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Network Structure and Model Projection Analysis of Depressive and Anxiety Symptoms, Sleep Disturbances, and Medical Coping Styles in Hospitalized Patients With Coexisting Hypertension and Diabetes: A Multicenter Cross-Sectional Study

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Abstract

Background: Patients with coexisting hypertension and diabetes mellitus commonly experience depressive and anxiety symptoms, sleep disturbances, and maladaptive coping. However, the conditional associations among psychological, sleep, and coping factors, as well as their projected effects under prespecified model perturbations, remain unclear. Guided by the Theory of Unpleasant Symptoms, this study examined the network structure of these factors and their model-implied responses to simulated perturbations.

Methods: This multicenter cross-sectional study included 529 hospitalized patients with coexisting hypertension and diabetes mellitus. A 26-node ordinal Gaussian graphical model (GGM) was estimated using the Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), Pittsburgh Sleep Quality Index (PSQI), and Medical Coping Modes Questionnaire (MCMQ). Expected influence, bridge expected influence, predictability, and network stability were assessed. Model-based projections across multiple perturbation levels were subsequently evaluated using the Gaussian Graphical Model NodeIdentifyR Algorithm (GGMNIRA). Projected effects under alleviation- and aggravation-oriented perturbations were further compared in a calibrated 23-node Ising network using the NodeIdentifyR algorithm (NIRA).

Results: The 26-node network contained 152 nonzero edges. Trouble relaxing, restlessness, and negative self-evaluation exhibited relatively high expected influence, whereas thoughts of self-harm or death, fear that something awful might happen, and trouble relaxing were among the leading nodes in bridge expected influence. In GGMNIRA, the five highest-priority nodes all belonged to the anxiety community, with trouble relaxing ranking first; only the

anxiety-to-depression pathway met the model-defined decision threshold. In Ising-NIRA, fatigue and sleep problems ranked highly under alleviation-oriented perturbations, whereas fear that something awful might happen and restlessness ranked highly under aggravation-oriented perturbations. Indirect changes in other nodes accounted for approximately 87%–88% of the total projected change associated with high-priority nodes. No robust evidence of network heterogeneity was identified.

Conclusions: An anxiety symptom cluster characterized by worry, trouble relaxing, and restlessness was prominent in both the network structure and model-based projections. Fatigue and sleep problems showed relatively high projected priority under alleviation-oriented perturbations, whereas fear that something awful might happen and restlessness ranked highly under aggravation-oriented perturbations. These findings suggest that improvement and worsening of psychological and sleep symptoms may be associated with distinct network patterns.

Keywords: hypertension; diabetes mellitus; comorbidity; depressive symptoms; anxiety; sleep quality; coping strategies; network analysis

Background

Hypertension and diabetes mellitus are common chronic noncommunicable diseases. Their coexistence can increase the risk of cardiovascular, cerebrovascular, and renal damage through mechanisms including insulin resistance, endothelial dysfunction, oxidative stress, inflammation, and vascular remodeling [1–3]. Patients are required to manage multiple disease-related tasks, including blood pressure and blood glucose monitoring, combination

pharmacotherapy, lifestyle modification, and complication management [3,4]. Consequently, they are more likely to experience depression, anxiety, and sleep problems, together with impaired quality of life and increased healthcare burden [5,6]. These problems may, in turn, undermine treatment engagement, self-management, and disease control [7–9]. Current diabetes care guidelines have incorporated depression, anxiety, coping, and sleep health into routine assessment [4]. However, examining these domains as separate outcomes may obscure the co-occurrence patterns and interrelationships among multidimensional symptoms and coping responses.

The Theory of Unpleasant Symptoms (TOUS) posits that multiple symptoms can co-occur and interact and that symptom experiences are influenced by physiological, psychological, and situational factors [10,11]. In the present study, coexisting hypertension and diabetes mellitus and related clinical characteristics are conceptualized as the physiological background; depression, anxiety, and sleep problems as interrelated unpleasant symptoms; and demographic, socioeconomic, residential, and care-resource characteristics as situational factors. Confrontation, avoidance, and resignation represent psychological and behavioral responses through which patients cope with disease-related threats and symptom experiences. These responses may influence how symptoms are interpreted and managed and may themselves change in the context of persistent psychological and sleep problems [10–12]. Previous research in patients with heart failure, guided by TOUS, has demonstrated complex relationships among depression, anxiety, sleep difficulties, and disease-related symptoms [13]. Accordingly, the present study uses TOUS as a framework for organizing variables and interpreting findings rather than as a model for testing the complete theoretical structure.

The relationships among depression, anxiety, sleep problems, and medical coping are likely to be symptom-specific. Among patients with diabetes, depression and anxiety may be interconnected through symptoms such as worry, difficulty relaxing, fatigue, concentration difficulties, and negative self-evaluation [7,8,14]. Reduced sleep efficiency and daytime dysfunction may also co-occur with fatigue, concentration difficulties, and depressed mood [9]. Adaptive coping is generally associated with better psychological and physical health, whereas maladaptive coping responses, such as avoidance and resignation, are associated with diabetes distress, depression, and poorer quality of life [12]. Conventional correlation and regression analyses primarily estimate average associations between total scale scores and therefore have limited ability to identify specific nodes that remain associated after conditioning on other variables or components that bridge different domains [15,16].

Regularized partial correlation networks can estimate conditional associations among symptom and coping dimensions [15,16,20]. Previous studies involving populations with diabetes, hypertension, and heart failure have identified central or bridge nodes within networks of depression, anxiety, sleep, and coping [14,17–19]. However, studies simultaneously integrating all four domains among patients with coexisting hypertension and diabetes mellitus remain scarce. Moreover, relatively few studies have distinguished the structural position of a node within a static network from its projected changes under prespecified model perturbations. Expected influence, bridge expected influence, and predictability can characterize overall connectivity, cross-community connectivity, and the extent to which a node can be explained by its neighboring nodes, respectively [20–22], whereas bootstrap procedures can be used to assess the accuracy and stability of network

estimates [23]. Because centrality does not directly represent the system-level consequences associated with changes in a given node [24], complementary model-based projection analyses are warranted to compare candidate nodes identified using different network metrics.

Accordingly, this study first employs a Gaussian graphical model (GGM) for ordinal data to identify stable conditional associations, central nodes, bridge nodes, and node predictability. We then conduct multi-level model-based projection analyses to evaluate single-node perturbations, cross-community pathways, and joint community perturbations, with distributional changes quantified using Kullback–Leibler (KL) divergence. Subsequently, within a calibrated binary Ising network, we adapt the logic of the NodeIdentifyR algorithm (NIRA) to compare node-level model projections in the alleviation and aggravation directions and to distinguish direct changes in the target node from indirect projected changes attributable to other nodes [25]. Finally, we compare sex-specific network differences and explore heterogeneity associated with demographic and clinical characteristics. By integrating theoretical interpretation, network structure, and model-based projection, this study aims to elucidate the interrelationships among psychological symptoms, sleep problems, and medical coping and to provide a basis for future research on symptom assessment and nursing interventions for patients with coexisting hypertension and diabetes mellitus.

Methods

Study design, setting, and participants

This multicenter cross-sectional study was conducted at four healthcare institutions in Hubei Province, China, between February and June 2024. Participants were recruited from the

departments of endocrinology, cardiology, respiratory medicine, nephrology, psychiatry and psychology, and other clinical departments involved in chronic disease care. Based on prespecified inclusion and exclusion criteria, the study team enrolled hospitalized patients with coexisting hypertension and diabetes mellitus, with both diagnoses verified through medical record review during hospitalization. The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [26].

Participants were recruited using convenience sampling. The inclusion criteria were as follows: (1) age ≥18 years; (2) diagnoses of both hypertension and diabetes mellitus confirmed through medical record review during hospitalization; (3) being alert and having basic reading, comprehension, and communication abilities; (4) being able to complete the questionnaire independently or with non-directive assistance from an investigator who did not prompt or influence responses; and (5) voluntary participation in the study and provision of written informed consent.

The exclusion criteria were as follows: (1) inability to complete the questionnaire reliably because of impaired consciousness, severe cognitive impairment, an acute psychiatric disorder, or an unstable clinical condition; (2) uncertain diagnostic information regarding hypertension or diabetes mellitus; (3) missing data on primary network nodes that precluded inclusion in the primary network analysis; and (4) major logical inconsistencies in the data that could not be verified or resolved. Patients documented as being seriously or critically ill were not automatically excluded if they remained able to complete the questionnaire.

The initial database contained records for 540 patients. After verification of variable coding, rechecking of scale scores, logical consistency checks, and assessment of network-node completeness, 529 patients had complete data for all 26 primary network nodes and were included in the Gaussian graphical model (GGM) analysis for ordinal data. No imputation was performed for missing data on the primary network nodes. Body mass index (BMI) data were missing for nine patients; therefore, BMI-stratified analyses included 520 patients. Other descriptive analyses and between-group comparisons were conducted using available cases with nonmissing data for the variables involved.

Research instruments and network nodes

Sociodemographic and clinical characteristics

Sociodemographic and clinical characteristics included age, sex, ethnicity, height, weight, marital status, educational attainment, healthcare payment method, occupation, monthly per-capita household income, place of residence, living arrangement, recurrence status, prespecified comorbidities, level of nursing care, disease severity, primary caregiver during hospitalization, nutritional risk score, disease stage, and hospital tier. Age was categorized as <65 years or ≥65 years. Based on the cutoff for overweight among Chinese adults, body mass index (BMI) was categorized as <24 kg/m² or ≥24 kg/m² [27]. Nutritional risk was assessed using the Nutritional Risk Screening 2002 (NRS 2002); scores <3 and ≥3 were classified as indicating no nutritional risk and nutritional risk, respectively [28]. Hospital, department, and hospital tier were treated as center- or design-level variables and were not used as the primary basis for drawing conclusions regarding patient-level network heterogeneity. The sample

distributions according to the prespecified age and BMI cutoffs are presented in Supplementary Fig. 4.

Depressive and anxiety symptoms

Depressive symptoms were assessed using the 9-item Patient Health Questionnaire (PHQ-9) [29,30]. The PHQ-9 consists of nine items, each rated from 0 to 3, yielding a total score ranging from 0 to 27. In the network, D1–D9 represented the nine PHQ-9 items. Cronbach's α for the PHQ-9 in the present sample was 0.915.

Anxiety symptoms were assessed using the 7-item Generalized Anxiety Disorder scale (GAD-7) [31,32]. The GAD-7 consists of seven items, each rated from 0 to 3, yielding a total score ranging from 0 to 21. In the network, A1–A7 represented the seven GAD-7 items. Cronbach's α for the GAD-7 in the present sample was 0.949.

