



## Original Article

## Identifying central symptom clusters and correlates in patients with lung cancer post-chemotherapy: A network analysis

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## ABSTRACT

**Objective:** This study aims to investigate the network structures of symptoms and symptom clusters in patients with lung cancer post-chemotherapy, with a focus on identifying the central symptom cluster. Understanding the central cluster is crucial for targeted and effective symptom management.

**Methods:** Symptom occurrence and severity were assessed using the Memorial Symptom Assessment Scale (MSAS). Principal component analysis (PCA) was employed to explore symptom clusters, while network analysis unveiled the network structure and pinpointed the central symptom cluster.

**Results:** The study included 512 patients with lung cancer. Four distinct symptom clusters emerged: sickness behavior, psychological, lung cancer-specific, and epithelial. The sickness behavior symptom cluster was identified as the central symptom cluster.

**Conclusions:** This research designates the sickness behavior symptom cluster as central in post-chemotherapy patients with lung cancer, offering valuable insights for clinical nurses in devising more effective symptom management strategies.

**Trial registration:** ChiCTR2300070944 (Chinese Clinical Trial Register).

## Introduction

Lung cancer is a malignant tumor with the highest prevalence and mortality rate in China.<sup>1</sup> The administration of chemotherapy is a frequently employed therapeutic approach for individuals diagnosed with lung cancer.<sup>2</sup> Patients with lung cancer often experience a multitude of concurrent symptoms following chemotherapy, significantly compromising their overall quality of life.<sup>3</sup> The term “symptom cluster” refers to the simultaneous occurrence of two or more symptoms that share a common underlying mechanism.<sup>4</sup> The presence of symptom clusters in cancer patients has been extensively documented.<sup>5</sup> Compared to individual symptoms, symptom clusters can inflict more significant harm upon patients.<sup>6</sup>

There have been many studies focusing on symptom clusters in patients with lung cancer post-chemotherapy. Ju et al. employed latent class growth analysis to investigate symptom clusters and sentinel symptoms in a cohort of 175 patients with lung cancer who received the first cycle of chemotherapy. The study identified five distinct symptom clusters (i.e., class 1: difficulty remembering-numbness-hemoptysis-

weight loss; class 2: cough-expectoration-chest tightness-shortness of breath; class 3: nausea-sleep disturbance-drowsiness-constipation; class 4: pain-distress-dry mouth-sadness-vomiting; class 5: fatigue-lack of appetite) along with the identification of sentinel symptoms (i.e., cough for class 2 and fatigue for class 5).<sup>6</sup> In a longitudinal study, Ma et al. employed a design to investigate sentinel symptoms in 180 patients with lung cancer during the initial two cycles of postoperative chemotherapy. They identified four distinct symptom clusters at cycle 1 (i.e., gastrointestinal symptom cluster, respiratory tract symptom cluster, psychological symptom cluster, and somatic symptom cluster), with nausea, cough, sadness, and fatigue as the prominent sentinel symptoms. During cycle two of chemotherapy, three symptom clusters were observed (i.e., gastrointestinal symptom cluster, respiratory tract symptom cluster, and psychological-somatic symptom cluster), with nausea, cough, and fatigue being the key sentinel symptoms.<sup>7</sup> In addition, some studies are investigating the stability of symptom clusters. Li et al. investigated the stability of symptom clusters across three time points: two weeks before chemotherapy, the first cycle of chemotherapy, and the fourth. Their findings revealed the consistent presence of three distinct symptom

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clusters (i.e., psychological symptom cluster, perceptual symptom cluster, and lung cancer-specific symptom cluster).<sup>8</sup> Russell et al. investigated the stability of symptom clusters at three time points (i.e., before chemotherapy, one week after chemotherapy, and two weeks after chemotherapy) and observed that the lung cancer-specific symptom cluster, the psychological symptom cluster, and the nutritional symptom cluster remained stable. Furthermore, they found that the severity of these symptom clusters was highest during the first week following chemotherapy.<sup>9</sup> Wang et al. conducted an analysis of the stability of symptom clusters across different dimensions (i.e., occurrence and severity). This study identified five distinct symptom clusters, including the sickness behavior symptom cluster, the lung cancer-specific symptom cluster, the psychological symptom cluster, the nutritional symptom cluster, and the epithelial symptom cluster. Notably, these symptom clusters exhibited consistent stability across both two dimensions.<sup>10</sup> Although they conducted a more comprehensive investigation into the stability of symptom clusters, they did not ascertain the relative significance among different symptom clusters. Moreover, in these previous studies, no study evaluated the strength of the relationships among multiple co-occurring symptoms and symptom clusters.

