NCW were involved in the analysis of the data. XYW, QL, WXZ, TW, NCW, ZZW were involved in the acquisition of the data. XYW, QL, WXZ, XYK, YF and JW were involved in the in-
terpretation of the results. XYW, QL, WXZ, XYK, YF and JW were involved in drafting the manuscript. All authors reviewed or revised the manuscript for important intellectual content, approved the final version of the manuscript, and are accountable for the work.

Data Availability

The authors declare that all supporting data are included in the manuscript. Additional data are available upon reasonable request to corresponding author.

Abbreviations

COVID-19: coronavirus disease 2019; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; WHO: World Health Organization; STROBE: Strengthening the Reporting of Observational Studies in Epidemiology

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