

# Health-Related Quality of Life and Utility Scores of Lung Cancer Patients Treated with Traditional Chinese Medicine in China

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**Purpose:** To assess health-related quality of life (HRQoL) and utility scores of lung cancer patients treated with traditional Chinese medicine (TCM) in China.

**Methods:** This cross-sectional study included lung cancer patients treated with TCM in seven tertiary hospitals in Shanghai, China. The HRQoL and utility scores of these patients were measured using the five-level EQ-5D (EQ-5D-5L). The EQ-5D-5L utility scores were derived from the Chinese EQ-5D-5L Value Set. The relationships between HRQoL and the socio-demographic and clinical characteristics of these patients were further explored by Tobit regression.

**Results:** This study included a total of 347 patients. Their mean  $\pm$  SD and median EQ-5D-5L utility scores were  $0.851 \pm 0.198$  and  $0.893$ , respectively. The highest proportion of participants reporting problems was observed in pain/discomfort dimension (57.9%) and anxiety/depression (45.5%). Lung cancer patients treated with TCM had poor HRQoL, influenced by cancer clinical stage.

**Conclusion:** Lung cancer patients treated with TCM have poor HRQoL, with many patients reporting problems in the pain/discomfort and anxiety/depression dimensions. The information on health utility scores and HRQoL of lung cancer patients treated with TCM could be useful for future supportive care, economic evaluations and decision-making in China.

**Keywords:** lung cancer, health-related quality of life, traditional Chinese medicine, EQ-5D-5L

## Introduction

Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer deaths, both worldwide<sup>1</sup> and in China.<sup>2</sup> In 2015, 787,000 patients in China were newly diagnosed with lung cancer and 631,000 patients died of this disease, accounting for 20.03% of patients diagnosed with cancer and 26.99% who died of cancer during that year.<sup>3</sup> In addition, the burden of lung cancer has increased in the past three decades. Lung cancer is one of the most aggressive malignant tumors, with a 5-year overall survival (OS) rate of about 19.7%,<sup>4</sup> much lower than the 5-year OS rate of 40.5% among all cancer patients in China.<sup>3</sup> In the treatment process, patients with lung cancers will suffer from the disease's malignant degree and its therapy toxicity.<sup>5</sup> At present, the leading treatment methods for lung cancer patients include surgery, chemotherapy, radiotherapy, and targeted therapy. Traditional Chinese Medicine (TCM), which has a long history in China, has been widely used to treat various diseases including lung cancer in China and other Asian countries or areas.<sup>6-8</sup> In addition to their physical symptoms, lung cancer patients frequently experience depression and anxiety,<sup>9,10</sup> having a negative impact on their health-related quality of life (HRQoL).

HRQoL, especially preference-based health-related QoL, has become an increasingly important outcome measure in the cost-utility analysis (CUA), a particular form of economic evaluation.<sup>11</sup> HRQoL can inform patient management and policy decisions, making it important to measure HRQoL.<sup>12</sup>

Although many studies in patients with lung cancer have investigated their HRQoL after surgery,<sup>13</sup> radiotherapy,<sup>14</sup> and/or chemotherapy,<sup>15–17</sup> few studies to date have evaluated their HRQoL after TCM treatment, which measured by disease-specific instruments, including the Functional Assessment of Cancer Therapy-Lung (FACT-L),<sup>18,19</sup> the quality-of-life (QoL) instrument for lung cancer based on Traditional Chinese Medicine (QLASTCM-Lu),<sup>20,21</sup> and European Organization for Research and the Treatment of Cancer Quality of Life Questionnaires (EORTC QLQ-C30 and EORTC QLQ-LC13).<sup>22,23</sup> Although these methods are valid and reliable, they are not preference-based instruments to elicit health utility scores for lung cancer patients. The present study, therefore, aimed to assess the HRQoL and utility scores in lung cancer patients who received TCM treatment and evaluate the relationships of quality of life outcomes with the socio-demographic and clinical characteristics among lung cancer patients in China.

## Materials and Methods

### Study Design and Setting

A cross-sectional questionnaire survey was conducted in Shanghai, China. Lung cancer patients treated with TCM were recruited successively from the seven tertiary hospitals of Shanghai in December 2020. All inpatients in the hospital ward who met the inclusion criteria were asked if they would like to participate in the survey. These seven hospitals are regional centers for TCM treatment of lung cancer; therefore, their patients are representative of lung cancer patients treated with TCM. The written informed consent was obtained from all participants prior to the interviews. The study was approved by the Ethics Review Board of the School of Public Health, Fudan University (IRB# 2020-09-0848), and it adhered to the tenets of the Declaration of Helsinki.

