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Original Article

Network analysis of fatigue symptoms in Chinese patients with advanced cancer

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ABSTRACT

Objective: This study was aimed at investigating the network structures of fatigue symptoms in patients with advanced cancer, with a focus on identifying the central symptom—an aspect crucial for targeted and effective fatigue symptom management.

Methods: In this cross-sectional study, patients with advanced cancer were recruited from the cancer treatment center of a tertiary hospital in China between January and December of 2022. Symptom occurrence and severity were assessed with the Cancer Fatigue Scale. Network analysis was conducted to explore the network structure and identify the core fatigue symptoms.

Results: The study included 416 patients with advanced cancer. Lack of energy (2.25 $\pm$ 1.24), lack of interest in anything (2.20 $\pm$ 1.22), and lack of self-encouragement (2.03 $\pm$ 1.25) were the most severe fatigue symptoms and belonged to the affective fatigue dimension. In the overall network, reluctance ($r_s = 5.622$), a heavy and tired body ($r_s = 5.424$), and tiring easily ($r_s = 5.319$) had the highest strength values. All these core symptoms were classified within the physical fatigue dimension and remained stable before and after adjustment for covariates.

Conclusions: This study identified reluctance, a heavy and tired body, and tiring easily as the core fatigue symptoms in patients with advanced cancer, thus providing valuable insight to help clinical nurses formulate more effective symptom management strategies. Future interventions could assess the efficacy of targeting the central symptom cluster in alleviating other symptoms and patient burden.

Introduction

Cancer poses a substantial disease burden in China. Approximately 4,824,700 new cancer cases have been estimated to have occurred in China,[1] and more than half of all newly diagnosed cancers are in advanced stages at the time of diagnosis.[2] Despite substantial improvements in the survival of patients with cancer in China, survival times remain shorter in China than other high-income countries, such as the US and the UK. Moreover, China has much higher age-standardized rates of cancer mortality than the US and UK (129.40 per 100,000 population, 86.30 per 100,000 population, and 100.50 per 100,000 population, respectively).[3] Cancer stage influences the treatment strategies and patient prognosis. Compared with patients with early-stage cancer, those with late-stage cancer are more likely to receive conservative treatments and are substantially more likely to have poorer prognosis.[4]

Numerous reports have indicated that patients with advanced cancer experience various symptoms.[5,6] Fatigue is among the most common and distressing adverse effects of cancer diagnosis and treatment in patients with advanced cancer. A systematic review has indicated that 49.2% of patients with cancer experience fatigue, and this percentage increases to 60.6% among those with advanced cancer.[7] Fatigue is the most prevalent and severe symptom among patients with advanced cancer.[8,9] The effects of fatigue on quality of life are both profound and pervasive, including diminished ability to work; to participate in social, leisure, and other activities; and to sustain meaningful relationships with family and others. Moreover, patients with fatigue are likely to interrupt cancer treatment, thus directly affecting treatment efficacy.[10] These findings highlight the

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importance of managing fatigue in patients with advanced cancer, not only to improve their quality of life, but also to aid in disease management and treatment.

Cancer-related fatigue is believed to be a distinct and central symptom with multi-dimensional content.[11] This fatigue, a persistent, often overwhelming feeling of physical, affective, and/or cognitive exhaustion, differs from the fatigue caused by exertion, in that it is not necessarily relieved by rest or sleep.[12,13] Instruments measuring various dimensions of fatigue are crucial to health care providers' understanding of the status of fatigue symptoms and match priori interventions. A systematic review has described 19 cancer-related fatigue instruments that have been developed, including the Cancer Fatigue Scale (CFS), Multidimensional Fatigue Inventory (MFI), Fatigue Symptom Inventory (FSI), and Brief fatigue inventory (BFI).[14] The CFS is a multidimensional, brief, and easy-to-use questionnaire that has three main benefits over other fatigue scales. First, it can be completed in several minutes, even by patients with advanced stages of cancer. This ease of use is a crucial benefit, given that the primary goal is to evaluate the fatigue encountered by patients with cancer who are already depleted. Second, the scale was specifically crafted to capture the essence of fatigue, and to measure its physical, emotional, and cognitive dimensions. Third, the scale has shown strong validity and reliability across substantial numbers of patients with cancer, and can adequately evaluate psychometric attributes through a 15-item instrument.[13]

Patients often experience multiple fatigue symptoms simultaneously during treatment.[15] Nevertheless, the correlation between various symptoms or symptom dimensions remains unclear. One study in 1403 patients with breast cancer has shown that, as physical fatigue worsens, mental fatigue also intensifies.[16] However, another study has indicated decreased total and physical fatigue after an exercise intervention, whereas the differences in affective or cognitive fatigue were not significant.[17] Notably, examining the associations among various dimensions or fatigue symptoms can help health care providers identify the core symptoms that most affect other symptoms. This, process can lead to the identification of core targets for complex fatigue interventions aimed at ameliorating fatigue symptoms.[18]

With information technology advances, symptom network analysis has become a practical method to address the above challenge. Network analysis provides a new approach to identifying core symptoms, and visualizing associations with various symptoms and symptom dimensions.[19,20] Empirical evidence is necessary for the development of personalized and precision fatigue symptom management strategies. Studies have used network analysis to explore the symptoms of patients with cancer. A scoping review published in 2024 has identified 23 studies focusing on physical, psychological, and social symptoms, or focusing solely on anxiety and depression symptoms of cancer. Fatigue was a core symptom in approximately half the studies in the scoping review.[21] However, a knowledge gap was identified regarding the interactions among different manifestations of fatigue symptoms. Therefore, this study was aimed at constructing a network of the fatigue symptoms of patients with advanced cancer through network analysis, to explore the core symptoms, and associations among symptoms or symptom dimensions.

