

# A Symptom Cluster and Sentinel Symptom Experienced by Women With Lung Cancer

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**A**lthough numerous researchers have reported the symptoms and severity of symptoms experienced by individuals with lung cancer (Cooley, 2000; Hollen, Gralla, Kris, Eberly, & Cox, 1999; Hollen, Gralla, Kris, & Potanovich, 1993; Kuo, Chen, Chao, Tsai, & Perng, 2000; Lutz et al., 1997, 2001; Tishelman, Degner, & Mueller, 2000), few studies have examined the symptom experience of women with lung cancer. Meanwhile, lung cancer continues to be the leading cause of cancer death in women, and its incidence in women has increased in the United States since the mid-1960s (American Cancer Society, 2011). Symptom clusters associated with lung cancer have been studied minimally as well, although such clusters may increase distress and complicate interventions for relief. In addition, unrelieved symptoms are related to poorer patient outcomes (Miaskowski, Aouizerat, Dodd, & Cooper, 2007; Miaskowski, Dodd, & Lee, 2004). To provide optimal symptom management for women with lung cancer, their symptom experience, patterns, and associated factors must be studied to develop targeted symptom assessment and management strategies.

## Background

### Symptom Prevalence

Fatigue, cough, dyspnea, anorexia, pain, and insomnia were reported by patients with lung cancer as their most common symptoms, with remarkable consistency across studies (Cooley, 2000; Fox & Lyon, 2006; Hollen et al., 1993, 1999; Kuo et al., 2000; Lutz et al., 1997, 2001; Tishelman et al., 2000). In addition, emotional distress (Lobchuk & Kristjanson, 1997; Lobchuk, Kristjanson, Degner, Blood, & Sloan, 1997; Sarna, 1993; Sarna & Brecht, 1997; Tishelman et al., 2000) as well as nausea, vomiting, hair loss, dysphagia, and sore throat relative to chemotherapy and radiotherapy were reported in several studies cited in a review by Cooley (2000). Only

**Purpose/Objectives:** To determine the symptom experience and a sentinel symptom and to describe the relationship of participant characteristics with symptom clusters.

**Design:** Prospective, correlational study.

**Setting:** Clinical sites in five U.S. states.

**Sample:** 196 women six months to five years after non-small cell lung cancer diagnosis.

**Methods:** Symptoms were measured during the past day and past four weeks. Symptom clusters were described using a novel dummy coding approach.

**Main Research Variables:** Symptom occurrence and severity, demographic and clinical characteristics, health status factors, and meaning of illness.

**Findings:** About 98% of women experienced three or more symptoms in the past day. The most common symptoms reported by more than 80% of the women were fatigue, shortness of breath, anorexia, cough, and pain, with fatigue and shortness of breath rated as most severe. Sleep problems, concentration problems, and weight loss also were reported during the past four weeks. A five-symptom cluster including fatigue, shortness of breath, cough, pain, and anorexia was reported by 64% of women. Pain was identified as a sentinel symptom for that cluster.

**Conclusions:** Most women experienced at least three symptoms in the past day, and a five-symptom cluster occurred frequently and continued post-treatment.

**Implications for Nursing:** Women who participated in the study were, on average, two years postdiagnosis, but most experienced three or more symptoms well past treatment; therefore, vigilant ongoing clinical assessment of these women is essential. A co-occurring sentinel symptom used as a clinical indicator for the presence of a symptom cluster may be useful for clinical assessment.

two of the studies (Sarna, 1993; Sarna & Brecht, 1997) described the symptom experience of women with lung cancer. Most studies of lung cancer symptoms have focused on individuals with advanced disease who were receiving treatment or palliative care.

## Symptom Distress

Individuals with lung cancer have been reported to have higher symptom distress than other individuals with cancer, and higher symptom distress scores were associated with shorter survival (Degner & Sloan, 1995; McCorkle & Quint-Benoliel, 1983). Fatigue, dyspnea, insomnia, and cough were reported as the most distressing symptoms for patients with advanced disease (Cooley, 2000; Gift, Jablonski, Stommel, & Given, 2004; Hollen et al., 1993, 1999; Lutz et al., 1997, 2001; Tishelman et al., 2000). In addition, pain, anorexia, and poor outlook were reported to be very distressing in several of those studies. Women with lung cancer reported that fatigue, frequent pain, insomnia, and poor outlook were the most prevalent and distressing symptoms in early and advanced disease (Sarna, 1993; Sarna & Brecht, 1997).

## Symptom Clusters

A symptom cluster has been defined as three or more co-occurring symptoms (Dodd, Miaskowski, & Paul, 2001). Few researchers have studied symptom clusters experienced by individuals with lung cancer. Krech, Davis, Walsh, and Curtis (1992) reported a median of nine symptoms experienced by patients with advanced lung cancer entering palliative care with pain, dyspnea, and anorexia—the most frequent and severe symptoms experienced. In samples of patients with advanced non-small cell lung cancer (NSCLC) receiving chemotherapy, Hollen et al. (1999) and Lutz et al. (2001) found that about 80% of patients experienced three or more symptoms, and Hollen et al. (1999) reported that 36% had five or more symptoms. The most common symptoms were fatigue, dyspnea, cough, pain, and anorexia. In one of the earliest reports of women with lung cancer, Sarna (1993) reported that 61% experienced more than one symptom, and 41% had fatigue, pain, and insomnia. Seventy-five percent of the women in that sample had NSCLC, and 43% were receiving treatment for a primary or recurrent diagnosis.

