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Trajectories of depression and predictors in lung cancer patients undergoing chemotherapy: growth mixture model

Yuanyuan Luo[1†], Dongmei Mao[1†], Le Zhang[1], Benxiang Zhu[1], Zhihui Yang[1], Jingxia Miao[2] and Lili Zhang[1*]

Abstract

Background Depression is prevalent among lung cancer patients undergoing chemotherapy, and the symptom cluster of fatigue-pain-insomnia may influence their depression. Identifying characteristics of patients with different depression trajectories can aid in developing more targeted interventions. This study aimed to identify the trajectories of depression and the fatigue-pain-insomnia symptom cluster, and to explore the predictive factors associated with the categories of depression trajectories.

Methods In this longitudinal study, 187 lung cancer patients who were undergoing chemotherapy were recruited and assessed at the first (T1), second(T2), and fourth(T3) months using the Patient Health Questionnaire-9 (PHQ-9), the Brief Pain Inventory (BPI), the Brief Fatigue Inventory (BFI), and the Athens Insomnia Scale (AIS). Growth Mixture Model (GMM) and Latent Class Analysis (LCA) were used to identify the different trajectories of the fatigue-pain-insomnia symptom cluster and depression. Binary logistic regression was utilized to analyze the predictive factors of different depressive trajectories.

Results GMM identified two depressive trajectories: a high decreasing depression trajectory (40.64%) and a low increasing depression trajectory (59.36%). LCA showed that 48.66% of patients were likely members of the high symptom cluster trajectory. Binary logistic regression analysis indicated that having a history of alcohol consumption, a higher symptom cluster burden, unemployed, and a lower monthly income predicted a high decreasing depression trajectory.

Conclusions Depression and fatigue-pain-insomnia symptom cluster in lung cancer chemotherapy patients exhibited two distinct trajectories. When managing depression in these patients, it is recommended to strengthen symptom management and pay particular attention to individuals with a history of alcohol consumption, unemployed, and a lower monthly income.

Keywords Depression, Longitudinal studies, Trajectory, Lung cancer patients, Growth mixture model

Background

In 2020, China reported 4,546,400 new cases of lung cancer, accounting for one-fourth of global new cases. It is projected that by 2023, China will become the country with the highest number of new lung cancer cases [1]. Lung cancer, the most common and deadliest cancer in China and globally, has become a major health challenge for society [2, 3]. The National Comprehensive

†Yuanyuan Luo is the first author and Dongmei Mao is the co-first author.

*Correspondence:
Lili Zhang
zhanglili_gzsmu@163.com
[1] School of Nursing, Southern Medical University, No.1023, South Shatai Road, Baiyun District, Guangzhou 510515, Guangdong, China
[2] Department of Medical Oncology, Nanfang Hospital, Southern Medical University, No.1838, North Guangzhou Avenue, Baiyun District, Guangzhou 510515, Guangdong, China

Cancer Network (NCCN) guidelines have identified psychological disorders in cancer patients as the sixth vital sign, apart from temperature, pulse, respiration, blood pressure, and pain [4]. Among various psychological disorders, depression is the most common among lung cancer patients. Studies have reported that the incidence of depression among Chinese lung cancer patients is as high as 57.1% [5].

Due to advancements in modern diagnostic and therapeutic methods, the lifespan of lung cancer patients has been extended [6]. However, frequent chemotherapy, immunotherapy, and targeted therapy have also brought severe side effects to patients; this is particularly true for chemotherapy, which serves as the cornerstone of various treatment regimens [7, 8]. Adverse reactions such as pain, fatigue, and insomnia are prevalent and significantly affect physical and mental health [9, 10]. In our previous study on lung cancer patients undergoing initial chemotherapy, the incidence rates of sleep disturbances, fatigue, and pain were 92.31%, 91.12%, and 69.82%, respectively [11]. Morrison [12] conducted a survey of 2205 lung cancer patients and found that greater symptom burden was associated with more severe emotional distress. Wang [13] implemented a cross-sectional study, and the results of a multivariate logistic regression showed that insomnia was a contributing factor to depression. Research has also indicated a significant correlation between pain, sleep disturbances, fatigue, and depression in cancer patients undergoing chemotherapy [14]. As research on symptoms progresses, scholars have gradually discovered that pain, fatigue, and insomnia, which have the highest incidence and most significant impact on patients, often occur together as a "symptom cluster"[15, 16]. Within the symptom cluster, the symptoms of pain, fatigue, and insomnia interact synergistically, potentially amplifying the risk of depression in lung cancer patients undergoing chemotherapy [17]. However, little is presently known about the impact of this symptom cluster on depression. Additionally, Shahedah's [18] study indicated that married individuals or those with partners had lower average depression scores compared to those who were single, widowed, unmarried, or divorced. Wu [19] found that depression was more prevalent among female and elderly patients. Other studies also suggested that educational level, economic status, and constipation might influence depression levels in lung cancer patients [13, 20, 21].

