





Risk factors for self-reported high symptom cluster burdens in patients with breast cancer undergoing chemotherapy in China: A cross-sectional study

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Abstract

Background and Aims: Further exploration is needed to recognize symptom clusters and categorize subgroups with distinct cluster patterns and associated risks, focusing on symptoms that are highly self-reported by patients with breast cancer undergoing chemotherapy. This study aimed to identify subgroups and risk factors for self-reported high symptom cluster burden among patients with breast cancer undergoing chemotherapy.

Methods: A total of 647 participants who met the inclusion criteria were included in the study, with data collected on demographics, disease information, self-reported symptoms, and psychosocial factors. Latent class analysis was utilized to identify the subgroup, while logistic regression was used to pinpoint predictive risk factors.

Results: Latent class analysis revealed three subgroups: the “high burden of all symptoms group” ($n = 107$, 16.54%), the “high burden of psychological symptoms group” ($n = 103$, 15.92%), and the “low burden of all symptoms group” ($n = 437$, 67.54%). Patients in the high burden of all symptom group and high burden of psychological symptom group exhibited significantly worse function outcomes ($p < 0.001$). Predictive risk factors for the “high burden of all symptom group” included older age, lower self-efficacy, worse body image, and a higher financial burden. Similarly, patients with high burden of psychological symptom were more likely to have low self-efficacy, poor body image, and a high financial burden.

Conclusion: The study demonstrated the importance of giving more attention to patients with breast cancer who are at risk of developing into membership of high symptom cluster burden group.

KEYWORDS

breast cancer, chemotherapy, latent class analysis, risk factor, symptom cluster

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1 | INTRODUCTION

Breast cancer (BC) poses a significant global health challenge, being the most frequently diagnosed cancer and a leading cause of cancer-related deaths among females worldwide and in China.^{1,2} Despite improved mortality rates for stage I–III BC in developed regions and China, attributed to advancements in early diagnosis, treatment, and disease management,^{3,4} patients often experience distressing short- and long-term symptoms in association with cancer treatment.^{5,6} Chemotherapy, a key adjuvant therapy for BC, induces a range of physical, psychological, and social symptoms.^{6–8} These symptoms often co-occur and form symptom clusters, resulting in a negative synergistic effect that significantly reduces the quality of life and functionality of patients with BC.^{9,10} Symptom clusters are thought to have a common or interconnected etiology,¹¹ offering valuable clues for developing strategies for symptom management. This knowledge enables healthcare providers to develop more targeted and effective interventions for the entire group of symptoms, rather than addressing a single symptom. Consequently, a fuller understanding of the burden of symptom clusters experienced by patients with BC can also enhance the quality of care provided, ultimately improving their quality of life.

Previous studies have consistently found that pain, fatigue, sleep disturbance, anxiety, and depression are the most prevalent symptoms in patients with BC,^{12,13} especially during chemotherapy.¹⁴ A systematic review of studies further supports the idea that the pain–fatigue–sleep disturbance cluster and the psychological cluster are the most commonly reported symptom clusters among patients with BC across various treatment stages. Moreover, the clustering of pain, sleep disturbance, and fatigue symptoms displays a consistent pattern over time, as do the psychological symptoms, particularly anxiety and depression.⁹ These frequently experienced symptoms can be referred to as core or defining symptoms.^{15,16} To our knowledge, few studies have concurrently assessed all five core symptoms (pain, fatigue, sleep disturbance, anxiety, and depression) in patients with BC undergoing chemotherapy using validated and reliable patient-reported outcome measures and explored the clusters within these symptoms, particularly distinguishing subgroups with unique cluster patterns and risks.

The methods used for symptom cluster analysis can influence cluster identification.⁹ Unlike traditional variable-centered methods such as exploratory factor analysis and principal component analysis, latent class models including latent class analysis (LCA) and latent profile analysis (LPA) have become increasingly popular for identifying symptom clusters in recent years.¹⁷ As person-centered approaches, LCA and LPA can more effectively explore inter-individual variability in patients experiencing multiple symptoms and identify subgroups of individuals with similar patterns.¹⁸

Considering the phased, long-term, and complex nature of BC treatment, and the fact that chemotherapy can exacerbate symptoms such as pain, fatigue, sleep disturbance, anxiety, and depression,¹⁴ our study aimed to homogenize a sample of patients with BC who were all undergoing chemotherapy.

