

# Mental Health Concerns in Patients with COVID-19: A Network Analysis

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**Purpose:** Patients with coronavirus disease 2019 (COVID-19) are predisposed to associated mental health problems, including intolerance of uncertainty (IUS), perceived stress (PSS), low sense of control, dysfunctional beliefs and attitudes about sleep (DBAS), insomnia, and impaired feeling of security. However, these mental health concerns have not been studied in a joint framework. This study aimed to investigate the relationships and putative causality among the aforementioned six variables and determine relatively important ones, indicating potential intervention strategies for the associated mental health concerns.

**Patients and Methods:** A total of 1015 inpatients with COVID-19 aged 18 years or older in the Shanghai shelter hospital completed validated self-report scales to assess relevant psychopathological constructs. Two network models, a Graphical Gaussian Model (GGM) and a Directed Acyclic Graph (DAG), were estimated based on collected cross-sectional data.

**Results:** The GGM network was reliably stable, highlighting five strongest associations such as the connection between IUS "Intolerance of uncertainty" and DBAS "Dysfunctional beliefs and attitudes about sleep". IUS was identified as the most central node. The DAG network suggested the key triggering role of PSS "Perceived stress" for other downstream variables.

**Conclusion:** This study provided insights into the complex pairwise connections between the mental health concerns and the pivotal roles of intolerance of uncertainty and perceived stress. The study findings were discussed in terms of both theoretical and clinical implications that might serve for the intervention of psychological distress and promotion of mental health in patients with COVID-19 or similar epidemics.

**Keywords:** directed acyclic graph, dysfunctional beliefs and attitudes about sleep, intolerance of uncertainty, network analysis, patients with COVID-19, perceived stress

## Introduction

The coronavirus disease 2019 (COVID-19) pandemic has been identified as a global public health concern, posing significant challenges. In late February 2022, the COVID-19 epidemic broke out in Shanghai, China. The number of newly infected cases peaked at 27,605 on April 13, 2022, and 593,336 cases were identified by May 4, 2022.<sup>1</sup> The COVID-19-associated mental health problems have attracted tremendous attention. People are generally susceptible to COVID-19-related mental health issues,<sup>2-5</sup> and individuals infected with COVID-19 are more seriously affected. Studies indicate that COVID-19-infected patients are distinguished by significant psychological distress and impaired mental health.<sup>6-9</sup>

The mass COVID-19-related facts, such as being kept in the isolation ward, requiring oxygen support, being admitted to intensive care units, and associated mortality, have led to significant fear of unknown and intolerance of uncertainty in

infected patients.<sup>6</sup> COVID-19 patients have also reported a high prevalence of perceived stress,<sup>10,11</sup> eg, 46.61% in a cross-sectional survey.<sup>11</sup> Perceived stress was found to be significantly associated with an increased risk of post-COVID-19 conditions among infected patients.<sup>12</sup> Additionally, sense of control (a subjective belief to what extent one can control events) was significantly impaired during the COVID-19 pandemic.<sup>13,14</sup> Previous studies showed that a majority of the patients with COVID-19 had dysfunctional beliefs and attitudes about sleep (DBAS) to varying degrees.<sup>15</sup> Studies also suggest that COVID-19 infection has led to increased odds of insomnia.<sup>16–18</sup> For example, a study showed that 20.5% of individuals infected with COVID-19 had insomnia.<sup>19</sup> Moreover, olfactory dysfunction resulting from infection was reported to lower the patients' feeling of security.<sup>9</sup> Extensive studies have investigated the relations between the aforementioned variables. Sense of control was closely related to mental health and buffers against psychological distress such as perceived stress.<sup>20–23</sup> A positive correlation between higher level of DBAS and the prevalence of insomnia was also confirmed.<sup>15,24</sup> Additionally, COVID-19-infected patients with insomnia also reported a low feeling of security.<sup>25</sup> The psychopathological variables such as intolerance of uncertainty, perceived stress, sense of control, DBAS, insomnia, and feeling of security have complex relationships with each other, for example, connections between insomnia and feeling of security.<sup>25</sup> However, the relations among all the relevant variables, the potential causality between them, and the relative importance of each variable in a joint framework have not yet been investigated, which can provide references for the targeted and efficient intervention of psychological distress and facilitate the promotion of the mental health of patients with COVID-19.

Although 4 years have passed since the start of the pandemic, COVID-19 shows no signs of settling into a seasonal pattern of spread, like influenza. A rise in COVID-19 infections is again reported, and it seems that COVID is likely to set new normal in terms of mini waves, as some countries are experiencing surges in infections three or four times a year.<sup>26</sup> The COVID-19 infections will continue, and the mental health issues caused by COVID-19 are long-lasting.<sup>27–29</sup> COVID-19 infection has been associated with long-term sequelae (Long COVID) including mental health consequences and it has been reported that anxiety and mood disorders are elevated and seen in about 25% of Long COVID patients.<sup>30,31</sup> It necessitates the integration of mental health services into the comprehensive care for patients with COVID-19.<sup>31</sup> However, studies on the mental health status of patients with COVID-19 are rare, especially for this wave occurred in February 2022 in Shanghai. Therefore, it was necessary to investigate the relationships between the aforementioned psychopathological variables in patients with COVID-19 in Shanghai, determine the important ones, and explore the possible causality of these variables. This study was critical in terms of providing insights for the intervention of psychological distress and promotion of mental health to address both recent and future challenges caused by the COVID-19 infection. The findings from this study can also be applicable to and be used as a reference for similar future epidemics to a certain extent.

