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Coping and health-related quality of life in patients with advanced lung cancer: The mediating role of positive and negative mood

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Keywords:	coping, quality of life, lung cancer, mood

Coping and health-related quality of life in patients with advanced lung cancer: The mediating role of positive and negative mood

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Abstract

Objectives: The ways patients coping with the life-threatening illness can influence their health-related quality of life (HRQoL). This study aims to examine the mediating role of positive and negative mood in the relationship between coping and HRQoL in patients with advanced lung cancer.

Methods: A sample of 261 patients (mean age: 59.99±9.53) with diagnosis of stage III or IV lung cancer was recruited from the inpatient unit in a hospital that specializes in chest-related disease in Shanghai, China. Participants completed measurements including Medical Coping Modes Questionnaire, Positive and Negative Affect Schedule, and 5-level EuroQol 5-dimension instrument.

Results: Despite the total effects of confrontation on HRQoL were not significant, competing indirect effects via mood were identified: (1) Positive indirect effects were found for confrontation on mobility, usual activities, pain/discomfort, and overall utility index through positive mood; (2) Negative indirect effects were found for confrontation on mobility, pain/discomfort, anxiety/depression, and overall utility index through negative mood. Resigned acceptance was negatively associated with HRQoL, and consistent indirect effects via mood were identified: (1) Negative indirect effects were found for resigned acceptance on mobility, self-care, usual activities, pain/discomfort, and overall utility index through positive mood; (2) Negative indirect effect were found for resigned acceptance on domains of HRQOL and overall utility index through negative mood.

Conclusions: Confronting advanced lung cancer can fuel ambivalent emotional experiences, which contribute to health outcomes. Nevertheless, accepting the illness in a resigned way can be maladaptive for health outcomes. Interventions are suggested to consider the role of

positive and negative mood, and their relationships with coping to help to improve or maintain quality of life in patients with advanced lung cancer.

Keywords: coping; quality of life; mood; lung cancer

Strengths and limitations of this study

- The study addressed health-related quality of life (HRQoL), an important health outcome of treatment for advanced lung cancer, and examined the psychological factors associated with HRQoL.
- The study examined the mediating role of positive and negative mood in relationship between coping and a range of health outcomes (mobility, self-care, usual activities, pain/discomfort, anxiety/depression, overall HRQoL), which identifies the potential pathways between coping and HRQoL in patients with advanced lung cancer.
- Convenience sampling could compromise the generalizability of the findings.
- Cross-sectional design.

1. Introduction

During the past decade, lung cancer has become a major cause of cancer incidence and mortality in China and many other countries [1, 2]. Lung cancer survival rates are poor, with a five-year survival rate in China of 16.1% [3]. As curative treatments are limited for advanced lung cancer, improving or maintaining quality of life is the main focus of treatment. Prognostic value of health-related quality of life (HRQoL) in patients with lung cancer is supported by a number of studies [4, 5]. In addition, positive mood is associated with increased longevity [6, 7], independent of negative affect, prior medical conditions, functional status and self-rated health [6].

The diagnosis of lung cancer can result in enormous stress for patients and their families, such as symptom burden [8], decisions about treatment options [9], and financial concerns [10]. The quality of life is significantly affected in patients with an advanced lung cancer [11]. Previous research has investigated correlates of HRQoL in cancer patients, such as sociodemographic characteristics (e.g., older age, being female), clinical factors (e.g., stage, metastasis, time since diagnosis, treatment options), and psychosocial factors (e.g., coping, social support) [12]. Specifically, the manner in which patients cope with the life-threatening illness is indicated to contribute to mood and HRQoL in patients with advanced cancer [13, 14]. Two coping strategies, confrontation and resigned acceptance, are regarded as important in cancer patients [15]. Confrontation is a form of active coping that involves seeking information from various sources, asking for advice, and cognitive redefinition [15]. Some studies indicated that confrontation was adaptive for cancer patients, which was associated with less negative mood [16-18], and better quality of life [19, 20]. However, other studies found insignificant associations between confrontation and health outcomes among cancer patients [21-23]. For instance, Nipp et al. [23] studied 350 patients with incurable lung or gastrointestinal cancer, and found that using active coping was not

associated with psychological distress or quality of life. It is suggested that confrontation could direct one's attention to the disease and its side effects, making it less effective in coping with cancer [15, 19]. On the other hand, resigned acceptance is a form of passive coping, in which individuals accept the stressful situation without endeavors to alter it [24, 25]. Research shows that resigned acceptance could be maladaptive, which was associated with less favorable outcomes, such as negative mood and low quality of life, in cancer patients and survivors [21, 26, 27].

Although research shows that coping is associated with HRQoL in cancer patients, the mechanism of the link between coping and HRQoL remains largely unexamined in cancer patients. Preliminary exploration suggests that behavioral, cognitive, mood factors may be potential pathways between coping and health outcomes [28-32]. Studies among cancer patients and survivors indicate that negative mood is associated with poor HRQOL, whereas positive mood is associated with better HRQoL [27, 33, 34]. Negative and positive mood involves different physiological responses (e.g., nervous, endocrine, and immune system functioning), which can influence overall physical health [35, 36]. Additionally, the broaden-and-build theory of positive mood indicates that positive mood can broaden one's attention scope and thought-action repertoires, which could be beneficial for physical health; In contrast, negative mood can fueled a narrowed, socially isolating thought-action tendencies, which could result in poor health outcomes [37, 38]. Several studies examined the mediating role of mood in linking coping and health outcomes [30-32]. For instance, in a prospective study among HIV caregivers, higher social coping predicted an increase in positive affect, which decreased levels of physical symptoms, whereas higher cognitive avoidance predicted enhanced negative affect, which resulted in higher levels of physical symptoms [30]. In another study involving a sample of hypertensive patients, depressive symptoms were found to mediate the relationship between emotional coping and quality of life [32]. However, in

the context of advanced cancer, to our knowledge, no study has examined the possible pathways between coping and HRQoL. Since patients with advanced cancer can encounter numerous stress, understanding the effect of coping on health and identifying the pathways through which patients maintain health and quality of life can provide important insights for clinical practice and interventions.

Taken together, the current study addresses the relationships between coping, mood, and HRQoL among patients with advanced lung cancer. We examined the effect of confrontation and resigned acceptance coping on positive mood, negative mood, and HRQoL, and tested mediating role of positive and negative mood in the relationship between coping and HRQoL.

2. Method

2.1 Participants and Public Involvement

Participants were recruited from the inpatient unit of the department of chest-oncology medicine at a public hospital that specializes in chest-related disease in Shanghai, China. The hospital is well recognized for its expertise, resources, and treatments for chest-related disease. A large number of patients with lung cancer in east China come to this hospital and receive treatment there. Patients were eligible in the study if they (a) were 18 years or older, (b) had been diagnosed with lung cancer, (c) had an expected survival time > 3 months, (d) had no significant cognitive impairment, and (e) were able to communicate with interviewers. Those who could not understand the questions were excluded from the sample. Between June 2016 and July 2016, 328 patients met the inclusion criteria and were enrolled in the study.

Data collection was conducted by trained undergraduate students majoring in medicine and public health. Doctors and nurses at the inpatient unit of department of chest-

oncology medicine recommended the eligible patients, and researcher approached them and introduced the study. Those who agreed to participate in the study provided informed consent. Face-to-face interviews were then conducted. Disease and treatment information was extracted from medical records. The study was approved by the Ethics Committee of Shanghai Chest Hospital, Shanghai Jiao Tong University (No. KS1353). According to our study aim, we focused on 267 patients with advanced-stage lung cancer (stage III or IV), and 261 participants who provided full information on the main study variables (coping, mood, and HRQoL) were included in the data analysis.

2.2 Measures

2.2.1 Health-related quality of life. The 5-level EuroQol 5-dimension (EQ-5D-5L) was used to measure HRQoL in this study [39]. It contained five questions to assess five health dimensions, as experienced in the recent days, namely mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Respondents rated the severity on 5 levels: “no” (1), “only a little” (2), “moderate” (3), “severe” (4), and “very severe” (5). In the current study, EQ-5D-5L domain scores and overall utility index were calculated. Domain scores were recoded reversely based on the original levels of each domain, with higher scores indicating better quality in the domain. EQ-5D-5L utility index was calculated based on value sets developed by the EuroQol Group. To our knowledge, no value sets have been developed in the Chinese representative sample for the calculation of utility index, and in this study, utility index was calculated based on value sets weighted from a representative sample of the English general population [40]. The EQ-5D-5L utility index ranged from -1 to 1, with 1 representing full health, 0 representing a state of death, and negative values representing a state worse than death.

2.2.2 Coping. Two subscales of the Chinese version of the Medical Coping Modes Questionnaire (MCMQ) were used to measure confrontation and resigned acceptance coping styles for lung cancer. MCMQ was developed by Feifel, Strack, and Nagy [15] among patients with a variety of life-threatening and chronic illnesses, and it is widely used for assessing coping strategies in patients in China [19, 41]. In the original questionnaire, acceptance-resignation had five items, and confrontation had eight items [15]. One item in the confrontation subscale assessing how often participants "obtained information through books, magazines, and newspapers in the past several months", in addition to that, we added one item assessing how often participants "obtained information through the Internet and new media in the past several months", as the Internet and new media have become important sources of information that supplement books, magazines, and newspaper. All the items were rated on a 4-point Likert scale ranging from 1 (*never*) to 4 (*very often*). The mean score of each coping style was calculated, with a higher score indicating higher probability of using that particular coping strategy. The Cronbach's α coefficients of confrontation and resigned acceptance in this study were 0.72 and 0.71, respectively.

2.2.3 Mood. Mood was measured using the Positive and Negative Affect Schedule (PANAS) in the current study [42]. The PANAS contained items to describe 10 positive affects (e.g., inspired, excited, determined) and 10 negative affects (e.g., afraid, upset, distressed). Respondents rated their experiences of each affect during the past two weeks on a 5-point Likert scale ranging from 1 (*very slightly*) to 5 (*extremely*). The mean scores of items on the two subscales were calculated for positive mood and negative mood, respectively. In the current study, the Cronbach's α coefficients of negative mood and positive mood were 0.91 and 0.86, respectively.

2.2.4 Covariates. Sociodemographic factors included age, gender, education (elementary school or lower, middle school, high school, college or higher), and marital

status (married, single, divorced, widowed). Perceived cancer-related financial burden was assessed by the question, "Have your disease and treatment caused you and your family financial difficulty", and participants answered on a 5-point scale ranging from 0 (*No*) to 4 (*Very much*). Clinical factors included time of diagnosis, cancer stage, lung cancer type (adenocarcinoma, squamous, poorly differentiated, small cell, not otherwise specified), metastasis (none, one location, multi-locations), and received treatment (surgery, chemotherapy, radiotherapy, targeted therapy).

2.3 Data Analysis

First, descriptive statistics were presented for sociodemographic and clinical characteristics, and main study variables. Mean and standard deviation, or frequency and percentage, were computed for continuous and categorical variables, respectively. Independent *t* test, analysis of variance, and post-hoc comparison were conducted to analyze the effect of sociodemographic and clinical factors on positive mood, negative mood, and HRQoL. Correlational analyses were performed to examine the associations between the continuous variables.

Second, multivariate, hierarchical, linear regression analyses were employed to examine the relationships among coping, mood, and HRQoL. The stepwise regressions with HRQoL (domain scores and EQ-5D utility index) as dependent variable involved three steps: In step one, gender, age, cancer stage, and covariates that were significantly correlated with mood and HRQoL (i.e., financial burden, poorly differentiated lung cancer, small cell lung cancer, received radiotherapy) were entered; In step two, confrontation and resigned acceptance were entered; In step three, positive and negative mood were entered.

Third, the mediating effects of positive and negative mood in the relationship between coping and HRQoL were tested using the MEDIATE macro for SPSS developed by Preacher

and Hayes [43]. Bootstrapping techniques using 5000 samples were used for the analysis, which was regarded as providing a more reliable estimate for the small sample size. Significant indirect effect was indicated by a 95% confidence interval of indirect effect without zero. All tests were two tailed, and a *p*-value of <0.05 was considered statistically significant.

3. Results

3.1 Sociodemographic and Clinical Characteristics

The sociodemographic and clinical characteristics for the samples are shown in Table 1. A total sample of 261 participants had a mean age of 59.99 years (*SD* = 9.53). Males represented 70.1% of the samples. Most participants were married (94.6%) and perceived a slight to very severe cancer-related financial burden (85.8%). More than half of the participants had been diagnosed in the past 6 months (55.2%), and multi-locations metastasis was present in 29.1% of the participants. More than 90% of the participants received chemotherapy (96.6%), whereas a certain proportion had ever received surgery (23.4%), radiotherapy (23.4%), or targeted therapy (14.6%).

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Table 1 Sample Characteristics

Variables	M(SD) / n (%)	Positive mood	Negative mood	Mobility	Self-care	Usual activities	Pain/ discomfort	Anxiety/ depression	EQ-5D utility index
Age (years)	59.99 (9.53)								
Gender									
Male	183 (70.1%)	2.41 (0.75)	1.80 (0.73)	4.39 (0.95)	4.63 (0.79)	4.33 (0.92)	4.03 (0.87)	4.24 (0.75)	0.81 (0.17)
Female	78 (29.9%)	2.34 (0.78)	1.93 (0.83)	4.21 (1.04)	4.50 (0.96)	4.06 (1.05)	3.91 (0.87)	4.21 (0.65)	0.78 (0.21)
Education									
Elementary school or lower	55 (21.1%)	2.28 (0.79)	1.82 (0.73)	4.54 (0.92)	4.64 (0.80)	4.31 (0.96)	3.98 (0.91)	4.11 (0.74)	0.80 (0.18)
Middle school	91 (34.9%)	2.35 (0.69)	1.94 (0.79)	4.24 (0.96)	4.57 (0.86)	4.14 (1.04)	3.90 (0.87)	4.16 (0.79)	0.78 (0.19)
High school	66 (25.3%)	2.46 (0.77)	1.71 (0.63)	4.32 (1.08)	4.59 (0.89)	4.29 (0.96)	4.05 (0.79)	4.32 (0.66)	0.82 (0.17)
College or higher	49 (18.8%)	2.51 (0.84)	1.83 (0.88)	4.41 (0.96)	4.59 (0.84)	4.35 (0.86)	4.10 (0.94)	4.35 (0.63)	0.83 (0.20)
Marital status									
Married	247 (94.6%)	2.40 (0.77)	1.83 (0.76)	4.34 (0.98)	4.60 (0.85)	4.25 (0.98)	3.98 (0.89)	4.23 (0.71)	0.80 (0.19)
Single/divorced/ widowed	14 (5.4%)	2.23 (0.58)	1.86 (0.82)	4.21 (1.05)	4.57 (0.85)	4.29 (0.83)	4.21 (0.58)	4.07 (1.00)	0.78 (0.18)
Perceived cancer-related financial burden									
None	37 (14.2%)	2.72 (0.89)	1.47 (0.50)	4.86 (0.42)	4.92 (0.28)	4.81 (0.46)	4.51 (0.56)	4.59 (0.50)	0.92 (0.08)

Slight	100 (38.3%)	2.27 (0.74)	1.74 (0.63)	4.21 (1.09)	4.54 (0.88)	4.23 (0.91)	3.91 (0.79)	4.22 (0.56)	0.78 (0.19)
Moderate	63 (24.1%)	2.53 (0.80)	1.87 (0.74)	4.43 (0.86)	4.65 (0.79)	4.17 (0.98)	3.90 (0.93)	4.27 (0.70)	0.80 (0.18)
Severe	36 (13.8%)	2.16 (0.51)	1.94 (0.84)	4.25 (0.77)	4.64 (0.68)	4.22 (0.90)	4.06 (1.01)	4.19 (0.71)	0.82 (0.14)
Very Severe	25 (9.6%)	2.38 (0.62)	2.52 (1.02)	3.96 (1.34)	4.12 (1.33)	3.76 (1.42)	3.68 (0.95)	3.64 (1.19)	0.68 (0.26)
Time since diagnosis									
Less than 6 months	144 (55.2%)	2.38 (0.77)	1.84 (0.77)	4.40 (0.96)	4.60 (0.84)	4.24 (1.02)	3.95 (0.90)	4.19 (0.76)	0.80 (0.19)
6-12months	32 (12.3%)	2.54 (0.68)	1.91 (0.72)	4.19 (1.28)	4.50 (1.05)	4.19 (1.12)	4.19 (0.78)	4.19 (0.82)	0.79 (0.23)
12-24 months	31 (11.9%)	2.54 (0.87)	1.71 (0.75)	4.35 (0.80)	4.71 (0.53)	4.42 (0.62)	3.97 (0.71)	4.32 (0.65)	0.83 (0.11)
More than 24 months	46 (17.6%)	2.25 (0.72)	1.86 (0.75)	4.17 (1.00)	4.48 (0.96)	4.17 (0.93)	3.91 (0.96)	4.26 (0.61)	0.78 (0.20)
Stage									
III	82 (31.4%)	2.50 (0.71)	1.96 (0.90)	4.35 (0.93)	4.55 (0.86)	4.20 (1.09)	3.95 (0.94)	4.13 (0.78)	0.79 (0.19)
IV	179 (68.6%)	2.34 (0.78)	1.78 (0.68)	4.33 (1.00)	4.61 (0.84)	4.28 (0.91)	4.01 (0.84)	4.27 (0.69)	0.81 (0.18)
Lung cancer type									
Adenocarcinoma	140 (53.6%)	2.39 (0.78)	1.88 (0.79)	4.28 (0.99)	4.56 (0.85)	4.20 (0.94)	3.91 (0.92)	4.18 (0.70)	0.79 (0.19)
Squamous	47 (18.0%)	2.50 (0.81)	1.84 (0.80)	4.45 (0.85)	4.68 (0.63)	4.32 (0.86)	4.00 (0.81)	4.26 (0.57)	0.81 (0.14)
Poorly differentiated	24 (9.2%)	2.46 (0.61)	1.77 (0.67)	4.08 (1.25)	4.38 (1.21)	3.88 (1.39)	3.75 (0.94)	4.13 (0.99)	0.72 (0.24)
Small cell	43 (16.5%)	2.26 (0.76)	1.76 (0.71)	4.49 (0.96)	4.67 (0.87)	4.49 (0.88)	4.26 (0.73)	4.35 (0.78)	0.85 (0.17)
Not otherwise	7 (2.7%)	2.30 (0.60)	1.64 (0.40)	4.71 (0.49)	5.00 (0.00)	4.71 (0.49)	4.71 (0.49)	4.57 (0.53)	0.92 (0.10)

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specified									
Metastasis									
None	85 (32.6%)	2.43 (0.68)	1.96 (0.88)	4.40 (0.85)	4.55 (0.85)	4.25 (1.01)	3.91 (0.91)	4.22 (0.70)	0.80 (0.19)
One location	100 (38.3%)	2.40 (0.83)	1.77 (0.78)	4.32 (1.06)	4.68 (0.75)	4.35 (0.89)	4.12 (0.78)	4.24 (0.77)	0.81 (0.17)
Multi-locations	76 (29.1%)	2.34 (0.75)	1.78 (0.57)	4.29 (1.02)	4.53 (0.96)	4.13 (1.01)	3.92 (0.93)	4.21 (0.70)	0.79 (0.20)
Treatment									
Received surgery									
Yes	61 (23.4%)	2.49 (0.78)	1.95 (0.85)	4.20 (0.98)	4.51 (0.83)	4.20 (0.96)	3.97 (0.86)	4.30 (0.74)	0.80 (0.18)
No	200 (76.6%)	2.36 (0.75)	1.80 (0.73)	4.38 (0.98)	4.62 (0.85)	4.27 (0.97)	4.00 (0.88)	4.21 (0.72)	0.80 (0.19)
Received chemotherapy									
Yes	252 (96.6%)	2.40 (0.76)	1.83 (0.76)	4.33 (0.99)	4.59 (0.86)	4.25 (0.98)	4.00 (0.87)	4.22 (0.73)	0.80 (0.19)
No	9 (3.4%)	2.16 (0.68)	1.83 (0.72)	4.44 (0.73)	4.67 (0.50)	4.33 (0.71)	3.67 (1.00)	4.33 (0.50)	0.81 (0.16)
Received radiotherapy									
Yes	61 (23.4%)	2.36 (0.70)	2.04 (0.87)	4.05 (1.19)	4.33 (1.21)	4.02 (1.09)	3.74 (1.05)	4.13 (0.62)	0.74 (0.23)
No	200 (76.6%)	2.40 (0.78)	1.77 (0.71)	4.43 (0.89)	4.68 (0.69)	4.33 (0.92)	4.07 (0.80)	4.26 (0.75)	0.82 (0.16)
Received targeted therapy									
Yes	38 (14.6%)	2.24 0.79)	1.83 (0.56)	4.21 (1.14)	4.47 (1.08)	4.11 (1.09)	3.79 (1.04)	4.26 (0.64)	0.77 (0.25)
No	223 (85.4%)	2.42 (0.75)	1.83 (0.79)	4.36 (0.95)	4.61 (0.80)	4.28 (0.95)	4.03 (0.84)	4.22 (0.74)	0.81 (0.17)

Scale range: Confrontation, resigned acceptance: 1 (never) – 4 (very often); Positive mood, negative mood: 1 (very slightly) – 5 (extremely); Mobility, self-care, usual activities, pain/discomfort, anxiety/depression: 1 (very severe) – 5 (no); EQ-5D utility index: -1 (worse than death) – 1 (full health)

Age was inversely correlated with positive mood (r = -0.14, p = 0.030), but not with negative mood and HRQoL. Perceived cancer-related financial burden was associated with health outcomes. Patients reporting no perceived financial burden had lower negative mood, and higher levels of positive mood and HRQoL (mobility, usual activities, pain/discomfort, anxiety/depression, and EQ-5D utility index), compared with those reporting financial burden ranging from slight to severe.

Analysis of variance test found HRQoL differed in lung cancer type, as those with poorly differentiated lung cancer had slightly lower EQ-5D utility index (M = 0.72, SD = 0.24) compared with those with small cell lung cancer (M = 0.85, SD = 0.17). Moreover, independent t test showed that the HRQoL and negative mood differed significantly in terms of having received radiotherapy. Patients treated with radiotherapy showed significantly lower EQ-5D utility index (M = 0.74, SD = 0.23) and reported more negative affect (M = 20.38, SD = 8.72) than those that were not (EQ-5D utility index: M = 0.82, SD = 0.16; Negative mood: M = 17.73, SD = 7.15). Other sociodemographic and clinical characteristics did not show a significant association with mood and HRQoL.

3.2 Coping, Mood, and HRQoL

Pearson correlation analysis was performed to examine the relationships between coping, mood, and HRQoL (see Table 2). A positive correlation was observed between confrontation coping and positive mood (r = 0.21). Resigned acceptance was positively correlated with negative mood (r = 0.46), but inversely correlated with positive mood (r = -0.27). Use of resigned acceptance was correlated with more difficulties in mobility (r = -0.21), self-care (r = -0.19), usual activities (r = -0.19), pain/discomfort (r = -0.19), anxiety/depression (r = -0.41), and lower EQ-5D utility index (r = -0.28).

Table 2 Correlation among coping, affect and HRQOL

	M (SD)	1	2	3	4	5	6	7	8	9
1. Confrontation	2.37 (0.49)	1								
2. Resigned acceptance	1.92 (0.62)	-0.03	1							
3. Positive mood	2.40 (0.76)	0.21**	-0.27**	1						
4. Negative mood	1.84 (0.76)	0.11	0.46**	-0.11	1					
5. Mobility	4.32 (0.99)	-0.05	-0.21**	0.19**	-0.28**	1				
6. Self-care	4.58 (0.86)	-0.06	-0.19**	0.15*	-0.28**	0.78**	1			
7. Usual activities	4.24 (0.97)	-0.10	-0.19**	0.16*	-0.27**	0.78**	0.73**	1		
8. Pain/discomfort	3.98 (0.87)	-0.08	-0.19**	0.14*	-0.28**	0.45**	0.43**	0.46**	1	
9. Anxiety/depression	4.22 (0.73)	-0.03	-0.41**	0.19**	-0.50**	0.21**	0.21**	0.25**	0.27**	1
10. EQ-5D utility index	0.80 (0.19)	-0.10	-0.28**	0.20**	-0.38**	0.84**	0.82**	0.84**	0.69**	0.45**

*p<0.05, **p<0.01

Hierarchical regression analyses were used to examine the relationship of confrontation and resigned acceptance coping with positive mood, negative mood, and HRQoL (see Table 3). Age, gender, cancer stage, and significant covariates found in descriptive statistics, including perceived cancer-related financial burden, having received radiotherapy, and lung cancer type (poorly differentiated versus small cell), were controlled in the hierarchical regression analyses. Regarding positive mood, in addition to covariates, confrontation and resigned acceptance were found to be significant factors, as confrontation was associated with higher positive mood ($\beta = 0.19$, $p = 0.002$), whereas resigned acceptance was associated lower positive mood ($\beta = -0.25$, $p < 0.001$). Regarding negative mood, in addition to covariates, confrontation and resigned acceptance were significant factors, as use of confrontation ($\beta = 0.11$, $p = 0.040$) and resigned acceptance ($\beta = 0.44$, $p < 0.001$) were associated with higher negative mood.