Sleep problems

Sleep status was assessed using the Pittsburgh Sleep Quality Index (PSQI) [33,34]. In the network, S1–S7 represented the seven PSQI components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction, respectively. Each component was scored from 0 to 3. Between-group comparisons were based on the PSQI total score after score verification. Because the PSQI is a multidimensional composite index, Cronbach's α across its seven component scores was not considered the primary evidence of internal consistency in this study.

Medical coping modes and node hierarchy

Medical coping modes were assessed using the Medical Coping Modes Questionnaire (MCMQ) [35,36], which comprises three dimensions: confrontation, avoidance, and resignation. In the network, C1–C3 represented these three dimensions, respectively.

The primary ordinal network comprised 26 nodes, including the nine PHQ-9 items, seven GAD-7 items, seven PSQI components, and three MCMQ dimensions. These nodes were prespecified into four communities: depression, anxiety, sleep problems, and medical coping. The binary Ising analysis included only the 23 psychological and sleep-related nodes (D1–D9, A1–A7, and S1–S7); the MCMQ dimensions were excluded to minimize the influence of differences in measurement level and the dichotomization of dimension-level scores on activated-node counts. Because the analytic dataset retained only MCMQ dimension scores and did not include the original item-level responses, the internal consistency of the individual MCMQ dimensions was not recalculated. Codes, names, community assignments, and scoring ranges for all 26 network nodes are provided in Supplementary Table 1.

Data collection and quality control

The coordinating research team developed a standardized survey protocol, questionnaire administration instructions, variable definitions, and quality-control procedures for implementation across all participating centers. At each center, the nursing department coordinated survey implementation and investigator training and facilitated data collection within the relevant clinical departments. Department heads oversaw participant screening, investigator assignment, survey implementation, and the initial review of completed questionnaires. Trained clinical nurses were designated as survey investigators.

Before the formal survey, investigators at all centers underwent standardized training on the inclusion and exclusion criteria, questionnaire administration, the permissible scope of clarification for scale items, procedures for verifying clinical information, informed consent, and protection of patient privacy. These standardized procedures were intended to minimize inter-center and inter-investigator variability in data collection.

At all centers, participants were screened according to uniform inclusion and exclusion criteria. Paper-based questionnaires were administered only after patients had been informed of the study purpose, survey content, voluntary nature of participation, and data-confidentiality principles and had provided written informed consent. Patients completed the questionnaires independently. For patients who had difficulty reading or writing but had intact comprehension and communication abilities, a trained investigator read each item aloud and recorded the response exactly as provided, without giving leading explanations or otherwise influencing the response.

Demographic and psychosocial data were primarily self-reported. Diagnoses of hypertension and diabetes, level of nursing care, severity of illness, Nutritional Risk Screening 2002 (NRS 2002) scores, and other clinical data were verified against medical records and nursing documentation.

After questionnaire collection, investigators in each clinical department first assessed the questionnaires for completeness and logical consistency, followed by a secondary review by the designated coordinator at each center. Questionnaires with evident logical inconsistencies,

missing key items, or discrepancies between data sources were verified against the original questionnaires, medical records, and nursing documentation.

Each center prepared its dataset using standardized variable names, coding rules, and scale-scoring criteria and submitted the data to the coordinating research team for consolidation. Data were independently entered by two data-entry personnel and cross-checked for consistency; any discrepancies were resolved by rechecking the original source documents. Before analysis, the consolidated dataset was systematically examined for allowable variable ranges, accuracy of scale scoring, logical consistency across variables, outliers, duplicate records, and missing data. All analyses were conducted using the locked node order, node labels, and community definitions.

Statistical analysis

Ordinal Gaussian graphical model

A mixed correlation matrix was computed using the cor_auto function in the qgraph package [38], with variables comprising no more than seven unique integer levels treated as ordinal. When the resulting correlation matrix was not positive definite, positive-definite adjustment was performed by specifying forcePD = TRUE. A regularized partial correlation network was subsequently estimated using the extended Bayesian information criterion–based graphical least absolute shrinkage and selection operator (EBICglasso), with the EBIC tuning parameter γ set to 0.50 [20]. Network edges represented conditional associations between pairs of nodes after controlling for all remaining nodes. Node predictability was quantified using R^2 [22]. Expected influence (EI) was defined as the signed sum of edge weights connecting a given

node to all adjacent nodes, whereas bridge expected influence (BEI) was defined as the signed sum of edge weights connecting that node to nodes in other communities [21]. EI and BEI were used to characterize the structural positions of nodes within the estimated network and were not interpreted as measures of intervention effects [46].

Network accuracy and stability

The accuracy of nonzero edge weights, EI, and BEI was evaluated using 1,000 successful nonparametric bootstrap resamples to obtain 95% confidence intervals. The stability of EI and BEI was assessed using case-dropping bootstrap and quantified using the correlation stability coefficient (CS). To ensure consistency of the estimation procedure between the primary and resampled networks, all resampled networks were re-estimated using the same analytical pipeline as the primary analysis, namely cor_auto(forcePD = TRUE) followed by EBICglasso with $\gamma = 0.50$. The CS coefficient was defined as the maximum proportion of cases that could be dropped while the correlation between the corresponding EI or BEI estimates from the reduced samples and those from the original sample remained ≥ 0.70 in at least 95% of the resamples. Network accuracy and centrality stability were evaluated in accordance with established bootstrap procedures [23].

Multilevel GGMNIRA model-projection analysis

To further evaluate model-implied changes in the overall distribution resulting from node manipulation under a fixed network model and prespecified manipulation conditions, multilevel model-projection analyses were conducted on the fixed 26-node ordinal Gaussian graphical model using GGMNIRA version 0.1.0. Node-joint analyses were first performed by

manipulating each node individually at the automatically determined manipulation intensity of I = 1. Kullback–Leibler (KL) divergence was used to quantify the change in the joint distribution of the entire network between the baseline and manipulated conditions. For the full 26-node network, the automatically derived interpretive threshold was 19.443. This threshold was used to facilitate interpretation of the relative magnitude of model-implied distributional changes and was not treated as a conventional frequentist cutoff for statistical significance. Larger KL divergence values indicated greater changes in the joint distribution under the specified network model and manipulation condition.

Building on the node-level analyses, target-community marginal distribution analyses were conducted for four prespecified cross-community source-to-target pathways: sleep problems → depression, sleep problems → anxiety, depression → anxiety, and anxiety → depression. Unit-norm community-joint manipulations were additionally performed for the depression, anxiety, sleep problems, and medical coping communities. Because these metrics were defined in different distributional spaces, node-joint KL divergence, target-community marginal KL divergence, and community-joint KL divergence were ranked only within their respective analytical frameworks, and their absolute values were not directly compared across analysis types.

The stability of KL-based rankings was assessed using case-dropping bootstrap, from which Pearson- and Spearman-based KL correlation stability coefficients (KL-CS) were calculated. In addition, 1,000 nonparametric bootstrap resamples were used to estimate the frequency with which each node met the interpretive threshold or ranked within the Top-1, Top-3, or Top-5 positions. Pairwise differences in KL divergence between the top-ranked node in the original

sample and all other nodes were evaluated with Holm adjustment for multiple comparisons. Finally, the analyses were repeated using a thresholded 26-node network and a network restricted to the 23 psychological and sleep-related nodes to evaluate the robustness of node and community rankings to the prespecified model specifications.

Binary Ising network estimation and fixed-edge-weight calibration

For the primary binary analysis, the 23 nodes from the Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), and Pittsburgh Sleep Quality Index (PSQI) were dichotomized such that an item score of 0 was coded as 0 and scores of 1–3 were coded as 1. Original scores of 0 were defined as inactive, whereas scores of 1–3 were defined as active. This dichotomization was used solely for model analysis and did not correspond to any clinical diagnostic cutoff. A binary Ising network was estimated using IsingFit version 0.4 [39], with an extended Bayesian information criterion (EBIC) tuning parameter of $\gamma = 0.25$ and the AND rule. Network accuracy and centrality stability were assessed using nonparametric bootstrap and case-dropping subset bootstrap procedures, respectively. The standard IsingFit model was designated M0.

Because M0, while retaining the estimated network structure, underestimated the observed node activation rates and the mean number of active nodes, node intercepts were further calibrated with edge weights held fixed. First, offset logistic regression based on the pseudolikelihood was used to obtain M1-PL. Next, within each of the three connected components, intercepts were calibrated using exact state enumeration and the joint likelihood, yielding M1-Exact. The largest connected component comprised 16 nodes and therefore

involved no more than 65,536 possible states, making exact enumeration computationally feasible. A parameterization audit confirmed an IsingSampler parameter scale of $\kappa = 1$. M1-Exact met the prespecified calibration criteria and was selected as the primary model for the Ising-based NodeIdentifyR algorithm (Ising-NIRA), whereas M0 was retained both to reproduce the conventional approach and as a sensitivity model.

Directional Ising-NIRA and simulation stability

To construct directional node-perturbation scenarios, the intercept of each node was separately decreased or increased by 2 within-model standard deviations (SDs), representing alleviation and aggravation scenarios, respectively. The alleviation effect was defined as the expected number of active nodes under the unperturbed model minus that under the alleviation scenario, whereas the aggravation effect was defined as the expected number under the aggravation scenario minus that under the unperturbed model.

Primary estimates were obtained by component-wise exact enumeration under M1-Exact. We additionally reported results based on a within-M0 perturbation of 2 SDs, an M1 perturbation using a common absolute magnitude, and conventional Monte Carlo simulations based on 5,000 Metropolis–Hastings states per scenario. The total effect was further decomposed into a direct component attributable to the change in the expected state of the target node itself and an indirect model-projected component arising from changes in the activation probabilities of all remaining nodes.

To evaluate the Monte Carlo stability of the conventional simulation approach, 100 independent replicates were performed for each of the M0 and M1-Exact models. In each replicate, 5,000 states were generated for both the alleviation and aggravation scenarios for

each of the 23 nodes. Top-1, Top-3, and Top-5 selection frequencies, rank ranges, and correlations with the exact results were calculated. The mgm package version 1.2-15 was used to estimate a regularized binary network allowing third-order interactions [40]. The primary specification used EBIC $\gamma = 0.25$, the AND rule, and the Loh–Wainwright threshold [41]; EBIC $\gamma = 0.50$ with the AND rule and EBIC $\gamma = 0.25$ with the OR rule were used as sensitivity specifications to evaluate the fixed-edge-weight assumption. Because third-order interactions were identified under the primary specification, the Ising-NIRA results were interpreted as conditional model projections under the fixed-edge-weight assumption.

Sex comparisons and exploratory heterogeneity analyses

Sex was prespecified as the primary network comparison. The Network Comparison Test was performed using 1,000 permutations of group labels under an independent-samples framework to compare the network structure invariance statistic (M) and the global strength invariance statistic (S). Individual edges, expected influence (EI), and bridge expected influence (BEI) were further compared, with Holm correction applied to these specific comparisons [42].