Network analysis can satisfy this research requirement. It is an emerging data-driven approach not dependent on prior assumptions of relations between variables, which has been applied extensively in psychopathology to examine and visualize relevant variables.<sup>32,33</sup> In the network theory, the variables are depicted as nodes and the edges represent the relations between variables.<sup>34</sup> The network represents and visualizes the interactions between distinct variables, indicating that the variables and their direct interactions lead to the maintenance of the psychopathological network.<sup>33,35,36</sup> The network analysis provides significant implications. It can help examine the complex relationships between individual variables,<sup>37–39</sup> uncovering the essential psychopathological pathways between variables via analyzing important edges. The network analysis can also provide indices to evaluate the roles the nodes play in the network. The expected influence (EI) index helps identify the central nodes that impact mostly on other nodes and the entire network,<sup>36,40</sup> providing potential intervention targets. Moreover, recent applications of the Bayesian approach allow for examining the strength and the direction of edges to explore admissible causal relationships in cross-sectional data, overcoming one of the key limitations of conventional networks (ie, partial correlation networks) whose edges are undirected.<sup>41</sup> This provided information about which associations between variables might be causally important, that is, which variables might play causal roles in triggering other symptoms.<sup>42,43</sup> The addition of the Bayesian approach to network analysis makes good sense because of the equivocality when interpreting findings from undirected networks, whereas the Bayesian approach permits a more confident interpretation of the network analysis.<sup>44–46</sup> Hence, network analysis offers novel insights into the complex interconnections among multiple variables, thereby deepening

our understanding of pathological pathways. By providing quantitative metrics to assess the significance of individual nodes within these networks, this approach opens new avenues for identifying intervention and therapeutic targets in mental disorders. Within the domain of psychopathology, these advantages substantiate the rationale and imperative for the adoption of this methodology.

To date, no network analysis has investigated the relationships among mental health concerns in patients with COVID-19, such as relations between intolerance of uncertainty, perceived stress, sense of control, DBAS, insomnia, and feeling of security. Considering the crucial implications for the intervention of psychological distress and promotion of mental health, this study constructed a network consisting of these variables in a sample of patients with COVID-19 who were treated in Shanghai shelter hospital. We aimed to (1) uncover the important pathways between the variables, (2) identify central nodes that mostly influenced the network, and (3) determine the putative direction of the causal relationship and which node had the highest predictive priority (ie, potentially causal).

## Materials and Methods

### Participants and Ethical Approval

This study was an online survey hosted on the Wenjuanwang platform (<https://www.wenjuan.com>). A total of 1104 inpatients with COVID-19 aged 18 years or older in the Shanghai shelter hospital were recruited through convenience sampling based on WeChat from April 18, 2022, to May 19, 2022. The inclusion criteria were: (1) participant age  $\geq 18$  years; (2) consent to participate in the study; (3) inpatients diagnosed with COVID-19. Eighty-nine invalid questionnaires were excluded to control data quality based on the following criteria: (1) the time used to complete the survey was  $< 100$  s, suggesting that it was completed without thinking about each question;<sup>47</sup> (2) the time used to complete the survey was  $> 60$  min, suggesting confusion in addressing relevant questions; and (3) the same option was selected for all items. The final sample comprised 1015 participants. This study was approved by the ethics committee of the Xijing Hospital of The Fourth Military Medical University and conducted according to the Declaration of Helsinki. All the participants provided their informed consent before commencing the survey.

### Measures

#### Perceived Stress

The 10-item Perceived Stress Scale was used to measure the perceived stress,<sup>48,49</sup> which had been validated in the Chinese population.<sup>50</sup> Each item was rated on a 5-point Likert-type scale (ranging from 0 = *never* to 4 = *very often*); the higher the score, the greater the perceived stress. In this study, Cronbach's  $\alpha$  coefficient of the scale was 0.88.

#### Insomnia

The severity of insomnia in patients was assessed using the Insomnia Severity Index (ISI-7), which had been used in Chinese inpatients with COVID-19.<sup>18</sup> All items were rated on a 5-point scale ranging from 0 = *none* to 4 = *very*. The total score ranged from 0 to 28, and the higher the score, the more severe the insomnia. In this study, Cronbach's  $\alpha$  coefficient of the scale was 0.83.

#### Feeling of Security

The Security Questionnaire was used to measure how secure an individual felt, which demonstrated good reliability and validity in Chinese samples.<sup>51–53</sup> All 16 items were rated on a 5-point scale ranging from 1 = *completely consistent* to 5 = *completely inconsistent*, with higher scores indicating a high feeling of security level. Cronbach's  $\alpha$  coefficient for this scale was 0.87 in our sample.