Regarding the EQ-5D domain scores, after controlling sociodemographic and clinical covariates, confrontation was not associated with all domains, whereas resigned acceptance was inversely associated with all domains. Positive mood was associated with less difficulty in mobility, usual activities, pain/discomfort, but not associated self-care and anxiety/depression. Negative mood was negatively associated with more difficulty in all domains.

Regarding EQ-5D utility index, after controlling sociodemographic and clinical covariates, resigned acceptance was inversely associated with EQ-5D utility index ($\beta = -0.22$, $p < 0.001$), whereas confrontation was not associated with EQ-5D utility index. Moreover, the effects of mood on EQ-5D utility index were significant, as positive mood was associated with higher EQ-5D utility index ($\beta = 0.17$, $p = 0.005$), whereas negative mood was associated with lower EQ-5D utility index ($\beta = -0.28$, $p < 0.001$).

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Table 3 Multiple regression results for predictors of mood and HRQOL

	Positive mood		Negative mood		Mobility		Self-care		Usual activities		Pain / discomfort		Anxiety / depression		EQ-5D utility index	
	β^e	*p*	β^e	*p*	β^e	*p*	β^e	*p*	β^e	*p*	β^e	*p*	β^e	*p*	β^e	*p*
Step 1																
Age	-0.15	**0.021**	-0.04	0.53	-0.13	**0.040**	-0.13	**0.046**	-0.06	0.31	-0.07	0.25	0.01	0.91	-0.10	0.09
Gender [a]	-0.07	0.32	0.05	0.40	-0.07	0.29	-0.06	0.35	-0.09	0.15	-0.01	0.85	0.02	0.76	-0.03	0.68
Financial burden [d]	-0.14	0.032	0.30	**<0.001**	-0.16	**0.010**	-0.15	**0.017**	-0.20	**0.002**	-0.15	**0.018**	-0.25	**<0.001**	-0.22	**0.001**
Cancer stage [b]	-0.09	0.16	-0.07	0.22	0.00	0.99	0.05	0.46	0.03	0.67	0.04	0.58	0.04	0.51	0.04	0.53
Cancer type-poorly differentiated [c]	0.01	0.93	-0.03	0.58	-0.07	0.26	-0.08	0.19	-0.12	0.053	-0.08	0.19	-0.04	0.51	-0.14	**0.027**
Cancer type-small cell [c]	-0.08	0.21	-0.01	0.85	0.05	0.44	0.03	0.66	0.08	0.22	0.14	**0.025**	0.07	0.29	0.10	0.12
Received radiotherapy [c]	-0.03	0.63	0.16	**0.009**	-0.17	**0.006**	-0.19	**0.003**	-0.14	**0.026**	-0.20	**0.002**	-0.07	0.24	-0.20	**0.001**
ΔR^2	0.054		0.141		0.079		0.081		0.097		0.094		0.080		0.124	
Step 2																
Confrontation	0.19	**0.002**	0.11	**0.040**	-0.05	0.40	-0.05	0.39	-0.07	0.25	-0.07	0.29	-0.01	0.81	-0.08	0.17
Resigned acceptance	-0.25	**<0.001**	0.44	**<0.001**	-0.16	**0.013**	-0.15	**0.019**	-0.16	**0.012**	-0.14	**0.029**	-0.41	**<0.001**	-0.22	**<0.001**

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ΔR^2	0.098	0.191	0.025		0.023		0.027		0.021		0.155		0.053	
Step 3														
Positive mood			0.16	**0.013**	0.12	0.078	0.14	**0.026**	0.14	**0.029**	0.10	0.076	0.17	**0.005**
Negative mood			-0.22	**0.003**	-0.20	**0.006**	-0.17	**0.020**	-0.20	**0.005**	-0.36	**<0.001**	-0.28	**<0.001**
ΔR^2			0.053		0.039		0.036		0.044		0.093		0.076	
Adjusted R^2	0.120	0.307	0.118		0.103		0.122		0.121		0.298		0.218	

Note. a. 0=Male, 1=Female; b. 1=stage III, 2=stage IV; c. 0=No, 1=Yes; d. range:1 (no difficulty) – 5 (very much); e. standardized coefficients

3.3 Mediating Effect of Mood on the Association between Coping and HRQoL

The MEDIATE macro was used to examine the mediating effect of mood in the relationship between coping and HRQoL, controlling for age, gender, cancer stage, perceived cancer-related financial burden, having received radiotherapy, and lung cancer type (poorly differentiated versus small cell; see Table 4). The indirect effect (ab) was estimated as the product of regression coefficients predicting mood from each coping (a), and HRQoL from mood (b) (see Figure 1). Bootstrapping techniques using 5000 samples revealed significant indirect effects for confrontation and resigned acceptance on HRQoL through positive and negative mood, respectively.

Despite the total effects of confrontation on EQ-5D domains scores and utility index were not significant, competing indirect effects via mood were identified. On one hand, positive indirect effects were found for confrontation on mobility (point estimate = 0.06, *SE* = 0.03, 95% CI [0.01, 0.13]), usual activities (point estimate = 0.05, *SE* = 0.03, 95% CI [0.01, 0.12]), pain/discomfort (point estimate = 0.05, *SE* = 0.03, 95% CI [0.004, 0.11]), and overall utility index (point estimate = 0.01, *SE* = 0.01, 95% CI [0.003, 0.03]) through positive mood. On the other hand, negative indirect effects were found for confrontation on mobility (point estimate = -0.05, *SE* = 0.03, 95% CI [-0.12, -0.002]), pain/discomfort (point estimate = -0.04, *SE* = 0.02, 95% CI [-0.10, -0.001]), anxiety/depression (point estimate = -0.06, *SE* = 0.03, 95% CI [-0.13, -0.003]), and overall utility index (point estimate = -0.01, *SE* = 0.01, 95% CI [-0.03, -0.001]) via negative mood. The direct effects of confrontation on EQ-5D domains scores and utility index were not significant.

Resigned acceptance has a significant negative total effect on EQ-5D domains scores and utility index. Furthermore, indirect effects of resigned acceptance on HRQoL via positive and negative mood were identified. Use of resigned acceptance was associated with decrease

in positive mood, and increase in negative mood, which could lead to more difficulty in mobility, self-care, usual activities, pain/discomfort, anxiety/depression, and overall utility index (indirect effect via positive mood: point estimate = -0.01, *SE* = 0.01, 95% CI [-0.03, -0.003]; indirect effect via negative mood: point estimate = -0.04, *SE* = 0.01, 95% CI [-0.06, -0.02]).

Table 4 Mediation model testing the direct and indirect effect of coping on HRQOL via mood

Outcome	Predictor	Mediator	Path a	Path b	Path ab: indirect effect of coping on HRQOL		Path c': Direct effect of coping on HRQOL	Path c: Total effect of coping on HRQOL
			coef (se)	coef (se)	coef (se)	95% CI	coef (se)	coef (se)
HRQOL	Confrontation	Positive mood	0.30** (0.09)	0.04** (0.01)	0.01 (0.01)	[0.003, 0.03]	-0.03 (0.02)	-0.03 (0.02)
		Negative mood	0.17* (0.08)	-0.07*** (0.02)	-0.01 (0.01)	[-0.03, -0.001]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.01 (0.01)	[-0.03, -0.003]	-0.02 (0.02)	-0.07*** (0.02)
		Negative mood	0.54*** (0.07)		-0.04 (0.01)	[-0.06, -0.02]		
Mobility	Confrontation	Positive mood	0.30** (0.09)	0.21* (0.08)	0.06 (0.03)	[0.01, 0.13]	-0.12 (0.13)	-0.10 (0.12)
		Negative mood	0.17* (0.08)	-0.28** (0.09)	-0.05 (0.03)	[-0.12, -0.002]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.06 (0.03)	[-0.13, -0.01]	-0.03 (0.11)	-0.25* (0.10)
		Negative mood	0.54*** (0.07)		-0.15 (0.06)	[-0.27, -0.05]		
Self-care	Confrontation	Positive mood	0.30** (0.09)	0.13 (0.07)	0.04 (0.03)	[-0.003, 0.10]	-0.09 (0.11)	-0.09 (0.11)
		Negative mood	0.17* (0.08)	-0.23** (0.08)	-0.04 (0.03)	[-0.10, 0.002]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.04 (0.03)	[-0.10, -0.003]	-0.04 (0.10)	-0.21* (0.09)
		Negative mood	0.54*** (0.07)		-0.14 (0.05)	[-0.24, -0.05]		
Usual Activities	Confrontation	Positive mood	0.30** (0.09)	0.18* (0.08)	0.05 (0.03)	[0.01, 0.12]	-0.16 (0.12)	-0.14 (0.12)
		Negative mood	0.17* (0.08)	-0.22* (0.09)	-0.04 (0.02)	[-0.09, 0.001]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.06 (0.03)	[-0.12, -0.01]	-0.07 (0.11)	-0.25* (0.10)
		Negative mood	0.54*** (0.07)		-0.12 (0.05)	[-0.22, -0.02]		

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Pain / Discomfort	Confrontation	Positive mood	0.30** (0.09)	0.16* (0.07)	0.05 (0.03)	[0.004, 0.11]	-0.12 (0.11)	-0.12 (0.11)
		Negative mood	0.17* (0.08)	-0.23** (0.08)	-0.04 (0.02)	[-0.10, -0.001]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.05 (0.03)	[-0.11, -0.005]	-0.02 (0.10)	-0.19* (0.09)
		Negative mood	0.54*** (0.07)		-0.13 (0.05)	[-0.23, -0.04]		
Anxiety / Depression	Confrontation	Positive mood	0.30** (0.09)	0.10 (0.05)	0.03 (0.02)	[-0.003, 0.74]	0.01 (0.08)	-0.02 (0.08)
		Negative mood	0.17* (0.08)	-0.34*** (0.06)	-0.06 (0.03)	[-0.13, -0.003]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.03 (0.02)	[-0.07, 0.003]	-0.26** (0.07)	-0.48*** (0.07)
		Negative mood	0.54*** (0.07)		-0.18 (0.04)	[-0.27, -0.11]		

Note. Age, gender, financial burden, disease stage, cancer type, and received radiotherapy were controlled in the mediation model. All coefficients (a, b, c', c) were unstandardized coefficients. *p<0.05, **p<0.01, *** p<0.001

4. Discussion

To our knowledge, this is the first study to examine the relationship between coping, positive and negative mood, and HRQoL, and the mediating role of mood in the relationship between coping and HRQoL among patients with advanced lung cancer. The findings of this study indicated that examining pathway via positive and negative mood can generate a new understanding of the effect of coping on HRQoL among patients with advanced lung cancer, regardless of sociodemographic and clinical factors. The confrontation coping strategy was not directly associated with domains of HRQoL or overall HRQoL, but two significant indirect pathways via mood were identified. On one hand, confrontation had positive indirect effect on mobility, usual activities, pain, and overall HRQoL via positive mood; On the other hand, confrontation had negative indirect effect on mobility, pain, anxiety, and overall HRQoL via negative mood; Positive and negative indirect effect of confrontation on mobility, pain, and overall HRQoL could counteract, resulting in a nonsignificant total effect. In contrast, use of resigned acceptance coping was associated with an increase in negative mood and decrease in positive mood, which could in turn result in more difficulty in mobility, self-care, usual activities, pain, and poor overall HRQoL. On the whole, this is a unique finding that indicates the ambivalence of confrontation and the maladaptive nature of resigned acceptance among patients with advanced lung cancer.

Research on the effects of coping on health indicated that the way people deal with stress can predict psychological and physical health [44]. Results support this theory and suggest that coping could play a role in adapting to the diagnosis and treatment of lung cancer, which could in turn influence health outcomes. In line with previous studies indicating resigned acceptance was associated with less favorable outcomes [21, 26], the current study indicated that use of resigned acceptance was associated with increased negative mood, decreased positive mood, and lower HRQoL among the patients with

advanced lung cancer. Although accommodative coping, such as acceptance and meaning-making coping, was suggested to be effective in dealing circumstances beyond a person's control, resigned acceptance—characterized as giving up control in the actual situation, or even other aspects of life; negative expectations about the future; and a loss of hope [24]—could still reduce positive mood, such as hope and inspiration, and contribute to the emotional distress and poor health outcomes.

Confrontation was found to be associated with increased positive and negative mood. In the current study, confrontation was characterized by attempts such as seeking information from various sources, asking for advice from family and clinicians, and conducting shared decision making. Through such efforts, patients may regain a sense of control and redirect energy to constructive actions during treatment and daily living, which might facilitate the occurrence of positive mood. However, it is also possible that individuals could encounter various stressful decisions and pieces of information when they actively confront the advanced disease, which might lead to negative mood.

Our findings are in line with other studies reporting a nonsignificant association between confrontation and overall HRQoL among cancer patients [21-23]. Particularly, the findings on the mediating role of mood can help to clarify the mechanisms underlying the nonsignificant association. Use of confrontation increased both positive and negative mood, which in turn were associated with overall HRQoL in opposite directions. Therefore, the coexisting positive and negative indirect effect could counteract one another, resulting in a null, or weak, total effect on overall HRQoL. We consider that this may reflect *ambivalence* of confrontation: despite that confronting the advanced cancer may have some benefits (e.g., sense of control, constructive actions and skills), it may also remind the patients of the life-threatening disease (e.g., ruminative thoughts) and increase distress.

This study indicated that mood can be a pathway between coping and health outcomes. One explanation is related to physiology of mood [45], as positive and negative mood are associated with physiological levels in different directions, which can lead to different health outcomes. The second explanation is related to thought-action repertoires [38]. Negative mood is suggested to narrow the thought-action repertoires, and increase unhealthy lifestyle and social isolation [38, 46], which could result in poor health outcomes; In contrast, positive affect is suggested to broaden the scope of attention and thought-action repertoires, and build up personal and social resources [38], which could be beneficial to health outcomes. Another explanation is related to attributional interpretation [30]. HRQoL refers to a self-perceived health status, and it is possible that participants in a negative mood tend to perceive lower health status (more difficulties in daily living and symptoms) than those in a positive mood.

This study has some limitations. First, causality on the relationships between coping, mood, and HRQoL could not be drawn out from the cross-sectional study. Second, although Medical Coping Modes Questionnaire measured three coping strategies (i.e., confrontation, acceptance-resignation, avoidance), reliability of avoidance, indicated by Cronbach' α coefficient, was low in current study, which restricted us to analyze the effect of avoidance strategy. Third, the sample was recruited from one hospital in China, which could compromise the generalizability of the findings.

Considering the effect of coping strategies, the findings of our study suggest specific attention to the use of resigned acceptance among patients with advanced cancer, which was associated with more negative mood and poor HRQoL. Despite patients accepting the reality of disease, practitioners may assist them to regain a sense of control and develop constructive and meaningful responses. Additionally, patients who actively confront the advanced cancer may experience both positive and negative mood. We suggest that practitioners consider this

ambivalent emotional experience and relieve patients' distress in the face of the life-threatening disease. Finally, when implementing interventions for the improvement of HRQoL, we suggest that practitioners consider the role of both positive and negative mood, which could serve as pathways between coping and HRQoL among patients with advanced lung cancer.

Figure 1 Positive and negative mood as mediators of the association between coping and HRQoL

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Contributors

HY, JH, LV, CJ designed the study. HY, JH, YM, ZJ, and LG collected data. HY and CJ analyzed the data. HY and CJ drafted the manuscript. HY, JH, YM, ZJ, LG, LV, CJ revised the manuscript.

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Competing interests

The authors declare that they have no conflict of interest.

Patient consent

Obtained.

Data sharing statement

No additional data were available.

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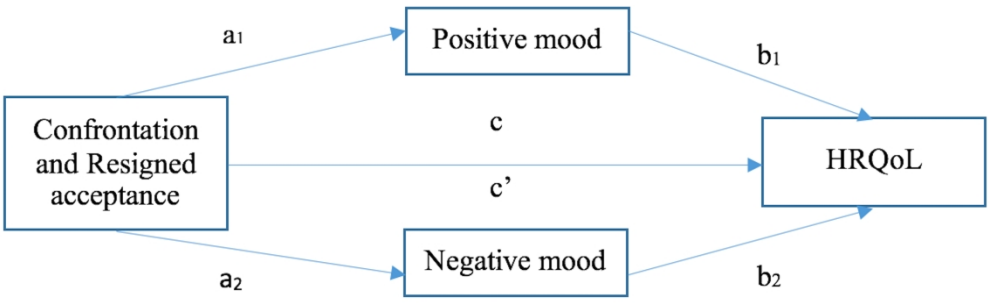

Positive and negative mood as mediators of the association between coping and HRQoL

The STROBE-Vet statement checklist.

	Item	*STROBE-Vet recommendation*	*Page #*
Title and Abstract	1	(a) Indicate that the study was an observational study and, if applicable, use a common study design term	1
		(b) Indicate why the study was conducted, the design, the results, the limitations, and the relevance of the findings	2
Background / rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	(a) State specific objectives, including any primary or secondary prespecified hypotheses or their absence	6
		(b) Ensure that the level of organization[a] is clear for each objective and hypothesis	4-6
Study design	4	Present key elements of study design early in the paper	6
Setting	5	(a) Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
		(b) If applicable, include information at each level of organization	
Participants [b]	6	(a) Describe the eligibility criteria for the owners/managers and for the animals, at each relevant level of organization	6
		(b) Describe the sources and methods of selection for the owners/managers and for the animals, at each relevant level of organization	6
		(c) Describe the method of follow-up	—
		(d) For matched studies, describe matching criteria and the number of matched individuals per subject (e.g., number of controls per case)	—
Variables	7	(a) Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. If applicable, give diagnostic criteria	7-8
		(b) Describe the level of organization at which each variable was measured	7-8
		(c) For hypothesis-driven studies, the putative causal-structure among variables should be described (a diagram is strongly encouraged)	Figure 1

Data sources / measurement	8*	(a) For each variable of interest, give sources of data and details of methods of assessment (measurement). If applicable, describe comparability of assessment methods among groups and over time	7-8
		(b) If a questionnaire was used to collect data, describe its development, validation, and administration	7-8
		(c) Describe whether or not individuals involved in data collection were blinded, when applicable	-
		(d) Describe any efforts to assess the accuracy of the data (including methods used for "data cleaning" in primary research, or methods used for validating secondary data)	-
Bias	9	Describe any efforts to address potential sources of bias due to confounding, selection, or information bias	8 (covariates)
Study size	10	(a) Describe how the study size was arrived at for each relevant level of organization	-
		(b) Describe how non-independence of measurements was incorporated into sample-size considerations, if applicable	-
		(c) If a formal sample-size calculation was used, describe the parameters, assumptions, and methods that were used, including a justification for the effect size selected	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	7-8
Statistical methods	12	(a) Describe all statistical methods for each objective, at a level of detail sufficient for a knowledgeable reader to replicate the methods. Include a description of the approaches to variable selection, control of confounding, and methods used to control for non-independence of observations	9
		(b) Describe the rationale for examining subgroups and interactions and the methods used	-
		(c) Explain how missing data were addressed	6
		(d) If applicable, describe the analytical approach to loss to follow-up, matching, complex sampling, and multiplicity of analyses	-
		(e) Describe any methods used to assess the robustness of the analyses (e.g., sensitivity analyses or quantitative bias assessment)	-
Participants	13*	(a) Report the numbers of owners/managers and animals at each stage of study and at each relevant level of organization - e.g., numbers eligible, included in the study, completing follow-up, and analyzed	6

		(b) Give reasons for non-participation at each stage and at each relevant level of organization	-
		(c) Consider use of a flow diagram and/or a diagram of the organizational structure	-
Descriptive data on exposures and potential confounders	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders by group and level of organization, if applicable	11
		(b) Indicate number of participants with missing data for each variable of interest and at all relevant levels of organization	7
		(c) Summarize follow-up time (e.g., average and total amount), if appropriate to the study design	-
Outcome data	15*	(a) Report outcomes as appropriate for the study design and summarize at all relevant levels of organization	10-23
		(b) For proportions and rates, report the numerator and denominator	11-14,16,18,19,22
		(c) For continuous outcomes, report the number of observations and a measure of variability	11-14,16,18,19,22
Main results	16	(a) Give unadjusted estimates and, if applicable, adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders and interactions were adjusted. Report all relevant parameters that were part of the model	11-14,16,18,19,22
		(b) Report category boundaries when continuous variables were categorized	-
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done,-such as sensitivity/robustness analysis and analysis of subgroups	-
Key results	18	Summarize key results with reference to study objectives	24
Strengths and Limitations	19	Discuss strengths and limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	24, 26
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	24-26
Generalizability	21	Discuss the generalizability (external validity) of the study results	26

~~Funding~~ Transparency	22	(a) Funding- Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based (b) Conflicts of interest-Describe any conflicts of interest, or lack thereof, for each author (c) Describe the authors' roles- Provision of an authors' declaration of transparency is recommended (d) Ethical approval- Include information on ethical approval for use of animal and human subjects (e) Quality standards-Describe any quality standards used in the conduct of the research	27

[a] Level of organization recognizes that observational studies in veterinary research often deal with repeated measures (within an animal or herd) or animals that are maintained in groups (such as pens and herds); thus, the observations are not statistically independent. This non-independence has profound implications for the design, analysis, and results of these studies.
[b] The word "participant" is used in the STROBE statement. However, for the veterinary version, it is understood that "participant" should be addressed for both the animal owner/manager and for the animals themselves.
*Give such information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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Mood mediates coping and health-related quality of life: A cross-sectional study in Chinese patients with advanced lung cancer

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Mood mediates coping and health-related quality of life: A cross-sectional study in Chinese patients with advanced lung cancer

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Abstract

Objectives: The ways patients cope with advanced cancer can influence their health-related quality of life (HRQoL). This study aims to examine the mediating role of positive and negative mood in the relationship between coping and HRQoL in patients with advanced lung cancer.

Methods: A consecutive sample of 261 patients (mean age: 59.99±9.53) diagnosed with stage III or IV lung cancer was recruited from the inpatient unit in a hospital that specializes in chest-related disease in Shanghai, China. Participants completed measurements including Medical Coping Modes Questionnaire, Positive and Negative Affect Schedule, and 5-level EuroQol 5-dimension instrument.

Results: Although the total effects of confrontation on HRQoL were not significant, competing indirect effects via mood were identified: (1) Positive indirect effects through positive mood were found for confrontation on mobility, usual activities, pain/discomfort, and overall utility index (indirect effect = 0.01, 95% CI 0.003 to 0.03); (2) Negative indirect effects through negative mood were found for confrontation on mobility, pain/discomfort, anxiety/depression, and overall utility index (indirect effect = -0.01, 95% CI -0.03 to -0.001). Resigned acceptance was negatively associated with HRQoL, and indirect effects via mood were identified: (1) Negative indirect effects through positive mood were found for resigned acceptance on mobility, self-care, usual activities, pain/discomfort, and overall utility index (indirect effect = -0.01, 95% CI -0.03 to -0.003); (2) Negative indirect effects through negative mood were found for resigned acceptance on domains of HRQoL and overall utility index (indirect effect = -0.04, 95% CI -0.06 to -0.02).

Conclusions: Confronting advanced lung cancer can fuel ambivalent emotional experiences. Nevertheless, accepting the illness in a resigned way can be maladaptive for health outcomes.