Fourteen variables—level of nursing care, place of residence, body mass index (BMI), recurrence, age, occupational status, disease severity, disease stage, health-care payment method, educational attainment, primary caregiver, comorbid heart disease, nutritional risk, and monthly income—were evaluated as exploratory screening factors for network heterogeneity. P values from the M and S tests were separately adjusted using the Benjamini–Hochberg false discovery rate (BH-FDR) procedure [37]. The grouping schemes, sample-size feasibility, variable overlap, and exclusions for the exploratory candidate variables are detailed in Supplementary Tables 5–7.

Statistical software

All analyses were conducted in R version 4.6.1, primarily using qgraph version 1.9.8 [38], bootnet version 1.8 [23], networktools version 1.6.0 [21], GGMNIRA version 0.1.0, IsingFit version 0.4 [39], IsingSampler version 0.2.4, nodeIdentifyR version 1.0.0 [25], and mgm version 1.2-15 [40]. All tests were two-sided, with $P < 0.05$ or an adjusted $q < 0.05$ considered statistically significant.

Ethical considerations

This study was reviewed and approved by the Ethics Committee of Renmin Hospital of Wuhan University (approval no. WDRY2022-K122). Before data collection, patients were informed of the study objectives, procedures, potential risks, measures to protect their privacy, and their right to withdraw from participation. Written informed consent was obtained from all patients. All study data were de-identified before analysis and used solely for the purposes of this study. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

Participant characteristics and data completeness

A total of 529 patients with comorbid hypertension and diabetes mellitus were included in the final analysis, comprising 307 men (58.0%) and 222 women (42.0%). The mean age was 64.82 ± 11.98 years, and the median age was 66 years. Body mass index (BMI) data were available for 520 participants, with a mean BMI of 23.94 ± 3.74 kg/m². The mean scores on the Patient

Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), and Pittsburgh Sleep Quality Index (PSQI) were 5.19 ± 5.29, 3.51 ± 4.42, and 5.36 ± 3.19, respectively.

The sociodemographic and clinical characteristics, scale scores, and distributions stratified by sex are presented in Table 1. Continuous variables are reported as both mean ± standard deviation (SD) and median (Q1–Q3). *P* values are provided solely for descriptive comparisons and were not used as criteria for the inclusion of network nodes or candidate variables. The distributional characteristics and data quality of the scales and their respective dimensions are presented in Supplementary Table 2.

385 **Table 1. Sociodemographic and clinical characteristics of patients with comorbid hypertension**
386 **and diabetes mellitus**

Variable	Category	Overall (n = 529)	Men (n = 307)	Women (n = 222)	Standardized difference	*P* value
Age (years)	—	64.82 ± 11.98; 66.00 (57.00–73.00)	63.48 ± 12.58; 64.00 (55.00–73.00)	66.67 ± 10.85; 68.00 (59.00–74.00)	−0.271	0.002
BMI (kg/m²)	—	23.94 ± 3.74; 23.73 (21.22–26.04)	24.10 ± 3.83; 23.74 (21.67–26.12)	23.74 ± 3.61; 23.73 (20.96–25.71)	0.097	0.396
	Missing	9 (1.7%)	8 (2.6%)	1 (0.5%)	—	—
Nutritional risk score	—	1.55 ± 1.65; 1.00 (0.00–2.00)	1.49 ± 1.64; 1.00 (0.00–2.00)	1.64 ± 1.66; 1.00 (0.00–2.00)	−0.091	0.218
PHQ-9 total score	—	5.19 ± 5.29; 4.00 (0.00–9.00)	4.75 ± 5.41; 3.00 (0.00–8.00)	5.80 ± 5.08; 5.00 (1.00–9.00)	−0.201	0.002
GAD-7 total score	—	3.51 ± 4.42; 2.00 (0.00–7.00)	3.29 ± 4.65; 1.00 (0.00–6.00)	3.81 ± 4.07; 2.50 (0.00–7.00)	−0.118	0.011
PSQI total score	—	5.36 ± 3.19; 5.00 (3.00–7.00)	5.02 ± 3.04; 5.00 (3.00–7.00)	5.83 ± 3.33; 6.00 (3.00–8.00)	−0.254	0.005
Medical Coping Modes Questionnaire (MCMQ), Confrontation subscale	—	17.64 ± 3.12; 17.00 (16.00–19.00)	17.79 ± 3.26; 17.00 (16.00–19.50)	17.44 ± 2.91; 17.00 (15.00–19.00)	0.114	0.405
MCMQ, Avoidance subscale	—	15.22 ± 2.75; 15.00 (14.00–17.00)	15.17 ± 2.87; 15.00 (13.50–17.00)	15.29 ± 2.59; 15.00 (14.00–17.00)	−0.046	0.273
MCMQ, Acceptance–Resignation subscale	—	10.34 ± 3.61; 11.00 (7.00–13.00)	9.99 ± 3.70; 10.00 (6.00–13.00)	10.83 ± 3.42; 12.00 (8.00–13.00)	−0.235	0.008
Marital status	Unmarried	13 (2.5%)	10 (3.3%)	3 (1.4%)	0.127	<0.001
	Married	480 (90.7%)	286 (93.2%)	194 (87.4%)	0.196	—
	Widowed	30 (5.7%)	6 (2.0%)	24 (10.8%)	−0.368	—
	Divorced	6 (1.1%)	5 (1.6%)	1 (0.5%)	0.116	—
Educational attainment	Primary school or below	197 (37.2%)	70 (22.8%)	127 (57.2%)	−0.750	<0.001
	Junior high school	183 (34.6%)	113 (36.8%)	70 (31.5%)	0.111	—
	Senior high school/technical secondary school	94 (17.8%)	74 (24.1%)	20 (9.0%)	0.415	—
	Junior college/bachelor's degree	54 (10.2%)	49 (16.0%)	5 (2.3%)	0.491	—
	Master's degree or above	1 (0.2%)	1 (0.3%)	0 (0.0%)	0.081	—
Medical expense payment method	Self-pay	7 (1.3%)	1 (0.3%)	6 (2.7%)	−0.196	<0.001
	Resident medical insurance	372 (70.3%)	198 (64.5%)	174 (78.4%)	−0.311	—
	Employee medical insurance	140 (26.5%)	101 (32.9%)	39 (17.6%)	0.359	—
	Government-funded medical care	9 (1.7%)	7 (2.3%)	2 (0.9%)	0.11	—
	Commercial health insurance	1 (0.2%)	0 (0.0%)	1 (0.5%)	−0.095	—
Occupation	Farmer	149 (28.2%)	67 (21.8%)	82 (36.9%)	−0.336	<0.001
	Worker	69 (13.0%)	51 (16.6%)	18 (8.1%)	0.261	—
	Enterprise/public-institution employee or civil servant	67 (12.7%)	58 (18.9%)	9 (4.1%)	0.479	—
	Self-employed	53 (10.0%)	35 (11.4%)	18 (8.1%)	0.111	—
	Unemployed	73 (13.8%)	28 (9.1%)	45 (20.3%)	−0.319	—

Variable	Category	Overall (n = 529)	Men (n = 307)	Women (n = 222)	Standardized difference	*P* value
	Retired	118 (22.3%)	68 (22.1%)	50 (22.5%)	−0.009	—
Monthly per capita household income	<3,000 CNY/month	213 (40.3%)	101 (32.9%)	112 (50.5%)	−0.362	<0.001
	3,000–5,000 CNY/month	213 (40.3%)	131 (42.7%)	82 (36.9%)	0.117	—
	5,000–10,000 CNY/month	92 (17.4%)	67 (21.8%)	25 (11.3%)	0.287	—
	>10,000 CNY/month	11 (2.1%)	8 (2.6%)	3 (1.4%)	0.09	—
Place of residence	Rural area	244 (46.1%)	126 (41.0%)	118 (53.2%)	−0.244	<0.001
	Town	101 (19.1%)	54 (17.6%)	47 (21.2%)	−0.091	—
	City	184 (34.8%)	127 (41.4%)	57 (25.7%)	0.337	—
Living arrangement	With spouse	288 (54.4%)	182 (59.3%)	106 (47.7%)	0.233	<0.001
	With children	68 (12.9%)	21 (6.8%)	47 (21.2%)	−0.422	—
	With spouse and children	114 (21.6%)	71 (23.1%)	43 (19.4%)	0.092	—
	Living alone	51 (9.6%)	25 (8.1%)	26 (11.7%)	−0.120	—
	With parents	8 (1.5%)	8 (2.6%)	0 (0.0%)	0.231	—
Recurrence	No	288 (54.4%)	171 (55.7%)	117 (52.7%)	0.06	0.494
	Yes	241 (45.6%)	136 (44.3%)	105 (47.3%)	−0.060	—
Comorbid heart disease	No	398 (75.2%)	236 (76.9%)	162 (73.0%)	0.09	0.305
	Yes	131 (24.8%)	71 (23.1%)	60 (27.0%)	−0.090	—
Comorbid stroke	No	454 (85.8%)	263 (85.7%)	191 (86.0%)	−0.011	0.905
	Yes	75 (14.2%)	44 (14.3%)	31 (14.0%)	0.011	—
Comorbid chronic respiratory disease	No	481 (90.9%)	277 (90.2%)	204 (91.9%)	−0.058	0.511
	Yes	48 (9.1%)	30 (9.8%)	18 (8.1%)	0.058	—
Comorbid cancer	No	516 (97.5%)	302 (98.4%)	214 (96.4%)	0.124	0.148
	Yes	13 (2.5%)	5 (1.6%)	8 (3.6%)	−0.124	—
Other comorbid chronic diseases	No	480 (90.7%)	276 (89.9%)	204 (91.9%)	−0.069	0.436
	Yes	49 (9.3%)	31 (10.1%)	18 (8.1%)	0.069	—
Level of nursing care	Level I nursing care	284 (53.7%)	158 (51.5%)	126 (56.8%)	−0.106	0.479
	Level II nursing care	237 (44.8%)	144 (46.9%)	93 (41.9%)	0.101	—
	Level III nursing care	8 (1.5%)	5 (1.6%)	3 (1.4%)	0.023	—
Illness severity	Neither severe nor critical	340 (64.3%)	213 (69.4%)	127 (57.2%)	0.255	0.013
	Severe	175 (33.1%)	86 (28.0%)	89 (40.1%)	−0.257	—
	Critical	14 (2.6%)	8 (2.6%)	6 (2.7%)	−0.006	—
Primary caregiver during hospitalization	None	134 (25.3%)	96 (31.3%)	38 (17.1%)	0.335	<0.001
	Parent(s)	20 (3.8%)	10 (3.3%)	10 (4.5%)	−0.065	—
	Spouse	185 (35.0%)	113 (36.8%)	72 (32.4%)	0.092	—
	Child(ren)	155 (29.3%)	69 (22.5%)	86 (38.7%)	−0.359	—
	Relative(s)	9 (1.7%)	4 (1.3%)	5 (2.3%)	−0.072	—
	Care attendant	26 (4.9%)	15 (4.9%)	11 (5.0%)	−0.003	—
Nutritional risk category	No nutritional risk (<3 points)	416 (78.6%)	245 (79.8%)	171 (77.0%)	0.068	0.442

Variable	Category	Overall (n = 529)	Men (n = 307)	Women (n = 222)	Standardized difference	*P* value
	Nutritional risk (≥3 points)	113 (21.4%)	62 (20.2%)	51 (23.0%)	−0.068	—
Disease stage	Acute phase	159 (30.1%)	94 (30.6%)	65 (29.3%)	0.029	0.762
	Stable phase	282 (53.3%)	165 (53.7%)	117 (52.7%)	0.021	—
	Recovery phase	88 (16.6%)	48 (15.6%)	40 (18.0%)	−0.064	—

Note: Continuous variables are presented as mean ± SD; median (Q1–Q3), and categorical variables as n (%). P values are provided for descriptive comparisons only. BMI, body mass index; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7; PSQI, Pittsburgh Sleep Quality Index; MCMQ, Medical Coping Modes Questionnaire; SD, standard deviation; Q1, first quartile; Q3, third quartile; CNY, Chinese yuan.