#### Sense of Control

The revised Chinese version of 12-item Sense of Control Scale (SCS) was used to measure the sense of control.<sup>54,55</sup> All items were scored on a 7-point Likert-like scale ranging from 1 = *completely disagree* to 7 = *completely agree*. The higher the SCS score, the greater the individual's sense of control. In this study, Cronbach's  $\alpha$  coefficient of the scale was 0.81.

## Intolerance of Uncertainty

The Chinese revision of the 12-item Intolerance of Uncertainty Scale was used to assess the intolerance of uncertainty.<sup>56,57</sup> Each item was scored on a Likert 5-point scale ranging from 1 = *completely inconsistent* to 5 = *completely consistent*, with a higher score indicating a lower degree of intolerance of uncertainty. Cronbach's  $\alpha$  coefficient of the scale in this study was 0.78.

## DBAS

The abbreviated version of the Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-16) was used to evaluate DBAS, and its validation has been established in the Chinese population.<sup>58,59</sup> Each item was rated on a 5-point scale ranging from 1 = *strongly agree* to 5 = *strongly disagree*. A lower score on the scale indicates a higher level of DBAS. In this study, Cronbach's  $\alpha$  coefficient of the scale was 0.82.

## Data Analysis

### Network Analysis

The network structure of perceived stress, insomnia, DBAS, sense of control, intolerance of uncertainty, and feeling of security was constructed and visualized via the R package *qgraph*.<sup>60</sup> The Graphical Gaussian Model (GGM) was employed to estimate the present network model.<sup>61,62</sup> In this model, each psychopathological construct was represented as a node, and the edges between nodes depicted the partial correlation between them after accounting for the influence of other nodes. The GGM estimation was performed using nonparametric Spearman correlations.<sup>62</sup> The Least Absolute Shrinkage and Selection Operator (LASSO) algorithm in combination with Extended Bayesian Information Criterion (EBIC) model selection was used to regularize the GGM.<sup>62,63</sup> The EBIC hyperparameter was set to 0.5 to determine the optimal network model.<sup>62</sup> During this process, spurious edges influenced by other nodes in the network were eliminated via computing regularized partial correlations. Any edges with trivial partial correlation were set to zero, resulting in a sparse network comprising only the strongest edges. The EI value of each node was calculated as the centrality index via the R package *qgraph*.<sup>40,60</sup> The EI value indicated the importance of the node for the entire network, with higher values indicating greater influence. The accuracy and stability of the network were evaluated via the R package *Bootnet*.<sup>34</sup> First, a nonparametric bootstrap approach (1000 bootstrapped samples) was employed to calculate the network accuracy, estimating the accuracy of edge weights by computing 95% confidence interval (CI); the narrower 95% CI, the more accurate the estimated edge weights.<sup>64,65</sup> Then, network stability (ie, the stability of node EI) was evaluated through a bootstrap person-dropping procedure by providing a correlation stability (CS) coefficient. A CS coefficient greater than 0.25 and preferably greater than 0.5 reflected sufficient network stability.<sup>34</sup> Finally, statistical differences between edge weights or EI values were examined using bootstrapped difference tests ( $\alpha = 0.05$ ; 1000 bootstrapped samples).

### Directed Acyclic Graph Analysis

We used the Bayesian network approach to model a network where edges were directed and acyclic [ie, directed acyclic graph (DAG)] and to identify possible causality.<sup>45,66</sup> The DAG was produced using a Bayesian hill-climbing algorithm furnished by R package *bnlearn*,<sup>67</sup> aiming to demonstrate the strength and directionality of the psychopathological construct relationships in the cross-sectional data and hence discern causality.<sup>41,68</sup> Through this algorithm, DAG added edges, removed them, and reversed their direction until a goodness-of-fit target score was reached, such as the Bayesian Information Criterion (BIC). Following previous studies,<sup>43,68</sup> this study involved an iterative procedure of randomly restarting the procedure five times with various edges potentially linking different symptom pairs to determine whether a certain edge existed. We performed 10 perturbations to randomly insert/remove/reverse an edge for each restart. As this iterative procedure unfolded, the algorithm discerned the best-fitting network structure based on this random restart/perturbation process. We bootstrapped 1000 samples with replacements to ensure the stability of the DAG, computing a network for each sample and averaging them to obtain the final network. Edge retention was set to determine the frequency at which an edge appeared in the 1000 bootstrapped networks, using the optimal cut-point method retaining edges with high sensitivity and specificity,<sup>69</sup> hence yielding edges almost certain to be genuine in such a sparse DAG. Finally, the BIC value was calculated for each edge, with higher values signifying the higher importance of an edge to the

model. Considering some of the shortcomings of equivalent separate DAGs,<sup>70</sup> we used the completed partially DAG (CPDAG) in this present study based on the study by Lazarov and co-workers.<sup>43</sup>

## Results

### Descriptive Statistics

Our sample included 603 (59.41%) male and 412 (40.59%) female patients; 322 (31.72%) patients were 30 years old or less, and 693 (68.28%) aged more than 30 years; 677 (66.70%) had high school education or less, and 338 (33.30%) were beyond high school. [Table 1](#) shows the abbreviations, means, standard deviations (SDs), skewness, kurtosis, and EI values for each variable.

