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Depression Symptom Trends and Health Domains among Lung Cancer Patients in the CanCORS Study

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Abstract

Objectives—Among lung cancer patients depression symptoms are common and impact outcomes. The aims of this study were to determine risk factors that contribute to persistent or new onset depression symptoms during lung cancer treatment, and examine interactions between depression symptoms and health domains that influence mortality.

Materials and Methods—Prospective observational study in five healthcare systems and 15 Veterans Affairs medical centers. Patients in the Cancer Care Outcomes Research and Surveillance (CanCORS) Consortium with lung cancer were eligible. The 8-item Center for Epidemiologic Studies Depression (CES-D) scale was administered at baseline and follow-up. Scores ≥4

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indicated elevated depressive symptoms. Health domains were measured using validated instruments. We applied logistic regression and Cox proportional hazards modeling to explore the association between depression symptoms, health domains, and mortality.

Results—Of 1,790 participants, 38% had depression symptoms at baseline and among those still alive 31% at follow-up. Risk factors for depression symptoms at follow-up included younger age (OR=2.81), female sex (OR=1.59), low income (OR=1.45), not being married (OR=1.74) and current smoking status (OR=1.80); high school education was associated with reduced odds of depression symptoms at follow-up, compared with lesser educational attainment (OR=0.74) (all p values <0.05). Patients with depression symptoms had worse health-related quality of life, vitality, cancer-specific symptoms, and social support than patients without depression symptoms (all p<0.001). The association between depression symptoms and increased mortality is greater among patients with more lung cancer symptoms (p=0.008) or less social support (p=0.04).

Conclusions—Patient risk factors for depression symptoms at follow-up were identified and these subgroups should be targeted for enhanced surveillance. Patients with depression symptoms suffer across all health domains; however, only more lung cancer symptoms or less social support are associated with worse mortality among these patients. These potentially modifiable health domains suggest targets for possible intervention in future studies.

Keywords

Lung cancer; depression symptoms; risk factors; health domains; quality of life; survival

1.1 Introduction

Cancer patients experience significant psychological distress and lung cancer patients are at especially high risk [1–3]. Depression symptoms may be understood as a normal reaction around the time of a lung cancer diagnosis. However, studies suggest symptoms are not transient, but can be lasting often persisting post-treatment [4–7]. The trajectory of depression symptoms during cancer treatment is understudied and patients continue to report unmet psychological needs at all stages of their cancer illness [8].

The development of depression and its association with worse survival is a multifactorial process that is not well understood in cancer patients. As a result, there is limited evidence to guide effective treatment [9], though recent trials of multicomponent collaborative care interventions had positive outcomes [3]. Depression development has been attributed to the interaction of multiple disease, individual and psychosocial-related factors [10]. At cancer diagnosis, risk factors that are associated with depression development include patient characteristics, family history of depression, less social support, poor communication with medical caregivers, and maladaptive coping strategies [11]. Risk factors for depression symptoms that occur or persist after a cancer diagnosis are not characterized, even though, the trajectory of depression is associated with worse patient outcomes [3, 11]

Quality of life (QOL) contributes to depression development and QOL at the time of lung cancer diagnosis is an independent prognostic indicator for survival [12, 13]. The interactions between health domains, such as QOL or physical symptoms, and depression

are likely impacted by cancer progression. Acquiring a better understanding of the trends in depression symptoms and health domains that contribute to the association between depression symptoms and mortality are essential. This knowledge may help establish better methods of identification of high-risk patients and allow providers to develop effective treatments.

Using data from the Cancer Care Outcomes Research and Surveillance (CanCORS) Consortium we sought to determine risk factors that contribute to persistent or new onset depression symptoms during lung cancer treatment. In addition, we examined the interactions between depression symptoms and health domains at baseline to determine their association with mortality.

1.2 Materials & Methods

The CanCORS Consortium was a prospective, observational study of practices and outcomes for patients with newly diagnosed lung cancer. The cohort was composed of 5,150 participants from five integrated health care delivery systems in the NCI-funded Cancer Research Network, 15 Veterans Affairs hospitals, and five geographically defined regions (northern California, Los Angeles County, North Carolina, Iowa, and Alabama). Participants or surrogates provided informed consent and IRBs at participating institutions approved the study. Baseline and follow-up patient telephone surveys were conducted. Demographic, cancer and treatment data was collected from medical records and cancer registries. Research staff also contacted hospitals and physicians to complete medical record reviews. Vital status was collected from: baseline and follow-up surveys, medical record abstraction, database updates, Social Security Death Index (SSDI) or the National Death Index (NDI). Vital status data was matched among data sources using the participants' social security number, gender and date of birth. End date of vital status query was April 2012. Full CanCORS study methods have been described previously [14, 15]. Our study was approved by the IRB at the Veterans Affairs Portland Health Care System.