The findings suggest interventions that facilitate adaptive coping, reduce negative mood, and enhance positive mood, as this could help to improve or maintain HRQoL in patients with advanced lung cancer.

Keywords: coping; quality of life; mood; lung cancer

Strengths and limitations of this study

- The study addressed health-related quality of life (HRQoL), an important health outcome of treatment for advanced lung cancer, and examined the psychological factors associated with HRQoL.
- The study examined the mediating role of positive and negative mood in the relationship between coping and a range of health outcomes (mobility, self-care, usual activities, pain/discomfort, anxiety/depression, overall HRQoL), which identifies the potential pathways between coping and HRQoL in patients with advanced lung cancer.
- Consecutive sampling could compromise the generalizability of the findings.
- Cross-sectional design.

1. Introduction

During the past decade, lung cancer has become the most common incident cancer and the leading cause of cancer mortality in China and many other countries [1, 2]. Lung cancer survival rates are poor, with a five-year survival rate in China of 16.1% [3]. As curative treatments are limited for advanced lung cancer, improving or maintaining quality of life is the main focus of treatment. The prognostic value of health-related quality of life (HRQoL) in patients with lung cancer is supported by a range of studies [4, 5].

The diagnosis of lung cancer can result in enormous stress for patients and their families, such as symptom burden [6], decisions about treatment options [7], and financial concerns [8]. The quality of life is significantly affected in patients with an advanced lung cancer [9]. Previous research has investigated socio-demographic, clinical, and psychosocial correlates of HRQoL in cancer patients [10]. Common risk factors identified from previous studies included older age, being female, financial burden, and advanced stage [11]. Specifically, the manner in which patients cope with the life-threatening illness is indicated to contribute to mood and HRQoL in patients with advanced cancer [12, 13]. Two coping strategies, confrontation and acceptance, have received considerable attention in patients with a life-threatening illness [14-17].

Confrontation is a form of active coping that involves seeking information from various sources, asking for advice, and cognitive redefinition [14]. Some studies indicated that confrontation was adaptive for cancer patients, which was associated with lower negative mood [18-20], and better quality of life [16, 17]. However, other studies found insignificant associations between confrontation and health outcomes among cancer patients [15, 21, 22]. For instance, Nipp et al. [15] studied 350 patients with incurable lung or gastrointestinal cancer, and found that using active coping was not associated with psychological distress or quality of life. It is suggested that confrontation could direct one's attention to the disease and its side effects, making it less effective in coping with cancer [14, 17].

Acceptance is regarded as a strategy to cope with unchangeable or uncontrollable negative events [23]. Resigned acceptance is a form of passive acceptance, in which individuals accept the stressful situation without endeavors to alter it [23, 24]. It is different from the concept of acceptance in Acceptance and Commitment Therapy, which is a form of active acceptance and characterized by active embracing of thoughts and feelings without unnecessary attempts to alter them [25]. Research shows that resigned acceptance could be maladaptive, which was associated with less favorable outcomes, such as negative mood and lower quality of life, in cancer patients and survivors [21, 26, 27].

Confrontation and resigned acceptance may be associated with cultural views of illness in the Chinese cancer population. Confucianism and Taoism are two dominant philosophical tenets in Chinese culture [28]. Confucian beliefs emphasize the importance of life, and death is a taboo and perceived as a negative event [29]. Consistent with this, the majority of patients and their families in China would choose to continue curative treatments to sustain and prolong life until the end of life [30]. On the other hand, cancer and other illness are believed to be an act of Ming (also known as fate) in the Taoist belief system [28]. The fatalistic attitude toward cancer may lead to resigned acceptance, which may affect health outcomes during the illness trajectory [28].

Although research shows that coping is associated with HRQoL in cancer patients, the mechanism of the link between coping and HRQoL remains largely unexamined in cancer patients. Preliminary exploration suggests that mood may be a potential pathway between coping and health outcomes [31-35]. Folkman and Greer developed a model of stress and coping for serious illness, and Roberts et al. revised the model based on studies among patients with advanced cancer [36, 37]. The models highlight the association between coping and emotional outcomes in the face of cancer, as the way patients cope with the stressors can influence the emotional outcomes, leading to positive and/or negative emotion [36, 37]. On

the other hand, studies indicate that mood is linked to health outcomes (e.g., HRQoL) in cancer patients and survivors [27, 38, 39]. Negative and positive mood involves different physiological responses (e.g., nervous, endocrine, and immune system functioning), which can influence overall physical health [40, 41]. Additionally, the broaden-and-build theory of positive mood indicates that positive mood can broaden one's attention scope and thought-action repertoires, which could be beneficial for physical health. In contrast, negative mood can fuel a narrowed, socially isolating thought-action tendencies, which could result in poor health outcomes [42, 43]. Given that coping strategies are related to mood, and that mood is related to HRQoL, it is possible that mood may be a mediational pathway between coping and HRQoL. In a prospective study among HIV caregivers, higher social coping predicted an increase in positive affect, which decreased levels of physical symptoms, whereas higher cognitive avoidance predicted enhanced negative affect, which resulted in higher levels of physical symptoms [33]. However, in the context of advanced cancer, to our knowledge, no study has examined the pathways between coping and HRQoL through mood. Since patients with advanced cancer can encounter numerous stresses, understanding the effect of coping on health and identifying the pathways through which patients maintain health and quality of life can provide important insights for clinical practice and interventions.

In summary, the current study addresses the relationships between coping, mood, and HRQoL among patients with advanced lung cancer. Specifically, we examined the effect of confrontation and resigned acceptance coping on positive mood, negative mood, and HRQoL. We also tested the mediating role of positive and negative mood in the relationship between coping and HRQoL among Chinese patients with advanced lung cancer.

2. Method

2.1 Participants and Public Involvement

Participants were recruited from the inpatient unit of the department of chest-oncology medicine at a public hospital that specializes in chest-related disease in Shanghai, China. The hospital is well recognized for its expertise, resources, and treatments for chest-related disease. A large number of patients with lung cancer in east China come to this hospital and receive treatment there. Patients were eligible in the study if they (a) were 18 years or older, (b) had been diagnosed with lung cancer, (c) had an expected survival time > 3 months, (d) had no significant cognitive impairment, and (e) were able to communicate with interviewers. Studies show that cancer patients may experience a steep decline in HRQoL during the last 3 months of life [44]. Therefore, we purposefully included only those with an expected survival time of at least 3 months. Those who could not understand the questions were excluded from the sample. Between June 2016 and July 2016, 328 patients met the inclusion criteria and were enrolled in the study.

Data collection was conducted by trained undergraduate students majoring in medicine and public health. Doctors and nurses in the inpatient unit of the department of chest-oncology medicine screened the eligible patients based on the inclusion and exclusion criteria, and researchers approached them and introduced the study. Those who agreed to participate in the study provided informed consent. Face-to-face interviews were then conducted. Disease and treatment information was extracted from medical records. The study was approved by the Ethics Committee of Shanghai Chest Hospital, Shanghai Jiao Tong University (No. KS1353). In accordance with our study aim, we focused on 267 patients with advanced-stage lung cancer (stage III or IV), and the 261 participants who provided full information on the main study variables (coping, mood, and HRQoL) were included in the data analysis. A flow chart of the sample selection procedure is presented in supplementary Figure 1.

2.2 Measures

2.2.1 Health-related quality of life. The 5-level EuroQol 5-dimension (EQ-5D-5L) was used to measure HRQoL in this study [45]. It contained five questions to assess five health dimensions, as experienced in the recent days, namely mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Respondents rated the severity on 5 levels ranging from 1 (*no*) to 5 (*very severe*). In the current study, EQ-5D-5L domain scores and overall utility index were calculated. Domain scores were recoded reversely based on the original levels of each domain, with higher scores indicating better quality in the domain. EQ-5D-5L utility index was calculated based on value sets developed by the EuroQol Group. To our knowledge, no value sets have been developed in a Chinese representative sample for the calculation of utility index, so in this study, utility index was calculated based on value sets weighted from a representative sample of the English general population [46]. The EQ-5D-5L utility index ranged from -1 to 1, with 1 representing full health, 0 representing a state of death, and negative values representing a state worse than death.

2.2.2 Coping. Two subscales of the Chinese version of the Medical Coping Modes Questionnaire (MCMQ) were used to measure confrontation and resigned acceptance coping strategies for lung cancer. MCMQ was developed by Feifel, Strack, and Nagy [14] among patients with a variety of life-threatening and chronic illnesses, and it is widely used for assessing coping strategies in patients in China [17, 47]. In the original questionnaire, acceptance-resignation had five items, and confrontation had eight items [14]. Sample items in acceptance-resignation subscale were as follows: “there is nothing you can do about your illness” and “you don’t care what happens to you.” One item in the confrontation subscale assessed how often participants “obtained information through books, magazines, and newspapers in the past several months”. In addition to that, we added one item assessing how often participants “obtained information through the Internet and new media in the past

several months," as the Internet and new media have become important sources of information that supplement books, magazines, and newspaper. All the items were rated on a 4-point Likert scale ranging from 1 (*never*) to 4 (*very often*). The mean score of each coping strategy was calculated, with a higher score indicating a higher probability of using that particular coping strategy. The Cronbach's α coefficients of confrontation and resigned acceptance in this study were 0.72 and 0.71, respectively.

2.2.3 Mood. Mood was measured using the Positive and Negative Affect Schedule (PANAS) [48]. The PANAS contained items to describe 10 positive affects (e.g., inspired, excited, determined) and 10 negative affects (e.g., afraid, upset, distressed). Respondents rated their experiences of each affect during the past two weeks on a 5-point Likert scale ranging from 1 (*very slightly*) to 5 (*extremely*). The mean scores of items on the two subscales were calculated for positive mood and negative mood, respectively. In the current study, the Cronbach's α coefficients of negative mood and positive mood were 0.91 and 0.86, respectively.

2.2.4 Covariates. Sociodemographic factors included age, gender, education (elementary school or lower, middle school, high school, college or higher), and marital status (married, single, divorced, widowed). Perceived cancer-related financial burden was assessed by the question, "Have your disease and treatment caused you and your family financial difficulty?" and participants answered on a 5-point scale ranging from 0 (*No*) to 4 (*Very much*). Clinical factors included time of diagnosis, cancer stage, lung cancer type (adenocarcinoma, squamous, poorly differentiated, small cell, not otherwise specified), and treatment history (surgery, chemotherapy, radiotherapy, targeted therapy).

2.3 Data Analysis

First, descriptive statistics were presented for sociodemographic and clinical characteristics, and main study variables. Mean and standard deviation, or frequency and percentage, were computed for continuous and categorical variables, respectively. Independent *t* test, analysis of variance, and post-hoc comparison were conducted to analyze the effect of sociodemographic and clinical factors on positive mood, negative mood, and HRQoL (see supplementary Table 1). Correlational analyses were performed to examine the associations between the continuous variables.

Secondly, multivariate, hierarchical, linear regression analyses were employed to examine the relationships among coping, mood, and HRQoL. The hierarchical regressions with HRQoL (domain scores and EQ-5D utility index) as a dependent variable involved three steps: In step one, gender, age, cancer stage, and covariates that were significantly correlated with mood and HRQoL (i.e., financial burden, lung cancer type, a history of radiotherapy) were entered; In step two, confrontation and resigned acceptance were entered; In step three, positive and negative mood were entered.

Thirdly, the mediating effects of positive and negative mood in the relationship between coping and HRQoL were tested using the MEDIATE macro for SPSS developed by Preacher and Hayes [49]. Bootstrapping techniques using 5000 samples were used for the analysis, which was regarded as providing a more reliable estimate for the small sample size. Significant indirect effect was indicated by a 95% confidence interval of indirect effect without including zero. Power analyses indicated that in a model with two parallel mediators, a sample of 260 has 80% power to detect a 95% confidence interval of indirect effect, assuming correlations of r = 0.20 between independent variable, the dependent variable, and the mediators. Schoemann, Boulton, and Short suggest that this power analytic method is an appropriate approach for determining power and sample size in mediation models [50]. All tests were two tailed, and a *p*-value of <0.05 was considered statistically significant.

3. Results

3.1 Sociodemographic and Clinical Characteristics

The sociodemographic and clinical characteristics for the samples are shown in Table 1. A total sample of 261 participants had a mean age of 59.99 years (*SD* = 9.53). Males represented 70.1% of the samples. Most participants were married (94.6%) and perceived a slight to very severe cancer-related financial burden (85.8%). More than half of the participants had been diagnosed in the past 6 months (55.2%). More than 90% of the participants had ever received chemotherapy (96.6%), whereas a certain proportion had ever received surgery (23.4%), radiotherapy (23.4%), or targeted therapy (14.6%).

Table 1 Sample Characteristics

Variables	M(SD) / n (%)
Age (years)	59.99 (9.53)
Gender	
Male	183 (70.1%)
Female	78 (29.9%)
Education	
Elementary school or lower	55 (21.1%)
Middle school	91 (34.9%)
High school	66 (25.3%)
College or higher	49 (18.8%)
Marital status	
Married	247 (94.6%)
Single/divorced/ widowed	14 (5.4%)
Perceived cancer-related financial burden	
None	37 (14.2%)
Slight	100 (38.3%)
Moderate	63 (24.1%)
Severe	36 (13.8%)
Very Severe	25 (9.6%)
Time since diagnosis [a]	
Less than 6 months	144 (55.2%)
6-12months	32 (12.3%)
12-24 months	31 (11.9%)
More than 24 months	46 (17.6%)
Stage	
III	82 (31.4%)
IV	179 (68.6%)
Lung cancer type [b]	
NSC - Adenocarcinoma	140 (53.6%)
NSC - Squamous	47 (18.0%)

NSC - Poorly differentiated	24 (9.2%)
NSC - Others	7 (2.7%)
Small cell	43 (16.5%)
Treatment history	
Received surgery	
Yes	61 (23.4%)
No	200 (76.6%)
Received chemotherapy	
Yes	252 (96.6%)
No	9 (3.4%)
Received radiotherapy	
Yes	61 (23.4%)
No	200 (76.6%)
Received targeted therapy	
Yes	38 (14.6%)
No	223 (85.4%)

Note. a. For time since diagnosis, the sum of number is not 261 due to missing data; b. NSC: Non-small cell.

3.2 Coping, Mood, and HRQoL

Pearson correlation analysis was performed to examine the relationships between coping, mood, and HRQoL (see Table 2). A small and positive correlation was observed between confrontation coping and positive mood ($r = 0.21$). Resigned acceptance was moderately and positively correlated with negative mood ($r = 0.46$), but moderately and inversely correlated with positive mood ($r = -0.27$). Use of resigned acceptance was correlated with more difficulties in mobility ($r = -0.21$), self-care ($r = -0.19$), usual activities ($r = -0.19$), pain/discomfort ($r = -0.19$), anxiety/depression ($r = -0.41$), and lower EQ-5D utility index ($r = -0.28$).

Table 2 Correlation among coping, affect and HRQOL

	M (SD)	1	2	3	4	5	6	7	8	9
1. Confrontation	2.37 (0.49)	1								
2. Resigned acceptance	1.92 (0.62)	-0.03	1							
3. Positive mood	2.40 (0.76)	0.21**	-0.27**	1						
4. Negative mood	1.84 (0.76)	0.11	0.46**	-0.11	1					
5. Mobility	4.32 (0.99)	-0.05	-0.21**	0.19**	-0.28**	1				
6. Self-care	4.58 (0.86)	-0.06	-0.19**	0.15*	-0.28**	0.78**	1			
7. Usual activities	4.24 (0.97)	-0.10	-0.19**	0.16*	-0.27**	0.78**	0.73**	1		
8. Pain/discomfort	3.98 (0.87)	-0.08	-0.19**	0.14*	-0.28**	0.45**	0.43**	0.46**	1	
9. Anxiety/depression	4.22 (0.73)	-0.03	-0.41**	0.19**	-0.50**	0.21**	0.21**	0.25**	0.27**	1
10. EQ-5D utility index	0.80 (0.19)	-0.10	-0.28**	0.20**	-0.38**	0.84**	0.82**	0.84**	0.69**	0.45**

*p<0.05, **p<0.01

Scale range: Confrontation, resigned acceptance: 1 (never) – 4 (very often); Positive mood, negative mood: 1 (very slightly) – 5 (extremely); Mobility, self-care, usual activities, pain/discomfort, anxiety/depression: 1 (very severe) – 5 (no); EQ-5D utility index: -1 (worse than death) – 1 (full health)

Hierarchical regression analyses were used to examine the relationship of confrontation and resigned acceptance coping with positive mood, negative mood, and HRQoL (see Table 3). Age, gender, cancer stage, and significant correlates of mood and/or HRQoL ($p < 0.05$), including perceived cancer-related financial burden, a history of radiotherapy, and lung cancer type (poorly differentiated non-small cell, small cell, other non-small cell), were controlled in the hierarchical regression analyses. Regarding positive mood, in addition to covariates, confrontation and resigned acceptance were found to be significant factors, as confrontation was associated with higher positive mood ($\beta = 0.19$, $p = 0.002$), whereas resigned acceptance was associated with lower positive mood ($\beta = -0.25$, $p < 0.001$). Regarding negative mood, in addition to covariates, confrontation and resigned acceptance were significant factors, as use of confrontation ($\beta = 0.11$, $p = 0.040$) and resigned acceptance ($\beta = 0.44$, $p < 0.001$) were associated with higher negative mood.

Regarding the EQ-5D domain scores, after controlling sociodemographic and clinical covariates, confrontation was not associated with the domain scores, whereas resigned acceptance was inversely associated with all domains. Positive mood was associated with less difficulty in mobility, usual activities, pain/discomfort, but not associated with self-care and anxiety/depression. Negative mood was negatively associated with more difficulty in all domains.

Regarding EQ-5D utility index, after controlling sociodemographic and clinical covariates, resigned acceptance was inversely associated with EQ-5D utility index ($\beta = -0.22$, $p < 0.001$), whereas confrontation was not associated with EQ-5D utility index. Moreover, the effects of mood on EQ-5D utility index were significant, as positive mood was associated with higher EQ-5D utility index ($\beta = 0.17$, $p = 0.005$), whereas negative mood was associated with lower EQ-5D utility index ($\beta = -0.28$, $p < 0.001$).

COPING, MOOD AND HRQOL IN LUNG CANCER PATIENTS

Table 3 Multiple regression results for predictors of mood and HRQOL

	Positive mood		Negative mood		Mobility		Self-care		Usual activities		Pain / discomfort		Anxiety / depression		EQ-5D utility index	
	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*
Step 1																
Age	-0.15	**0.021**	-0.04	0.53	-0.13	**0.040**	-0.13	**0.046**	-0.06	0.31	-0.07	0.25	0.01	0.91	-0.10	0.09
Gender [a]	-0.07	0.32	0.05	0.40	-0.07	0.29	-0.06	0.35	-0.09	0.15	-0.01	0.85	0.02	0.76	-0.03	0.68
Financial burden [b]	-0.14	**0.032**	0.30	**<0.001**	-0.16	**0.010**	-0.15	**0.017**	-0.20	**0.002**	-0.15	**0.018**	-0.25	**<0.001**	-0.22	**0.001**
Cancer stage [c]	-0.09	0.16	-0.07	0.22	0.00	0.99	0.05	0.46	0.03	0.67	0.04	0.58	0.04	0.51	0.04	0.53
Cancer type- other non-small cell (Reference)	0		0		0		0		0		0		0		0	
Cancer type- undifferentiated [d]	0.01	0.93	-0.03	0.58	-0.07	0.26	-0.08	0.19	-0.12	0.053	-0.08	0.19	-0.04	0.51	-0.14	**0.027**
Cancer type- small cell [d]	-0.08	0.21	-0.01	0.85	0.05	0.44	0.03	0.66	0.08	0.22	0.14	**0.025**	0.07	0.29	0.10	0.12
Received radiotherapy [e]	-0.03	0.63	0.16	**0.009**	-0.17	**0.006**	-0.19	**0.003**	-0.14	**0.026**	-0.20	**0.002**	-0.07	0.24	-0.20	**0.001**
ΔR^2	0.054		0.141		0.079		0.081		0.097		0.094		0.080		0.124	
Step 2																

Confrontation	0.19	**0.002**	0.11	**0.040**	-0.05	0.40	-0.05	0.39	-0.07	0.25	-0.07	0.29	-0.01	0.81	-0.08	0.17
Resigned acceptance	-0.25	**<0.001**	0.44	**<0.001**	-0.16	**0.013**	-0.15	**0.019**	-0.16	**0.012**	-0.14	**0.029**	-0.41	**<0.001**	-0.22	**<0.001**
ΔR^2	0.098		0.191		0.025		0.023		0.027		0.021		0.155		0.053	
Step 3																
Positive mood					0.16	**0.013**	0.12	0.078	0.14	**0.026**	0.14	**0.029**	0.10	0.076	0.17	**0.005**
Negative mood					-0.22	**0.003**	-0.20	**0.006**	-0.17	**0.020**	-0.20	**0.005**	-0.36	**<0.001**	-0.28	**<0.001**
ΔR^2					0.053		0.039		0.036		0.044		0.093		0.076	
Adjusted R^2	0.120		0.307		0.118		0.103		0.122		0.121		0.298		0.218	

Note. a. 0=Male, 1=Female; b. range:1 (no difficulty) – 5 (very much); c. 1=stage III, 2=stage IV; d. other non-small cell lung cancers was the reference group; e. 0=No, 1=Yes; f. standardized coefficients

3.3 Mediating Effect of Mood on the Association between Coping and HRQoL

The MEDIATE macro was used to examine the mediating effect of mood in the relationship between coping and HRQoL, controlling for age, gender, cancer stage, perceived cancer-related financial burden, history of radiotherapy, and lung cancer type (poorly differentiated non-small cell, small cell, other non-small cell). The indirect effect (ab) was estimated as the product of regression coefficients predicting mood from each coping strategy (a), and HRQoL from mood (b) (see Figure 1). Bootstrapping techniques using 5000 samples revealed significant indirect effects for confrontation and resigned acceptance on HRQoL through positive and negative mood, respectively. The results are presented in Table 4.

Although the total effects of confrontation on EQ-5D domains scores and utility index were not significant, competing indirect effects via mood were identified. On one hand, positive indirect effects were found for confrontation on mobility (point estimate = 0.06, *SE* = 0.03, 95% CI [0.01, 0.13]), usual activities (point estimate = 0.05, *SE* = 0.03, 95% CI [0.01, 0.12]), pain/discomfort (point estimate = 0.05, *SE* = 0.03, 95% CI [0.004, 0.11]), and overall utility index (point estimate = 0.01, *SE* = 0.01, 95% CI [0.003, 0.03]) through positive mood. On the other hand, negative indirect effects were found for confrontation on mobility (point estimate = -0.05, *SE* = 0.03, 95% CI [-0.12, -0.002]), pain/discomfort (point estimate = -0.04, *SE* = 0.02, 95% CI [-0.10, -0.001]), anxiety/depression (point estimate = -0.06, *SE* = 0.03, 95% CI [-0.13, -0.003]), and overall utility index (point estimate = -0.01, *SE* = 0.01, 95% CI [-0.03, -0.001]) through negative mood. The direct effects of confrontation on EQ-5D domains scores and utility index were not significant.

Resigned acceptance has a significant negative total effect on EQ-5D domains scores and utility index. Furthermore, indirect effects of resigned acceptance on HRQoL via positive and negative mood were identified. Use of resigned acceptance was associated with decrease

in positive mood, and increase in negative mood, which could lead to more difficulty in mobility, self-care, usual activities, pain/discomfort, anxiety/depression, and overall utility index (indirect effect via positive mood: point estimate = -0.01, *SE* = 0.01, 95% CI [-0.03, -0.003]; indirect effect via negative mood: point estimate = -0.04, *SE* = 0.01, 95% CI [-0.06, -0.02]).