### Graphical LASSO Network

[Figure 1A](#) depicts the resultant regularized partial correlation network comprising 6 nodes (each node representing one psychopathological variable) and 13 non-zero edges (with weights ranging from  $-0.59$  to  $0.22$ ) out of 15 possible edges. Five strongest pairwise connections stood out: between IUS “Intolerance of uncertainty” and DBAS “Dysfunctional beliefs and attitudes about sleep” (weight =  $-0.59$ ), ISI “Insomnia” and SQ “Feeling of security” (weight =  $-0.42$ ), PSS “Perceived stress” and SQ “Feeling of security” (weight =  $-0.26$ ), SQ “Feeling of security” and CS “Sense of control” (weight =  $0.22$ ), and between CS “Sense of control” and DBAS “Dysfunctional beliefs and attitudes about sleep” (weight =  $0.20$ ). [Table S1](#) in [Supplementary Material](#) shows all the edge weights in the network. Regarding the results of certainty and precision of the edge weights, the bootstrapped 95% CI was narrow (see [Figure 2](#)), suggesting that the edge weights were accurately estimated. The bootstrapped difference test for edge weights in this network is shown in [Figure S1](#) in [Supplementary Material](#).

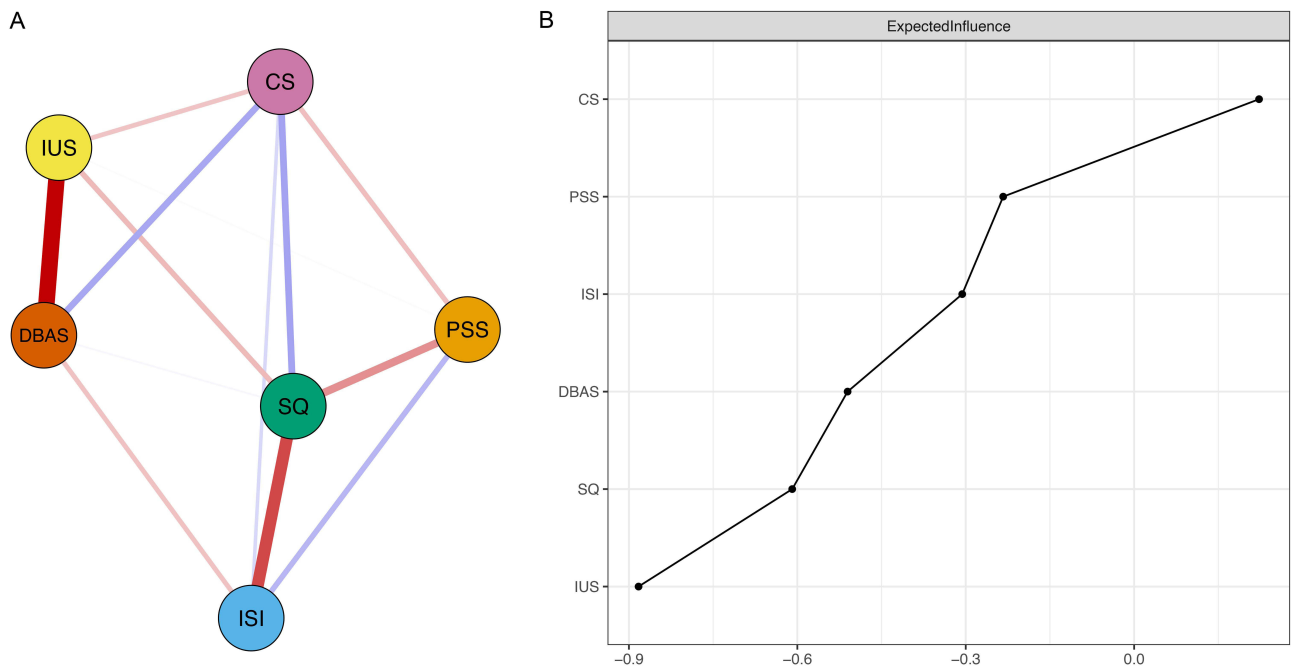
[Figure 1B](#) shows the raw values of EI for each node within the network. IUS “Intolerance of uncertainty” had the highest absolute EI value (EI =  $-0.88$ ), followed by SQ “Feeling of security” (EI =  $-0.61$ ), DBAS “Dysfunctional beliefs and attitudes about sleep” (EI =  $-0.51$ ), ISI “Insomnia” (EI =  $-0.31$ ), PSS “Perceived stress” (EI =  $-0.23$ ), and CS “Sense of control” (EI =  $0.22$ ). The larger the absolute EI value, the more central the node would be. This result indicated that IUS “Intolerance of uncertainty” was the most central node in the present network. The CS coefficient for EI was  $0.75$ , exceeding the preferred threshold of  $0.5$ , indicating that the estimation of node EIs was adequately stable (see [Figure 3](#)). The result of the bootstrapped difference test for node EIs is shown in [Figure S2](#) in [Supplementary Material](#), which revealed that the most central node, namely IUS “Intolerance of uncertainty”, had significantly higher absolute EI value than less central nodes.

