

**Review Article**

# Symptoms in Adults with Lung Cancer: A Systematic Research Review

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**Abstract**

*Health care providers play a key role in providing adequate symptom management and promoting quality of life during chronic illness. Several studies have noted that adults with lung cancer experience more symptom distress than patients with other types of cancer. Therefore, symptom management in this group of patients is particularly important. An understanding of the research conducted in this area is important for further knowledge development and for potentially improving symptom management. This paper presents a systematic review of empirical studies examining symptoms in adults with lung cancer. The results of this systematic review revealed that although major strides have been made in understanding symptoms associated with lung cancer, further progress is needed to decrease the morbidity associated with uncontrolled symptoms. Theoretical, conceptual, and/or methodological issues identified through this review must be addressed in future research. In particular, the researcher should provide information about the theoretical or empirical framework guiding the study, give an explicit definition about the dimensions of the symptom experience being studied, report refusal rates and attrition, and use instruments that are reliable and valid.* J Pain Symptom Manage 2000;19:137–153. © U.S. Cancer Pain Relief Committee, 2000.

**Key Words**

*Symptoms and lung cancer, symptom distress and lung cancer, symptom management and lung cancer*

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**Introduction**

Lung cancer is the second most common cancer in both men and women in the United States and the number one cause of cancer mortality in both men and women.<sup>1</sup> Twenty-five percent of all cancer deaths are due to lung cancer. Unfortunately, most adults with lung cancer present with advanced stages of disease.<sup>2,3</sup> Symptoms are common and typically progress if the disease cannot be controlled

with therapy. Treatment, however, may cause additional symptoms.

Weisman and Worden<sup>4</sup> underscored the importance of adequate symptom management in this population of patients. In their now classic study, they examined psychosocial responses to the diagnosis of cancer. One hundred sixty-three adults with newly diagnosed Hodgkin's disease, malignant melanoma, breast, colon, or lung cancer were followed every 4 to 6 weeks from 10 days after diagnosis until 6 months. Results suggested that adults with advanced stage lung cancer experienced the highest number of symptoms and concerns related to health and existential issues. The

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number of physical symptoms was highly correlated with level of emotional distress.<sup>4</sup> Peak levels of emotional distress and concerns related to health and existential issues occurred within the first 100 days after diagnosis. Although a gradual resolution of emotional distress and concerns was noted in most patients, high levels of physical symptoms and emotional distress persisted at every assessment in those with lung cancer.

Because symptoms in adults with lung cancer are an important focus for clinical intervention, an understanding of symptom-related research in this area is important. The purpose of this paper is to present a systematic review of empirical studies examining symptoms in adults with lung cancer. Computer searches were performed using MEDLINE and Cumulative Index to Nursing and Allied Health Literature from January 1982 to August 1998. Key words used to access the articles were "symptoms and lung cancer" and "symptom distress and lung cancer." A hand search of the references noted in the articles provided additional studies. The published reports that explicitly included symptoms of lung cancer in the title were identified as appropriate for analysis. Phase I and Phase II clinical trials and studies that primarily examined quality of life, as reflected in the title of the article, were not included. Studies that examined the relationship between symptom distress and quality of life, however, were included. The final review encompassed 18 studies that include a discussion of the theoretical framework, design, sample, measures, and selected findings (Table 1). Implications for future theory development and research are also discussed.

### ***Theoretical Framework***

Only three studies (17%) were guided by an explicit theoretical framework. McCorkle and Benoliel<sup>5</sup> used Crisis Theory to describe symptom distress, current concerns, and mood disturbance in patients with either newly diagnosed lung cancer or recent myocardial infarction, whereas Sarna and colleagues used a theoretical model of variables derived from the empirical literature to guide their studies.<sup>12,13</sup> The other 15 studies used an atheoretical approach in studying symptoms in lung cancer.

### ***Study Design***

Ten of the studies used a longitudinal study design and eight studies used a cross-sectional design. Eight of the longitudinal studies used a prospective design, whereas the other two used a retrospective chart review.<sup>15,18</sup> All of the longitudinal studies followed the same patients over time. The time that patients were followed varied among studies. Six of the studies followed the patients for an average of 12 weeks (range 7–24 weeks).<sup>5,8,12,13,18,22</sup> Three followed patients for an average of 3 years (range 1–5 years).<sup>6,10,14</sup> The remaining study did not specify the length of time that patients were followed.<sup>15</sup>

Attrition was a problem in five of the longitudinal studies.<sup>8,10,12,13,22</sup> At the end of 14 weeks, Kaasa and colleagues<sup>8</sup> reported that 73% of the subjects completed the questionnaires. The authors did not provide information, however, about the reason for attrition. Similarly, Muers and Round<sup>10</sup> noted a 43% attrition rate at 12 months but did not provide information about the reasons for loss of subjects. As expected, death of subjects and decline in physical condition were responsible for the high attrition rates found in the other three studies.<sup>12,13,22</sup>

Data were collected prospectively in seven of the cross-sectional studies.<sup>9,11,14,16,17,19,20</sup> One of the researchers collected data from a retrospective chart review.<sup>7</sup> Secondary analysis of previously collected data was used in a number of the studies.<sup>7,12,13,21</sup>