Network structure, node metrics, and stability of the ordinal GGM

The zero-order correlation matrix for the 26 nodes is provided in Supplementary Data 1, and the corresponding heatmap is shown in Supplementary Fig. 1.

The 26-node network comprised 325 possible edges, of which 152 were estimated as nonzero, yielding a network density of 0.468 and a global strength of 13.107. Of the nonzero edges, 122 were positive and 30 were negative. The strongest within-community edges were observed between sleep duration and habitual sleep efficiency (S3–S4, 0.673), use of sleep medication and daytime dysfunction (S6–S7, 0.498), nervousness or anxiety and inability to control worrying (A1–A2, 0.422), and trouble relaxing and restlessness (A4–A5, 0.408). The strongest intercommunity edge was between thoughts of self-harm or death and fear that something awful might happen (D9–A7, 0.234). Key edges and node metrics are presented in Table 2; complete edge lists and edge-weight matrices are provided in Supplementary Data 1, and complete node metrics are provided in Supplementary Table 3. The estimated network is shown in Fig. 1.

The highest Expected Influence (EI) values were observed for trouble relaxing (A4, 1.173), restlessness (A5, 1.158), and negative self-evaluation (D6, 1.124). Bridge Expected Influence

(BEI) was highest for thoughts of self-harm or death (D9, 0.625), fear that something awful might happen (A7, 0.550), and trouble relaxing (A4, 0.370). The five nodes with the highest predictability all belonged to the anxiety community and, in descending order, were A4, A5, A3, A2, and A1. Standardized EI and BEI values for all network nodes are shown in Fig. 2.

All 1,000 nonparametric bootstrap iterations were completed successfully. The bootstrap mean estimates for the stronger edges were close to the original edge-weight estimates. The 95% confidence intervals (CIs) for S3–S4, S6–S7, A1–A2, and A4–A5 were 0.573–0.779, 0.388–0.658, 0.294–0.640, and 0.261–0.621, respectively, whereas weaker edges generally had wider CIs. The case-dropping bootstrap analysis yielded correlation stability (CS) coefficients of 0.75 for EI and 0.60 for BEI, indicating good stability of the principal centrality measures. Summary results for network accuracy and stability are provided in Supplementary Table 4 and Supplementary Figs. 2, 3, and 9; complete bootstrap confidence intervals are provided in Supplementary Data 1.

Table 2. Key edges, node centrality, and predictability in the ordinal Gaussian graphical model

Panel A. Ten edges with the largest absolute edge weights

Rank	Node 1	Node 1 name	Node 2	Node 2 name	Edge weight	Absolute edge weight	Edge sign	Connection type
1	S3	Sleep duration	S4	Habitual sleep efficiency	0.673	0.673	Positive	Within-community edge
2	S6	Use of sleeping medication	S7	Daytime dysfunction	0.498	0.498	Positive	Within-community edge
3	A1	Nervousness or anxiety	A2	Inability to control worrying	0.422	0.422	Positive	Within-community edge
4	A4	Difficulty relaxing	A5	Restlessness	0.408	0.408	Positive	Within-community edge
5	A3	Excessive worrying	A4	Difficulty relaxing	0.37	0.37	Positive	Within-community edge
6	A1	Nervousness or anxiety	A6	Irritability	0.357	0.357	Positive	Within-community edge
7	S5	Sleep disturbances	S7	Daytime dysfunction	0.321	0.321	Positive	Within-community edge
8	S2	Sleep latency	S5	Sleep disturbances	0.286	0.286	Positive	Within-community edge
9	D1	Loss of interest	D2	Depressed mood	0.278	0.278	Positive	Within-community edge
10	S1	Subjective sleep quality	S7	Daytime dysfunction	0.254	0.254	Positive	Within-community edge

Panel B. Ten cross-community edges with the largest absolute edge weights

Rank	Node 1	Node 1 name	Node 1 community	Node 2	Node 2 name	Node 2 community	Edge weight	Absolute edge weight	Edge sign
1	D9	Thoughts of self-harm or	Depressive symptoms	A7	Fear that something	Anxiety symptoms	0.234	0.234	Positive

Panel A. Ten edges with the largest absolute edge weights

Rank	Node 1	Node 1 name	Node 2	Node 2 name	Edge weight	Absolute edge weight	Edge sign		Connection type
		death			awful might happen				
2	D6	Negative self-evaluation	Depressive symptoms	A2	Inability to control worrying	Anxiety symptoms	0.154	0.154	Positive
3	D9	Thoughts of self-harm or death	Depressive symptoms	C3	Resignation	Medical coping	0.149	0.149	Positive
4	D8	Psychomotor changes	Depressive symptoms	A5	Restlessness	Anxiety symptoms	0.133	0.133	Positive
5	D9	Thoughts of self-harm or death	Depressive symptoms	A4	Difficulty relaxing	Anxiety symptoms	0.123	0.123	Positive
6	A7	Fear that something awful might happen	Anxiety symptoms	C3	Resignation	Medical coping	0.12	0.12	Positive
7	D3	Sleep problems	Depressive symptoms	S3	Sleep duration	Sleep problems	0.118	0.118	Positive
8	D6	Negative self-evaluation	Depressive symptoms	C3	Resignation	Medical coping	0.113	0.113	Positive
9	D9	Thoughts of self-harm or death	Depressive symptoms	C2	Avoidance	Medical coping	0.108	0.108	Positive
10	D9	Thoughts of self-harm or death	Depressive symptoms	S1	Subjective sleep quality	Sleep problems	−0.108	0.108	Negative

Panel C. Top five nodes ranked by expected influence, bridge expected influence, and predictability

Metric	Rank	Node code	Node name	Community	Raw value
Expected influence (EI)	1	A4	Difficulty relaxing	Anxiety symptoms	1.173
Expected influence (EI)	2	A5	Restlessness	Anxiety symptoms	1.158
Expected influence (EI)	3	D6	Negative self-evaluation	Depressive symptoms	1.124
Expected influence (EI)	4	A7	Fear that something awful might happen	Anxiety symptoms	1.113
Expected influence (EI)	5	D2	Depressed mood	Depressive symptoms	1.074
Bridge expected influence (BEI)	1	D9	Thoughts of self-harm or death	Depressive symptoms	0.625
Bridge expected influence (BEI)	2	A7	Fear that something awful might happen	Anxiety symptoms	0.55
Bridge expected influence (BEI)	3	A4	Difficulty relaxing	Anxiety symptoms	0.37
Bridge expected influence (BEI)	4	C3	Resignation	Medical coping	0.343
Bridge expected influence (BEI)	5	A2	Inability to control worrying	Anxiety symptoms	0.304
Predictability (R^2)	1	A4	Difficulty relaxing	Anxiety symptoms	0.847
Predictability (R^2)	2	A5	Restlessness	Anxiety symptoms	0.838
Predictability (R^2)	3	A3	Excessive worrying	Anxiety symptoms	0.821
Predictability (R^2)	4	A2	Inability to control worrying	Anxiety symptoms	0.816
Predictability (R^2)	5	A1	Nervousness or anxiety	Anxiety symptoms	0.803

Abbreviations: EI, expected influence; BEI, bridge expected influence; R^2, coefficient of determination. Positive and negative denote the sign of the corresponding edge.

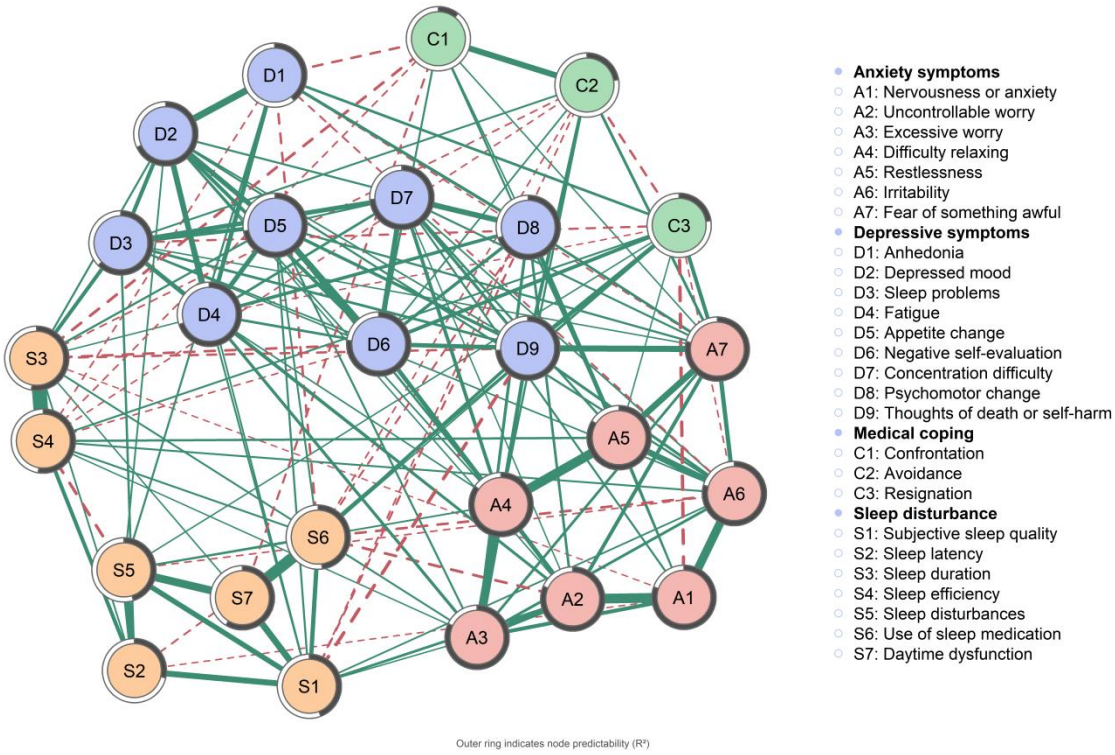


Figure 1. Network of psychological symptoms, sleep problems, and medical coping

Note: Solid green lines indicate positive conditional associations, whereas dashed red lines indicate negative conditional associations. Thicker edges represent larger absolute edge weights. The outer ring of each node represents its predictability (R^2).