### Directed Acyclic Graph

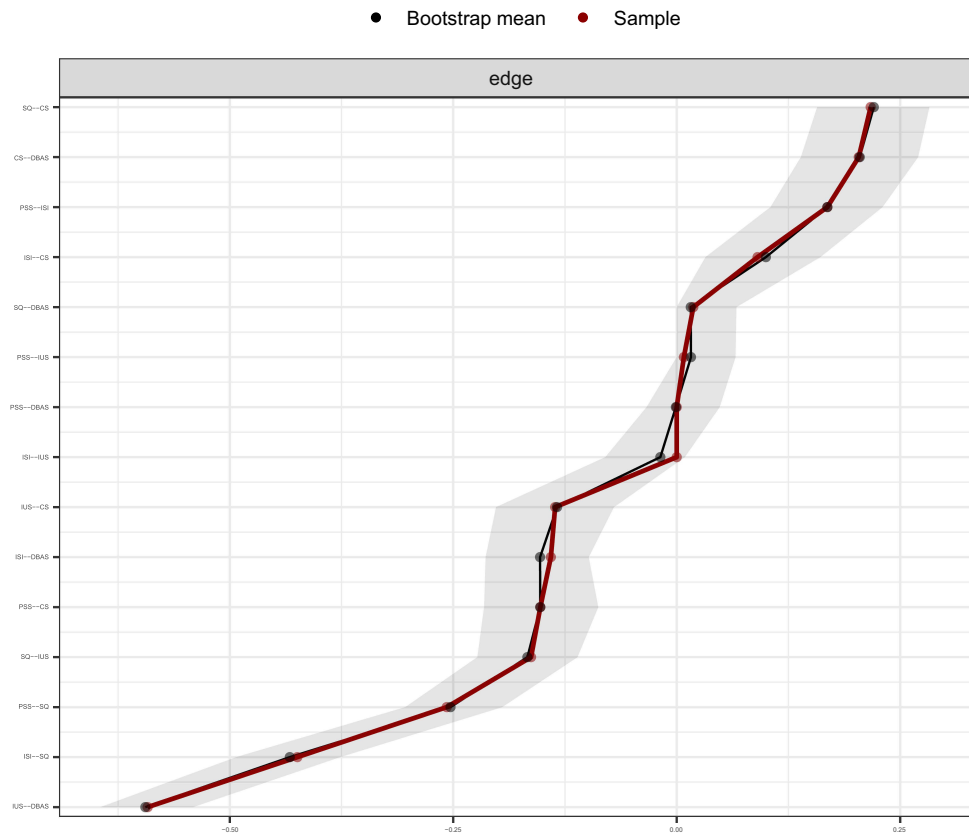
[Figure 4](#) depicts the DAG resulting from averaging the 1000 bootstrapped networks whereby edge thickness represented the changes in BIC when that edge was removed from the DAG and indicated the importance of an edge to the overall DAG structure; the thicker the edge, the more vital it was to model-fit. The direction of arrows signified the direction of predictive (ie, causal) relationships. In the present DAG, two features were notable. First, PSS “Perceived stress”, situated at the top of the network (ie, the most upstream node), emerged as the most pivotal network node and was estimated to have the highest predictive priority compared with other nodes. It was the only variable exhibiting only

**Table 1** Abbreviations, Means, SDs, Skewness, Kurtosis, and EI Values for Each Variable

Variable	Abbreviation	Mean	SD	Skewness	Kurtosis	EI
Perceived stress	PSS	26.77	6.32	-0.01	0.42	-0.23
Insomnia	ISI	15.81	6.13	0.67	0.01	-0.31
Dysfunctional beliefs and attitudes about sleep	DBAS	50.49	15.55	0.06	-0.13	-0.51
Sense of control	CS	53.22	10.15	0.67	0.52	0.22
Intolerance of uncertainty	IUS	35.04	11.44	-0.14	0.04	-0.88
Feeling of security	SQ	61.24	14.51	-0.47	-0.38	-0.61