### Participants

Patients diagnosed with lung cancer who were treated with TCM were invited to enroll in this study. Patients were excluded if they were younger than 16 years at the time of the survey, as were those unwilling to provide informed consent, unable to understand the questionnaires or with serious complications.

### Data Collection

The enrolled patients completed the survey questionnaires. The questionnaire consisted of three parts: (1) socio-demographic information; (2) clinical information; and (3) HRQoL instrument. Socio-demographic information included sex, age, level of education, employment status, medical insurance and annual household income. The clinical information included type and severity of lung cancer and the duration since diagnosis. HRQoL was evaluated using the validated Chinese version of EQ-5D-5L.

### EQ-5D-5L

The EQ-5D instrument is one of the most widely used generic preference-based HRQoL instruments internationally, and has been validated in patients with cancer.<sup>24</sup> To reduce the ceiling effects and improve the sensitivity of the three-level version of EQ-5D (EQ-5D-3L) introduced by the EuroQol Group in the 1990s,<sup>25</sup> the new five-level EQ-5D questionnaire (EQ-5D-5L) was developed in 2011.<sup>26</sup> It retains the same five dimensions as the EQ-5D-3L (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), with each dimension having five levels: no problems, slight problems, moderate problems, severe problems, and unable to/extreme problems, resulting in 3125 ( $5^5$ ) unique health states. The Chinese version of the EQ-5D-5L has been validated.<sup>27</sup> The health utility values can be derived by the Chinese-specific scoring algorithm of the EQ-5D-5L developed by Luo et al,<sup>28</sup> which yielded scores ranging from  $-0.391$  to  $1.000$ , with zero representing being dead,  $1.000$  indicating a state of full health, and negative scores indicating health status worse than death. The other component of EQ-5D-5L, the EQ Visual Analogue Scale (EQ-VAS), allowed patients to describe their current overall health on a scale ranging from 0 (the worst health state they can imagine) to 100 (the best health state they can imagine).

## Statistical Analysis

Patients who supplied complete socio-demographic and clinical information and completed both the EQ-5D and EQ-VAS were included in the analysis. Continuous variables were reported as means and standard deviations (SD); due to the skewed distribution, the non-parametric Mann–Whitney U or Kruskal–Wallis test were applied to examine the differences of EQ-5D-5L health state utility scores among the various subgroups. Because the maximum health state utility score was 1, which was reported by large percentage of patients, the Tobit model was used to explore the impact of socio-demographic variables (sex, geographical region, age, educational level, employment status, medical insurance and annual household income in 2020) and clinical variables (duration since diagnosis, type and clinical stage of Lung cancer) on utility scores of lung cancer patients. All statistical analyses were performed using Stata version 16.0 (StataCorp LP, College Station, TX, USA).

## Results

### Characteristics of the Participants

The 347 patients with lung cancer included 187 men and 160 women, mean age  $64.8 \pm 8.7$  years and an average duration since diagnosis of 27.3 months (Table 1). Of these patients, 82.7% lived in urban areas, 63.7% were retired, and 98.8% had health insurance. Most (58.7%) reported annual per capita household incomes ranging from 50,000 to 149,999 Chinese yuan (approximately US\$ 7657 to 22,971), whereas 18.5% reported incomes below 50,000 Chinese yuan (US \$7657). Of these patients, 79.5% had non-small cell lung cancer (NSCLC) and 7.5% had small cell lung cancer, with 26.4%, 14.0%, 19.2%, and 40.4% having stages I-IV lung cancer, respectively.

### EQ-5D-5L Dimensions

The proportion of patients reporting problems in each dimension of the EQ-5D-5L is shown in Table 2 and Figure 1. Problems in the pain/discomfort dimension were reported by 57.9% of these patients, followed by problems in the anxiety/depression (45.5%), usual activities (34.0%), mobility (33.7%), and self-care (21.9%) dimensions. A total of 94 patients (27.1%) reported no problems in any of the five dimensions.