### ***Sample***

Sample size for the various studies ranged from 37 to 1640 subjects. Eleven studies had a sample size less than or equal to 100. The remaining seven had sample sizes ranging from 240 to 1640. Although all studies used convenience sampling techniques, the majority of studies used multiple sites to recruit subjects. The researchers who did not use a multicenter approach to recruit patients either used a randomized clinical trial design or selected a sequential patient procedure to reduce selection bias. Only two researchers provided information about the number of patients who were eligible but did not participate in their studies.<sup>16,18</sup>

Table 1  
Summary of Studies Examining Symptoms in Adults with Lung Cancer

Investigator	Theoretical framework	Design	Sample	Instruments used to measure symptoms	Selected findings
McCorkle and Benoliel <sup>5</sup>	Crisis Theory	Short-term longitudinal	56 newly diagnosed lung cancer patients 65 recent myocardial infarction patients	SDS	Patients with lung cancer experienced significantly more symptom distress than patients with myocardial infarction. Symptom distress affected current concerns and mood disturbance for both groups at both occasions. An increase in symptom distress was associated with more concerns and greater mood disturbance. Most troublesome symptoms for lung cancer patients were fatigue, pain, cough, lack of appetite, and insomnia.
Kukull et al. <sup>6</sup>	None	Longitudinal	53 newly diagnosed lung cancer patients	SDS, Pain-McGill Pain Questionnaire	Forty-five subjects had died, four were alive, two were lost to follow-up, and two had died of other causes at the end of 3 1/2 years. The patients' SDS scores shortly after their diagnosis was the most important predictor of survival after adjusting for age, personality factors, and functional status.
DeMaria and Cohen <sup>7</sup>	None	Cross-sectional secondary analysis of previously abstracted medical record data	364 adults with lung cancer age 40-50 822 adults with lung cancer age 51-69 209 adults with lung cancer age 70 and above	Standard Assessment Tool	The elderly cohort, age 70 and above, demonstrated more presenting symptoms of dyspnea, fewer symptoms of chest pain, but similar frequency of weight loss as compared with the younger cohort.
Kaasa et al. <sup>8</sup>	None	Randomized clinical trial. Longitudinal	95 adults with advanced NSCLC 51 received radiation therapy 44 received chemotherapy with cisplatin and VP-16	Toxicity Questionnaire	Sleeping disturbance, pain, tiredness, and lack of appetite were the predominant symptoms for both groups of patients. Nausea, vomiting and hair loss were the predominant symptoms in the chemotherapy group. Dysphagia and sore throat were more common in the radiation therapy group.
Krech et al. <sup>9</sup>	None	Cross-sectional	100 adults with lung cancer referred to palliative care service	Standard Assessment Tool	Median number of symptoms was 9. Most common and severe symptoms were pain, dyspnea, and anorexia. There was no difference in symptoms between men and women. Males less than age 64 had higher levels of easy fatigue, taste changes, and sleep problems. Males older than age 64 had a higher incidence of cough and weight loss greater than 10%.
Muers and Round <sup>10</sup>	None	Longitudinal	289 adults with NSCLC 64 had surgery 122 had radiation therapy 103 had best supportive care	Standard Assessment Tool	Most common and severe symptoms at presentation were cough and breathlessness. Hemoptysis and chest pain were also common. Chest pain, breathlessness, malaise, and anorexia worsened over time. Breathlessness was a particular problem in those receiving supportive care

(continued)

Table 1 continued

Investigator	Theoretical framework	Design	Sample	Instruments used to measure symptoms	Selected findings
Sarna <sup>11</sup>	None	Cross-sectional	69 women with lung cancer	SDS	Sixty-one percent of patients experienced more than one symptom. Most prevalent and distressing symptoms were fatigue, pain, and insomnia. Poor outlook, dyspnea, and appetite disruptions were other common symptoms. Forty-one percent of patients with fatigue also experienced frequent pain and insomnia. Concurrent respiratory disease, previous chemotherapy, recurrent disease, no surgical treatment and low income were associated with high levels of symptom distress. Average weight change and nutritional intake showed little variation over time.
Sarna et al. <sup>12</sup>	Model of nutritional intake, functional status, symptom distress, and weight change derived from the empirical literature	Design: Longitudinal, descriptive, correlational (secondary analysis)	Subsample of 26 adults with advanced lung cancer	SDS	Lower intake of kilocalories was moderately related to functional status. Kilocalorie status at a previous time was related to subsequent functional decline at 2 of the 6 data points. Weight change was not directly related to Kcal intake. Percentage of weight loss over time was greater in patients less than 65 years of age, those with small cell lung cancer, and those receiving chemotherapy. Symptom distress and symptoms of hunger, nausea, and appetite disturbance showed subtle fluctuations over time and had an inconsistent relationship with food.
Sarna et al. <sup>13</sup>	Model of variables influencing weight change derived from the empirical literature	Design: Longitudinal descriptive, correlational (secondary analysis)	Subsample of 60 adults with advanced lung cancer	SDS	Weight loss of 10% or more at study entry occurred in 35% of patients; 37% lost weight at three or more intervals and 25% lost weight at only 1 interval. Preillness weight loss was moderately correlated with subsequent decrease in functional status. Weight loss correlated with subsequent increase in symptom distress. Chemotherapy and smoking predicted weight loss from time 1 to 5, explaining 28% of variance.
Degner and Sloan <sup>14</sup>	None	Cross-sectional for ambulatory care cancer patients and longitudinal for lung cancer patients	434 newly diagnosed cancer patients 82 of these patients had lung cancer	SDS	Patients with lung cancer had the highest level of symptom distress as compared with the other cancer patients in ambulatory care. Symptom distress at baseline was predictive of survival. Patients with higher symptom distress were more likely to die than those with lower levels of symptom distress. Fatigue, pain, loss of appetite, coughing, and insomnia were the most frequent symptoms.