Current research mostly consists of cross-sectional surveys conducted to explore factors influencing depression. However, the results of single-time measurements may be influenced by recent physical conditions or life events. The few available longitudinal studies have not focused on lung cancer patients undergoing chemotherapy. Stommel [22] and Chang [23] conducted longitudinal tracking of patients and found that the patients' depression gradually decreased over time. However, Andersen [24] reported a slight increase in depression before the decline. Another study revealed that depression levels slightly increased after the decline [25]. Currently, there is no unified consensus on the trajectory of depression among lung cancer patients undergoing chemotherapy. These studies analyzed all patients as an entity, thereby failing to analyze the heterogeneity of different change trajectories.

Trajectory analysis, by identifying multiple potential individual subgroups presenting similar longitudinal patterns, may provide a deeper understanding of the data. Growth mixture modeling (GMM) can consider individual differences and identify potential subgroups in a population that follow different trajectories over time [26, 27]. This person-centered approach shifts the focus from diagnosing depression symptoms to understanding their changes over time. Summarizing these changes into several classes of similar developmental trajectories can enhance our understanding of the development of depression [28]. Therefore, the aim of this study was to track the development of depression and fatigue-pain-insomnia symptom cluster among lung cancer patients after their initial chemotherapy and analyze their change trajectories. Furthermore, "fatigue-pain-insomnia symptom cluster" were considered a composite predictor to explore the factors associated with changes in different depression trajectories.

Methods

Study design and participants

This longitudinal study was conducted at Nanfang Hospital from February 2023 to January 2024. Nanfang Hospital is a comprehensive hospital located in the urban center of Guangzhou, Guangdong Province, China. The Department of Medical Oncology has more than 130 beds and admits over 9,000 patients annually. Patients come primarily from the city and surrounding areas and represent diverse socioeconomic backgrounds, ranging from affluent company executives to low-income rural residents. This diversity ensured the recruitment of a balanced patient baseline for the study. Two trained research nurses screened all eligible patients according to the established inclusion and exclusion criteria. On the day of admission, the nurses explained the study's purpose and procedures to all eligible patients and asked if they were willing to participate. If the patients agreed to participate and signed the informed consent form, the research nurses guided them to a separate, quiet room to complete the questionnaire. After the patients finished, the nurses immediately checked for any missing items and requested the patients to complete them. This study

collected patient questionnaires at the first (T1), second (T2), and fourth (T3) months. The inclusion criteria were as follows: (1) age > 18 years, (2) histologically diagnosis of lung cancer, (3) treatment with chemotherapy, and (4) expected survival of more than 6 months. The exclusion criteria were as follows: (1) a history of severe mental illness or current use of psychotropic drugs, (2) cognitive impairment or inability to communicate normally, and (3) unwillingness to participate in the study. Initially, 212 patients were enrolled, 25 of whom were excluded due to patient death, loss to follow-up, or voluntary withdrawal. A total of 187 patients completed all three follow-up assessments in this study.

Measurements

Sociodemographic and disease-related characteristics

Sociodemographic and disease-related characteristics, including age, BMI, sex, smoking history, history of alcohol consumption, marital status, educational level, work status, monthly income, and cancer stage, were collected via self-report and the electronic medical records system of the hospital.

Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 is a self-reported depression screening questionnaire based on the nine diagnostic criteria of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [29]. It consists of nine items, each with four scoring options: 0 points indicating not at all, 1 point indicating several days, 2 points indicating more than half the days, and 3 points indicating nearly every day. The total score is the sum of all items, ranging from 0 to 27 points. A higher total score indicates more severe depression, with scores of 0–4 indicating no depression, 5–9 indicating mild depression, 10–14 indicating moderate depression, 15–19 indicating moderately severe depression, and 20–27 indicating severe depression [30, 31]. The Cronbach's α coefficients at the three time points in this study were 0.852, 0.845, and 0.868.

