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# Patient-reported Outcomes of Patients With Breast Cancer During the COVID-19 Outbreak in the Epicenter of China: A Cross-sectional Survey Study

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## Abstract

**During the coronavirus disease 2019 (COVID-19) outbreak in China, fear about COVID-19, together with worry about progression of cancer, caused strong emotional stress in patients with cancer. We evaluated patient-reported outcome in 658 patients with breast cancer (BC) and survivors recruited from multiple BC centers in Hubei Province using 4 standardized assessment scales. Multivariable logistic regression analysis was used to identify potential affecting factors on mental health outcomes. High rates of anxiety, depression, distress, and insomnia were observed in patients with BC during the COVID-19 outbreak. Based on our results, living in Wuhan, poor general condition by self-identification, shorter duration after BC diagnosis, aggressive BC molecular subtypes, metastatic BC clinical stage, treatment discontinuation, central venous catheter flushing delay, or close contact with patients with COVID-19 are associated risk factors for poorer psychological status. Special attention should be paid to the psychological status of patients with BC, especially those with poor general condition, treatment discontinuation, aggressive molecular subtypes, and metastatic BC.**

**Introduction:** We aimed to analyze the psychological status in patients with breast cancer (BC) in the epicenter of the coronavirus disease 2019 (COVID-19) pandemic. **Patients and Methods:** A total of 658 individuals were recruited from multiple BC centers in Hubei Province. Online questionnaires were conducted, and these included demographic information, clinical features, and 4 patient-reported outcome scales (Generalized Anxiety Disorder Questionnaire [GAD-7], Patient Health Questionnaire [PHQ-9], Insomnia Severity Index [ISI], and Impact of Events Scale-Revised [IES-R]). Multivariable logistic regression analysis was designed to identify potential factors on mental health outcomes. **Results:** Questionnaires were collected from February 16, 2020 to February 19, 2020, the peak time point of the COVID-19 outbreak in China. Of patients with BC, 46.2% had to modify planned necessary anti-cancer treatment during the outbreak. Severe anxiety and severe depression were reported by 8.9% and 9.3% of patients, respectively.

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Severe distress and insomnia were reported by 20.8% and 4.0% of patients, respectively. Multivariable logistic regression analysis demonstrated poor general condition, shorter duration after BC diagnosis, aggressive BC molecular subtypes, and close contact with patients with COVID-19 as independent factors associated with anxiety. Poor general condition and central venous catheter flushing delay were factors that were independently associated with depression. In terms of insomnia, poor general condition was the only associated independent factor. Poor physical condition and treatment discontinuation were underlying risk factors for distress based on multivariable analysis. **Conclusion:** High rates of anxiety, depression, distress, and insomnia were observed in patients with BC during the COVID-19 outbreak. Special attention should be paid to the psychological status of patients with BC, especially those with poor general condition, treatment discontinuation, aggressive molecular subtypes, and metastatic BC.

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**Keywords:** Breast cancer, COVID-19, Epicenter, Psychological status

## Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was initially identified in patients in Wuhan, Hubei Province, in December, 2019.<sup>1</sup> The pandemic disease caused by this virus was named by the World Health Organization (WHO) as coronavirus disease 2019 (COVID-19).<sup>2</sup> In late January of 2020, Chinese authorities placed a lockdown on Hubei Province to contain this disease.<sup>1,3</sup> In addition, nearly all the medical resources were organized and more than 40,000 healthcare workers from other cities were dispatched to work together in Wuhan and other cities of Hubei.<sup>4</sup> These measures and sacrifices have resulted in decreased rates of transmission and better outcomes in China.<sup>5</sup>

Studies from China have demonstrated that patients with cancer are significantly more likely to experience worse outcomes to COVID-19 infection,<sup>6,7</sup> which has led to a re-evaluation of the risk/benefit balance in cancer therapies.<sup>8,9</sup> Indeed, almost all the patients with cancer in Wuhan, the epicenter of COVID-19 in China, had to discontinue or delay their normal anticancer therapy owing to lockdown policies, limited medical resources, and the predicted increased risk of infection at the initial time of the outbreak. After the outbreak was under control, modified therapeutic regimens were recommended, and online prescriptions were available for patients with cancer because nearly all the cancer clinics were still not active. These changes can lead to significant increases in the psychological burden of patients with cancer, especially for those with breast cancer (BC).

BC is the most common cancer among women worldwide. The mean age of patients with BC in China is 45 to 55 years, which is considerably younger than for Western women, according to epidemiologic data from China.<sup>10</sup> A diagnosis of BC can result in long-lasting mental health effects on women,<sup>11</sup> such as physical hardship, traumatic events during treatment, fear of recurrence, etc. Furthermore, mental illness can further exacerbate the quality of life of patients with BC, resulting in worse BC outcomes.<sup>12</sup> During the COVID-19 crisis, patients with BC in Hubei Province were exposed to a very high risk of COVID-19 infection and interruptions of standard medical care. Therefore, it is crucial to understand quality of life factors so they may be addressed during this outbreak and hopefully result in less stress for patients with BC.

In this study, we conducted a survey to measure the psychological status of patients with BC and survivors and to identify potential affecting factors in the epicenter of COVID-19 in China at the peak time point of the crisis.