In a large family homecare study of older adult (i.e., older than 65 years) patients with cancer (Gift, Stommel, Jablonski, & Given, 2003; Given, Given, Azzouz, & Stommel, 2001; Given, Given, Azzouz, Kozachik, & Stommel, 2001; Given et al., 2002), 89% of participants with newly diagnosed lung cancer experienced two or more symptoms (Gift et al., 2004). Participants with early-stage lung cancer had an average of 4.9 symptoms during the first year after diagnosis, and late-stage patients had an average of 5.7 symptoms during this time period (Given, Given, Azzouz, Kozachik, et al., 2001). Using factor analysis and the Cronbach alpha, Gift et al. (2004) described a seven-symptom cluster of fatigue, nausea, weakness, appetite loss, weight loss, altered taste, and vomiting, but this cluster was experienced by only 5% of the participants at baseline measurement.

The most common symptom clusters consisted of two (19%) and three (19%) symptoms, but the symptoms contributing to these clusters were not reported. Over time, fatigue, weakness, poor appetite, altered taste, and nausea were reported more consistently than weight loss and vomiting (Gift et al., 2003). Fox and Lyon (2006) also reported a two-symptom cluster of fatigue and depression in a secondary analysis of 51 patients with early- and advanced-stage lung cancer in which only fatigue, depression, and pain were studied.

Although some overlap exists in the symptom clusters described in these studies, no consistent symptom cluster has emerged, most likely because of differences in sample characteristics, symptoms studied, measurement, and analytic techniques. Considerable agreement exists, however, that a large number (41%–89%) of study participants experienced at least two or three co-occurring symptoms, suggesting the presence of symptom clusters.

## Factors Related to the Occurrence of Symptom Clusters

Factors associated with the lung cancer symptom experience also have received limited study. Sarna (1993) reported several factors that were positively associated with greater symptom distress in women with NSCLC, including number of symptoms, recurrent disease, severity of respiratory symptoms, previous chemotherapy, and poverty. Poverty and recurrent disease explained 26% of the symptom distress in those women. In addition, Herndon et al. (1999) found that symptoms of dyspnea and weight loss in the last three months of life were among clinical predictors of survival in a large sample of mostly male patients with advanced NSCLC who were participating in a Cancer and Leukemia Group B clinical trial of hydrazine sulfate. Factors associated with differences in symptoms by gender have not been elucidated; nor have co-occurring sentinel symptoms, which are indicators or markers of the presence of symptom clusters, been described.

## Analysis of Symptom Clusters

To date, most symptom cluster research has been conducted with existing data sets using symptoms determined a priori. Symptoms available for analysis were based on primary study aims and/or theoretical frameworks (Barsevick, 2007). Several correlational approaches to symptom cluster analysis, such as factor analysis, cluster analysis, and canonical correlation, have been used and proposed (Barsevick, Whitmer, Nail, Beck, & Dudley, 2006; Miaskowski et al., 2007). Although valid, those approaches do not fully describe the clinical patterns of symptoms or symptom severity within a cluster or identify co-occurring sentinel symptoms that could serve as indicators or markers for the presence of a symptom cluster that would be useful to clinicians.

## Conclusions of Previous Literature

Fatigue, cough, dyspnea, anorexia, pain, insomnia, and emotional distress consistently have been reported as the most common symptoms experienced by patients with advanced lung cancer in samples with a high percentage of males. Of those symptoms, fatigue, dyspnea, insomnia, and cough were reported as the most distressing. In the two studies of women with local and advanced disease, fatigue, pain, insomnia, and emotional distress were the most prevalent and distressing symptoms (Sarna, 1993; Sarna & Brecht, 1997). Reports of symptom clusters were inconsistent, with no clear symptom cluster emerging for men or women. However, consistency exists in findings that a large number of patients with lung cancer experienced two to three co-occurring symptoms. The only common symptom across the five studies describing symptom clusters in NSCLC was fatigue. Thus, little research describes the symptom experience of women with lung cancer, conflicting evidence exists regarding symptom clusters experienced by individuals with lung cancer, and no evidence exists describing the pattern of symptoms or symptom severity within clusters or a co-occurring sentinel symptom. In addition, most studies of symptoms of the NSCLC population predate current treatment regimens.

## Conceptual Framework

The University of California, San Francisco, Symptom Management Model developed by Dodd, Janson, et al. (2001), which describes three inter-related concepts (symptom experience, symptom management strategies, and patient outcomes), was used as the conceptual framework. The current study focused on the symptom experience portion of the model by describing the symptom occurrence, severity, clusters, and a sentinel symptom of women with NSCLC. Personal and health and illness factors within which the symptom experience occur, as posited by the model, were conceptualized as demographic and clinical characteristics, health status factors, and the personal meaning of illness in the current study.

