

Impact of COVID-19 on Anxiety, Stress, and Coping Styles in Nurses in Emergency Departments and Fever Clinics: A Cross-Sectional Survey

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Background: During the Coronavirus Disease 2019 (COVID-19) pandemic, emergency departments and fever clinics nurses acted as gatekeepers to the health care system. To manage the psychological problems that these nurses experience, we should develop appropriate training and intervention programs.

Objective: To identify the impact of COVID-19 on the psychology of Chinese nurses in emergency departments and fever clinics and to identify associated factors.

Methods: This online cross-sectional study recruited participants through snowball sampling between 13 February and 20 February 2020. Nurses self-administered the online questionnaires, including a general information questionnaire, the Self-Rating Anxiety Scale, the Perceived Stress Scale-14, and the Simplified Coping Style Questionnaire.

Results: We obtained 481 responses, of which 453 were valid, an effective response rate of 94.18%. Participants who had the following characteristics had more mental health problems: female gender, fear of infection among family members, regretting being a nurse, less rest time, more night shifts, having children, lack of confidence in fighting transmission, not having emergency protection training, and negative professional attitude.

Conclusion: Effective measures are necessary to preserve mental health of nurses in emergency departments and fever clinics. These include strengthening protective training, reducing night shifts, ensuring adequate rest time, and timely updating the latest pandemic situation.

Keywords: COVID-19, nurses, psychological health, mental health, stress, anxiety

Introduction

Starting in December of 2019, COVID-19 spread worldwide. A rapid infection rate and human-to-human transmission characterize COVID-19.^{1,2} Although the pandemic has been under effective control, numbers of confirmed and suspected cases continue to rise. Physicians, nurses, and ambulance workers are more likely to be infected than any other group. Of the confirmed cases worldwide, 6%, or 90,000, were healthcare workers.³ As of 11 February 2020, 1716 (3.8% of the country's confirmed cases) medical workers in China were infected, six of whom died, accounting for 0.4% of China's total deaths.⁴

Nurses play essential roles in the fight against infectious diseases. During the COVID-19 pandemic, nurses faced higher risks of death than physicians in some

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countries.⁵ The pandemic caused not only morbidity and mortality but also psychological and social problems.⁶ High expectations, lack of time, skills, and social support may lead to occupational stress that, in turn, causes anxiety, post-traumatic stress disorder, distress, burnout, and other psychological problems.^{3,7} Nurses may also experience a range of somatic symptoms, including palpitations, nausea, dyspnea, and dizziness.⁸ Unclear disease status and uncertainty regarding COVID-19 treatment and care policies exacerbate stress on nurses, affecting nursing care quality⁷ and even causing resignations.⁹

In public health crises, several factors influence the mental health status of nurses. Common risk factors that cause stress and anxiety during a pandemic include a lack of effective hospital management systems,¹⁰ lack of personal protective equipment (PPE) and training,¹¹ exposure to confirmed cases,^{6,12} fear of being infected,¹³ fear of spreading the virus to family members,¹⁴ concerns about their children for not being taken care of,¹⁵ long working hours, and heavy workloads.^{9,13} Previous studies showed that the effect on mental health varies by sex. During an Ebola outbreak, male health workers experienced more mental distress.¹⁶

Many hospitals closed outpatient clinics while maintaining open emergency departments and fever clinics (EDFC) to reduce human-to-human transmission in hospitals. Hospitals establish fever clinics for the prevention and control of acute infectious diseases. As gatekeepers to the health care system, EDFC nurses distinguish confirmed cases from suspected patients through carefully evaluating their clinical manifestations, contact history, and travel history. EDFC nurses hold the key to controlling transmission among patients, staff, visitors, and the community.¹⁰ EDFC nurses are most likely to contact suspected patients, imparting a higher risk of exposure to the virus. Compared with the nurses in the isolation wards, some EDFC nurses may place less emphasis on protective measures. During the COVID-19 pandemic, many studies focused on nurses' mental health while caring for patients with confirmed disease in isolation wards.^{17–19} A better understanding of EDFC nurses' anxiety, stress, and coping mechanisms can help design intervention and training programs.