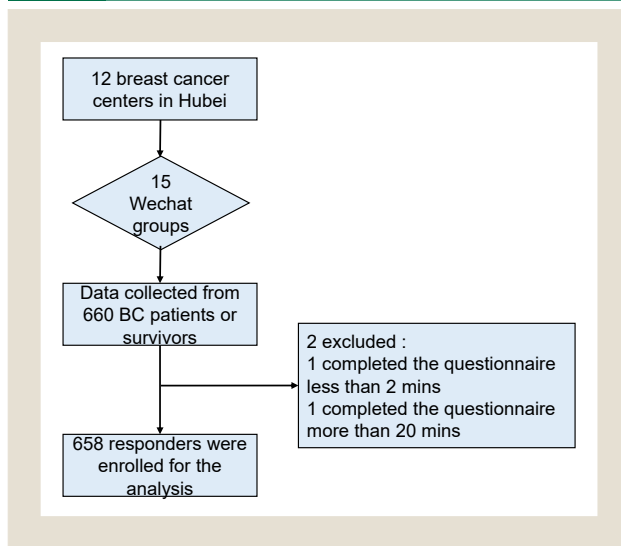
## Patients and Methods

### Patients

Patients with BC and survivors from the epicenter of COVID-19 in China, Hubei Province, were enrolled for this survey study. The study was sponsored by the BC center in Renmin Hospital of Wuhan University and was supported by several BC centers in Hubei province. All the enrolled patients signed digital informed consent before accessing the questionnaire online, consisting of a series of questions including demographic characteristics, clinical features of BC, current treatment, and patient-reported outcomes (PROs) using 4 validated psychological assessment scales. The 4 scales included Generalized Anxiety Disorder Questionnaire (GAD-7), Patient Health Questionnaire (PHQ-9), Insomnia Severity Index (ISI), and Impact of Events Scale-Revised (IES-R). Patients with BC were asked to answer all the questions anonymously through Wechat software, a popular social media platform in China. The local Wechat communication groups were set up originally for patients with BC to connect with their doctors for daily medical consultant and support. The questionnaires were issued to each local WeChat group for patients with BC from February 16 to 19, 2020. Data were collected from 660 patients with BC automatically after the questionnaires were returned. Two participants who completed the entire questionnaire less than 2 minutes or more than 20 minutes were excluded. Therefore, after the evaluation of questionnaires for eligibility, 658 participants were enrolled for analysis. The flowchart of the patient selection is shown in [Figure 1](#). This study protocol was approved by the Institutional Ethics Committee in Renmin Hospital of Wuhan University.

### Patient-reported Outcomes

PROs of patients with BC in the epicenter of the COVID-19 outbreak in China were evaluated using 4 Chinese versions of validated questionnaires.<sup>13-16</sup> GAD-7, a 7-item self-reported scale, was used to briefly measure anxiety disorders of the patients.

**Figure 1** The Flowchart of the Recruitment of Participants Enrolled for the Analysis

Abbreviation: BC = breast cancer.

Evaluation scores of 0, 1, 2, and 3 for 7 items represent the response categories of 'not at all,' 'several days,' 'more than half the days,' and 'nearly every day,' respectively. The cutoff point of the sum score for mild is a score of 5; for moderate is 10 and for severe is 15. Depression was measured by PHQ-9, a 9-question instrument, to screen for the presence and severity of depression. Responses of each question range from "0" (not at all) to "3" (nearly every day). Depression severity was classified into none (0-4), mild (5-9), moderate (10-14), and severe (> 15) according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition criteria. ISI is a self-assessment tool measuring the patient's perception of both nocturnal and diurnal symptoms of insomnia. It has 7 questions. A 4-point Likert scale is used to rate each item (eg, 0 = none, 4 = very severe), yielding a total score ranging from 0 to 28. The total score is interpreted as follows: absent of insomnia (0-7); sub-threshold insomnia (8-14); moderate insomnia (15-21); and severe insomnia (22-28). The IES-R, also a self-reported questionnaire, yields a total score (ranging from 0 to 88). It was used to measure distress symptoms caused by the COVID-19 outbreak. The IES-R and subscale scores can also be calculated for the intrusion, avoidance, and hyperarousal status. These PRO tools have established sensitivity, specificity, reliability, and factorial and procedural validity.

### Statistical Analysis

All statistical analysis were carried out with R software (version 3.5.1). Based on nonnormal distribution, the nonparametric Wilcoxon rank-sum test and Kruskal-Wallis test were used to compare the severity of each symptom among 2 or more groups. The univariable and multivariable logistic regression models were used to identify potential risk factors affecting psychological status for patients with BC. The association between risk factors and PROs are presented as odds ratios (ORs) and 95% confidence intervals (CIs). The statistical significance level was set at  $P < .05$ , and all tests were 2-tailed.

## Results

### Baseline Characteristics of Patients With BC in the Center of COVID-19 Outbreak in China

After excluding 2 patients who completed the entire questionnaire in less than 2 minutes or more than 20 minutes, a total of 658 patients with BC were enrolled in this analysis, including 247 (37.5%) cases from Wuhan (the epicenter of the outbreak in China), and 411 (62.5%) cases from cities outside Wuhan in Hubei Province. The baseline characteristics of patients with BC are shown in Table 1. The majority of the patients were from cities (485/658; 73.8%), younger than 55 years old (516/658; 78.4%), no bachelor's or higher degree (515/658; 78.3%), married (584/658; 88.9%), and annual income less than \$15,000 (554/658; 84.2%). Most of the patients presented with good or average physical condition by self-identification (496/658; 75.4%), had early stage BC (392/658; 59.6%), reported a history of prior breast surgery (628/658; 95.4%), and were recommend to undergo BC treatment during COVID-19 (474/658; 72.0%). Of 474 patients with BC recommended to undergo BC treatment, 219 (46.2%) patients had to discontinue or modify their planned necessary anticancer treatments, including systemic therapy and local therapy, during the outbreak. It also led to delays in the central venous catheter (CVC) flushing of over 4 weeks in 40.6% (164/276) of patients with implanted CVCs. The efficacy of compromised anti-cancer therapeutic regimens (519/966; 53.7%) was the main concern among these patients with BC, followed by the fear about infection of COVID-19 (191/966; 19.8%).

### PRO Measurements of Patients With BC

The mean scores were  $6.01 \pm 5.35$  and  $5.80 \pm 5.66$  for the GAD-7 and PHQ-9, respectively (Table 2). There were 34.0%, 13.3%, and 8.9% patients categorized into the mild, moderate, and severe anxiety categories, respectively. There were 25.2%, 12.8%, and 9.3% patients who reported mild, moderate, and severe depression, respectively. The mean scores were  $8.66 \pm 6.29$  and  $28.17 \pm 18.23$  for the ISI and IES-R, respectively (Table 2). There were 36.2%, 12.9%, and 4.0% patients, respectively, who reported mild, moderate, and severe insomnia. There were 30.7%, 31.5%, and 20.8% patients who described mild, moderate, and severe distress symptoms. Subscale scores of IES-R were calculated to evaluate the intrusion, avoidance, and hyperarousal status (Table 2).