## Purpose

The purposes of the study were to (a) describe the occurrence, severity, and clusters of symptoms experienced by women with NSCLC, (b) describe the relationships of demographic and clinical characteristics, health status factors, and meaning of illness with symptom experience and symptom clusters, and (c) determine if a co-occurring sentinel symptom was associated with the presence of symptom clusters. A symptom cluster was defined as three or more co-occurring symptoms (Dodd, Janson, et al., 2001). A sentinel symptom was defined as a co-occurring indicator or marker of the presence of a

symptom cluster. Baseline data from a prospective, six-month, multisite study of women with lung cancer were used for analysis. Other findings from this project related to quality of life in women with lung cancer and their families, tobacco use, and complementary and alternative therapy use have been reported elsewhere (Cooley et al., 2007; Sarna et al., 2005, 2006, 2010; Wells et al., 2007).

## Methods

### Design, Settings, and Sample

In this prospective, correlational study, data were collected from multiple clinical sites in Alabama, California, Georgia, Massachusetts, and New York. Three hundred thirteen women with NSCLC who were six months to five years from diagnosis were screened and eligible to participate. Women were eligible if a physician, tumor registry, or medical record verified their diagnosis of NSCLC, including a recurrence or second primary lung cancer diagnosis. Women were ineligible if they had small cell lung cancer or other types of cancer of the lung. Of the 231 women with NSCLC who agreed to participate, 196 (85%) met the inclusion criteria of complete symptom data and were included in the analysis. Thirty-five (15%) women with incomplete symptom data were excluded.

### Measurement

The following variables were measured: symptom occurrence and severity during the past day, symptom occurrence during the past four weeks, demographic and clinical characteristics, health status factors, and meaning of illness.

Symptom occurrence and severity during the past day were measured using the patient version of the **Lung Cancer Symptom Scale (LCSS)**, which was designed to measure current symptoms. The instrument has well-established psychometric properties (Hollen et al., 1993; Hollen, Gralla, Kris, & Cox, 1994; Hollen, Gralla, Kris, Cox, Belani, et al., 1994; Hollen et al., 1999). Presence and severity of six symptoms (fatigue, shortness of breath, poor appetite, cough, pain, and blood in sputum) were rated on visual analog scales from 0–100 mm, as well as overall symptom severity and ability to carry out normal activities. Higher ratings indicated more severe symptoms. The occurrence of a symptom was indicated by ratings greater than zero.

Symptoms experienced during the past four weeks were measured using the **Symptom Query Questionnaire (SQQ)**, a semistructured interview developed by Van Servellen, Sarna, and Jablonski (1998). Women were asked to report whether or not they experienced fatigue, difficulty breathing, pain, loss of appetite, or weight loss, in addition to listing any other symptoms related to their lung cancer that they experienced in the past four weeks. Content validity was established with a panel of experts.

**Table 1. Demographic Characteristics**

Characteristic	n	%
<b>Race</b>		
Caucasian	165	84
Black	21	11
Asian or Pacific Islander	3	2
Other	7	4
<b>Marital status</b>		
Married	95	49
Widowed	54	28
Divorced or separated	37	19
Never married	10	5
<b>Employment (N = 191)</b>		
Retired	136	71
Employed	50	26
Unemployed	5	3
<b>Geographic region</b>		
Northeast (New York and Connecticut)	81	41
West Coast (California)	70	36
South (Alabama and Georgia)	45	23

N = 196, unless otherwise noted.

Note. Because of rounding, not all percentages total 100.

Health status factors for the current study included depressed mood, presence of comorbidities, tobacco history, and current smoking status. The **Center for Epidemiologic Studies–Depression scale (CES-D)** (Lewinsohn, Seeley, Roberts, & Allen, 1997; Radloff, 1977; Radloff & Teri, 1986) was used to measure depressed mood. The CES-D has been used extensively in cancer research and has established reliability and validity. Possible scores range from 0–60, and scores of 16 or greater are categorized as depressed mood. The **Charlson Comorbidity Index** (Charlson, Pompei, Ales, & MacKenzie, 1987; Elixhauser, Steiner, Harris, & Coffey, 1998; Katz, Chang, Sangha, Fossel, & Bates, 1996), a well-established tool, was used to measure the presence of other comorbidities. History of tobacco use and current smoking status were measured using self-report. Current smoking status also was verified biochemically at the time of interview using urine cotinine (NicoMeter™) (Parker et al., 2002; SRNT Subcommittee on Biochemical Verification, 2002).

Meaning of illness (Degner, Hack, O’Neil, & Kristjanson, 2003) was measured to determine women’s views of their disease as positive, negative, or another meaning. The instrument was stable over six months with the women in the current sample, demonstrating test-retest reliability (Sarna et al., 2005).

Demographic characteristics included age, race, marital status, employment status, and geographic region; and clinical factors included histology, stage at diagnosis and interview, presence of recurrence, type of surgery, treatment status, smoking status, and comorbidities. These data were obtained from medical records and patient questionnaires.