Methods

Sample/Participants

We selected candidates using snowball sampling from 13 to 20 February 2020. We used the Questionnaire Star

platform (<https://www.wjx.cn>) to conduct an online survey. To obtain help and support, we collected data by sending the questionnaire link to relevant professional groups using QQ and WeChat (the most popular social media applications in China). We uploaded response data to the platform after nurses completed and submitted the questionnaires. Only one submission was allowed for each IP address, computer, or mobile phone. The inclusion criteria were as follows: registered nurse; working in hospitals in Jiangsu Province; EDFC nurses who had exposure to COVID-19 for more than one month. Finally, we obtained 481 responses. After removing 28 questionnaires that showed non-Jiangsu IP addresses, non-emergency departments, or fever clinics nurses, we recovered 453 valid questionnaires, an effective response rate of 94.18%.

Data Collection

General Information Questionnaire

The research team developed a general information questionnaire based on a literature review.^{6,11,12} An expert panel evaluated the questionnaire content; the panel included a fever clinic nurse, an emergency nurse, two head nurses, a nurse administrator, and two nursing professors. This questionnaire consisted of two parts; one was demographic characteristics (ie, sex, age, education level, designation, marital status, and having children); the other related to socio-psychological and working conditions during the COVID-19 pandemic, including rest time per week, the number of night shifts in the previous month, professional attitude, confidence, willingness to fight transmission, whether they have been in contact with confirmed patients, and whether they had recently attended infection prevention training.

Self-Rating Anxiety Scale (SAS)

The SAS, compiled by ZUNG in 1971,²⁰ measures anxiety levels. This scale includes 20 items and uses a 4-point scoring system to measure the frequency of symptoms (1 = no or little time, 2 = a small part of the time, 3 = a considerable amount of time, and 4 = most or all of the time). Of these, 15 items use negative words (eg, I feel more nervous and anxious than usual; I feel afraid for no reason) scored on the 1 to 4 scale. The other five items use positive words (eg, I feel calm and sit still easily; I can breathe in and out easily), scored in reverse. Adding the scores of all items produces the raw score, and multiplying the score by 1.25 produces the standard score. The higher the standard SAS score, the higher the anxiety level

(Chinese norm: the standard deviation of SAS is 50 points; 50 to 59 points for mild anxiety; 60 to 69 points for moderate anxiety; and above 69 points for severe anxiety).

Perceived Stress Scale (PSS)

PSS is a tool for measuring stress. The scale consists of 14 items and two dimensions.²¹ The Chinese version of PSS-14 scale adopts a 5-point scoring system (0 = never, 1 = almost never, 2 = sometimes, 3 = fairly often, 4 = always).²² Of these, items 1, 2, 3, 8, 11, 12, and 14 belonging to the negative dimension are scored from 0 to 4, while the remainder (items 4, 5, 6, 7, 9, 10, 13), belonging to positive dimension, are scored in reverse. Items in the negative dimension include not coping with all the things one has to do and the inability to control the important things in one's life, etc. Items such as things were going one's way and effectively coping with important changes occurring in one's life belong to the positive dimension. The PSS score is the sum of the 14 items; the higher the score, the greater the perceived stress (Chinese norm: normal: ≤ 25 points; stress: > 25 points).

Simplified Coping Style Questionnaire (SCSQ)

Xie compiled the SCSQ based on a non-Chinese pressure coping style scale and the Chinese population's characteristics.²³ It is a sensitive instrument for measuring stress responses. It includes two dimensions: positive coping (12 items, including asking relatives, friends, or classmates for advice and finding several different ways to solve the problem); and negative coping (eight items, including reliance on others to solve problems). It uses a 4-point scoring system (0 = never, 1 = seldom, 2 = sometimes, and 3 = often). When individuals are under stress, they adopt various coping measures, including positive and negative coping styles. Researchers use the following formula to judge an individual's coping style:²⁴ Coping tendency = positive coping standard score – negative coping standard score. Positive coping standard score = Individual positive coping dimension mean – Sample positive coping dimension mean / Sample positive coping dimension standard deviation. Negative coping standard score = Individual negative coping dimension mean – Sample negative coping dimension mean / Sample negative coping dimension standard deviation. Coping tendency scores above 0 suggest a positive coping style; below 0 suggests a negative coping style.