Table 4 Mediation model testing the direct and indirect effect of coping on HRQOL via mood

Outcome	Predictor	Mediator	Path a	Path b	Path ab: indirect effect of coping on HRQOL		Path c': Direct effect of coping on HRQOL	Path c: Total effect of coping on HRQOL
			coef (se)	coef (se)	coef (se)	95% CI	coef (se)	coef (se)
HRQOL	Confrontation	Positive mood	0.30** (0.09)	0.04** (0.01)	0.01 (0.01)	[0.003, 0.03]	-0.03 (0.02)	-0.03 (0.02)
		Negative mood	0.17* (0.08)	-0.07*** (0.02)	-0.01 (0.01)	[-0.03, -0.001]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.01 (0.01)	[-0.03, -0.003]	-0.02 (0.02)	-0.07*** (0.02)
		Negative mood	0.54*** (0.07)		-0.04 (0.01)	[-0.06, -0.02]		
Mobility	Confrontation	Positive mood	0.30** (0.09)	0.21* (0.08)	0.06 (0.03)	[0.01, 0.13]	-0.12 (0.13)	-0.10 (0.12)
		Negative mood	0.17* (0.08)	-0.28** (0.09)	-0.05 (0.03)	[-0.12, -0.002]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.06 (0.03)	[-0.13, -0.01]	-0.03 (0.11)	-0.25* (0.10)
		Negative mood	0.54*** (0.07)		-0.15 (0.06)	[-0.27, -0.05]		
Self-care	Confrontation	Positive mood	0.30** (0.09)	0.13 (0.07)	0.04 (0.03)	[-0.003, 0.10]	-0.09 (0.11)	-0.09 (0.11)
		Negative mood	0.17* (0.08)	-0.23** (0.08)	-0.04 (0.03)	[-0.10, 0.002]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.04 (0.03)	[-0.10, -0.003]	-0.04 (0.10)	-0.21* (0.09)
		Negative mood	0.54*** (0.07)		-0.14 (0.05)	[-0.24, -0.05]		
Usual Activities	Confrontation	Positive mood	0.30** (0.09)	0.18* (0.08)	0.05 (0.03)	[0.01, 0.12]	-0.16 (0.12)	-0.14 (0.12)
		Negative mood	0.17* (0.08)	-0.22* (0.09)	-0.04 (0.02)	[-0.09, 0.001]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.06 (0.03)	[-0.12, -0.01]	-0.07 (0.11)	-0.25* (0.10)
		Negative mood	0.54*** (0.07)		-0.12 (0.05)	[-0.22, -0.02]		

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Pain / Discomfort	Confrontation	Positive mood	0.30** (0.09)	0.16* (0.07)	0.05 (0.03)	[0.004, 0.11]	-0.12 (0.11)	-0.12 (0.11)
		Negative mood	0.17* (0.08)	-0.23** (0.08)	-0.04 (0.02)	[-0.10, -0.001]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.05 (0.03)	[-0.11, -0.005]	-0.02 (0.10)	-0.19* (0.09)
		Negative mood	0.54*** (0.07)		-0.13 (0.05)	[-0.23, -0.04]		
Anxiety / Depression	Confrontation	Positive mood	0.30** (0.09)	0.10 (0.05)	0.03 (0.02)	[-0.003, 0.74]	0.01 (0.08)	-0.02 (0.08)
		Negative mood	0.17* (0.08)	-0.34*** (0.06)	-0.06 (0.03)	[-0.13, -0.003]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.03 (0.02)	[-0.07, 0.003]	-0.26** (0.07)	-0.48*** (0.07)
		Negative mood	0.54*** (0.07)		-0.18 (0.04)	[-0.27, -0.11]		

Note. Age, gender, financial burden, disease stage, lung cancer type, and history of radiotherapy were controlled in the mediation model. All coefficients (a, b, c', c) were unstandardized coefficients. *p<0.05, **p<0.01, *** p<0.001

4. Discussion

To our knowledge, this is the first study to examine the relationship between coping, positive and negative mood, and HRQoL and the mediating role of mood in the relationship between coping and HRQoL among patients with advanced lung cancer. The findings of this study indicate that examining the pathway via positive and negative mood can generate a new understanding of the effect of coping on HRQoL among patients with advanced lung cancer, regardless of sociodemographic and clinical factors. The confrontation coping strategy was not directly associated with domains of HRQoL or overall HRQoL, but two significant indirect pathways via mood were identified. On one hand, confrontation had positive indirect effects on mobility, usual activities, pain, and overall HRQoL via positive mood; On the other hand, confrontation had negative indirect effects on mobility, pain, anxiety, and overall HRQoL via negative mood; Positive and negative indirect effect could counteract, resulting in a nonsignificant total effect. In contrast, use of resigned acceptance coping was associated with an increase in negative mood and a decrease in positive mood, which could in turn result in more difficulty in mobility, self-care, usual activities, pain, and poor overall HRQoL. On the whole, this is a unique finding that indicates the ambivalence of confrontation and the maladaptive nature of resigned acceptance among patients with advanced lung cancer.

The mean EQ-5D utility index in the current study was found to be 0.80, which was comparable to a study among patients with advanced non-small cell lung cancer in China with a utility index of 0.81 [51]. Consistent with previous studies, patients perceiving higher financial burden were more likely to report poor HRQoL compared to those perceiving lower financial burden related to cancer [11, 52]. Financial burden may restrict access to some drugs and treatment [52], and it may also lead to a sense of guilt for relying on families [29], which may affect health outcomes.

The current findings support the theory of stress and coping in the context of advanced cancer by indicating that coping can play a role in adapting to the experience of lung cancer, which could in turn influence emotional and health outcomes [36, 37]. The current study is in line with previous studies indicating that resigned acceptance was associated with less favorable outcomes [21, 26]. Resigned acceptance is related to the fatalistic attitude toward illness in traditional Taoist beliefs [28]. Giving up control in the actual situation, or even other aspects of life and holding negative expectations about the future could reduce positive mood, such as hope and inspiration, and contribute to the emotional distress and poor health outcomes in patients with advanced cancer.

Confrontation was found to be associated with increased positive and negative mood. In the current study, confrontation was characterized by attempts such as seeking information from various sources, asking for advice from family and clinicians, and conducting shared decision making. Through such efforts, patients may regain a sense of control and redirect energy to constructive actions during treatment and daily living, which might facilitate the occurrence of positive mood. However, it is also possible that individuals could encounter various stressful decisions and pieces of information when they actively confront the advanced disease, which might lead to negative mood.

Our findings are in line with other studies reporting a nonsignificant association between confrontation and HRQoL among cancer patients [15, 21, 22]. Particularly, the findings on the mediating role of mood can help clarify the mechanisms underlying the nonsignificant association. The coexisting positive and negative indirect effect via mood could counteract one another, resulting in a null, or weak, total effect of confrontation on HRQoL. The ambivalence of confrontation may also reflect the effect of fighting attitude towards life-threatening illness in Chinese population, in which the patients and their families would seek, try, and continue available curative treatments to sustain and prolong life. Even

though actively confronting the advanced cancer may have some benefits (e.g., sense of control, constructive actions and skills), it may also remind patients of the potential incurable nature of advanced cancer and increase distress.

This study indicated that mood can be a pathway between coping and health outcomes. One explanation is related to physiology of mood [53], as positive and negative mood are associated with physiological levels in different directions, which can lead to different health outcomes. The second explanation is related to thought-action repertoires [43]. Negative mood is suggested to narrow the thought-action repertoires and increase unhealthy lifestyle and social isolation [43, 54], which could result in poor health outcomes. In contrast, positive affect is suggested to broaden the scope of attention and thought-action repertoires and build up personal and social resources [43], which could be beneficial to health outcomes. The third explanation is related to attributional interpretation [33]. HRQoL refers to a self-perceived health status, and it is possible that participants in a negative mood tend to perceive lower health status (more difficulties in daily living and symptoms) than those in a positive mood.

This study has some limitations. First, causality on the relationships between coping, mood, and HRQoL could not be drawn out from this cross-sectional study. Secondly, although Medical Coping Modes Questionnaire measured three coping strategies (i.e., confrontation, acceptance-resignation, avoidance), reliability of avoidance, indicated by Cronbach' α coefficient, was low in the current study. This restricted us from analyzing the effect of the avoidance strategy. Thirdly, although EuroQol 5-dimension was used to measure HRQoL among patients with advanced cancer in a range of studies [51, 55], the measurement properties of the instrument is needed to be examined further in patients with advanced cancer [56]. Fourthly, the sample was recruited from one hospital in China, which could compromise the generalizability of the findings.

Considering the effect of coping strategies, the findings of our study suggest specific attention to resigned acceptance among patients with advanced cancer, which was associated with negative mood and poor HRQoL. Despite patients accepting the reality of disease, practitioners may help them to regain a sense of control and develop constructive and meaningful responses. Acceptance-based interventions, such as Acceptance and Commitment Therapy, may be a worthwhile approach, which are suggested to reduce emotional distress and improve quality of life by facilitating the active acceptance of unpleasant thoughts and feelings in cancer patients [57, 58]. Additionally, patients who actively confront the advanced cancer may experience both positive and negative mood. We suggest that practitioners consider this ambivalent emotional experience and relieve patients' distress in the face of the life-threatening disease. Finally, when implementing interventions for the improvement of HRQoL, we suggest that practitioners consider the role of both positive and negative mood, which could serve as pathways between coping and HRQoL among patients with advanced lung cancer. Early palliative care may be integrated into standard oncology care, which is suggested to facilitate adaptive coping, reduce emotional distress, and improve quality of life in patients with advanced cancer [59].

Figure 1 Positive and negative mood as mediators of the association between coping and HRQoL

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Contributors

HY, JH, LV, CJ designed the study. HY, JH, YM, ZJ, and LG collected data. HY and CJ analyzed the data. HY and CJ drafted the manuscript. HY, JH, YM, ZJ, LG, LV, CJ revised the manuscript.

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Competing interests

The authors declare that they have no conflict of interest.

Patient consent

Obtained.

Data sharing statement

No additional data were available.

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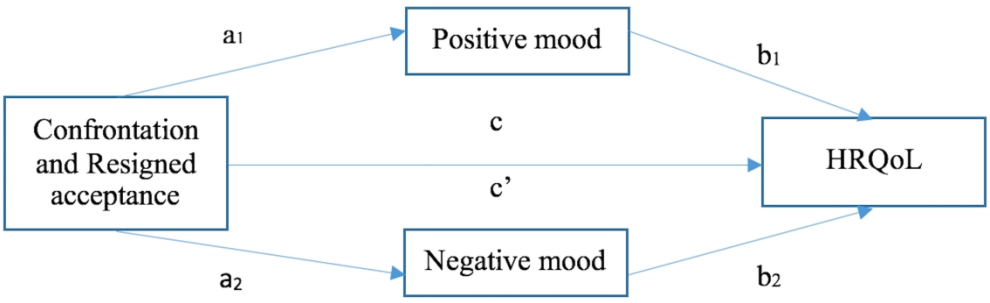


Positive and negative mood as mediators of the association between coping and HRQoL

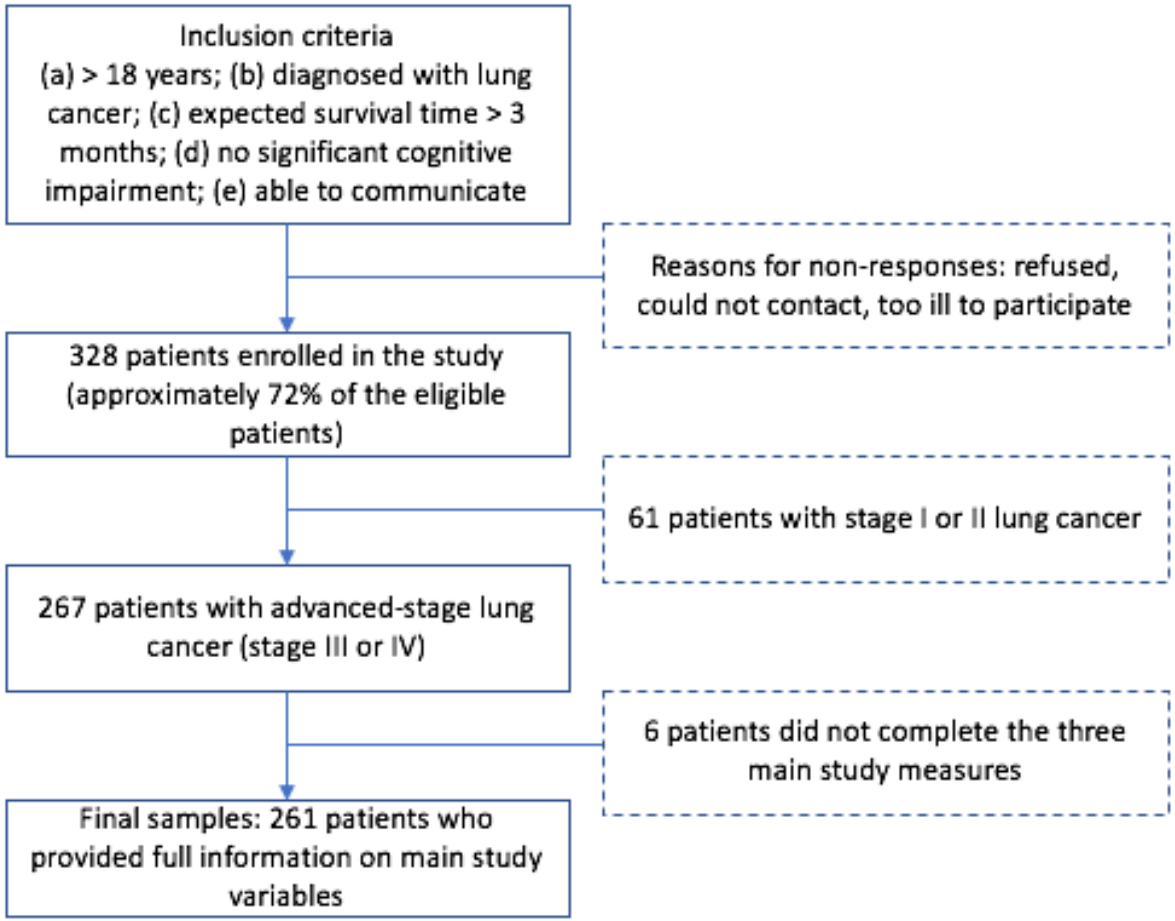
Table 1 Mood and Health-related Quality of Life by Socio-demographic and Clinical Characteristics

Variables	M(SD) / n (%)	Positive mood	Negative mood	Mobility	Self-care	Usual activities	Pain/ discomfort	Anxiety/ depression	EQ-5D utility index
Age (years)	59.99 (9.53)								
Gender									
Male	183 (70.1%)	2.41 (0.75)	1.80 (0.73)	4.39 (0.95)	4.63 (0.79)	4.33 (0.92)	4.03 (0.87)	4.24 (0.75)	0.81 (0.17)
Female	78 (29.9%)	2.34 (0.78)	1.93 (0.83)	4.21 (1.04)	4.50 (0.96)	4.06 (1.05)	3.91 (0.87)	4.21 (0.65)	0.78 (0.21)
Education									
Elementary school or lower	55 (21.1%)	2.28 (0.79)	1.82 (0.73)	4.54 (0.92)	4.64 (0.80)	4.31 (0.96)	3.98 (0.91)	4.11 (0.74)	0.80 (0.18)
Middle school	91 (34.9%)	2.35 (0.69)	1.94 (0.79)	4.24 (0.96)	4.57 (0.86)	4.14 (1.04)	3.90 (0.87)	4.16 (0.79)	0.78 (0.19)
High school	66 (25.3%)	2.46 (0.77)	1.71 (0.63)	4.32 (1.08)	4.59 (0.89)	4.29 (0.96)	4.05 (0.79)	4.32 (0.66)	0.82 (0.17)
College or higher	49 (18.8%)	2.51 (0.84)	1.83 (0.88)	4.41 (0.96)	4.59 (0.84)	4.35 (0.86)	4.10 (0.94)	4.35 (0.63)	0.83 (0.20)
Marital status									
Married	247 (94.6%)	2.40 (0.77)	1.83 (0.76)	4.34 (0.98)	4.60 (0.85)	4.25 (0.98)	3.98 (0.89)	4.23 (0.71)	0.80 (0.19)
Single/divorced/ widowed	14 (5.4%)	2.23 (0.58)	1.86 (0.82)	4.21 (1.05)	4.57 (0.85)	4.29 (0.83)	4.21 (0.58)	4.07 (1.00)	0.78 (0.18)
Perceived cancer-related financial burden									
None	37 (14.2%)	2.72 (0.89)	1.47 (0.50)	4.86 (0.42)	4.92 (0.28)	4.81 (0.46)	4.51 (0.56)	4.59 (0.50)	0.92 (0.08)
Slight	100 (38.3%)	2.27 (0.74)	1.74 (0.63)	4.21 (1.09)	4.54 (0.88)	4.23 (0.91)	3.91 (0.79)	4.22 (0.56)	0.78 (0.19)
Moderate	63 (24.1%)	2.53 (0.80)	1.87 (0.74)	4.43 (0.86)	4.65 (0.79)	4.17 (0.98)	3.90 (0.93)	4.27 (0.70)	0.80 (0.18)
Severe	36 (13.8%)	2.16 (0.51)	1.94 (0.84)	4.25 (0.77)	4.64 (0.68)	4.22 (0.90)	4.06 (1.01)	4.19 (0.71)	0.82 (0.14)
Very Severe	25 (9.6%)	2.38 (0.62)	2.52 (1.02)	3.96 (1.34)	4.12 (1.33)	3.76 (1.42)	3.68 (0.95)	3.64 (1.19)	0.68 (0.26)
Time since diagnosis[a]									
Less than 6 months	144 (55.2%)	2.38 (0.77)	1.84 (0.77)	4.40 (0.96)	4.60 (0.84)	4.24 (1.02)	3.95 (0.90)	4.19 (0.76)	0.80 (0.19)
6-12months	32 (12.3%)	2.54 (0.68)	1.91 (0.72)	4.19 (1.28)	4.50 (1.05)	4.19 (1.12)	4.19 (0.78)	4.19 (0.82)	0.79 (0.23)
12-24 months	31 (11.9%)	2.54 (0.87)	1.71 (0.75)	4.35 (0.80)	4.71 (0.53)	4.42 (0.62)	3.97 (0.71)	4.32 (0.65)	0.83 (0.11)

More than 24 months	46 (17.6%)	2.25 (0.72)	1.86 (0.75)	4.17 (1.00)	4.48 (0.96)	4.17 (0.93)	3.91 (0.96)	4.26 (0.61)	0.78 (0.20)
Stage									
III	82 (31.4%)	2.50 (0.71)	1.96 (0.90)	4.35 (0.93)	4.55 (0.86)	4.20 (1.09)	3.95 (0.94)	4.13 (0.78)	0.79 (0.19)
IV	179 (68.6%)	2.34 (0.78)	1.78 (0.68)	4.33 (1.00)	4.61 (0.84)	4.28 (0.91)	4.01 (0.84)	4.27 (0.69)	0.81 (0.18)
Lung cancer type[b]									
NSC-Adenocarcinoma	140 (53.6%)	2.39 (0.78)	1.88 (0.79)	4.28 (0.99)	4.56 (0.85)	4.20 (0.94)	3.91 (0.92)	4.18 (0.70)	0.79 (0.19)
NSC-Squamous	47 (18.0%)	2.50 (0.81)	1.84 (0.80)	4.45 (0.85)	4.68 (0.63)	4.32 (0.86)	4.00 (0.81)	4.26 (0.57)	0.81 (0.14)
NSC-Poorly differentiated	24 (9.2%)	2.46 (0.61)	1.77 (0.67)	4.08 (1.25)	4.38 (1.21)	3.88 (1.39)	3.75 (0.94)	4.13 (0.99)	0.72 (0.24)
NSC-others	7 (2.7%)	2.30 (0.60)	1.64 (0.40)	4.71 (0.49)	5.00 (0.00)	4.71 (0.49)	4.71 (0.49)	4.57 (0.53)	0.92 (0.10)
Small cell	43 (16.5%)	2.26 (0.76)	1.76 (0.71)	4.49 (0.96)	4.67 (0.87)	4.49 (0.88)	4.26 (0.73)	4.35 (0.78)	0.85 (0.17)
Treatment									
Received surgery									
Yes	61 (23.4%)	2.49 (0.78)	1.95 (0.85)	4.20 (0.98)	4.51 (0.83)	4.20 (0.96)	3.97 (0.86)	4.30 (0.74)	0.80 (0.18)
No	200 (76.6%)	2.36 (0.75)	1.80 (0.73)	4.38 (0.98)	4.62 (0.85)	4.27 (0.97)	4.00 (0.88)	4.21 (0.72)	0.80 (0.19)
Received chemotherapy									
Yes	252 (96.6%)	2.40 (0.76)	1.83 (0.76)	4.33 (0.99)	4.59 (0.86)	4.25 (0.98)	4.00 (0.87)	4.22 (0.73)	0.80 (0.19)
No	9 (3.4%)	2.16 (0.68)	1.83 (0.72)	4.44 (0.73)	4.67 (0.50)	4.33 (0.71)	3.67 (1.00)	4.33 (0.50)	0.81 (0.16)
Received radiotherapy									
Yes	61 (23.4%)	2.36 (0.70)	2.04 (0.87)	4.05 (1.19)	4.33 (1.21)	4.02 (1.09)	3.74 (1.05)	4.13 (0.62)	0.74 (0.23)
No	200 (76.6%)	2.40 (0.78)	1.77 (0.71)	4.43 (0.89)	4.68 (0.69)	4.33 (0.92)	4.07 (0.80)	4.26 (0.75)	0.82 (0.16)
Received targeted therapy									
Yes	38 (14.6%)	2.24 0.79)	1.83 (0.56)	4.21 (1.14)	4.47 (1.08)	4.11 (1.09)	3.79 (1.04)	4.26 (0.64)	0.77 (0.25)
No	223 (85.4%)	2.42 (0.75)	1.83 (0.79)	4.36 (0.95)	4.61 (0.80)	4.28 (0.95)	4.03 (0.84)	4.22 (0.74)	0.81 (0.17)

Scale range: Confrontation, resigned acceptance: 1 (never) – 4 (very often); Positive mood, negative mood: 1 (very slightly) – 5 (extremely); Mobility, self-care, usual activities, pain/discomfort, anxiety/depression: 1 (very severe) – 5 (no); EQ-5D utility index: -1 (worse than death) – 1 (full health)

Figure 1 Flow Chart of the Sample Selection Procedure



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Coping, mood, and health-related quality of life: A cross-sectional study in Chinese patients with advanced lung cancer

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Coping, mood, and health-related quality of life: A cross-sectional study in Chinese patients with advanced lung cancer

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Abstract

Objectives: The ways patients cope with advanced cancer can influence their health-related quality of life (HRQoL). This study aims to examine the mediating role of positive and negative mood in the relationship between coping and HRQoL in patients with advanced lung cancer.

Methods: A consecutive sample of 261 patients (mean age: 59.99±9.53) diagnosed with stage III or IV lung cancer was recruited from the inpatient unit in a hospital that specializes in chest-related disease in Shanghai, China. Participants completed measurements including Medical Coping Modes Questionnaire, Positive and Negative Affect Schedule, and 5-level EuroQol 5-dimension instrument.

Results: Although the total effects of confrontation on HRQoL were not significant, competing indirect effects via mood were identified: (1) Positive indirect effects through positive mood were found for confrontation on mobility, usual activities, pain/discomfort, and overall utility index (indirect effect = 0.01, 95% CI 0.003 to 0.03); (2) Negative indirect effects through negative mood were found for confrontation on mobility, pain/discomfort, anxiety/depression, and overall utility index (indirect effect = -0.01, 95% CI -0.03 to -0.001). Resigned acceptance was negatively associated with HRQoL, and indirect effects via mood were identified: (1) Negative indirect effects through positive mood were found for resigned acceptance on mobility, self-care, usual activities, pain/discomfort, and overall utility index (indirect effect = -0.01, 95% CI -0.03 to -0.003); (2) Negative indirect effects through negative mood were found for resigned acceptance on domains of HRQoL and overall utility index (indirect effect = -0.04, 95% CI -0.06 to -0.02).

Conclusions: Confronting advanced lung cancer can fuel ambivalent emotional experiences. Nevertheless, accepting the illness in a resigned way can be maladaptive for health outcomes.

The findings suggest interventions that facilitate adaptive coping, reduce negative mood, and enhance positive mood, as this could help to improve or maintain HRQoL in patients with advanced lung cancer.