Methods

Study design and participants

This study used a cross-sectional design. Participants were recruited from the cancer treatment center of a tertiary hospital in China between January and December of 2022. Participants were included if they (1) were older than 18 years; (2) were diagnosed with stage III or IV cancer; (3) were receiving cycle therapy, in which treatments were repeated every several weeks; (4) were in the period between two repeated treatments; and (5) provided informed consent to participate. Furthermore, participants were excluded if they (1) were unable to communicate because of self-reported hearing impairment or loss of voice, (2) were diagnosed with dementia, and/or (3) were receiving palliative care at end of life. The research methods have been presented elsewhere.[9]

Measure

Fatigue

Fatigue was measured with the Chinese version of the CFS.[13] The scale consists of three dimensions: physical fatigue (seven items), affective fatigue (four items), and cognitive fatigue (four items). A five-point Likert scale is used, ranging from 0 (not at all) to 4 (very much), with a total score of 60. Items 5, 8, 11, and 14 are scored with a reverse scoring method. A higher score indicates greater fatigue severity. Cronbach's α was 0.88 in the original research and 0.86 in this study (Supplementary Table S1).

Sociodemographic and clinical data

We collected sociodemographic and clinical data with a self-designed general information questionnaire. Sociodemographic data included age (continuous), sex (male or female), educational level (primary school or lower, junior high school, senior high school, associate, or higher), marital status (married or single), current residence area (urban or rural), living alone (yes or no), family monthly income per capita ($<$ 3000, 3000–6000, 6000–10,000, or $\geq$ 10,000 yuan), body mass index (BMI; underweight, normal, overweight, or obese), and major payment source for medical services (insurance or self-payment). Clinical data included cancer diagnosis (gastrointestinal cancer, lung cancer, breast cancer, urinary cancer, gynecologic cancer, or other cancer), cancer survivorship duration (continuous), previous cancer therapy (surgery, radiotherapy, chemotherapy, or other), complications (hypertension, diabetes, cardiovascular disease, kidney disease, liver diseases, other, or no comorbidities), and malnutrition risk (high or low). Malnutrition risk was evaluated with the Nutrition Risk Screening scale (NRS 2002), consisting of three components: undernutrition, disease severity, and age. The total score is 7, and scores of 0–3 indicate low malnutrition risk.

Study procedures

Registered nurses with more than 1 year of experience served as research assistants. Unified training in administering the questionnaire and data collection was provided to the research assistants by the researchers. After an eligible patient with advanced cancer was admitted to the cancer treatment center, a research assistant provided a comprehensive explanation of the study's objectives and content to the patients who were willing to participate in the research. Enrollment was based on the inclusion and exclusion criteria. Questionnaires were collected on the day of hospitalization. The researchers obtained written informed consent from the patients willing to participate, and the patients were informed that they could withdraw from the study at any time. The entire questionnaires were completed independently, on the basis of self-assessment by patients. A researcher assistant was present throughout the entire process and explained items that were difficult for patients to understand. Missing entries were immediately confirmed with the patients, to ensure data completeness.

Sample size calculation

Moreover, a priori and a posteriori sample size estimation was conducted. The network, represented as an undirected graph, described a set of random variables possessing the Markov property, constituting the pairwise Markov random field. As the network expands, the quantity of parameters to be estimated for a pairwise Markov random field rapidly increases. In our 15-node networks, at least 120 parameters (15 threshold parameters and $15 \times 14/2 = 105$ pairwise association parameters) needed to be estimated.[22] The net simulator estimate was used for a posteriori sample size estimation.[23] This method was used to simulate network data and estimate the recoverability of the network structure under various conditions. Additionally, this method can be used to calculate the minimum sample size required for constructing robust network models. A correlation coefficient greater than 0.9 was considered to indicate a stable network model. The results are presented in Supplementary Fig. S1.

Data analysis

Initially, we employed mode imputation as a method to handle missing data within the covariate variables. Then the prevalence and severity of fatigue symptoms were described with means, standard deviations, medians, interquartile ranges, frequencies, and percentages. Subsequently, linear regression analysis was performed to evaluate the statistical significance between covariates and overall symptom severity.