Data Analysis

Descriptive statistics included frequency, proportions (%), mean, and standard deviations. We used multiple linear regression analysis with a stepwise selection of predictor variables. We adopted three separate models to identify the influencing factors of anxiety, perceived stress, and stress coping among EDFC nurses. Each time we introduced an independent variable in the stepwise regression equation, we performed an F-test based on the sum of partial regression squares for each newly-introduced independent variable. We eliminated independent variables with no statistical significance. We repeated the process until we could no longer introduce independent variables. The test level for introducing independent variables was 0.05, and that of removing independent variables was 0.10. We checked linearity assumptions by tolerance > 0.1 and variance inflation factor (VIF) < 10 . We checked the homogeneity of variances using scatterplots. The multicollinearity test found that minimum and maximum VIF were 1.001 and 1.160, respectively, and the tolerance range was 0.862 to 0.999, suggesting no multicollinearity. In the final adjusted multiple regression, we considered variables with $p < 0.05$ to be significantly correlated with measured values. We calculated standardized beta and 95% confidence interval (CI) coefficients to evaluate multivariate regression analysis's statistical significance.

Ethical Considerations

The Committee on Ethics of Medical Research at the Navy Medical University (HJEC number: 2020-LW-001) approved the study. We conducted the study according to the principles of the Helsinki Declaration. Before initiating the survey, we explained the purpose of the study and the selection criteria to participants. All participants gave written consent, and we assured them that we would maintain their confidentiality, and we would publish only anonymized survey results.

Results

Descriptive Statistics

We display demographic statistics, work characteristics, and socio-psychological variables of the participants in Table 1. Of the 453 nurses, 16 (3.53%) were males, and 437 (96.47%) were females. The mean age was 33.15 years (SD = 8.38). The mean working time was 11.33 years (SD = 9.25).

Table I Demographic Characteristics, Socio-Psychological and Working Condition Variables (n = 453)

Variables	Variable Categories	N (%)
Sex	Female Male	437 (96.47%) 16 (3.53%)
Designation	Primary nurse Nurse practitioner Nurse-in-charge Co-chief superintendent nurse and above	9 (20.53%) 217 (47.90%) 118 (26.05%) 25 (5.52%)
Education level	College degree Bachelor's degree Master's degree or above	116 (25.61%) 333 (73.51%) 4 (0.88%)
Marital status	Married Unmarried	312 (68.87%) 141 (31.13%)
Having children	Yes No	290 (64.02%) 163 (35.98%)
The level of the hospital where you work	Grade II Class B hospital and below Grade II Class A hospital Grade III Class B hospital Grade III Class A hospital	39 (8.61%) 63 (13.91%) 197 (43.49%) 154 (34.00%)
Rest time each week in the past month	Less than 1 day per week One day per week Two days per week More than two days per week	17 (3.75%) 111 (24.50%) 257 (56.73%) 68 (15.01%)
Number of night shifts in a week	Zero One night shift a week Two night shifts a week Three or more night shifts a week	147 (32.45%) 87 (19.21%) 109 (24.06%) 110 (24.28%)
Contact with a confirmed patient	Yes No	65 (14.35%) 388 (85.65%)
Regretting being a nurse	Yes No	20 (4.42%) 433 (95.58%)
Professional attitude	Negative General Positive Strongly positive	3 (0.66%) 19 (4.19%) 97 (21.41%) 334 (73.73%)
Confidence in fighting transmission	Lack of confidence General confident Quite confident	1 (0.22%) 26 (5.74%) 426 (94.04%)
Signed up to go to Hubei Province for support	Yes No	385 (84.99%) 68 (15.01%)
Having attended infection prevention training	Yes No	328 (72.41%) 125 (27.59%)
Family support	Yes No	435 (96.03%) 18 (3.97%)

(Continued)

Table 1 (Continued).

Variables	Variable Categories	N (%)
Hospital for confirmed patient	Yes	181 (39.96%)
	No	272 (60.04%)
Fear of infecting family members	Yes	361 (79.69%)
	No	92 (20.31%)

We display the overall results of the scales in [Table 2](#). Among the participants, 281 (62.03%) reported no anxiety symptoms, 154 (34.00%) reported mild anxiety, 16 (3.53%) reported moderate anxiety, and two (0.44%) reported severe anxiety. There were 146 (32.23%) participants with scores greater than 25 in the PSS, suggesting excessive stress; 229 (50.55%) participants were more likely to respond positively to stress, while 224 (49.45%) were more likely to respond negatively ([Table 2](#)).

