

**Original Article**

# Stability of Symptom Clusters in Patients With Lung Cancer Receiving Chemotherapy



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**Abstract**

**Context.** Patients with lung cancer who undergo chemotherapy (CTX) experience multiple symptoms. Evaluation of how these symptoms cluster together and how these symptom clusters change over time are salient questions in symptom clusters research.

**Objectives.** The purposes of this analysis, in a sample of patients with lung cancer ( $n = 145$ ) who were receiving CTX, were to 1) evaluate for differences in the number and types of symptom clusters at three time points (i.e., before their next cycle of CTX, the week after CTX, and two weeks after CTX) using ratings of symptom occurrence and severity and 2) evaluate for changes in these symptom clusters over time.

**Methods.** At each assessment, a modified version of the Memorial Symptom Assessment Scale was used to assess the occurrence and severity of 38 symptoms. Exploratory factor analyses were used to extract the symptom clusters.

**Results.** Across the two symptom dimensions (i.e., occurrence and severity) and the three assessments, six distinct symptom clusters were identified; however, only three of these clusters (i.e., lung cancer specific, psychological, nutritional) were relatively stable across both dimensions and across time. Two additional clusters varied by time but not by symptom dimension (i.e., epithelial/gastrointestinal and epithelial). A sickness behavior cluster was identified at each assessment with the exception of the week before CTX using only the severity dimension.

**Conclusion.** Findings provide insights into the most common symptom clusters in patients with lung cancer undergoing CTX. Most common symptoms within each cluster appear to be relatively stable across the two dimensions, as well as across time. *J Pain Symptom Manage* 2019;57:909–922. © 2019 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

**Key Words**

*Symptoms, symptom clusters, lung cancer, chemotherapy, exploratory factor analysis, symptom occurrence, symptom severity*

**Introduction**

Patients with lung cancer have an extremely high symptom burden that negatively affects their physical and emotional well-being.<sup>1</sup> Given the high rates of multiple co-occurring symptoms, an evaluation of symptom clusters in these patients is highly relevant. As noted in a recent report from the National Institute

of Nursing Research,<sup>2</sup> two of the most salient questions in symptom clusters research are whether symptom clusters are stable across symptom dimensions (e.g., occurrence versus severity) and whether symptom clusters are stable over time. An increased understanding of the dynamic nature of symptom clusters will provide direction for the assessment and

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management of symptoms in this vulnerable group of patients.<sup>2</sup>

In the first study of symptom clusters in patients with lung cancer,<sup>3</sup> the authors hypothesized that the treatment of symptoms associated with chemotherapy (CTX) might improve if we understood the relationships among symptoms and symptom distress. In a sample of 60 women with advanced lung cancer, four groups of related symptoms were identified using factor analysis (i.e., emotional and physical suffering, gastrointestinal [GI] distress, respiratory distress, and malaise).

Since this publication in 1997, eight studies have evaluated for symptom clusters in patients with lung cancer. Four of these studies,<sup>4–7</sup> along with Sarna and Brecht's study,<sup>3</sup> were summarized in a systematic review by Chen et al.<sup>8</sup> Three additional studies,<sup>9</sup> including one from our research team,<sup>9</sup> were published following the systematic review. Although the number of symptom clusters across these eight studies ranged from two to five, no common symptom cluster was found; however, an emotional/psychological symptom cluster was identified in five studies,<sup>3,7,9–11</sup> with sad being the most common symptom. In addition, a lung cancer–specific symptom cluster was found in four studies,<sup>3,7,9,10</sup> with cough being the most common symptom. Finally, a GI symptom cluster was identified in four studies,<sup>3,5,6,11</sup> with nausea being the most common symptom. Comparisons of findings across these eight studies are difficult because different dimensions of the symptom experience were evaluated, different assessment tools were used, and different statistical procedures were used to identify the symptom clusters. Of note, except for our own study,<sup>9</sup> none of these studies evaluated for differences in symptom clusters using different dimensions of the symptom experience or evaluated for changes in symptom clusters over time.