This study chooses a Gaussian graphical model (GGM) to examine ordinal data variables. A contemporaneous network based on symptom severity was constructed with the extended Bayesian criterion, in conjunction with least absolute shrinkage and selection operator regression analysis. Node centrality served as an indicator for identifying relative importance of the symptoms from a mechanistic perspective. Centrality analysis was performed with three centrality indices: strength, betweenness, and closeness. Strength was defined as the sum of the absolute values of the edge weights between a node and all nodes with direct links. Closeness was characterized by the inverse of the mean distance between a node and the nodes to which it was linked. Betweenness referred to the number of times in which a node appeared in all the shortest paths in the network. Among these indicators, strength was considered the most reliable indicator of centrality. A higher value indicated that a symptom occupied a more central position within the network regarding its underlying mechanisms. The centrality index serves as a measure for nodes, whereas network density is a metric that characterizes the overall network. And the absolute value of all spearman correlation coefficients between two nodes was identified as the network density, which is considered an indicator of long-term prognosis.[24] Bridge symptoms were broadly defined as symptoms connecting different clusters of symptoms. The centrality indicators for bridge symptoms were classified as previously described.[25]

We conducted a difference test to determine whether variations existed in the estimates of network connections and centrality across various variables. The bootstrapped values can be used to test if two edge-weights or centralities significantly differ from one-another. This can be done by taking the difference between bootstrap values of one edge-weight or centrality and another edge-weight or centrality, and constructing a bootstrapped confidence interval (CI) around those difference scores. We determined the 95% CI for each edge weight by using 1000 bootstrap replicates. This allows for a null-hypothesis test if the edge-weights or centralities differ from one-another by checking if zero is in the bootstrapped CI.

Bootstrapping techniques were used to access the accuracy and stability of the network. To assess network accuracy, we determined the 95% CI for each edge weight by using 1000 bootstrap replicates. Furthermore, network stability was evaluated according to the correlation stability coefficient (CS coefficient) based on 1000 bootstrap replicates. The CS coefficient should preferably be > 0.5 and at least > 0.25.[26]

In sensitivity analysis, we conducted network analysis with covariates and subgroup analysis. Refer to the previous study,[27,28] in the network analysis with covariates, the most significant factors ($P < 0.001$) in the regression analysis were included in the network analyses as confounders. The subgroup analysis in the network was conducted with the network comparison test. The network invariance and global strength invariance were tested with the network comparison test. All data analyses were performed in R software (version 4.4.0). Statistical significance was defined as a P value less than 0.05.

Ethical considerations

This study was approved by the institutional ethics committee (IRB No. 2021BJYYEC-325-01). Written informed consent was obtained from all participants before the initiation of the research.

Results

Participants' characteristics

The patients' ($n = 416$) mean age was 62.02 ± 12.08 years. All patients were in stage III ($n = 279$, 67.1%) and IV ($n = 137$, 32.9%). Lung

Table 1
Characteristics of participants ($N = 416$).

Variables	n (%)
Age (years), Mean ± SD (range)	62.02 ± 12.08 (20–88)
< 65	215 (51.7)
≥ 65	201 (48.3)
Gender	
Male	212 (51.0)
Female	204 (49.0)
Educational level	
Primary school, or lower	46 (11.1)
Junior high school	118 (28.4)
Senior high school	92 (22.1)
Associate or higher	160 (38.5)
Marital status	
Married	371 (89.2)
Single	45 (10.8)
Current residence	
Urban	350 (84.1)
Rural	66 (15.9)
Live alone	
Yes	30 (7.2)
No	386 (92.8)
Family monthly income per capita (yuan)	
<3000	58 (13.9)
3000-6000	163 (39.2)
6000-10,000	121 (29.1)
≥10,000	74 (17.8)
Body mass index (kg/m^2)	
Underweight (< 18.5)	33 (7.9)
Normal (18.5-24.0)	225 (54.1)
Overweight (24.0-28.0)	129 (31.0)
Obesity (≥ 28.0)	29 (7.0)
Major payment source for medical services	
Insurance	403 (96.9)
Self-payment	13 (3.1)
Malnutrition risk	
Increased	33 (7.9)
Low	383 (92.1)
Cancer diagnosis	
Gastrointestinal cancer	127 (30.5)
Lung cancer	138 (33.2)
Breast cancer	61 (14.7)
Urinary cancer	25 (6.0)
Gynecologic cancer	7 (1.7)
Otherwise	58 (13.9)
Cancer survivorships duration (year), median (IQR)	2 (1–3)
Previous cancer therapy[a]	
Surgery	215 (51.7)
Radiotherapy	102 (24.5)
Chemotherapy	353 (84.9)
Otherwise	39 (9.4)
Comorbidities[a]	
Hypertension	137 (32.9)
Diabetes	74 (17.8)
Cardiovascular disease	57 (13.7)
Kidney disease	13 (3.1)
Liver diseases	22 (5.3)
Otherwise	23 (5.5)
No comorbidities	212 (51.0)

SD, standard deviation; IQR, interquartile range.
[a] More than one answer is possible.

cancer accounted for the greatest proportion of cases ($n = 138$, 33.2%), and was followed by gastrointestinal ($n = 127$, 30.5%), breast ($n = 61$, 14.7%), urinary ($n = 25$, 6.0%), and gynecological ($n = 7$, 1.7%) cancers. Most patients received chemotherapy ($n = 353$, 84.9%), followed by surgery ($n = 215$, 51.7%) and radiotherapy ($n = 102$, 24.5%). Detailed information on general characteristics is presented in Table 1.

