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Original Article

Symptom cluster study undergoing chemotherapy in breast cancer patients: Latent class analysis and contemporaneous network analysis

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ABSTRACT

Objective: This study aims to explore the subgroups and networks of symptom clusters in breast cancer patients undergoing chemotherapy, and to provide effective interventions for the core symptoms.
Methods: A cross-sectional survey was conducted at four comprehensive hospitals in Foshan City, China, from August to November 2023. A total of 292 participants completed the social determinants of health questionnaire, the numerical rating scale (NRS), the Pittsburgh sleep quality index (PSQI), the Chinese version of the cancer fatigue scale (CFS), and the hospital anxiety and depression Scale (HADS). Latent class analysis (LCA) was utilized to distinguish subgroups, and network analysis was utilized to identify core symptoms among different subgroups.
Results: Breast cancer patients undergoing chemotherapy exhibit symptoms were divided into two subgroups: the high burden group of symptoms (72.3%, Class 1) and the low burden group of symptoms (27.7%, Class 2). Education attainment, work status, family monthly income per capita, and daily sleep duration (hours) were associated with subgroup membership. "Panic feelings" (# HADS-A11) were the core symptom in both the full sample and Class 2, while "tension or pain" (# HADS-A1) was the core symptom in Class 1.
Conclusions: The core symptoms of fear, enjoyment, nervousness, and pain varied across subgroups of patients and could inform the current strategies for symptom management in breast cancer chemotherapy patients.

Introduction

According to the latest global cancer data,[1] there are approximately 2.3 million new cases of breast cancer worldwide, ranking it as the second most common cancer globally, the disease claims about 670,000 lives each year. In China, breast cancer ranks as the second most prevalent cancer among women and poses a significant threat to their health.[1] The diagnosis and treatment of breast cancer often lead to a series of physical and psychological symptoms,[2] with the most common symptom cluster among breast cancer patients consisting of pain, fatigue, anxiety, depression, and sleep disorders,[3–5] with an occurrence rate exceeding 40%, particularly during the chemotherapy period.[6,7] These symptoms may exhibit synergistic and reinforcing effects, cyclic recurrence, and remain stable or reappear during the treatment process. Some symptoms also exhibit cumulative effects as treatment progresses.[8] They can have a multiplicative negative impact on patients' quality of life and functional status, leading to treatment delays or discontinuations, increased medical costs, and decreased overall well-being.[9] Therefore, effective management of symptoms during the chemotherapy period is crucial for breast cancer patients. Successful symptom management relies on understanding the distinct characteristics of symptom presentation in different patients, accurate identification and targeted interventions.

Currently, research on breast cancer symptom clusters primarily relies on measuring overall symptom burden using total scores on scales. However, due to individual differences in experiences and characteristics, it is possible for individuals to have high scores on a few specific symptoms while having a lower overall symptom level. This can mask the specificity of certain symptoms and overlook individual differences.[10–13] The Symposium on Symptom Science in the United States pointed out that due to the individual variability in symptoms, distinguishing heterogeneous symptom subgroups based on individual variations in symptom expression may be the key to effective symptom management.[14] LCA is a person-centered statistical method that provides a new approach to gain a deeper understanding of the symptom characteristics of different patients. It can visually demonstrate response patterns within the study population and heterogeneity between groups, enabling the Classification of patient subgroups based on different symptom profiles.[15]

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In addition, most studies on symptoms focus on symptom clusters composed of one or more independent symptoms.[16,17] However, many researchers have pointed out that symptoms are not independent of each other but rather interrelated and mutually influential.[18] The Symposium on Symptom Science in the United States also emphasized the need for innovative techniques and strategies to classify these symptoms and explore their underlying causes.[14] Symptom network refers to a method that explores the interactions and associations among different symptoms by studying their co-linearity, correlations, and levels of influence in specific diseases or disease states and presents them in a graphical manner. Symptom networks can help us understand the complexity of diseases and the interactions between symptoms. By identifying important symptom nodes based on network centrality indices, they provide guidance for the diagnosis, treatment, and management of diseases. Research has shown that interventions targeting important symptom nodes in the core symptoms not only have a greater impact on the network but also facilitate improvements in other symptoms associated with them.[4,14] Such an approach, focusing on managing core symptom nodes, is more beneficial for symptom relief compared to interventions targeting non-central symptom nodes. This management approach improves symptom management efficiency, optimizes the intervention process, and enables more effective symptom management.

Therefore, this study focuses on the core symptom cluster (pain, fatigue, anxiety, depression, sleep disorders) experienced by breast cancer patients during chemotherapy. By using LCA, it explores different symptom patterns or subgroups that arise from individual differences during breast cancer chemotherapy and identifies social determinants of health (SDOH) data, such as sociodemographic or disease characteristics, among the subgroups. Building upon LCA, the study identifies important symptom nodes within different subgroups and reveals the complex interactions and relationships between symptom nodes using symptom networks. By combining these two methods, it enables personalized and precise identification of symptoms experienced by breast cancer patients during chemotherapy, thereby promoting patient-centered precision care and efficient symptom management.

Methods

Study design and participants

This is a cross-sectional study that uses convenience sampling to choose breast cancer patients who undergoing chemotherapy in the hospital during breast surgery at four tertiary hospitals in Foshan City, Guangdong Province, China, from August to November 2023. The participants need to meet criteria such as being female, being older than 18 years old when diagnosed with breast cancer, currently undergoing chemotherapy, having clear awareness, having no difficulties in communication, and being willing to provide written informed consent.

Research instruments

Social determinants of health questionnaire

Data from the participants were collected using the social determinants of health questionnaire, which included information such as age, body mass index (BMI), residence place, education attainment, marital status, work status, and monthly family income per capita. Clinical information, including the Charlson comorbidity index (CCI),[19] months since cancer diagnosis, stage of breast cancer, lymph node metastasis, surgical method, chemotherapy cycles and daily sleep duration, was obtained from medical records.