Brief Pain Inventory (BPI)

The BPI is a concise tool for rapidly assessing the severity of pain and its impact on functioning [32, 33]. In this study, pain severity was determined by calculating the arithmetic mean of four pain severity items from the questionnaire. These items included the worst pain, least pain, average pain, and current pain intensity, each scored using a 0–10 Likert scale where 0 indicates no pain and 10 indicates the most severe pain. The Cronbach's α coefficients at the three time points in this study were 0.954, 0.960, and 0.953.

Brief Fatigue Inventory (BFI)

The BFI consists of nine items, three of which measure the current severity of fatigue, usual fatigue, and worst fatigue, scored on a 0–10 Likert scale where 0 indicates no fatigue and 10 indicates the most severe fatigue. The remaining six items assess the impact of fatigue on patients' mood, general activities, walking ability, normal work (including housework), relationships with other people, and enjoyment of life and are scored on a 0–10 Likert scale, where 0 indicates no interference and 10 indicates the most severe interference [34, 35]. The total score is the average score across all items, with higher scores indicating higher levels of fatigue. The Cronbach's α coefficients at the three time points in this study were 0.969, 0.968, and 0.969.

Athens Insomnia Scale (AIS)

The AIS is a self-assessment psychometric instrument designed for quantifying sleep difficulty based on the ICD-10 criteria [36]. The first five items assess sleep induction, awakening during the night, early morning awakening, total sleep time, and sleep quality. The last three items evaluate the impact on daytime mood, functioning, and sleepiness. Scores range from 0 (no problem) to 1 (slight impact), 2 (noticeable impact), and 3 (significant impact). The total score is the sum of all items, ranging from 0 to 24, with an AIS score exceeding 6 indicating insomnia [37]. Previous studies have confirmed that the AIS is well-applied among Chinese cancer patients [38–40]. The Cronbach's α coefficients at the three time points in this study were 0.883, 0.871, and 0.884.

Statistical analysis

Data analysis was conducted using Mplus version 8.7 and SPSS version 26.0. General sociodemographic information and disease-related characteristics were analyzed descriptively. Normality tests were conducted for the data. Continuous variables that followed a normal distribution were presented as mean ± standard deviation, while non-normally distributed continuous variables were expressed as median (interquartile range). Categorical variables were presented as counts (percentages).

We employed growth mixture modeling (GMM) to explore the longitudinal trajectories of pain, fatigue, insomnia, and depression. GMM can identify classes with different changing patterns over time based on participants' temporal variations [41]. This involves categorizing participants into homogeneous classes within each category but with heterogeneous differences between categories. GMM requires presetting the number of classifications. In this study, we gradually increased the number of classifications from one category, added

trajectory classes each time, and compared model fit indices between models to determine the best fit model. For each classification, the estimation was repeated using 200 random initial values to avoid any spurious convergence toward a local maximum. Lower values of the Akaike information criterion (AIC), Bayesian information criterion (BIC), and sample-size adjusted BIC (SSA-BIC) indicate better model fit. The entropy value ranges between 0 and 1, with higher values indicating higher classification accuracy. Identifying the optimal trajectory solution with the best data fit involves examining the following indices: the Lo-Mendell-Rubin likelihood ratio test (LMR-LRT) and the bootstrap likelihood ratio test (BLRT). The statistical significance of their p values indicates that adding classes significantly improves the model fit. To determine the optimal number of latent classes, we selected the AIC, BIC, and SSA-BIC values that were minimized, along with statistically significant p values for LMR-LRT and BLRT and the maximum entropy value [42]. This process was repeated separately for pain, fatigue, insomnia, and depression. Since the ultimate aim of this study was to analyze the impact of the symptom cluster on depression, after completing longitudinal classification for these three symptoms, a latent class analysis (LCA) of the symptom cluster (pain, fatigue, and insomnia) was conducted based on the classification results of individual symptoms. Specifically, we first used Growth Mixture Modeling (GMM) to analyze individual trajectories for each symptom, then used the membership of these trajectories as input variables for Latent Class Analysis (LCA). This method allowed us to identify patient groups with similar symptom trajectories. For example, patients in Class 1 trajectories in the GMM were assigned a value of "0", and those in Class 2 trajectories were assigned a value of "1". After reassigning values for fatigue, pain, and insomnia patients, the reassigned data were analyzed using LCA. Similar to GMM analysis, LCA depends on model fit indices (e.g., AIC, BIC, SSA-BIC, LMR-LRT, and entropy) to assess model parsimony and interpretability to finalize model selection [43]. Subsequently, we conducted a backward stepwise binary logistic regression, with depression levels as the dependent variable. The independent variables included symptom cluster classifications from the LCA, along with other sociodemographic and disease-related characteristics that were significant in the univariate analysis, to investigate the factors influencing depressive.