1.2.1 Cohort—Patients aged 21 years or older with newly diagnosed invasive non–small-cell or small-cell lung cancer were eligible if they were identified within 3 months of cancer diagnosis. Participants completed a baseline and follow-up survey approximately 5 and 12 months after cancer diagnosis, respectively. CanCORS enrolled a demographically and clinically representative cohort, reflective of newly diagnosed patients with lung cancer in all Surveillance, Epidemiology, and End Results (SEER) regions [16]. For this analysis, 1,790 CanCORS participants who completed the full baseline survey were eligible. Participants who were deceased or too ill to complete full surveys were excluded. Also participants who did not have medical records available for review were excluded.

1.2.2 Variables and Measures—A brief version of the Center for Epidemiologic Studies Depression (CES-D) scale [17, 18], including eight yes/no items, was administered to measure depression symptoms at baseline and follow-up. Its internal consistency, reliability and validity are almost identical to the full 20-item version [19]. The brief CES-D shows very high internal consistency, adequate test- retest repeatability and good factor structure and internal consistency in cancer patients [20]. Scores ≥ 4 on the brief CES-D indicate

elevated depression symptoms [21–23]. Persistent depression symptoms were defined by elevated symptoms at both baseline and follow-up. New onset depression symptoms were defined as no depression symptoms at baseline and depression symptoms at follow-up. The following health domains were assessed using validated instruments [14, 15]administered at the baseline visit.

Health-related (HR) QOL: HRQOL was assessed using the Medical Outcomes Study (MOS) 12-item short form (SF-12) and EuroQol questionnaire (EQ-5D). The SF-12 is a shorter version of the SF-36 and consists of a physical component summary (PCS) and mental component summary (MCS). A higher score indicates a better QOL and scores greater than 50 represent above average health status [24]. The EQ-5D is a well-validated five-item questionnaire, to characterize the patient's current HRQOL in five health dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression [25]. These questions are then used to calculate the EQ-5D index score based upon the U.S. population's preference weights with an outcome score from −0.2 to 1.0 with higher scores representing better HRQOL [26].

Vitality: The MOS 36-item short form (SF-36) was constructed to survey health status. It measures eight dimensions of health status, but to avoid redundancy only the vitality scale was included in this study which reflects energy and fatigue [27, 28]. Scores range from 0 to 100 with higher scores indicating a better health state [29].

Cancer-specific Symptoms: Cancer-specific symptoms using selected items from the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ-C30) and the EORTC QLQ Lung Cancer (LC13) Modular Questionnaire. The EORTC QLQ-C30 is a cancer-specific questionnaire that measures physical, psychological and social functioning of patients incorporating symptoms as well as perceived financial effect of the disease and treatment [30, 31]. The EORTC QLQ-LC13 is a 13-item tool for assessing disease and treatment-specific symptoms in lung cancer patients [32, 33]. Scores for each questionnaire represent a composite of all symptom scores; for each questionnaire a score of 0 to 100 is used with higher scores corresponding to more severe symptoms.

Fatalism: Fatalistic beliefs were assessed with four items from the Powe Fatalism Inventory (PFI) that measures cancer fatalism, which is a situational manifestation of fatalism in which individuals may feel powerless in the face of cancer and may view a diagnosis of cancer as a struggle against insurmountable odds. The PFI is based on four philosophical components: fear, predetermination, pessimism, and inevitable death [34, 35]. Higher scores on the PFI indicate higher degrees of fatalism and a mean score greater than eight indicates high cancer fatalism.

Social Support: Social support was measured using the 19-item MOS Social Support Survey (MOS-SSS) which focuses on perceived "functional" social support [36]. This survey supports the dimensionality of four functional support sub-scales: emotional/ informational, tangible/instrumental, positive social interaction and affectionate. However, due to the evidence of some independence among support subscales the developers

recommend scoring and using the subscales separately. In order to reduce participant burden only a subset of the emotional/informational (i.e., empathetic understanding, information, guidance) and tangible/instrumental (i.e., material aid or behavioral assistance) subscales were included. The items are easy to understand and administer to chronically ill patients of all ages, including patients with cancer [37, 38]. Scores are calculated and transformed from 0–100; higher scores indicate greater support [36, 39].