Network analysis enables the visualization and quantitative elucidation of relationships among diverse symptoms and symptom clusters, thus serving as a novel approach for identifying core symptoms and symptom clusters.<sup>11</sup> This approach has been extensively employed for the management of symptoms. The symptom clusters in 1116 human immunodeficiency virus (HIV) patients were analyzed using network analysis by Zhu et al. who identified cognitive dysfunction as the central symptom cluster.<sup>12</sup> Han et al. conducted a network analysis to investigate the central symptom and symptom cluster in a cohort of 518 HIV patients, revealing that sadness emerged as the core symptom within the single symptom network. In contrast, the negative affect symptom cluster exhibited the highest centrality within the symptom cluster network.<sup>13</sup> Fang et al. conducted a network analysis and found that the gastrointestinal cluster was the most central symptom cluster.<sup>14</sup> Based on the results of the central symptom clusters, clinical practitioners can develop more precise and efficient schemes for managing symptoms.

However, the inter-relationships of symptom clusters in patients with lung cancer post-chemotherapy remain unclear. To address this knowledge gap, we conducted the present study using a network approach to examine (1) the network structure and relationship of symptom clusters in patients with lung cancer post-chemotherapy, and (2) the most central symptom cluster among all identified clusters.

## Methods

### Sample and procedure

This cross-sectional study was conducted at the Affiliated Hospital of Jiangnan University in Wuxi, Jiangsu, China, from September 2022 to June 2023. Participants were eligible if they met the following criteria: (1) received a pathological diagnosis of primary lung cancer with or without solitary metastases; (2) were aged 18 years or older; (3) were native Chinese speakers; and (4) had undergone chemotherapy before enrollment. Exclusion criteria included participants who exhibited abnormal communication abilities or had cognitive impairment, mental illness, or other malignancies.

Posters were sent out to patients in the wards to reach respondents interested in this study. The researchers provided a comprehensive explanation of the study's objectives and content to the patients, and invited interested respondents to participate. The enrolled participants were determined according to the inclusion and exclusion criteria. Researchers obtained written informed consent from the patients willing to participate and told them they could withdraw from the study at any point. Well-trained researchers collected the information through face-to-face, one-on-one interviews.

### Measure

The demographic and clinical characteristics were assessed using a structured questionnaire. The demographic variables encompassed age, gender, education status, current employment, registered residence, smoking history, drinking history, multimorbidity, cancer stage, tumor classification, treatment, and chemotherapy regimen.

The prevalence and severity of symptoms in patients with lung cancer post-chemotherapy were assessed using the Memorial Symptom Assessment Scale (MSAS). This scale measured 32 symptoms experienced by patients over the past week, with each symptom being rated on a scale from 0 (not present) to 4 (very severe). MSAS comprised three subscales, namely the physical symptom subscale, the psychological symptom subscale, and the global distress index. The Cronbach's  $\alpha$  values for these subscales ranged from 0.782 to 0.874.<sup>15</sup> The Chinese version of MSAS was translated by Cheng et al.<sup>16</sup> The construct validity of the scale demonstrated consistency with the original version, and the content validity yielded a coefficient of 0.94. Overall, MSAS demonstrated robust reliability and validity when applied to cancer patients.<sup>9</sup>

### Data analysis

Categorical variables were analyzed using frequencies and percentages to conduct descriptive analysis. For continuous variables that exhibited a normal distribution, mean and standard deviation were employed to describe the distribution. Otherwise, medians and quartiles were utilized.

Principal component analysis (PCA) was conducted to identify symptom clusters with the severity of symptoms via the "stats package" in R (version 4.3.1). The Kaiser–Meyer–Olkin test and Bartlett's test of sphericity were used to determine whether the data met the criteria for factor analysis. The symptom cluster consisted of factors that experienced orthogonal transformation (varimax rotation) with Eigen values greater than 1.0 and factor loading greater than 0.4.<sup>17</sup> We only included symptoms with an occurrence rate of over 20% to ensure adequate variability and covariation within the dataset.<sup>10</sup> The research team members engaged in discussion to ensure the clinical applicability of the analyzed symptom clusters.