Patient self-reported symptoms

The intensity of discomfort was gauged using the numerical rating scale (NRS),[20] which assigns a value between 0 and 10. A higher value signifies a greater degree of pain, with 0 representing no pain, 1–3 mild pain, 4–6 moderate pain, and 7–10 severe pain. The Pittsburgh sleep quality index (PSQI), developed by Buysse,[21] assessed subjective sleep quality, measuring seven aspects, including sleep duration and efficiency. The sleep quality of breast cancer patients was evaluated using a subjective scale with a single entry and a 3-point grading system, where one represents good sleep quality, two average, and three poor. The Chinese version of the cancer fatigue scale (CFS), based on the research of Zhang et al.,[22] is primarily used to assess fatigue symptoms in cancer patients. It comprises 15 items divided into three categories: physical exhaustion, emotional fatigue, and cognitive weariness. The scale was evaluated using a Likert 5-point scale, ranging from 0 to 4, where 0 indicates no fatigue, and 4 indicates extreme fatigue. The scale ranges from 0 to 60, with a clinical fatigue threshold for CFS set at scores above 18. As the score rises, so does the patient's level of fatigue. The Hospital Anxiety and Depression Scale (HADS), established in 1983 by Zigmond and Snaith,[23] consists of two separate scales for assessing anxiety and depression. Each scale contains 14 items, seven evaluating anxiety (A) and seven evaluating depression (D). Each item is scored on a scale of 0–3. A score of 8 signifies the absence of symptoms, while scores between 8 and 10 suggest the presence of anxiety or severe depression. Higher scores on the scale indicate a higher probability of experiencing anxiety or depression.

Data collection

The research received formal sanction from the ethics committee of the People's Hospital situated in the Nanhai District of Foshan City (IRB No. 2023280). Data collection was conducted by a trained nursing researcher. This researcher independently completed the data collection in the four hospitals, and the study participants were referred by physicians. The study participants were referred by physicians and enrolled in this study during their hospitalization in four hospitals. Researchers obtained written informed consent from the participants, which included information on the purpose, significance, benefits and risks of the study. Participants were also informed of their right to withdraw from the study at any time. If there are any missing or incomplete data entries, researchers promptly inform the study participants to provide the necessary supplements. In case of any unclear items, researchers should explain them from an objective standpoint, ensuring that participants have a full understanding and cooperate with the study.

Data analysis

Statistical analyses were conducted using SPSS Statistics 26.0, Mplus 8.0, and R 4.3.2. Descriptive statistics examined the social determinants of health, clinical factors, and patient-reported symptoms. Categorical variables were depicted using frequencies and percentages, while continuous variables were expressed as mean ± standard deviation. The evaluation of LCA[2] involved the use of indicators such as Akaike information criterion (AIC), Bayesian information criterion (BIC), and adjusted BIC (aBIC). Lower values for these criteria indicate a superior fit for the model. The likelihood ratio test (Lo-Mendell-Rubin, LMR) and the bootstrap-based likelihood ratio test (BLRT) were used to evaluate differences in model fitting. A statistically significant value of $P < 0.05$ implies that a model with k categories is preferable to a model with k–1 categories. Entropy values are used to assess the accuracy of model categorization. A value nearing 1 denotes higher classification accuracy, with values exceeding 0.8, indicating accuracy above 90%.[15] Finally, by assessing the fitting indicators of models in each category, we determine the most optimal category model and assign it a name.[24] Once the suitable latent category has been identified, we utilize the χ^2 test and Fisher exact tests to evaluate and compare the differences among various categories. The binary logistic regression model includes significant variables, and all statistical tests have a significance criterion of $P < 0.05$.[15] We utilized R4.3.2. Version to carry out network analysis. The Fruchterman-Reingold force-directed layout was employed to position nodes

with the strongest correlations at the center of the network.[25] The symptomatic network of this study represents symptoms as nodes and independent conditional linkages between the nodes as edges. The thickness of the edges indicates the strength of the association. Additionally, the study employed two primary variables (strength and closeness) to identify core symptoms under numerous potential groups. Strength is determined by calculating the absolute weight of the correlation coefficient between a node and all other nodes, and then adding these values. It is an indicator of the importance of a node within a network. The more intense the strength, the greater the importance of the symptom and its potential influence on other symptoms. Proximity calculates the average distance between a single node and all others.[26] The symptoms were more central when there was a higher strength and closeness.[26]

Results

We distributed 314 questionnaires, excluding 22 invalid questionnaires owing to missing entries and obtained 292 valid questionnaires, with a questionnaire response rate of 93.0%.

Characteristics of the sample

All participants in the study were female, with ages ranging from 26 to 81 years and an average age of approximately 52.32 ± 11.07 years. The majority of the participants had *n* normal BMI index (54.8%) and lived in either urban (50.0%) or rural areas (50.0%). Most of the participants had an education attainment of secondary school or below (71.2%), were married (94.5%), were sick leave (69.9%), had one or two children (80.1%), and had a monthly family income of less than 5000 yuan (84.2%). The disease characteristic data includes those who have a Charlson comorbidity index of CCI ≥ 3 points (72.3%); an illness duration of fewer than six months (45.9%); disease staging at stage II (46.9%); occurrence of lymph node metastasis (49.3%); underwent breast-conserving surgery (68.5%); received chemotherapy four or more times (77.7%); and daily sleep duration six to seven hours (49.7%).

Latent class analysis

This study proposes five potential category models. Table 1 demonstrates that category three has the highest entropy value, while category two also has an entropy value above 0.9, suggesting that category two also exhibits a significant level of accuracy. The statistical indicators AIC, BIC, and aBIC reach their minimum values in category 2, indicating the effectiveness of this model in representing the data. When only two categories are considered, the LMRT and BLRT values are statistically significant ($P < 0.001$), thus validating that the two-category model is optimal.

According to the probability distribution chart shown in Fig. 1, it is evident that the intensity of two possible sub-symptoms in breast cancer chemotherapy patients differs All symptoms are significantly heightened within the High Symptom Burden group (Class 1), accounting for 210 cases (72.3%). Conversely, in the Low Symptom Burden group (Class 2), the severity of symptoms in these patients is comparatively lower, with 82 cases (27.7%). Both categories displayed the highest degree of fatigue symptoms, a comparatively lower response rate regarding sleep quality, and a minimum distinction between the two groupings. The primary distinction between the two groups is predominantly evident in psychological symptoms, especially in symptoms related to anxiety and depression.

Table 1
Comparison of latent class models' goodness of fit.

Model	AIC	BIC	aBIC	Entropy	LMR *P* value	BLRT *P* value	Latent class probability
1	1569.47	1587.85	1571.99	–	–	–	1
2	1431.04	1471.49	1436.61	0.97	< 0.001	< 0.001	0.72/0.28
3	1431.78	1494.29	1440.37	0.95	0.069	0.061	0.09/0.19/0.72
4	1440.55	1525.11	1452.17	0.78	0.256	0.667	0.19/0.09/0.52/0.20
5	1451.35	1557.98	1466.01	0.75	0.459	1	0.50/0.22/0.01/0.07/0.21

aBIC, Adjusted Bayesian information criterion; AIC, Akaike information criterion; BIC, Bayesian information criterion; BLRT, Bootstrap likelihood ratio test; LMRT, Lo–Mendell–Rubin likelihood ratio test.