1.2.3 Statistical Analysis—Descriptive statistics, at the time of the baseline survey, summarize participants' characteristics categorized by depression symptoms at baseline and follow-up. Item nonresponse rate was <5% across variables for patients who completed the baseline survey. At baseline, participants were categorized as having or not having depression symptoms based on CES-D scores. At follow-up, participants were categorized by the longitudinal changes in their depression symptoms based on baseline and follow-up CES-D scores, e.g., the new onset depression symptoms group included participants who did not have depression symptoms at baseline and had depression symptoms at follow-up. Overall patient drop-out rate at follow-up, not including deaths, was <10% and was not significantly different between participants with and without depression symptoms. Patient risk factors for persistent or new onset depression symptoms at follow-up were evaluated using univariate and multivariate logistic regression modeling and odds ratio are presented. Patient and treatment characteristics were examined including: age, sex, race, cancer stage and histology, income, education, marital status, smoking history, Adult Comorbidity Evaluation-27 (ACE-27) index [40], and cancer therapy received. Final multivariate models presented included significant risk factors although, models including all characteristics examined were similar. Odds ratios, 95% confidence intervals, and p-values are reported.

Health domain score differences between participants with and without depression symptoms were examined using t-tests. Health domain scores were standardized to units of one standard deviation for the sake of comparison. Separate Cox's proportional-hazards regression models were fitted to obtain hazard ratios and corresponding confidence intervals for survival. The hazard ratios (HR) presented represent the HR for a one standard deviation increase in the health domain. Survival was measured from the date of initial baseline survey until the date of death or censoring. Further Cox's proportional-hazards regression models including an interaction term between the health domain score and depression symptoms were fitted. The adjusted regression models were adjusted for age, sex, race, cancer stage and histology, income, education, marital status, smoking history, and ACE-27 index. All analyses were performed using STATA version 14 (StataCorp LP, College Station, TX) and two-sided statistical significance was defined as a resultant p-value of <0.05.

1.3 Results

Among 1,790 participants with lung cancer who completed the baseline survey, 57% were ≥65 years old, 55% were male, 72% were white, 56% were married/partnered, 29% were current tobacco smokers and 40% were diagnosed with early stage (stage I & II) lung cancer. At baseline 681 (38%) participants had depression symptoms. At follow-up, among 1155 participants who were still alive, 359 (31%) participants had depression symptoms. (Table 1)

1.3.1 Patient Risk Factors for Depression Symptoms at Follow-up—Patient risk factors for depression symptoms at follow-up, which includes persistent or new onset depression symptoms, included: age less than 55 years-old (OR 2.81, 95% CI: 1.91–4.13, p<0.001), female sex (OR 1.59, 95% CI: 1.24–2.05, p<0.001), low income (< $20,000) (OR 1.45, 95% CI: 1.09–1.94, p=0.012) not being married/partnered (OR 1.74, 95% CI: 1.34–2.27, p<0.001) and current smoking status (OR 1.80, 95% CI: 1.36–2.38, p<0.001). High school education was associated with reduced odds of depression symptoms at follow-up, compared with lesser educational attainment (OR 0.74, 95% CI: 0.55–0.98, p=0.04). (Table 2)

1.3.3 Health Domain Differences—At baseline, participants with depression symptoms had significantly lower SF-12 PCS and MCS, EQ-5D, SF-36 (Vitality) and MOS-SSS scores (all p<0.001) corresponding to worse HRQOL, vitality and less social support, respectively. Participants with depression symptoms had significantly higher EORTC QLQ-30 and EORTC QLQ-LC13 scores (p<0.001) corresponding to more cancer-specific symptoms. PFI scores corresponding to fatalism beliefs were not significantly different between participants with and without depression symptoms (p=0.82). (Table 3)