We used internationally standardized patient-reported outcome measures and advanced statistical methods to identify the symptom clusters accurately for these patients. Specifically, the objectives of this study were to: (1) identify a distinct latent cluster of five self-reported core symptoms (pain, sleep disturbance, fatigue, anxiety, and depression) among Chinese patients with BC receiving chemotherapy and, in particular, to identify patients in subgroups with a high burden of symptom clusters, (2) validate differences in functional outcomes over the same time period in subgroups of patients with distinct symptom clusters, and (3) identify predictive risk factors (e.g., demographic, disease-related, and psychosocial) for membership in the subgroups with a high burden of symptom clusters. The goals of this study were to provide a comprehensive understanding of symptom clusters among patients with BC and identify higher-risk subpopulations requiring additional attention.

2 | METHODS

2.1 | Study design and participant recruitment

This cross-sectional study used convenience sampling to enrol patients with BC from four tertiary hospitals in Southeast China (Shandong, Jiangsu, Shanghai, and Zhejiang Provinces) between October 2019 and May 2021. The inclusion criteria were a diagnosis of stage I–III BC, confirmed by preoperative puncture or postoperative histopathology, age ≥ 18 years, postoperative or preoperative adjuvant chemotherapy, disease awareness, and the ability to read and write independently. The exclusion criteria were other cancer diagnoses, serious diseases and patients who were unconscious or uncooperative. A sample size of >200 was considered adequate to ensure sufficient statistical power for LCA¹⁸. All procedures adhered to the ethical standards of the institutional research committee and the 1964 Declaration of Helsinki and its subsequent amendments. The study protocol was approved by the Ethical Review Board of the author's institution (IRB No. 2018-12-13) and written informed consent was obtained from all participants.

2.2 | Data collection

Investigators for this study were recruited from our network of research collaborators and underwent training to ensure consistency in explaining and reviewing the questionnaire items. Paper questionnaires were then mailed to each investigator, who guided the participants in their completion during the middle stage of chemotherapy (i.e., within 2 days after the end of the third cycle for six-cycle chemotherapy and within 2 days after the end of the fourth cycle for eighth-cycle chemotherapy), to collect a homogenous sample. After obtaining written informed consent, the questionnaires were distributed and collected on-site, then returned after quality review.

2.3 | Measures

2.3.1 | Demographic and disease-related information

A self-designed questionnaire was used to collect demographic and disease-related information, including age, marital status, religion, educational level, monthly family income, living status, employment status, location of residence, menstrual status, and height and weight for calculating the body mass index (BMI) of the participants.

2.3.2 | Symptom assessment of pain, sleep disturbance, fatigue, anxiety, depression

Symptoms were assessed using the Chinese version of the Patient-Reported Outcome Measurement Information System[®] (PROMIS[®]) short forms, including PROMIS pain interference 8a, sleep disturbance 8a, fatigue 8a, anxiety 8a and depression 8a (the numbers represent the item count in each short form).¹⁹ All five short forms were unidimensional, with responses recorded on five-point Likert scales. The internal consistency of these measures was reliable, with Cronbach's α coefficients ranging from 0.86 to 0.94 in this study. Raw scores for each short form were obtained by summing all item scores, which were then converted into T-scores ranging from 0 to 100, following the *PROMIS[®] Scoring Manual* (2023).²⁰ For LCA data input, T-scores from each short form were converted into dichotomized variables (0 = no depression, 1 = depression) based on established T-score thresholds in the PROMIS measures (<55, within normal limits; ≥ 55 , at least mild symptom distress).²¹

2.3.3 | Functional outcomes

Functional outcomes included physical function, cognitive function and social function; evaluated using the PROMIS[®] short forms for physical function 8b,¹⁹ cognitive function 4a,²² ability to participate in social roles and activities 4a, and satisfaction with social roles and activities 4a.²³ The internal consistency of these measures was strong, with Cronbach's α coefficients of 0.93, 0.95, 0.90, and 0.95, respectively, in this sample. The T-score from each short form was calculated, with higher scores indicating higher function levels.

2.3.4 | Self-efficacy

Self-efficacy was assessed using the Chinese Patient-Reported Outcome Measurement System-Breast-Chemotherapy (PROMS-B-C) self-efficacy scale, developed by our research team in a previous study.²² The scale includes nine items for assessing general self-efficacy and five items for assessing chemotherapy-related self-efficacy, with each item scored on a five-point Likert scale. Higher scores indicate greater self-efficacy. The scale

demonstrated high reliability with a Cronbach's α coefficient of 0.93 in this study.