Patients with Wuhan exposure, poor general condition by self-identification, treatment discontinuation, and who had metastatic BC were more likely to report experiencing severe symptoms of anxiety, depression, insomnia, and distress (Table 3; Supplemental Table 1 and Supplemental Figure 1 in the online version). Patients with BC with Wuhan exposure ( $P = .001$ ), poor general condition by self-identification ( $P < .001$ ), treatment discontinuation ( $P < .001$ ), metastatic BC ( $P = .018$ ), CVC flushing delay exceeding 4 weeks ( $P = .002$ ), and BC diagnosis within 1 year ( $P = .029$ ) were found to have an association with symptoms of anxiety. In addition, patients with Wuhan exposure ( $P = .010$ ), poor general physical condition ( $P < .001$ ), treatment discontinuation ( $P < .001$ ), and metastatic BC ( $P < .001$ ), close contact to a patient with COVID-19 ( $P = .027$ ), CVC flushing delay exceeding 4 weeks ( $P = .004$ ), and BC diagnosis within 1 year ( $P = .034$ ) tended to have an association with symptoms of depression. The patients with BC who had poor

# Psychological Status of Patients With BC During COVID-19

**Table 1** Patients Characteristics

Characteristic	N (%) <sup>a</sup>
No. patients	658
Wuhan exposure	
Yes	247 (37.5)
No	411 (62.5)
Residence location	
Urban	485 (73.8)
Rural	173 (26.2)
Age, y	
<40	152 (23.1)
40-54	364 (55.3)
55-64	123 (18.7)
≥65	19 (2.9)
Highest level of education	
Elementary school or less	44 (6.7)
Middle school	184 (28.0)
High school	287 (43.6)
Bachelor's degree or higher	143 (21.7)
Annual income, US dollars	
<\$7500	351 (53.3)
\$7500-\$15,000	203 (30.9)
\$15,000-\$43,000	95 (14.4)
>\$43,000	9 (1.4)
Marital status	
Unmarried	19 (2.9)
Married	584 (88.9)
Divorced/widowed	55 (8.2)
General health condition by self-identification	
Well	269 (40.9)
Average	227 (34.5)
Poor	162 (24.6)
BC diagnosis time	
Within 1 year	296 (45.0)
1-5 years	313 (47.6)
More than 5 years	49 (7.4)
Stage of BC	
Early	392 (59.6)
Metastatic	115 (17.5)
Unknown	151 (22.9)
Molecular subtype of BC	
TNBC	127 (19.3)
Luminal	177 (26.9)
HER2	196 (29.8)
Unknown	158 (24.0)
History of BC surgery	
Yes	628 (95.4)
No	30 (4.6)
Recommend anti-cancer therapy	
Yes	474 (72.0)
No	184 (28.0)

**Table 1** Continued

Characteristic	N (%) <sup>a</sup>
Discontinued anticancer therapy <sup>b</sup>	
Endocrine therapy	168 (32.9)
Targeted therapy	105 (20.6)
Chemotherapy	133 (26.1)
Radiotherapy	27 (5.3)
Traditional Chinese medicine	77 (15.1)
Duration of therapy interruption <sup>c</sup>	
Less than 2 weeks	135 (28.5)
2-4 weeks	102 (21.5)
Undefined	131 (27.6)
Unknown	88 (18.6)
No therapy discontinued	18 (3.8)
CVC maintenance	
Not delayed	112 (17.0)
Delayed	164 (24.9)
No CVC	382 (58.1)
Diagnosis of COVID-19	
Yes	1 (0.2)
No	637 (96.8)
Unknown	20 (3.0)
Close contact with patient with COVID-19	
Yes	48 (7.3)
No	561 (85.3)
Unknown	49 (7.4)
Worried about <sup>d</sup>	
Changed BC therapeutic regimen	53 (5.5)
Delayed BC therapeutic regimen	266 (27.5)
Suboptimal therapy for BC	200 (20.7)
Infection of COVID-19	191 (19.8)
Discrimination	21 (2.2)
Other	101 (10.4)
None	134 (13.9)

Abbreviations: BC = breast cancer; COVID-19 = coronavirus disease 2019; CVC = central venous catheter; HER2 = human epidermal growth factor receptor 2; TNBC = triple negative breast cancer.

<sup>a</sup>Percentages are weighted to account for the sample size (n = 658).

<sup>b</sup>Percentages are weighted to account for the total responder size (n = 510).

<sup>c</sup>Percentages are weighted to the size of the group of patients recommended for anti-cancer therapy (n = 474).

<sup>d</sup>Percentages are weighted to account for the size of the total responder group (n = 966).

general condition ( $P < .001$ ), treatment discontinuation ( $P = .031$ ), and metastatic BC ( $P < .001$ ) were more likely to have severe insomnia. Furthermore, patients with Wuhan exposure ( $P = .026$ ) and who had poor general condition ( $P < .001$ ), treatment discontinuation ( $P = .031$ ), metastatic BC ( $P = .004$ ), and close contact with a patient with COVID-19 ( $P = .004$ ) had a higher risk of distress during the outbreak.

### Independent Risk Factors for Specific PRO Measurement

Univariable logistic regression analysis showed that patients with Wuhan exposure ( $P = .014$ ), poor general condition by self-identification ( $P = .008$ ), less than 4 months after BC diagnosis

**Table 2** Overview of the Scores on the 4 Scales Including 3 Subscales of IES-R Among Patients With BC

Scales	Mean ± SD	Min, Max	Median	IQR
GAD-7	6.01 ± 5.35	0, 21	5	1-9
PHQ-9	5.80 ± 5.66	0, 27	4	1-9
ISI	8.66 ± 6.29	0, 28	8	4-13
IES-R total	28.17 ± 18.23	0, 88	27	15-41
Intrusion	10.41 ± 6.81	0, 32	10	6-15
Avoidance	10.28 ± 6.94	0, 32	10	5-15
Hyperarousal	7.47 ± 5.35	0, 24	7	3-11

Abbreviations: BC = breast cancer; GAD-7 = Generalized Anxiety Disorder Questionnaire; IES-R = Impact of Events Scale-Revised; IQR = interquartile range; ISI = Insomnia Severity Index; PHQ-9 = Patient Health Questionnaire; SD = standard deviation.

( $P = .003$ ), aggressive BC molecular subtypes ( $P = .014$ ), treatment discontinuation ( $P = .003$ ), CVC flushing delay exceeding 4 weeks ( $P = .032$ ), and close contact with a patient with COVID-19 ( $P = .006$ ) were more likely to report moderate and severe anxiety symptoms (see [Supplemental Figure 2A](#) in the online version). In addition, patients with BC with poor general condition ( $P = .010$ ), metastatic BC ( $P = .010$ ), treatment discontinuation ( $P < .001$ ), and CVC flushing delay exceeding 4 weeks ( $P < .001$ ) had a higher risk of falling into moderate or severe depression (see [Supplemental Figure 2B](#) in the online version). Furthermore, patients with poor general condition ( $P = .003$ ), treatment discontinuation ( $P = .033$ ), or CVC flushing delay exceeding 4 weeks ( $P = .028$ ) were more likely to have moderate or severe insomnia (see [Supplemental Figure 2C](#) in the online version). In addition, patients with BC with Wuhan exposure ( $P = .037$ ), poor general condition ( $P = .021$ ), metastatic BC ( $P = .024$ ), and with treatment discontinuation ( $P = .004$ ) might harbor a greater chance to present with distress (see [Supplemental Figure 2D](#) in the online version). With multivariate logistic regression analysis, poor general condition ( $P = .006$ ), less than 4 months after BC diagnosis ( $P = .010$ ), aggressive BC molecular subtypes ( $P = .026$ ), and close contact with patients with COVID-19 ( $P = .005$ ) were independent affecting risk factors for moderate or severe anxiety ([Figure 2A](#)). In addition, poor general condition ( $P = .031$ ) and CVC flushing interval exceeding 4 weeks ( $P = .005$ ) were shown as independently associated factors with moderate or severe depression based on multivariate logistic regression analysis ([Figure 2B](#)). In terms of moderate or severe insomnia, poor general condition ( $P = .008$ ) was the only independent affecting factor ([Figure 2C](#)). Poor physical condition ( $P = .028$ ) and treatment discontinuation ( $P = .046$ ) were independent risk markers for distress based on the multivariate analysis ([Figure 2D](#)).