Prevalence and severity of fatigue symptoms

Table 2 presents the prevalence and severity of each fatigue symptom. Lack of energy ($n = 373$, 89.7%), lack of interest in anything ($n = 372$, 89.4%), and lack of self-encouragement ($n = 367$, 88.2%) were the most prevalent symptoms. Regarding symptom severity, lack of energy (2.25 ± 1.24), lack of interest in anything (2.20 ± 1.22), and lack of self-encouragement (2.03 ± 1.25) were the most severe fatigue symptoms.

Factors associated with overall symptom severity

The linear regression analysis of overall symptom severity indicated that living alone ($\beta = 5.179$, $P = 0.008$), family monthly income per capita ($\beta = -1.558$, $P = 0.006$), urinary cancer ($\beta = 4.643$, $P = 0.044$), and malnutrition risk ($\beta = -6.013$, $P < 0.001$) were associated with overall symptom severity (Supplementary Table S2).

Network of fatigue symptoms

Fig. 1A shows the symptom network of the fatigue symptom experienced by advanced cancer survivors. A spring layout was used to generate undirected association networks. Each node represented one fatigue symptom. In the network, edges indicated the conditional independence relationships between nodes. Greater edge thickness indicated stronger association between nodes. Color indicated the direction of correlation between two nodes, with green indicating positive correlation and red indicating negative correlation. Supplementary Table S3 shows the weight of each connection in the network. The density of this network was 32.14.

Node centrality and predictability

As shown in Fig. 1B and Supplementary Table S5, reluctance ($r_s = 5.622$), a heavy and tired body ($r_s = 5.424$) and tiring easily ($r_s = 5.319$) had the highest strength values. Furthermore, reluctance ($r_c = 0.022$), a heavy and tired body ($r_c = 0.021$), and tiring easily ($r_c = 0.021$) had the largest closeness values. Reluctance ($r_b = 12$), lack of energy ($r_b = 12$), and lack of interest in anything ($r_b = 10$) had the largest betweenness values. The circles around each node indicated the predictability, which ranged from 55.3% to 81.0% for the 15 nodes of the network (Fig. 1A). Symptom nodes with high predictability might potentially be managed by interventions targeting the surrounding nodes. The most predictable symptoms were lack of energy, aimlessness due to fatigue, and being fed up, at 81.0%, 79.7%, and 79.2%, respectively. For bridge centrality, slowed thinking ($r_{bs} = 3.420$), carelessness ($r_{bs} = 2.969$), and making more errors while speaking ($r_{bs} = 2.902$) had the highest bridge centrality values (Fig.1C, Supplementary Table S6).

Accuracy, stability, and difference test

The bootstrapped CIs were small, thus indicating that the network had good accuracy, on the basis of the edge weight bootstrap (Fig. 2A). The bootstrap subset revealed that the network had good stability. The CS coefficient was 0.594 for expected influence and 0.594 for strength (Fig. 2B). Furthermore, the bootstrapped difference test for edge weights revealed that tiring easily and urge to lie down significantly differed from the other edge weights (Fig. 3A). The bootstrapped node difference test revealed that reluctance significantly differed from the other nodes (DTs = 1.20) (Fig. 3B).

Sensitivity analysis

Referring to previous studies, we constructed a new network after controlling for clinical covariates (malnutrition risk). The results with covariate adjustments are shown in the supplementary materials (Supplementary Tables S4–6, Supplementary Figs. S2–4). The symptom network with and without covariates did not exhibit any statistically significant differences (all P values > 0.05) (Supplementary Table S7). Furthermore, for subgroup analysis, the symptom network did not exhibit any statistically significant differences (all P values > 0.05) by age, sex, educational level, family monthly income per capita, BMI, comorbidities, or previous cancer therapy (Supplementary Tables S8–9, Supplementary Fig. S5).

Discussion

This study represents a novel effort in using network analysis to identify the central fatigue symptom among patients with advanced cancer. The most severe symptoms in patients with advanced cancer were lack of energy, lack of interest in anything, and lack of self-encouragement. Notably, these three symptoms, all belonging to the affective fatigue dimension, had lower centrality than most other symptoms. The core fatigue symptoms in patients with advanced cancer, characterized by reluctance, a heavy and tired body, and tiring easily, remained consistent before and after adjustment for covariates. Notably, these core symptoms were all classified within the physical fatigue dimension. Contemporaneous symptom networks can aid in identifying

Table 2
Prevalence and severity of fatigue symptoms ($N = 416$).

Dimension	Fatigue symptom	Number of participants	Prevalence (%)	Severity (0–4) (Mean ± SD)	Severity [Median (IQR)]
Affective fatigue	Lack of energy	373	89.7	2.25 ± 1.24	2 (1, 3)
Affective fatigue	Lack of interest in anything	372	89.4	2.20 ± 1.22	2 (1, 3)
Affective fatigue	Lack of self-encouragement	367	88.2	2.03 ± 1.25	2 (1, 3)
Affective fatigue	Unable to focus	363	87.3	1.92 ± 1.24	2 (1, 3)
Physical fatigue	Urge to lie down	339	81.5	1.75 ± 1.16	2 (1, 3)
Physical fatigue	Tiring easily	338	81.3	1.72 ± 1.12	2 (1, 2)
Physical fatigue	A heavy and tired body	317	76.2	1.61 ± 1.18	2 (1, 2)
Cognitive fatigue	Forgetfulness	295	70.9	1.41 ± 1.12	2 (0, 2)
Physical fatigue	Exhaustion	283	68.0	1.36 ± 1.19	1 (0, 2)
Cognitive fatigue	Slowed thinking	273	65.6	1.24 ± 1.10	1 (0, 2)
Cognitive fatigue	Carelessness	256	61.5	1.10 ± 1.04	1 (0, 2)
Physical fatigue	Reluctance	256	61.5	1.09 ± 1.07	1 (0, 2)
Physical fatigue	Aimlessness due to fatigue	251	60.3	1.14 ± 1.11	1 (0, 2)
Cognitive fatigue	Making errors while speaking	237	57.0	0.98 ± 1.02	1 (0, 2)
Physical fatigue	Being fed up	248	59.6	0.88 ± 0.90	1 (0, 1)