The relationships and network structures among symptoms and symptom clusters were explored using network analysis (NA) through the utilization of the "qgraph and bootnet package" in R (version 4.3.1).<sup>18</sup> Firstly, a weighted and undirected network was constructed using the data. The nodes represented the symptoms or symptom clusters. The edges in the network indicated conditional independent relationships among the nodes, estimated through Spearman correlation coefficients between symptom severity scores or standardized severity scores of symptom clusters. Secondly, we employed the "EBICglasso" method (tuning = 0.5) to shrink the network and eliminate spurious relationships. Finally, we utilized the Fruchterman–Reingold algorithm to visualize the network, where edge width denoted correlation strength and color indicated correlation direction (blue for positive and red for negative correlation).

Four centrality indices (i.e., strength, closeness, betweenness, and expected influence) were employed to ascertain the most significant symptoms and symptom clusters. Strength is the sum of the weighted values of all edges of a node and can be used to evaluate the strongest connected node. Closeness represents the strength of indirect connections between a node and other nodes. Betweenness represents the degree of relationship between a node and the other two nodes and can identify bridge symptoms. Expected influence (EI) represented the sum of the original values of all edges of a node and measured the node's centrality. The node with the highest strength was defined as the central symptom or the central symptom cluster.<sup>12</sup> The stability of centrality was assessed using the case-dropping bootstrap test, while the accuracy of network edges was evaluated through bootstrap confidence intervals

(CIs). A correlation coefficient greater than 0.5 indicated reliable centrality stability; narrower CIs reflected higher accuracy in estimating network edges.<sup>19</sup>

The subgroup analysis in the network was conducted by the network comparison test (NCT). The network invariance and global strength invariance were tested by NCT. The data analysis was performed using R (version 4.3.1). Statistical significance was defined as a *P*-value less than 0.05.

**Results**

*Participant characteristics*

As presented in Fig. 1, 610 potential participants were recruited in this study. After eligibility screening, 547 patients were eligible for inclusion, followed by 512 participants who signed the informed consent and completed interviews. As shown in Table 1, the majority of participants were male (72.85%), retired (76.56%), and urban residents (68.55%). The proportion of participants with a middle school education level was 56.45%. The mean age was 65.21 years. Approximately 68.55% of the participants had advanced stage IV lung cancer, while adenocarcinoma accounted for 63.09% of the patient population. All the individuals included in the study had undergone chemotherapy.

*Prevalence and severity of symptoms*

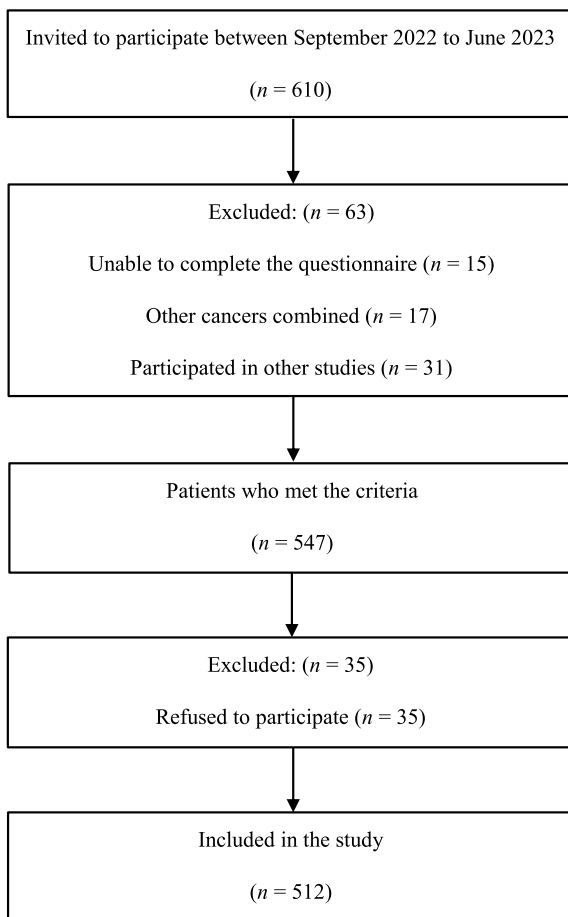
As presented in Table 2, 15 symptoms met the study criteria out of the 32 evaluated. The predominant symptom was lack of energy (72.46%),