## Discussion

Wuhan, a metropolis of 11 million residents in central China's Hubei Province, became the epicenter of COVID-19 in January 2020. Rapidly rising numbers of infected cases put the local health care system under tremendous stress,<sup>3</sup> occupying and affecting the medical needs for patients with non-COVID-19, especially for patients with cancer. In addition, patients with cancer were exposed to a higher risk of infection with COVID-19, and experienced

worse outcomes after infection during the COVID-19 epidemic.<sup>6,7</sup> Under this unique circumstance, patients with cancer faced COVID-19 infections and interruption of cancer treatment, resulting in significant mental stress. In this study, we investigated PROs in patients with BC in the epicenter at the peak timepoint of the COVID-19 outbreak.

We found a wide range of abnormal quality of life metrics that patients with BC experienced, including stress, anxiety, fear, depression, and distress. Approximate 10% of patients with BC showed severe depression and anxiety. Over one-fifth of patients with BC presented severe distress symptoms during the COVID-19 outbreak. The scores in our study were significantly higher than patients with BC under normal conditions in previous studies, which showed about only 3.5% patients reported severe anxiety and depression,<sup>17-21</sup> indicating an additional increase of mental stress on the patients with BC by the COVID-19 crisis.

We identified factors affecting PROs of the patients with BC during the COVID-19 pandemic that may help to make effective measures to reduce stress for these patients. Based on our results, living in Wuhan, poor general condition by self-identification, shorter duration after BC diagnosis, aggressive BC molecular subtypes, metastatic BC clinical stage, treatment discontinuation, CVC flushing delay, or close contact with patients with COVID-19 are associated risk factors for poorer psychological status. Notably, poor general condition, namely with comorbidities, was the only overlapping independent affecting factor for all 4 PRO metrics. Several studies have found that patients with BC with comorbidities have worse outcome than patients without comorbidities under normal conditions.<sup>22,23</sup> In addition, the death rate among patients with COVID-19 with one or more comorbidities was much higher than those without comorbidities.<sup>24-27</sup> Therefore, patients with BC with comorbidities faced more stress, which can affect their mental health under this unique circumstance, which we demonstrated. Thus more attention should be paid and some effective measures should be taken to reduce the stress during the COVID-19 crisis among patients with comorbidities.

During the outbreak, changes to usual clinical practice for patients with BC were necessary.<sup>28-32</sup> Notably, the efficacy of compromised anti-cancer therapeutic regimens (519/966; 53.7%) was the main concern among these patients with BC, followed by the fear about infection of COVID-19 (191/966; 19.8%). A number of modifications to standard treatment paradigms were implemented. For example, during the outbreak, capecitabine was preferentially prescribed for patients with triple negative BC. Pyrotinib, an oral pan-HER receptor tyrosine kinase inhibitor, which was approved in China, was recommended for human epidermal growth factor receptor 2 (HER2)-positive patients with BC. Several months of neoadjuvant endocrine therapy and delay in surgery was recommended for hormone receptor-positive patients with early BC. In terms of CVC maintenance delay, we opened a special clinic to care for CVC weekly. In addition, we rapidly established and expanded telemedicine efforts through social media, offering outpatient service and prescription or medical consulting. Optimization of physician-to-patient communication was critical for shared decision-making of therapeutic changes.

There are several limitations of our study. There was a possible selection bias for the patients enrolled in this study. Those patients