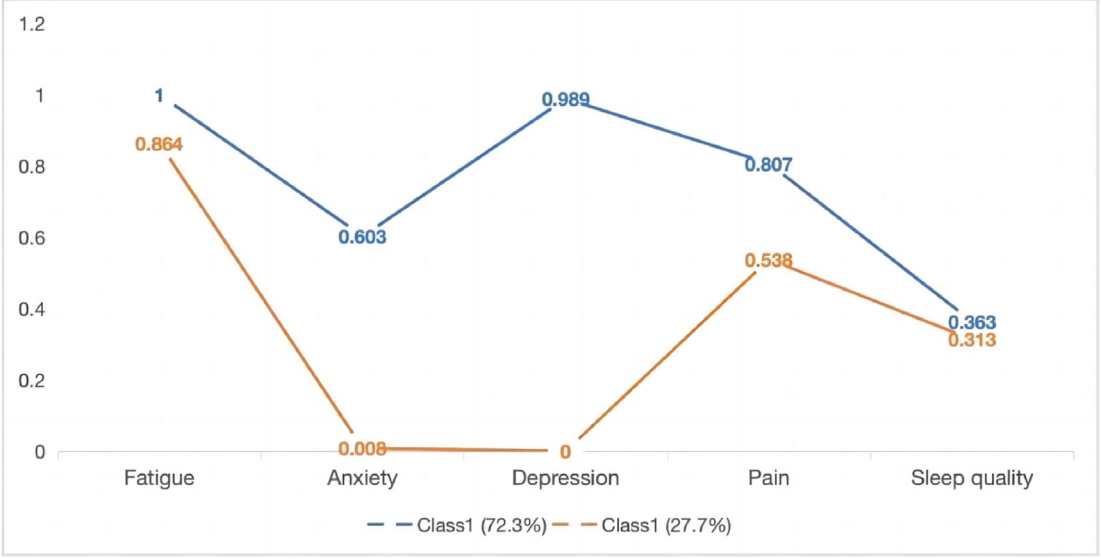

Fig. 1. Distribution of severity of symptoms in two potential subgroups.

The social determinants of health factors across latent classes

A univariate analysis was conducted, revealing two distinct subgroups that demonstrated significant statistical differences ($P < 0.05$) in several areas, including education attainment, work status, family monthly income per capita, surgical methods, and daily sleep duration (hours). The binary logistic regression analysis incorporated the significant variables identified in the univariate analysis as independent variables, with the two subgroups acting as dependent variables. The "Symptom Low Burden Group" (Class 2) was used as the reference for comparison. The results, presented in Table 2, and Fig. 2, demonstrate that both employed (OR = 4.73, $P = 0.009$) and sick leave (OR = 5.87, $P = 0.001$) patients had a higher probability of being categorized as Class 1. Conversely, individuals with an education level of secondary school (OR = 0.38, $P = 0.028$), post-secondary (OR = 0.14, $P < 0.001$), university or above (OR = 0.28, $P = 0.028$), and an income exceeding 8000 (OR = 0.14, $P = 0.030$) have a higher probability of being classified as Class 2.

Symptom network analysis plot and centrality indices

Symptom network plot

Fig. 3 presents a network model that depicts the relationships among symptoms in the full sample of patients undergoing chemotherapy for breast cancer, as well as in two distinct subgroups. The graphic illustrates positive correlations using solid lines and negative correlations using dotted lines. Within the symptom network, the strength of the connection between nodes is directly related to the numerical value of the connection weight. A more substantial link indicates a stronger correlation between the two nodes. Upon analysis, it is evident that symptoms exhibit a tight clustering pattern within the network, apart from pain and sleep, which seem to be situated on the outskirts of this symptom network.

Symptom network centrality indices

Fig. 4 displays the strength index (rs) and closeness (rc) of every symptom node across the full sample and two subgroups. Within the full sample network, "I immediately experienced a feeling of terror" (#HADS-A11, rs = 18.34) emerges with the highest strength, whereas the symptom that shows the greatest proximity is "My heart is full of troubles" (#HADS-A5, rc = 0.02). The "I feel nervous or in pain" symptom (#HADS-A1) has the maximum strength and closeness in the high symptom burden group, with a correlation coefficient of 16.78 (rs) and a correlation coefficient of 0.02 (rc). In the low symptom burden group, the maximum strength is "I suddenly found a sense of panic" (#HADS-A11, rs = 15.88), and the maximum closeness is " feel very pleased" (#HADS-D6, rc = 0.01).

Comparison of symptom networks between two subgroups

The study revealed significant distinctions in the global strength index between two subgroups ($P = 0.04$). The Class 1 group scored 14.29, while the Class 2 group scored 12.75. This indicates that the symptom load in the Class 1 group is significantly higher than that in the Class 2 group.

Table 2
Differences in sample characteristics among the latent classes.