**Table 1**  
Participant characteristics (N = 512).

Characteristics	n (%) or Mean (SD)
Age (years)	65.21 (8.94)
Gender	
Male	373 (72.85)
Female	139 (27.15)
Education status	
Primary school or below	133 (25.98)
Middle school	289 (56.45)
High school	62 (12.11)
College or above	28 (5.47)
Current employment	
Full-time employed	27 (5.27)
Part-time employed	10 (1.95)
Retired	392 (76.56)
Unemployed	83 (16.21)
Registered residence	
Urban	351 (68.55)
Rural	161 (31.45)
Smoking history	
No	225 (43.95)
Yes	287 (56.05)
Drinking history	
No	335 (65.43)
Yes	177 (34.57)
Multimorbidity	
No	305 (59.57)
Yes	207 (40.43)
Cancer stage	
Stage I	30 (5.86)
Stage II	38 (7.42)
Stage III	93 (18.16)
Stage IV	351 (68.55)
Tumor classification	
Squamous carcinoma	94 (18.36)
Adenocarcinoma	323 (63.09)
Large cell carcinoma	4 (0.78)
Small-cell lung carcinoma	91 (17.77)
Treatment	
Chemotherapy	222 (43.36)
Chemotherapy + radiotherapy	83 (16.21)
Surgery + chemotherapy	117 (22.85)
Surgery + chemotherapy + radiotherapy	90 (17.58)
Chemotherapy regimen	
Paclitaxel and cisplatin/carboplatin	155 (30.27)
Pemetrexed and cisplatin/carboplatin	202 (39.45)
Etoposide and cisplatin/carboplatin	87 (16.99)
others	68 (13.28)

**Table 2**  
Prevalence and severity of symptoms (N = 512).

Variable of symptom	Number of participants	Prevalence (%)	Severity (0–4) (Mean ± SD)
Lack of energy	371	72.46	2.02 ± 1.46
Feeling nervous	353	68.95	1.49 ± 1.40
Feeling drowsy	294	57.42	1.46 ± 1.42
Feeling irritable	289	56.45	1.00 ± 1.12
Difficulty sleeping	286	55.86	1.45 ± 1.47
Pain	283	55.27	1.39 ± 1.44
Shortness of breath	240	46.88	1.20 ± 1.43
Feeling sad	225	43.95	0.74 ± 1.07
Cough	195	38.09	0.76 ± 1.09
Dry mouth	176	34.38	0.73 ± 1.09
Lack of appetite	174	33.98	0.84 ± 1.26
Itching	156	30.47	0.78 ± 1.27
Sweats	145	28.32	0.59 ± 0.98
Numbness/tingling in hands/feet	126	24.61	0.54 ± 1.02
Nausea	106	20.70	0.51 ± 1.06



**Fig. 1.** Flow chart of the recruiting patients.

**Table 3**  
Summary of symptom clusters (N = 512).

Symptom cluster	Cluster composition	Factor loading	Number of participants (%)
Sickness behavior symptom cluster	Difficulty sleeping	0.876	172 (33.59)
	Feeling drowsy	0.872	
	Pain	0.467	
	Lack of energy	0.431	
Psychological symptom cluster	Feeling irritable	0.847	157 (30.66)
	Feeling nervous	0.772	
	Feeling sad	0.764	
Lung cancer-specific symptom cluster	Cough	0.722	67 (13.09)
	Shortness of breath	0.625	
	Lack of appetite	0.610	
Epithelial symptom cluster	Numbness/tingling in hands/feet	0.692	20 (3.91)
	Nausea	0.645	
	Itching	0.598	
	Dry mouth	0.473	

followed by feeling nervous (68.95%), feeling drowsy (57.42%), feeling irritable (56.45%), difficulty sleeping (55.86%), and pain (55.27%). Lack of energy also exhibited the highest severity score ( $2.02 \pm 1.46$ ), followed by feeling nervous ( $1.49 \pm 1.40$ ), feeling drowsy ( $1.46 \pm 1.42$ ), difficulty sleeping ( $1.45 \pm 1.47$ ), pain ( $1.39 \pm 1.44$ ), and shortness of breath ( $1.20 \pm 1.43$ ).