(continued)

Table 1 continued

Investigator	Theoretical framework	Design	Sample	Instruments used to measure symptoms	Selected findings
Furuta et al. <sup>15</sup>	None	Retrospective chart review Longitudinal	240 adults with NSCLC receiving treatment with definitive radiation therapy	Chart review by investigator. Instrument not specified.	Only 15% of adults were symptomatic at the beginning of therapy. Chest pain, fatigue, breathlessness, and weight loss correlated with decreased survival while cough, sputum production, and fever were favorable symptoms in adults with squamous cell histology. In contrast, weight loss was the only symptom that correlated with decreased survival in those with adenocarcinoma. Although symptoms were related to clinical stage and performance status, they were not an independent prognostic factor. Performance status, stage, histology, and weight loss were related to survival. Most common symptoms at presentation were tiredness, lack of energy, worry, anxiety, cough, shortness of breath, lack of appetite, and difficulty sleeping. No differences in symptoms were noted between those with SCLC and those with NSCLC. Women reported more psychological symptoms than men.
Hopwood and Stephens <sup>16</sup>	None	Cross-sectional	655 patients with lung cancer 232 SCLC patients receiving chemotherapy 423 NSCLC patients receiving chemotherapy	Rotterdam Symptom Checklist. Five additional symptoms added to make the checklist more specific to lung cancer patients	
Vainio and Auvinen <sup>17</sup>	None	Cross-sectional	1640 patients with advanced cancer referred to palliative care service	Standardized Assessment Tool	Significant differences for prevalence of all symptoms were noted among various primary cancer sites except for constipation, insomnia, and confusion.
Lutz et al. <sup>18</sup>	None	Retrospective chart review Longitudinal	54 patients with NSCLC who received palliative radiation therapy	Observer portion of the Lung Cancer Symptom Scale	Dyspnea was most common in the patients with lung cancer. Sixty-five percent of patients had post-therapy improvement of symptoms. Significant reduction in cough, hemoptysis, and dyspnea were noted.
Lobchuk et al. <sup>19</sup>	None	Cross-sectional	37 adults with lung cancer and their family caregivers	SDS	Patients with lung cancer identified fatigue, cough, pain frequency, outlook, breathing, and insomnia as the most distressing symptoms, whereas family caregivers identified fatigue, outlook, insomnia, cough, and pain frequency as the most distressing symptoms for patients. Family caregivers tended to rate the degree of distress as slightly more severe than the patients for all symptoms except for concentration. Dyad members appeared to agree most often on symptoms that patients rated as most distressing.

(continued)

Table 1 continued

Investigator	Theoretical framework	Design	Sample	Instruments used to measure symptoms	Selected findings
Lobchuk and Kristjanson <sup>20</sup>	None	Cross-sectional	37 adults with lung cancer and their family caregivers	SDS open-ended questionnaire to elicit behavioral assessment cues that family caregivers used when assessing patient symptom distress	Family caregivers used the behavioral assessment categories of impaired functioning and verbal cues as the most frequent indices of symptom distress. Family caregivers tend to limit the number of cue categories to one cue dimension. Behavioral observation did not have a significant influence on closing the gap between patient and family caregiver perceptions of symptom distress.
Sarna and Brecht <sup>21</sup>	None	Cross-sectional (secondary analysis)	60 women with advanced lung cancer	SDS	The most common symptoms were fatigue, disruptions in outlook, frequent pain, and insomnia. A four-factor solution for low symptom distress (symptoms rated as 1–2): emotional and physical suffering (five items), gastrointestinal distress (3 items), respiratory distress (3 items), and malaise (2 items). A five-factor solution was identified for high symptom distress (symptoms rated as 3–5): gastrointestinal distress (three items), respiratory distress (three items), malaise (two items), physical distress (three items), and emotional distress (two items).
Stephens et al. <sup>22</sup>	None	Longitudinal	810 adults with advanced lung cancer who participated in clinical trials and their doctors.	Rotterdam Symptom Checklist plus an additional 4 items for lung cancer (patients). Clinical report forms depicting the presence and severity of symptoms (doctors).	Complete agreement on symptoms between patients and doctors was 78%. There was no change in levels of agreement over time but there was increasing disagreement when patients had increased severity of symptoms. Doctors consistently underestimated the severity of patient symptoms. 66% of doctors provided data on symptoms as compared with 52% of patients during the first 6 months of one clinical trial. In the other clinical trial, 68% of doctors provided data on symptoms as compared with 61% of patients during the first 6 months.

NSCLC = non-small cell lung cancer; SCLC = small cell lung cancer; SDS = Symptom Distress Scale.