## Data Collection Procedures

After approval from the institutional review boards at each of the participating sites, a variety of recruitment strategies were used, including flyers in oncology offices and clinics, advertisements, and letters sent to potential participants from physicians and tumor registries (Cooley et al., 2003). Interested women were screened for eligibility by telephone using the same script at each site to ensure a consistent approach. Informed consent was obtained, and a copy of the document was given to each woman. Data were collected by medical record review and interviews in women’s homes or in study offices. Women received \$25 per face-to-face interview for their participation.

## Data Analysis

Data entry was verified with a 20% random sample. No imputation of missing data was conducted because participants with missing symptom data were excluded. Occurrence of LCSS symptoms was dummy coded (0 = LCSS score of 0, 1 = LCSS score of greater than 0). Descriptive statistics appropriate to the level of measurement were computed for all variables. A novel strategy was used to identify symptom clusters. Symptoms were coded uniquely and analyzed to determine patterns of co-occurring symptoms (i.e., symptom clusters). Specifically, a new LCSS pattern variable was computed by summing each of the six LCSS symptoms that were uniquely coded as 000001, 000010, 000100, 001000, 010000, and 100000 if the symptom was reported with a LCSS score greater than zero. Frequency analysis then was used to determine co-occurring patterns. For example, a participant who reported all six LCSS symptoms would have a summed total of 111111. Presence or absence of a symptom cluster then was dummy coded (0 = not present, 1 = present) and used in descriptive analysis of symptom clusters and in Pearson correlation and logistic regression analysis to determine the relationship of demographic and clinical characteristics, health status factors, and meaning of illness with symptom clusters. Analysis of the co-occurring sentinel symptom was conducted with Pearson correlations. Each symptom was correlated with the presence or absence of the predominant, dummy-coded symptom cluster. SPSS®, version 18.0, was used for data analysis, and alpha was set at 0.05.

## Results

### Sample Characteristics

The average age of study participants was 65.4 years (range = 33–89, SD = 11.4). The mean years of education were 13.2 (range = 6–24, SD = 2.6). Average annual income (n = 163) was \$38,010 (range = \$1,206–\$300,000, SD = \$38,060). Eighty-four percent were Caucasian (see Table

1). As seen in Table 2, most women were diagnosed with adenocarcinoma, had local or regional disease, had surgical treatment, and were former smokers. The average time since initial diagnosis was 24 months (SD = 15.9), ranging from 5–60 months. Twenty-four (12%) had recurrent disease, and 25 (13%) were currently on treatment. Average body mass index was 27.6 kg/m<sup>2</sup> (SD = 6), ranging from 16.7–46.4 kg/m<sup>2</sup>.

## Symptom Occurrence and Severity

The women's symptom experience was examined for two time periods, the past day (LCSS) and the past four weeks (SQQ). The occurrence and severity of symptoms during the past day by stage of disease are shown in Figures 1 and 2, respectively. The five most common symptoms experienced during the past day by more than 80% of the women were fatigue, shortness of breath, anorexia, cough, and pain, with fatigue and shortness of breath rated on average as most severe. The LCSS item overall symptom severity was rated 17 on average (SD = 22.6) on the 0–100 LCSS scale.

During the past four weeks, fatigue (65%), difficulty breathing (53%), and pain (49%) were reported by at least half of the women, and several additional symptoms not included in the LCSS were identified, including sleep problems (25%), concentration problems (16%), and weight loss (13%). The mean total symptoms experienced in the past four weeks were 3 (SD = 1.8, range = 0–7).

## Symptom Clusters

Based on LCSS data, symptom clusters of three or more co-occurring symptoms were experienced in the past day by 98% of the participants. Ninety-eight percent of women with symptom clusters reported fatigue, and 88% reported shortness of breath. Women with three-symptom clusters (6%) did not report any predominant pattern of symptoms. Fourteen of the 32 women with a four-symptom cluster (16%) had fatigue, shortness of breath, cough, and anorexia. The predominant symptom pattern for five- and six-symptom clusters included fatigue, shortness of breath, cough, pain, and anorexia and was reported by 64% of the women. Those with six co-occurring symptoms (50%) also experienced hemoptysis of minimal severity ( $\bar{X}$  = 4 on a 100-point scale). Because of the minimal severity of hemoptysis, those with five- and six-symptom clusters were combined for the remaining analysis and are identified as the five-symptom cluster of fatigue, shortness of breath, cough, pain, and anorexia. Although no predominant symptom cluster was identified for the past four weeks, 50% of the women experienced three or more symptoms.

The severity of the five-symptom cluster during the past day for all symptomatic (i.e., LCSS score greater than 0) women (n = 126) is shown in Figure 3, along with the five-symptom cluster severity for women with

fatigue and shortness of breath symptom severity scores of 10 or greater on a 100-point scale (n = 91), an estimate of clinically significant severity (Hollen et al., 1999).

The five-symptom cluster was reported by 67% (n = 111) of the women with local or regional disease and 50% (n = 15) of those with metastases. It was the predominant symptom cluster for both groups. The severity of symptoms by stage of disease for women with the five-symptom cluster is shown in Figure 4.