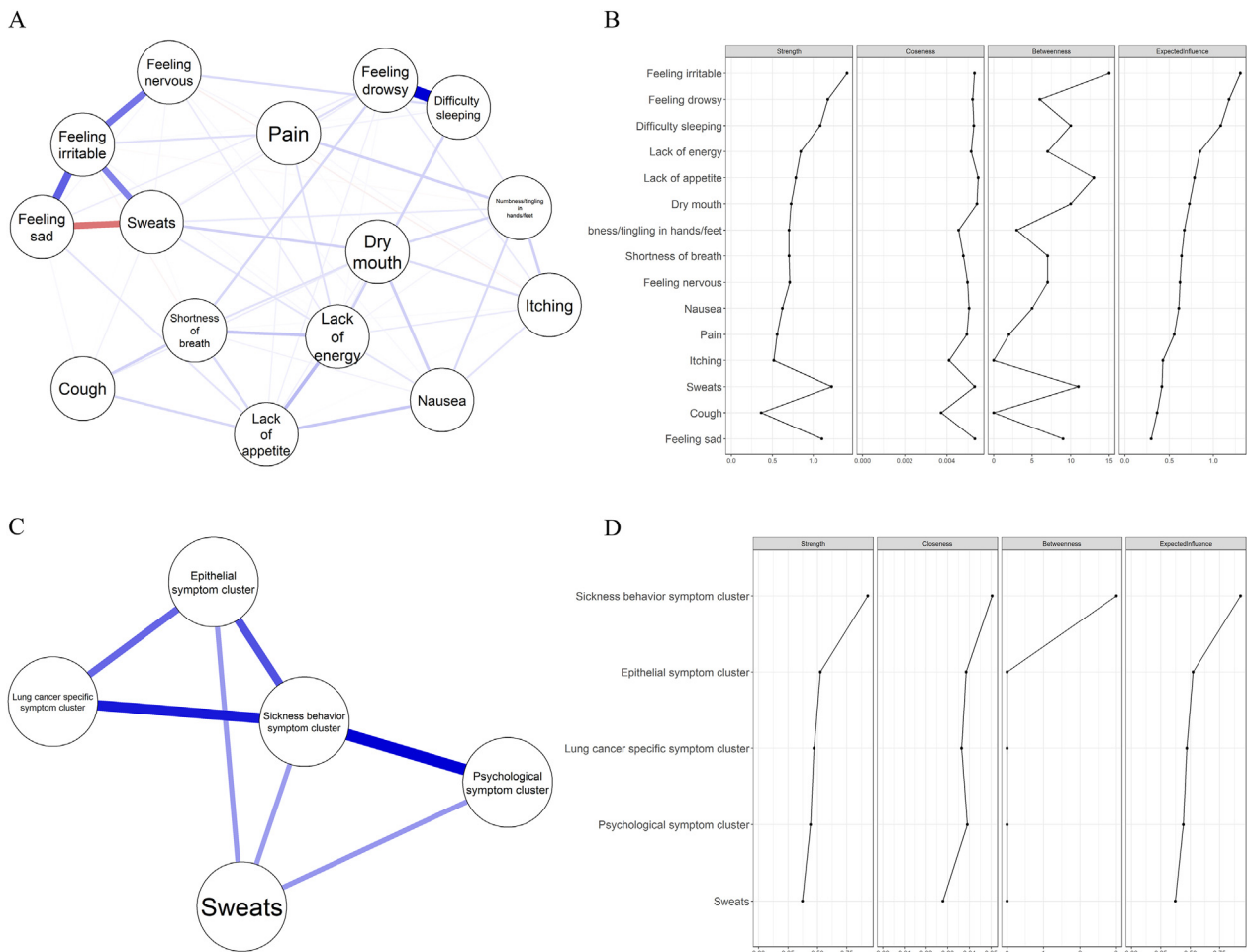
*Prevalence and composition of symptom clusters*

As presented in Table 3, PCA identified four symptom clusters. The Kaiser–Meyer–Olkin was 0.746, and Bartlett’s test of sphericity was