2.3.5 | Body image

Body image was assessed using the Chinese PROMS-B-C Body Image Scale, which consists of 16 items. The responses were scored using a five-point Likert scale, with higher scores indicating poorer body image. The scale has shown strong internal consistency with Cronbach's α coefficients > 0.90 , and confirmatory factor analysis showed an acceptable model fit, suggesting good structural validity.²²

2.3.6 | Social support

Social support consisted of instrumental support, informational support, emotional support, and companionship, evaluated using the Chinese versions of PROMIS short forms for instrumental support 4a, informational support 4a, emotional support 4a, and companionship 4a, respectively. Previous research by our team has demonstrated good psychometric properties of these scales, with all Cronbach's α coefficients > 0.90 , indicating high interrater reliability.²² The T-score was calculated for each short form, with higher scores indicating higher support levels.

2.3.7 | Family relationships

Family relationships were assessed using the Chinese PROMS-B-C family relationship scale. This scale comprises two subscales, relationship with a spouse (19 items) and relationship with a child (four items), having Cronbach's α coefficients of 0.885 and 0.869, respectively. Each item was scored using a five-point Likert scale, with higher scores indicating better relationships.²²

2.3.8 | Financial burden

Financial burden was assessed using the Chinese version of the Comprehensive Score for Financial Toxicity, an 11-item instrument for which items are scored on a five-point Likert scale.²⁴ Scores ranged from 0 to 44, with lower scores indicating greater financial burden. The scale showed reliable internal consistency in this study, with a Cronbach's α coefficient of 0.89.

2.4 | Statistical analysis

Continuous variables are presented as means \pm standard deviations, or as medians (I and III quartiles) based on the normal distribution results from the Kolmogoro-Smirnov test, while categorical variables are displayed as numbers and percentages. The latent class model,

by using multiple observed variables, effectively identifies unobserved subgroups or classes of individuals sharing similar symptom patterns. In this study, LCA was applied to categorical data on pain, sleep disturbance, fatigue, anxiety, and depression, to identify distinct subgroups of patients with BC with similar cluster patterns during chemotherapy, particularly those experiencing high levels of symptom cluster burden.

A robust maximum-likelihood estimator was used to estimate the LCA model parameters. Model goodness of fit was assessed using the Akaike information criterion, Bayesian information criterion (BIC), and sample-size adjusted BIC, with smaller values indicating better model fit.¹⁸ An entropy value >0.8 indicated accurate classification.¹⁸ The Lo-Mendell-Rubin likelihood ratio test (LMR-LRT) and bootstrap likelihood ratio tests (BLRT) were used to compare the models, with a significant *p*-value indicating a significant improvement in the *k*-class model.¹⁸ The optimal number of subgroups was determined based on all indicators. Bayesian posterior probability was used to assign class membership for each individual after identifying a model with good fit.

For functional outcomes, a univariate analysis of variance (ANOVA) and pairwise post hoc comparisons were conducted to examine omnibus and between-class differences. Univariate analyses, including one-way ANOVA, or Kruskal–Wallis test, or the chi-square test, were used to select potential predictive factors. Variables significant in the univariate analysis ($p \leq 0.2$, two-sided probability) were entered into the multinomial logistic regression model. $p < 0.05$ was set as the threshold for the inclusion of a variable in the final model. Statistical analyses were performed using software of SPSS 21.0 (IBM Corp.) or Mplus version 8.0 (Muthen & Muthen).

3 | RESULTS

3.1 | Sample characteristics

A total of 647 patients with BC undergoing chemotherapy were included in the final data analysis. The mean participant age was 48.11 ± 9.97 years (range: 23–76 years). The majority of the patients were married (93.8%), and 43.1% had attained a high education level (senior middle school and above). Additionally, 69.9% of the participants were from villages or rural areas of China, and over half (51.2%) reported a low monthly family income ($\leq 3,000$ ¥). Only 35.4% of the patients were employed. Additionally, 52.7% were premenopausal, and 12.8% were classified as overweight (BMI ≥ 28 kg/m²). Further information on patient characteristics is presented in Table 1.

3.2 | Latent clusters of pain, sleep disturbance, fatigue, anxiety, and depression based on symptom occurrence

During chemotherapy, Patients with BC had an incidence rate of 28% for pain, 30.6% for sleep disturbances, 26.3% for fatigue, 33.8% for

anxiety and 36.1% for depression. The optimal model was determined by comparing the fit indices of the candidate models. The three-class model was selected as it had the lowest BIC (Table 2). The LMR and bootstrap likelihood ratio tests also supported the three-class model over the four-class model. The latent class classification quality for the three-class model was deemed acceptable (entropy: 0.895).