Effects of Socio-Psychological and Working Condition Variables on Scores of Anxiety, Stress, and Stress Coping Tendency

We found that variables in the model explained 19.2% total variation in the anxiety (adjusted $R^2 = 0.192$, $P = 0.032$). Fear of infecting family members ($\beta = 0.263$, $P = 0.000$), regretting being a nurse ($\beta = 0.216$, $P = 0.000$), and

having children ($\beta = 0.096$, $P = 0.028$) positively correlated with reporting anxiety. Confidence in fighting the pandemic ($\beta = -0.147$, $P = 0.001$), sex ($\beta = -0.106$, $P = 0.015$), and rest time each week in the previous month ($\beta = -0.092$, $P = 0.032$) inversely correlated with reporting anxiety. Being female, having less rest time, having children, having a lack of confidence in fighting the pandemic, regretting being a nurse, and fearing infection in the family were risk factors for reporting anxiety ([Table 3](#)).

In the perceived stress domain, the variables in the model explained 13.7% of total variance (adjusted $R^2 = 0.137$, $P = 0.014$). Fear of infecting family members ($\beta = 0.239$, $P = 0.000$), regretting being a nurse ($\beta = 0.199$, $P = 0.000$) and the number of night shifts in a week ($\beta = 0.109$, $P = 0.014$) positively correlated with reporting stress. Having attended infection prevention training ($\beta = -0.122$, $P = 0.006$) correlated associated with stress. Regretting being a nurse, not receiving emergency protection training, fear of infection in family, and more night shifts were risk factors for perceived stress ([Table 4](#)).

Variables in the model explained 13.2% of total variation in stress coping tendency (adjusted $R^2 = 0.132$, $P = 0.029$). Professional attitude ($\beta = 0.125$, $P = 0.008$), having attended infection prevention training ($\beta = 0.108$, $P = 0.015$), and signing up to go to Hubei Province for rescue ($\beta = 0.099$, $P = 0.029$) positively correlated with stress coping tendency. Fear of infecting family members ($\beta = -0.188$, $P = 0.000$) and regretting being a nurse ($\beta = -0.155$, $P = 0.001$) inversely correlated with stress coping tendency. In other words, participants with positive professional attitudes, who did not regret being a nurse, who trained in emergency preparedness, who were willing to go to Hubei Province for rescue, and who did not fear infecting family members responded more positively to stress ([Table 5](#)).

Discussion

In this study, we explored the effects of socio-psychological variables and working conditions on

Table 2 Descriptive Statistics of the Anxiety, Stress, and Coping Style (n = 453)

Variables	N (%)	Mean	SD
Self-rating anxiety scale		49.01	5.46
None (< 50 points)	281 (62.03%)		
Mild anxiety (50 to 59 points)	154 (34.00%)		
Moderate anxiety (60 to 69 points)	16 (3.53%)		
Severe anxiety (>69 points)	2 (0.44%)		
Perceived stress scale		21.09	7.76
Normal (≤ 25 points)	307 (67.77%)		
Stress (>25 points)	146 (32.23%)		
Simplified Coping Style Questionnaire			
Coping tendency > 0	229 (50.55%)		
Coping tendency < 0	224 (49.45%)		
Positive coping dimension		1.97	0.57
Negative coping dimension		1.13	0.48

Table 3 Multiple Linear Regression Analysis Model Showing Independently-Associated Variables with Anxiety Among EDFC Nurses (n = 453)

Socio-Psychological and Working Condition Variables with Anxiety	Unstandardized Coefficient (β)		Standardized Coefficient (β)	95% CI for β	P-value
	β	Standard Error	Beta		
Constant	56.722	3.015		50.797 to 62.647	<0.001
Fear of infecting family members	3.567	0.582	0.263	2.424 to 4.710	<0.001
Regretting being a nurse	5.724	1.147	0.216	3.469 to 7.978	<0.001
Confidence in fighting transmission	-3.205	0.944	-0.147	-5.061 to -1.349	0.001
Having children	1.092	0.497	0.096	0.116 to 2.068	0.028
Sex	-3.132	1.279	-0.106	-5.646 to -0.619	0.015
Rest time each week in the past month	-0.697	0.325	-0.092	-1.335 to -0.059	0.032