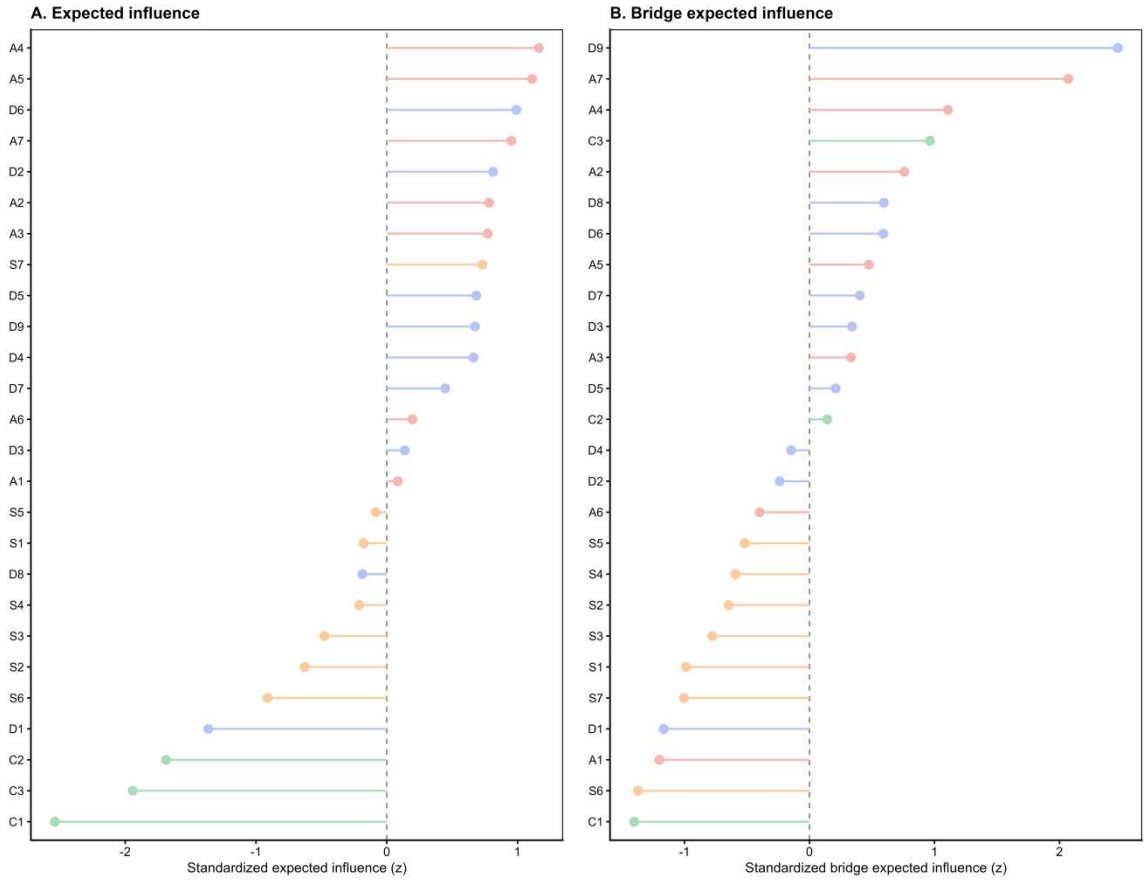


Figure 2. Expected influence and bridge expected influence of network nodes

Note: The x-axis represents standardized centrality *Z* scores. Node colors denote the four communities: depression, anxiety, sleep, and medical coping.

GGMNIRA model-projection results

In the joint node perturbation analysis, A4 (trouble relaxing) showed the largest sample Kullback–Leibler (KL) divergence (21.435) and was the only node exceeding the network-wide decision threshold of 19.443 in the 26-node network. A5 (restlessness; 19.042), A3 (excessive worrying; 15.525), A2 (inability to control worrying; 14.732), and A1 (nervousness or anxiety; 12.873) ranked second through fifth, respectively; all five of the highest-ranked nodes belonged to the anxiety symptom community. In the nonparametric

bootstrap analysis, A4 exceeded the decision threshold in 95.7% of bootstrap samples and ranked in the Top 1, Top 3, and Top 5 in 55.7%, 91.8%, and 99.5% of samples, respectively. None of the pairwise KL differences between A4 and A5, A3, A2, or A1 remained statistically significant after Holm adjustment. These findings support interpreting A4 as the highest-ranked candidate within a group of prominent anxiety nodes rather than as a uniquely identified node.

Among the four prespecified cross-community pathways, only the anxiety symptoms → depressive symptoms pathway showed projected changes exceeding the model-derived decision threshold in the marginal distribution of the target community. A4 produced the largest projected change along this pathway (maximum KL = 15.734), and four anxiety nodes exceeded the pathway-specific threshold. In the community-level joint perturbation analysis, the anxiety and depressive symptom communities yielded KL divergences of 87.809 and 35.244, respectively, both exceeding the decision threshold of 19.443. By contrast, the corresponding KL divergences for the sleep problems and medical coping communities were 5.031 and 1.004, respectively, and neither exceeded the threshold.

In the case-dropping analysis, the Pearson- and Spearman-based correlation stability (CS) coefficients for the KL values were both 0.75. Node rankings in the thresholded 26-node network and the 23-node psychological-and-sleep network were highly consistent with those in the main model, with Spearman correlations of 0.997 and 0.999, respectively. A4 retained the top rank in both sensitivity models, and the anxiety symptom community consistently showed the largest community-level joint KL divergence across all sensitivity models. Results are

462 presented in Table 3 and Figure 3; complete results are provided in Supplementary Tables 9–14,

463 Supplementary Data 1, and Supplementary Figs. 11–12.

464 Table 3. GGMNIRA results for joint node perturbations, cross-community pathways,

465 community-level joint perturbations, and stability analyses

Panel A. Top 10 nodes in the joint node perturbation analysis and bootstrap stability

Rank	Node	Node label	Community	Sample KL	Frequency exceeding threshold	Top 1	Top 3	Top 5	95% rank interval
1	A4	Trouble relaxing	Anxiety symptoms	21.435	95.70%	55.70%	91.80%	99.50%	1.0–4.0
2	A5	Restlessness	Anxiety symptoms	19.042	89.60%	22.90%	73.70%	93.20%	1.0–7.0
3	A3	Excessive worrying	Anxiety symptoms	15.525	84.30%	4.00%	47.80%	85.60%	1.0–7.0
4	A2	Inability to control worrying	Anxiety symptoms	14.732	82.50%	10.00%	43.40%	80.90%	1.0–7.0
5	A1	Nervousness or anxiety	Anxiety symptoms	12.873	70.30%	5.30%	24.00%	54.50%	1.0–9.0
6	A6	Irritability	Anxiety symptoms	11.545	63.60%	0.80%	7.50%	35.60%	2.0–9.0
7	A7	Fear that something bad might happen	Anxiety symptoms	11.155	58.70%	1.10%	7.90%	32.70%	2.0–10.0
8	D6	Negative self-evaluation	Depressive symptoms	9.359	36.40%	0.20%	2.80%	12.50%	3.0–11.0
9	D7	Difficulty concentrating	Depressive symptoms	7.368	6.30%	0.00%	0.10%	0.90%	7.0–14.0
10	D9	Thoughts of self-harm or death	Depressive symptoms	7.335	23.80%	0.00%	1.00%	4.20%	5.0–13.0

Panel B. Results for the prespecified cross-community pathways

Pathway	Maximum-effect	Node label	Maximum	Pathway threshold	No. of nodes

	trigger node		KL		exceeding threshold
Sleep problems → Depressive symptoms	S3	Sleep duration	0.216	8.459	0
Sleep problems → Anxiety symptoms	S4	Sleep efficiency	0.145	7.034	0
Depressive symptoms → Anxiety symptoms	D6	Negative self-evaluation	6.297	7.034	0
Anxiety symptoms → Depressive symptoms	A4	Trouble relaxing	15.734	8.459	4

Panel C. Community-level joint perturbation results

Rank	Community	No. of nodes	Per-node perturbation	Joint KL	Decision threshold	Threshold exceeded
1	Anxiety symptoms	7	0.378	87.809	19.443	Yes
2	Depressive symptoms	9	0.333	35.244	19.443	Yes
3	Sleep problems	7	0.378	5.031	19.443	No
4	Medical coping	3	0.577	1.004	19.443	No

Note: The Pearson- and Spearman-based correlation stability (CS) coefficients for the KL values were both 0.75. Spearman correlations of node rankings between the main model and the thresholded 26-node network and the 23-node psychological-and-sleep network were 0.997 and 0.999, respectively, with A4 ranked first in both sensitivity models. Full stability and sensitivity results are provided in Supplementary Tables 12–14 and Supplementary Data 1.