Results

Participant characteristics

The median age of the 187 lung cancer patients undergoing chemotherapy was 57 years; 63.10% were male, and the majority of patients were married. A total of 32.62% of patients were retired, and 30.48% were unemployed. More than half of the patients had advanced-stage cancer. The sociodemographic and disease characteristics of the patients were presented in Table 1.

Model fit indices of growth mixture models for pain, fatigue, insomnia, and depression

Based on the fit indices of the class solutions, all classifications retained models with two trajectories as the

Table 1 Sociodemographic and disease-related characteristics of the participants ($N = 187$)

Variables	Mean (SD)/ Median (interquartile range)/N (%)
Age, years	
Median (interquartile range)	57 (50, 65)
BMI	
M ± SD	22.17 ± 3.06
Sex	
Male	118 (63.10)
Female	69 (36.90)
Smoking history	
No	99 (52.94)
Yes	88 (47.06)
Alcohol consumption history	
No	106 (56.68)
Yes	81 (43.32)
Marital status	
Married	167 (89.30)
Divorced / Widowed / Never married	20 (10.70)
Educational level	
Elementary school or lower	62 (33.16)
Middle school	66 (35.29)
High school / Vocational school or greater	59 (31.55)
Work status	
Working or self-employed	39 (20.86)
On sick leave	30 (16.04)
Retired	61 (32.62)
Unemployed	57 (30.48)
Monthly income, CNY	
< 3000	29 (15.51)
3000—5999	69 (36.90)
6000—8999	74 (39.57)
≥ 9000	15 (8.02)
Cancer stage	
Stage I	10 (5.35)
Stage II	22 (11.76)
Stage III	59 (31.55)
Stage IV	96 (51.34)

CNY Chinese Yuan, *BMI* body mass index

Table 2 Model fit indices of growth mixture models for pain, fatigue, insomnia, and depression

Item	Classes	AIC	BIC	SSA-BIC	Entropy	LMR-LRT (*P*)	BLRT (*P*)	Proportion
BPI	1	2423.722	2449.571	2424.231	/	/	/	1
	2	**2388.485**	**2424.027**	**2389.185**	**0.852**	**38.767(0.0240)**	**0.0000**	**43(0.22995)/144(0.77005)**
	3	2367.860	2413.095	2368.751	0.848	25.030 (0.0736)	0.0000	17(0.09091)/45(0.24064)/125(0.66845)
BFI	1	2451.793	2477.642	2452.303	/	/	/	1
	2	**2441.071**	**2476.613**	**2441.772**	**0.674**	**15.720(0.0301)**	**0.0000**	**96(0.51337)/91(0.48663)**
	3	2440.874	2486.110	2441.766	0.722	5.826(0.2426)	0.5000	64(0.34225)/62(0.33155)/61(0.32620)
AIS	1	3396.478	3422.326	3396.987	/	/	/	1
	2	**3373.458**	**3409.001**	**3374.159**	**0.866**	**27.281(0.0077)**	**0.0000**	**168(0.89840)/19(0.10160)**
	3	3349.086	3394.322	3349.978	0.868	28.553(0.0254)	0.0000	59(0.31551)/16(0.08556)/112(0.59893)
PHQ	1	3344.177	3370.026	3344.687	/	/	/	1
	2	**3325.644**	**3361.186**	**3326.344**	**0.768**	**23.064(0.0165)**	**0.0000**	**111(0.59358)/76(0.40642)**
	3	3318.231	3363.467	3319.123	0.839	12.609(0.2719)	0.0128	121(0.64706)/61(0.32620)/5(0.02674)

The best-fitting models are indicated in bold font. *AIC* Akaike Information Criteria, *BIC* Bayesian Information Criteria, *SSA-BIC* Sample-Size Adjusted BIC, *LMR-LRT* Lo-Mendell-Rubin likelihood Ratio Test, *BLRT* Bootstrap Likelihood Ratio Test

optimal solution (Table 2). For pain (BPI), although the AIC, BIC, and SSA-BIC decreased when comparing the three-class classification to the two-class classification, the statistical value of LMR-LRT was not significant ($P=0.0736$), and the entropy value decreased. Therefore, the two-class classification was chosen as the best fitting model. For fatigue (BFI) and depression (PHQ), the BIC values of the three-class classification increased compared to those of the two-class classification, and the LMR-LRT statistic was not significant. Thus, the two-class classification was chosen as the best fitting model. For insomnia (AIS), the BIC value of the three-class classification increased; hence, the two-class classification was chosen as the best fitting model.