$\chi^2 = 2159.474$  ( $P < 0.001$ ), confirming the suitability of the data for factor analysis. These statistical results provide evidence for the reliability of PCA findings. Based on previous studies and our research team members’ understanding of symptoms, we named these symptom clusters as follows: the sickness behavior symptom cluster (i.e., difficulty sleeping, feeling drowsy, pain, and lack of energy), the psychological symptom cluster (i.e., feeling irritable, feeling nervous, and feeling sad), the lung cancer-specific symptom cluster (i.e., cough, shortness of breath, and lack of appetite), and the epithelial symptom cluster (numbness/tingling in hands/feet, nausea, itching, and dry mouth). Sweating did not belong to any specific symptom cluster. By applying diagnostic criteria that required severity scores greater than 0 within each respective symptom cluster, the most prevalent one was the sickness behavior symptom cluster (33.59%), followed by the psychological symptom cluster (30.66%), the lung cancer-specific symptom cluster (13.09%), and the epithelial symptom cluster (3.91%).

*Networks of symptoms and symptom clusters*

The network relationship and centrality indices of 15 symptoms are depicted in Fig. 2(A) and (B). The top three strongest edges were between “difficulty sleeping” and “feeling drowsy” ( $r = 0.748$ ), “feeling irritable” and “feeling sad” ( $r = 0.467$ ), and “feeling irritable” and “feeling nervous” ( $r = 0.405$ ). Among all symptoms, “feeling irritable” ( $r_S = 1.412$ ,  $r_C = 0.005$ ,  $r_B = 15.000$ , and  $EI = 1.305$ ) was the core symptom among all symptoms, followed by “feeling drowsy” ( $r_S = 1.177$ ,  $r_C = 0.005$ ,  $r_B = 6.000$ , and  $EI = 1.177$ ), “difficulty sleeping” ( $r_S = 1.083$ ,  $r_C = 0.005$ ,  $r_B = 10.000$ , and  $EI = 1.083$ ), and “lack of energy” ( $r_S = 0.848$ ,  $r_C = 0.005$ ,  $r_B = 7.000$ , and  $EI = 0.848$ ).



**Fig. 2.** Network structures of symptoms and symptom clusters in patients with lung cancer post-chemotherapy. (A) Network relationship map of symptoms. (B) The centrality indices of the symptom network. (C) Network relationship map of symptom clusters. (D) The centrality indices of the symptom cluster network.

The network relationship and centrality indices of four symptom clusters along with sweats are illustrated in Fig. 2(C) and (D). The top three strongest edges were between the “sickness behavior symptom cluster” and the “psychological symptom cluster” ( $r = 0.312$ ), the “sickness behavior symptom cluster” and the “lung cancer-specific symptom cluster” ( $r = 0.283$ ), and the “sickness behavior symptom cluster” and the “epithelial symptom cluster” ( $r = 0.212$ ). In the entire symptom cluster network, the “sickness behavior symptom cluster” ( $r_S = 0.928$ ,  $r_C = 0.051$ ,  $r_B = 3.000$ , and  $EI = 0.928$ ) was the most central symptom cluster among all symptom clusters, followed by the “epithelial symptom cluster” ( $r_S = 0.524$ ,  $r_C = 0.038$ ,  $r_B = 0.000$ , and  $EI = 0.524$ ), the “lung cancer-specific symptom cluster” ( $r_S = 0.471$ ,  $r_C = 0.036$ ,  $r_B = 0.000$ , and  $EI = 0.471$ ), and the “psychological symptom cluster” ( $r_S = 0.441$ ,  $r_C = 0.039$ ,  $r_B = 0.000$ , and  $EI = 0.441$ ). Moreover, the subgroup analysis was conducted to identify differences in networks among people with different characteristics. As shown in Supplementary Table S1, the symptom cluster network did not exhibit any statistically significant differences (all  $P$  values  $> 0.05$ ) concerning gender, registered residence, smoking history, drinking history, multimorbidity, cancer stage, tumor classification, and treatment.

The correlation coefficients of the four centrality indices in both the symptom and symptom cluster networks exceeded 0.5, indicating their stability (Supplementary Fig. S1 and Fig. S3). The small bootstrap confidence intervals for both networks suggest high accuracy (Supplementary Fig. S2 and Fig. S4).