In our previous analysis of 145 patients receiving CTX for lung cancer,<sup>9</sup> differences in the number and types of symptom clusters were evaluated using the occurrence and severity ratings of 38 symptoms from the Memorial Symptom Assessment Scale (MSAS) obtained one week after the administration of the patients' second or third cycle of CTX. Across both dimensions, five relatively similar symptom clusters were identified (i.e., sickness behavior, lung cancer specific, psychological, nutritional, and epithelial). In addition, across the two symptom dimensions, the specific symptoms within each of the symptom clusters were relatively similar.

Given that no studies of changes in symptom clusters over time in patients with lung cancer were identified, this study expands on our previous analysis with this sample.<sup>9</sup> The purposes of this study, in a sample of patients with lung cancer ( $n = 145$ ) who had received

one or two cycles of CTX, were to 1) evaluate for differences in the number and types of symptom clusters at three time points (i.e., in the week before the next cycle of CTX, approximately one week after CTX administration, and approximately two weeks after CTX administration) using ratings of occurrence and severity and 2) evaluate for changes in these symptom clusters over time.

## Materials and Methods

### Patients and Settings

This longitudinal analysis is part of a larger study, funded by the National Cancer Institute, which evaluated the symptom experience of oncology outpatients receiving CTX.<sup>12</sup> Details of the methods from the parent study are published elsewhere.<sup>12,13</sup> In brief, the parent study enrolled adults who were  $\geq 18$  years of age with lung, breast, GI, or gynecological cancer. Patients were recruited from two comprehensive cancer centers, one Veterans Affairs hospital, and four community-based oncology programs. All patients had received CTX within the preceding four weeks and were scheduled to receive at least two additional cycles. Patients were required to read, write, and understand English and provided written informed consent. In the parent study, of 2234 patients approached, 1343 consented to participate (60.1% response rate). The major reason for refusal was being overwhelmed with cancer treatment. In the current analysis, only patients with lung cancer ( $n = 145$ ) were evaluated.

### Instruments

Patients completed a demographic questionnaire, the Karnofsky Performance Status (KPS) scale,<sup>14–16</sup> and the Self-Administered Comorbidity Questionnaire (SCQ).<sup>17</sup>

A modified version of the MSAS<sup>18</sup> evaluated the occurrence and severity of 38 symptoms commonly associated with cancer and its treatment. The six symptoms that were added were chest tightness, difficulty breathing, increased appetite, weight gain, abdominal cramps, and hot flashes. Patients indicated if they experienced each symptom in the past week (i.e., symptom occurrence). If yes, they rated its severity, frequency, and distress. Symptom severity was rated using a four-point Likert scale. Only symptom occurrence and severity were included in the current analysis. The reliability and validity of the MSAS are well established.<sup>18,19</sup>

### Study Procedures

The study was approved by the Institutional Review Board at the University of California, San Francisco and at each study site. Patients completed questionnaires in their homes six times over two cycles of

CTX. For this analysis, the first, second, and third assessments that obtained data in the week before the second or third cycle of CTX (T1; recovery from their previous cycle), approximately one week after CTX administration (T2; acute symptoms), and approximately two weeks after the administration of CTX (T3; potential nadir) were used to assess for symptom clusters. Medical records were reviewed for clinical information.

### Data Analysis

Data were analyzed using Stata/SE, version 15,<sup>20</sup> and Mplus, version 7.4.<sup>21</sup> Descriptive statistics and frequency distributions were calculated for the demographic and clinical characteristics.

### Identification of Symptom Clusters

Exploratory factor analyses (EFAs) were done to identify symptom clusters using dichotomous occurrence and ordinal severity items.<sup>22,23</sup> Factor loadings of  $\geq 0.40$  were considered meaningful.<sup>19,23,24</sup> Factors were considered to be adequately defined if at least two symptoms had loadings of  $\geq 0.40$ .<sup>18</sup> Although it is common to require that each item load strongly on only one factor, we retained items that loaded on two factors (i.e., cross loaded) if they met our prespecified criteria of  $\geq 0.40$ . The cross loading of symptoms may be beneficial in the interpretation of potential causal mechanisms.<sup>20,25–27</sup> To have sufficient variation and covariation in the data to perform the EFAs, only symptoms that were present in  $>20\%$  but  $<80\%$  of the patients were included in the analyses.