### EQ-5D-5L Utility Scores

The mean and median of EQ-5D-5L utility scores for patients with lung cancer using the Chinese preference weights were 0.851 ( $SD=0.198$ ) and 0.893 respectively (Table 3). The Shapiro–Wilk test statistics suggested that the null hypothesis of normal distribution of EQ-5D-5L utility scores was rejected ( $P < 0.001$ ). Figure 2 shows the EQ-5D-5L utility scores skewed towards the right higher values.

According to the non-parametric test, the results showed EQ-5D-5L utility scores differed significant among patients living in urban, rural and other areas ( $P < 0.05$ ). Those who were at III or IV stage of lung cancer had lower utility scores compared with the patients being at I stage ( $p < 0.05$ ). In addition, utility scores tended to differ between employed and retired patients, as well as in patients treated according to different decision-making models and with different types of health-care insurance ( $P < 0.1$  each) (Table 3).

### Factors Associated with Health Utility Scores

The results of Tobit regression analysis are presented in Table 4. The EQ-5D utility scores were significantly lower in women than in men ( $P = 0.026$ ). Lower utility scores were associated with stage III ( $P = 0.036$ ) or IV ( $P = 0.005$ ) cancer at diagnosis. Time since diagnosis of 13–24 months was a significant predictor of low EQ-5D-5L utility scores ( $P = 0.013$ ). The residence was also significantly predicted utility scores after controlling for other factors.

## Discussion

To our knowledge, this study is the first to report the EQ-5D-5L utility scores and HRQoL of lung cancer patients treated with TCM in China. These findings may be applicable to health economic evaluations of clinical and resource allocations for lung cancer within the health-care sector.

**Table I** Socio-Demographic and Clinical Characteristics of Patients with Lung Cancer

Characteristic	N (%)
	347 (100)
Sex	
Male	187 (53.9)
Female	160 (46.1)
Age (years)	
<60	89 (25.7)
60–69	150 (43.2)
>69	108 (31.1)
Residence	
Rural area	53 (15.3)
Urban area	287 (82.7)
Other	7 (2.0)
Education level <sup>a</sup>	
Primary school or lower	32 (9.3)
Secondary school	122 (35.4)
High school or technical secondary school	124 (35.9)
University degree and above	67 (19.4)
Employment status	
Employment	126 (36.3)
Retirement	221 (63.7)
Annual household income per capita in 2020, Chinese yuan <sup>b</sup>	
<50,000	64 (18.5)
50,000–99,999	113 (32.7)
100,000–149,999	90 (26.0)
≥150,000	79 (22.8)
Decision-making model	
Shared decision-making	315 (90.8)
Other	32 (9.2)
Health-care insurance	
No insurance	4 (1.2)
Urban employee basic medical insurance	187 (53.9)
Urban and rural resident basic medical insurance	59 (17.0)
Other insurance	97 (28.0)
Duration of disease since diagnosis (month)	
<8	76 (21.9)
8–12	71 (20.5)
13–24	79 (22.8)
>24	121 (34.9)
Clinical stage <sup>c</sup>	
I	91 (26.4)
II	48 (14.0)
III	66 (19.2)
IV	139 (40.4)
Type of lung cancer	
Non-small cell lung cancer (NSCLC)	276 (79.5)
Small cell lung cancer (SCLC)	26 (7.5)
Other	45 (13.0)

**Notes:** <sup>a</sup>Level of education missing for two patients; <sup>b</sup>per capita annual household income missing for one patient; <sup>c</sup>clinical stage missing for three patients.

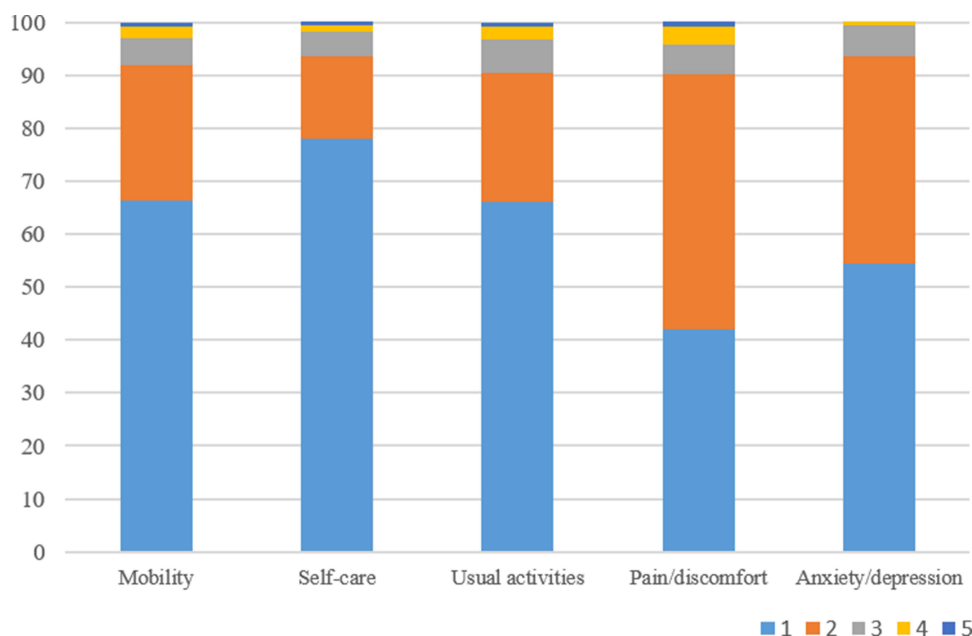
**Table 2** Frequency of Item Response in Each EQ-5D-5L Dimension Reported by Participants