SD, standard deviation; IQR, interquartile range.

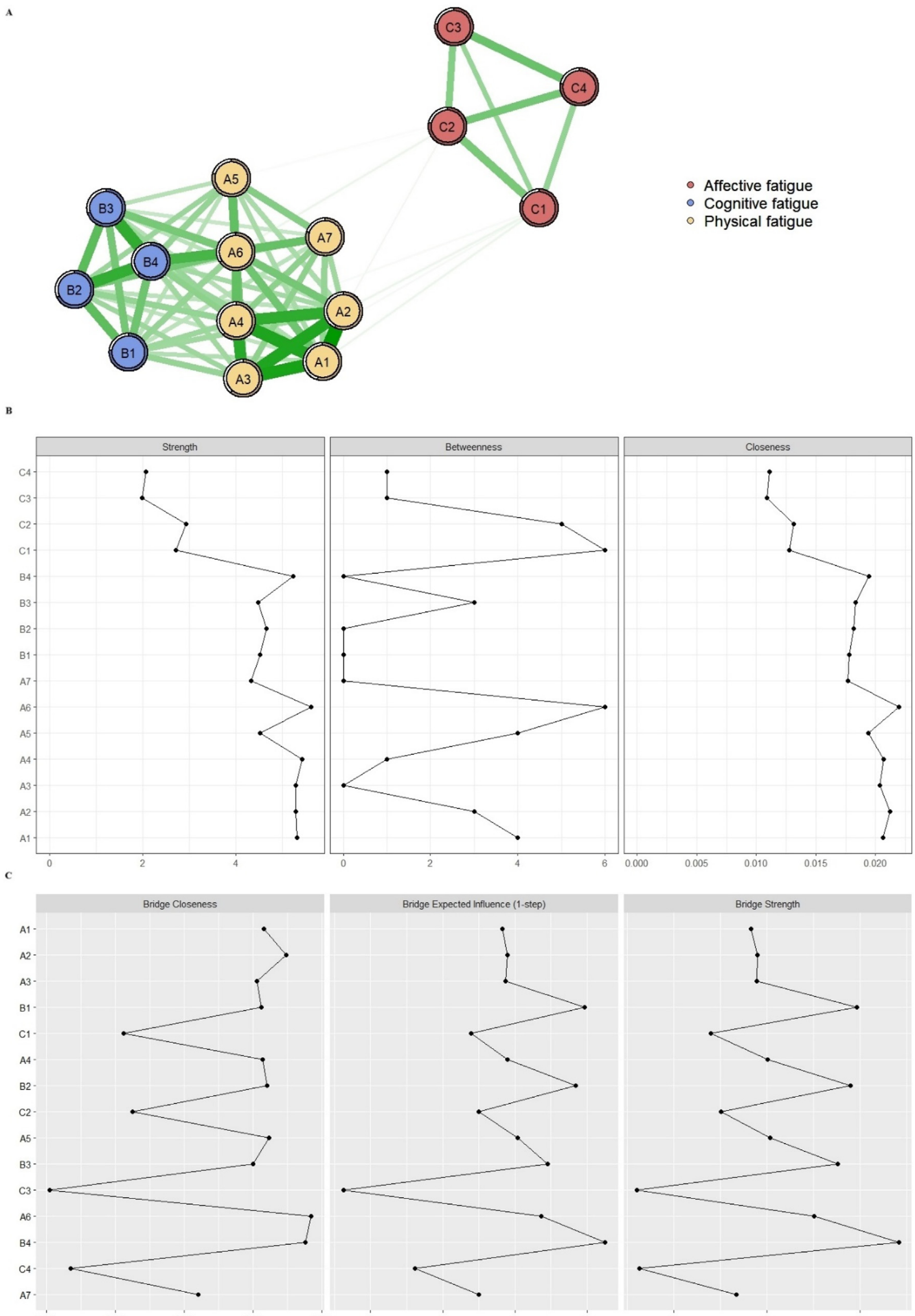

Fig. 1. Symptom networks and centrality measures in the full sample networks. (A) Symptom networks and predictability of 15 symptoms; (B) strength, betweenness, and closeness of 15 symptoms; (C) Bridge centrality index of 15 symptoms. Note: A1: Tiring easily, A2: Urge to lie down, A3: Exhaustion, B1: Carelessness, C1: Lack of energy, A4: A heavy and tired body, B2: Making errors while speaking, C2: Lack of interest in anything, A5: Being fed up, B3: Forgetfulness; C3: Unable to focus, A6: Reluctance, B4: Slowed thinking, C4: Lack of self-encouragement, A7: Aimlessness due to fatigue.