Table 2  
Instruments Used to Measure Symptoms in Adults with Lung Cancer

Instrument	Symptom dimension measured	Method of administration	Reliability	Validity
Lung Cancer Symptom Scale <sup>23,24</sup>	Intensity	Patient self-report Observer scale	Cronbach alpha Test-retest Interrater agreement	Content Construct Criterion
Rotterdam Symptom Checklist <sup>25</sup>	Distress	Patient self-report	Cronbach alpha	Construct
Standard Assessment Instrument <sup>7</sup>	Presence	Clinician report	NR	NR
Standard Assessment Instrument <sup>9,10,17</sup>	Intensity	Clinician report	NR	NR
Standard Assessment Instrument <sup>15</sup>	Not indicated	Clinician report	NR	NR
Symptom Distress Scale <sup>26-28</sup>	Distress Frequency	Patient self-report	Cronbach alpha Test-retest	Content Construct Criterion
Toxicity Questionnaire <sup>29</sup>	Frequency	Patient self-report	NR	Needed further development

NR = not reported.

Almost 40% of the studies ( $n = 7$ ) were conducted using a heterogeneous sample of patients with lung cancer. The phase of illness that was examined varied in the remaining studies; three studies were conducted with newly diagnosed patients, six studies were conducted with patients receiving active treatment with chemotherapy or radiation therapy, and two studies were conducted with patients who had advanced disease and were receiving palliative care services.

The majority of studies were conducted with white, middle-income males with advanced stage non-small cell lung cancer. Two of the studies examined symptoms in white, middle-income females with lung cancer.<sup>11,21</sup> The majority of women in these studies also had advanced stage non-small cell lung cancer.

## Measures

The instruments used to measure symptoms are listed in Table 2. The Symptom Distress Scale (SDS) was the most common instrument used to measure symptoms ( $n = 9$ ). A variety of other instruments were also used, including the Rotterdam Symptom Checklist ( $n = 2$ ), Lung Cancer Symptom Scale Observer Portion (LCSS) ( $n = 1$ ), Toxicity Questionnaire ( $n = 1$ ), and an investigator-developed Standard As-

essment Tool ( $n = 5$ ). The instruments measured a variety of dimensions of the symptom experience (Table 2). A brief discussion of each instrument is provided below.

The SDS provides a measure of symptom distress defined as "The degree of comfort from specific symptom being experienced as reported by the patient" (reference 26, p. 374). This is a 13-item patient self-report instrument assessing the level of symptom distress for 11 symptoms (nausea, appetite, insomnia, pain, fatigue, bowel pattern, concentration, appearance, outlook, breathing, and cough) and the frequency of two symptoms (nausea and pain). A 5-point Likert type format is used to assess each symptom. A score of 1 indicates normal or no distress for a symptom, whereas a score of 5 represents extreme distress. Similarly, the frequency items are on a scale from 1 to 5, where 1 represents almost never experiencing the symptom and 5 represents experiencing the symptom almost constantly. The sum of the 13 items provides a measure of total symptom distress. Scores can range from 13 to 65 with higher scores indicating higher levels of symptom distress. Internal consistency and test-retest reliability have been reported in patients with lung cancer.<sup>27</sup> Content, construct, and criterion validity have been established for this instrument.<sup>28</sup> Reference values for the SDS in various samples are also available.<sup>28</sup>

The Rotterdam Symptom Checklist is a patient self-report instrument that measures physical symptom distress, psychological distress, activity level, and overall quality of life. Subscales are available for each construct. The physical symptom distress scale consists of 23 different physical symptoms. The psychological distress scale consists of 7 different psychological symptoms. The activity level scale consists of 8 items regarding functional status. One question assesses overall quality of life. The symptom subscales use a four-point Likert type format ranging from "not at all" to "very much" to assess the degree to which patients were bothered by the symptom. Internal consistency, reliability, and construct validity have been established in patients with cancer.<sup>25</sup> The researchers using the Rotterdam Symptom Checklist, in this review, added items believed to be important in patients with lung cancer. Reliability and validity of the revised instrument were not reported.<sup>16,22</sup>

The LCSS is a site-specific instrument that has both a patient and an observer form.<sup>24</sup> The patient form uses a 100-mm Visual Analogue Scale format to measure the intensity of symptoms specific to lung cancer (appetite, fatigue, cough, shortness of breath, hemoptysis, pain, overall symptoms), perception of activity status, and overall quality of life. Individual scores, obtained for each item, can range from zero representing the lowest score to 100 representing the highest. An aggregate score ranging from zero to 900 can also be used.

The observer portion of the LCSS scale allows health care providers to assess the symptoms experienced by the patient. Six questions related to the most common symptoms experienced by patients are graded on a five-point ordinal scale ranging from none to severe. No symptoms are scored as 100 and severe symptoms are scored as zero. Individual scores are obtained for each item. An aggregate score ranging from zero to 600 can also be used.