## Discussion

This study represents a pioneering effort in utilizing network analysis to identify the central symptom clusters among patients with lung cancer post-chemotherapy. Among the 15 symptoms examined, “lack of energy” emerged as the most prevalent and severe. Furthermore, “feeling irritable” was identified as the core symptom within the comprehensive symptom network. The Kaiser–Meyer–Olkin was above 0.5, indicating that data were sufficient for the principal component analysis.<sup>20</sup> Four distinct clusters were discerned: the sickness behavior symptom cluster, the psychological symptom cluster, the lung cancer-specific symptom cluster, and the epithelial symptom cluster. Notably, within this framework, the sickness behavior symptom cluster (i.e., difficulty sleeping, feeling drowsy, pain, and lack of energy) constituted the central symptom cluster.

The symptom of “lack of energy” was found to be the most prevalent and severe among the 15 symptoms assessed. This finding aligned with a previous study, which also identified “lack of energy” as the most common adverse symptom experienced by patients following chemotherapy, significantly impacting their overall quality of life.<sup>3,21</sup> The underlying mechanism of “lack of energy” remains elusive, potentially involving inflammation and immune system dysregulation, hypothalamic-pituitary-adrenal (HPA) axis dysfunction, as well as impaired energy metabolism.<sup>22</sup> However, “lack of energy” has often been overlooked in clinical practice, being considered a normative response following chemotherapy.<sup>23</sup> Clinical nurses should prioritize identifying and managing “lack of energy” while developing evidence-based nursing strategies. Moderate physical exercise, nutraceutical treatment, and psychosocial interventions (such as cognitive behavioral therapy, mind-body interventions, and yoga) have demonstrated efficacy in ameliorating symptoms of “lack of energy”.<sup>24</sup> However, the core symptom of “feeling irritable” served as a catalyst for the manifestation of other symptoms in the present study.<sup>23</sup> This finding diverged from a previous study that identified fatigue as the core symptom among cancer patients.<sup>17</sup> This discrepancy may be attributed to the specific cancer type. Due to the impairment of the respiratory system, individuals diagnosed with lung cancer commonly experience significant psychological distress, including irritability, anxiety, and depression.<sup>25</sup> “Feeling irritable” can be considered a significant psychological concern, with the potential to

progress into depressive symptoms.<sup>26</sup> Patients exhibiting a heightened sense of irritability were found to be more prone to reporting elevated levels of symptom burden and diminished quality of life.<sup>27</sup> Therefore, early identification and intervention of irritability can be beneficial in improving the prognosis. Moreover, this study revealed a disparity between the most prevalent or severe symptom (i.e., lack of energy) and the core symptom (i.e., feeling irritable), necessitating clinical nurses to reassess their prioritization of nursing interventions to achieve optimal cost-effectiveness.

The present study identified four distinct symptom clusters, with the sickness behavior symptom cluster emerging as the most prevalent and central cluster. These findings were consistent with prior research and have been widely corroborated across various cancer types.<sup>5</sup> The cluster of symptoms, including difficulty sleeping, feeling drowsy, pain, and lack of energy, may be attributed to the involvement of inflammatory mediators such as IL-4 or IL-6.<sup>28</sup> Previous studies demonstrated that comorbid conditions, functional status, age, and stress were significant risk factors for the manifestation of the sickness behavior symptom cluster.<sup>29,30</sup> Numerous intervention studies were conducted on this symptom cluster, including mind-body treatments and psychoeducational interventions.<sup>31–34</sup> However, these studies failed to differentiate the subgroups within the sickness behavior symptom cluster. To implement more precise intervention measures, Hammer et al. identified three distinct profiles of this symptom cluster (i.e., low, moderate, and high class) in gynecologic cancer patients.<sup>35</sup> Therefore, future research should aim to identify the risk and subgroups associated with the symptom cluster of sickness behavior in patients with lung cancer post-chemotherapy, to provide personalized and targeted nursing interventions.

The psychological symptom cluster (i.e., feeling irritable, feeling nervous, and feeling sad) emerged as the second most prevalent symptom cluster among patients with lung cancer post-chemotherapy in this study. Relevant findings were also reported by Choi et al. and Russell et al. who identified a similar symptom cluster among patients with lung cancer.<sup>9,36</sup> Meanwhile, we observed a robust correlation between the psychological symptom cluster and the sickness behavior symptom cluster, suggesting a potential causal relationship between these two clusters of symptoms. The manifestation of severe physical symptoms can contribute to the development of psychological problems in patients, while profound psychological distress can exacerbate the burden of overall symptoms.<sup>25</sup> Refractory psychological symptom clusters may contribute to treatment delays and disease exacerbations.<sup>37,38</sup> Therefore, it was imperative for clinical nurses to promptly assess patients’ psychological symptoms and implement efficacious interventions such as mind-body therapy and cognitive-behavioral therapy.<sup>39</sup>