Dimensions	No Problem N (%)	Slight Problem N (%)	Moderate Problem N (%)	Severe Problem N (%)	Extreme Problem N (%)
Mobility	230 (66.3)	89 (25.6)	18 (5.2)	7 (2.0)	3 (0.9)
Self-care	271 (78.1)	54 (15.6)	16 (4.6)	4 (1.2)	2(0.6)
Usual activities	229 (66.0)	85 (24.5)	22 (6.3)	8 (2.3)	3 (0.9)
Pain/discomfort	146 (42.1)	167 (48.1)	19 (5.5)	12 (3.5)	3 (0.9)
Anxiety/depression	189 (54.5)	136 (39.2)	20 (5.8)	2 (0.6)	0 (0.0)

The mean health state utility score, as determined by the EQ-5D-5L, in these patients was 0.851, lower than those reported in urban Chinese population (0.957)<sup>29</sup> and in urban and rural residents in four cities in China (0.951),<sup>30</sup> but equivalent to that of patients with non-small cell lung cancer in Taiwan of China.<sup>31</sup> Before our study, a cross-sectional study of advanced non-small-cell lung cancer patients in a hospital in China found that their mean health utility score was 0.814, somewhat lower than in our patient populations.<sup>32</sup> In comparison, patients with advanced lung cancer in France and Germany were found to have a mean EQ-5D-3L index score of 0.58,<sup>33</sup> and patients with lung cancer in Canada also had a lower mean EQ-5D index score.<sup>34</sup>

The differences among these scores may be due to differences among treatment types and clinical stage. Previous studies examined the HRQoL of patients with advanced lung cancer who received drug treatment, including targeted and chemotherapeutic agents. In contrast, the patients in the present study were recruited at tertiary hospitals, were at all stages of disease, and tended to be treated with TCM. The adverse effects of targeted drugs and chemotherapeutic agents may result in chronicity and a decrease in health utility,<sup>35</sup> whereas, TCM is thought to reduce chemotherapy-related side effects and improve HRQoL.<sup>36</sup> In addition, previous studies in lung cancer measured health status values using the EQ-5D-3L which has a higher ceiling effect and lower discriminatory power than the EQ-5D-5L.<sup>29</sup>