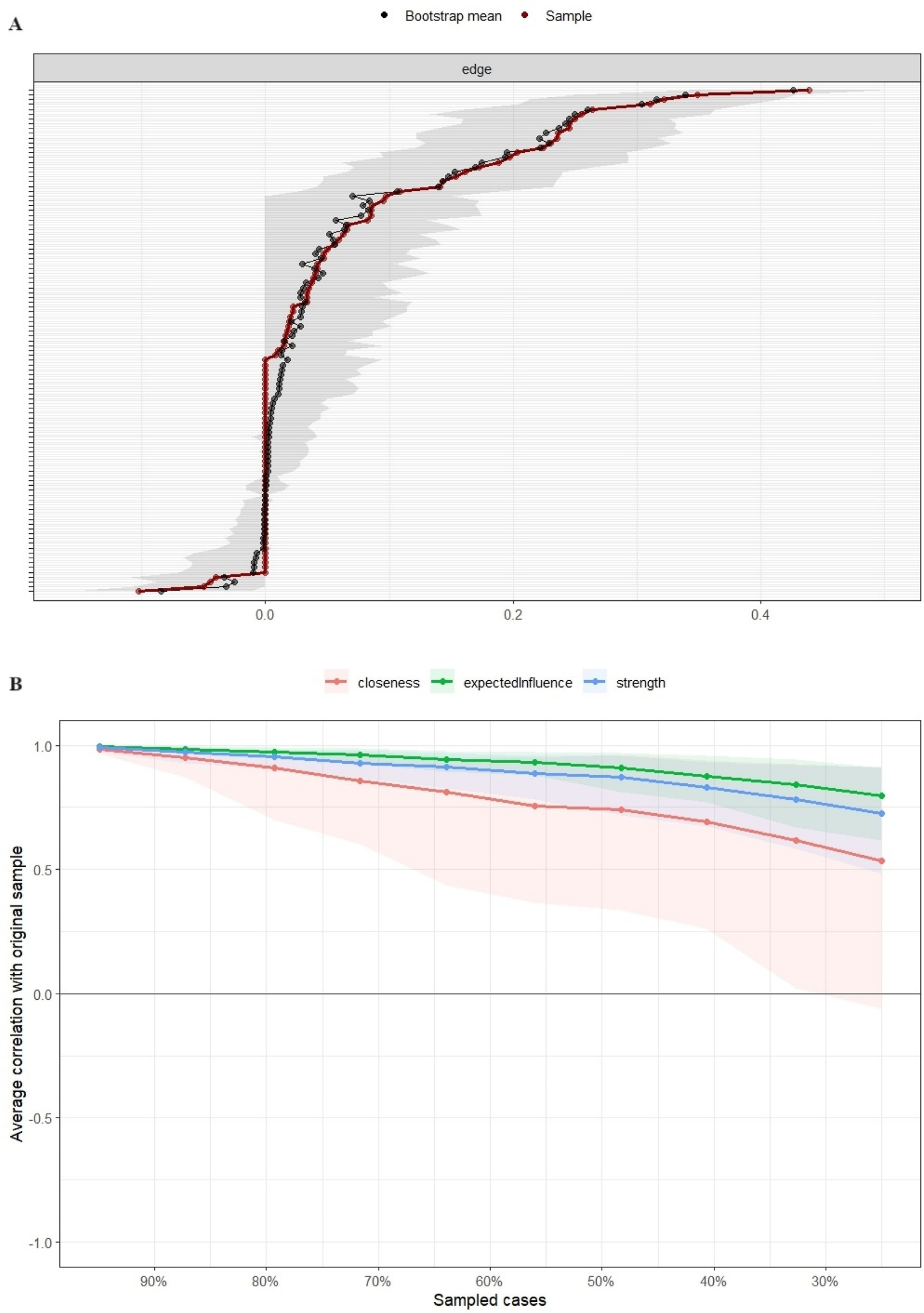

Fig. 2. Accuracy and stability of the symptom networks. (A) Bootstrap analysis results of the edge weights; (B) correlation stability coefficient for strength, closeness, and expected influence.