Keywords: coping; quality of life; mood; lung cancer

Strengths and limitations of this study

- The study addressed health-related quality of life (HRQoL), an important health outcome of treatment for advanced lung cancer, and examined the psychological factors associated with HRQoL.
- The study examined the mediating role of positive and negative mood in the relationship between coping and a range of health outcomes (mobility, self-care, usual activities, pain/discomfort, anxiety/depression, overall HRQoL), which identifies the potential pathways between coping and HRQoL in patients with advanced lung cancer.
- Consecutive sampling could compromise the generalizability of the findings.
- Cross-sectional design.

1. Introduction

During the past decade, lung cancer has become the most common incident cancer and the leading cause of cancer mortality in China and many other countries [1, 2]. The diagnosis of lung cancer can result in enormous stress for patients and their families, such as symptom burden [3], decisions about treatment options [4], and financial concerns [5]. The quality of life is significantly affected in patients with an advanced lung cancer [6]. The curative treatments are limited for advanced lung cancer, and the five-year survival rate of lung cancer is16.1% in China [7]. Improving or maintaining quality of life is the main focus of treatment. The prognostic value of health-related quality of life (HRQoL) in patients with lung cancer is supported by a range of studies [8, 9].

Previous research has investigated socio-demographic, clinical, and psychosocial correlates of HRQoL in cancer patients [10]. Common risk factors identified from previous studies included older age, being female, financial burden, and advanced stage [11]. Specifically, coping strategy is indicated to contribute to HRQoL in patients with advanced cancer [12, 13]. The manner in which patients cope with the life-threatening illness may affect patients' emotional state, perceptions of illness, and health behaviors, which can have an impact on the treatment course and ultimately health outcomes [14]. Two coping strategies, confrontation and acceptance, have received considerable attention in patients with a life-threatening illness [14-17].

Confrontation is defined as a set of coping strategies that involves seeking information and advice from various sources, seeking support from family and friends, and engaging in decision making [15]. It is actively oriented, which is indicated to be adaptive for cancer patients and associated with lower negative mood [18-20] and better quality of life [16, 17]. However, other studies found insignificant associations between confrontation and

health outcomes among cancer patients [14, 21, 22]. For instance, Nipp et al. [14] studied 350 patients with incurable lung or gastrointestinal cancer, and found that using active coping was not associated with psychological distress or quality of life. It is suggested that confrontation could direct one's attention to the disease and its side effects, making it less effective in coping with cancer [15, 17].

Acceptance is regarded as a strategy to cope with unchangeable or uncontrollable negative events [23]. Resigned acceptance is a form of acceptance, specifically, a passive form of acceptance, in which individuals accept the stressful situation and give up endeavors or hope to deal with it [23, 24]. It is different from the concept of acceptance in Acceptance and Commitment Therapy, which is a form of active acceptance and characterized by active embracing of thoughts and feelings without unnecessary attempts to alter them [25]. Research shows that resigned acceptance could be maladaptive, which was associated with less favorable outcomes, such as negative mood and lower quality of life, in cancer patients and survivors [21, 26, 27].

Confrontation and resigned acceptance may be associated with cultural views of illness in the Chinese cancer population. Confucianism and Taoism are two dominant philosophical tenets in Chinese culture [28]. Confucian beliefs emphasize the importance of life, and death is a taboo and perceived as a negative event [29]. Consistent with this, the majority of patients and their families in China would choose to continue curative treatments to sustain and prolong life until the end of life [30]. On the other hand, cancer and other illness are believed to be an act of Ming (also known as fate) in the Taoist belief system [28]. The fatalistic attitude toward cancer may lead to resigned acceptance, which may affect health outcomes during the illness trajectory [28].

Although research shows that coping is associated with HRQoL in cancer patients, the mechanism of the link between coping and HRQoL remains largely unexamined in cancer patients. Preliminary exploration suggests that mood may be a potential pathway between coping and health outcomes [31-35]. Folkman and Greer developed a model of stress and coping for serious illness, and Roberts et al. revised the model based on studies among patients with advanced cancer [36, 37]. The models highlight the association between coping and emotional outcomes in the face of cancer, as the way patients cope with the stressors can influence the emotional outcomes, leading to positive and/or negative emotion [36, 37]. On the other hand, studies indicate that mood is linked to health outcomes (e.g., HRQoL) in cancer patients and survivors [27, 38, 39]. Negative and positive mood involves different physiological responses (e.g., nervous, endocrine, and immune system functioning), which can influence overall physical health [40, 41]. Additionally, the broaden-and-build theory of positive mood indicates that positive mood can broaden one's attention scope and thought-action repertoires, which could be beneficial for physical health. In contrast, negative mood can fuel a narrowed, socially isolating thought-action tendencies, which could result in poor health outcomes [42, 43]. Given that coping strategies are related to mood, and that mood is related to HRQoL, it is possible that mood may be a mediational pathway between coping and HRQoL. In a prospective study among HIV caregivers, higher social coping predicted an increase in positive affect, which decreased levels of physical symptoms, whereas higher cognitive avoidance predicted enhanced negative affect, which resulted in higher levels of physical symptoms [33]. However, in the context of advanced cancer, to our knowledge, no study has examined the pathways between coping and HRQoL through mood. Since patients with advanced cancer can encounter numerous stresses, understanding the effect of coping on health and identifying the pathways through which patients maintain health and quality of life can provide important insights for clinical practice and interventions.

In summary, the current study addresses the relationships between coping, mood, and HRQoL among patients with advanced lung cancer. Specifically, we examined the effect of confrontation and resigned acceptance coping on positive mood, negative mood, and HRQoL. We also tested the mediating role of positive and negative mood in the relationship between coping and HRQoL among Chinese patients with advanced lung cancer.

2. Method

2.1 Study setting and participants

Participants were recruited from the inpatient unit of the department of chest-oncology medicine at a public hospital that specializes in chest-related disease in Shanghai, China. The hospital is well recognized for its expertise, resources, and treatments for chest-related disease. A large number of patients with lung cancer in east China come to this hospital and receive treatment there. Patients were eligible in the study if they (a) were 18 years or older, (b) had been diagnosed with lung cancer, (c) had an expected survival time > 3 months, (d) had no significant cognitive impairment, and (e) were able to communicate with interviewers. Studies show that cancer patients may experience a steep decline in HRQoL during the last 3 months of life [44]. Therefore, we purposefully included only those with an expected survival time of at least 3 months. Those who could not understand the questions were excluded from the sample. Between June 2016 and July 2016, 328 patients met the inclusion criteria and were enrolled in the study.

Data collection was conducted by trained undergraduate students majoring in medicine and public health. Doctors and nurses in the inpatient unit of the department of chest-oncology medicine screened the eligible patients based on the inclusion and exclusion criteria, and researchers approached them and introduced the study. Those who agreed to

participate in the study provided informed consent. Face-to-face interviews were then conducted. Disease and treatment information was extracted from medical records. The study was approved by the Ethics Committee of Shanghai Chest Hospital, Shanghai Jiao Tong University (No. KS1353). In accordance with our study aim, we focused on 267 patients with advanced-stage lung cancer (stage III or IV), and the 261 participants who provided full information on the main study variables (coping, mood, and HRQoL) were included in the data analysis. A flow chart of the sample selection procedure is presented in supplementary Figure 1.

2.2 Participant involvement

The participants were not involved in the design or recruitment process of this study. However, the patients in department of oncology who worked with the 2nd author (an oncologist) provided insights for the development of the research question. Permission to conduct the study was obtained from relevant hospital authorities and participants.

2.3 Measures

2.3.1 Health-related quality of life. The 5-level EuroQol 5-dimension (EQ-5D-5L) was used to measure HRQoL in this study [45]. It contained five questions to assess five health dimensions, as experienced in the recent days, namely mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Respondents rated the severity on 5 levels ranging from 1 (*no*) to 5 (*very severe*). In the current study, EQ-5D-5L domain scores and overall utility index were calculated. Domain scores were recoded reversely based on the original levels of each domain, with higher scores indicating better quality in the domain. EQ-5D-5L utility index was calculated based on value sets developed by the EuroQol Group. To our knowledge, no value sets have been developed in a Chinese representative sample for the calculation of utility index, so in this study, utility index was calculated based on value

sets weighted from a representative sample of the English general population [46]. The EQ-5D-5L utility index ranged from -1 to 1, with 1 representing full health, 0 representing a state of death, and negative values representing a state worse than death.

2.3.2 Coping. Two subscales of the Chinese version of the Medical Coping Modes Questionnaire (MCMQ) were used to measure confrontation and resigned acceptance coping strategies for lung cancer. MCMQ was developed by Feifel, Strack, and Nagy [15] among patients with a variety of life-threatening and chronic illnesses, and it is widely used for assessing coping strategies in patients in China [17, 47]. Acceptance-resignation subscale had five items, and confrontation subscale had nine items [15]. Sample items in acceptance-resignation subscale were as follows: "there is nothing you can do about your illness", "you don't care what happens to you", and "feel there is really no hope for your recovery." Sample items in confrontation subscale were as follows: "obtained information through books, magazines, and newspapers in the past several months", "try to talk about your illness with friends or relatives", "be involved in decisions regarding your treatment." In addition to original confrontation subscale with eight items, we added one item assessing how often participants "obtained information through the Internet and new media in the past several months," as the Internet and new media have become important sources of information that supplement books, magazines, and newspaper. All the items were rated on a 4-point Likert scale ranging from 1 (*never*) to 4 (*very often*). The mean score of each coping strategy was calculated, with a higher score indicating a higher probability of using that particular coping strategy. The Cronbach's α coefficients of confrontation and resigned acceptance in this study were 0.72 and 0.71, respectively.

2.3.3 Mood. Mood was measured using the Positive and Negative Affect Schedule (PANAS) [48]. The PANAS contained items to describe 10 positive affects (e.g., inspired, excited, determined) and 10 negative affects (e.g., afraid, upset, distressed). Respondents

rated their experiences of each affect during the past two weeks on a 5-point Likert scale ranging from 1 (*very slightly*) to 5 (*extremely*). The mean scores of items on the two subscales were calculated for positive mood and negative mood, respectively. In the current study, the Cronbach's α coefficients of negative mood and positive mood were 0.91 and 0.86, respectively.

2.3.4 Covariates. Sociodemographic factors included age, gender, education (elementary school or lower, middle school, high school, college or higher), and marital status (married, single, divorced, widowed). Perceived cancer-related financial burden was assessed by the question, "Have your disease and treatment caused you and your family financial difficulty?" and participants answered on a 5-point scale ranging from 0 (*No*) to 4 (*Very much*). Clinical factors included time of diagnosis, cancer stage, lung cancer type (adenocarcinoma, squamous, poorly differentiated, small cell, not otherwise specified), and treatment history (surgery, chemotherapy, radiotherapy, targeted therapy).

2.4 Data Analysis

First, descriptive statistics were presented for sociodemographic and clinical characteristics, and main study variables. Mean and standard deviation, or frequency and percentage, were computed for continuous and categorical variables, respectively. Independent *t* test, analysis of variance, and post-hoc comparison were conducted to analyze the effect of sociodemographic and clinical factors on positive mood, negative mood, and HRQoL (see supplementary Table 1). Correlational analyses were performed to examine the associations between the continuous variables.

Secondly, hierarchical, multiple, linear regression analyses were employed to examine the relationships among coping, mood, and HRQoL. The hierarchical regressions with HRQoL (domain scores and EQ-5D utility index) as a dependent variable involved three

steps: In step one, gender, age, cancer stage, and covariates that were significantly correlated with mood and HRQoL (i.e., financial burden, lung cancer type, a history of radiotherapy) were entered; In step two, confrontation and resigned acceptance were entered; In step three, positive and negative mood were entered.

Thirdly, the mediating effects of positive and negative mood in the relationship between coping and HRQoL were tested using the MEDIATE macro for SPSS developed by Preacher and Hayes [49]. Bootstrapping techniques using 5000 samples were used for the analysis, which was regarded as providing a more reliable estimate for the small sample size. Significant indirect effect was indicated by a 95% confidence interval of indirect effect without including zero. Power analyses indicated that in a model with two parallel mediators, a sample of 260 has 80% power to detect a 95% confidence interval of indirect effect, assuming correlations of r = 0.20 between independent variable, the dependent variable, and the mediators. Schoemann, Boulton, and Short suggest that this power analytic method is an appropriate approach for determining power and sample size in mediation models [50]. All tests were two tailed, and a *p*-value of <0.05 was considered statistically significant.

3. Results

3.1 Sociodemographic and Clinical Characteristics

The sociodemographic and clinical characteristics for the samples are shown in Table 1. A total sample of 261 participants had a mean age of 59.99 years (*SD* = 9.53). Males represented 70.1% of the samples. Most participants were married (94.6%) and perceived a slight to very severe cancer-related financial burden (85.8%). More than half of the participants had been diagnosed in the past 6 months (55.2%). More than 90% of the participants had ever received chemotherapy (96.6%), whereas a certain proportion had ever received surgery (23.4%), radiotherapy (23.4%), or targeted therapy (14.6%).

Table 1 Sample Characteristics

Variables	M(SD) / n (%)
Age (years)	59.99 (9.53)
Gender	
Male	183 (70.1%)
Female	78 (29.9%)
Education	
Elementary school or lower	55 (21.1%)
Middle school	91 (34.9%)
High school	66 (25.3%)
College or higher	49 (18.8%)
Marital status	
Married	247 (94.6%)
Single/divorced/ widowed	14 (5.4%)
Perceived cancer-related financial burden	
None	37 (14.2%)
Slight	100 (38.3%)
Moderate	63 (24.1%)
Severe	36 (13.8%)
Very Severe	25 (9.6%)
Time since diagnosis [a]	
Less than 6 months	144 (55.2%)
6-12months	32 (12.3%)
12-24 months	31 (11.9%)
More than 24 months	46 (17.6%)
Stage	
III	82 (31.4%)
IV	179 (68.6%)
Lung cancer type [b]	
NSC - Adenocarcinoma	140 (53.6%)
NSC - Squamous	47 (18.0%)

NSC - Poorly differentiated	24 (9.2%)
NSC - Others	7 (2.7%)
Small cell	43 (16.5%)
Treatment history	
Received surgery	
Yes	61 (23.4%)
No	200 (76.6%)
Received chemotherapy	
Yes	252 (96.6%)
No	9 (3.4%)
Received radiotherapy	
Yes	61 (23.4%)
No	200 (76.6%)
Received targeted therapy	
Yes	38 (14.6%)
No	223 (85.4%)

Note. a. For time since diagnosis, the sum of number is not 261 due to missing data; b. NSC: Non-small cell.

3.2 Coping, Mood, and HRQoL

Pearson correlation analysis was performed to examine the relationships between coping, mood, and HRQoL (see Table 2). A small and positive correlation was observed between confrontation coping and positive mood (r = 0.21). Resigned acceptance was moderately and positively correlated with negative mood (r = 0.46), but moderately and inversely correlated with positive mood (r = -0.27). Use of resigned acceptance was correlated with more difficulties in mobility (r = -0.21), self-care (r = -0.19), usual activities (r = -0.19), pain/discomfort (r = -0.19), anxiety/depression (r = -0.41), and lower EQ-5D utility index (r = -0.28).

Table 2 Correlation among coping, affect and HRQOL

	M (SD)	1	2	3	4	5	6	7	8	9
1. Confrontation	2.37 (0.49)	1								
2. Resigned acceptance	1.92 (0.62)	-0.03	1							
3. Positive mood	2.40 (0.76)	0.21**	-0.27**	1						
4. Negative mood	1.84 (0.76)	0.11	0.46**	-0.11	1					
5. Mobility	4.32 (0.99)	-0.05	-0.21**	0.19**	-0.28**	1				
6. Self-care	4.58 (0.86)	-0.06	-0.19**	0.15*	-0.28**	0.78**	1			
7. Usual activities	4.24 (0.97)	-0.10	-0.19**	0.16*	-0.27**	0.78**	0.73**	1		
8. Pain/discomfort	3.98 (0.87)	-0.08	-0.19**	0.14*	-0.28**	0.45**	0.43**	0.46**	1	
9. Anxiety/depression	4.22 (0.73)	-0.03	-0.41**	0.19**	-0.50**	0.21**	0.21**	0.25**	0.27**	1
10. EQ-5D utility index	0.80 (0.19)	-0.10	-0.28**	0.20**	-0.38**	0.84**	0.82**	0.84**	0.69**	0.45**

*p<0.05, **p<0.01

Scale range: Confrontation, resigned acceptance: 1 (never) – 4 (very often); Positive mood, negative mood: 1 (very slightly) – 5 (extremely); Mobility, self-care, usual activities, pain/discomfort, anxiety/depression: 1 (very severe) – 5 (no); EQ-5D utility index: -1 (worse than death) – 1 (full health)

Hierarchical regression analyses were used to examine the relationship of confrontation and resigned acceptance coping with positive mood, negative mood, and HRQoL (see Table 3). Age, gender, cancer stage, and significant correlates of mood and/or HRQoL ($p < 0.05$), including perceived cancer-related financial burden, a history of radiotherapy, and lung cancer type (poorly differentiated non-small cell, small cell, other non-small cell), were controlled in the hierarchical regression analyses. Regarding positive mood, in addition to covariates, confrontation and resigned acceptance were found to be significant factors, as confrontation was associated with higher positive mood ($\beta = 0.19$, $p = 0.002$), whereas resigned acceptance was associated with lower positive mood ($\beta = -0.25$, $p < 0.001$). Regarding negative mood, in addition to covariates, confrontation and resigned acceptance were significant factors, as use of confrontation ($\beta = 0.11$, $p = 0.040$) and resigned acceptance ($\beta = 0.44$, $p < 0.001$) were associated with higher negative mood.

Regarding the EQ-5D domain scores, after controlling sociodemographic and clinical covariates, confrontation was not associated with the domain scores, whereas resigned acceptance was inversely associated with all domains. Positive mood was associated with less difficulty in mobility, usual activities, pain/discomfort, but not associated with self-care and anxiety/depression. Negative mood was associated with more difficulty in all domains of HRQOL.

Regarding EQ-5D utility index, after controlling sociodemographic and clinical covariates, resigned acceptance was inversely associated with EQ-5D utility index ($\beta = -0.22$, $p < 0.001$), whereas confrontation was not associated with EQ-5D utility index. Moreover, the effects of mood on EQ-5D utility index were significant, as positive mood was associated with higher EQ-5D utility index ($\beta = 0.17$, $p = 0.005$), whereas negative mood was associated with lower EQ-5D utility index ($\beta = -0.28$, $p < 0.001$).

Table 3 Multiple regression results for predictors of mood and HRQOL

	Positive mood		Negative mood		Mobility		Self-care		Usual activities		Pain / discomfort		Anxiety / depression		EQ-5D utility index	
	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*
Step 1																
Age	-0.15	**0.021**	-0.04	0.53	-0.13	**0.040**	-0.13	**0.046**	-0.06	0.31	-0.07	0.25	0.01	0.91	-0.10	0.09
Gender [a]	-0.07	0.32	0.05	0.40	-0.07	0.29	-0.06	0.35	-0.09	0.15	-0.01	0.85	0.02	0.76	-0.03	0.68
Financial burden [b]	-0.14	**0.032**	0.30	**<0.001**	-0.16	**0.010**	-0.15	**0.017**	-0.20	**0.002**	-0.15	**0.018**	-0.25	**<0.001**	-0.22	**0.001**
Cancer stage [c]	-0.09	0.16	-0.07	0.22	0.00	0.99	0.05	0.46	0.03	0.67	0.04	0.58	0.04	0.51	0.04	0.53
Cancer type- other non-small cell (Reference)	0		0		0		0		0		0		0		0	
Cancer type- undifferentiated [d]	0.01	0.93	-0.03	0.58	-0.07	0.26	-0.08	0.19	-0.12	0.053	-0.08	0.19	-0.04	0.51	-0.14	**0.027**
Cancer type- small cell [d]	-0.08	0.21	-0.01	0.85	0.05	0.44	0.03	0.66	0.08	0.22	0.14	**0.025**	0.07	0.29	0.10	0.12
Received radiotherapy [e]	-0.03	0.63	0.16	**0.009**	-0.17	**0.006**	-0.19	**0.003**	-0.14	**0.026**	-0.20	**0.002**	-0.07	0.24	-0.20	**0.001**
ΔR^2	0.054		0.141		0.079		0.081		0.097		0.094		0.080		0.124	
Step 2																

Confrontation	0.19	**0.002**	0.11	**0.040**	-0.05	0.40	-0.05	0.39	-0.07	0.25	-0.07	0.29	-0.01	0.81	-0.08	0.17
Resigned acceptance	-0.25	**<0.001**	0.44	**<0.001**	-0.16	**0.013**	-0.15	**0.019**	-0.16	**0.012**	-0.14	**0.029**	-0.41	**<0.001**	-0.22	**<0.001**
ΔR^2	0.098		0.191		0.025		0.023		0.027		0.021		0.155		0.053	
Step 3																
Positive mood					0.16	**0.013**	0.12	0.078	0.14	**0.026**	0.14	**0.029**	0.10	0.076	0.17	**0.005**
Negative mood					-0.22	**0.003**	-0.20	**0.006**	-0.17	**0.020**	-0.20	**0.005**	-0.36	**<0.001**	-0.28	**<0.001**
ΔR^2					0.053		0.039		0.036		0.044		0.093		0.076	
Adjusted R^2	0.120		0.307		0.118		0.103		0.122		0.121		0.298		0.218	

Note. a. 0=Male, 1=Female; b. range:1 (no difficulty) – 5 (very much); c. 1=stage III, 2=stage IV; d. other non-small cell lung cancers was the reference group; e. 0=No, 1=Yes; f. standardized coefficients

3.3 Mediating Effect of Mood on the Association between Coping and HRQoL

The MEDIATE macro was used to examine the mediating effect of mood in the relationship between coping and HRQoL, controlling for age, gender, cancer stage, perceived cancer-related financial burden, history of radiotherapy, and lung cancer type (poorly differentiated non-small cell, small cell, other non-small cell). The indirect effect (ab) was estimated as the product of regression coefficients predicting mood from each coping strategy (a), and HRQoL from mood (b) (see Figure 1). Bootstrapping techniques using 5000 samples revealed significant indirect effects for confrontation and resigned acceptance on HRQoL through positive and negative mood, respectively. The results are presented in Table 4.

Although the total effects of confrontation on EQ-5D domains scores and utility index were not significant, competing indirect effects via mood were identified. On one hand, positive indirect effects were found for confrontation on mobility (point estimate = 0.06, *SE* = 0.03, 95% CI [0.01, 0.13]), usual activities (point estimate = 0.05, *SE* = 0.03, 95% CI [0.01, 0.12]), pain/discomfort (point estimate = 0.05, *SE* = 0.03, 95% CI [0.004, 0.11]), and overall utility index (point estimate = 0.01, *SE* = 0.01, 95% CI [0.003, 0.03]) through positive mood. On the other hand, negative indirect effects were found for confrontation on mobility (point estimate = -0.05, *SE* = 0.03, 95% CI [-0.12, -0.002]), pain/discomfort (point estimate = -0.04, *SE* = 0.02, 95% CI [-0.10, -0.001]), anxiety/depression (point estimate = -0.06, *SE* = 0.03, 95% CI [-0.13, -0.003]), and overall utility index (point estimate = -0.01, *SE* = 0.01, 95% CI [-0.03, -0.001]) through negative mood. The direct effects of confrontation on EQ-5D domains scores and utility index were not significant.

Resigned acceptance has a significant negative total effect on EQ-5D domains scores and utility index. Furthermore, indirect effects of resigned acceptance on HRQoL via positive and negative mood were identified. Use of resigned acceptance was associated with decrease

in positive mood, and increase in negative mood, which could lead to more difficulty in mobility, self-care, usual activities, pain/discomfort, anxiety/depression, and overall utility index (indirect effect via positive mood: point estimate = -0.01, *SE* = 0.01, 95% CI [-0.03, -0.003]; indirect effect via negative mood: point estimate = -0.04, *SE* = 0.01, 95% CI [-0.06, -0.02]).