Variables	Class 1 (n=211)	Class 2 (n=81)	F-value	P-value
Age (years)			4.46	0.107
20–39	26 (12.3)	15 (18.5)		
40–59	126 (59.7)	52 (64.2)		
≥ 60	59 (28.0)	14 (17.3)		
Body mass index (kg/m^2)			7.73	0.02
≤ 18.5	9 (4.3)	6 (7.4)		
18.5–23.9	126 (59.7)	34 (42.0)		
> 23.9	76 (36.0)	41 (50.6)		
Residence place			1.38	0.24
Urban area	110 (52.1)	36 (44.4)		
Rural area	101 (47.9)	45 (55.6)		
Education attainment			12.15	0.01
Primary school or below	90 (42.7)	22 (27.2)		
Secondary school	72 (34.1)	24 (29.6)		
Post-secondary	28 (13.3)	20 (24.7)		
University or above	21 (10.0)	15 (18.5)		
Marital status			3.09	0.08
Single	8 (3.8)	8 (9.9)		
Married	203 (96.2)	73 (90.1)		
Childbearing history			1.09	0.59
None	8 (3.8)	5 (6.2)		
One or two child	169 (80.1)	65 (80.2)		
Three or more children	34 (16.1)	11 (13.6)		
Occupation			19.12	< 0.001
Retired	14 (6.6)	16 (19.8)		
Employed	35 (16.6)	23 (28.4)		
Sick leave	162 (76.8)	42 (51.9)		
Family monthly income per capita (RMB)			20.96	< 0.001
< 2000	99 (46.9)	29 (35.8)		
2000–5000	90 (42.7)	28 (34.6)		
5000–8000	20 (9.5)	14 (17.3)		
> 8000	2 (0.9)	10 (12.3)		
Comorbidities			3.64	0.06
1–2	52 (24.6)	29 (35.8)		
≥ 3	159 (75.4)	52 (64.2)		
Months since cancer diagnosis			1.66	0.44
≤ 6	93 (44.1)	41 (50.6)		
6–12	53 (25.1)	21 (25.9)		
> 12	65 (30.8)	19 (23.5)		
Stage of breast cancer			1.10	0.78
I	54 (25.6)	18 (22.2)		
II	95 (45.0)	42 (51.9)		
III	38 (18.0)	13 (16.0)		
IV	24 (11.4)	8 (9.9)		
Lymph node metastasis			1.06	0.30
Yes	108 (51.2)	36 (44.4)		
No	103 (48.8)	45 (55.6)		
Surgical method			10.63	0.01
None	37 (17.5)	19 (23.5)		
Breast-conserving	155 (73.5)	45 (55.6)		
Radical mastectomy	19 (9.0)	17 (21.0)		
Cycles of chemotherapy			4.19	0.24
First chemotherapy cycle	7 (3.3)	7 (8.6)		
Second chemotherapy cycle	21 (10.0)	5 (6.2)		
Third chemotherapy cycle	18 (8.5)	7 (8.6)		
Fourth chemotherapy cycle or above	165 (78.2)	62 (76.5)		
Daily sleep duration (hours)			28.54	< 0.001
< 6	82 (38.9)	17 (21.0)		
6–7	109 (51.7)	36 (44.4)		
≥ 7	20 (9.5)	28 (34.6)		

Discussion

Subgroups of symptoms

Upon examining PROs the analysis resulted in two unique subgroups. The majority, accounting for around 72.3% of participants, is classified as the "High Symptom Burden Group." The remaining 27.7% of individuals are categorized as the "Low Symptom Burden Group." The conclusion drawn from the LCA and symptom network analysis indicates that patients in the High Symptom Burden Group experience much more severe symptoms than those in the Low Symptom Burden Group.

In both categories, the occurrence rate of fatigue is relatively high, implying that it may be a key factor affecting the quality of life for patients undergoing chemotherapy for breast cancer. This observation aligns with previous research, underscoring that fatigue is not just a concern unique to breast cancer treatment but a significant challenge for all cancer patients.[27] Numerous studies suggest that cancer-related fatigue is more severe, lasts longer, and is associated with more significant physical impairment compared to the "usual" tiredness caused by lack of sleep or overexertion.[28–30] It cannot be relieved by sufficient sleep or rest. An extensive study on fatigue among breast cancer survivors has revealed that fatigue is the most distressing and prevalent symptom they

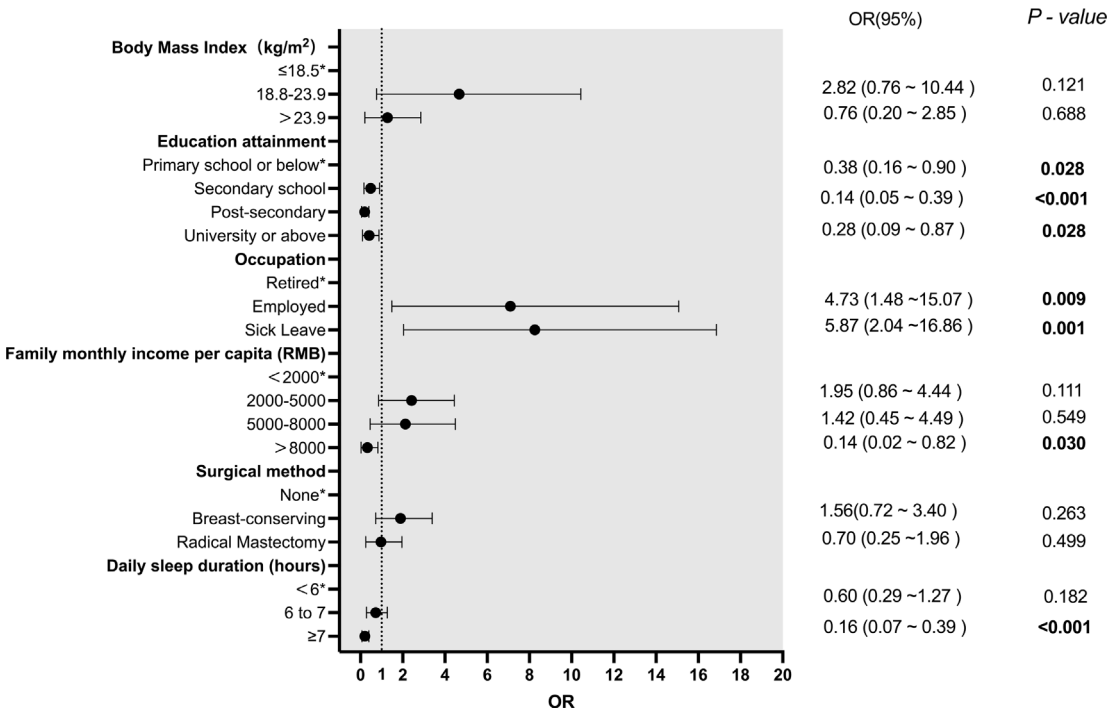

Fig. 2. Potential predictors of latent class membership. 95%CI, 95% confidence interval of OR; OR, odds ratio.

experience.[11] The heightened intensity of fatigue in women undergoing chemotherapy for breast cancer is closely linked to the negative effects of the treatment.[19] Despite their sleep quality, both groups show relatively mild levels of various symptoms with minor differences. The root of this issue could be the adverse reactions during chemotherapy, leading to a widespread issue of poor sleep quality among patients in these two groups. Certain studies also suggest a strong correlation between sleep quality and symptoms like fatigue, muscle weakness, and other physical symptoms.[2]

This study reveals significant disparities in psychological symptoms across two subgroups. The group characterized by a high symptom burden demonstrates the most severe of depression and anxiety. Hu et al.[31] conducted a subgroup analysis of the symptoms of individuals with advanced cancer stages. The findings indicate that patients in the subgroup exhibiting the most severe symptoms demonstrate moderate levels of anxiety and depression. In contrast, individuals in the moderate and mild symptom groups exhibit typical psychological symptoms. These findings suggest that various factors, including disease progression, treatment methods, and sociodemographic characteristics, influence how individuals perceive psychological symptoms.[32]