Internal consistency and test-retest reliability have been established for the patient form. Repeated interrater agreement for the provider scale has been established and it is highly acceptable.<sup>30</sup> Content, construct, and criterion validity have also been established for both the patient and observer forms.<sup>23</sup>

The Toxicity Questionnaire is part of a patient self-report instrument designed to mea-

sure quality of life in lung cancer patients.<sup>29</sup> The Toxicity Questionnaire measures the frequency of 10 symptoms (nausea, vomiting, hair loss, trouble swallowing, sore throat, sore and red skin, tired, lack of appetite, trouble sleeping, pain) on a four-point scale ranging from never to a great deal. Initial reliability and validity testing suggested that further refinement of the instrument was necessary.<sup>29</sup>

Investigator-developed Standard Assessment Instruments were developed for five of the studies.<sup>7,9,10,15,17</sup> All five instruments used clinician report to measure symptoms. Reliability and validity of the instruments were not reported.

### *Selected Findings*

Selected findings of the studies are summarized in Table 1. There were four main clusters of studies: symptoms in lung cancer; the relationship between symptoms and quality and/or quantity of life; the relationship among patient and clinical characteristics and symptom distress; and the feasibility of using either family caregivers or health care providers (physicians) to provide proxy measures of symptom distress. Salient findings from each of these clusters of studies are highlighted in the following section.

#### *Symptoms in Lung Cancer*

Two of the studies confirmed that patients with lung cancer experience more symptom distress than other samples of patients.<sup>5,14</sup> McCorkle and Benoliel<sup>5</sup> described symptom distress, current concerns, and mood disturbance in patients with either newly diagnosed lung cancer or a recent myocardial infarction. Patients with lung cancer experienced significantly higher levels of symptom distress at 1 and 2 months after the diagnosis than the myocardial infarction patients. In another study, Degner and Sloan<sup>14</sup> assessed the level of symptom distress in newly diagnosed ambulatory cancer patients. Results from this study suggested that the patients with lung cancer had the highest level of symptom distress, as compared with the other cancer patients in ambulatory care.

The majority of studies described symptoms in various samples of patients with lung cancer. Symptoms were described in newly diagnosed



patients, those receiving active treatment, and in those receiving palliative care. Two studies were conducted in newly diagnosed patients with lung cancer.<sup>5,14</sup> The findings of these studies suggested that the most common symptoms in newly diagnosed patients are fatigue, pain, loss of appetite, coughing, and insomnia. It is important to recognize that although the studies were conducted in different countries (United States and Canada) and at different points in time (1983 and 1995), the symptoms experienced by the patients were the same in both studies. Furthermore, the mean score on the SDS was similar in both studies (mean score of 26.8 and 26.9), respectively.<sup>5,14</sup>

One study examined the difference in symptoms between patients with advanced non-small cell lung cancer receiving treatment with either chemotherapy or radiation therapy.<sup>8</sup> Results of this study suggested that the predominant symptoms in those receiving chemotherapy were nausea, vomiting, and hair loss, whereas the more common symptoms in the radiation therapy group were dysphagia and sore throat.

The high prevalence of uncontrolled symptoms in patients with advanced lung cancer was highlighted in three studies.<sup>9,10,17</sup> In one of these studies, Krech and colleagues<sup>9</sup> reported that patients with advanced lung cancer admitted to a palliative care service had a median of nine symptoms. Pain, dyspnea, and anorexia were the most common and most intense symptoms experienced by the patients in all three studies. Vainio and colleagues<sup>17</sup> identified that the incidence and severity of dyspnea were highest in the lung cancer population, as compared with other patients with advanced cancer.

Taken together, these studies suggest that most patients with lung cancer experience multiple symptoms; symptoms may differ at various points in the illness trajectory, and among various treatments. Furthermore, some of these symptoms may tend to cluster together. For example, Sarna<sup>11</sup> found that the symptoms of fatigue, frequent pain, and insomnia tended to occur together in women with lung cancer.

#### *Relationship Between Symptoms and Quality and/or Quantity of Life*

The relationship between symptoms and quality and/or quantity of life was examined in

four studies.<sup>5,6,14,15</sup> McCorkle and Benoliel<sup>5</sup> investigated the relationship among symptom distress, current concerns, and mood disturbance in patients with either newly diagnosed lung cancer or recent myocardial infarction. Symptom distress was noted to have a positive relationship to current concerns and mood disturbance at 1 month after the diagnosis of a life-threatening illness. As the symptom distress increased, current concerns and mood disturbance also increased. Interestingly, concerns and mood disturbance decreased after 2 months. Since the authors used Crisis Theory to guide the study, results of the study supported their hypothesis that assimilation of the threat of a serious illness occurs over time.

Symptom distress at diagnosis was also a significant predictor of survival. The relationship between symptom distress and survival was examined in two studies.<sup>6,14</sup> Kukull and colleagues<sup>6</sup> examined the influence of various psychosocial variables on survival in patients with advanced stage lung cancer. Fifty-seven patients with advanced lung cancer were followed for approximately 4 years. Higher levels of symptom distress at time of diagnosis were the most significant predictor of survival when age, functional status, and personality traits were controlled. In a subsequent study, Degner and Sloan<sup>14</sup> followed 82 patients with advanced stage lung cancer for 5 years. Similar to Kukull and colleagues,<sup>6</sup> the single measure of symptom distress was a significant predictor of survival. In contrast to these two studies, however, Furuta and colleagues<sup>15</sup> did not find that symptoms were an independent prognostic factor in adults receiving definitive radiation therapy.