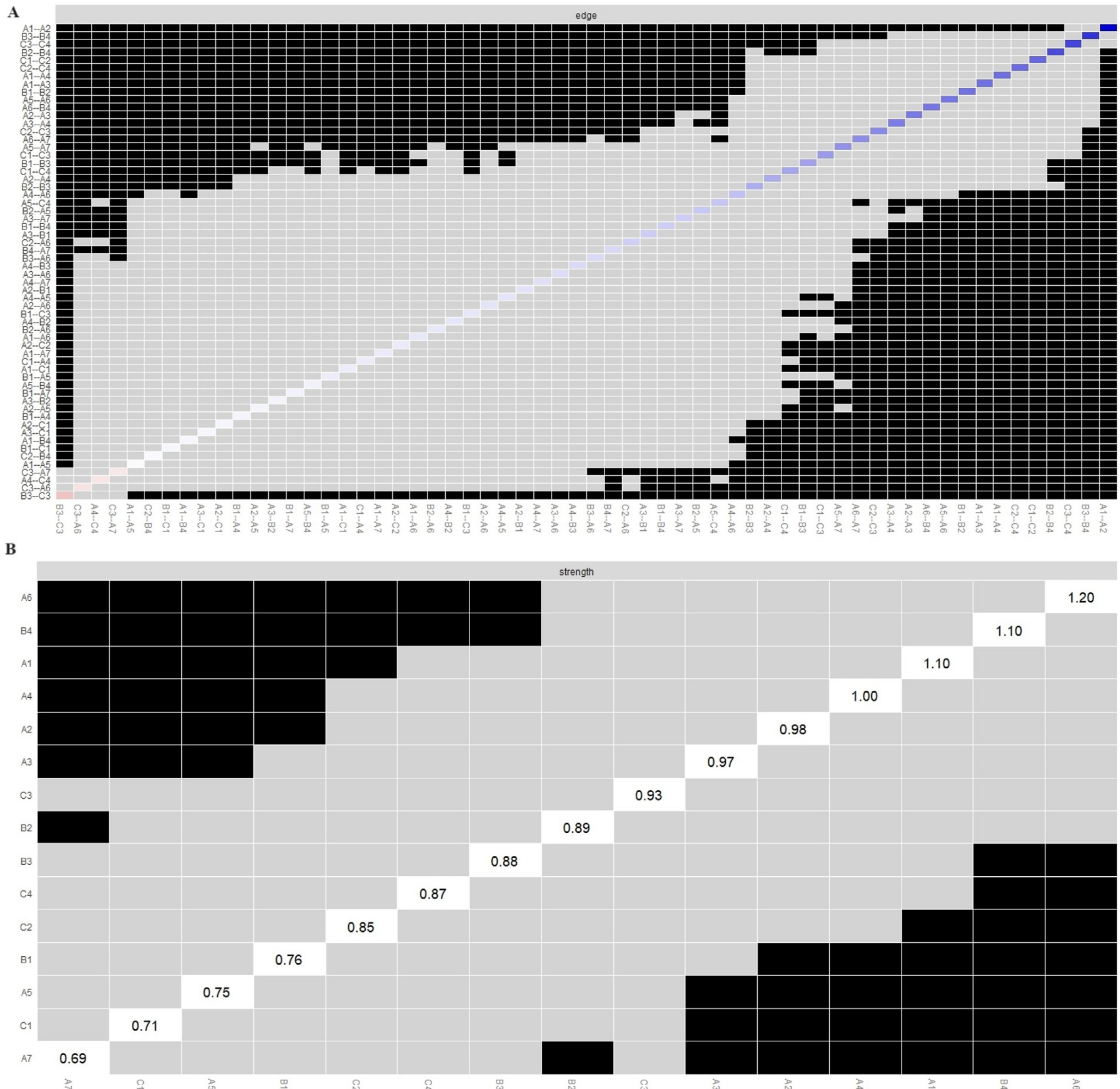

Fig. 3. Results of different tests. (A) Bootstrapped different test for edges; (B) bootstrapped difference test for nodes. Note: A1: Tiring easily, A2: Urge to lie down, A3: Exhaustion, B1: Carelessness, C1: Lack of energy, A4: A heavy and tired body, B2: Making errors while speaking, C2: Lack of interest in anything, A5: Being fed up, B3: Forgetfulness; C3: Unable to focus, A6: Reluctance, B4: Slowed thinking, C4: Lack of self-encouragement, A7: Aimlessness due to fatigue.

the most critical symptom within a network's architecture, and supporting health care providers and researchers in crafting precisely tailored treatment plans.

The four symptoms in the affective fatigue symptom dimension were the most prevalent and severe among the 15 symptoms assessed. This finding aligned with a previous study in a cohort comprising 65% patients with advanced cancer.[29] However, this finding contrasts with those from previous studies suggesting that the physical fatigue symptom dimension is the most severe in patients with cancer who have undergone chemotherapy.[30,31] These contradictory findings might have been because physical frailty was the most sensitive to chemotherapy. A prior study that repeatedly assessed the fatigue status of patients with breast cancer during, and as many as 12 months after, cancer therapy has indicated a significant effect of chemotherapy only for physical fatigue, but not cognitive or affective fatigue.[32] Therefore, physical frailty in patients with cancer who have recently undergone chemotherapy might be the most severe. Another possible explanation is that having advanced disease might be a significant risk factor for psychological outcomes among patients with cancer. For individuals with advanced disease, the psychological effects may arise from the awareness of the severity of their health status, the uncertainty of prognosis, and the possible effects on their quality of life.[33,34] However, affective fatigue has been largely overlooked in clinical practice and is considered a normative response. Therefore, including mental health care in the overall care plan is crucial for patients with advanced cancer. Health care providers should pay attention to how these patients are feeling emotionally, and provide medical treatments, emotional help, and resources to address the difficulties that patients might encounter.