Trajectories of pain, fatigue, insomnia and depression

Figure 1 illustrates the separate classifications of the two trajectories for pain, fatigue, insomnia, and depression. For pain, 77.00% of patients experienced an increase from 1.39 points (T1) to 1.77 points (T3), thus

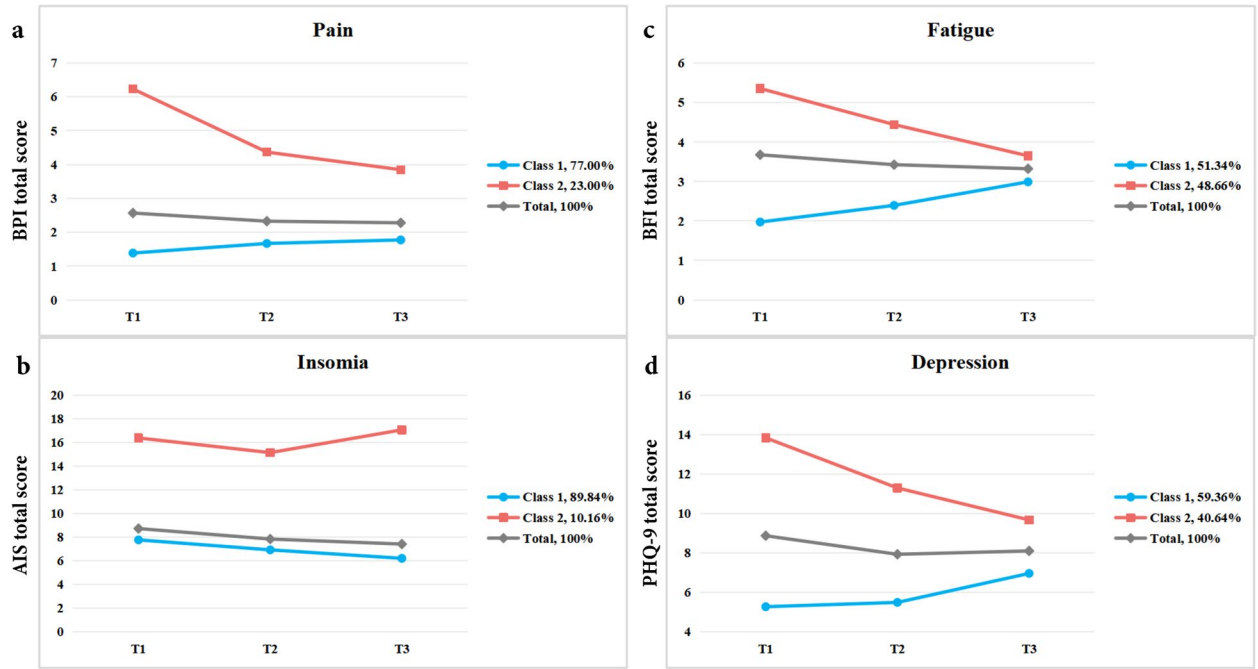

Fig. 1 Trajectories of (**a**) pain, (**b**) insomnia, (**c**) fatigue, and (**d**) depression

this class was named Low increasing (Class 1). Conversely, 23.00% of patients experienced a decrease from 6.23 points (T1) to 3.85 points (T3), thus this class was named High decreasing (Class 2). In terms of fatigue, 51.34% of patients experienced an increase from 1.97 points (T1) to 2.99 points (T3), thus this class was named Low increasing (Class 1), while 48.66% of patients experienced a decrease from 5.35 points (T1) to 3.65 points (T3), thus this class was named High decreasing (Class 2). For insomnia, 89.84% of patients experienced a decrease from 7.77 points (T1) to 6.21 points (T3), thus this class was named Low decreasing (Class 1), while 10.16% of patients experienced an initial decrease from 16.38 points (T1) to 15.14 points (T2), followed by an increase to 17.07 points (T3), thus this class was named High-decrease-increasing (Class 2). Regarding depression, 59.36% of patients experienced an increase from 5.27 points (T1) to 6.96 points (T3), thus this class was named Low increasing (Class 1), while 40.64% of patients experienced a decrease from 13.84 points (T1) to 9.67 points (T3), thus this class was named High decreasing (Class 2).