## Factors Related to the Symptom Experience and Symptom Clusters

Significant Pearson correlations of demographic and clinical characteristics, health status factors, and meaning of illness are shown in Table 3. Depressed mood, time since diagnosis, number of comorbid diseases, and whether the patient was currently on treatment were variables significantly related to overall symptom severity during the past day. Somewhat similarly, depressed mood, time

**Table 2. Clinical Characteristics**

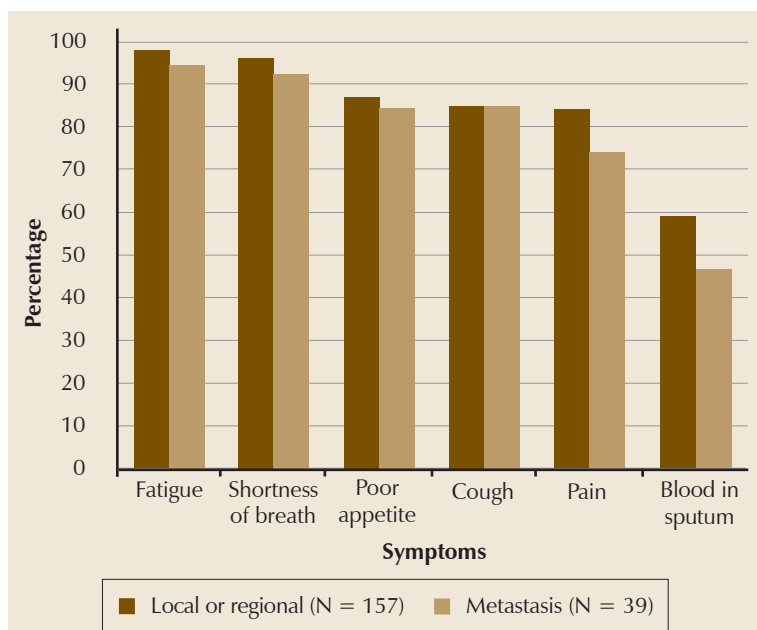
Characteristic	n	%
<b>Histology</b>		
Adenocarcinoma	150	77
Squamous	31	16
Other	15	8
<b>Stage at diagnosis</b>		
Local or regional	166	85
Metastasis	30	15
<b>Stage at interview</b>		
Local or regional	157	80
Metastasis	39	20
<b>Type of surgery</b>		
Lobectomy and resection	147	75
Pneumonectomy	9	5
Other	2	1
None	35	18
Missing	3	2
<b>Other treatment</b>		
Chemotherapy	21	11
Radiotherapy	2	1
Combined	2	1
<b>Smoking status</b>		
Former	150	77
Never	28	14
Current	18	9
<b>Comorbid diseases<sup>a</sup></b>		
Depressed mood (CES-D score of 16 or greater)	69	35
Chronic obstructive pulmonary disease	60	31
Other cancers	43	22
Rheumatoid arthritis	31	16
Heart disease	30	15
Stomach or peptic ulcers	23	12
Other	58	30

N = 196

<sup>a</sup>Some participants reported multiple comorbid diseases.

CES-D—Center for Epidemiologic Studies–Depression scale

Note. Because of rounding, not all percentages total 100.



**Figure 1. Percent of Lung Cancer Symptom Scale Symptoms Reported During Past Day by Stage of Disease**

since diagnosis, number of comorbid diseases, age, and meaning of illness were variables significantly related to the number of symptoms experienced in the past four weeks and effect of symptoms on normal activities.

Occurrence of the five-symptom cluster of fatigue, shortness of breath, cough, pain, and anorexia during the past day was regressed on variables significantly correlated to number of symptoms in the past day and past four weeks, overall symptom severity, and effect of symptoms on normal activities, using logistic regression. Independent variables included age, number of comorbid diseases, depressed mood, time since diagnosis, whether the patient was on treatment currently, and meaning of illness. The model was not statistically significant ( $\chi^2 = 7.788$ , degrees of freedom [df] = 6,  $p = 0.25$ ). Only current treatment had a significant regression coefficient ( $B = -478$ ,  $df = 1$ ,  $p < 0.05$ ), with an odds ratio of 0.98.