**Table 3** Severity Categories of Anxiety, Depression, Insomnia, and Distress in Patients With BC

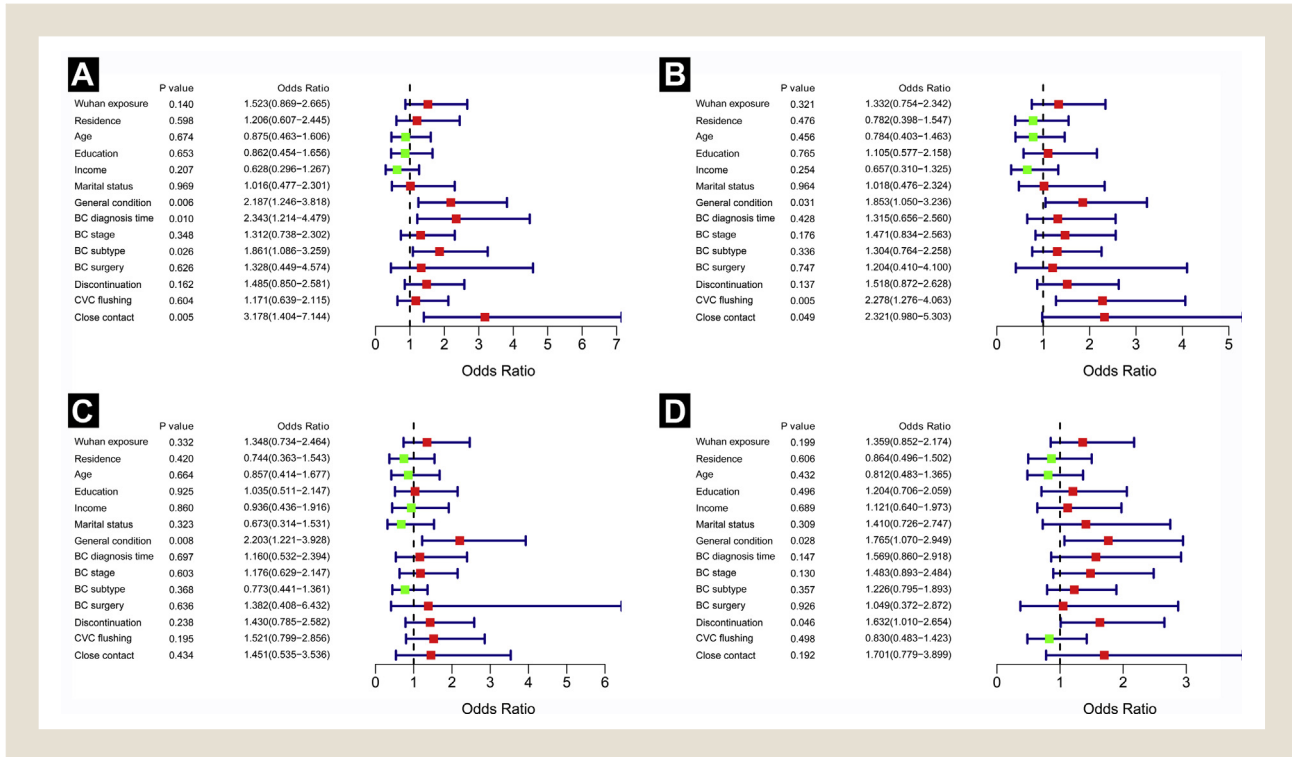
Severity Category	Total, N (%)	Wuhan Exposure			General Condition by Self-identification				Treatment Discontinuation <sup>a</sup>			BC Clinical Stage			
		N (%)		P Value	N (%)			P Value	N (%)		P Value	N (%)			P Value
		Yes	No		Well	Average	Poor		Yes	No		Early	Metastatic	N/A	
GAD-7, anxiety symptoms															
Normal	287 (43.6)	90 (36.4)	197 (47.9)	.001	133 (49.4)	104 (45.8)	50 (30.9)	<.001	119 (41.6)	80 (42.5)	<.001	175 (44.7)	41 (35.7)	71 (47.0)	.018
Mild	224 (34.0)	91 (36.8)	133 (32.4)		93 (34.6)	73 (32.2)	58 (35.8)		103 (36.0)	75 (39.9)		139 (35.4)	40 (34.8)	45 (29.8)	
Moderate	88 (13.4)	39 (15.8)	49 (11.9)		22 (8.2)	34 (15.0)	32 (19.8)		36 (12.6)	21 (11.2)		50 (12.8)	22 (19.1)	16 (10.6)	
Severe	59 (9.0)	27 (11.0)	32 (7.8)		21 (7.8)	16 (7.0)	22 (13.6)		28 (9.8)	12 (6.4)		28 (7.1)	12 (10.4)	19 (12.6)	
PHQ-9, depression symptoms															
Normal	347 (52.7)	118 (47.8)	229 (55.7)	.010	164 (61.0)	124 (54.6)	59 (36.4)	<.001	89 (40.7)	153 (60.0)	<.001	221 (56.4)	43 (37.4)	83 (55.0)	<.001
Mild	166 (25.2)	68 (27.5)	98 (23.8)		60 (22.3)	57 (25.1)	49 (30.2)		62 (28.3)	65 (25.5)		98 (25.0)	34 (29.6)	34 (22.5)	
Moderate	84 (12.8)	32 (13.0)	52 (12.7)		25 (9.3)	27 (11.9)	32 (19.8)		39 (17.8)	25 (9.8)		41 (10.5)	22 (19.1)	21 (13.9)	
Severe	61 (9.3)	29 (11.7)	32 (7.8)		20 (7.4)	19 (8.4)	22 (13.6)		29 (13.2)	12 (4.7)		32 (8.1)	16 (13.9)	13 (8.6)	
ISI, insomnia symptoms															
Normal	309 (47.0)	114 (46.2)	195 (47.4)	.096	160 (59.5)	102 (44.9)	47 (29.0)	<.001	92 (42.0)	131 (51.4)	.031	202 (51.5)	39 (33.9)	68 (45.0)	<.001
Mild	238 (36.2)	86 (34.8)	152 (37.0)		83 (30.9)	82 (36.1)	73 (45.1)		84 (38.4)	89 (34.9)		134 (34.2)	48 (41.7)	56 (37.1)	
Moderate	85 (12.9)	36 (14.6)	49 (11.9)		20 (7.4)	34 (15.0)	31 (19.1)		34 (15.5)	28 (11.0)		43 (11.0)	23 (20.0)	19 (12.6)	
Severe	26 (3.9)	11 (4.4)	15 (3.7)		6 (2.2)	9 (4.0)	11 (6.8)		9 (4.1)	7 (2.7)		13 (3.3)	5 (4.4)	8 (5.3)	
IES-R, distress symptoms															
Normal	112 (17.0)	32 (13.0)	80 (19.5)	.026	59 (21.9)	36 (15.9)	17 (10.5)	<.001	33 (15.1)	47 (18.4)	.031	73 (18.6)	10 (8.7)	29 (19.2)	.004
Mild	202 (30.7)	74 (30.0)	128 (31.1)		80 (29.8)	81 (35.7)	41 (25.3)		59 (26.9)	81 (31.8)		125 (31.9)	34 (29.6)	43 (28.5)	
Moderate	207 (31.5)	84 (34.0)	123 (29.9)		84 (31.2)	64 (28.2)	59 (36.4)		73 (33.3)	83 (32.5)		125 (31.9)	33 (28.7)	49 (32.4)	
Severe	137 (20.8)	57 (23.0)	80 (19.5)		46 (17.1)	46 (20.2)	45 (27.8)		54 (24.7)	44 (17.3)		69 (17.6)	38 (33.0)	30 (19.9)	

P value was calculated using the nonparametric Wilcoxon rank-sum test and Kruskal-Wallis test.

Abbreviation: BC = breast cancer; GAD-7 = Generalized Anxiety Disorder Questionnaire; IES-R = Impact of Events Scale-Revised; ISI = Insomnia Severity Index; N/A = Not provided or not available; PHQ-9 = Patient Health Questionnaire.

<sup>a</sup>Total size is the patients who were recommended for anti-cancer treatment during COVID-19 period: n = 474.

**Figure 2** Forest Plots to Identify Independent Affecting Factors for Anxiety (A), Depression (B), Insomnia (C), and Distress (D) Symptoms Among Patients With BC in the Center of COVID-19 in China Using Multivariable Logistic Regression Analysis. (Interpretations: Wuhan Exposure: Yes vs. No; Residence: Urban vs. Rural; Age:  $\geq 55$  years Old vs.  $\leq 54$  years Old; Education: High School or More vs. Middle School or less; Income:  $\leq \$15,000$  per Year vs.  $> \$15,000$  per Year; Marital Status: Single (including Widowed/Divorced) vs. Married; General Condition by Self-Identification: Poor vs. Well/Average; BC Diagnosis Time:  $\leq 1$  Year vs.  $> 1$  year; BC Stage: Metastatic vs. Early; BC Subtype: TNBC/HER2 vs. Luminal; BC Surgery History: Yes vs. No; Treatment Discontinuation: Yes vs. No; CVC Flushing: Interval Exceeding 4 weeks vs. Interval Within 4 Weeks; Close Contact: Close Contact With Patient With COVID-19 vs. No Close Contact With Patient With COVID-19)



Abbreviations: BC = breast cancer; COVID-19 = coronavirus disease 2019; CVC = central venous catheter; HER2 = human epidermal growth factor receptor 2; TNBC = triple negative breast cancer.

without smartphones or not in the local Wechat groups may not be involved in our survey. In addition, this is a cross-sectional observational study; we need a control cohort to compare the differences of psychological status under different situations and to confirm the effect of COVID-19 in patients with BC. Furthermore, our population was diverse and heterogeneous in terms of disease states, which limits the power to each relevant clinical subgroup.