For the EFAs using dichotomous occurrence items, tetrachoric correlations were used to create the matrix of associations. For the EFAs using ordinal severity items, polychoric correlations were used to create the matrix of associations.<sup>23,28</sup> The simple structure for the occurrence and severity EFAs were estimated using the method of unweighted least squares with geomin (i.e., oblique) rotation. The geomin rotation method was chosen to create the best fit for the model and improve the interpretability of each factor solution.<sup>23,29</sup> The unweighted least-squares estimator<sup>23,26</sup> was selected to achieve more reliable results because the scales for the MSAS items are dichotomous and ordinal.

The EFAs for severity were conducted using severity ratings that ranged from 0 (symptom not present) to 4 (very severe). A preliminary analysis was conducted using severity ratings that ranged from 1 (mild) to 4, omitting observations when the symptom was not present. However, the pairwise missingness was over 90% for many pairs, and the estimation failed. Therefore, the EFAs for the severity ratings were estimated including zeros.

Factor solutions were estimated for two through six factors. After examining all the factor solutions, the factor solution with the greatest interpretability and clinical meaningfulness was selected, given that it met the criteria set for evaluating simple structure. Then, each symptom cluster was evaluated to determine a clinically appropriate name based on the majority of the symptoms in the cluster. By conducting EFAs at three specific time points, we were able to compare the stability of symptom clusters over time.

### Differences in the Number and Types of Symptom Clusters

To evaluate agreement among the symptoms within the same cluster using occurrence and severity ratings, within and across each assessment, we used the criteria proposed by Kirkova and Walsh.<sup>30</sup> They suggested that to be in agreement with each other, at least 75% of the symptoms in the clusters should be present including the prominent and important symptom, namely the symptom with the greatest weight from the factor analyses.

## Results

### Demographic and Clinical Characteristics

The majority of patients were female (56.6%), white (71.8%), and married or partnered (64.6%). The majority of the patients (69.7%) had a current or former smoking history and an average of 3.2 ( $\pm 1.6$ ) comorbid conditions (Table 1).

### Symptom Clusters Based on Occurrence

Using occurrence rates, a five-factor solution was found for the T1 assessment (Table 2; for each of the EFAs, the specific symptoms within each cluster are found on Tables 2–7 and are summarized in Table 8). Factor 1 contained six symptoms and was named the *sickness behavior* cluster. Factor 2 consisted of five symptoms and was named the *lung cancer-specific* cluster. Factor 3 consisted of eight symptoms and was named the *psychological* cluster. Factor 4 contained nine symptoms and was named the *epithelial/GI* cluster. Factor 5 contained three symptoms and was named the *nutritional* cluster.

For the T2 assessment, a five-factor solution was found (Table 3). Factor 1 with 8 symptoms was named the *sickness behavior* cluster. Factor 2 with four symptoms was named the *lung cancer-specific* cluster. Factor 3 with seven symptoms was named the *psychological* cluster. Factor 4 with four symptoms was named *nutritional* cluster. Factor 5 with four symptoms was named the *epithelial* cluster.<sup>9</sup>

A five-factor solution was found for the T3 assessment (Table 4). Factor 1 with four symptoms was

Table 1  
Demographic and Clinical Characteristics of Patients  
With Lung Cancer Receiving CTX (N = 145)<sup>a</sup>