### Sentinel Symptom for Five-Symptom Cluster

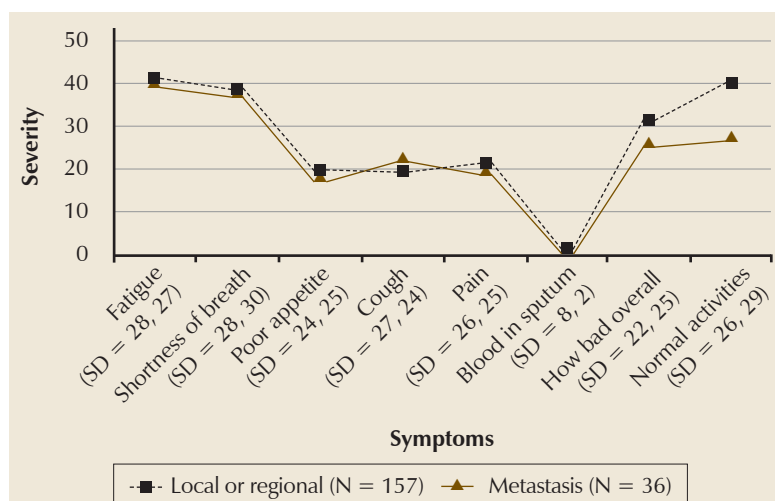
The presence or absence of the five-symptom cluster was correlated with the occurrence of pain ( $r = 0.63$ ,  $p < 0.05$ ), cough ( $r = 0.56$ ,  $p < 0.05$ ), loss of appetite ( $r = 0.54$ ,  $p < 0.05$ ), shortness of breath ( $r = 0.29$ ,  $p < 0.05$ ), and fatigue ( $r = 0.24$ ,  $p < 0.05$ ) using Pearson correlations to determine if a co-occurring sentinel symptom was evident. The occurrence of pain was most highly correlated with the presence of the five-symptom cluster.

## Discussion

The current study is the first to describe the symptom experience of women with mostly local and regional NSCLC (85%) who have had surgical treatment (81%). The diverse geographic sample was made up of women who were, on average, two years from diagnosis (range = 0.5–5 years). Only 13% were receiving cancer treatment currently and about one-third had comorbid conditions, with depressed mood and chronic obstructive pulmonary disease being most common. Most (69%) were retired, and about 50% were married. Previous studies consisted mostly of men with advanced disease, so the findings of the study describe the symptom experience of women with NSCLC, about whom little research evidence exists.

### Symptom Occurrence

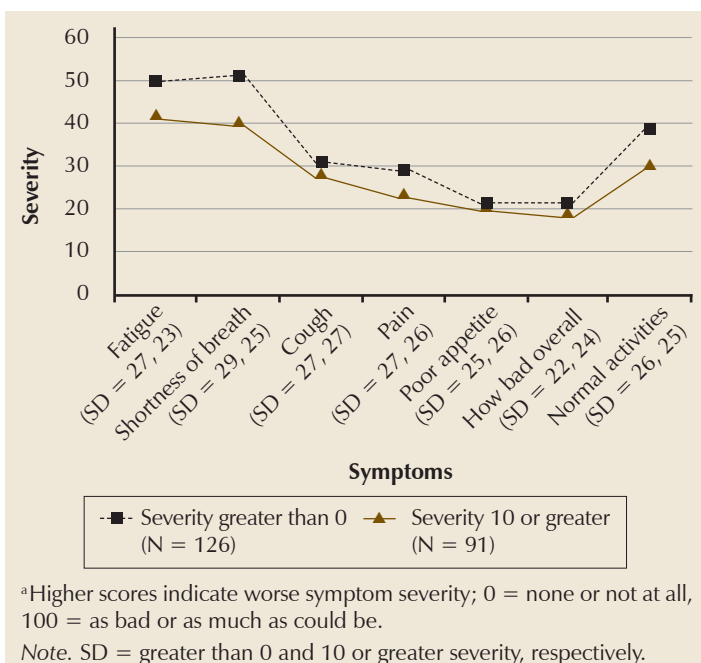
The most frequently occurring symptoms experienced by women with all stages of disease during the past day were fatigue, shortness of breath, anorexia, cough, and pain, which is consistent with previous studies that included women and men; however, those studies focused primarily on individuals with advanced disease who were in treatment or palliative care (Cooley, 2000; Hollen et al., 1993, 1999; Kuo et al., 2000; Lutz et al., 1997, 2001; Tishelman et al., 2000, 2005). During the past four weeks, more than half the women in the current sample reported fatigue, difficulty breathing, and pain; and women with advanced disease reported more symptoms than women with local or regional disease. Other symptoms not included on the LCSS were



<sup>a</sup>Lung Cancer Symptom Scale 0–100 mm, where 0 = none or not at all and 100 = as bad or much as could be

Note. SD = local or regional and metastasis, respectively.

**Figure 2. Mean Severity<sup>a</sup> Scores of the Lung Cancer Symptom Scale During the Past Day by Stage of Disease**



<sup>a</sup>Higher scores indicate worse symptom severity; 0 = none or not at all, 100 = as bad or as much as could be.  
 Note. SD = greater than 0 and 10 or greater severity, respectively.

**Figure 3. Mean Severity<sup>a</sup> of Symptoms in the Five-Symptom Cluster**

reported, including sleep problems, concentration problems, and weight loss. Insomnia and weight loss have been reported in the literature, but problems with concentration in this population were only reported previously by Sarna (1993). Thus, these women, who had for the most part received curative surgical treatment, were experiencing the same symptoms as individuals with advanced disease receiving treatment or palliative care.

Symptom occurrence reported on the LCSS for the past day was substantially greater than reported on the SQQ for the past four weeks. That is probably a recall issue, reflecting the poorer measurement reliability of instruments using participant memory for self-report. The greatest accuracy of symptom measurement may be for the current time frame, rather than a four-week recall, but that needs to be addressed in future research.