As illustrated in Figure 1, according to the probability of symptom occurrence for each latent subgroup by LCA model, 16.54% ($n = 107$) of the patients were classified into the “high burden of all symptoms group” (class 1, red line), corresponding to a high probability of occurrence for all symptoms (pain, sleep

TABLE 1 Sample characteristics ($n = 647$).

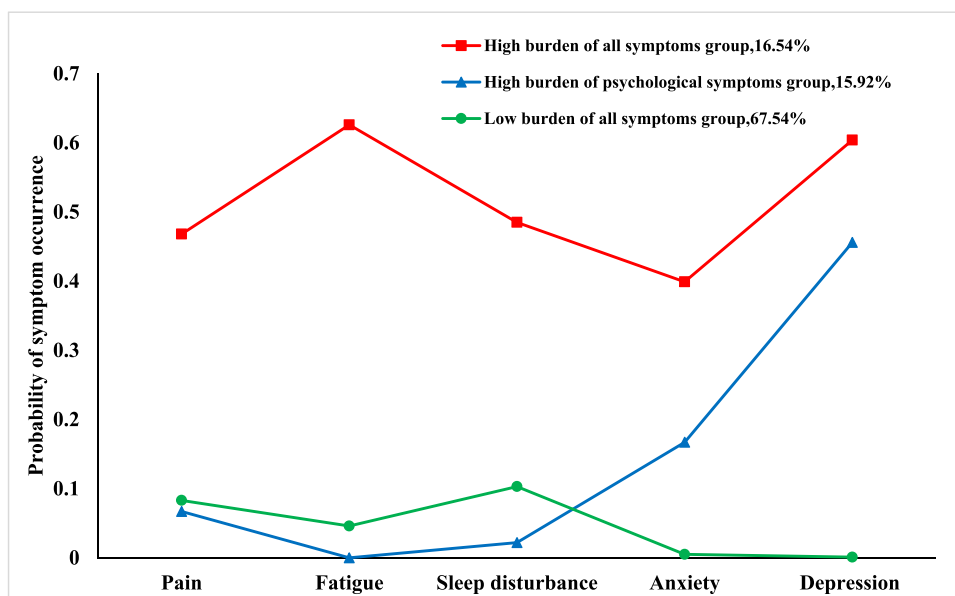
Variables	Mean/ <i>n</i>	SD/%
Age (years)	48.11	9.97
Marriage status		
Married	607	93.8%
Single/Widowed/Divorced	40	6.2%
Religion		
Yes (any religion)	54	8.3%
No religion	593	91.7%
Educational level		
9 years or less	368	56.9%
10 years and above	279	43.1%
Monthly family income		
Low (≤ 3000 ¥)	331	51.2%
High (>3000 ¥)	316	48.8%
Living status		
Living with family	610	94.3%
Living alone or others	37	5.7%
Employment		
Employed	229	35.4%
Unemployed or retired	418	64.6%
Residence		
City	195	30.1%
Villages or countryside	452	69.9%
BMI (Kg/m ²)		
Obese (≥ 28.0)	83	12.8%
No obese (<28.0)	564	87.2%
Menstrual status		
Premenopausal	341	52.7%
Postmenopausal	306	47.3%

Abbreviation: SD, standard deviation.

TABLE 2 Latent class model fit comparison.

Model	AIC	BIC	aBIC	Entropy	LMR-LRT <i>p</i> -value	BLRT <i>p</i> -value
Model 1	5326.798	5371.522	5339.772	-	-	-
Model 2	4812.392	4906.311	4839.637	0.863	<0.001	<0.001
Model 3	4715.827	4858.942	4757.343	0.895	<0.001	<0.001
Model 4	4692.359	4884.670	4748.146	0.906	0.115	0.120

Abbreviations: aBIC, adjusted-Bayesian information criterion; AIC, Akaike information criterion; BIC, Bayesian information criterion; BLRT, bootstrapped likelihood ratio test; LMR-LRT, Lo-Mendell-Rubin likelihood ratio test.