1.3.4 Interaction between Health Domains and Depression Symptoms with Associated Mortality—Lower scores on the SF-12, EQ-5D, and SF-36 Vitality were associated with increased mortality (all p<0.001). Higher symptom scores on the EORTC QLQ-30 and EORTC QLQ-LC13 were associated with increased mortality (all p<0.001). Scores on the PFI and MOS Social Support Survey were not associated with increased mortality (p>0.05). Results were similar when adjusted by patient and tumor characteristics. There were no significant interactions between depression symptoms and SF-12, EQ-5D, SF-36 Vitality, EORTC QLQ-30 and PFI scores. There were significant interactions between the EORTC QLQ-LC13 lung cancer symptoms scores and the MOS Social Support Survey scores, emotional/informational sub-scale, and depression symptoms on mortality p=0.008 and p=0.04, respectively. (Table 4) There was a greater association between EORTC QLQ-LC13 lung cancer symptom scores and mortality among patients without depression symptoms compared to patients with depression symptoms. There was an associated interaction between MOS Social Support Survey scores and mortality among patients with depression symptoms; there was no associated interaction among patients without depression symptoms.

1.4 Discussion

Risk factors for depression symptoms among lung cancer patients at follow-up were younger age (<55 years-old), female sex, low income (<$20,000), less education (<high school), unmarried/unpartnered marital status, and current smoking status. Patients with depression symptoms suffered significantly worse HRQOL, vitality, cancer-related symptoms, and social support than patients without depression symptoms. There were no differences in fatalism beliefs among those with and without depression symptoms. Worse HRQOL, vitality and cancer-related symptom were all associated with increased mortality among lung cancer patient with depression symptoms. However, among these health domains only

increased symptoms and low social support moderated the association between depression symptoms and worse mortality.

Patient risk factors for changes in depression symptoms during treatment are understudied compared to assessments at cancer diagnosis [4, 41]. We found some notable differences in risk factors at these two time points. Around the time of cancer diagnosis, younger lung cancer patients have reported lower rates of depression and depression symptoms [42, 43]. Hopwood et al. [4] found a higher trend for symptoms of depression in younger patients at cancer diagnosis which failed to reach statistical significance. Among cancer patients, female sex has been associated with more distress [44], depressive symptoms [45], and increased anxiety [46] at follow-up; however, sex differences have not been consistent across studies [47, 48]. Traditionally, low income patients are less likely to receive antidepressants or mental health services [49, 50], and many encounter economic barriers to cancer care [51] which may explain their increased risk of depression. Our study was in agreement with previous research that found lower education level was a significant predictor of depression 12 months after lung cancer curative resection [52]. Income and education are indexes of socioeconomic status (SES) [53], and low SES is associated with numerous health disparities among cancer patients including worse survival [54] and increased depression symptom severity among lung cancer patients [55].

Other important patient risk factors for depression symptoms at follow-up were identified. Among lung [44] and colorectal [56] cancer patients, married or partnered patients had lower levels of distress at follow-up. Marriage is associated with better overall survival in cancer patients which has been partially attributed to better adherence with prescribed treatments [44, 57, 58]. Depression symptoms may mediate the relationship between marriage and adherence to medical treatments as there is a strong relationship between depression and non-adherence [59]. Smoking is frequently comorbid with depression [60, 61], whether depression increases the risks of smoking [62, 63] or there is a causal link between smoking and depression [64] is unknown. Our study results support the integration of depression screening with smoking cessation programs among lung cancer patients. Providers should pay particular attention to these vulnerable patient subgroups at high-risk for persistent or new onset depression symptoms during cancer treatment; the use of timely depression screening and regular evaluations may improve quality of life.

QOL assessed around the time of lung cancer diagnosis [12] and before treatment [65] has been identified as a prognostic variable for survival. However, among lung cancer patients a systematic review found the relationship between HRQOL, which included physical symptoms, role functioning, and global health status assessed using the EuroQol, EORTC QLQ-C30 and EORTC QLQ-LC13 among other instruments, and overall survival was not consistent [66]. Depression is also associated with worse survival among lung cancer patients [67–69], however, health domains, such as QOL, that interact with depression to increase mortality are understudied.

QOL among cancer patients is multidimensional and includes as least five aspects: physical, social, functional, and emotional as well as an overall global index [70]. According to a hierarchical model, the main impact of depression is on the psychological functioning

domain of QOL [71, 72]. Instruments that measure HRQOL or vitality significantly overlap with depression symptoms in terms of their psychological assessment. Besides the psychological domain, depression may involve the physical domain of QOL as it has been reported to amplify physical symptom severity [4, 73]. Data from three randomized trials during lung cancer treatment found increasing physical symptom burden was associated with depression symptoms [4]. Although the relationship between physical symptoms and depression symptoms has been characterized [4], this is the first study to demonstrate an interaction between lung cancer symptoms and depression symptoms on mortality. Considering the high physical symptom burden experienced by many patients, frequent surveillance and concurrent physical and mental symptom management should be a focus of any depression treatment program. Identifying potentially modifiable health domains that are associated with mortality may support implementation of depression screening and help identify potential targets for interventions.