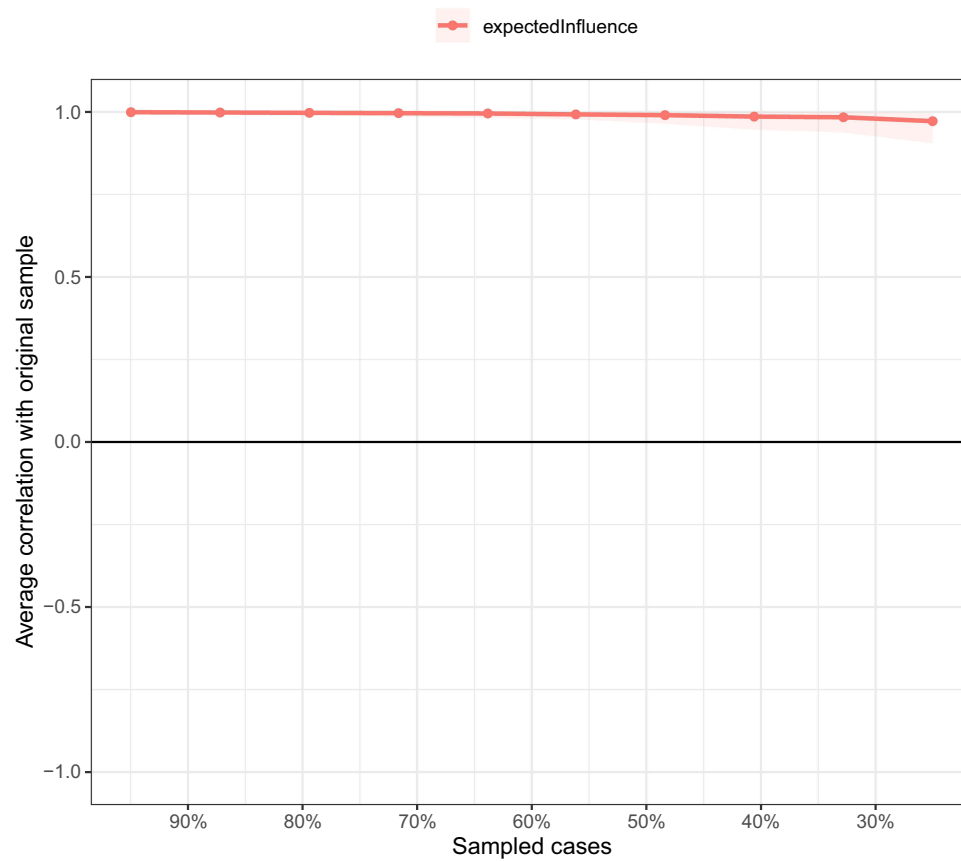


**Figure 1** Network structure and raw values of EI for each node in the present network. **(A)** Graphical LASSO network. The specific meanings of each node are shown in [Table 1](#). Blue edges represent positive correlations, whereas red edges represent negative correlations. Thicker and more saturated edges reflect stronger connections between nodes. Nodes with stronger connections are closer to each other. The weights of the edges are provided in [Table S1](#). **(B)** EI indexes of the nodes in the network (raw values). The specific meanings of each node are shown in [Table 1](#).

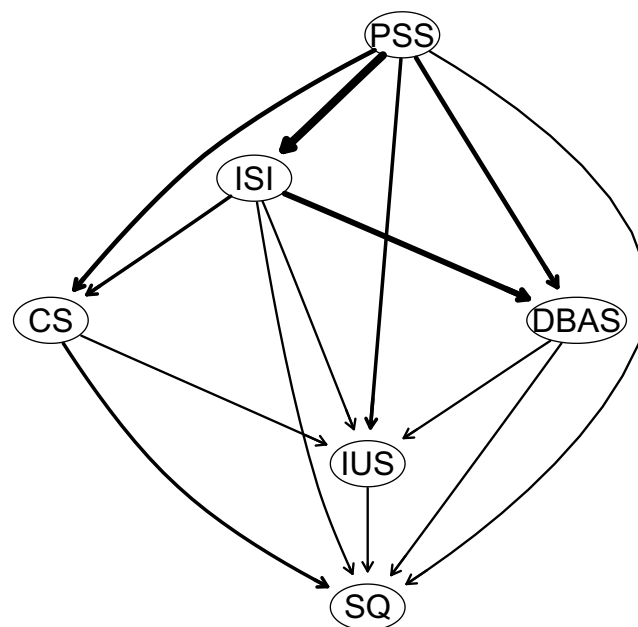


**Figure 2** Accuracy of edge weights in the network. The red line depicts the sample edge weights, the black line represents bootstrap means, and the gray bar depicts the bootstrapped confidence interval. Each horizontal line represents one edge of the network, ordered from the edge with the highest edge-weight to the edge with the lowest edge-weight.





**Figure 3** Stability of node El's in the network. The red bar represents the average correlation between node El's in the full sample and subsample, with the red area depicting the 2.5th quantile to the 97.5th quantile.



**Figure 4** DAG of included psychopathological variables. DAG assumes that nodes are connected in a unidirectional, non-looping fashion, and attempts to generate a model that most closely approximates the data given these assumptions. Nodes represent variables and edges represent directed connections between variables. See Table 1 for node names. Edge thickness signifies the magnitude of the BIC. Thicker edges indicate that the removal of the edge would significantly impact model-fit.

outgoing edges in the network and predicted the activation of five other psychopathological variables, with the strongest connection being from PSS “Perceived stress” to ISI “Insomnia” (changes in BIC value:  $-289.98$ ). The change in BIC values for each edge is depicted in [Table S2](#) in [Supplementary Material](#). Second, the most downstream variables were IUS “Intolerance of uncertainty” and SQ “Feeling of security”, with SQ “Feeling of security” being mostly triggered by other variables and triggering no other nodes.