**FIGURE 1** The probability of symptom occurrence for each latent subgroup by latent class analysis.

disturbance, fatigue, anxiety, and depression). Conversely, 67.54% ($n = 437$) of the patients belonged to the “low burden of all symptoms group” (class 3, green line), corresponding to a low probability of symptom occurrence. Another group, comprising 15.92% ($n = 103$) of the patients, exhibited a high probability of experiencing anxiety and depression only, labeled as the “high burden of psychological symptoms group” (class 2, blue line).

3.3 | Differences in functional outcomes among subgroups

As shown in Table 3, analysis of differences in functional outcomes among the three subgroups with distinct symptom cluster characteristics revealed that the “high burden of all symptoms group” and “high burden of psychological symptoms group” exhibited significantly poorer physical and cognitive functioning compared to patients in the “low burden of all symptoms group” ($p < 0.001$). However, no differences in social functioning were observed among the subgroups. Additionally, except for slight differences in “Satisfaction with Social Roles and Activities” ($p < 0.001$), there were no differences in

physical or cognitive functioning between the “high burden of all symptoms group” and the “high burden of psychological symptoms group.”

3.4 | Risk factors for patients in subgroups with a high burden of all symptoms and a high burden of psychological symptoms

The potential risk variables identified in univariate analysis are shown in Table 4. Age ($p = 0.131$), religion ($p = 0.033$), education level ($p = 0.085$), monthly family income ($p = 0.007$), living status ($p = 0.032$) and employment status ($p = 0.145$) were significantly associated with the risk of developing a high burden of all symptoms. Additionally, patients in the high burden of symptoms group reported significantly poorer self-efficacy, social support, and family relationships, along with a poorer body image and heavier financial burden.

To validate the potential risk factors, multivariate logistic regression analysis was conducted taking the “low burden of all symptoms group” as the reference. As shown in Table 5, patients with

TABLE 3 Differences in physical, cognitive, and social functions among three subgroups.

Outcomes	Class 1 (n = 107)	Class 2 (n = 103)	Class 3 (n = 437)	F	P
Physical function	45.86 ± 8.71	47.67 ± 10.20	51.57 ± 9.87	18.165	<0.001 1,2 < 3
Cognitive function	45.68 ± 7.73	46.21 ± 7.32	51.96 ± 10.46	27.907	<0.001
Social function					1,2 < 3
Ability to Participate in Social Roles and Activities	51.33 ± 9.48	50.08 ± 8.12	49.66 ± 10.50	1.168	0.312
Satisfaction with Social Roles and Activities	45.24 ± 10.87	49.32 ± 9.37	51.30 ± 9.58	16.321	<0.001 1 < 2,3

Note: Class 1 = high burden of all symptoms group; Class 2 = high burden of psychological symptoms group; Class 3 = low burden of all symptoms group.

a high burden of all symptoms were older (odds ratio [OR] = 1.031, $p = 0.024$) and had lower self-efficacy (OR = 0.942, $p < 0.001$), worse body image (OR = 1.089, $p < 0.001$) and a higher financial burden (OR = 1.036, $p = 0.016$). Similarly, patients with a high burden of psychological symptoms had lower levels of self-efficacy (OR = 0.939, $p < 0.001$), worse body image (OR = 1.034, $p = 0.016$), and a higher financial burden (OR = 1.074, $p = 0.016$).

4 | DISCUSSION

Recognizing symptom clusters and distinguishing subgroups with specific cluster patterns and risks is essential for improving symptom management efficacy and quality of care for patients with BC. However, previous studies have shown inconsistencies in the number and types of symptom clusters identified due to variations in assessment methods, instruments, and statistical approaches.^{10,12,14,25–30} Additionally, sample heterogeneity among studies may contribute to the inconsistency of symptom cluster results. Several researchers have highlighted the need for studies focusing on homogenous samples.^{29,31,32} By homogenizing a sample of Chinese patients with BC undergoing chemotherapy and focusing on five highly self-reported core symptoms (pain, sleep disturbance, fatigue, anxiety, and depression), we identified three different subgroups with distinct symptom clusters using LCA. Accounting for 32.46% of the overall sample, patients in class 1 (high burden of all symptoms group) and class 2 (high burden of psychological symptoms group) both exhibited high symptomatic features and reported worse functional outcomes, as expected.