## Conclusions

In summary, our study indicates that the psychological status of patients with BC deserves more attention during the COVID-19 pandemic. Patients with BC are likely to experience adverse mental well-being. Effective measures should be taken to minimize mental health issues and to provide psychological support.

### Clinical Practice Points

- During the COVID-19 outbreak in China, fear about COVID-19, together with worry about progression of cancer, causes strong

emotional stress in patients with cancer. High rates of anxiety, depression, distress, and insomnia were observed in patients with breast cancer during the COVID-19 outbreak.

- Special attention should be paid to the psychological status of patients with breast cancer, especially those with poor general condition, treatment discontinuation, aggressive molecular subtypes, and metastatic breast cancer.

## Acknowledgments

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## Disclosure

The authors have stated that they have no conflicts of interest.

## Supplemental Data

Supplemental table and figures accompanying this article can be found in the online version at <https://doi.org/10.1016/j.clbc.2020.06.003>.

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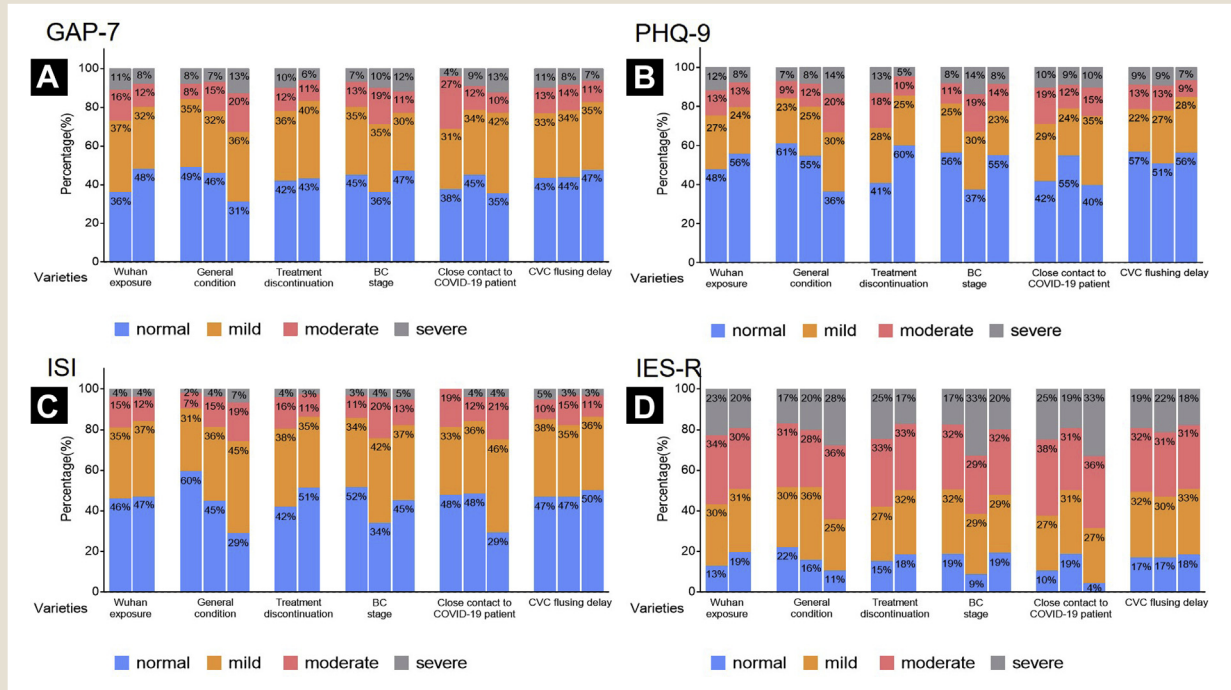
**Supplemental Table 1** Severity Categories of Anxiety, Depression, Insomnia, and Distress in Patients With BC