The third prevalent symptom cluster observed in patients with lung cancer was the lung cancer-specific symptom cluster, characterized by cough, shortness of breath, and lack of appetite. Numerous prior studies have consistently reported the presence of this particular symptom cluster among individuals diagnosed with lung cancer.<sup>6,40</sup> Coughing and shortness of breath were prevalent among patients with lung cancer due to the impact of pulmonary parenchymal lesions and treatment, consequently leading to a lack of appetite.<sup>41</sup> This finding can assist clinical nurses in implementing targeted nursing interventions for respiratory symptoms, enhancing patients’ respiratory function and nutritional status. The final symptom cluster observed was the epithelial symptom cluster, including numbness/tingling in hands/feet, nausea, itching, and dry mouth. However, the composition of this symptom cluster was inconsistent with the previous studies.<sup>9,42</sup> The discrepancy may arise from variations in measurement tools or an inadequate sample size. Further investigations were warranted to assess the composition and stability of the epithelial symptom cluster.

The accuracy and stability of the symptom and symptom cluster networks were significantly high, further demonstrating the reliability of our findings. The subgroup analysis results revealed no statistically significant differences in the symptom clusters of patients with lung cancer

post-chemotherapy among individuals with diverse characteristics, which can be attributed to the following factors: the limited sample size and the inability to control for all other clinical covariates in the subgroup network analysis. In the future, a large-scale study should be conducted to further investigate the differences in the symptom cluster networks among individuals with different characteristics.

#### Implications for nursing practice and research

This study found that the sickness behavior symptom cluster was the central symptom cluster, which was positively correlated with other symptom clusters. The findings can facilitate clinical nurses in comprehensively understanding of the inter-relationships among symptom clusters in patients with lung cancer post-chemotherapy. Future interventions targeting the central symptom cluster (the sickness behavior symptom cluster) could be implemented to assess their efficacy in ameliorating other symptom clusters to alleviate patient burden.

#### Limitations

There were several limitations in this study. Firstly, our analysis only encompassed 15 symptoms, neglecting many others. Future studies should aim to investigate a broader range of symptoms and establish the core symptom and symptom cluster more comprehensively in a large-scale, multi-center study. Secondly, we solely relied on one dimension of self-reported symptoms (severity), which may impact the reliability of our findings. To enhance the reliability of identifying central symptom clusters, future research should incorporate additional dimensions such as prevalence, frequency, distress, and objective measurements. Lastly, this study can't explore causal relationships among different symptoms or symptom clusters. Dynamic network analysis utilizing longitudinal data can be employed to address this limitation in future studies.

#### Conclusions

This study has contributed novel insights into the symptom cluster in patients with lung cancer post-chemotherapy using network analysis. Four distinct symptom clusters were identified: the sickness behavior symptom cluster, the psychological symptom cluster, the lung cancer-specific symptom cluster, and the epithelial symptom cluster. The sickness behavior symptom cluster exhibited a central role in patients' experiences across these various clusters. These findings hold significant implications for clinical nurses to develop targeted interventions to enhance patients' quality of life.

#### Ethics statement

The ethical review was conducted by the Ethics Committee of Jiangnan University (Approval No. JNU20220901IRB05). It was conducted according to the guidelines of the Declaration of Helsinki. Written informed consent was obtained from those individuals who were willing to participate in this study before starting any study procedure.

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#### CRediT authorship contribution statement

**Liping Teng:** Conceptualization, Methodology, Supervision, and Writing – Review & Editing. **Zhou Zhou:** Conceptualization, Methodology, Investigation, Formal analysis, and Writing – Original Draft. **Yiting Yang:** Methodology, Investigation, and Formal analysis. **Jun Sun, Yajun Dong, and Min Zhu:** Methodology, and Investigation. **Teng Wang:** Methodology, and Supervision. The authors have read and approved the final manuscript. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

#### Declaration of competing interest

The authors declare no conflict of interest.

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#### Data availability statement

Datasets used and/or analyzed during the current study are available from the corresponding author, Liping Teng, upon reasonable request.

#### Declaration of Generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.apjon.2024.100383>.

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