Latent categories of the fatigue-pain-insomnia symptom cluster in lung cancer patients

As the aim of this study was to explore the impact of symptom cluster severity on patient depression, we classified pain, fatigue, and insomnia using LCA. The results showed that the AIC, BIC, and SSA-BIC values of the three-class classification were higher than those of the two-class classification. Additionally, the statistical value of the BLRT was not statistically significant ($P=0.6667$). Therefore, the two-class classification was chosen as the optimal classification for the symptom cluster (Table 3). Figure 2 illustrated the two latent classes of the symptom cluster. The figure shows that patients in Class 2 had a greater probability of experiencing severe pain, fatigue, and insomnia than patients in Class 1. Thus, we named Class 2 the "High symptom cluster class" and Class 1 the "Low symptom cluster class" (Fig. 2).

Identifying important determinants of depression trajectory patterns

Sociodemographic characteristics, disease-related characteristics, and symptom cluster burden classification were treated as independent variables, while depression classification served as the dependent variable in the

Table 3 Model fit indices of latent class analysis for the symptom cluster

Item	Classes	AIC	BIC	SSA-BIC	Entropy	LMR-LRT (*P*)	BLRT (*P*)	Proportion
symptom cluster trajectory classification	1	589.663	599.356	589.854	/	/	/	1
	2	**562.741**	**585.359**	**563.187**	**0.758**	**33.329(0.0000)**	**0.0000**	**91(0.48663)/96(0.51337)**
	3	569.962	605.505	570.663	0.829	0.743(0.0116)	0.6667	36(0.19251)/138(0.73797)/13(0.06952)

The best-fitting models are indicated in bold font. *AIC* Akaike Information Criteria, *BIC* Bayesian Information Criteria, *SSA-BIC* Sample-Size Adjusted BIC, *LMR-LRT* Lo-Mendell-Rubin likelihood Ratio Test, *BLRT* Bootstrap Likelihood Ratio Test

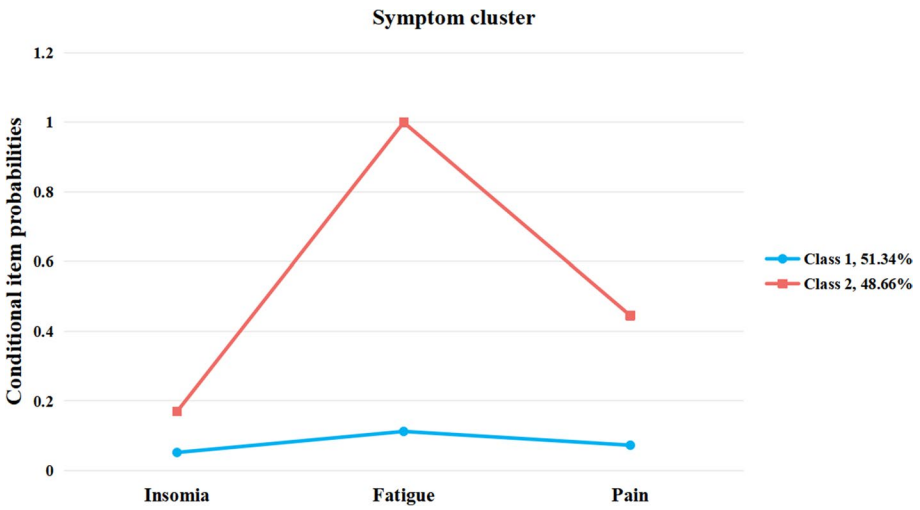

Fig. 2 Latent class analysis of the fatigue-pain-insomnia symptom cluster trajectory classification

univariate analysis. For symptom cluster burden classification, patients with a low symptom cluster class in the LCA were assigned a score of 0, while those with a high symptom cluster class were assigned a score of 1. For depression classification, patients categorized under the low increasing depression class were assigned a score of 0, and those classified under the high decreasing depression class were assigned a score of 1. The results revealed statistically significant differences in age, smoking history, alcohol consumption history, work status, monthly income, and symptom cluster burden classification (Supplementary Table 1). Variables showing statistical significance in the univariate analysis were included in the binary logistic regression analysis. The results indicated that patients who had an alcohol consumption history (OR = 2.694, 95% CI: 1.300—5.584), had a high symptom cluster burden (OR = 9.031, 95% CI: 4.276—19.073), were on sick leave (OR = 4.144, 95% CI: 1.235—13.899) or were in retirement (OR = 3.349, 95% CI: 1.166—9.618) were more likely to experience a high depression burden trajectory. Conversely, patients with lower monthly incomes (OR = 0.504, 95% CI: 0.177—1.430 for income between 3000 and 5999; OR = 0.318, 95% CI: 0.111—0.914 for income between 6000 and 8999; OR = 0.198, 95% CI: 0.042—0.922 for income ≥ 9000) were more likely to experience a low depression burden trajectory (Table 4).