Factors affecting the low burden group of symptoms

Patients who have at least a high school education are more likely to be classified as Class 2. This study has found that breast cancer patients with higher educational attainment have a relatively lower likelihood of experiencing anxiety or depression. On the other hand, individuals with lower levels of education are more prone to feelings of worry and sadness due to their limited understanding of the disease, this is in line with the results of the TSARAS study.[32] Cancer is a formidable disease for most people. Individuals with higher education levels could learn about the disease through various means. Individuals with a deeper understanding of the disease and a clearer awareness of the prognosis of breast cancer treatment can adopt a rational approach to face the various challenges that cancer may pose. They can effectively manage and adapt their emotional health, thereby reducing the chances of experiencing depression and anxiety. Patients with salaries exceeding 8000 yuan are more likely to be classified as Class 2. This study suggests that breast cancer patients who bear a significant financial burden and undergo chemotherapy are more likely to exhibit symptoms of anxiety or depression. These findings are consistent with previous research.[33] Medical expenses present a continuous challenge throughout the entire treatment period, from the diagnosis stage of breast cancer to the successive series of adjuvant therapy measures. This is an inevitable reality for every cancer patient and their families. Furthermore, several expensive medications are not covered by medical insurance, leading to increased psychological stress for financially challenged patients and a higher likelihood of experiencing anxiety or depression.

Factors affecting the high burden group of symptoms

Whether employed or not, people are more likely to fall into Class 1. Prior research has indicated[34] that cancer treatment could lead to changes in body image, causing concerns such as hair loss. This can negatively impact patients' self-esteem and confidence, adversely affecting their social behavior and increasing psychological stress at work. Sick leave breast cancer patients undergoing chemotherapy who stay at home every day may experience strong feelings of loneliness and helplessness, which can negatively affect their mental health. Furthermore, the lack of a stable job can put individuals under financial stress, thereby exacerbating their levels of anxiety and depression. In addition to the physical discomfort and worry about the disease, this can increase the psychological burden.

Centrality of symptom networks

This research underscores the significant role of anxiety and depression in the symptom network related to cancer, both in terms of severity and closeness. Hence, anxiety and melancholy are the main symptoms associated with cancer in individuals receiving chemotherapy for breast cancer. Earlier research[35] has also shown that young and middle-aged

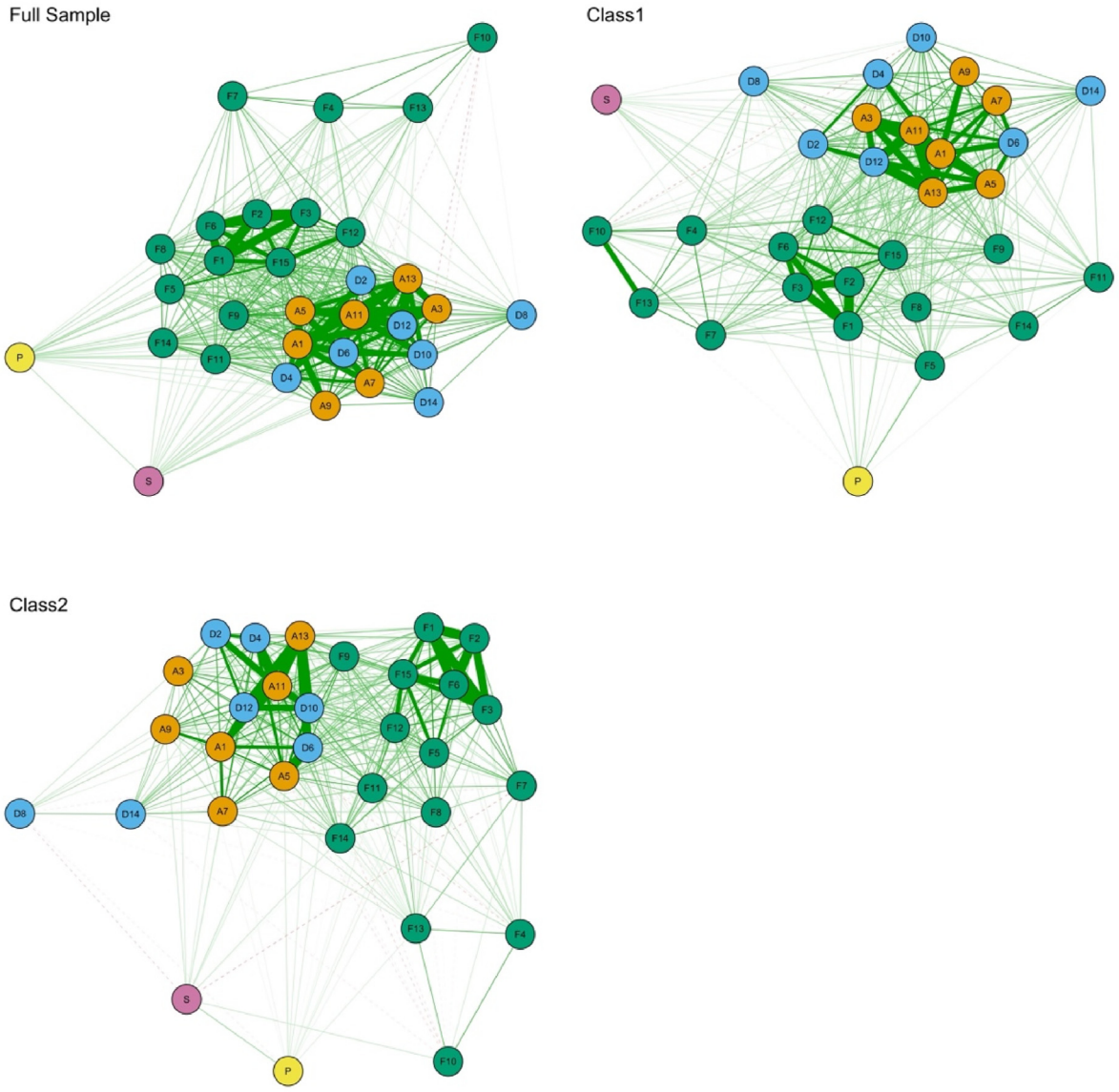

Fig. 3. Symptom networks in the full sample and two latent classes.