Table 4 Multiple Linear Regression Analysis Model Showing Independently-Associated Variables with Perceived Stress Among EDFC Nurses (n = 453)

Socio-Psychological and Working Condition Variables with Perceived Stress	Unstandardized Coefficient (β)		Standardized Coefficient (β)	95% CI for β	P-value
	β	Standard Error	Beta		
Constant	17.627	1.004		15.653 to 19.601	<0.001
Fear of infecting family members	4.598	0.852	0.239	2.924 to 6.273	<0.001
Regretting being a nurse	7.489	1.667	0.199	4.213 to 10.766	<0.001
Having attended infection prevention training	-2.119	0.762	-0.122	-3.616 to -0.622	0.006
Number of night shift in a week	0.720	0.292	0.109	0.147 to 1.294	0.014

anxiety, stress, and stress coping tendency. In the critical stage of controlling the spread of the virus, assessing the EDFC nurses' psychological state is very important for helping design intervention and training strategies.

Anxiety, Stress, and Stress Coping Styles of EDFC Nurses

We found a mean anxiety score of 49.01 ± 5.46 , which was slightly higher than those reported by Liu.²⁵ Among

Table 5 Multiple Linear Regression Analysis Model Showing Independently-Associated Variables with Stress Coping Tendency Among EDFC Nurses (n = 453)

Socio-Psychological and Working Condition Variables with Stress Coping Tendency (>0)	Unstandardized Coefficient (β)		Standardized Coefficient (β)	95% CI for β	P-value
	β	Standard Error	Beta		
Constant	-0.710	0.321		-1.340 to -0.080	0.027
Fear of infecting family members.	-0.567	0.135	-0.188	-0.832 to -0.302	<0.001
Regretting being a nurse	-0.919	0.275	-0.155	-1.460 to -0.379	0.001
Professional attitude	0.262	0.099	0.125	0.068 to 0.456	0.008
Having attended infection prevention training	0.294	0.121	0.108	0.057 to 0.531	0.015
Signed up to go to Hubei Province for support	0.337	0.154	0.099	0.034 to 0.640	0.029

453 EDFC nurses, the proportion of reported anxiety symptoms was 37.97%, consistent with those of Than et al.²⁶ We found that 32.23% of EDFC nurses had perceived stress; previous studies also found that being a nurse was highly stressful,^{27,28} especially for nurses working in emergency departments.²⁹ Uncertainty characterizes the working environment in emergency departments, and emergency department healthcare workers were more vulnerable to medical workplace violence. During the COVID-19 pandemic, healthcare workers who experienced violence in the medical environment were more likely to suffer from mental health problems.³⁰ Factors such as excessive workload, fear of infecting family members, and medical staff death can also lead to stress and anxiety.^{31,32} We found 229 (50.55%) were more likely to respond positively to stress, while 224 (49.45%) were more likely to respond negatively. Negative coping behaviors such as fantasy, avoidance, self-blame and indulgence have a negative impact on psychological well-being.³³ Previous studies have shown that in emergency events, negative coping was associated with lower psychological endurance, lower perceptual control and higher anxiety-like behavior.^{34,35} Nearly half of EDFC nurses negatively responded to stress, suggesting the need for appropriate interventions to improve coping styles.

Predictors of Stress, Anxiety, and Stress Coping Tendency

Socio-psychological variables and working conditions serve as predictors, accounting for 19.2% of the variance in anxiety, 13.7% in the stress domain, and 13.2% in stress coping tendency. Among variables, fear of infecting family members was the most influential and predictive of all three criteria. During the pandemic, it was difficult for hospital workers to return home from the hospital because they worried about infecting family members.¹³ Nurses are vulnerable to infection during outbreaks of infectious disease,^{36,37} especially when there are emerging infectious diseases of unclear infectious nature. During the COVID-19 outbreak, EDFC in Chinese hospitals were high-risk workplaces, where nurses were likely to be exposed to the virus. COVID-19 is highly infectious, and this causes nurses to worry more about their family members, subsequently making them more anxious, stressed, and more inclined to adopt negative coping methods.