Social support may mitigate the negative effects of stressful life events [74], and enhance physical and mental health particularly among older adults [75–77]. Among breast and head/neck cancer patients, social support reduced distress [76, 78]. Marriage is likely a surrogate of social support partly explaining why marriage is associated with increased survival in cancer patients, as partners can share the emotional disease burden. After adjustment for marital status in our analyses, social support still interacted with depression symptoms to influence mortality potentially demonstrating the importance of a network of close relatives or friends. Unfortunately, social support is seldom assessed in clinical settings [79] and cancer patients report unmet emotional needs and a desire for support during and after completion of cancer treatment [8]. Ensuring patients have adequate social support should be a key focus of any depression treatment program as part of comprehensive lung cancer care. The importance of support may explain why an integrated collaborative approach to depression treatment was successful [80].

Not surprisingly, many lung cancer patients had high fatalism beliefs; however, patients with and without depression symptoms had comparable beliefs. Cancer fatalism is a situational manifestation of fatalism in which individuals feel powerless in the face of cancer and view their diagnosis as a struggle against predetermined, insurmountable odds [81–83]. Cancer fatalism has been identified as a barrier to participation in cancer treatment [83]. Perceptions of fatalism occur over time along a continuum after cancer diagnosis [84]; the early assessment at baseline in our study may explain why these perceptions were similar between patients with and without depression symptoms as they did not have adequate time to diverge. Alternatively, if high cancer fatalism is not a significant factor among patients with depression symptoms, this might infer depression treatment may enjoy a higher likelihood of success, as there are significant limitations in modifying cancer fatalism [83].

This study has limitations. Patients were interviewed soon after diagnosis; however, some died or were too ill to complete surveys, limiting generalizability. A validated, reliable brief depression screening tool[17, 85, 86] was used which measures depression symptoms other than clinical depression and may have led to a misclassification for some patients. Only baseline measures of health domains were compiled and longitudinal assessments were not available. A comprehensive list of covariates was used in modeling; however, the potential

for unmeasured confounding exists. Our results cannot prove causation and it is possible patients' anticipated mortality is associated with depression.

1.5 Conclusions

Among lung cancer patients, risk factors for persistent or new onset depression symptoms during treatment include younger age, female sex, low income, less education, unmarried/unpartnered marital status and current smoking status. These at-risk patient subgroups should be identified by providers for enhanced depression symptom detection and timely treatment. Worse health domains existed among lung cancer patients with depression symptoms; however, only lung-cancer symptoms and social support significantly interact with depression symptoms to influence mortality. Future research should focus on developing a better understanding of the mechanisms of depression development and persistence, and targeting cancer symptoms and social support as key components of any depression treatment program.

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Highlights

- Depression symptoms are often persistent among lung cancer patients
- Patient characteristics stratify risk for depression during cancer treatment
- Lung cancer patients with depression symptoms suffer significantly worse QOL
- Cancer symptoms and social support are important determinants for survival