Table 4 Identifying important determinants of a high depression trajectory

Predictors	*β*	S.E	*P*	OR (95% CI)
Alcohol consumption history				
No	Ref			
Yes	0.991	0.372	0.008*	2.694 (1.300, 5.584)
Symptom cluster burden classification				
Low	Ref			
High	2.201	0.381	< 0.001*	9.031 (4.276, 19.073)
Work status			0.087	
Working or self-employed	Ref			
On sick leave	1.422	0.617	0.021*	4.144 (1.235, 13.899)
Retired	1.209	0.538	0.025*	3.349 (1.166, 9.618)
Unemployed	0.858	0.545	0.115	2.359 (0.811, 6.863)
Monthly income, CNY			0.098	
< 3000	Ref			
3000—5999	-0.686	0.532	0.198	0.504 (0.177, 1.430)
6000—8999	-1.146	0.538	0.033*	0.318 (0.111, 0.914)
≥ 9000	-1.621	0.785	0.039*	0.198 (0.042, 0.922)
Constant	-2.074	0.648	0.001	

* Correlation is significant at the 0.05 level (2-tailed). *OR* odds ratio, *95% CI* 95% confidence interval

Discussion

Trajectories of depression

This study identified two trajectories of depression in lung cancer patients undergoing chemotherapy based on longitudinal data, with "low increasing" accounting for 59.36% and "high decreasing" accounting for 40.64%. Previous studies have also identified these two trajectory patterns. Longitudinal studies by Kurtz [44], Stommel [22], and Chang [23] showed a decrease in depression levels over time. However, Boyes [45] reported no decrease in depression during the first year after diagnosis, Andersen [24] reported a slight increase in depression before the decline, and McFarland [46] reported an increase in depression levels over time. The differences observed among these research findings may be attributed to variations in demographic characteristics, follow-up intervals, or differences in the tools used to measure depression symptom. These differences also confirm the heterogeneity in the developmental trajectories of depression. The results of this study indicated that 59.36% of patients experienced worsening depressive after the first chemotherapy session. The reasons for such worsening could be long-term accumulated psychological stress, persistent physical discomfort, and insufficient social support [47]. This finding suggests the need for routine psychological screening during the patient survival period to achieve the goal of "early detection, early intervention". Additionally, at Nanfang Hospital, patients only receive routine oncology care and conventional health guidance such as smoking cessation, alcohol abstinence, and exercise, with minimal access to social services care or psycho-oncological care. In the future, training in psychological education and self-management techniques can be offered to help patients understand their emotional changes and learn how to effectively cope with the psychological stress.

Predictors of the trajectory class

Considering the diverse progression of depressive symptoms among individuals, exploring the predictive factors of trajectory categories can provide insights for precision management in the future. The results of this study indicate that the "high decreasing" trajectory and the "low increasing" trajectory can be predicted by factors such as alcohol history, symptom cluster burden, work status, and monthly income. First, lung cancer patients with a history of alcohol consumption who are undergoing chemotherapy are more likely to belong to the "high decreasing" depression class. This finding is consistent with the study by Chau [48], who found through a cross-sectional survey that an alcohol consumption history is a risk factor for depression in lung cancer patients. However, in a survey of newly diagnosed lung cancer patients, Shahedah [18] found no association between

alcohol consumption history and depressive symptoms. The reasons for this difference may be related to differences in the characteristics of the study populations and variations in the measurement standards for alcohol consumption. Large-scale longitudinal studies are needed in the future to validate the impact of alcohol consumption on depression. Furthermore, lung cancer patients with more severe symptoms in the "fatigue-pain-insomnia" symptom cluster (high symptom cluster class) were more likely to belong to the "high decreasing" depression class. Two longitudinal studies have also highlighted the importance of symptom management for depression among lung cancer patients [22, 44]. In addition, Lee [21] found fatigue to be a factor influencing depression, Park [49] found pain to be a risk factor for depression, and Riemann [50] suggested that insomnia and depression are inseparable. Another study proposed the selection of antidepressants based on this symptom cluster [51]. Such consistent conclusions may be due to the shared inflammatory response mechanisms among these symptoms [46, 52]. Therefore, future depression interventions may need to consider incorporating the severity of the "fatigue-pain-insomnia" symptom cluster [53].