breast cancer patients commonly experience anxiety, sadness, fatigue, and pain interference as their primary symptoms during chemotherapy. Moreover, there is a strong interrelation among these critical symptoms. In the symptom network analyzed in this study, the link between anxiety and other symptoms (especially depression) is very close, indicating a strong correlation and mutual influence between anxiety and depression symptoms. However, the findings of the study conducted by Rha SY[8] differ from those of this research. The study focused on a group of 209 cancer survivors undergoing chemotherapy, with fatigue being their main symptom. As the chemotherapy cycles progress, particularly after the fourth cycle, the intensity of fatigue decreases. This could be due to different patient cohorts, as breast cancer mainly affects a specific demographic characterized by women, making it more difficult for them to accept changes in feminine characteristics. Earlier research has also suggested that individuals diagnosed with cancer often face a variety of psychological issues, including anxiety and despair, which present challenges for effective management. For cancer patients, it is essential to prioritize the reduction of psychological distress and discomfort as a critical part of symptom management. The onset of mental disorders may be associated with medical interventions, financial stress, and concerns about the future.[36] Previous studies have demonstrated that the implementation of mindfulness therapies can effectively alleviate symptoms of anxiety and sadness.[37–39] Integrating mindfulness intervention strategies and exploring more beneficial approaches in future medical practices is recommended to enhance patients' physical and mental health. This approach can help reduce the spread of cancer-related symptoms online, reducing the overall symptom burden.

This study identifies "I suddenly feel panic," "My heart is full of troubles" and "I feel pleased" as the most significant symptoms among the overall sample and the Class 2 group, respectively. There is a potent and direct connection between these two symptoms and other symptoms in the network, suggesting that the activation of these symptoms is likely to spread throughout the network through their links with other symptoms. Panic is a unique emotional expression associated with anxiety symptoms, indicating that cancer patients must endure physical discomfort during treatment and be alert to the panic symptoms stemming from the uncertainty of the disease. They often face difficulties in understanding and managing these emotions. A network analysis study investigating anxiety and depression in individuals with HIV infection found that "sudden feelings of fear" are also considered one of the core symptoms within the cluster of anxiety symptoms.[40] Within the cluster of depression symptoms, the symptom of "difficulty experiencing pleasure"

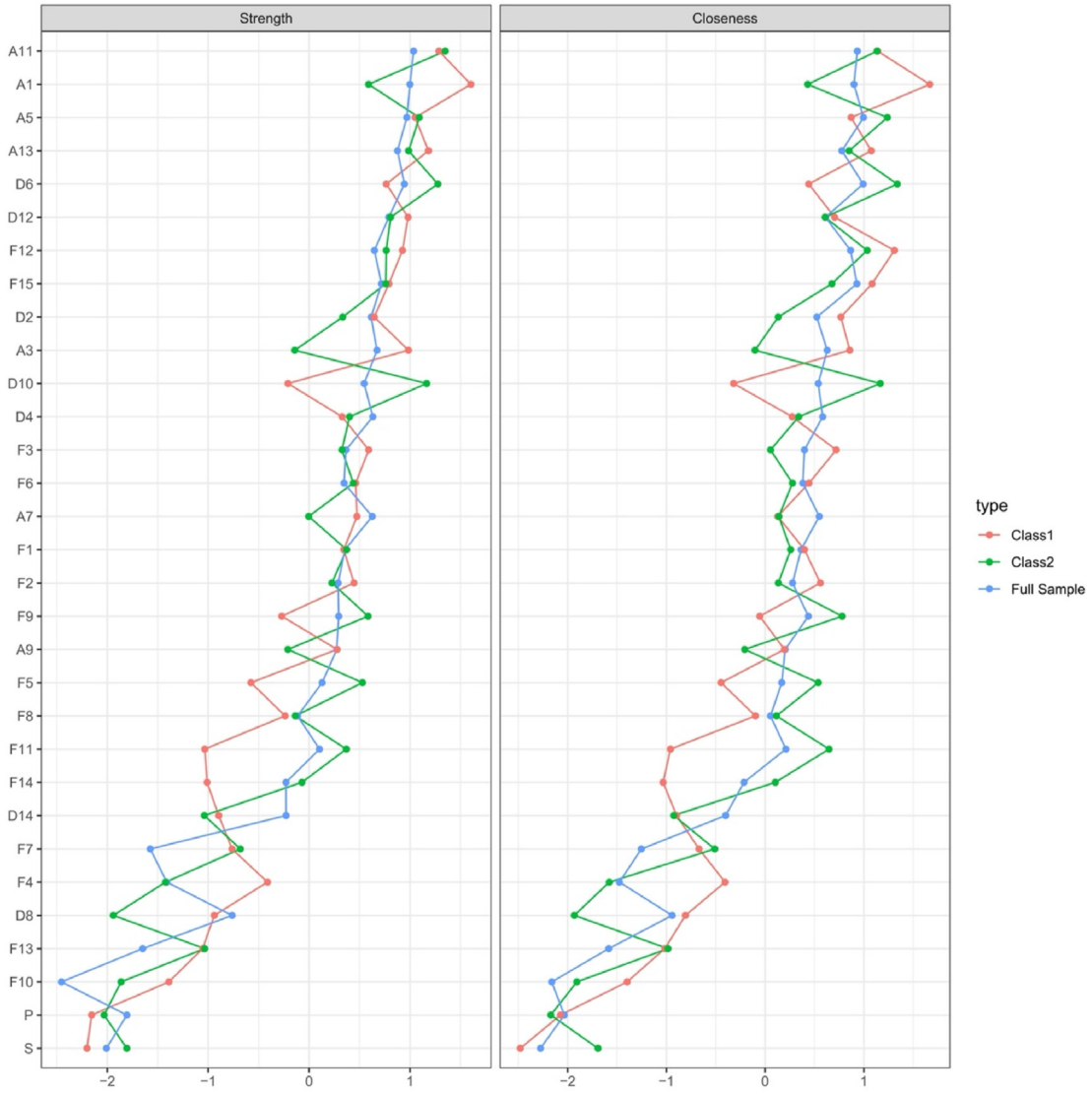

Fig. 4. Centrality indices of the full sample and the two subgroups.

is recognized as a connecting symptom that is likely to have a greater impact, consistent with the findings of this study. Indeed, when faced with the unpredictability caused by the disease, patients typically have a dominant psychological response characterized by fear and panic. They have concerns about their future and the potential impact of the disease on their daily lives. At the same time, the fear and panic response to the disease is linked to a variety of psychological problems, especially anxiety.[41,42] Regarding the symptom 'I suddenly feel panic' in (# HADS-A11), therapies aimed at addressing this symptom have shown more effectiveness in alleviating patients' anxiety and depressive symptoms compared to interventions targeting other symptoms. This suggests that clinical healthcare providers should enhance their connection with patients, meet their need for disease-related knowledge, and alleviate their fear of unfamiliar situations.