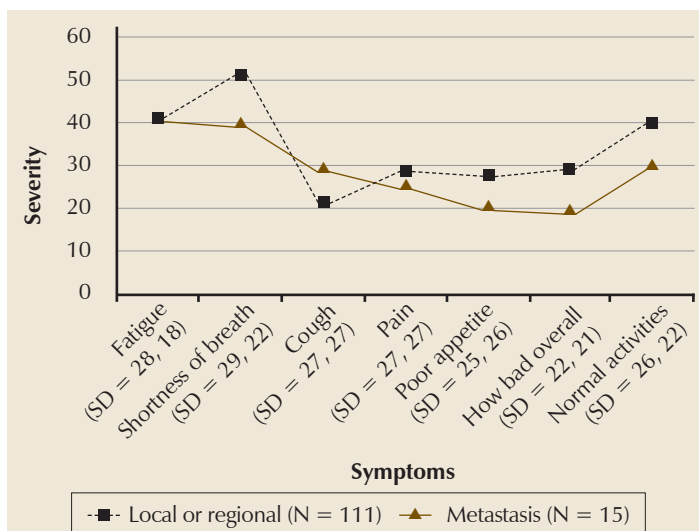
### Symptom Severity

Fatigue and shortness of breath were rated as most severe during the past 24 hours and past four weeks by women with all stages of disease, consistent with the symptoms rated most distressing in previous studies (Cooley, 2000; Gift et al., 2004; Hollen et al., 1993, 1999; Lutz et al., 1997, 2001; Tishelman et al., 2000); however, symptom severity cannot necessarily be equated with symptom distress, as noted by Hollen, Gralla, Kris, and Cox (1994) and Tishelman et al. (2005). Women with local and regional disease rated their symptoms during the past day as less severe than women with advanced disease, but the

mean difference for each symptom between these two groups was, on average, 3 mm (range = 1–6 mm) on the 100 mm LCSS item scale. According to Hollen et al. (1999), a meaningful clinical change has been demonstrated for 10 mm and 25 mm changes on the LCSS, so the differences in symptom severity by stage of disease do not appear to be clinically significant in these women. However, a 10 mm difference in ability to carry out normal activities was observed, which would be clinically significant. Women with advanced disease reported their illness as having a greater effect on their ability to carry out normal activities. When compared with hospitalized patients with advanced NSCLC (Hollen et al., 1999), women in the current sample reported much less symptom severity (mean difference = 15–25 mm) on all symptoms except shortness of breath (mean difference = 6 mm) and blood in sputum (mean difference = 4). Thus, the severity of symptoms these women experienced was consequential in their lives, and severity of shortness of breath was comparable for women with local or regional as well as advanced disease.

### Symptom Clusters

Almost all women in the sample experienced three or more symptoms in the past day, most of which included fatigue. A five-symptom cluster of fatigue, shortness of breath, cough, pain, and anorexia was experienced by 64% of the women, and about 75% of those women also experienced blood in the sputum of minimal severity ( $\bar{X}$  = 2, SD = 7.09, median = 0.5). The five-symptom cluster



<sup>a</sup>Higher scores indicate worse symptom severity; 0 = none or not at all, 100 = as bad or as much as could be.  
 Note. SD = local or regional and metastasis, respectively.

**Figure 4. Mean Severity<sup>a</sup> of Symptoms in the Five-Symptom Cluster by Stage of Disease**

**Table 3. Significant Correlations of Studied Factors With Symptom Experience and Symptom Cluster Variables**

Factor	Number of Symptoms: Past Day	Number of Symptoms: Past Four Weeks	Presence of Five-Symptom Cluster	Overall Symptom Severity: Past Day <sup>a</sup>	Effect of Symptoms on Normal Activities <sup>a</sup>
Age	-0.02	-0.27*	0.03	-0.12	-0.14*
Time since diagnosis	-0.18*	-0.2*	-0.14	-0.19*	-0.17*
Metastatic disease <sup>b</sup>	-0.13	0.07	-0.13	0.12	0.14
Currently on treatment <sup>b</sup>	-0.07	0.12	-0.07	0.15*	0.11
Number of comorbid diseases	0.07	0.2*	0.07	0.19*	0.22*
Currently smoking <sup>b</sup>	0.04	0.09	0.05	0.002	0.03
Depressed mood	0.11	0.44*	0.04	0.41*	0.49*
Meaning of illness <sup>b</sup>	-0.07	-0.17*	-0.1	-0.14	-0.24*

N = 196  
\* p < 0.05  
<sup>a</sup>Lung Cancer Symptom Scale 0–100 mm, where 0 = none or not at all and 100 = as bad or much as could be  
<sup>b</sup>Coded 0 = no, 1 = yes

persisted for women whose fatigue and shortness of breath were 10 mm or greater (an estimate of clinically significant severity, based on Hollen et al. [1999]). For those women, shortness of breath and fatigue increased sharply in severity, with mean LCSS scores greater than 50; however, anorexia, cough, and pain increased only slightly (3–4 mm, on average) in severity. The five-symptom cluster also persisted when examined by stage of disease with women with advanced disease having substantially greater severity of shortness of breath. No predominant symptom cluster was identified for the past four weeks, but 50% of the women experienced three or more symptoms.