Table 4 Mediation model testing the direct and indirect effect of coping on HRQOL via mood

Outcome	**Predictor**	**Mediator**	**Path a**	**Path b**	**Path ab: indirect effect of coping on HRQOL**		**Path c': Direct effect of coping on HRQOL**	**Path c: Total effect of coping on HRQOL**
			coef (se)	coef (se)	coef (se)	95% CI	coef (se)	coef (se)
HRQOL	Confrontation	Positive mood	0.30** (0.09)	0.04** (0.01)	0.01 (0.01)	[0.003, 0.03]	-0.03 (0.02)	-0.03 (0.02)
		Negative mood	0.17* (0.08)	-0.07*** (0.02)	-0.01 (0.01)	[-0.03, -0.001]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.01 (0.01)	[-0.03, -0.003]	-0.02 (0.02)	-0.07*** (0.02)
		Negative mood	0.54*** (0.07)		-0.04 (0.01)	[-0.06, -0.02]		
Mobility	Confrontation	Positive mood	0.30** (0.09)	0.21* (0.08)	0.06 (0.03)	[0.01, 0.13]	-0.12 (0.13)	-0.10 (0.12)
		Negative mood	0.17* (0.08)	-0.28** (0.09)	-0.05 (0.03)	[-0.12, -0.002]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.06 (0.03)	[-0.13, -0.01]	-0.03 (0.11)	-0.25* (0.10)
		Negative mood	0.54*** (0.07)		-0.15 (0.06)	[-0.27, -0.05]		
Self-care	Confrontation	Positive mood	0.30** (0.09)	0.13 (0.07)	0.04 (0.03)	[-0.003, 0.10]	-0.09 (0.11)	-0.09 (0.11)
		Negative mood	0.17* (0.08)	-0.23** (0.08)	-0.04 (0.03)	[-0.10, 0.002]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.04 (0.03)	[-0.10, -0.003]	-0.04 (0.10)	-0.21* (0.09)
		Negative mood	0.54*** (0.07)		-0.14 (0.05)	[-0.24, -0.05]		
Usual Activities	Confrontation	Positive mood	0.30** (0.09)	0.18* (0.08)	0.05 (0.03)	[0.01, 0.12]	-0.16 (0.12)	-0.14 (0.12)
		Negative mood	0.17* (0.08)	-0.22* (0.09)	-0.04 (0.02)	[-0.09, 0.001]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.06 (0.03)	[-0.12, -0.01]	-0.07 (0.11)	-0.25* (0.10)
		Negative mood	0.54*** (0.07)		-0.12 (0.05)	[-0.22, -0.02]		

Pain / Discomfort	Confrontation	Positive mood	0.30** (0.09)	0.16* (0.07)	0.05 (0.03)	[0.004, 0.11]	-0.12 (0.11)	-0.12 (0.11)
		Negative mood	0.17* (0.08)	-0.23** (0.08)	-0.04 (0.02)	[-0.10, -0.001]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.05 (0.03)	[-0.11, -0.005]	-0.02 (0.10)	-0.19* (0.09)
		Negative mood	0.54*** (0.07)		-0.13 (0.05)	[-0.23, -0.04]		
Anxiety / Depression	Confrontation	Positive mood	0.30** (0.09)	0.10 (0.05)	0.03 (0.02)	[-0.003, 0.74]	0.01 (0.08)	-0.02 (0.08)
		Negative mood	0.17* (0.08)	-0.34*** (0.06)	-0.06 (0.03)	[-0.13, -0.003]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.03 (0.02)	[-0.07, 0.003]	-0.26** (0.07)	-0.48*** (0.07)
		Negative mood	0.54*** (0.07)		-0.18 (0.04)	[-0.27, -0.11]		

Note. Age, gender, financial burden, disease stage, lung cancer type, and history of radiotherapy were controlled in the mediation model. All coefficients (a, b, c', c) were unstandardized coefficients. *p<0.05, **p<0.01, *** p<0.001

4. Discussion

To our knowledge, this is the first study to examine the relationship between coping, positive and negative mood, and HRQoL and the mediating role of mood in the relationship between coping and HRQoL among patients with advanced cancer. The findings of this study indicate that examining the pathway via positive and negative mood can generate a new understanding of the effect of coping on HRQoL among patients with advanced lung cancer, regardless of sociodemographic and clinical factors. The confrontation coping strategy was not directly associated with domains of HRQoL or overall HRQoL, but two significant indirect pathways via mood were identified. On one hand, confrontation had positive indirect effects on mobility, usual activities, pain, and overall HRQoL via positive mood; On the other hand, confrontation had negative indirect effects on mobility, pain, anxiety, and overall HRQoL via negative mood; Positive and negative indirect effect could counteract, resulting in a nonsignificant total effect. In contrast, use of resigned acceptance coping was associated with an increase in negative mood and a decrease in positive mood, which could in turn result in more difficulty in mobility, self-care, usual activities, pain, and poor overall HRQoL. On the whole, this is a unique finding that indicates the ambivalence of confrontation and the maladaptive nature of resigned acceptance among patients with advanced lung cancer.

The mean EQ-5D utility index in the current study was found to be 0.80, which was comparable to a study among patients with advanced non-small cell lung cancer in China with a utility index of 0.81 [51]. Consistent with previous studies, patients perceiving higher financial burden were more likely to report poor HRQoL compared to those perceiving lower financial burden related to cancer [11, 52]. Financial burden may restrict access to some drugs and treatment [52], and it may also lead to a sense of guilt for relying on families [29], which may affect health outcomes.

The current findings support the theory of stress and coping in the context of advanced cancer by indicating that coping can play a role in adapting to the experience of lung cancer, which could in turn influence emotional and health outcomes [36, 37]. The current study is in line with previous studies indicating that resigned acceptance was associated with less favorable outcomes [21, 26]. Resigned acceptance is related to the fatalistic attitude toward illness in traditional Taoist beliefs [28]. Giving up control in the actual situation, or even other aspects of life and holding negative expectations about the future could be associated with low levels of positive mood, and increase negative mood, which contribute to poor health outcomes in patients with advanced cancer. Moreover, it should be noted that PANAS mainly measured the high-activated affect [53]. It is possible that giving up attempt and hope may induce high-activated negative mood (e.g., distressed, scared, ashamed), rather than the high-activated positive mood (e.g., active, alert, interested). However, further study is suggested to investigate the relationship between resigned acceptance and low-activated mood, for instance, if low-activated positive mood (e.g., peace, calm) may emerge by accepting the advanced cancer despite in a passive way.

Confrontation was found to be associated with increased positive and negative mood. In the current study, confrontation was characterized by attempts such as seeking information and support from various sources and being involved in decision making. Through such efforts, patients may regain a sense of control and redirect energy to constructive actions during treatment and daily living, which might facilitate the occurrence of positive mood. However, it is also possible that individuals could encounter various stressful decisions and pieces of information when they actively confront the advanced disease, which might lead to negative mood.

Our findings are in line with other studies reporting a nonsignificant association between confrontation and HRQoL among cancer patients [14, 21, 22]. Particularly, the

findings on the mediating role of mood can help clarify the mechanisms underlying the nonsignificant association. The coexisting positive and negative indirect effect via mood could counteract one another, resulting in a null, or weak, total effect of confrontation on HRQoL. The ambivalence of confrontation may also reflect the effect of fighting attitude towards life-threatening illness in Chinese population, in which the patients and their families would seek, try, and continue available curative treatments to sustain and prolong life. Even though actively confronting the advanced cancer may have some benefits (e.g., sense of control, constructive actions and skills), it may also remind patients of the potential incurable nature of advanced cancer and increase distress.

This study indicated that mood can be a pathway between coping and health outcomes. One explanation is related to physiology of mood [54], as positive and negative mood are associated with physiological levels in different directions, which can lead to different health outcomes. The second explanation is related to thought-action repertoires [43]. Negative mood is suggested to narrow the thought-action repertoires and increase unhealthy lifestyle and social isolation [43, 55], which could result in poor health outcomes. In contrast, positive affect is suggested to broaden the scope of attention and thought-action repertoires and build up personal and social resources [43], which could be beneficial to health outcomes. The third explanation is related to attributional interpretation [33]. HRQoL refers to a self-perceived health status, and it is possible that participants in a negative mood tend to perceive lower health status (more difficulties in daily living and symptoms) than those in a positive mood.

This study has some limitations. First, causality on the relationships between coping, mood, and HRQoL could not be drawn out from this cross-sectional study. Secondly, although Medical Coping Modes Questionnaire measured three coping strategies (i.e., confrontation, acceptance-resignation, avoidance), reliability of avoidance, indicated by

Cronbach' α coefficient, was low in the current study. This restricted us from analyzing the effect of the avoidance strategy. Thirdly, although EuroQol 5-dimension was used to measure HRQoL among patients with advanced cancer in a range of studies [51, 56], the measurement properties of the instrument is needed to be examined further in patients with advanced cancer [57]. Fourthly, the sample was recruited from one hospital in China, which could compromise the generalizability of the findings.

Considering the effect of coping strategies, the findings of our study suggest specific attention to resigned acceptance among patients with advanced cancer. Despite patients accepting the reality of advanced disease, practitioners may help them to regain a sense of control and develop constructive responses. Acceptance-based interventions, such as Acceptance and Commitment Therapy, may be a worthwhile approach, which are suggested to reduce emotional distress and improve quality of life by facilitating the active acceptance of unpleasant thoughts and feelings in cancer patients [58, 59]. Resigned acceptance is associated with a variety of negative feelings such as fear and distressed. Support from family and a positive environment is suggested to relieve the fears and fatalistic attitude [60, 61]. Additionally, the associations of confrontation with both positive and negative mood indicates the need to consider this ambivalent emotional experience among patients who actively confront the advanced cancer. Being actively to deal with the stressors during the illness trajectory may enhance the positive mood, but practitioners is suggested to pay attention to the excessive information- or treatment-seeking behaviors, and help relieve anxiety and fear among patients. Finally, when implementing interventions for the improvement of HRQoL, we suggest that practitioners consider the role of both positive and negative mood, which could serve as pathways between coping and HRQoL among patients with advanced lung cancer. Early palliative care may be integrated into standard oncology

care, which is suggested to facilitate adaptive coping, reduce emotional distress, and improve quality of life in patients with advanced cancer [62].

Figure 1 Positive and negative mood as mediators of the association between coping and HRQoL

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Contributors

HY, JH, LV, CJ designed the study. HY, JH, YM, ZJ, and LG collected data. HY and CJ analyzed the data. HY and CJ drafted the manuscript. HY, JH, YM, ZJ, LG, LV, CJ revised the manuscript.

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Competing interests

The authors declare that they have no conflict of interest.

Patient consent

Obtained.

Data sharing statement

No additional data were available.

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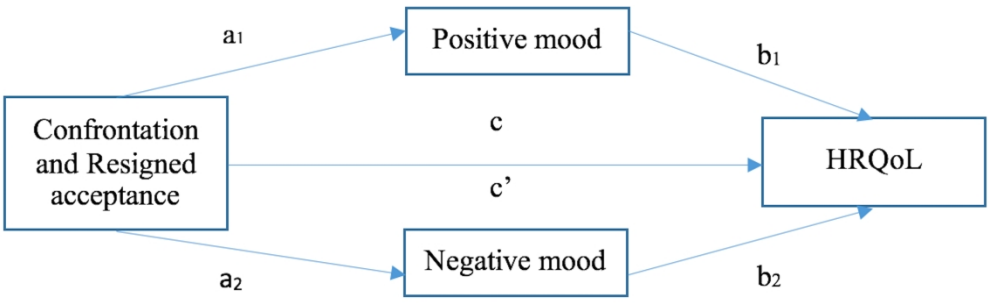


Positive and negative mood as mediators of the association between coping and HRQoL

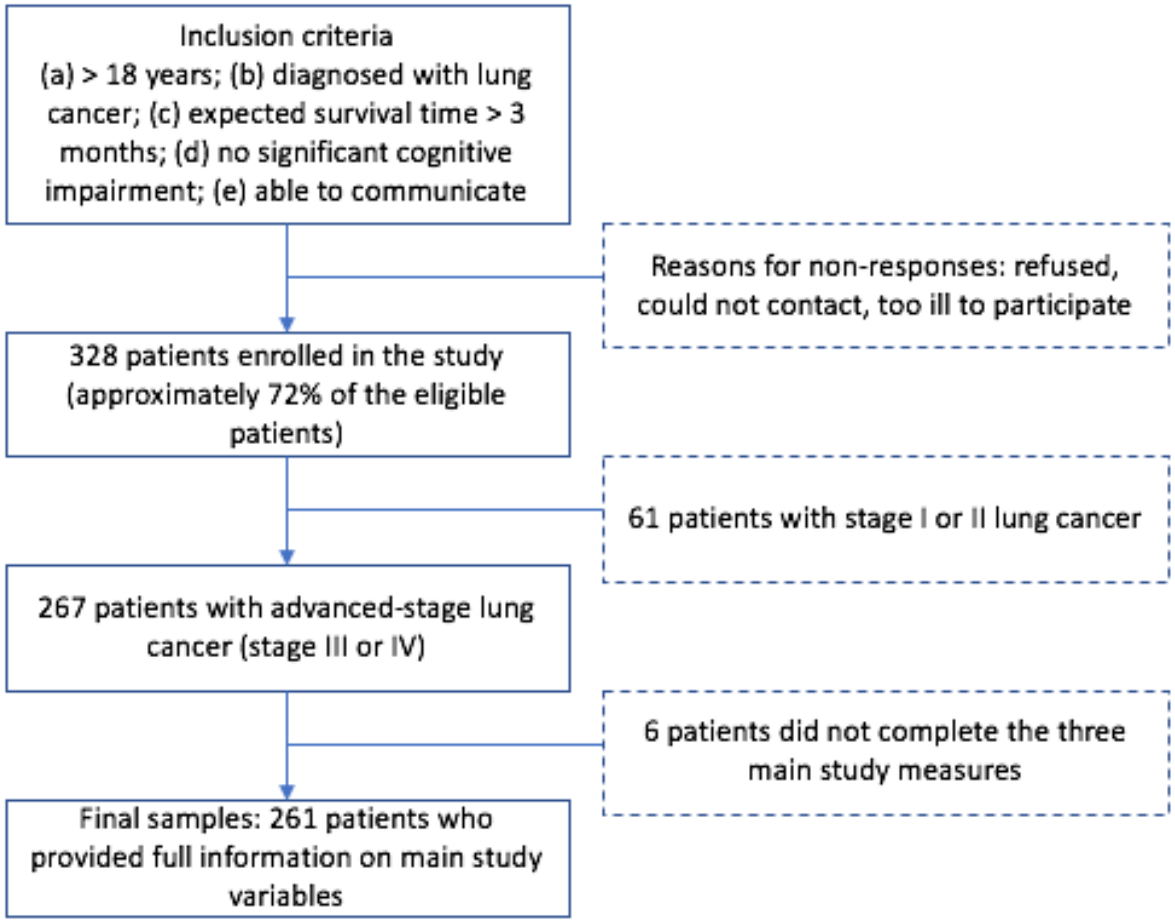
Table 1 Mood and Health-related Quality of Life by Socio-demographic and Clinical Characteristics

Variables	M(SD) / n (%)	Positive mood	Negative mood	Mobility	Self-care	Usual activities	Pain/ discomfort	Anxiety/ depression	EQ-5D utility index
Age (years)	59.99 (9.53)								
Gender									
Male	183 (70.1%)	2.41 (0.75)	1.80 (0.73)	4.39 (0.95)	4.63 (0.79)	4.33 (0.92)	4.03 (0.87)	4.24 (0.75)	0.81 (0.17)
Female	78 (29.9%)	2.34 (0.78)	1.93 (0.83)	4.21 (1.04)	4.50 (0.96)	4.06 (1.05)	3.91 (0.87)	4.21 (0.65)	0.78 (0.21)
Education									
Elementary school or lower	55 (21.1%)	2.28 (0.79)	1.82 (0.73)	4.54 (0.92)	4.64 (0.80)	4.31 (0.96)	3.98 (0.91)	4.11 (0.74)	0.80 (0.18)
Middle school	91 (34.9%)	2.35 (0.69)	1.94 (0.79)	4.24 (0.96)	4.57 (0.86)	4.14 (1.04)	3.90 (0.87)	4.16 (0.79)	0.78 (0.19)
High school	66 (25.3%)	2.46 (0.77)	1.71 (0.63)	4.32 (1.08)	4.59 (0.89)	4.29 (0.96)	4.05 (0.79)	4.32 (0.66)	0.82 (0.17)
College or higher	49 (18.8%)	2.51 (0.84)	1.83 (0.88)	4.41 (0.96)	4.59 (0.84)	4.35 (0.86)	4.10 (0.94)	4.35 (0.63)	0.83 (0.20)
Marital status									
Married	247 (94.6%)	2.40 (0.77)	1.83 (0.76)	4.34 (0.98)	4.60 (0.85)	4.25 (0.98)	3.98 (0.89)	4.23 (0.71)	0.80 (0.19)
Single/divorced/ widowed	14 (5.4%)	2.23 (0.58)	1.86 (0.82)	4.21 (1.05)	4.57 (0.85)	4.29 (0.83)	4.21 (0.58)	4.07 (1.00)	0.78 (0.18)
Perceived cancer-related financial burden									
None	37 (14.2%)	2.72 (0.89)	1.47 (0.50)	4.86 (0.42)	4.92 (0.28)	4.81 (0.46)	4.51 (0.56)	4.59 (0.50)	0.92 (0.08)
Slight	100 (38.3%)	2.27 (0.74)	1.74 (0.63)	4.21 (1.09)	4.54 (0.88)	4.23 (0.91)	3.91 (0.79)	4.22 (0.56)	0.78 (0.19)
Moderate	63 (24.1%)	2.53 (0.80)	1.87 (0.74)	4.43 (0.86)	4.65 (0.79)	4.17 (0.98)	3.90 (0.93)	4.27 (0.70)	0.80 (0.18)
Severe	36 (13.8%)	2.16 (0.51)	1.94 (0.84)	4.25 (0.77)	4.64 (0.68)	4.22 (0.90)	4.06 (1.01)	4.19 (0.71)	0.82 (0.14)
Very Severe	25 (9.6%)	2.38 (0.62)	2.52 (1.02)	3.96 (1.34)	4.12 (1.33)	3.76 (1.42)	3.68 (0.95)	3.64 (1.19)	0.68 (0.26)
Time since diagnosis[a]									
Less than 6 months	144 (55.2%)	2.38 (0.77)	1.84 (0.77)	4.40 (0.96)	4.60 (0.84)	4.24 (1.02)	3.95 (0.90)	4.19 (0.76)	0.80 (0.19)
6-12months	32 (12.3%)	2.54 (0.68)	1.91 (0.72)	4.19 (1.28)	4.50 (1.05)	4.19 (1.12)	4.19 (0.78)	4.19 (0.82)	0.79 (0.23)
12-24 months	31 (11.9%)	2.54 (0.87)	1.71 (0.75)	4.35 (0.80)	4.71 (0.53)	4.42 (0.62)	3.97 (0.71)	4.32 (0.65)	0.83 (0.11)

More than 24 months	46 (17.6%)	2.25 (0.72)	1.86 (0.75)	4.17 (1.00)	4.48 (0.96)	4.17 (0.93)	3.91 (0.96)	4.26 (0.61)	0.78 (0.20)
Stage									
III	82 (31.4%)	2.50 (0.71)	1.96 (0.90)	4.35 (0.93)	4.55 (0.86)	4.20 (1.09)	3.95 (0.94)	4.13 (0.78)	0.79 (0.19)
IV	179 (68.6%)	2.34 (0.78)	1.78 (0.68)	4.33 (1.00)	4.61 (0.84)	4.28 (0.91)	4.01 (0.84)	4.27 (0.69)	0.81 (0.18)
Lung cancer type[b]									
NSC-Adenocarcinoma	140 (53.6%)	2.39 (0.78)	1.88 (0.79)	4.28 (0.99)	4.56 (0.85)	4.20 (0.94)	3.91 (0.92)	4.18 (0.70)	0.79 (0.19)
NSC-Squamous	47 (18.0%)	2.50 (0.81)	1.84 (0.80)	4.45 (0.85)	4.68 (0.63)	4.32 (0.86)	4.00 (0.81)	4.26 (0.57)	0.81 (0.14)
NSC-Poorly differentiated	24 (9.2%)	2.46 (0.61)	1.77 (0.67)	4.08 (1.25)	4.38 (1.21)	3.88 (1.39)	3.75 (0.94)	4.13 (0.99)	0.72 (0.24)
NSC-others	7 (2.7%)	2.30 (0.60)	1.64 (0.40)	4.71 (0.49)	5.00 (0.00)	4.71 (0.49)	4.71 (0.49)	4.57 (0.53)	0.92 (0.10)
Small cell	43 (16.5%)	2.26 (0.76)	1.76 (0.71)	4.49 (0.96)	4.67 (0.87)	4.49 (0.88)	4.26 (0.73)	4.35 (0.78)	0.85 (0.17)
Treatment									
Received surgery									
Yes	61 (23.4%)	2.49 (0.78)	1.95 (0.85)	4.20 (0.98)	4.51 (0.83)	4.20 (0.96)	3.97 (0.86)	4.30 (0.74)	0.80 (0.18)
No	200 (76.6%)	2.36 (0.75)	1.80 (0.73)	4.38 (0.98)	4.62 (0.85)	4.27 (0.97)	4.00 (0.88)	4.21 (0.72)	0.80 (0.19)
Received chemotherapy									
Yes	252 (96.6%)	2.40 (0.76)	1.83 (0.76)	4.33 (0.99)	4.59 (0.86)	4.25 (0.98)	4.00 (0.87)	4.22 (0.73)	0.80 (0.19)
No	9 (3.4%)	2.16 (0.68)	1.83 (0.72)	4.44 (0.73)	4.67 (0.50)	4.33 (0.71)	3.67 (1.00)	4.33 (0.50)	0.81 (0.16)
Received radiotherapy									
Yes	61 (23.4%)	2.36 (0.70)	2.04 (0.87)	4.05 (1.19)	4.33 (1.21)	4.02 (1.09)	3.74 (1.05)	4.13 (0.62)	0.74 (0.23)
No	200 (76.6%)	2.40 (0.78)	1.77 (0.71)	4.43 (0.89)	4.68 (0.69)	4.33 (0.92)	4.07 (0.80)	4.26 (0.75)	0.82 (0.16)
Received targeted therapy									
Yes	38 (14.6%)	2.24 0.79)	1.83 (0.56)	4.21 (1.14)	4.47 (1.08)	4.11 (1.09)	3.79 (1.04)	4.26 (0.64)	0.77 (0.25)
No	223 (85.4%)	2.42 (0.75)	1.83 (0.79)	4.36 (0.95)	4.61 (0.80)	4.28 (0.95)	4.03 (0.84)	4.22 (0.74)	0.81 (0.17)

Scale range: Confrontation, resigned acceptance: 1 (never) – 4 (very often); Positive mood, negative mood: 1 (very slightly) – 5 (extremely); Mobility, self-care, usual activities, pain/discomfort, anxiety/depression: 1 (very severe) – 5 (no); EQ-5D utility index: -1 (worse than death) – 1 (full health)

Figure 1 Flow Chart of the Sample Selection Procedure



STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2,3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-7
Objectives	3	State specific objectives, including any pre-specified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	8
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-10
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10-11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10-11
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	Not applicable

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	Supplementary figure 1
		(c) Consider use of a flow diagram	Supplementary figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11-13
		(b) Indicate number of participants with missing data for each variable of interest	13
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Not applicable
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	14,15
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	14-22
		(*b*) Report category boundaries when continuous variables were categorized	14-22
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	23
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	25-26
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	23-26
Generalisability	21	Discuss the generalisability (external validity) of the study results	25-26
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	27

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Coping, mood, and health-related quality of life: A cross-sectional study in Chinese patients with advanced lung cancer

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Secondary Subject Heading:	Patient-centred medicine
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Coping, mood, and health-related quality of life: A cross-sectional study in Chinese patients with advanced lung cancer

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Abstract

Objectives: The ways patients cope with advanced cancer can influence their health-related quality of life (HRQoL). This study aims to examine the mediating role of positive and negative mood in the relationship between coping and HRQoL in patients with advanced lung cancer.

Methods: A consecutive sample of 261 patients (mean age: 59.99±9.53) diagnosed with stage III or IV lung cancer was recruited from the inpatient unit in a hospital that specializes in chest-related disease in Shanghai, China. Participants completed measurements including Medical Coping Modes Questionnaire, Positive and Negative Affect Schedule, and 5-level EuroQol 5-dimension instrument.