In the Class 1 group, the primary symptom identified is "feeling nervous or distressed." This finding aligns with the work of Akash and his team,[32] who also found that emotional tension is a crucial symptom common to both anxiety and depression, significantly affecting patients' overall well-being. However, this study contrasts with the work of Ye et al.[43] who argue that melancholy is the core symptom in the symptom network of cancer patients. The difference in findings could be due to the use of different symptom evaluation tools in the two studies. The diagnosis of breast cancer is a significant source of stress for patients, often accompanied by chemotherapy. While chemotherapy can effectively eliminate tumor cells, it can also cause a range of physiological discomforts, including nausea, vomiting, reduced appetite, hair loss, and peripheral neuropathy. In addition, the removal of the breast, a significant symbol for women, dramatically affects patients' physiological processes, self-perception, evaluation, and social interaction. Moreover, managing personal, family, and job responsibilities while undergoing treatment is a critical concern that could potentially trigger feelings of "strain" and "distress" in patients. In this study, half of the patients come from rural areas, and due to their families' unfavorable economic conditions, they bear a significant disease burden. More than 80% of the patients have a relatively low cultural level, suggesting a lack of understanding and awareness of the disease in this group, thereby intensifying their worry. Research indicates that individuals' emotional expression may be influenced by their personal knowledge of their own circumstances. Lack of information during treatment may cause patients to experience anxiety, intensifying their distress. Multiple negative emotions can mutually reinforce and persist. Furthermore, various studies[3,5] suggest that anxiety emotions, such as tension and suffering, can interfere with the sympathetic nervous system and the hypothalamic–pituitary–adrenal axis. This interference triggers the production of pro-inflammatory cytokines, which exacerbate the patients' physical discomfort and, to some extent, hinder the treatment and recovery of the

disease. Therefore, when administering chemotherapy to patients, it is crucial to properly and effectively assess their psychological state. While improving physical discomfort symptoms, it is also essential to prioritize their feelings of tension and distress. One might analyze the symptoms to identify the underlying causes of the patient's tension. Provide targeted psychological treatment to alleviate the patient's anxiety symptoms, taking into account their condition and psychological characteristics.

Limitations

Firstly, due to the cross-sectional design, causal relationships between symptoms cannot be determined. For instance, it remains unclear whether the central node triggers other nodes, if other nodes trigger the central node, or if both scenarios coexist. Therefore, conducting more in-depth longitudinal studies is essential to gain a deeper understanding of the trajectory of symptom changes in breast cancer patients undergoing chemotherapy and to uncover causal relationships. Furthermore, the recruitment of participants from four medical institutions limits the generalizability of our findings. Thus, it is necessary to conduct similar studies in multiple research institutions to enhance the external validity of the research results. Lastly, the data-driven nature of network analysis methods may impose limitations on the generalizability of our findings. Therefore, further empirical research is warranted before applying our results to other populations.

Conclusions

This research employed latent class analysis and network analysis methodologies to explore a variety of symptoms that breast cancer patients might experience during chemotherapy. The study underscores the necessity of developing tailored intervention approaches that consider each patient's unique experiences. Factors such as Education attainment, work status, family monthly income per capita, and daily sleep duration (hours) significantly contribute to the diversity among breast cancer patients. By focusing on improving primary symptoms like fear, joy, stress, and pain in different patient subgroups, we can gain valuable insights to enhance symptom management strategies for patients undergoing chemotherapy for breast cancer. This can serve as a valuable reference for the ongoing optimization of symptom management strategies for these patients.

Ethics statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Medical Ethics Committee of Nanhai People's Hospital (IRB No. 2023280). Informed consent was obtained from all subjects involved in the study.

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CRediT authorship contribution statement

Guangting Chang: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft preparation; **Xiaoyuan Lin**: Conceptualization, Methodology, Data curation, Software, Validation, Writing – review & editing; **Meijiao Qin**: Formal analysis, Data curation, Visualization; **Lixia Wang**: Visualization, Validation; **Shu Cai**: Methodology, Project administration, Supervision. 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 that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability statement

The datasets presented in this article are not readily available because the datasets involve unfinished research projects. If necessary, requests to access the datasets should contact the corresponding author.

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

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

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74(3):229–263.
2. Fox RS, Ancoli-Israel S, Roesch SC, et al. Sleep disturbance and cancer-related fatigue symptom cluster in breast cancer patients undergoing chemotherapy. *Support Care Cancer*. 2020;28(2):845–855.
3. Ho SY, Rohan KJ, Parent J, Tager FA, McKinley PS. A longitudinal study of depression, fatigue, and sleep disturbances as a symptom cluster in women with breast cancer. *J Pain Symptom Manag*. 2015;49(4):707–715.
4. Browall M, Brandberg Y, Nasic S, et al. A prospective exploration of symptom burden clusters in women with breast cancer during chemotherapy treatment. *Support Care Cancer*. 2017;25(5):1423–1429.
5. Doong SH, Dhruva A, Dunn LB, et al. Associations between cytokine genes and a symptom cluster of pain, fatigue, sleep disturbance, and depression in patients prior to breast cancer surgery. *Biol Res Nurs*. 2015;17(3):237–247.
6. Han CJ, Reding K, Cooper BA, et al. Symptom clusters in patients with gastrointestinal cancers using different dimensions of the symptom experience. *J Pain Symptom Manag*. 2019;58(2):224–234.
7. Lim CC, Devi MK, Ang E. Anxiety in women with breast cancer undergoing treatment: a systematic review. *Int J Evid Base Healthc*. 2011;9(3):215–235.
8. Rha SY, Lee J. Stable symptom clusters and evolving symptom networks in relation to chemotherapy cycles. *J Pain Symptom Manag*. 2021;61(3):544–554.
9. Gapstur RL. Symptom burden: a concept analysis and implications for oncology nurses. *Oncol Nurs Forum*. 2007;34(3):673–680.
10. Snyder S, Kroll JL, Chen AB, Antonoff MB, Yang CC, Milbury K. Moderators of the association between stigma and psychological and cancer-related symptoms in women with non-small cell lung cancer. *Psycho Oncol*. 2022;31(9):1581–1588.
11. Ruiz-Casado A, Álvarez-Bustos A, de Pedro CG, Méndez-Otero M, Romero-Elías M. Cancer-related fatigue in breast cancer survivors: a review. *Clin Breast Cancer*. 2021;21(1):10–25.
12. Wang M, Fang J, Hu X, Cai T, Wu F, Lin Y. Chemotherapy-related symptoms in children with leukemia: application of latent profile analysis and network analysis. *Support Care Cancer*. 2024;32(3):207.
13. Peng P, Liao Y. Six addiction components of problematic social media use in relation to depression, anxiety, and stress symptoms: a latent profile analysis and network analysis. *BMC Psychiatr*. 2023;23(1):321.
14. Miaskowski C, Barsevick A, Berger A, et al. Advancing symptom science through symptom cluster research: expert panel proceedings and recommendations. *J Natl Cancer Inst*. 2017;109(4):djw253.
15. Mori M, Krumholz HM, Allore HG. Using latent class analysis to identify hidden clinical phenotypes. *JAMA*. 2020;324(7):700–701.
16. Kwekkeboom KL. Cancer symptom cluster management. *Semin Oncol Nurs*. 2016;32(4):373–382.
17. Oh PJ, Cho JR. Changes in fatigue, psychological distress, and quality of life after chemotherapy in women with breast cancer: a prospective study. *Cancer Nurs*. 2020;43(1):E54–E60.
18. Zhu Z, Xing W, Hu Y, Wu B, So WKW. Paradigm shift: moving from symptom clusters to symptom networks. *Asia Pac J Oncol Nurs*. 2022;9(1):5–6.
19. Jacobsen PB, Hann DM, Azzarello LM, Horton J, Balducci L, Lyman GH. Fatigue in women receiving adjuvant chemotherapy for breast cancer: characteristics, course, and correlates. *J Pain Symptom Manag*. 1999;18(4):233–242.