Severity Category	Total, N (%)	Marital Status			Close Contact With Patient With COVID-19				CVC Flushing				BC Diagnosis Time			Annual Income		
		N (%)		P Value	N (%)			P Value	N (%)			P Value	N (%)		P Value			
		Married	Single <sup>a</sup>		Yes	No	N/A		Delay Over 4 Weeks	Delay Less Than 4 Weeks	No CVC		≤1 Year	>1 Year		≤\$15,000	>\$15,000	
GAD-7, anxiety symptoms																		
Normal	287 (43.6)	255 (43.7)	32 (43.2)	.881	18 (37.5)	252 (44.8)	17 (35.4)	.079	61 (43.4)	45 (43.7)	181 (47.4)	.002	123 (41.6)	164 (45.3)	.029	243 (43.9)	44 (42.3)	.327
Mild	224 (34.0)	199 (34.1)	25 (33.8)		15 (31.2)	189 (33.6)	20 (41.7)		52 (33.3)	38 (34.4)	134 (35.1)		99 (33.4)	125 (34.5)		180 (32.4)	44 (42.3)	
Moderate	88 (13.4)	78 (13.3)	10 (13.5)		13 (27.1)	70 (12.5)	5 (10.4)		26 (13.2)	20 (13.5)	42 (11.0)		39 (13.2)	49 (13.6)		79 (14.3)	9 (8.7)	
Severe	59 (9.0)	52 (8.9)	7 (9.5)		2 (4.2)	51 (9.1)	6 (12.5)		25 (10.1)	9 (8.4)	25 (6.5)		35 (11.8)	24 (6.6)		52 (9.4)	7 (6.7)	
PHQ-9, depression symptoms																		
Normal	347 (52.7)	314 (53.8)	33 (44.6)	.205	20 (41.7)	308 (54.8)	19 (39.6)	.027	80 (56.6)	52 (50.7)	215 (56.3)	.004	150 (50.7)	197 (54.4)	.034	289 (52.2)	58 (55.8)	.393
Mild	166 (25.2)	146 (25.0)	20 (27.0)		14 (29.2)	135 (24.0)	17 (35.4)		26 (21.9)	31 (27.0)	109 (28.5)		72 (24.3)	94 (26.0)		136 (24.5)	30 (28.8)	
Moderate	84 (12.8)	72 (12.3)	12 (16.2)		9 (18.7)	68 (12.1)	7 (14.6)		36 (12.7)	15 (12.8)	33 (8.6)		40 (13.5)	44 (12.1)		74 (13.4)	10 (9.6)	
Severe	61 (9.3)	52 (8.9)	9 (12.2)		5 (10.4)	51 (9.1)	5 (10.4)		22 (8.8)	14 (9.5)	25 (6.6)		34 (11.5)	27 (7.5)		55 (9.9)	6 (5.8)	
ISI, insomnia symptoms																		
Normal	309 (47.0)	278 (47.6)	31 (41.9)	.193	23 (47.9)	272 (48.4)	14 (29.2)	.092	67 (46.9)	51 (47.0)	191 (50.0)	.112	134 (45.3)	175 (48.3)	.220	252 (45.5)	57 (54.8)	.099
Mild	238 (36.2)	214 (36.6)	24 (32.4)		16 (33.3)	200 (35.6)	22 (45.8)		55 (38.2)	45 (35.1)	138 (36.1)		111 (37.5)	127 (35.1)		205 (37.0)	33 (31.7)	
Moderate	85 (12.9)	73 (12.5)	12 (16.2)		9 (18.8)	66 (11.7)	10 (20.8)		34 (9.6)	11 (14.7)	40 (10.5)		41 (13.8)	44 (12.2)		73 (13.2)	12 (11.6)	
Severe	26 (3.9)	19 (3.3)	7 (9.5)		0 (0)	24 (4.3)	2 (4.2)		8 (5.3)	5 (3.2)	13 (3.4)		10 (3.4)	16 (4.4)		24 (4.3)	2 (1.9)	
IES-R, distress symptoms																		
Normal	112 (17.0)	99 (17.0)	13 (17.5)	.920	5 (10.4)	105 (18.7)	2 (4.2)	.004	31 (17.1)	11 (17.0)	70 (18.3)	.056	38 (12.8)	74 (20.4)	.177	92 (16.6)	20 (19.2)	.243
Mild	202 (30.7)	179 (30.6)	23 (31.1)		13 (27.1)	176 (31.3)	13 (27.1)		41 (32.0)	37 (30.0)	124 (32.5)		96 (32.4)	106 (29.3)		170 (30.7)	32 (30.8)	
Moderate	207 (31.5)	188 (32.2)	19 (25.7)		18 (37.5)	172 (30.6)	17 (35.4)		44 (31.6)	43 (31.4)	120 (31.4)		100 (33.8)	107 (29.6)		171 (30.9)	36 (34.6)	
Severe	137 (20.8)	118 (20.2)	19 (25.7)		12 (25.0)	109 (19.4)	16 (33.3)		48 (19.3)	21 (21.6)	68 (17.8)		62 (21.0)	75 (20.7)		121 (21.8)	16 (15.4)	

Supplemental Table 1 Continued																	
Severity category	Total, N (%)	Residence			Age, y			Education			History of BC Surgery			BC Molecular Subtype			
		N (%)		P Value	N (%)		P Value	N (%)		P Value	N (%)		P Value	N (%)			P Value
		Urban	Rural		≤55	>55		Middle School or Less	High School or Higher		Yes	No		TNBC and HER2	Luminal	N/A	
GAD-7, anxiety symptoms																	
Normal	287 (43.6)	212 (43.7)	75 (43.3)	.576	222 (43.0)	65 (45.8)	.645	99 (43.4)	188 (43.7)	.937	274 (43.6)	13 (43.3)	.387	134 (41.4)	75 (42.4)	78 (49.4)	.126
Mild	224 (34.0)	163 (33.6)	61 (35.3)		183 (35.5)	41 (28.9)		76 (33.3)	148 (34.4)		216 (34.4)	8 (26.7)		103 (31.9)	74 (41.8)	47 (29.7)	
Moderate	88 (13.4)	66 (13.6)	22 (12.7)		67 (13.0)	21 (14.8)		30 (13.2)	58 (13.5)		85 (13.6)	3 (10.0)		48 (14.9)	19 (10.7)	21 (13.3)	
Severe	59 (9.0)	44 (9.1)	15 (8.7)		44 (8.5)	15 (10.5)		23 (10.1)	36 (8.4)		53 (8.4)	6 (20.0)		38 (11.8)	9 (5.1)	12 (7.6)	
PHQ-9, depression symptoms																	
Normal	347 (52.7)	258 (53.2)	89 (51.4)	.822	272 (52.7)	75 (52.8)	.968	129 (56.6)	218 (50.7)	.135	332 (52.9)	15 (50.0)	.288	163 (50.4)	94 (53.1)	90 (57.0)	.072
Mild	166 (25.2)	121 (25.0)	45 (26.0)		130 (25.2)	36 (25.3)		50 (21.9)	116 (27.0)		162 (25.8)	4 (13.3)		81 (25.1)	50 (28.2)	35 (22.2)	
Moderate	84 (12.8)	55 (11.3)	29 (16.8)		71 (13.8)	13 (9.2)		29 (12.7)	55 (12.8)		79 (12.6)	5 (16.7)		40 (12.4)	24 (13.6)	20 (12.6)	
Severe	61 (9.3)	51 (10.5)	10 (5.8)		43 (8.3)	18 (12.7)		20 (8.8)	41 (9.5)		55 (8.7)	6 (20.0)		39 (12.1)	9 (5.1)	13 (8.2)	
ISI, insomnia symptoms																	
Normal	309 (47.0)	229 (47.2)	80 (46.2)	.866	238 (46.1)	71 (50.0)	.351	107 (46.9)	202 (47.0)	.357	296 (47.1)	13 (43.4)	.334	150 (46.9)	79 (44.6)	80 (50.6)	.173
Mild	238 (36.2)	175 (36.1)	63 (36.4)		190 (36.8)	48 (33.8)		87 (38.2)	151 (35.1)		226 (36.0)	12 (40.0)		114 (35.6)	66 (37.3)	58 (36.7)	
Moderate	85 (12.9)	65 (13.4)	20 (11.6)		69 (13.4)	16 (11.3)		22 (9.6)	63 (14.7)		81 (12.9)	4 (13.3)		41 (12.8)	26 (14.7)	15 (9.5)	
Severe	26 (3.9)	16 (3.3)	10 (5.8)		19 (3.7)	7 (4.9)		12 (5.3)	14 (3.2)		25 (4.0)	1 (3.3)		15 (4.7)	6 (3.4)	5 (3.2)	
IES-R, distress symptoms																	
Normal	112 (17.0)	84 (17.3)	28 (16.2)	.484	78 (15.1)	34 (23.9)	.210	39 (17.1)	73 (17.0)	.698	109 (17.4)	3 (10.0)	.099	50 (15.5)	30 (16.9)	32 (20.3)	.117
Mild	202 (30.7)	151 (31.1)	51 (29.5)		164 (31.8)	38 (26.8)		73 (32.0)	129 (30.0)		195 (31.0)	7 (23.4)		96 (29.7)	55 (31.1)	51 (32.3)	
Moderate	207 (31.5)	153 (31.6)	54 (31.2)		166 (32.2)	41 (28.9)		72 (31.6)	135 (31.4)		197 (31.4)	10 (33.3)		100 (31.0)	55 (31.1)	52 (32.9)	
Severe	137 (20.8)	97 (20.0)	40 (23.1)		108 (20.9)	29 (20.4)		44 (19.3)	93 (21.6)		127 (20.2)	10 (33.3)		77 (23.8)	37 (20.9)	23 (14.5)	