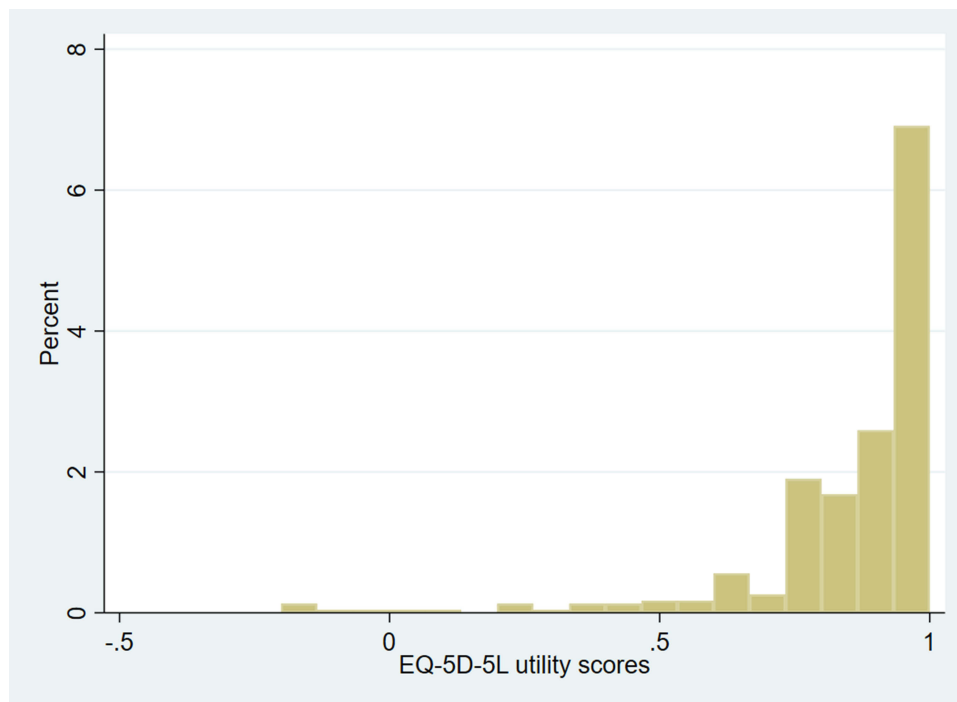
In this study, pain/discomfort (57.9%) and anxiety/depression (45.5%) were the problems most frequently reported by respondents, similar to previous findings Chinese patients with advanced lung cancer.<sup>32,37</sup> Lung cancer therefore had a significant effect on the physiological and psychological status of these patients. Pain has been reported to be an inevitable symptom in lung cancer patients and the main physical symptom causing psychological problems in elderly

**Figure 1** Patients reporting problems percentage in five levels of EQ-5D.

**Table 3** EQ-5D-5L Utility Scores of Participants with Lung Cancer in Different Characteristics

	Range	Mean	SD	Median	P values
Sex					0.216
Male	-0.200-1.000	0.850	0.214	0.897	
Female	-0.190-1.000	0.853	0.178	0.893	
Age (years)					0.817
<60	-0.190-1.000	0.864	0.190	0.893	
60-69	-0.160-1.000	0.849	0.203	0.893	
>69	-0.200-1.000	0.844	0.198	0.893	
Residence					0.014
Rural area	0.360-1.000	0.881	0.136	0.906	
Urban area	-0.200-1.000	0.853	0.197	0.893	
Other	-0.160-0.940	0.562	0.385	0.702	
Education level					0.549
Primary school or lower	0.450-1.000	0.848	0.171	0.918	
Secondary school	-0.190-1.000	0.844	0.196	0.893	
High school or technical secondary school	-0.160-1.000	0.856	0.200	0.902	
University degree and above	-0.200-1.000	0.864	0.210	0.897	
Employment status					0.066
Employment	-0.160-1.000	0.873	0.183	0.942	
Retirement	-0.200-1.000	0.839	0.205	0.893	
Annual household income per capita in 2020, Chinese yuan					0.113
<50,000	0.260-1.000	0.855	0.169	0.893	
50,000-99,999	-0.200-1.000	0.825	0.218	0.893	
100,000-149,999	-0.190-1.000	0.868	0.218	0.942	
≥150,000	0.030-1.000	0.868	0.163	0.893	
Decision-making model					0.080
Shared decision-making	-0.200-1.000	0.852	0.204	0.897	
Other	0.470-1.000	0.841	0.130	0.862	
Health-care insurance					0.064
No insurance	-0.750-0.940	0.864	0.095	0.883	
Urban employee basic medical insurance	-0.190-1.000	0.861	0.208	0.934	
Urban and rural resident basic medical insurance	0.430-1.000	0.836	0.146	0.848	
Other insurance	-0.200-1.000	0.841	0.211	0.893	
Duration of disease since diagnosis (month)					0.738
<8	-0.160-1.000	0.867	0.181	0.900	
8-12	-0.190-1.000	0.857	0.200	0.888	
13-24	-0.200-1.000	0.810	0.258	0.893	
>24	0.030-1.000	0.864	0.157	0.893	
Clinical stage					0.013
I	0.200-1.000	0.886	0.144	0.906	
II	-0.120-1.000	0.889	0.181	0.942	
III	-0.160-1.000	0.842	0.224	0.893	
IV	-0.200-1.000	0.819	0.218	0.893	
Type of lung cancer					0.145
Non-small cell lung cancers (NSCLC)	-0.200-1.000	0.860	0.193	0.895	
Small cell lung cancers (SCLC)	-0.016-1.000	0.765	0.282	0.848	
Other	0.200-1.000	0.848	0.154	0.893	
Total	-0.200-1.000	0.851	0.198	0.893	

**Abbreviation:** SD, standard deviation.



**Figure 2** Distribution of EQ-5D-5L utility scores among lung cancer patients.

lung cancer patients.<sup>38</sup> A more severe degree of pain is associated with the aggravation of patients' anxiety, depression and other negative psychological emotions.<sup>39</sup> Efforts are therefore needed to alleviate pain/discomfort and anxiety/depression during the treatment of lung cancer.