20. Yan G. NRS numerical rating scale for pain. *Chinese J Orthopedic Surgery (Online Edition)*. 2014;8(3):410.
21. Buysse DJ, Reynolds 3rd CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatr Res*. 1989;28(2):193–213.
22. Zhang F, Ding Y, Han L. Reliability and validity of the Chinese version of the cancer fatigue scale. *Chin J Ment Health*. 2011;25(11):810–813.
23. Snaith RP. The hospital anxiety and depression scale. *Health Qual Life Outcomes*. 2003;1:29.
24. Sinha P, Calfee CS, Delucchi KL. Practitioner's guide to latent class analysis: methodological considerations and common pitfalls. *Crit Care Med*. 2021;49(1):e63–e79.
25. Borsboom D, Cramer AO. Network analysis: an integrative approach to the structure of psychopathology. *Annu Rev Clin Psychol*. 2013;9:91–121.
26. Zhu Z, Guo M, Dong T, Han S, Hu Y, Wu B. Assessing psychological symptom networks related to HIV-positive duration among people living with HIV: a network analysis. *AIDS Care*. 2022;34(6):725–733.
27. Joachim Weis. Cancer-related fatigue: prevalence, assessment and treatment strategies. *Expert Rev Pharmacoecon Outcomes Res*. 2011.
28. Madmoli M. Evaluation of chemotherapy complications in patients with cancer: a systematic review. *Int J Res Stud Sci Eng Technol*. 2018;5(12):58–63.
29. Imanian M, Imanian M, Karimyar M. Sleep quality and fatigue among breast cancer patients undergoing chemotherapy. *Int J Hematol Oncol Stem Cell Res*. 2019;13(4):196–200.
30. Weis J. Cancer-related fatigue: prevalence, assessment and treatment strategies. *Expert Rev Pharmacoecon Outcomes Res*. 2011;11(4):441–446.
31. Hu H, Zhao Y, Sun C, Wang P, Yu L, Peng K. Symptom profiles and related factors among patients with advanced cancer: a latent profile analysis. *Asia Pac J Oncol Nurs*. 2023;10(11):100296.
32. Tsaras K, Papathanasiou IV, Mitsi D, et al. Assessment of depression and anxiety in breast cancer patients: prevalence and associated factors. *Asian Pac J Cancer Prev APJCP*. 2018;19(6):1661–1669.
33. Dijkstra-Kersten SM, Biesheuvel-Leliefeld KE, van der Wouden JC, Penninx BW, van Marwijk HW. Associations of financial strain and income with depressive and anxiety disorders. *J Epidemiol Community Health*. 2015;69(7):660–665.
34. Magnavita N, Di Prinzio RR, Meraglia I, et al. Supporting return to work after breast cancer: a mixed method study. *Healthcare (Basel)*. 2023;11(16):2343.
35. Cai T, Zhou T, Huang Q, Wu F, Ni F, Yuan C. Cancer-related symptoms among young and middle-aged women undergoing chemotherapy for breast cancer: application of latent class analysis and network analysis. *Eur J Oncol Nurs*. 2023;63:102287.
36. Chan RJ, Gordon LG, Tan CJ, et al. Relationships between financial toxicity and symptom burden in cancer survivors: a systematic review. *J Pain Symptom Manag*. 2019;57(3):646–660.e641.
37. Bockting CL, Hollon SD, Jarrett RB, Kuyken W, Dobson K. A lifetime approach to major depressive disorder: the contributions of psychological interventions in preventing relapse and recurrence. *Clin Psychol Rev*. 2015;41:16–26.
38. Clarke K, Mayo-Wilson E, Kenny J, Pilling S. Can non-pharmacological interventions prevent relapse in adults who have recovered from depression? A systematic review and meta-analysis of randomised controlled trials. *Clin Psychol Rev*. 2015;39:58–70.
39. Khoury B, Lecomte T, Fortin G, et al. Mindfulness-based therapy: a comprehensive meta-analysis. *Clin Psychol Rev*. 2013;33(6):763–771.
40. Camara A, Sow MS, Touré A, et al. Anxiety and depression among HIV patients of the infectious disease department of Conakry University Hospital in 2018. *Epidemiol Infect*. 2020;148:e8.
41. Duijts SF, Stolk-Vos AC, Oldenburg HS, van Beurden M, Aaronson NK. Characteristics of breast cancer patients who experience menopausal transition due to treatment. *Climacteric*. 2011;14(3):362–368.
42. Lei YY, Ho SC, Cheng A, et al. The association between soy isoflavone intake and menopausal symptoms after breast cancer diagnosis: a prospective longitudinal cohort study on Chinese breast cancer patients. *Breast Cancer Res Treat*. 2020;181(1):167–180.
43. Ye Y, Qin L, Zeng K, Liang J, Zhang L. Identification of core symptoms and symptom clusters during treatment breaks in cancer patients. *J Nurs*. 2022;37(1):20–24.