#### *Relationship Among Patient and Clinical Characteristics and Symptom Distress*

The third cluster of studies examined the relationship among various patient and clinical characteristics and symptom distress. Age, gender, stage of disease, type of treatment, comorbidities, income, and weight loss were associated with symptom distress. A number of studies reported that age of the patient may be related to the type of symptom and degree of symptom distress experienced.<sup>7,9,14</sup> Two of the studies identified that older patients may experience a difference in the type of symptom.<sup>7,9</sup> For example, DeMaria and Cohen<sup>7</sup> identified

that patients older than 70 years of age had more presenting symptoms of dyspnea but fewer symptoms of chest pain than younger patients. Degner and Sloan<sup>14</sup> reported that older patients tended to have less symptom distress than younger patients.

Several studies examined the influence of gender on the type of symptom and the overall level of symptom distress.<sup>9,14,16</sup> Although the results of the study conducted by Krech and colleagues<sup>9</sup> suggested that there were no differences in type of symptoms between men and women, two other studies did report significant differences. Hopwood and Stephens<sup>16</sup> found that women with lung cancer reported more psychological symptoms than men. Similarly, Degner and Sloan<sup>14</sup> identified that women had higher symptom distress scores than the men. Stage of disease was related to symptom distress. Both Sarna<sup>11</sup> and Degner and Sloan<sup>14</sup> identified that patients with recurrent disease or those with advanced stages of disease experienced more symptom distress than those with early-stage disease.

In an exploratory study examining correlates of symptom distress in women with lung cancer, Sarna<sup>11</sup> observed that type of treatment, comorbidity, and income were associated with high levels of symptom distress. Previous chemotherapy, no surgical treatment, concurrent respiratory disease, and low income were associated with high symptom distress in women with lung cancer.

Similarly, Sarna and colleagues<sup>13</sup> identified that weight loss was associated with increased symptom distress. Factors associated with weight loss were treatment with chemotherapy, smoking, age greater than 65 years, and small cell histology.<sup>12,13</sup>

### *Proxy Measures of Symptom Distress*

The last cluster of studies examined the congruence of perceived symptom distress between family caregivers or physicians and patients with lung cancer.<sup>19,20,22</sup> Results of these studies suggest that gathering information about symptoms from the patient is the most reliable source of information. Family caregivers tend to rate the degree of symptom distress as slightly more severe than the patient, whereas physicians consistently underrated the severity of the patients' symptoms.

## **Discussion**

This is the first systematic review of empirical studies examining symptoms in adults with lung cancer. The results reveal a number of theoretical, conceptual, and methodological issues that should be addressed in future studies.

### *Theoretical Issues*

One major finding of this review is the lack of explicit theoretical frameworks used to guide research. Only three studies used a theoretical framework to guide the study. The use of theoretical frameworks is essential for the development of knowledge because they present an organized view of phenomena. An important function of theories is that they can help describe, explain, or predict a phenomenon. Therefore, they can be used to guide the selection of appropriate variables used in clinical research. While the lack of conceptual models and/or theoretical frameworks has been identified as a problem in quality-of-life research, few papers have identified this as an issue in research examining symptoms associated with cancer.<sup>31-34</sup>

Several promising conceptual models and/or theoretical frameworks for future research have been highlighted. Lenz and colleagues<sup>35</sup> recently described a Middle Range Theory of Unpleasant Symptoms that proposes a way to integrate information about the complexity and interactive nature of the symptom experience. Because symptoms are often conceptualized as a dimension of health-related quality of life, frameworks used in health-related quality-of-life research may also offer a promising avenue for future research of symptoms.<sup>32</sup> For example, two potential frameworks may be the Model of Patient Outcomes proposed by Wilson and Cleary<sup>36</sup> or the Roy Adaptation Model.<sup>37,38</sup> Both models link clinical variables with health-related quality-of-life outcomes. Symptoms are integral parts of these models. Finally, Teel and colleagues<sup>39</sup> recently suggested a Symptom Interpretation Model that links an individual's interpretation of symptoms and the behaviors that are selected for management of the symptoms. In contrast to the other frameworks, this theory directs the researcher to examine the relationship between cognitive appraisal of the symptoms and the resulting health-seeking behaviors. As one

can see, each of the conceptual models and/or theoretical frameworks presented provides a different approach to the study of symptoms in lung cancer.

Empirical data may also be used to develop a theoretical framework to guide a study. In this particular situation, a theoretical framework is derived from empirical studies. Once the new data are collected and the model is tested, changes may be needed in the theoretical framework underscoring the dynamic nature of theory development and testing.<sup>40</sup>

### *Conceptual Issues*

The lack of a consistent conceptual definition of the symptom experience was identified as another problem in this review (see Table 2). Other authors have noted the confusion surrounding the construct of the symptom experience.<sup>33,41</sup> McDaniel and Rhodes<sup>41</sup> have attempted to clarify this concept by suggesting that the symptom experience consists of symptom occurrence and symptom distress. Symptom occurrence is the frequency, duration, and intensity (severity) of the symptom.<sup>41</sup> Symptom distress is the degree of discomfort reported by the patient in response to the specific symptom being experienced.<sup>42</sup>