In line with previous research,⁹ our findings reinforce the substantial variations in symptom clusters experienced by patients with BC and emphasize that patients with a high burden of symptoms require prioritized attention from healthcare providers. Interestingly, our study discovered that those in the high burden of psychological symptoms group exhibited functional outcomes similar to those in the high burden of all symptoms group, suggesting the need for similar levels of attention and intervention strategies for these subgroups and emphasizing the importance of psychological stress management. Moreover, the results of this study indicate that functional outcomes, including physical, cognitive, and social function of patients with BC have deteriorated by the midway point of

chemotherapy, highlighting the importance of early intervention to prevent long-term functional decline.

This study provided further evidence regarding the risk factors associated with high symptomatic cluster patterns. While previous research often associated a high burden of symptoms with younger age,^{10,26,29,33,34} our findings indicated that older patients were more likely to experience a greater symptom burden. In previous studies, increased symptoms in younger patients may have been attributable to more aggressive BC types and treatments.^{10,29,34} However, our study focused solely on chemotherapy, which can exacerbate symptoms across all ages,⁸ with more pronounced effects seen in older patients who are more susceptible to the effects of acute symptoms. Additionally, our study primarily included middle-aged adults, with only 4.3% of the patients being aged ≥ 65 years, contrasting with Lee et al.²⁹ who analyzed a cohort where 25% of the patients were aged ≥ 65 years. Song et al.³⁵ reported that the mean age at BC diagnosis in China is nearly 10 years younger than in Western countries. Therefore, the age distribution of diagnosed patients with BC in China may also explain the differences between our results and previous findings.

Previous studies have suggested that patients with higher socioeconomic status, indicated by higher education and income levels, are less likely to belong to the “high burden of all symptoms group”. This is attributed to their increased engagement in healthy lifestyle behaviors, including physical activities, as well as better access to healthcare services and enhanced knowledge and skills regarding symptom management.^{10,29,33,36} Consistent with previous findings, our study revealed differences in educational level, income level, and employment status among the patient subgroups, with the “high burden of all symptoms group” having a lower educational level, lower monthly family income, and a higher unemployment rate. However, these variables were not retained in the subsequent multinomial logistic regression model, consistent with our previous findings using non-PROMIS measures in a small sample of Chinese patients with BC.³⁷ Further exploration of the predictive effects of these socioeconomic variables is warranted.

Although several studies have investigated the correlations of sociodemographic and clinical variables with symptom clusters in patients with BC, these unmodifiable variables may not clearly indicate actionable intervention plans for healthcare providers. The present study is among the few to consider interventional factors,

TABLE 4 Potential risk factors for patients with high burden of symptom cluster by univariate analysis.

Variables	Class 1 (n = 107)	Class 2 (n = 103)	Class 3 (n = 437)	Statistics	p
Age	49.39 ± 9.23	46.62 ± 8.87	48.14 ± 10.35	2.042	0.131
Marriage status				1.117	0.572
Married	100 (93.5%)	99 (96.1%)	408 (93.4%)		
Single/Widowed/Divorced	7 (6.5%)	4 (3.9%)	29 (6.6%)		
Religion (No)	104 (97.2%)	90 (87.4%)	399 (91.3%)	6.828	0.033
Educational level				4.928	0.085
9 years or less	65 (60.7%)	67 (65.0%)	236 (54.0%)		
10 years and above	42 (17.7%)	36 (35.0%)	201 (46.0%)		
Monthly income				9.835	0.007
Low (≤3000¥)	63 (58.9%)	63 (61.2%)	205 (46.9%)		
High (>3000¥)	44 (41.1%)	40 (38.8%)	232 (53.1%)		
Living status				6.896	0.032
Living with family	96 (89.7%)	101 (98.1%)	413 (94.5%)		
Living alone or others	11 (10.3%)	2 (1.9%)	24 (5.5%)		
Employment				3.855	0.145
Employed	29 (27.1%)	38 (36.9%)	162 (37.1%)		
Unemployed or retired	78 (72.9%)	65 (63.1%)	275 (62.9%)		
Residence				5.152	0.076
City	27 (25.2%)	24 (23.3%)	144 (33.0%)		
Villages or countryside	80 (74.8%)	79 (76.7%)	293 (67.0%)		
BMI (Obese, ≥28.0)	13 (12.1%)	11 (10.7%)	59 (13.5%)	0.646	0.724
Menstrual status				0.261	0.878
Premenopausal	54 (50.5%)	55 (53.4%)	232 (53.1%)		
Postmenopausal	53 (49.5%)	48 (46.6%)	205 (46.9%)		
Self-efficacy	45.90 [37.54–48.91]	46.82 [38.47–48.91]	52.10 [46.82–59.82]	57.989	<0.001
Body image	55.74 [50.02–61.48]	54.55 [46.70–56.88]	47.74 [42.02–54.60]	67.720	<0.001
Social support					
Instrumental support	47.49 [47.49–59.25]	47.49 [41.61–59.25]	53.37 [47.49–59.25]	3.241	0.198
Informational support	47.30 [38.28–53.31]	50.31 [41.29–59.33]	50.31 [44.30–61.74]	16.246	<0.001
Emotional support	47.18 [38.33–53.08]	50.13 [41.28–58.99]	50.13 [44.23–61.94]	18.485	<0.001
Companionship	45.05 [39.49–50.61]	50.61 [39.49–58.96]	50.61 [45.05–61.74]	26.760	<0.001
Family relationship					
Spouse relationship	48.30 [43.30–52.60]	49.73 [45.09–54.74]	52.60 [46.16–56.89]	24.604	<0.001
Children relationship	49.07 [41.76–56.39]	49.07 [46.64–58.83]	51.51 [46.64–58.83]	7.873	0.002
Financial burden	51.15 [47.81–58.94]	55.60 [45.59–62.28]	47.81 [41.69–54.49]	45.373	<0.001