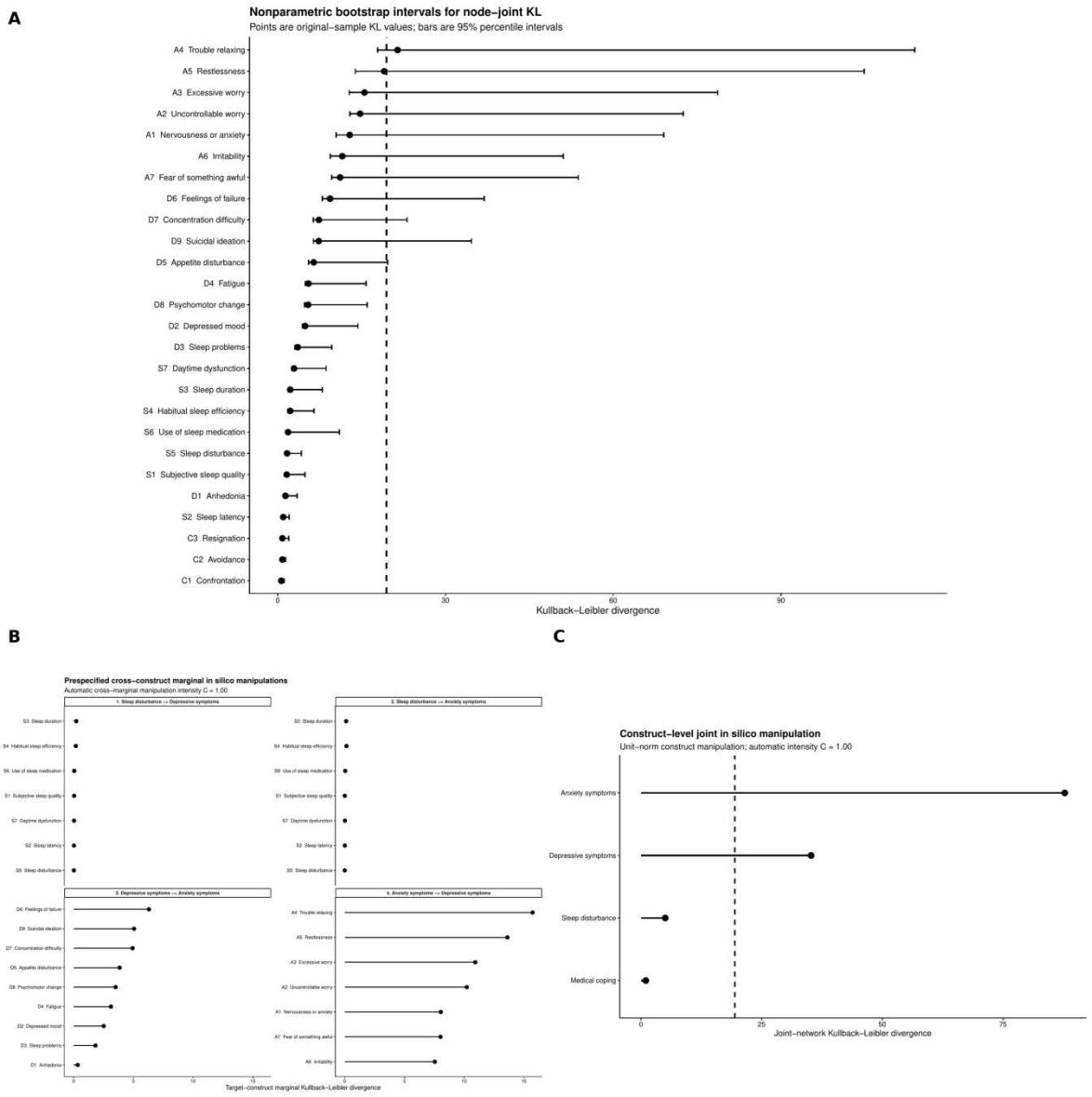


Figure 3. Projection results of the GGMNIRA model

Note: Panel A shows joint node-perturbation KL divergences and nonparametric bootstrap intervals. Panel B shows marginal KL divergences in the target community for the four prespecified cross-community pathways. Panel C shows unit-norm joint-perturbation KL divergences for the four communities. Dashed lines indicate the automatically determined decision threshold for the corresponding analysis. Because the panels represent different distributional spaces, absolute KL values should not be directly compared across panels.

Binary Ising network calibration and directional Ising-NIRA results

The primary 23-node binary Ising network contained 63 nonzero edges. The correlation-stability (CS) coefficients for both expected influence (EI) and strength were 0.75. In-sample reproduction of the observed node activation levels using the standard M0 model yielded a mean number of active nodes of 7.797, which was substantially lower than the observed value of 10.518. The M1-PL model improved this value to 9.729 but still failed to meet the prespecified calibration criteria. In contrast, the M1-Exact model yielded a mean absolute error (MAE) of 0.0009 for node endorsement rates, with a maximum error of 0.0029. The mean number of active nodes was 10.535, corresponding to an absolute difference of 0.017 from the observed value. The M1-Exact model therefore satisfied the prespecified calibration criteria and was selected as the primary Ising–NodeIdentifyR algorithm (NIRA) model.

Under the 2-SD perturbation in the M1-Exact model, the five highest-ranked nodes in the amelioration direction were fatigue (D4, 3.553), sleep problems (D3, 3.081), excessive worry (A3, 3.014), depressed mood (D2, 2.983), and difficulty relaxing (A4, 2.962). D4 ranked first in both the M0 and M1 models and was identified as the Top-1 node in 100% of the 100 replicate simulations for both models.

In the exacerbation direction, the five highest-ranked nodes were fear that something awful might happen (A7, 4.326), restlessness (A5, 4.261), nervousness or anxiety (A1, 4.178), difficulty concentrating (D7, 4.048), and thoughts of self-harm or death (D9, 3.959). Across the 100 replicate simulations, A7 and A5 were identified as the Top-1 node in 74% and 23% of simulations, respectively, in the M1 model. The 2.5th–97.5th percentile interval for the A7-minus-A5 effect difference ranged from −0.197 to 0.264, indicating that the simulations

did not clearly distinguish their ordering and supporting their interpretation as a top-tier set of candidate nodes in the exacerbation direction. The Spearman correlation between the amelioration and exacerbation rankings in the M1 model was 0.528, indicating that the two directional processes were not simple mirror images of one another.

For the high-priority nodes, most of the total projected effect was attributable to indirect changes in other nodes. In the M1 model, the indirect component accounted for 87.4% of the amelioration effect for D4, 87.9% of that for A4, 88.2% of the exacerbation effect for A7, and 88.0% of that for A5. Within the M1 model, Pearson correlations between the exact effects and the mean effects obtained from 100 conventional Monte Carlo simulations ranged from 0.998 to 0.999, while Spearman correlations between the corresponding rankings ranged from 0.988 to 0.991, supporting the Monte Carlo stability of the overall rankings. The primary specification of the regularized moderated network identified six third-order interactions, indicating the presence of higher-order dependency structures in the model. The results are presented in Table 4 and Figure 4, with complete results provided in Supplementary Tables 15–22, Supplementary Data 1, and Supplementary Figs. 13–18.

Table 4. Ising model calibration, directional node effects, and replicate-simulation stability

Panel A. Reproduction performance and calibration of the Ising models

Model	Endorsement-rate MAE	Maximum endorsement-rate error	Observed mean total	Model mean total	Absolute error in mean total	Phi RMSE	Calibration conclusion
M0 Standard IsingFit	0.1203	0.2141	10.518	7.797	2.721	0.189	Calibration inadequate
M1-PL Fixed-edge offset	0.0362	0.0707	10.518	9.729	0.788	0.144	Calibration inadequate
M1-Exact Selected calibrated	0.0009	0.0029	10.518	10.535	0.017	0.128	Calibration passed

518 **Abbreviations:** MAE, mean absolute error; RMSE, root-mean-square error.

Panel B. Top five nodes in the amelioration and exacerbation directions in the M1-Exact model

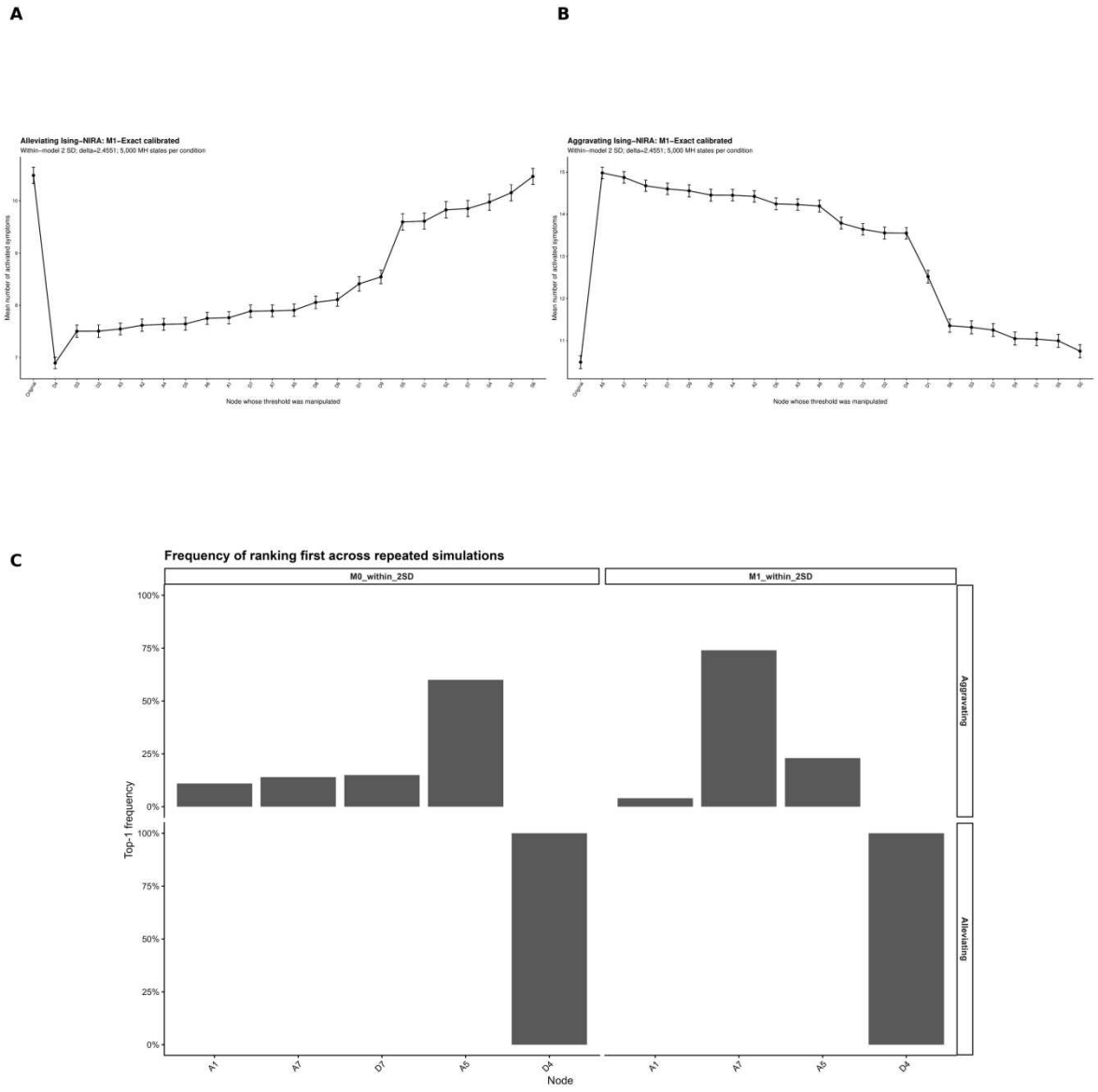
Direction	Rank	Node	Node label	Exact projected effect	Direct effect	Indirect effect	Indirect proportion
Amelioration	1	D4	Fatigue	3.553	0.449	3.104	87.4%
Amelioration	2	D3	Sleep problems	3.081	0.422	2.659	86.3%
Amelioration	3	A3	Excessive worry	3.014	0.373	2.641	87.6%
Amelioration	4	D2	Depressed mood	2.983	0.414	2.570	86.1%
Amelioration	5	A4	Difficulty relaxing	2.962	0.358	2.604	87.9%
Exacerbation	1	A7	Fear that something awful might happen	4.326	0.510	3.816	88.2%
Exacerbation	2	A5	Restlessness	4.261	0.513	3.748	88.0%
Exacerbation	3	A1	Nervousness or anxiety	4.178	0.498	3.680	88.1%
Exacerbation	4	D7	Difficulty concentrating	4.048	0.504	3.544	87.5%
Exacerbation	5	D9	Thoughts of self-harm or death	3.959	0.531	3.428	86.6%