Results: Although the total effects of confrontation on HRQoL were not significant, competing indirect effects via mood were identified: (1) Positive indirect effects through positive mood were found for confrontation on mobility, usual activities, pain/discomfort, and overall utility index (indirect effect = 0.01, 95% CI 0.003 to 0.03); (2) Negative indirect effects through negative mood were found for confrontation on mobility, pain/discomfort, anxiety/depression, and overall utility index (indirect effect = -0.01, 95% CI -0.03 to -0.001). Resigned acceptance was negatively associated with HRQoL, and indirect effects via mood were identified: (1) Negative indirect effects through positive mood were found for resigned acceptance on mobility, self-care, usual activities, pain/discomfort, and overall utility index (indirect effect = -0.01, 95% CI -0.03 to -0.003); (2) Negative indirect effects through negative mood were found for resigned acceptance on domains of HRQoL and overall utility index (indirect effect = -0.04, 95% CI -0.06 to -0.02).

Conclusions: Confronting advanced lung cancer can fuel ambivalent emotional experiences. Nevertheless, accepting the illness in a resigned way can be maladaptive for health outcomes.

The findings suggest interventions that facilitate adaptive coping, reduce negative mood, and enhance positive mood, as this could help to improve or maintain HRQoL in patients with advanced lung cancer.

Keywords: coping; quality of life; mood; lung cancer

Strengths and limitations of this study

- The study addressed health-related quality of life (HRQoL), an important health outcome of treatment for advanced lung cancer, and examined the psychological factors associated with HRQoL.
- The study examined the mediating role of positive and negative mood in the relationship between coping and a range of health outcomes (mobility, self-care, usual activities, pain/discomfort, anxiety/depression, overall HRQoL), which identifies the potential pathways between coping and HRQoL in patients with advanced lung cancer.
- Consecutive sampling could compromise the generalizability of the findings.
- Cross-sectional design.

1. Introduction

During the past decade, lung cancer has become the most common incident cancer and the leading cause of cancer mortality in China and many other countries [1, 2]. The diagnosis of lung cancer can result in enormous stress for patients and their families, such as symptom burden [3], decisions about treatment options [4], and financial concerns [5]. The quality of life is significantly affected in patients with an advanced lung cancer [6]. The curative treatments are limited for advanced lung cancer, and the five-year survival rate of lung cancer is16.1% in China [7]. Improving or maintaining quality of life is the main focus of treatment. The prognostic value of health-related quality of life (HRQoL) in patients with lung cancer is supported by a range of studies [8, 9].

Previous research has investigated socio-demographic, clinical, and psychosocial correlates of HRQoL in cancer patients [10]. Common risk factors identified from previous studies included older age, being female, financial burden, and advanced stage [11]. Specifically, coping strategy is indicated to contribute to HRQoL in patients with advanced cancer [12, 13]. The manner in which patients cope with the life-threatening illness may affect patients' emotional state, perceptions of illness, and health behaviors, which can have an impact on the treatment course and ultimately health outcomes [14]. Two coping strategies, confrontation and acceptance, have received considerable attention in patients with a life-threatening illness [14-17].

Confrontation is defined as a set of coping strategies that involves seeking information and advice from various sources, seeking support from family and friends, and engaging in decision making [15]. It is actively oriented, which is indicated to be adaptive for cancer patients and associated with lower negative mood [18-20] and better quality of life [16, 17]. However, other studies found insignificant associations between confrontation and

health outcomes among cancer patients [14, 21, 22]. For instance, Nipp et al. [14] studied 350 patients with incurable lung or gastrointestinal cancer, and found that using active coping was not associated with psychological distress or quality of life. It is suggested that confrontation could direct one's attention to the disease and its side effects, making it less effective in coping with cancer [15, 17].

Acceptance is regarded as a strategy to cope with unchangeable or uncontrollable negative events [23]. Resigned acceptance is a form of acceptance, specifically, a passive form of acceptance, in which individuals accept the stressful situation and give up endeavors or hope to deal with it [23, 24]. It is different from the concept of acceptance in Acceptance and Commitment Therapy, which is a form of active acceptance and characterized by active embracing of thoughts and feelings without unnecessary attempts to alter them [25]. Research shows that resigned acceptance could be maladaptive, which was associated with less favorable outcomes, such as negative mood and lower quality of life, in cancer patients and survivors [21, 26, 27].

Confrontation and resigned acceptance may be associated with cultural views of illness in the Chinese cancer population. Confucianism and Taoism are two dominant philosophical tenets in Chinese culture [28]. Confucian beliefs emphasize the importance of life, and death is a taboo and perceived as a negative event [29]. Consistent with this, the majority of patients and their families in China would choose to continue curative treatments to sustain and prolong life until the end of life [30]. On the other hand, cancer and other illness are believed to be an act of Ming (also known as fate) in the Taoist belief system [28]. The fatalistic attitude toward cancer may lead to resigned acceptance, which may affect health outcomes during the illness trajectory [28].

Although research shows that coping is associated with HRQoL in cancer patients, the mechanism of the link between coping and HRQoL remains largely unexamined in cancer patients. Preliminary exploration suggests that mood may be a potential pathway between coping and health outcomes [31-35]. Folkman and Greer developed a model of stress and coping for serious illness, and Roberts et al. revised the model based on studies among patients with advanced cancer [36, 37]. The models highlight the association between coping and emotional outcomes in the face of cancer, as the way patients cope with the stressors can influence the emotional outcomes, leading to positive and/or negative emotion [36, 37]. On the other hand, studies indicate that mood is linked to health outcomes (e.g., HRQoL) in cancer patients and survivors [27, 38, 39]. Negative and positive mood involves different physiological responses (e.g., nervous, endocrine, and immune system functioning), which can influence overall physical health [40, 41]. Additionally, the broaden-and-build theory of positive mood indicates that positive mood can broaden one's attention scope and thought-action repertoires, which could be beneficial for physical health. In contrast, negative mood can fuel a narrowed, socially isolating thought-action tendencies, which could result in poor health outcomes [42, 43]. Given that coping strategies are related to mood, and that mood is related to HRQoL, it is possible that mood may be a mediational pathway between coping and HRQoL. In a prospective study among HIV caregivers, higher social coping predicted an increase in positive affect, which decreased levels of physical symptoms, whereas higher cognitive avoidance predicted enhanced negative affect, which resulted in higher levels of physical symptoms [33]. However, in the context of advanced cancer, to our knowledge, no study has examined the pathways between coping and HRQoL through mood. Since patients with advanced cancer can encounter numerous stresses, understanding the effect of coping on health and identifying the pathways through which patients maintain health and quality of life can provide important insights for clinical practice and interventions.

In summary, the current study addresses the relationships between coping, mood, and HRQoL among patients with advanced lung cancer. Specifically, we examined the effect of confrontation and resigned acceptance coping on positive mood, negative mood, and HRQoL. We also tested the mediating role of positive and negative mood in the relationship between coping and HRQoL among Chinese patients with advanced lung cancer.

2. Method

2.1 Study setting and participants

Participants were recruited from the inpatient unit of the department of chest-oncology medicine at a public hospital that specializes in chest-related disease in Shanghai, China. The hospital is well recognized for its expertise, resources, and treatments for chest-related disease. A large number of patients with lung cancer in east China come to this hospital and receive treatment there. Patients were eligible in the study if they (a) were 18 years or older, (b) had been diagnosed with lung cancer, (c) had an expected survival time > 3 months, (d) had no significant cognitive impairment, and (e) were able to communicate with interviewers. Studies show that cancer patients may experience a steep decline in HRQoL during the last 3 months of life [44]. Therefore, we purposefully included only those with an expected survival time of at least 3 months. Those who could not understand the questions were excluded from the sample. Between June 2016 and July 2016, 328 patients met the inclusion criteria and were enrolled in the study.

Data collection was conducted by trained undergraduate students majoring in medicine and public health. Doctors and nurses in the inpatient unit of the department of chest-oncology medicine screened the eligible patients based on the inclusion and exclusion criteria, and researchers approached them and introduced the study. Those who agreed to

participate in the study provided informed consent. Face-to-face interviews were then conducted. Disease and treatment information was extracted from medical records. The study was approved by the Ethics Committee of Shanghai Chest Hospital, Shanghai Jiao Tong University (No. KS1353). In accordance with our study aim, we focused on 267 patients with advanced-stage lung cancer (stage III or IV), and the 261 participants who provided full information on the main study variables (coping, mood, and HRQoL) were included in the data analysis. A flow chart of the sample selection procedure is presented in supplementary Figure 1.

2.2 Participant and public involvement

The participants were not involved in the design or recruitment process of this study. However, the patients in department of oncology who worked with the 2nd author (an oncologist) provided insights for the development of the research question. Permission to conduct the study was obtained from relevant hospital authorities and participants.

2.3 Measures

2.3.1 Health-related quality of life. The 5-level EuroQol 5-dimension (EQ-5D-5L) was used to measure HRQoL in this study [45]. It contained five questions to assess five health dimensions, as experienced in the recent days, namely mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Respondents rated the severity on 5 levels ranging from 1 (*no*) to 5 (*very severe*). In the current study, EQ-5D-5L domain scores and overall utility index were calculated. Domain scores were recoded reversely based on the original levels of each domain, with higher scores indicating better quality in the domain. EQ-5D-5L utility index was calculated based on value sets developed by the EuroQol Group. To our knowledge, no value sets have been developed in a Chinese representative sample for the calculation of utility index, so in this study, utility index was calculated based on value

sets weighted from a representative sample of the English general population [46]. The EQ-5D-5L utility index ranged from -1 to 1, with 1 representing full health, 0 representing a state of death, and negative values representing a state worse than death.

2.3.2 Coping. Two subscales of the Chinese version of the Medical Coping Modes Questionnaire (MCMQ) were used to measure confrontation and resigned acceptance coping strategies for lung cancer. MCMQ was developed by Feifel, Strack, and Nagy [15] among patients with a variety of life-threatening and chronic illnesses, and it is widely used for assessing coping strategies in patients in China [17, 47]. Acceptance-resignation subscale had five items, and confrontation subscale had nine items [15]. Sample items in acceptance-resignation subscale were as follows: "there is nothing you can do about your illness", "you don't care what happens to you", and "feel there is really no hope for your recovery." Sample items in confrontation subscale were as follows: "obtained information through books, magazines, and newspapers in the past several months", "try to talk about your illness with friends or relatives", "be involved in decisions regarding your treatment." In addition to original confrontation subscale with eight items, we added one item assessing how often participants "obtained information through the Internet and new media in the past several months," as the Internet and new media have become important sources of information that supplement books, magazines, and newspaper. All the items were rated on a 4-point Likert scale ranging from 1 (*never*) to 4 (*very often*). The mean score of each coping strategy was calculated, with a higher score indicating a higher probability of using that particular coping strategy. The Cronbach's α coefficients of confrontation and resigned acceptance in this study were 0.72 and 0.71, respectively.

2.3.3 Mood. Mood was measured using the Positive and Negative Affect Schedule (PANAS) [48]. The PANAS contained items to describe 10 positive affects (e.g., inspired, excited, determined) and 10 negative affects (e.g., afraid, upset, distressed). Respondents

rated their experiences of each affect during the past two weeks on a 5-point Likert scale ranging from 1 (*very slightly*) to 5 (*extremely*). The mean scores of items on the two subscales were calculated for positive mood and negative mood, respectively. In the current study, the Cronbach's α coefficients of negative mood and positive mood were 0.91 and 0.86, respectively.

2.3.4 Covariates. Sociodemographic factors included age, gender, education (elementary school or lower, middle school, high school, college or higher), and marital status (married, single, divorced, widowed). Perceived cancer-related financial burden was assessed by the question, "Have your disease and treatment caused you and your family financial difficulty?" and participants answered on a 5-point scale ranging from 0 (*No*) to 4 (*Very much*). Clinical factors included time of diagnosis, cancer stage, lung cancer type (adenocarcinoma, squamous, poorly differentiated, small cell, not otherwise specified), and treatment history (surgery, chemotherapy, radiotherapy, targeted therapy).

2.4 Data Analysis

First, descriptive statistics were presented for sociodemographic and clinical characteristics, and main study variables. Mean and standard deviation, or frequency and percentage, were computed for continuous and categorical variables, respectively. Independent *t* test, analysis of variance, and post-hoc comparison were conducted to analyze the effect of sociodemographic and clinical factors on positive mood, negative mood, and HRQoL (see supplementary Table 1). Correlational analyses were performed to examine the associations between the continuous variables.

Secondly, hierarchical, multiple, linear regression analyses were employed to examine the relationships among coping, mood, and HRQoL. The hierarchical regressions with HRQoL (domain scores and EQ-5D utility index) as a dependent variable involved three

steps: In step one, gender, age, cancer stage, and covariates that were significantly correlated with mood and HRQoL (i.e., financial burden, lung cancer type, a history of radiotherapy) were entered; In step two, confrontation and resigned acceptance were entered; In step three, positive and negative mood were entered.

Thirdly, the mediating effects of positive and negative mood in the relationship between coping and HRQoL were tested using the MEDIATE macro for SPSS developed by Preacher and Hayes [49]. Bootstrapping techniques using 5000 samples were used for the analysis, which was regarded as providing a more reliable estimate for the small sample size. Significant indirect effect was indicated by a 95% confidence interval of indirect effect without including zero. Power analyses indicated that in a model with two parallel mediators, a sample of 260 has 80% power to detect a 95% confidence interval of indirect effect, assuming correlations of r = 0.20 between independent variable, the dependent variable, and the mediators. Schoemann, Boulton, and Short suggest that this power analytic method is an appropriate approach for determining power and sample size in mediation models [50]. All tests were two tailed, and a *p*-value of <0.05 was considered statistically significant.

3. Results

3.1 Sociodemographic and Clinical Characteristics

The sociodemographic and clinical characteristics for the samples are shown in Table 1. A total sample of 261 participants had a mean age of 59.99 years (*SD* = 9.53). Males represented 70.1% of the samples. Most participants were married (94.6%) and perceived a slight to very severe cancer-related financial burden (85.8%). More than half of the participants had been diagnosed in the past 6 months (55.2%). More than 90% of the participants had ever received chemotherapy (96.6%), whereas a certain proportion had ever received surgery (23.4%), radiotherapy (23.4%), or targeted therapy (14.6%).

Table 1 Sample Characteristics

Variables	M(SD) / n (%)
Age (years)	59.99 (9.53)
Gender	
Male	183 (70.1%)
Female	78 (29.9%)
Education	
Elementary school or lower	55 (21.1%)
Middle school	91 (34.9%)
High school	66 (25.3%)
College or higher	49 (18.8%)
Marital status	
Married	247 (94.6%)
Single/divorced/ widowed	14 (5.4%)
Perceived cancer-related financial burden	
None	37 (14.2%)
Slight	100 (38.3%)
Moderate	63 (24.1%)
Severe	36 (13.8%)
Very Severe	25 (9.6%)
Time since diagnosis [a]	
Less than 6 months	144 (55.2%)
6-12months	32 (12.3%)
12-24 months	31 (11.9%)
More than 24 months	46 (17.6%)
Stage	
III	82 (31.4%)
IV	179 (68.6%)
Lung cancer type [b]	
NSC - Adenocarcinoma	140 (53.6%)
NSC - Squamous	47 (18.0%)

NSC - Poorly differentiated	24 (9.2%)
NSC - Others	7 (2.7%)
Small cell	43 (16.5%)
Treatment history	
Received surgery	
Yes	61 (23.4%)
No	200 (76.6%)
Received chemotherapy	
Yes	252 (96.6%)
No	9 (3.4%)
Received radiotherapy	
Yes	61 (23.4%)
No	200 (76.6%)
Received targeted therapy	
Yes	38 (14.6%)
No	223 (85.4%)

Note. a. For time since diagnosis, the sum of number is not 261 due to missing data; b. NSC: Non-small cell.

3.2 Coping, Mood, and HRQoL

Pearson correlation analysis was performed to examine the relationships between coping, mood, and HRQoL (see Table 2). A small and positive correlation was observed between confrontation coping and positive mood (r = 0.21). Resigned acceptance was moderately and positively correlated with negative mood (r = 0.46), but moderately and inversely correlated with positive mood (r = -0.27). Use of resigned acceptance was correlated with more difficulties in mobility (r = -0.21), self-care (r = -0.19), usual activities (r = -0.19), pain/discomfort (r = -0.19), anxiety/depression (r = -0.41), and lower EQ-5D utility index (r = -0.28).

Table 2 Correlation among coping, affect and HRQOL

	M (SD)	1	2	3	4	5	6	7	8	9
1. Confrontation	2.37 (0.49)	1								
2. Resigned acceptance	1.92 (0.62)	-0.03	1							
3. Positive mood	2.40 (0.76)	0.21**	-0.27**	1						
4. Negative mood	1.84 (0.76)	0.11	0.46**	-0.11	1					
5. Mobility	4.32 (0.99)	-0.05	-0.21**	0.19**	-0.28**	1				
6. Self-care	4.58 (0.86)	-0.06	-0.19**	0.15*	-0.28**	0.78**	1			
7. Usual activities	4.24 (0.97)	-0.10	-0.19**	0.16*	-0.27**	0.78**	0.73**	1		
8. Pain/discomfort	3.98 (0.87)	-0.08	-0.19**	0.14*	-0.28**	0.45**	0.43**	0.46**	1	
9. Anxiety/depression	4.22 (0.73)	-0.03	-0.41**	0.19**	-0.50**	0.21**	0.21**	0.25**	0.27**	1
10. EQ-5D utility index	0.80 (0.19)	-0.10	-0.28**	0.20**	-0.38**	0.84**	0.82**	0.84**	0.69**	0.45**

*p<0.05, **p<0.01

Scale range: Confrontation, resigned acceptance: 1 (never) – 4 (very often); Positive mood, negative mood: 1 (very slightly) – 5 (extremely); Mobility, self-care, usual activities, pain/discomfort, anxiety/depression: 1 (very severe) – 5 (no); EQ-5D utility index: -1 (worse than death) – 1 (full health)

Hierarchical regression analyses were used to examine the relationship of confrontation and resigned acceptance coping with positive mood, negative mood, and HRQoL (see Table 3). Age, gender, cancer stage, and significant correlates of mood and/or HRQoL ($p < 0.05$), including perceived cancer-related financial burden, a history of radiotherapy, and lung cancer type (poorly differentiated non-small cell, small cell, other non-small cell), were controlled in the hierarchical regression analyses. Regarding positive mood, in addition to covariates, confrontation and resigned acceptance were found to be significant factors, as confrontation was associated with higher positive mood ($\beta = 0.19$, $p = 0.002$), whereas resigned acceptance was associated with lower positive mood ($\beta = -0.25$, $p < 0.001$). Regarding negative mood, in addition to covariates, confrontation and resigned acceptance were significant factors, as use of confrontation ($\beta = 0.11$, $p = 0.040$) and resigned acceptance ($\beta = 0.44$, $p < 0.001$) were associated with higher negative mood.

Regarding the EQ-5D domain scores, after controlling sociodemographic and clinical covariates, confrontation was not associated with the domain scores, whereas resigned acceptance was inversely associated with all domains. Positive mood was associated with less difficulty in mobility, usual activities, pain/discomfort, but not associated with self-care and anxiety/depression. Negative mood was associated with more difficulty in all domains of HRQOL.

Regarding EQ-5D utility index, after controlling sociodemographic and clinical covariates, resigned acceptance was inversely associated with EQ-5D utility index ($\beta = -0.22$, $p < 0.001$), whereas confrontation was not associated with EQ-5D utility index. Moreover, the effects of mood on EQ-5D utility index were significant, as positive mood was associated with higher EQ-5D utility index ($\beta = 0.17$, $p = 0.005$), whereas negative mood was associated with lower EQ-5D utility index ($\beta = -0.28$, $p < 0.001$).

Table 3 Multiple regression results for predictors of mood and HRQOL

	Positive mood		Negative mood		Mobility		Self-care		Usual activities		Pain / discomfort		Anxiety / depression		EQ-5D utility index	
	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*	β^f	*p*
Step 1																
Age	-0.15	**0.021**	-0.04	0.53	-0.13	**0.040**	-0.13	**0.046**	-0.06	0.31	-0.07	0.25	0.01	0.91	-0.10	0.09
Gender [a]	-0.07	0.32	0.05	0.40	-0.07	0.29	-0.06	0.35	-0.09	0.15	-0.01	0.85	0.02	0.76	-0.03	0.68
Financial burden [b]	-0.14	**0.032**	0.30	**<0.001**	-0.16	**0.010**	-0.15	**0.017**	-0.20	**0.002**	-0.15	**0.018**	-0.25	**<0.001**	-0.22	**0.001**
Cancer stage [c]	-0.09	0.16	-0.07	0.22	0.00	0.99	0.05	0.46	0.03	0.67	0.04	0.58	0.04	0.51	0.04	0.53
Cancer type- other non-small cell (Reference)	0		0		0		0		0		0		0		0	
Cancer type- undifferentiated [d]	0.01	0.93	-0.03	0.58	-0.07	0.26	-0.08	0.19	-0.12	0.053	-0.08	0.19	-0.04	0.51	-0.14	**0.027**
Cancer type- small cell [d]	-0.08	0.21	-0.01	0.85	0.05	0.44	0.03	0.66	0.08	0.22	0.14	**0.025**	0.07	0.29	0.10	0.12
Received radiotherapy [e]	-0.03	0.63	0.16	**0.009**	-0.17	**0.006**	-0.19	**0.003**	-0.14	**0.026**	-0.20	**0.002**	-0.07	0.24	-0.20	**0.001**
ΔR^2	0.054		0.141		0.079		0.081		0.097		0.094		0.080		0.124	
Step 2																

Confrontation	0.19	**0.002**	0.11	**0.040**	-0.05	0.40	-0.05	0.39	-0.07	0.25	-0.07	0.29	-0.01	0.81	-0.08	0.17
Resigned acceptance	-0.25	**<0.001**	0.44	**<0.001**	-0.16	**0.013**	-0.15	**0.019**	-0.16	**0.012**	-0.14	**0.029**	-0.41	**<0.001**	-0.22	**<0.001**
ΔR^2	0.098		0.191		0.025		0.023		0.027		0.021		0.155		0.053	
Step 3																
Positive mood					0.16	**0.013**	0.12	0.078	0.14	**0.026**	0.14	**0.029**	0.10	0.076	0.17	**0.005**
Negative mood					-0.22	**0.003**	-0.20	**0.006**	-0.17	**0.020**	-0.20	**0.005**	-0.36	**<0.001**	-0.28	**<0.001**
ΔR^2					0.053		0.039		0.036		0.044		0.093		0.076	
Adjusted R^2	0.120		0.307		0.118		0.103		0.122		0.121		0.298		0.218	

Note. a. 0=Male, 1=Female; b. range:1 (no difficulty) – 5 (very much); c. 1=stage III, 2=stage IV; d. other non-small cell lung cancers was the reference group; e. 0=No, 1=Yes; f. standardized coefficients

3.3 Mediating Effect of Mood on the Association between Coping and HRQoL

The MEDIATE macro was used to examine the mediating effect of mood in the relationship between coping and HRQoL, controlling for age, gender, cancer stage, perceived cancer-related financial burden, history of radiotherapy, and lung cancer type (poorly differentiated non-small cell, small cell, other non-small cell). The indirect effect (ab) was estimated as the product of regression coefficients predicting mood from each coping strategy (a), and HRQoL from mood (b) (see Figure 1). Bootstrapping techniques using 5000 samples revealed significant indirect effects for confrontation and resigned acceptance on HRQoL through positive and negative mood, respectively. The results are presented in Table 4.

Although the total effects of confrontation on EQ-5D domains scores and utility index were not significant, competing indirect effects via mood were identified. On one hand, positive indirect effects were found for confrontation on mobility (point estimate = 0.06, *SE* = 0.03, 95% CI [0.01, 0.13]), usual activities (point estimate = 0.05, *SE* = 0.03, 95% CI [0.01, 0.12]), pain/discomfort (point estimate = 0.05, *SE* = 0.03, 95% CI [0.004, 0.11]), and overall utility index (point estimate = 0.01, *SE* = 0.01, 95% CI [0.003, 0.03]) through positive mood. On the other hand, negative indirect effects were found for confrontation on mobility (point estimate = -0.05, *SE* = 0.03, 95% CI [-0.12, -0.002]), pain/discomfort (point estimate = -0.04, *SE* = 0.02, 95% CI [-0.10, -0.001]), anxiety/depression (point estimate = -0.06, *SE* = 0.03, 95% CI [-0.13, -0.003]), and overall utility index (point estimate = -0.01, *SE* = 0.01, 95% CI [-0.03, -0.001]) through negative mood. The direct effects of confrontation on EQ-5D domains scores and utility index were not significant.