Note: Class 1 = high burden of all symptoms group; Class 2 = high burden of psychological symptoms group; Class 3 = low burden of all symptoms group.

including psychological (e.g., self-efficacy and body image), social (e.g., social support), family (e.g., relationships with spouse and children), and financial factors, as predictors of symptom clusters. Self-efficacy, body image, and financial burden were retained in the

final multinomial regression model. Lower self-efficacy, worse body image, and a heavier financial burden were common risk factors in the “high burden of all symptoms group” and “high burden of psychological symptoms group”. A study by St. Fleur et al.¹⁰ also

TABLE 5 Final risk factors for patients with high symptom cluster burden by multinomial logistics regression.

Risk factors	Low burden of all symptoms group (refer) versus					
	High burden of all symptoms group			High burden of psychological symptoms group		
	OR	95% CI	<i>p</i>	OR	95% CI	<i>p</i>
Age	1.031	1.004–1.059	0.024	0.996	0.970–1.023	0.781
Religion (No)	3.057	0.875–10.682	0.080	0.659	0.3041–1.428	0.290
Education level						
9 years or less	0.884	0.493–1.584	0.678	1.815	0.980–3.361	0.058
10 years and above	Refer	Refer	Refer	Refer	Refer	Refer
Monthly income (Low)	1.092	0.627–1.903	0.755	1.138	0.654–1.979	0.648
Lifestyle (living alone or others)	1.484	0.528–4.168	0.454	0.181	0.022–1.496	0.113
Employment (unemployed or retired)	0.848	0.453–1.587	0.606	0.543	0.293–1.006	0.052
Residence (villages or countryside)	1.348	0.718–2.529	0.353	1.141	0.604–2.158	0.684
Self-efficacy	0.942	0.911–0.973	<0.001	0.939	0.909–0.970	<0.001
Body image	1.089	1.056–1.123	<0.001	1.034	1.006–1.063	0.016
Informational support	1.036	0.984–1.091	0.175	0.967	0.915–1.022	0.234
Emotional support	0.981	0.939–1.024	0.371	1.045	0.995–1.098	0.078
Companionship	0.982	0.940–1.027	0.432	1.012	0.968–1.059	0.589
Spouse relationship	0.985	0.958–1.013	0.290	0.985	0.957–1.015	0.325
Children relationship	0.994	0.969–1.021	0.666	1.021	0.991–1.052	0.174
Financial burden	1.036	1.007–1.066	0.016	1.074	1.045–1.105	<0.001

Abbreviation: CI, confidence interval; OD, odds ratio.

reported an association between lower self-efficacy and membership of the “high burden of all symptoms group.” Previous research has demonstrated that high self-efficacy is associated with healthy behaviors (e.g., physical activity) that promote well-being and reduce physical and psychological symptoms in patients with BC.^{38,39} Our findings validated the relationship between low self-efficacy and high symptom burden among patients with BC undergoing chemotherapy, highlighting its importance for future interventions. Body image, defined as the subjective impression of an individual's physical appearance,⁴⁰ is significantly influenced by treatment-related changes, such as mastectomy and chemotherapy-related hair loss.^{40,41} Donghua Ma et al.,⁴² revealed that significant proportions of patients with BC in China considered their bodies imperfect (60.34%), were unwilling to look at themselves without clothes (65.52%), and avoided social contact because of their physical appearance (31.03%). Several other studies have also highlighted the critical role of body image in the psychological well-being and social integration of patients with BC, with those experiencing poor body image being more susceptible to anxiety, depression, low self-esteem, pessimism, hopelessness, and social impairment, negatively affecting marriage and family dynamics. The results of this study further demonstrated that poorer body image was linked to an increased likelihood of patients with BC being included in the high burden of all symptoms group or high burden of psychological