Table 1

Patient Characteristics by Depression Symptom Status

	Baseline		Follow-up	
Characteristic	**Depression Symptoms N=681**	**No Depression Symptoms N=1109**	**Depression Symptoms N=359**	**No Depression Symptoms N=796**
	no. (%)	**no. (%)**	**no. (%)**	**no. (%)**
Age, years				
< 55	124 (18)	125 (11)	80 (22)	72 (9)
55–64	227 (33)	287 (26)	102 (28)	220 (28)
65–74	212 (31)	401 (36)	117 (33)	296 (37)
75+	118 (17)	296 (27)	60 (17)	208 (26)
Sex, Female	345 (51)	458 (41)	191 (53)	329 (41)
Race/Ethnicity				
White	494 (73)	791 (71)	261 (73)	599 (75)
African American	67 (10)	139 (13)	43 (12)	84 (11)
Other/Unknown/Mixed Race	120 (18)	179 (16)	55 (15)	113 (14)
Cancer Stage				
Stage I	184 (27)	367 (33)	131 (36)	329 (41)
Stage II	70 (10)	92 (8)	37 (10)	85 (11)
Stage III	202 (30)	286 (26)	105 (29)	203 (26)
Stage IV	197 (29)	279 (25)	63 (18)	127 (16)
Unknown	28 (4)	85 (8)	23 (6)	52 (7)
Histology				
NSCLC	443 (65)	734 (66)	251 (70)	563 (71)
SCLC	77 (11)	134 (12)	31 (9)	73 (9)
Other/Unknown	161 (24)	241 (22)	77 (21)	160 (20)
Income Level				
< $20,000	267 (39)	277 (25)	128 (36)	207 (26)
$20,000–59,000	264 (39)	518 (47)	156 (43)	367 (46)
≥$60,000	94 (14)	219 (20)	51 (14)	164 (21)
Unknown	56 (8)	95 (9)	24 (7)	58 (7)
Education				
< High School	326 (48)	490 (44)	178 (50)	335 (42)
High School	230 (34)	374 (34)	111 (31)	282 (35)
>High School	125 (18)	242 (22)	70 (19)	178 (22)
Unknown	-	3 (<1)	-	1 (<1)
Marital Status				
Married/Partner	348 (51)	663 (60)	183 (51)	500 (63)
Not Married	301 (44)	373 (34)	158 (44)	246 (31)
Refused/Unknown/Missing	32 (5)	73 (7)	18 (5)	50 (6)

	Baseline		Follow-up	
Characteristic	**Depression Symptoms N=681**	**No Depression Symptoms N=1109**	**Depression Symptoms N=359**	**No Depression Symptoms N=796**
	no. (%)	**no. (%)**	**no. (%)**	**no. (%)**
Smoking Status				
Former	361 (53)	694 (63)	187 (52)	494 (62)
Never	70 (10)	139 (13)	40 (11)	103 (13)
Current	247 (36)	267 (24)	131 (36)	193 (24)
Unknown	3 (<1)	9 (1)	1 (<1)	7 (<1)
Comorbidity (ACE-27)				
ACE 0	107 (16)	210 (19)	58 (16)	160 (20)
ACE 1	277 (41)	445 (40)	148 (41)	327 (41)
ACE 2	168 (25)	231 (21)	86 (24)	176 (22)
ACE 3	129 (19)	223 (20)	67 (19)	143 (18)
Site				
VA	105 (15)	155 (14)	62 (17)	116 (15)
Other	576 (85)	954 (86)	297 (83)	680 (85)
Cancer Treatment Received				
Surgery	323 (47)	531 (48)	220 (61)	493 (62)
Radiation	354 (52)	506 (46)	154 (43)	315 (40)
Chemotherapy	446 (65)	675 (61)	195 (54)	463 (58)

May not add to 100% due to rounding;

*Abbreviations: ACE-27= Adult Comorbidity Index 27, VA= Veterans Affairs.

Table 2

Patient Risk Factors for Depression Symptoms at Follow-up

	Univariate		Multivariate[#]	
	Depression Symptoms at Follow-up[*] OR (95% CI)	**p value**	**Depression Symptoms at Follow-up[*] OR (95% CI)**	**p value**
Characteristic				
Age, years				
< 55	**2.81 (1.91–4.13)**	**<0.001**	**3.28 (2.17–4.96)**	**<0.001**
55–64	1.17 (0.85–1.61)	0.33	1.30 (0.94–1.82)	0.12
65–74	1.0 (Reference)	-	1.0 (Reference)	-
75+	0.73 (0.51–1.04)	0.09	0.80 (0.55–1.15)	0.23
Sex, Female	**1.59 (1.24–2.05)**	**<0.001**	**1.53 (1.17–2.01)**	**<0.001**
Income Level				
< $20,000	**1.45 (1.09–1.94)**	**0.01**	1.30 (0.94–1.80)	0.11
$20,000–59,000	1.0 (Reference)	-	1.0 (Reference)	-
≥$60,000	0.73 (0.51–1.05)	0.09	**0.60 (0.40–0.90)**	**0.01**
Unknown	0.95 (0.57–1.59)	0.86	0.93 (0.55–1.59)	0.80
Education				
< High School	1.0 (Reference)	-	1.0 (Reference)	-
High School	**0.74 (0.55–0.98)**	**0.04**	**0.71 (0.53–0.96)**	**0.03**
>High School	0.74 (0.53–1.03)	0.07	0.96 (0.67–1.39)	0.85
Marital Status				
Married/Partner	1.0 (Reference)	-	1.0 (Reference)	-
Not Married	**1.74 (1.34–2.27)**	**<0.001**	**1.37 (1.01–1.85)**	**0.04**
Refused/Missing/Unknown	0.98 (0.56–1.73)	0.949	0.97 (0.52–1.78)	0.91
Smoking Status				
Former	1.0 (Reference)	-	1.0 (Reference)	-
Current	**1.80 (1.36–2.38)**	**<0.001**	**1.44 (1.07–1.94)**	**0.02**
Never	1.03 (0.69–1.53)	0.90	0.88 (0.58–1.35)	0.57
Unknown	0.38 (0.46–3.09)	0.36	0.33 (0.04–2.87)	0.31