Panel C. Agreement between exact results and 100 replicate simulations

Model	Direction	Pearson correlation of effects	Spearman rank correlation	Top-1 recovery rate	Top-3 overlap	Top-5 overlap	A4 Top-5 frequency
M0	Exacerbation	0.999	0.990	60.0%	2.37	4.38	60.0%
M0	Amelioration	0.994	0.990	100.0%	2.95	4.66	0.0%
M1	Exacerbation	0.999	0.988	73.0%	2.86	4.39	43.0%
M1	Amelioration	0.998	0.991	100.0%	2.51	4.28	60.0%

Panel D. Replicate-simulation comparisons of leading candidate nodes

Comparison	Direction	Node 1	Node 2	Mean effect difference	Difference interval/conclusion
D4 vs D3	Amelioration	D4	D3	0.473	Difference interval did not include 0
A7 vs A5	Exacerbation	A7	A5	0.054	2.5th–97.5th percentile interval: −0.197 to 0.264



519

520 **Figure 4. Directional model-projected effects and replicate-simulation stability of the calibrated**

521 **Ising–NIRA model**

522 **Note:** Panel A shows the amelioration direction for the M1-Exact model, and Panel B shows the
523 exacerbation direction. Points and error bars are based on 5,000 Metropolis–Hastings (MH) states per
524 scenario. Panel C shows the frequency with which each node was identified as Top-1 across 100 replicate
525 simulations. Primary effect estimates were obtained by exact enumeration, whereas conventional Monte
526 Carlo simulations were used to assess simulation stability.

527

Secondary scores and network heterogeneity analyses

Of the 120 between-group comparisons across score measures, 41 had unadjusted P values < 0.05, of which 29 remained significant after global Benjamini–Hochberg false discovery rate (BH-FDR) correction. Group differences were most extensive by disease severity and nursing-care level. Female patients had higher Generalized Anxiety Disorder-7 (GAD-7), Pittsburgh Sleep Quality Index (PSQI), and resignation scores than male patients, whereas patients aged ≥65 years had higher PSQI scores than those aged <65 years. Full results are provided in Supplementary Data 1 and Supplementary Fig. 5.

In sex-stratified analyses, global network strength was 12.013 in men and 13.192 in women. The network structure invariance test yielded M = 0.402 (P = 0.049), representing only a nominal signal at the conventional 0.05 threshold, whereas the global strength test yielded S = 1.179 (P = 0.366). After Holm correction, no between-sex differences in individual edges, expected influence (EI), or bridge expected influence (BEI) remained significant. Among the 14 exploratory candidate variables, none showed BH-FDR-significant differences in either network structure or global strength; only disease severity and place of residence showed nominal signals of structural heterogeneity. Full results are provided in Supplementary Table 8, Supplementary Data 1, and Supplementary Figs. 6–10.

Discussion

Main findings in the context of the Theory of Unpleasant Symptoms

Guided by the Theory of Unpleasant Symptoms (TOUS), this study constructed a multidomain network encompassing depressive symptoms, anxiety symptoms, sleep problems, and medical

549 coping among patients with coexisting hypertension and diabetes. Candidate nodes were
550 evaluated from three complementary perspectives: static network structure, model-based
551 projections from an ordinal Gaussian graphical model (GGM) using the Gaussian Graphical
552 Model NodeIdentifyR Algorithm (GGMNIRA), and projections from a calibrated Ising model.
553 Several key findings emerged. First, anxiety nodes reflecting difficulty relaxing, restlessness,
554 excessive worry, and inability to control worry consistently ranked highly in expected
555 influence, predictability, and GGMNIRA-based projections, suggesting that the symptom
556 cluster characterized by worry and heightened arousal may occupy a particularly salient
557 position within the network. Second, thoughts of self-harm or death, fear that something bad
558 might happen, and resignation exhibited relatively strong cross-community connectivity. Third,
559 the nodes prioritized in the symptom-alleviation direction differed from those prioritized in the
560 symptom-exacerbation direction. Fatigue, sleep problems, and worry were more relevant to the
561 alleviation direction, whereas fear that something bad might happen, restlessness, and tension
562 were more prominent in the exacerbation direction. Fourth, for most high-priority nodes, much
563 of the projected overall change was accounted for by indirect changes in other nodes,
564 highlighting the potential importance of network-wide responses beyond changes in the focal
565 node itself. Fifth, although female patients had higher scores on some measures, no robust sex-
566 or clinical characteristic-related differences in network structure were identified.
567 The TOUS emphasizes that multiple symptoms may co-occur and interact with one another
568 [10,11]. The present findings are consistent with this multisymptom interaction perspective and
569 are also in line with previous network research in patients with heart failure [13]. In the present

study, the TOUS provided a theoretical framework for interpreting the multidimensional interrelationships among psychological symptoms, sleep problems, and medical coping.

Anxiety-related hyperarousal symptoms in network structure and model-based projections

In the present study, trouble relaxing and restlessness showed relatively high expected influence, while trouble relaxing, restlessness, excessive worry, inability to control worry, and nervousness or anxiety ranked among the most predictable nodes. The Gaussian Graphical Model NodeIdentifyR Algorithm (GGMNIRA) further indicated that the five nodes with the highest model-based projected importance all belonged to the anxiety community; at the community level, the anxiety community also showed a greater projected change in the joint distribution than the other communities. Rather than implicating a single isolated symptom, these findings suggest a relatively concentrated network position for a cluster characterized by persistent worry, difficulty controlling worry, nervousness, trouble relaxing, and motor restlessness. In patients with type 2 diabetes, excessive worry, inability to control worry, and trouble relaxing have likewise been identified as key symptoms connecting anxiety, depression, and diabetes distress [14]. Studies involving patients with hypertension, diabetes, or both conditions have also identified anxiety symptoms as potentially important components of cross-domain network connectivity [17]. Among patients undergoing percutaneous coronary intervention (PCI), sleep problems, irritability, and inability to control worry showed relatively high expected influence, whereas excessive worry and trouble relaxing exhibited bridging roles [43]. Taken together, these findings suggest that the sustained demands of monitoring blood pressure and blood glucose, recognizing signs of hypoglycemia and target-organ damage,

managing multiple medications, and coping with uncertainty regarding disease outcomes may be associated with persistent threat monitoring and anxiety-related hyperarousal.

The high predictability of anxiety nodes suggests strong local conditional dependencies among worry, nervousness, trouble relaxing, and restlessness [22]. In patients with diabetes, sleep quality is associated with multiple psychological, clinical, behavioral, and social factors, including depression, anxiety, disease-related characteristics, lifestyle, and social support [9]. Consistent with these observations, the hyperarousal model of insomnia proposes that persistent worry and rumination may be accompanied by heightened physiological and cortical arousal, thereby disrupting sleep maintenance [44]. When considered alongside the present findings, trouble relaxing and its neighboring symptoms may constitute a symptom cluster linking persistent worry and anxiety-related hyperarousal with sleep disturbance.

Cross-community bridging, self-harm risk, and medical coping

Although thoughts of death or self-harm did not show the highest expected influence, they exhibited the highest bridge expected influence and had cross-community connections with fear that something awful might happen, trouble relaxing, resignation, avoidance, and several sleep-related nodes. Bridge expected influence quantifies a node's connectivity with nodes in other prespecified communities and therefore provides information distinct from conventional centrality measures of overall network connectivity [21]. Systematic reviews and meta-analyses have documented elevated risks of suicide mortality, suicidal ideation, and suicide attempts among individuals with diabetes [45]. Accordingly, a positive response to the item assessing thoughts of death or self-harm should warrant standardized assessment of self-harm and suicide risk and, when clinically indicated, referral to specialist mental health

614 services. The clinical safety implications of such a response should take precedence over its
615 interpretation in terms of network centrality. A self-reported response to a single item of the
616 Patient Health Questionnaire-9 (PHQ-9) cannot substitute for a structured suicide risk
617 assessment.
618 Within the medical coping community, resignation showed the highest bridge expected
619 influence and had relatively strong cross-community connections with thoughts of death or
620 self-harm, negative self-appraisal, and fear that something awful might happen. Resignation
621 may reflect patients' perceptions that their disease is uncontrollable, that treatment is difficult
622 to sustain, or that they lack the capacity to cope effectively; these perceptions may, in turn, be
623 associated with helplessness, passive acceptance of symptoms, and reduced treatment
624 engagement. A systematic review of coping among patients with diabetes found that
625 maladaptive, emotion-focused, or withdrawal-based coping was associated with depression,
626 anxiety, diabetes distress, and poorer health outcomes, whereas problem-focused coping was
627 generally associated with better psychological adjustment [12]. Studies incorporating coping
628 dimensions alongside anxiety and depression within the same network have similarly
629 suggested that coping may contribute to structural connections among psychological
630 symptoms and to model-based projections [19]. Thus, the prominent bridging role of
631 resignation in the present study is best interpreted as indicating cross-domain connectivity
632 between medical coping and psychological symptoms and sleep problems.

Concordance and divergence between static network structure and GGMNIRA projections

The static ordinal network and Gaussian Graphical Model NodeIdentifyR Algorithm (GGMNIRA) analyses showed substantial convergence in highlighting anxiety-related nodes. Difficulty relaxing had relatively high expected influence and predictability and ranked first in the node-level projection based on changes in the joint distribution. At the community level, the anxiety community likewise showed the largest projection under joint perturbation. Of the four prespecified cross-community pathways, anxiety → depression was the only pathway to meet the model-defined threshold, suggesting a comparatively strong cross-domain link between the anxiety symptom cluster and the depression community within the estimated model. This pattern is consistent with previous findings in populations with diabetes and cardiovascular disease, in which worry and difficulty relaxing have been identified as symptoms linking anxiety and depression communities [14,17,43].

Expected influence, predictability, and Kullback–Leibler (KL) divergence quantify distinct properties of the network: connectivity, the extent to which a node is explained by its neighboring nodes, and the change in the joint distribution following a modeled perturbation, respectively. These measures therefore address complementary rather than interchangeable questions. Centrality indices characterize the static topological position of nodes within an estimated network [24], whereas the NodeIdentifyR algorithm (NIRA) and related simulation-based models characterize projected distributional changes under prespecified perturbations [25]. In the present study, these approaches converged in highlighting the anxiety symptom cluster but yielded distinct directional rankings. Combining structural network

measures with model-based projection measures may therefore provide a more comprehensive characterization of potentially influential symptoms than centrality rankings alone.