Many researchers argue that a multidimensional assessment of symptoms, which includes the frequency, duration, intensity, and distress of a symptom, is necessary to capture the complexity of multiple symptoms.<sup>33,35,43,44</sup> In response to this need, Portenoy and colleagues<sup>45</sup> developed an instrument to capture the multidimensional aspects of the symptom experience. This instrument was subsequently tested for validity. Results from this study suggested that the distress measurement provided the most information about quality of life and that frequency but not severity measure added significant information. Thus, this study identified that if a single symptom measurement is preferred, symptom distress will provide the most useful information. In contrast, a study examining the factor structure of a Symptom Experience Scale did not support the usefulness of separating the frequency, intensity, and distress components of the symptom experience.<sup>46</sup>

### *Methodological Issues*

The SDS was the most common instrument ( $n = 9$ ) used to measure symptoms in this re-

view. A variety of other instruments were used to measure symptoms in the other studies. Unfortunately, many studies not using the SDS had serious problems with the reliability and/or validity of the instruments used to measure symptoms. For example, five of the instruments used to measure symptoms were developed by the investigators.<sup>7,9,10,15,17</sup> The investigators do not discuss issues regarding reliability or validity of these instruments. Thus, the findings of these studies are difficult to interpret given the lack of information about the performance of these instruments in measuring symptoms. Although two other studies used a previously developed instrument, the investigators added items that they felt were important in lung cancer.<sup>16,22</sup> The reliability and validity of this adapted measure were not reported. Similarly, Lutz and colleagues<sup>18</sup> used the observer portion of the LCSS but did not report procedures done to reduce observer bias. Often, it is important to implement procedures, such as tests for interobserver bias and measures of interobserver agreement (Kappa), to ensure that an individual performs reliable and valid coding of an instrument.<sup>47</sup> Finally, one-third ( $n = 6$ ) of the studies used clinician-rated reports of patient symptoms.<sup>7,9,10,15,17,20</sup> Because symptoms are a subjective experience, patient self-report is the preferred method of measurement.<sup>41,48</sup> The importance of using patient self-report of symptoms was highlighted in three of the studies.<sup>19,20,22</sup> For example, Stephens and colleagues<sup>22</sup> observed that physicians consistently underestimated symptom severity. Furthermore, the discrepancy between clinician report and patient self-report increased as the symptoms became more severe. This finding underscores the difficulties of using clinician report of patient symptoms.

Major advances in instrument development related to symptoms and health-related quality of life (HR-QOL) have been made over the past decade.<sup>49,50</sup> A variety of reliable and valid instruments are now available. Selection of the most appropriate instrument depends on the research question and characteristics of the patient population. Symptom assessment instruments such as the SDS, Symptom Experience Scale, or the Memorial Symptom Assessment Scale are available if the researcher is interested in measuring aspects of the symptom experience.<sup>28,45,46</sup> In some cases, however, the re-

searcher may be interested in measuring concepts related to HR-QOL. Emotional function, social function, functional status, and spiritual well-being, in addition to physical symptoms, are considered other dimensions of HR-QOL.<sup>51,52</sup>

A single instrument or a battery of instruments may be used to measure the HR-QOL construct of interest. Single instruments can be multidimensional and may either be generic or disease-specific. Generic instruments are developed for use in the general population and are useful for comparisons across groups, whereas disease-specific instruments are developed for use in a particular group of patients and are best for capturing changes unique to the group being studied.<sup>49</sup> The Medical Outcomes Study Short Form 36 is an example of a generic instrument, whereas the European Organization for Research and Treatment of Cancer Quality of Life–LC13 (lung cancer module), Functional Assessment of Cancer Therapy–Lung, and LCSS are disease-specific instruments that may be used for measuring HR-QOL in adults with lung cancer.<sup>24,53–55</sup> For a more comprehensive discussion of the instruments used to measure HR-QOL in adults with lung cancer, the reader is referred to another source.<sup>30</sup>

A battery of instruments may also be used to target the specific dimensions that the researcher wishes to measure. For example, if the researcher wishes to measure symptom distress, depression, and functional status, the SDS may be used to measure symptom distress, the Center for Epidemiological Studies–Depression Scale may be used to measure depression, and the Karnofsky Performance Status may be used to measure functional status.<sup>28,56,57</sup> In general, HR-QOL instruments should be patient self-report, measure at least three dimensions, be easy to use, minimize respondent burden, and include both a generic and cancer-specific instrument.<sup>49,58,59</sup> Moreover, measurement of HR-QOL should occur more than once; before, during, and after treatment is recommended.<sup>59,60</sup>

A major strength of the studies examined was the use of longitudinal study designs. Fifty percent of the studies used a longitudinal, panel design. Longitudinal panel designs are an ideal method to assess changes over time.<sup>61,62</sup> Unfortunately, attrition is a frequent

problem associated with this type of design. In fact, most of the studies reported loss of subjects. Several of the researchers did not provide information about reasons for loss of subjects. It is important to recognize that attrition can jeopardize the internal validity of a study,<sup>63</sup> address the problem if possible, and provide data on the reasons that subjects may have left. For example, the Consolidated Standards of Reporting Clinical Trials issued a statement recommending that published reports contain information about the number of subjects who died, withdrew, were lost to follow-up, or left the study for other reasons.<sup>64</sup> In addition, analyses can be done to assess whether the subjects who left the study differ on major characteristics from the subjects who remained in the study.<sup>63</sup> This type of analysis would be important to check for sample bias and also to ascertain the best method for handling missing data.<sup>63,65–67</sup>