Resigned acceptance has a significant negative total effect on EQ-5D domains scores and utility index. Furthermore, indirect effects of resigned acceptance on HRQoL via positive and negative mood were identified. Use of resigned acceptance was associated with decrease

in positive mood, and increase in negative mood, which could lead to more difficulty in mobility, self-care, usual activities, pain/discomfort, anxiety/depression, and overall utility index (indirect effect via positive mood: point estimate = -0.01, *SE* = 0.01, 95% CI [-0.03, -0.003]; indirect effect via negative mood: point estimate = -0.04, *SE* = 0.01, 95% CI [-0.06, -0.02]).

Table 4 Mediation model testing the direct and indirect effect of coping on HRQOL via mood

Outcome	**Predictor**	**Mediator**	**Path a**	**Path b**	**Path ab: indirect effect of coping on HRQOL**		**Path c': Direct effect of coping on HRQOL**	**Path c: Total effect of coping on HRQOL**
			coef (se)	coef (se)	coef (se)	95% CI	coef (se)	coef (se)
HRQOL	Confrontation	Positive mood	0.30** (0.09)	0.04** (0.01)	0.01 (0.01)	[0.003, 0.03]	-0.03 (0.02)	-0.03 (0.02)
		Negative mood	0.17* (0.08)	-0.07*** (0.02)	-0.01 (0.01)	[-0.03, -0.001]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.01 (0.01)	[-0.03, -0.003]	-0.02 (0.02)	-0.07*** (0.02)
		Negative mood	0.54*** (0.07)		-0.04 (0.01)	[-0.06, -0.02]		
Mobility	Confrontation	Positive mood	0.30** (0.09)	0.21* (0.08)	0.06 (0.03)	[0.01, 0.13]	-0.12 (0.13)	-0.10 (0.12)
		Negative mood	0.17* (0.08)	-0.28** (0.09)	-0.05 (0.03)	[-0.12, -0.002]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.06 (0.03)	[-0.13, -0.01]	-0.03 (0.11)	-0.25* (0.10)
		Negative mood	0.54*** (0.07)		-0.15 (0.06)	[-0.27, -0.05]		
Self-care	Confrontation	Positive mood	0.30** (0.09)	0.13 (0.07)	0.04 (0.03)	[-0.003, 0.10]	-0.09 (0.11)	-0.09 (0.11)
		Negative mood	0.17* (0.08)	-0.23** (0.08)	-0.04 (0.03)	[-0.10, 0.002]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.04 (0.03)	[-0.10, -0.003]	-0.04 (0.10)	-0.21* (0.09)
		Negative mood	0.54*** (0.07)		-0.14 (0.05)	[-0.24, -0.05]		
Usual Activities	Confrontation	Positive mood	0.30** (0.09)	0.18* (0.08)	0.05 (0.03)	[0.01, 0.12]	-0.16 (0.12)	-0.14 (0.12)
		Negative mood	0.17* (0.08)	-0.22* (0.09)	-0.04 (0.02)	[-0.09, 0.001]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.06 (0.03)	[-0.12, -0.01]	-0.07 (0.11)	-0.25* (0.10)
		Negative mood	0.54*** (0.07)		-0.12 (0.05)	[-0.22, -0.02]		

Pain / Discomfort	Confrontation	Positive mood	0.30** (0.09)	0.16* (0.07)	0.05 (0.03)	[0.004, 0.11]	-0.12 (0.11)	-0.12 (0.11)
		Negative mood	0.17* (0.08)	-0.23** (0.08)	-0.04 (0.02)	[-0.10, -0.001]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.05 (0.03)	[-0.11, -0.005]	-0.02 (0.10)	-0.19* (0.09)
		Negative mood	0.54*** (0.07)		-0.13 (0.05)	[-0.23, -0.04]		
Anxiety / Depression	Confrontation	Positive mood	0.30** (0.09)	0.10 (0.05)	0.03 (0.02)	[-0.003, 0.74]	0.01 (0.08)	-0.02 (0.08)
		Negative mood	0.17* (0.08)	-0.34*** (0.06)	-0.06 (0.03)	[-0.13, -0.003]		
	Resigned acceptance	Positive mood	-0.31*** (0.08)		-0.03 (0.02)	[-0.07, 0.003]	-0.26** (0.07)	-0.48*** (0.07)
		Negative mood	0.54*** (0.07)		-0.18 (0.04)	[-0.27, -0.11]		

Note. Age, gender, financial burden, disease stage, lung cancer type, and history of radiotherapy were controlled in the mediation model. All coefficients (a, b, c', c) were unstandardized coefficients. *p<0.05, **p<0.01, *** p<0.001

4. Discussion

To our knowledge, this is the first study to examine the relationship between coping, positive and negative mood, and HRQoL and the mediating role of mood in the relationship between coping and HRQoL among patients with advanced cancer. The findings of this study indicate that examining the pathway via positive and negative mood can generate a new understanding of the effect of coping on HRQoL among patients with advanced lung cancer, regardless of sociodemographic and clinical factors. The confrontation coping strategy was not directly associated with domains of HRQoL or overall HRQoL, but two significant indirect pathways via mood were identified. On one hand, confrontation had positive indirect effects on mobility, usual activities, pain, and overall HRQoL via positive mood; On the other hand, confrontation had negative indirect effects on mobility, pain, anxiety, and overall HRQoL via negative mood; Positive and negative indirect effect could counteract, resulting in a nonsignificant total effect. In contrast, use of resigned acceptance coping was associated with an increase in negative mood and a decrease in positive mood, which could in turn result in more difficulty in mobility, self-care, usual activities, pain, and poor overall HRQoL. On the whole, this is a unique finding that indicates the ambivalence of confrontation and the maladaptive nature of resigned acceptance among patients with advanced lung cancer.

The mean EQ-5D utility index in the current study was found to be 0.80, which was comparable to a study among patients with advanced non-small cell lung cancer in China with a utility index of 0.81 [51]. Consistent with previous studies, patients perceiving higher financial burden were more likely to report poor HRQoL compared to those perceiving lower financial burden related to cancer [11, 52]. Financial burden may restrict access to some drugs and treatment [52], and it may also lead to a sense of guilt for relying on families [29], which may affect health outcomes.

The current findings support the theory of stress and coping in the context of advanced cancer by indicating that coping can play a role in adapting to the experience of lung cancer, which could in turn influence emotional and health outcomes [36, 37]. The current study is in line with previous studies indicating that resigned acceptance was associated with less favorable outcomes [21, 26]. Resigned acceptance is related to the fatalistic attitude toward illness in traditional Taoist beliefs [28]. Giving up control in the actual situation, or even other aspects of life and holding negative expectations about the future could be associated with low levels of positive mood, and increase negative mood, which contribute to poor health outcomes in patients with advanced cancer.

Confrontation was found to be associated with increased positive and negative mood. In the current study, confrontation was characterized by attempts such as seeking information and support from various sources and being involved in decision making. Through such efforts, patients may regain a sense of control and redirect energy to constructive actions during treatment and daily living, which might facilitate the occurrence of positive mood. However, it is also possible that individuals could encounter various stressful decisions and pieces of information when they actively confront the advanced disease, which might lead to negative mood.

Our findings are in line with other studies reporting a nonsignificant association between confrontation and HRQoL among cancer patients [14, 21, 22]. Particularly, the findings on the mediating role of mood can help clarify the mechanisms underlying the nonsignificant association. The coexisting positive and negative indirect effect via mood could counteract one another, resulting in a null, or weak, total effect of confrontation on HRQoL. The ambivalence of confrontation may also reflect the effect of fighting attitude towards life-threatening illness in Chinese population, in which the patients and their families would seek, try, and continue available curative treatments to sustain and prolong life. Even

though actively confronting the advanced cancer may have some benefits (e.g., sense of control, constructive actions and skills), it may also remind patients of the potential incurable nature of advanced cancer and increase distress.

This study indicated that mood can be a pathway between coping and health outcomes. One explanation is related to physiology of mood [53], as positive and negative mood are associated with physiological levels in different directions, which can lead to different health outcomes. The second explanation is related to thought-action repertoires [43]. Negative mood is suggested to narrow the thought-action repertoires and increase unhealthy lifestyle and social isolation [43, 54], which could result in poor health outcomes. In contrast, positive affect is suggested to broaden the scope of attention and thought-action repertoires and build up personal and social resources [43], which could be beneficial to health outcomes. The third explanation is related to attributional interpretation [33]. HRQoL refers to a self-perceived health status, and it is possible that participants in a negative mood tend to perceive lower health status (more difficulties in daily living and symptoms) than those in a positive mood.

This study has some limitations. First, causality on the relationships between coping, mood, and HRQoL could not be drawn out from this cross-sectional study. Secondly, although Medical Coping Modes Questionnaire measured three coping strategies (i.e., confrontation, acceptance-resignation, avoidance), reliability of avoidance, indicated by Cronbach' α coefficient, was low in the current study. This restricted us from analyzing the effect of the avoidance strategy. Thirdly, the PANAS mostly measured the high-activated positive and negative affect [55]. Further study is suggested to investigate the relationship between resigned acceptance and low-activated mood (e.g., peace, calm). Fourthly, although EuroQol 5-dimension was used to measure HRQoL among patients with advanced cancer in a range of studies [51, 56], the measurement properties of the instrument is needed to be

examined further in patients with advanced cancer [57]. Finally, the sample was recruited from one hospital in China, which could compromise the generalizability of the findings.

Our finding that coping strategies is associated with mood and quality of life suggest that oncology providers need to pay attention to how patients are coping with the advanced cancer. Despite fostering realistic expectation for treatment and prognosis, oncology providers should watch for resigned acceptance and help the patients to learn what they can still do to regain a sense of control. On the other hand, when patients are engaging in excessive information- or treatment-seeking behaviors (i.e., part of confrontation), oncology providers should be aware that if it might a signal of underlying anxiety and make sure patients have appropriate mental health care and support. Mental health providers may help to address coping, mood, and quality of life through evidence-based interventions for advanced cancer patients. For instance, Acceptance and Commitment Therapy is indicated to reduce emotional distress and improve quality of life by facilitating the active acceptance of unpleasant thoughts and feelings in cancer patients [58, 59], which may a worthwhile approach. Finally, Early palliative care is a comprehensive, multidisciplinary, evidence-based approach for improving quality of life, which may be integrated into standard oncology care for patients with advanced cancer [60].

Figure 1 Positive and negative mood as mediators of the association between coping and HRQoL

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Contributors

HY, JH, LV, CJ designed the study. HY, JH, YM, ZJ, and LG collected data. HY and CJ analyzed the data. HY and CJ drafted the manuscript. HY, JH, YM, ZJ, LG, LV, CJ revised the manuscript.

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Competing interests

The authors declare that they have no conflict of interest.

Patient consent

Obtained.

Data sharing statement

No additional data were available.

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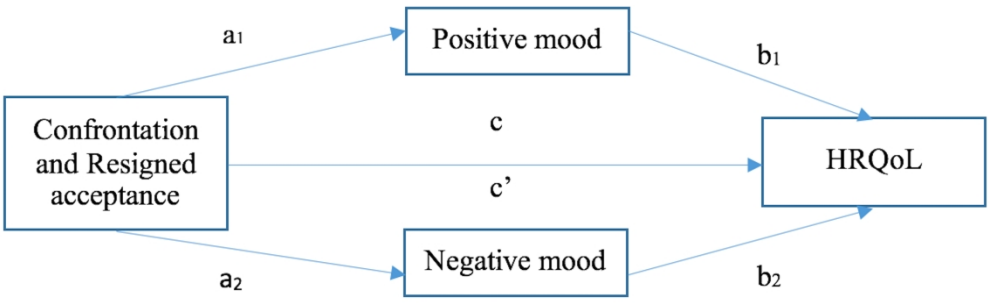


Positive and negative mood as mediators of the association between coping and HRQoL

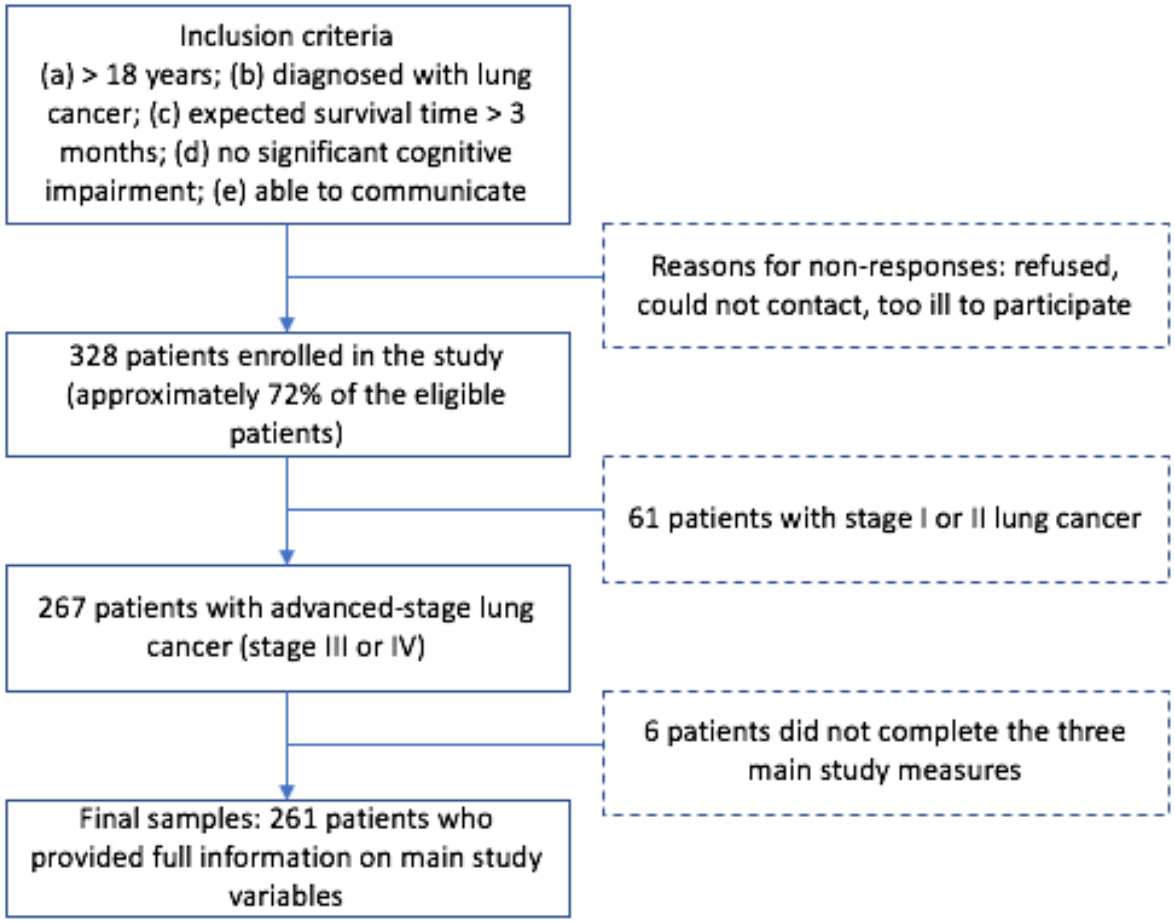
Table 1 Mood and Health-related Quality of Life by Socio-demographic and Clinical Characteristics

Variables	M(SD) / n (%)	Positive mood	Negative mood	Mobility	Self-care	Usual activities	Pain/ discomfort	Anxiety/ depression	EQ-5D utility index
Age (years)	59.99 (9.53)								
Gender									
Male	183 (70.1%)	2.41 (0.75)	1.80 (0.73)	4.39 (0.95)	4.63 (0.79)	4.33 (0.92)	4.03 (0.87)	4.24 (0.75)	0.81 (0.17)
Female	78 (29.9%)	2.34 (0.78)	1.93 (0.83)	4.21 (1.04)	4.50 (0.96)	4.06 (1.05)	3.91 (0.87)	4.21 (0.65)	0.78 (0.21)
Education									
Elementary school or lower	55 (21.1%)	2.28 (0.79)	1.82 (0.73)	4.54 (0.92)	4.64 (0.80)	4.31 (0.96)	3.98 (0.91)	4.11 (0.74)	0.80 (0.18)
Middle school	91 (34.9%)	2.35 (0.69)	1.94 (0.79)	4.24 (0.96)	4.57 (0.86)	4.14 (1.04)	3.90 (0.87)	4.16 (0.79)	0.78 (0.19)
High school	66 (25.3%)	2.46 (0.77)	1.71 (0.63)	4.32 (1.08)	4.59 (0.89)	4.29 (0.96)	4.05 (0.79)	4.32 (0.66)	0.82 (0.17)
College or higher	49 (18.8%)	2.51 (0.84)	1.83 (0.88)	4.41 (0.96)	4.59 (0.84)	4.35 (0.86)	4.10 (0.94)	4.35 (0.63)	0.83 (0.20)
Marital status									
Married	247 (94.6%)	2.40 (0.77)	1.83 (0.76)	4.34 (0.98)	4.60 (0.85)	4.25 (0.98)	3.98 (0.89)	4.23 (0.71)	0.80 (0.19)
Single/divorced/ widowed	14 (5.4%)	2.23 (0.58)	1.86 (0.82)	4.21 (1.05)	4.57 (0.85)	4.29 (0.83)	4.21 (0.58)	4.07 (1.00)	0.78 (0.18)
Perceived cancer-related financial burden									
None	37 (14.2%)	2.72 (0.89)	1.47 (0.50)	4.86 (0.42)	4.92 (0.28)	4.81 (0.46)	4.51 (0.56)	4.59 (0.50)	0.92 (0.08)
Slight	100 (38.3%)	2.27 (0.74)	1.74 (0.63)	4.21 (1.09)	4.54 (0.88)	4.23 (0.91)	3.91 (0.79)	4.22 (0.56)	0.78 (0.19)
Moderate	63 (24.1%)	2.53 (0.80)	1.87 (0.74)	4.43 (0.86)	4.65 (0.79)	4.17 (0.98)	3.90 (0.93)	4.27 (0.70)	0.80 (0.18)
Severe	36 (13.8%)	2.16 (0.51)	1.94 (0.84)	4.25 (0.77)	4.64 (0.68)	4.22 (0.90)	4.06 (1.01)	4.19 (0.71)	0.82 (0.14)
Very Severe	25 (9.6%)	2.38 (0.62)	2.52 (1.02)	3.96 (1.34)	4.12 (1.33)	3.76 (1.42)	3.68 (0.95)	3.64 (1.19)	0.68 (0.26)
Time since diagnosis[a]									
Less than 6 months	144 (55.2%)	2.38 (0.77)	1.84 (0.77)	4.40 (0.96)	4.60 (0.84)	4.24 (1.02)	3.95 (0.90)	4.19 (0.76)	0.80 (0.19)
6-12months	32 (12.3%)	2.54 (0.68)	1.91 (0.72)	4.19 (1.28)	4.50 (1.05)	4.19 (1.12)	4.19 (0.78)	4.19 (0.82)	0.79 (0.23)
12-24 months	31 (11.9%)	2.54 (0.87)	1.71 (0.75)	4.35 (0.80)	4.71 (0.53)	4.42 (0.62)	3.97 (0.71)	4.32 (0.65)	0.83 (0.11)

More than 24 months	46 (17.6%)	2.25 (0.72)	1.86 (0.75)	4.17 (1.00)	4.48 (0.96)	4.17 (0.93)	3.91 (0.96)	4.26 (0.61)	0.78 (0.20)
Stage									
III	82 (31.4%)	2.50 (0.71)	1.96 (0.90)	4.35 (0.93)	4.55 (0.86)	4.20 (1.09)	3.95 (0.94)	4.13 (0.78)	0.79 (0.19)
IV	179 (68.6%)	2.34 (0.78)	1.78 (0.68)	4.33 (1.00)	4.61 (0.84)	4.28 (0.91)	4.01 (0.84)	4.27 (0.69)	0.81 (0.18)
Lung cancer type[b]									
NSC-Adenocarcinoma	140 (53.6%)	2.39 (0.78)	1.88 (0.79)	4.28 (0.99)	4.56 (0.85)	4.20 (0.94)	3.91 (0.92)	4.18 (0.70)	0.79 (0.19)
NSC-Squamous	47 (18.0%)	2.50 (0.81)	1.84 (0.80)	4.45 (0.85)	4.68 (0.63)	4.32 (0.86)	4.00 (0.81)	4.26 (0.57)	0.81 (0.14)
NSC-Poorly differentiated	24 (9.2%)	2.46 (0.61)	1.77 (0.67)	4.08 (1.25)	4.38 (1.21)	3.88 (1.39)	3.75 (0.94)	4.13 (0.99)	0.72 (0.24)
NSC-others	7 (2.7%)	2.30 (0.60)	1.64 (0.40)	4.71 (0.49)	5.00 (0.00)	4.71 (0.49)	4.71 (0.49)	4.57 (0.53)	0.92 (0.10)
Small cell	43 (16.5%)	2.26 (0.76)	1.76 (0.71)	4.49 (0.96)	4.67 (0.87)	4.49 (0.88)	4.26 (0.73)	4.35 (0.78)	0.85 (0.17)
Treatment									
Received surgery									
Yes	61 (23.4%)	2.49 (0.78)	1.95 (0.85)	4.20 (0.98)	4.51 (0.83)	4.20 (0.96)	3.97 (0.86)	4.30 (0.74)	0.80 (0.18)
No	200 (76.6%)	2.36 (0.75)	1.80 (0.73)	4.38 (0.98)	4.62 (0.85)	4.27 (0.97)	4.00 (0.88)	4.21 (0.72)	0.80 (0.19)
Received chemotherapy									
Yes	252 (96.6%)	2.40 (0.76)	1.83 (0.76)	4.33 (0.99)	4.59 (0.86)	4.25 (0.98)	4.00 (0.87)	4.22 (0.73)	0.80 (0.19)
No	9 (3.4%)	2.16 (0.68)	1.83 (0.72)	4.44 (0.73)	4.67 (0.50)	4.33 (0.71)	3.67 (1.00)	4.33 (0.50)	0.81 (0.16)
Received radiotherapy									
Yes	61 (23.4%)	2.36 (0.70)	2.04 (0.87)	4.05 (1.19)	4.33 (1.21)	4.02 (1.09)	3.74 (1.05)	4.13 (0.62)	0.74 (0.23)
No	200 (76.6%)	2.40 (0.78)	1.77 (0.71)	4.43 (0.89)	4.68 (0.69)	4.33 (0.92)	4.07 (0.80)	4.26 (0.75)	0.82 (0.16)
Received targeted therapy									
Yes	38 (14.6%)	2.24 0.79)	1.83 (0.56)	4.21 (1.14)	4.47 (1.08)	4.11 (1.09)	3.79 (1.04)	4.26 (0.64)	0.77 (0.25)
No	223 (85.4%)	2.42 (0.75)	1.83 (0.79)	4.36 (0.95)	4.61 (0.80)	4.28 (0.95)	4.03 (0.84)	4.22 (0.74)	0.81 (0.17)

Scale range: Confrontation, resigned acceptance: 1 (never) – 4 (very often); Positive mood, negative mood: 1 (very slightly) – 5 (extremely); Mobility, self-care, usual activities, pain/discomfort, anxiety/depression: 1 (very severe) – 5 (no); EQ-5D utility index: -1 (worse than death) – 1 (full health)

Figure 1 Flow Chart of the Sample Selection Procedure



STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2,3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-7
Objectives	3	State specific objectives, including any pre-specified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	8
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-10
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10-11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10-11
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	Not applicable

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	Supplementary figure 1
		(c) Consider use of a flow diagram	Supplementary figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11-13
		(b) Indicate number of participants with missing data for each variable of interest	13
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Not applicable
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	14,15
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	14-22
		(*b*) Report category boundaries when continuous variables were categorized	14-22
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	23
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	25-26
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	23-26
Generalisability	21	Discuss the generalisability (external validity) of the study results	25-26
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	27

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.