Asymmetry between alleviation and aggravation projections

In the calibrated Ising-NIRA analysis, fatigue ranked highest in the alleviation direction, followed by sleep problems, excessive worry, depressed mood, and difficulty relaxing. Although fatigue did not have the highest expected influence in the ordinal network, it generated the largest projected change under the alleviation scenario. This finding further underscores that static centrality and model-based perturbation analyses capture different aspects of the symptom system. Fatigue in patients with type 2 diabetes is multifactorial and may be associated with disease status, inflammation, psychological factors, and lifestyle characteristics [47]. Among patients with coexisting hypertension and diabetes, fatigue may also occur alongside insufficient sleep, glycemic variability, adverse medication effects, nutritional risk, anemia, physical inactivity, and depressive symptoms. Fatigue may therefore represent a useful entry point for comprehensive nursing assessment, provided that potential underlying somatic contributors are evaluated concurrently.

The aggravation analysis yielded a different pattern. Fear that something awful might happen, restlessness, feeling nervous or anxious, difficulty concentrating, and thoughts of self-harm or death were among the highest-ranked nodes. The alleviation and aggravation rankings were only moderately correlated, indicating that these two directions were not simple mirror images. Fear of adverse events may coexist with persistent threat appraisal, tension, and hypervigilance and may be associated with disturbances in sleep, attention, and emotion regulation.

Hyperarousal theory provides a plausible mechanistic framework for the observed associations among fear, worry, restlessness, and sleep disturbance [44]. Previous simulation research on coping–emotion networks has similarly shown that alleviation and aggravation scenarios can generate different rankings of candidate nodes [19]. When both projected effect size and consistency across repeated simulations were considered, A7 and A5 formed the leading cluster of nodes in the aggravation direction.

For the high-priority nodes, approximately 87%–88% of the total projected change was attributable to indirect changes in other nodes. Thus, the modeled consequences of node perturbation appeared to arise predominantly through coordinated changes across related symptoms rather than through changes in the target node alone. This pattern supports a multisymptom perspective in nursing assessment and management. When fatigue, sleep problems, worry, or fear is considered as a potential point of entry, concurrent attention to related emotional, cognitive, and coping difficulties may better reflect the organization of the symptom network than management focused on a single symptom in isolation.

Network heterogeneity associated with sex and clinical characteristics

Female patients had higher levels of anxiety, sleep problems, and resignation than male patients. However, evidence for sex-related differences in network structure was limited. The overall structural difference was only close to the statistical threshold, and no significant differences were identified in global strength or, after correction for multiple comparisons, in specific edges, expected influence, or bridge expected influence. These results indicate that

between-group differences in symptom burden do not necessarily correspond to differences in the organization of symptom relationships.

A previous study of patients undergoing percutaneous coronary intervention (PCI) reported a sex difference in global network strength [43], whereas sex-based comparisons in other cardiovascular and chronic disease network studies have yielded inconsistent results [17,18]. Overall, the present study found no robust evidence of network heterogeneity associated with sex or the clinical characteristics examined. These findings suggest that nursing assessment should prioritize patients' actual symptom burden and symptom configurations rather than relying solely on a single demographic or clinical characteristic for stratification.

Implications for clinical nursing and future intervention research

The findings of this study provide a basis for a tiered approach to psychological and sleep-related nursing assessment in patients with coexisting hypertension and diabetes. At the first tier, assessment may focus on anxiety-related hyperarousal symptoms, including difficulty controlling worry, excessive worry, difficulty relaxing, restlessness, and apprehension that something bad may happen. At the second tier, fatigue and sleep-related functioning should be assessed, with potential contributors considered in relation to glycemic variability, nocturnal hypoglycemia, medication effects, anemia, nutritional status, physical activity, and depressive symptoms [9,47]. At the third tier, medical coping modes should be evaluated to identify resignation, a perceived lack of control over illness, treatment fatigue, and persistent, inflexible avoidance [12]. At the fourth tier, patient safety should be prioritized; when thoughts of self-harm or death are endorsed, a standardized risk assessment should be conducted, followed

by referral and supportive management according to the level of risk [45]. Diabetes care guidelines have incorporated depression, anxiety, sleep health, and adaptive coping into routine psychosocial care [4]. Our findings suggest that these domains may be considered jointly as part of nursing assessment.

Future nursing intervention studies may develop hypotheses along two complementary lines: reducing symptom burden and managing the risk of symptom worsening. Symptom-burden reduction may target fatigue, sleep disturbances, excessive worry, and low mood, while integrating sleep hygiene, principles of cognitive behavioral therapy for insomnia (CBT-I), relaxation training, graded activity, energy management, problem-solving strategies, and management of underlying somatic contributors. A systematic review of randomized trials in patients with diabetes showed that cognitive behavioral therapy–based interventions could improve overall sleep quality and total sleep time, although effects were not consistent across all sleep outcomes [48]. Management of the risk of symptom worsening may focus on apprehension that something bad may happen, restlessness, thoughts of self-harm, and resignation, combined with clarification of illness-related knowledge, enhancement of perceived control, safety planning, and proactive follow-up. Previous studies of collaborative care and nurse-led psychological interventions suggest that multicomponent, patient-centered management may improve some psychological and chronic disease outcomes, although treatment effects are heterogeneous [49,50]. Together, these findings provide a basis for developing stratified nursing strategies that address both symptom burden and the risk of symptom worsening.

Strengths and limitations

This study has several strengths. First, by simultaneously integrating depression, anxiety, sleep problems, and medical coping modes in a multicenter sample of hospitalized patients with coexisting hypertension and diabetes, this study extends the scope of previous network research, which has largely focused on depression–anxiety or sleep–mood networks. Second, the Theory of Unpleasant Symptoms was used as an organizing framework for physiological context, symptom experiences, and psychological and behavioral factors, thereby conceptually distinguishing medical coping modes from symptom nodes. Third, the primary network was estimated using an ordinal Gaussian graphical model (GGM), preserving ordinal information while simultaneously reporting edge weights, expected influence, bridge expected influence, and predictability. The accuracy and stability of the network were evaluated using nonparametric and case-dropping bootstrap procedures. Finally, the study integrated static network structure with GGM-based model projections at the node, cross-community pathway, and community levels. For the binary Ising model, intercept calibration, exact enumeration, bidirectional analyses of alleviating and aggravating projections, and repeated simulation-based validation were also performed. The structurally central nodes, cross-community bridge nodes, and direction-specific projection-priority nodes identified across these analyses did not fully overlap, providing complementary insights into the distinction between network topology and candidate intervention targets [24,25].

Several limitations should also be acknowledged. First, the cross-sectional design and convenience sampling preclude inferences regarding temporal ordering. Moreover, the participants were predominantly hospitalized patients, and a relatively high proportion were

recruited from Grade A tertiary hospitals. Therefore, the applicability of these findings to community settings, primary care settings, and clinically stable populations requires further evaluation.

Second, the Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), Pittsburgh Sleep Quality Index (PSQI), and Medical Coping Modes Questionnaire (MCMQ) were primarily self-administered. Some item content overlapped across instruments, and the network nodes differed in measurement granularity because they represented individual items, components, and dimensions. These factors may have influenced some edge estimates and node-level metrics.

Third, the Ising analyses dichotomized the nodes and generated model projections using fixed edge weights, which may have resulted in some loss of information regarding symptom severity. The study also did not incorporate physiological measures such as objective sleep measures, continuous glucose monitoring, or ambulatory blood pressure monitoring. Future studies combining repeated assessments with objective monitoring may help characterize dynamic changes in network structure more comprehensively.

Conclusions

Guided by the Theory of Unpleasant Symptoms, this study characterized a multidomain network of depression, anxiety, sleep problems, and medical coping modes in patients with coexisting hypertension and diabetes. An anxiety-related symptom cluster characterized by worry, difficulty relaxing, and restlessness was prominent in both the static network and GGM-based model projections. Thoughts of self-harm or death showed relatively strong

cross-community connectivity and should be prioritized as a clinical safety signal during assessment. Directional analysis using the Ising-based nodeIdentifyR algorithm (Ising-NIRA) showed that fatigue and sleep problems had relatively high projected priority in the alleviating direction, whereas apprehension that something bad may happen and restlessness ranked highly in the aggravating direction, suggesting that alleviation and aggravation are not simply mirror-image processes. These findings suggest that psychological and sleep-related nursing care for patients with coexisting hypertension and diabetes should prioritize anxiety-related hyperarousal symptoms, fatigue, and sleep problems, while integrating assessment of self-harm risk and medical coping modes into comprehensive care.

List of abbreviations

BEI, bridge expected influence; BH-FDR, Benjamini–Hochberg false discovery rate; BMI, body mass index; CI, confidence interval; CS, correlation stability; EI, expected influence; GAD-7, Generalized Anxiety Disorder-7; GGM, Gaussian graphical model; GGMNIRA, Gaussian Graphical Model NodeIdentifyR Algorithm; KL, Kullback–Leibler; MAE, mean absolute error; MCMQ, Medical Coping Modes Questionnaire; MH, Metropolis–Hastings; NIRA, NodeIdentifyR algorithm; NRS 2002, Nutritional Risk Screening 2002; PHQ-9, Patient Health Questionnaire-9; PSQI, Pittsburgh Sleep Quality Index; RMSE, root-mean-square error; SD, standard deviation; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; TOUS, Theory of Unpleasant Symptoms.

Declarations

Ethics approval and consent to participate

This study was reviewed and approved by the Ethics Committee of Renmin Hospital of Wuhan University (approval no. WDRY2022-K122). Written informed consent was obtained from all participants before data collection. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Clinical trial number: not applicable.

Consent for publication

Not applicable.

Data Availability

The data supporting the findings of this study are provided within the Article, the Supplementary Information, and the accompanying Supplementary Data 1 file. De-identified participant-level data are not publicly available because they contain potentially sensitive clinical information and are subject to institutional and ethical restrictions. Additional de-identified data may be made available by the corresponding author upon reasonable request, subject to approval by the relevant institutional and ethics authorities and to applicable data-protection requirements.

Competing interests

The authors declare no competing interests.

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Authors' contributions

Z.W. contributed to conceptualization, methodology, formal analysis, visualization, writing of the original draft, and review and editing of the manuscript. T.L. contributed to conceptualization, supervision, project administration, and review and editing of the manuscript. Y.L. contributed to investigation, data curation, validation, and review and editing of the manuscript. T.C. contributed to data curation, formal analysis, and review and editing of the manuscript. Y.S. contributed to investigation, validation, and review and editing of the manuscript. Y.W. contributed to investigation, data curation, methodology, validation, and review and editing of the manuscript. Z.C. contributed to supervision, project administration, resources, and critical review and editing of the manuscript. Z.W., T.L., and Y.L. contributed equally to this work and share first authorship. All authors read and approved the final manuscript.

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