Strategies for minimizing attrition in longitudinal studies have been identified by several researchers.<sup>68,69</sup> Clinical deterioration, however, may not be amenable to intervention. In this situation, several authors have recommended the use of proxy measures, asserting that some data is better than no data.<sup>49,70,71</sup> Given the poor correlation between proxy respondents and patients, however, it is important to exercise caution when using this approach. Gathering data from both the patient and proxy respondent, at several points in time, should be done if the researcher can anticipate the use of proxy measures. The proxy response can then be used, when the patient is no longer able to respond, if the responses are well correlated.<sup>49</sup>

All of the studies used a convenience sample. Although convenience samples are the most common method of obtaining subjects, problems may occur with obtaining a representative sample.<sup>61,72</sup> Most of the studies tried to minimize selection bias by using large samples from multiple sites, randomizing patients to a treatment group, or selecting sequential patients. One major limitation of the studies in this review, however, is the lack of information on the number of subjects who agreed to participate in the study. McCorkle and colleagues<sup>69</sup> pointed out that subject accrual can be difficult in a vulnerable population such as lung cancer. This issue was underscored by the

fact that only 32% of eligible subjects agreed to participate in a longitudinal, randomized clinical trial. Thus, future studies should include information about response rate and refusal rate so that the external validity of the study and possible systematic bias in sampling can be evaluated.<sup>73</sup>

### *Suggestions for Future Research*

Areas needing further study were identified through this review. Because symptoms are influenced by biological, psychological, social, and cultural factors, new models for research are needed to gain a better understanding of this phenomenon.<sup>74-76</sup> The use of conceptual models and/or theoretical frameworks to guide research will help identify variables that explain or predict the relationship among symptoms, clinical and patient characteristics, and outcome measures.<sup>77,78</sup> The addition of qualitative research methodologies will be useful to enhance our understanding of the complexity of the symptom experience and to further theory development.<sup>79</sup>

Future studies must incorporate reliable and valid measures of symptoms. Selection of the most appropriate research instrument will vary depending on the research question. A multi-dimensional instrument may be useful for understanding the complexity of the symptom experience. Given the conflicting results about the importance of the various dimensions of the symptom experience, further research is warranted.<sup>45,46</sup> In the meantime, for researchers who are concerned with instrument burden in patients with lung cancer, the single measurement of symptom distress is recommended.

The disparity between clinician report and patient self-report underscores the importance of using patients as the primary source for gathering data whenever possible. Instruments assessing symptoms have been used more often in research settings. Because health care providers consistently underestimate the severity of patient symptoms, modification and refinement of these instruments for use in the clinical practice setting is the next step toward improving patient outcomes.<sup>80,81</sup> Potential benefits of using these instruments in clinical practice may include identification of patients at risk for high symptom distress, im-

proved communication between health care providers and patients, and monitoring patient responses to treatment. Although early studies have suggested a role for the use of health status assessment in geriatrics, widespread use has not occurred.<sup>82,83</sup> To date, no studies have compared the use of various symptom assessment measures in the oncology clinical setting. Comparison of various instruments is needed to identify which measures work best in various samples of patients and to determine clinically significant changes in scores.<sup>84,85</sup> Subsequently, the effectiveness of using these instruments to improve patient outcomes in the clinical setting can then be ascertained.

Unfortunately, adults with lung cancer often have progressive disease and may not be able to report their symptoms in the latter part of their illness. Therefore, additional research directed toward the potential role of proxies in rating symptoms is needed. Expanding the scope of inquiry to include behavioral assessment may offer new perspectives on adequately assessing symptoms when patients are no longer able to communicate.<sup>86-88</sup>

It is important to note that the majority of studies in this review were conducted with white, middle-income males with advanced lung cancer. A small number of studies were conducted with white, middle-income females with advanced lung cancer. Research with other racial and ethnic groups is necessary to reflect the diversity among patients with lung cancer. In particular, research in black Americans is important because lung cancer rates are increasing at a significant rate in this population.<sup>89,90</sup> Recruitment of various racial and ethnic groups into research studies may be difficult.<sup>91</sup> Special recruitment strategies designed to increase the likelihood of minority participation must be considered in future research.<sup>92</sup>

It is evident from this review that strategies for improved symptom management are needed. The majority of studies conducted so far have been descriptive and/or correlational studies. These studies provide a rich data base upon which intervention studies can be developed and tested. Because adults with lung cancer often experience multiple symptoms that cluster and change throughout the illness trajectory, symptom management services need to be integrated across the illness trajectory.<sup>90,93,94</sup>

New models of care have been suggested to address this issue.<sup>94,95</sup> For example, the World Health Organization has proposed that pain and symptom management be included as part of total care at the time of diagnosis rather than used as a last resort.<sup>95</sup>

## Conclusion

It is apparent from the results of this review that although major strides have been made in understanding the symptoms associated with lung cancer, further progress is needed to decrease the morbidity associated with uncontrolled symptoms. In particular, intervention studies that seek to improve symptom management are needed. In order for future studies to be useful, however, the theoretical, conceptual, and/or methodological problems identified through this review must be addressed.

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