P value was calculated using the nonparametric Wilcoxon signed-rank test and Kruskal-Wallis test.  
 Abbreviations: BC = breast cancer; COVID-19 = coronavirus disease 2019; CVC = central venous catheter; GAD-7 = Generalized Anxiety Disorder Questionnaire; HER2 = human epidermal growth factor receptor 2; IES-R = Impact of Events Scale-Revised; ISI = Insomnia Severity Index; N/A = Not provided or not available; PHQ-9 = Patient Health Questionnaire; TNBC = triple negative breast cancer.  
 \*Single category included widowed and divorced participants.

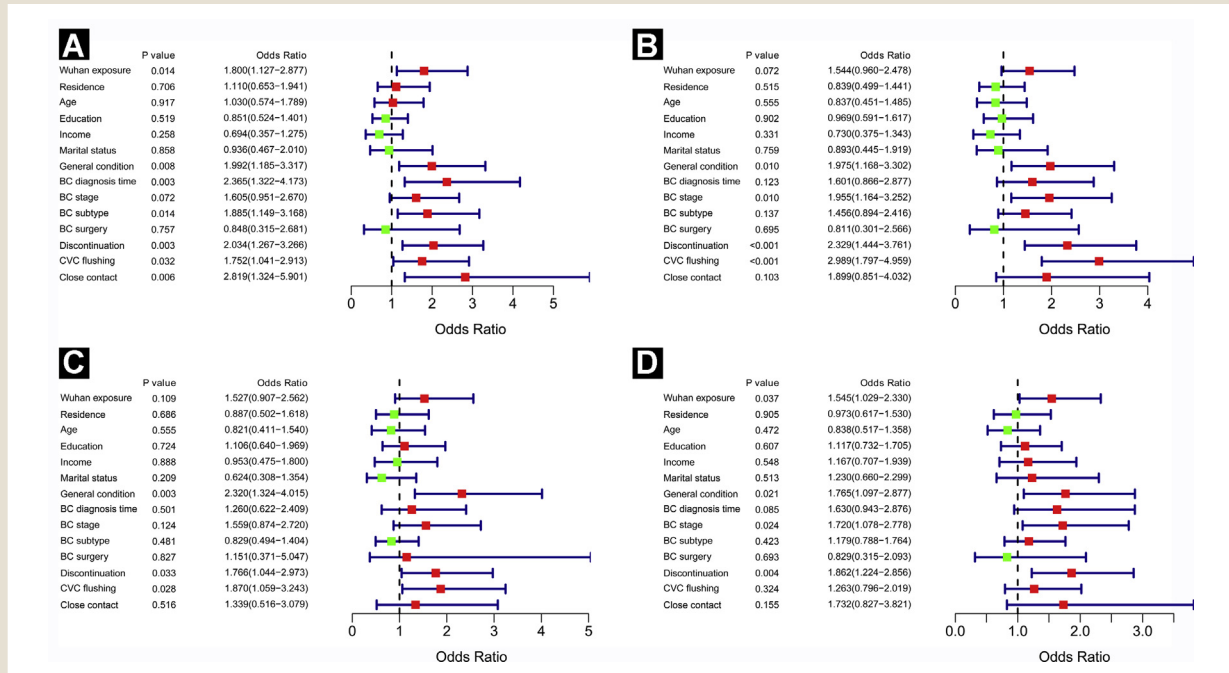
**Supplemental Figure 1** Stacked bar Plots to Identify Severity of Measurements and Associated Factors for Anxiety (A), Depression (B), Insomnia (C), and Distress (D) Symptoms Among Patients With BC in the Center of COVID-19 in China. (Interpretations: Wuhan Exposure: Yes vs. No; General Condition by Self-Identification: Well vs. Average vs. Poor; Treatment Discontinuation: Yes vs. No; Breast Cancer Stage: Early vs. Metastatic vs. N/A; Close Contact With Patient With COVID-19: Yes vs. No vs. N/A; CVC Flushing Delay: Delay vs. No Delay vs. No CVC)



Abbreviations: BC = breast cancer; CVC = central venous catheter; COVID-19 = coronavirus disease 2019.

# Psychological Status of Patients With BC During COVID-19

**Supplemental Figure 2** Forest Plots to Identify Independent Affecting Factors for Anxiety (A), Depression (B), Insomnia (C), and Distress (D) Symptoms Among Patients With BC in the Center of COVID-19 in China Using Univariable Logistic Regression Analysis. (Interpretations: Wuhan Exposure: Yes vs. No; Residence: Urban vs. Rural; Age:  $\geq 55$  years Old vs.  $\leq 54$  years Old; Education: High School or More vs. Middle School or less; Income:  $\leq \$15,000$  per Year vs.  $> \$15,000$  per Year; Marital Status: Single (including Widowed/Divorced) vs. Married; General Condition by Self-Identification: Poor vs. Well/Average; BC Diagnosis Time:  $\leq 1$  Year vs.  $> 1$  year; BC Stage: Metastatic vs. Early; BC Subtype: TNBC/HER2 vs. Luminal; BC Surgery History: Yes vs. No; Treatment Discontinuation: Yes vs. No; CVC Flushing: Interval Exceeding 4 weeks vs. Interval Within 4 Weeks; Close Contact: Close Contact With Patient With COVID-19 vs. No Close Contact With Patient With COVID-19.)



Abbreviations: BC = breast cancer; COVID-19 = coronavirus disease 2019; CVC = central venous catheter; HER2 = human epidermal growth factor receptor 2; TNBC = triple negative breast cancer.