## Discussion

The patients with COVID-19 are susceptible to perceived stress, insomnia, intolerance of uncertainty, low feeling of security, impaired sense of control, and DBAS. This study constructed a network comprising the aforementioned mental health concerns in patients with COVID-19 who received treatment in the Shanghai shelter hospital to examine the complex relationships among psychological distress. This was the first network study investigating the interrelatedness among these psychopathological variables in a joint framework. The results emphasized certain relatively strong edges, such as the edge between IUS “Intolerance of uncertainty” and DBAS “Dysfunctional beliefs and attitudes about sleep”. The results also determined important nodes such as IUS “Intolerance of uncertainty” that had great influence on the whole network. Moreover, the DAG analysis revealed the putative causality between the aforementioned variables. PSS “Perceived stress” was the variable with the highest predictive priority. Although the findings of this study are preliminary and derived from cross-sectional data, they may advance our understanding of the relations underlying these variables and provide important insights into intervention targets and strategies for addressing relevant psychological distress.

Five strongest edges were identified in the present network. IUS “Intolerance of uncertainty” was negatively correlated with DBAS “Dysfunctional beliefs and attitudes about sleep”. In this study, the lower the DBAS-16 score, the more severe the DBAS. Hence, this study actually signified a positive correlation between intolerance of uncertainty and DBAS. This finding was consistent with a study showing that intolerance of uncertainty was positively correlated with cancer-related dysfunctional beliefs about sleep, and they mediated the relationship of fear of progression with insomnia, depression, or anxiety.<sup>71</sup> However, the direct relationship between IUS and DBAS remains understudied to date, which warrants verification through future research. ISI “Insomnia” and SQ “Feeling of security” were negatively correlated. This result was consistent with a study showing a negative correlation between the feeling of security and sleep disturbance.<sup>72</sup> A previous study also showed that feeling of insecurity and mental distress including insomnia were positively correlated,<sup>73</sup> implying a negative correlation between insomnia and feeling of security from the opposite angle.

Additionally, SQ “Feeling of security” was negatively correlated with PSS “Perceived stress” but positively correlated with CS “Sense of control”. These findings were in line with the studies showing a positive correlation of perceived insecurity with perceived stress,<sup>74,75</sup> the feeling of security and sense of control were positively correlated.<sup>76</sup> Moreover, the relationship between the feeling of security and sense of control was expected to some extent because the sense of control was part of the feeling of security in a certain sense of security questionnaire.<sup>52,53,77</sup> One further relatively strong edge was observed between CS “Sense of control” and DBAS, suggesting that the sense of control was positively correlated with the decreased severity of DBAS, in other words, negatively correlated with DBAS. Prior findings showed that the sense of control was related to reduced sleep problems, which was considered as a protective factor against sleep disorders,<sup>78–80</sup> conversely, dysfunctional beliefs about sleep was a risk factor for sleep disorders.<sup>15,24,81</sup> Predictably, the correlation between the sense of control and DBAS was negative, as revealed in this study.

IUS “Intolerance of uncertainty” was identified as the most central node based on the EI values, highlighting the significant impact of this variable in the network. This importance was mainly because of the connection between intolerance of uncertainty and DBAS. However, our finding was inconsistent with previous studies reporting that intolerance of uncertainty had a lower EI compared with other nodes in the network comprising intolerance of uncertainty, worry, attention bias towards threat, and meta-worry in male undergraduate students.<sup>39</sup> This inconsistency likely resulted from the differences in the variables included in the network and participants recruited. The network analysis is data-driven and hence specific to the characteristics of the study sample and variables.<sup>82,83</sup> Thus, this may partly explain the inconsistencies between this study and previous studies. Few studies examined the role of intolerance of uncertainty as a whole in the psychopathological network. Most studies



examined it at a fine-grained level,<sup>83–85</sup> and therefore, these studies were not directly comparable with our study. Overall, our findings are preliminary and largely exploratory. Hence, further investigations are needed to explore this topic further.

We used the DAG to explore the predictive (and potentially causal) priority of these variables to inform the hypotheses about potential causal associations. Although this study was cross-sectional, the DAG could provide admissible causal insights.<sup>41,68,86</sup> The results showed that PSS “Perceived stress” was situated at the most upstream and triggered the activation of all the other variables, indicating that all downstream variables were probabilistically dependent on it. This means that if patients with COVID-19 perceive stress, they are more susceptible to psychological distress such as insomnia, intolerance of uncertainty, low sense of control, and impaired feeling of security. Our findings are partly contradictory with previous studies showing that the intolerance of uncertainty and high-level perceived insecurity positively predicted stress in undergraduate students.<sup>74,87</sup> This contradiction may result from the difference that patients with COVID-19 perceive stress in the very early stage even prior to infection.<sup>12</sup> IUS “Intolerance of uncertainty” and SQ “Feeling of security” were the most downstream variables; however, the former was of particular interest to us. IUS “Intolerance of uncertainty” was identified as the most central node. However, as the graphical LASSO network is undirected, whether highly central nodes exert significant influence on other nodes in the network or are especially influenced by other nodes in the network is unclear. The DAG results showed that IUS “Intolerance of uncertainty” was probabilistically dependent on variables such as CS “Sense of control” and PSS “Perceived stress”, supplementing the analysis and resolving relevant concerns.