Ninety-eight percent of women in the current study experienced three or more symptoms during the past day, which is substantially greater than the 41%–89% with two or three co-occurring symptoms reported for previous samples of individuals with NSCLC (Gift et al., 2004; Hollen et al., 1999; Lutz et al., 2001; Sarna, 1993). The five-symptom cluster of fatigue, shortness of breath, cough, pain, and anorexia reported by participants in the current study was consistent with the findings of Hollen et al. (1999) and Lutz et al. (2001) for patients with advanced NSCLC who were hospitalized or receiving chemotherapy.

Notably, the LCSS inherently captured the five-symptom cluster described in the current study. The development of the LCSS was based on major symptoms identified by an expert panel of oncology nurses, oncology physicians, and patients with NSCLC (Hollen et al., 1993). Thus, the LCSS appears to have been created to measure a symptom cluster at the time of its development long before the idea of symptom clusters was posited.

### Factors Related to the Symptom Experience and Symptom Clusters

The symptom experience was examined relative to demographic and clinical characteristics, health status factors, and meaning of illness. Depressed mood and less time since diagnosis were related to a more severe symptom experience during the past day, more symptoms during the past four weeks, and greater effect of symptoms on normal activities during the past day. Less time since diagnosis also was related to more symptoms during the past day. Those findings provide new insights into personal and health and illness factors associated with the symptom experience of women with NSCLC and are consistent with previous findings that the greater number of co-occurring symptoms experienced, the greater the symptom distress (Sarna, 1993).

Demographic, clinical, and health status variables were not associated with occurrence of the five-symptom cluster. Only one variable, time since diagnosis, was significantly related to the occurrence of the five-symptom cluster when the other variables were controlled. As time since diagnosis decreased, the occurrence of the five-symptom cluster increased. Personal and health and illness factors related to the symptom experience of women with NSCLC have not been reported in previous studies.

### Sentinel Symptom

The idea of a co-occurring sentinel symptom that is associated with the presence of a symptom cluster is new to symptom cluster research. The idea was conceived from the perspective of improving clinical symptom assessment and management. In the current sample, women



who had pain were more likely to have the five-symptom cluster. The authors believe that could be a useful assessment indicator in clinical practice. Clinicians who assess patients with pain could use the symptom as a cue to assess further for other symptoms in the cluster (fatigue, shortness of breath, cough, and anorexia).

## Limitations

The current study provides a snapshot at one point in time of a convenience sample of women who were six months to five years from NSCLC diagnosis. Thus, generalizability is limited. Although the LCSS is a very well-established instrument measuring symptoms of NSCLC, it does not include symptoms related to sleeping problems, loss of weight, and loss of concentration reported by 10%–23% of this sample. The SQQ has received less psychometric validation and depends on participants' recall of symptoms experienced during the past four weeks, which probably led to underreporting of symptoms for the past four weeks.

## Future Directions

This is the first study of symptoms experienced by women with primarily early-stage NSCLC treated surgically. More studies are needed to better understand their symptom experience, particularly predictors of symptom severity and distress. Little is known about the post-thoracotomy symptom trajectory or the best interventions to manage these symptoms. Interventions need to be developed and tested to help patients effectively manage their multiple symptoms, which is their predominant symptom experience.

This study introduced two new approaches to symptom cluster research. First, a novel approach using dummy coding for the presence or absence of each symptom was used to fully describe the pattern of symptoms within a cluster based on prospective, empirical data. That strategy can be useful to researchers and clinicians in the development of interventions and measurement of relevant outcomes because it describes patterns of symptoms within a cluster. Longitudinal studies using that approach could answer questions related to changes in patterns of symptoms and related symptom severity within the symptom cluster over time. For example, does a rise or fall in the severity of one symptom

affect the pattern of occurrence and severity of other symptoms in the cluster? Second, the idea of a co-occurring sentinel symptom as an indicator or marker for the presence of a symptom cluster was introduced as a clinical strategy that could improve symptom cluster assessment. Additional research is needed to determine if the identification of a sentinel symptom leads to better clinical assessment of the total symptom cluster and better overall symptom management.

## Implications for Nursing

These findings demonstrated that fatigue and shortness of breath continue over time for women with NSCLC and often were combined in a symptom cluster with cough, pain, and anorexia. Pain appeared to be a co-occurring sentinel symptom for this symptom cluster. Thus, it could be used as an indicator of the need for additional clinical assessment for the presence of the symptom cluster including fatigue, shortness of breath, cough, pain, and anorexia. Women survivors of NSCLC experience clinically significant symptoms long after completion of treatment that require vigilant assessment and ongoing follow-up by oncology healthcare providers. The symptoms those women experience have adverse effects on their ability to carry out normal activities and need to be managed with ongoing diligence if optimal quality of life is to be achieved.

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