Those who regretted becoming a nurse reported higher levels of anxiety, stress, and adoption of negative coping styles. Nurses who served voluntarily were less stressed than those who were appointed.³⁸ Wong et al found that 76.9% of community nurses were unwilling to work because of psychological stress and fear of being infected by H1N1 influenza. Those who reported unwillingness were more depressed and stressed.³⁹ It is unclear why respondents regretted becoming nurses during the COVID-19 pandemic. We can only speculate as to the following reasons: protective working conditions or facilities may have been unavailable, they feared infection, labored under excessive workloads, or had childcare responsibilities, and they prioritized family members.⁴⁰

We also noted that 72.41% (328) respondents attended infection prevention training, which resulted in lower levels of stress and the adoption of positive coping styles. Inadequate training in infection control, a lack of knowledge, and unclear specific tasks increased perceived personal risk but reduced willingness to work.³⁹ All involved staff need to be trained for the skills necessary to protect them from infection.⁴¹ Institutional preparedness predicts individual perceptions of preventive measures. Protection training is necessary, especially for the highly infectious COVID-19. Medical institutions should attach great importance to improving the protection training system, and they should implement online and offline comprehensive training to improve the occupational protection skills among EDFC nurses.

Those who took fewer breaks and more night shifts each week had higher levels of anxiety and stress. The length of rest time and the number of night shifts can reflect whether the nursing resources are sufficient. Previous studies suggested that long hours and large workloads predict stress.^{9,41} Overwork may cause a sense of loss of control in the EDFC nurse, produce feelings of powerlessness, and even cause insomnia, headache, loss of appetite, and other physical problems.⁴² Therefore, hospitals should ensure that the nursing staffing of EDFC is adequate, and the head nurse should arrange the shift of nurses in a coordinated way to ensure that they can rest sufficiently.

The 64.02% (290) of the respondents with children had higher levels of anxiety, which is similar to the results of Shanafelt et al.¹⁵ This result differed from that of Chen et al³⁸ who found that nurses with more than two children reported the lowest levels of job stress. In contrast, nurses without children reported the highest levels of job stress

and were more likely than other nurses to employ destructive stress coping strategies. The opposite finding may be due to the timing of the survey. During the pandemic, nurses protected their children from infection. The burden of caring for children increased as schools closed. The double burden from both family and work made them more anxious.

Female nurses comprised the majority (96.47%) of our respondents; they reported higher anxiety levels. This finding is consistent with Zhang et al, who found that being female was the most common risk factor for insomnia, anxiety, and depression.⁴³ Other studies showed that sex had differential effects on mental health. During an Ebola outbreak, male health workers experienced more mental distress.¹⁶ This differed from our results because, during the COVID-19 pandemic, EDFC performed most of the diagnosis and treatment work. However, there were only 16 male nurses in this study; therefore, the findings should be applied only in the appropriate context, and further research is needed.

Confidence in fighting the outbreak negatively correlated with anxiety levels among EDFC nurses. Confident nurses tend to have more abundant clinical professional knowledge and higher abilities and can effectively manage their time and tasks.⁴⁴ Professional attitude predicted stress coping tendency. More positive attitudes increased the likelihood that these nurses would adopt positive coping tendency. Lam and Hung found that, during an influenza outbreak, nurses endured a considerable amount of hardship. They overcame the fear of infection and provided nursing service primarily because of professional loyalty, mission, and obligation.³⁷ Therefore, we recommend that medical institutions summarize pandemic prevention and control work daily and encourage nurses to share their clinical experience and feelings, recognize their professional value, and improve their professional identity and confidence in fighting pandemic.

Limitations

The study has some limitations. First, the method of snowball sampling may make reduce the generalizability of our results. Second, the data's cross-sectional nature constrained us from concluding causality among anxiety, stress, and coping tendency. Finally, the present survey relied only on self-reported questionnaires, which may reduce data collection objectivity.

Conclusion

Psychological intervention is necessary, and hospitals should take adequate measures. These measures include strengthening protective training, ensuring sufficient numbers of nurses for emergency departments and fever clinics, reducing the number of night shifts, ensuring adequate rest time, updating the latest information promptly, and encouraging EDFC nurses to share clinical experiences and feelings. There should be greater attention to female EDFC nurses and those with children, providing more support for their families.

We performed this study during the peak of the COVID-19 outbreak in China, when knowledge of the pandemic was limited, and information was rapidly changing. In a subsequent investigation, we will combine qualitative and quantitative methods to understand the psychosocial impact on nurses better.

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Disclosure

The authors declare no competing financial interest and report no conflicts of interest for this work.

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