## Theoretical and Clinical Implications

Our findings will be of significance both theoretically and clinically. Theoretically, this study was novel in investigating the complex pairwise relationships between psychopathological constructs after controlling for interference from other constructs in the network. These findings advanced our understanding of the psychopathological pathways among mental health concerns in patients with COVID-19, including undirected and directed associations between variables. These findings also provided preliminary insights into the possible correlations that were never studied, such as the connection between IUS “Intolerance of uncertainty” and DBAS. Regarding the clinical implications, this study focused on two indexes of node importance, which may provide a reference for targeted intervention and prevention. First, we computed EI centrality and found that IUS “Intolerance of uncertainty” stood out as the most central node. Second, we estimated a DAG, which aimed to identify a directional model exhibiting the highest probability given the data, and we found that PSS “Perceived stress” was situated at the top of a cascade of variables and had the highest predictive priority. From the perspective of network theory, central nodes can be regarded as promising targets for effective interventions.<sup>33,88–91</sup> Additionally, the upstream node can also provide implications for intervention because it may cause a beneficial therapeutic cascade.<sup>68,92</sup> Hence, in the present study, IUS “Intolerance of uncertainty” and PSS “Perceived stress” were emphasized, suggesting they were potential intervention targets for mitigating psychological distress and promoting mental health in patients with COVID-19. Cognitive behavioral therapy (CBT) strategies such as cognitive restructuring can be effective in coping with intolerance of uncertainty, while stress appraisal modification contributes to the management of stress. Consequently, CBT empowers individuals to tolerate uncertainty and reduce stress by modifying unhelpful thought patterns, engaging in adaptive behaviors, and cultivating acceptance. Also, the findings provided implications for practice applied to other epidemics that are similar to COVID-19 to a certain extent.

## Limitations

Despite the novel findings, this study had several limitations. First, the study adopted a cross-sectional design without temporal antecedence, preventing us from directly examining the temporal nature and the causal direction.<sup>43,86</sup> Although DAG was used to explore causal relationships, which advanced cross-sectional data closer to a causal interpretation, the cross-sectional design of our study limited the ability to confirm causal relationships.<sup>42,92</sup> Experimental designs remain the gold standard for achieving fully causal claims, indicating the need for longitudinal experiments to determine the causal relationships between the variables in the future. Second, the relatively short timeframe of our study may indeed limit our ability to fully capture the longitudinal dynamics of mental health outcomes. Future research with longitudinal

designs, such as multi-wave cohort studies, would be essential to provide comprehensive understanding of mental health dynamics. Third, the sample in our study comprised patients with COVID-19 in Shanghai, which might limit the generalizability of our findings due to variations in cultural backgrounds and environmental exposure such as patients in Western countries. Future studies should broaden the applicability of the results by replicating them with other populations with COVID-19. Fourth, this study was based on data from self-reported scales, suggesting that the results might have been impacted by subjective biases. Our results should, therefore, be interpreted with caution. Fifth, our approaches were exploratory, not experimental. Although we identified important nodes that might be potential targets for intervening in psychological distress and promoting mental health, the effectiveness of any strategy thereby developed would require further validation. Sixth, although the findings of this study reflected between-subject effects at a group level, individual experiences might vary. The examination of relationship mode within an individual could be implemented via idiographic network analysis using intensive longitudinal data. Finally, the current dataset's demographic variables are insufficiently comprehensive, which limits the ability to implement rigorous research controls. Future studies incorporating more detailed consideration of confounding factors in statistical analysis would enhance the credibility of findings.

## Conclusion

This study was novel in investigating the relationships among perceived stress, insomnia, intolerance of uncertainty, feeling of security, sense of control, and DBAS in patients with COVID-19 using both GGM and DAG networks. Our findings outlined the complex relationships among these variables, enhancing our understanding of the relations previously unexplored. The node IUS “Intolerance of uncertainty” with the highest absolute EI value and the node PSS “Perceived stress” with the highest predictive priority were identified, providing references for potentially effective targets for the intervention of psychological distress and promotion of mental health in patients with COVID-19 and similar epidemic-infected patients.

## Abbreviations

COVID-19, coronavirus disease 2019; GGM, Graphical Gaussian Model; DAG, Directed Acyclic Graph; DBAS, dysfunctional beliefs and attitudes about sleep; IUS, intolerance of uncertainty; PSS, perceived stress; EI, expected influence; LASSO, Least Absolute Shrinkage and Selection Operator; EBIC, Extended Bayesian Information Criterion; CI, confidence interval; CS, correlation stability; BIC, Bayesian Information Criterion; CBT, cognitive behavioral therapy.

## Data Sharing Statement

The datasets used during the study are available from the corresponding author on reasonable request.

## Ethical Approval and Informed Consent

All methods were carried out in accordance with the Declaration of Helsinki and with relevant guidelines and regulations. Informed consent was obtained from all participants included in this study. The ethical approval of the study was obtained from the Ethics Committee of Xijing Hospital of The Fourth Military Medical University.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; reviewed and agreed on all versions of the article before submission, during revision, the final version accepted for publication, and any significant changes introduced at the proofing stage; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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