symptoms group. Considering this, interventions focusing on improving self-efficacy and body image could potentially mitigate the symptom burden of patients with BC. Therefore, healthcare professionals should tailor interventions aimed at enhancing self-efficacy and body image perceptions among patients, to reduce suffering and improve their quality of life and overall health outcomes.

Although monthly family income was not included in the final regression analysis, financial burden emerged as a significant independent predictor of inclusion in the high burden of all symptoms subgroup. Financial burden encompasses both the objective economic strain of medical expenses and the subjective perception of financial distress. The present study assumed that the perceived financial burden experienced by patients with BC could have a more immediate impact on their symptoms compared to the actual income level. However, it remains uncertain whether financial burden is a cause of high symptom burden or a consequence of symptoms that lead patients to perceive a heavy financial burden. Healthcare providers should prioritize patients facing high financial burdens and make efforts to secure financial assistance for them.

This study also had certain limitations that must be considered. Firstly, the cross-sectional design precluded exploration of causality or directionality between variables and symptom cluster patterns, as well as the investigation of changes in symptom cluster membership over time. Secondly, due to a substantial number of missing values

pertaining to disease-related variables, such as chemotherapy cycle, disease stage, and comorbidities, associations between these variables and symptom cluster membership could not be examined. Future longitudinal studies are needed to address these limitations and provide a more comprehensive understanding of symptom cluster dynamics in patients with BC.

5 | CONCLUSION

This study, focusing on the five core symptoms of pain, fatigue, sleep disturbance, anxiety, and depression, identified three distinct subgroups within a large patient with BC cohort undergoing chemotherapy in China. It contributes to the existing research on the complexity and heterogeneity of symptom clusters among these patients. Furthermore, our findings demonstrated that older age was a predictor of high symptom cluster burden, while low self-efficacy, worse body image, and heavier financial burden emerged as risk factors for high symptom clustering.

6 | RELEVANCE FOR CLINICAL PRACTICE

Through LCA, our study highlighted the significant disparities in symptom experiences among patients with BC undergoing chemotherapy. Patients exhibiting a high symptom burden represented a high-risk group, necessitating priority attention from healthcare providers. Interestingly, our findings suggested that patients in the high burden of psychological symptoms group had similar, poor functional outcomes as those in the high burden of all symptoms group, despite primarily displaying psychological symptoms. This highlights the importance of equal attention and tailored interventions, with a focus on addressing psychological stress and providing psychological interventions. Our study provides additional evidence regarding the risk factors for highly symptomatic cluster profiles. In particular, older patients with lower self-efficacy, poor body image, and heavy financial burdens were more likely to experience a high symptom cluster burden during chemotherapy. These findings can guide the development of tailored interventions for optimizing health outcomes in patients with BC undergoing chemotherapy.

AUTHOR CONTRIBUTIONS

Qingmei Huang: Conceptualization; writing—original draft; methodology; formal analysis; project administration; funding acquisition; writing—review and editing. **Xuqian Zong:** Data curation; investigation; software; validation. **Changrong Yuan:** Conceptualization; methodology; project administration. **Meimei Shang:** Investigation; data curation; resources. **Rong Yan:** Data curation; investigation; resources. **Yeping Zheng:** Investigation; data curation; resources. **Meie Niu:** Investigation; data curation; resources. **Yang Yang:** Investigation; data curation; resources; validation. **Fulei Wu:** Conceptualization; methodology; writing—original draft; writing—review and editing; project administration; funding acquisition; supervision;

validation. All authors have read and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available due to privacy or ethical restrictions. The corresponding author had full access to all of the data in this study and took complete responsibility for the integrity of the data and the accuracy of the data analysis.

ETHICS STATEMENT

The study was approved by the Ethical Review Board of Fudan University, School of Nursing (IRB No. 2018-12-13) and written informed consent was obtained from all participants.

TRANSPARENCY STATEMENT

The lead author Fulei Wu affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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