The present results showed three independent factors influenced the HRQoL of lung cancer patients: sex, tumor clinical stage, and residence. Women exhibited lower utility than men, in agreement with previous studies in China<sup>40,41</sup> and Japan.<sup>42</sup> HRQoL tended to decrease in patients with more advanced clinical stage, consistent with previous reports on patients with lung cancer in China,<sup>32</sup> France and Germany<sup>33</sup> and in patients with other types of cancer.<sup>43</sup> Patients with advanced stage cancers have more obvious physical symptoms related to the disease, and the difficulty of treatment may lead to poor prognosis or death,<sup>38</sup> increasing anxiety and depression and worsening quality of life. Our results showed that residential disparities influenced the HRQoL of patients, consistent with findings previously reported in China.<sup>44</sup>

This study had several limitations. First, the study population consisted of lung cancer patients from several tertiary hospitals in Shanghai, China, which may not be representative of all lung cancer patients in mainland China. However, the study population included patients at different stages of lung cancer. Second, this study was cross-sectional survey in design, and therefore could not determine the causal relationships between HRQoL and other influencing factors. These causal relationships should be examined in future longitudinal studies. In addition, we only pay attention to whether the patient has received TCM, and not whether the patient has received other treatments at the same time, which may have a certain impact on the results. Although additional studies are required, the results of this study may provide information on HRQoL on Chinese lung cancer patients receiving TCM treatment.

## Conclusion

This study found that lung cancer patients treated with TCM had a low health state utility and poor HRQoL. The dimensions of reduced HRQoL most frequently reported by patients were pain/discomfort and anxiety/depression. More advanced stage tumors were associated with lower HRQoL. These results can provide basic information on health utility scores and HRQoL of lung cancer patients treated with TCM for future supportive care, economic evaluations and decision-making in China. In addition, the HRQoL of lung cancer patients may be improved by reducing pain and depression during the process of treatment.

**Table 4** Factors Influencing EQ-5D-5L Utility Scores as Determined by a Tobit Regression Model

	Coefficients	SE	P values
Sex			
Male	Ref		
Female	-0.067	0.030	0.026
Age (years)			
<60	Ref		
60–69	-0.006	0.034	0.851
>69	-0.033	0.038	0.387
Residence			
Other	Ref		
Rural area	0.536	0.117	<0.001
Urban area	0.485	0.112	<0.001
Education level			
Primary school or lower	Ref		
Secondary school	-0.064	0.053	0.223
High school or technical secondary school	-0.045	0.054	0.405
University degree and above	-0.057	0.060	0.342
Employment status			
Employment	Ref		
Retirement	-0.045	0.030	0.137
Annual household income per capita in 2020, Chinese yuan			
<50,000	Ref		
50,000–99,999	-0.036	0.040	0.363
100,000–149,999	0.032	0.043	0.447
≥150,000	-0.005	0.045	0.913
Decision-making model			
Shared decision-making	Ref		
Other	-0.063	0.047	0.182
Health-care insurance			
No insurance	Ref		
Urban employee basic medical insurance	0.124	0.121	0.307
Urban and rural resident basic medical insurance	0.047	0.124	0.702
Other insurance	0.081	0.122	0.508
Duration of disease since diagnosis (months)			
<8	Ref		
8–12	-0.010	0.042	0.814
13–24	-0.107	0.043	0.013
>24	-0.025	0.041	0.534
Clinical stage			
I	Ref		
II	-0.007	0.046	0.876
III	-0.091	0.043	0.036
IV	-0.100	0.036	0.005
Type of lung cancer			
Other	Ref		
Non-small cell lung cancers (NSCLC)	0.050	0.040	0.210
Small cell lung cancers (SCLC)	-0.033	0.063	0.604

**Abbreviation:** SE, standard error.

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## Disclosure

The authors have no conflict of interest to report.

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