Moreover, this study revealed a difference between the most prevalent or severe symptom (affective fatigue dimension) and the core symptom (physical fatigue dimension). Notably, reluctance, a heavy and tired body, and tiring easily served as a catalyst for the manifestation of other symptoms in this study. One previous study used network analysis to explore core symptoms among patients with terminal illnesses and identified three symptom clusters: physical, psychological, and practical. That study revealed that symptoms in physical clusters were the core symptoms, in line with findings from our study.[35] The mechanism underlying the core symptoms in our study remains elusive and may potentially involve the inability of muscles to perform tasks in response to stimulation, diminished endurance, or dysregulation of cortisol levels in the blood.[36] Given that reluctance, a heavy and tired body, and tiring easily were core symptoms among patients with advanced cancer on the day of hospitalization, and were strongly correlated with other symptoms, those three symptoms might be the most effective intervention targets. Health care professionals could develop an integrated symptom management strategy focusing on the above core symptoms to address the additional symptoms experienced by patients with advanced cancer. Specially, aerobic exercise, yoga, and cognitive-behavioral therapy have shown efficacy in ameliorating symptoms of physical fatigue.[37]

Bridge symptoms are broadly defined as symptoms that link various symptom clusters in various diseases or various symptom subgroups of the same disease.[25] In the network in this study, slowed thinking showed the highest bridge centrality. Slower thinking often requires patients to expend more energy in processing information and completing tasks. Concurrently, making repeated cognitive mistakes can cause awkward moments or difficulty in talking with others, thus affecting patients' sense of self-efficacy. A decrease in self-efficacy can lead to diminished motivation and depletion of mental resources, and, over time, to affective fatigue and physical fatigue.[38,39] Consequently, slowed thinking may link the cognitive fatigue symptom dimension, affective fatigue symptom dimension, and physical fatigue symptom dimension. Focusing on bridge symptoms can help decrease interactions between symptom clusters in treatments, and targeting these bridge symptoms might be more effective than broader treatments.[40] Therefore, health care providers should promptly identify patients with slowed thinking, and guide them toward measures such as cognitive training, to decrease the incidence and severity of slowed thinking and thus the symptom transmission between symptom groups.

Implications for nursing practice and research

This study revealed differences between the most prevalent or severe symptom (affective fatigue dimension) and the core symptom (physical fatigue dimension). Reluctance, a heavy and tired body, and tiring easily composed the central symptom cluster, which was positively correlated with other symptoms. Our findings may help clinical nurses comprehensively understand the inter-relationships among fatigue symptoms in patients with advanced cancer. Furthermore, our findings provide a reminder that clinical nurses, while focusing on overt emotional fatigue symptoms, should also pay attention to underlying physical fatigue symptoms. Future interventions targeting the central symptom cluster could be implemented to assess efficacy in alleviating other symptoms and patient burden.

Limitations

This study has several limitations. First, the cross-sectional design allowed us to explore correlations among symptoms but did not identify the temporal dynamics of symptom relationships. Second, participants in our study were recruited from a tertiary hospital that admits patients nationwide. The variety in cancer types and therapy methods suggests that this study may possess a degree of representativeness of the broader population of advanced cancer patients. However, the predominance of gastrointestinal and lung cancers, along with the prevalent use of chemotherapy, may render the findings of this study more representative of the clinical characteristics associated with these patient populations. Besides, differences across distinct clinical contexts might exist, such as discrepancies in the cancer disease spectrum may thus limiting the ability our findings to be extended to other clinical settings. Finally, the limitations related to sample sizes for each subgroup must be considered in interpreting the results. The estimate method might have influenced the visualization of the networks for small sample sizes, thus generating networks overfitted to the data and affecting the stability of the centrality indexes. Subsequent studies, such as multicenter studies, should be conducted to validate the findings of our study across a broader range of settings. Furthermore, longitudinal symptom networks could be further used to explore causal relationships between symptoms, and randomized controlled trials targeting core symptoms could provide stronger verification of the credibility of the results of this study.

Conclusions

This study contributed novel insights regarding fatigue symptoms in patients with advanced cancer by performing network analysis. Three symptoms—reluctance, a heavy and tired body, and tiring easily—had a central role in the fatigue symptoms experienced by patients with advanced cancer. These findings have major implications that may help clinical nurses develop targeted interventions enhancing patients' quality of life.

Ethics statement

This study was approved by Ethics Committee of Beijing Hospital (IRB No. 2021BJYYEC-325-01). All participants provided written informed consent.

CRediT authorship contribution statement

Huixiu Hu: Conceptualization, Methodology, Data curation, Software, Visualization, Writing – Original draft preparation. **Yajie Zhao:** Conceptualization, Methodology, Data curation, Software, Visualization, Writing-Original draft preparation. **Huanhuan Luo**: Methodology, Data curation, Software, Visualization, Writing – Original draft preparation. **Yuqing Hao**: Software, Writing – Original draft preparation. **Pei Wang:** Investigation, Supervision, Writing – Reviewing and Editing. **Lijuan Yu**: Investigation, Writing – Reviewing and Editing. **Chao Sun:** Supervision, Writing – Reviewing and Editing. 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.

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Declaration of competing interest

All authors declare no conflicts of interest. Professor Chao Sun, the corresponding author, serves on the editorial board of the *Asia-Pacific Journal of Oncology Nursing*. The article underwent standard review procedures of the journal, with peer review conducted independently of Professor Sun and their research groups.

Data availability statement

The data that support the findings of this study are available from the corresponding author, SC, 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.2024.100641.

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