[*] Includes persistent and new onset depression symptoms participants;

[#] Adjusted by age, sex, income, education, marital status, and smoking status

Table 3

Health Instruments at Baseline by Depression Symptoms Status

	Depression Symptoms* mean (SD)	No Depression Symptoms mean (SD)	p value
Instrument			
SF-12			
Physical Component	33.2 (10.4)	38.9 (11.2)	<0.001
Mental Component	41.9 (10.8)	55.9 (8.2)	<0.001
EQ-5D	0.68 (0.18)	0.84 (0.14)	<0.001
SF-36 (Vitality)	30.8 (19.3)	55.2 (21.5)	<0.001
EORTC QLQ-30#	33.7 (19.7)	15.6 (14.1)	<0.001
EORTC QLQ-LC13	30.5 (16.7)	19.3 (13.2)	<0.001
Powe Fatalism Inventory#	9.2 (2.5)	9.2 (2.6)	0.82
MOS Social Support Survey			
Emotional/Informational	78.1 (26.7)	86.2 (22.8)	<0.001
Tangible/Instrumental	76.8 (25.2)	88.6 (17.8)	<0.001

*Includes persistent and new onset depression symptoms participants,

#Selected items

Abbreviations: SF-12= Medical Outcomes Study 12-item short form, EQ-5D=EuroQol questionnaire, SF-36 Medical Outcomes Study 36-item short form vitality scale, EORTC QLQ-30= European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, LC13=Lung Cancer Modular Questionnaires, and MOS=Medical Outcomes Study.

Table 4

Association between Instrument Scores and Mortality

	HR* (CI 95%)	p value	Adj HR*# (CI 95%)	p value	p value Interaction*# (depression symptoms x instrument)
Instrument					
SF-12					
PCS	0.80 (0.75–0.85)	<0.001	0.87 (0.82–0.93)	<0.001	0.94
MCS	0.90 (0.85–0.95)	<0.001	0.94 (0.89–1.01)	0.078	0.66
EQ-5D	0.84 (0.80–0.89)	<0.001	0.89 (0.84–0.95)	<0.001	0.59
SF-36 (Vitality)	0.83 (0.79–0.88)	<0.001	0.91 (0.85–0.96)	0.002	0.25
EORTC QLQ-30^	1.18 (1.12–1.25)	<0.001	1.09 (1.03–1.16)	0.004	1.00
EORTC QLQ-LC13	1.24 (1.18–1.31)	<0.001	1.14 (1.08–1.21)	<0.001	**0.008**
Powe Fatalism Inventory^	0.95 (0.90–1.01)	0.11	0.96 (0.90–1.03)	0.25	0.38
MOS Social Support Survey^					
Emotional/Informational	0.96 (0.91–1.02)	0.21	1.01 (0.95–1.07)	0.71	**0.04**
Tangible/instrumental	0.96 (0.91–1.01)	0.12	0.98 (0.93–1.04)	0.53	0.26

*Scores standardized to unit of one standard deviation for comparison;

#Adjusted by age, race, sex, income, education, smoking history, marital status, comorbidities and cancer stage and histology;

^Selected items

Abbreviations: SF-12= Medical Outcomes Study 12-item short form, EQ-5D=EuroQol questionnaire, SF-36 Medical Outcomes Study 36-item short form vitality scale, EORTC QLQ-30= European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, LC-13=Lung Cancer Modular Questionnaire, and MOS=Medical Outcomes Study.