With the aging population and improved cancer survival rates, an increasing number of cancer patients are experiencing financial toxicity. The results of this study indicated that patients who are currently on sick leave, are retired, are unemployed, or have lower monthly incomes are more likely to belong to the "high decreasing" depression class. A review indicated that compared to nonworking cancer survivors, employed cancer survivors have a lower prevalence of depression [54]. Andersen's study also indicated that patients with severe depressive symptoms have more limited social and economic resources [55]. Employment is a significant factor in fulfilling social needs, and not being employed implies a decline in participation in social activities, which is closely related to mental health [56, 57]. Employment status facilitates patients' participation in social interactions, and clinical practitioners should encourage capable patients to continue working. Economic income is also associated with the trajectory of depression development. The results of this study indicate that patients with lower monthly incomes are more likely to belong to the "high decreasing" trajectory. Previous studies have also indicated that lower economic status tends to be an adverse prognostic factor for cancer patients [58, 59]. Lung cancer incurs the highest treatment costs among all cancers, imposing significant economic burdens on patients and their families [60, 61]. Additionally, lung cancer survivors face higher unemployment rates and reduced income compared to the general population, highlighting the persistent impact of financial toxicity [62]. Frequent chemotherapy treatments lead to increased costs for treatment, transportation, and nutritional supplements, further exacerbating economic toxicity and making lung cancer patients more susceptible to depression. This underscores the need for policymakers to optimize health insurance policies to alleviate the financial toxicity on patients. Furthermore, attending physicians can discuss the potential economic toxicity of treatments with patients and provide information on financial assistance and available resources.

In our study, although age and smoking history were significantly associated with depression in univariate analysis, they did not retain statistical significance in the final model. This suggests that, after controlling for the effects of other variables, age and smoking history were no longer independent predictors of depression. This may be due to the influence of age and smoking history being overshadowed by stronger effects of other variables in the model. Therefore, we recommend that future research further explore the relationship between age, smoking history, and depression, and consider validation in larger samples.

This study also has several limitations. We selected patients from only a single medical center, which may limit the representativeness of the sample among lung cancer patients undergoing chemotherapy. Additionally, the relatively short follow-up period in this study may have affected the trajectory shapes. Therefore, multicenter, long-term longitudinal studies are needed to validate the results of this study.

Conclusions

This study revealed that the trajectories of depression and the fatigue-pain-insomnia symptom cluster in lung cancer patients from the first to the fourth month post-chemotherapy followed two distinct patterns. This finding underscores the necessity for healthcare providers to conduct regular follow-ups throughout the treatment process and to develop personalized intervention strategies based on patients' specific depression trajectories. Additionally, the study identified key predictors influencing the trajectories of depression. Among demographic characteristics, a history of alcohol consumption, employment status, and monthly income level were significant predictors. This suggests that healthcare providers should pay close attention to these factors for early identification and intervention of patients at risk for depression. Furthermore, the severity of the fatigue-pain-insomnia symptom cluster was also a significant factor affecting depression. Therefore, future interventions targeting depression should consider incorporating symptom cluster management to achieve more comprehensive and effective treatment outcomes.

Abbreviations

PHQ-9	Patient Health Questionnaire-9
BPI	Brief Pain Inventory
BFI	Brief Fatigue Inventory
AIS	Athens Insomnia Scale
GMM	Growth Mixture Modeling
NCCN	The National Comprehensive Cancer Network
OR	Odds Ratio
95% CI	95% Confidence Interval
DSM	Diagnostic and Statistical Manual of Mental Disorders
LMR-LRT	Lo-Mendell-Rubin Likelihood Ratio Test
BLRT	Bootstrap Likelihood Ratio Test
AIC	Akaike Information Criterion
BIC	Bayesian Information Criterion
SSA-BIC	Sample-size Adjusted BIC
LCA	Latent Class Analysis
CNY	Chinese Yuan
BMI	Body Mass Index

Supplementary Information

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Supplementary Material 1.

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Authors' contributions
YYL and DMM conducted the initial analyzes and wrote original draft; YYL, DMM, LZ and BXZ collected the data; JXM and ZHY supervised data collection and revised the manuscript; LLZ designed the study. All authors critically reviewed the manuscript and approved the final manuscript. YYL and DMM contributed equally as co-first authors.

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Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study has been reviewed and approved by the Ethics Committee of Nanfang Hospital, Southern Medical University (NFEC-2023–540). All procedures conducted in this study adhere to the Declaration of Helsinki. Eligible participants provided written informed consent before completing the survey.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

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