| Characteristic                               | n (%)          |
|--|----------------|
| Age in years, mean (SD)                      | 64.0 (11.1)    |
| Gender                                       |                |
| Female                                       | 82 (56.6)      |
| Male   | 63 (43.4)      |
| Race/ethnicity                               |                |
| White  | 102 (71.8)     |
| Asian or Pacific Islander                    | 14 (9.9)       |
| Black  | 14 (9.9)       |
| Hispanic, Mixed, or other                    | 12 (8.5)       |
| Annual household income                      |                |
| <\$30,000                                    | 37 (27.6)      |
| \$30,000 to \$69,999                         | 31 (23.1)      |
| \$70,000 to \$99,999                         | 21 (15.7)      |
| >\$100,000                                   | 45 (33.6)      |
| Currently employed                           | 36 (24.8)      |
| Education in years, mean (SD)                | 16.1 (3.4)     |
| Married or partnered                         | 93 (64.6)      |
| Lives alone                                  | 36 (25.0)      |
| Smoking history                              |                |
| Current or former smoker                     | 99 (69.7)      |
| Never smoker                                 | 43 (30.3)      |
| BMI kg/m <sup>2</sup> , mean (SD)            | 25.3 (4.6)     |
| Patient-reported KPS score, mean (SD)        | 79.1 (14.6)    |
| SCQ score, mean (SD)                         | 7.3 (3.9)      |
| No. of comorbidities, mean (SD)              | 3.2 (1.6)      |
| Comorbidities                                |                |
| Lung disease                                 | 87 (60.0)      |
| Hypertension                                 | 58 (40.0)      |
| Back pain                                    | 53 (36.6)      |
| Depression                                   | 26 (17.9)      |
| Osteoarthritis                               | 21 (14.5)      |
| Heart disease                                | 20 (13.8)      |
| Diabetes                                     | 18 (12.4)      |
| Anemia or other blood disease                | 12 (8.3)       |
| Liver disease                                | 12 (8.3)       |
| Rheumatoid arthritis                         | 12 (8.3)       |
| Ulcer or stomach disease                     | 9 (6.2)        |
| Kidney disease                               | 1 (0.7)        |
| Type of lung cancer                          |                |
| Non-small cell lung cancer                   | 126 (88.1)     |
| Small cell lung cancer                       | 17 (11.9)      |
| Months since cancer diagnosis, mean (SD)     | 15.1 (31.7)    |
| Months since cancer diagnosis, median (IQR)  | 4.2 (2.5–14.5) |
| Metastatic disease at time of study          | 110 (76.9)     |
| Number of prior cancer treatments, mean (SD) | 1.4 (1.4)      |
| Prior treatment                              |                |
| No prior treatment                           | 54 (38.9)      |
| Surgery only                                 | 17 (12.2)      |
| CTX only                                     | 12 (8.6)       |
| Radiation only                               | 18 (13.0)      |
| Surgery and CTX                              | 5 (3.6)        |
| Surgery and radiation                        | 3 (2.2)        |
| CTX and radiation                            | 13 (9.4)       |
| Surgery, CTX, and radiation                  | 17 (12.2)      |
| CTX regimen at time of study                 |                |
| Platinum-doublet                             | 113 (77.9)     |
| Single agent CTX                             | 29 (20.0)      |
| Monoclonal antibody alone                    | 3 (2.1)        |
| Cycle length                                 |                |
| 14 days                                      | 4 (3.5)        |
| 21 days                                      | 124 (85.5)     |
| 28 days                                      | 16 (11.0)      |
| Mean number of MSAS symptoms (of 38, SD)     | 14.3 (7.1)     |

BMI = body mass index; CTX = chemotherapy; IQR = interquartile range; kg/m<sup>2</sup> = kilogram per meter squared; KPS = Karnofsky Performance Status; MSAS = Memorial Symptom Assessment Scale; SCQ = Self-Administered Comorbidity Questionnaire; SD = standard deviation.

<sup>a</sup>Reprinted with permission from reference 9.

named the *sickness behavior* cluster. Factor 2 with seven symptoms was named the *lung cancer-specific* cluster. Factor 3 with 13 symptoms was named the *epithelial/GI* cluster. Factor 4 with six symptoms was named the *psychological* cluster. Factor 5 with three symptoms was named the *nutritional* cluster.

#### Symptom Clusters Based on Severity Ratings

Using severity ratings, a four-factor solution was found for the T1 assessment (Table 5). Factor 1 with eight symptoms was named the *lung cancer-specific* cluster. Factor 2 with eight symptoms was named the *epithelial/GI* cluster. Factor 3 with seven symptoms was named the *psychological* cluster. Factor 4 with four symptoms was named the *nutritional* cluster.

A five-factor solution was found for the T2 assessment (Table 6). Factor 1 with 17 symptoms was named the *sickness behavior* cluster. Factor 2 with five symptoms was named the *lung cancer-specific* cluster. Factor 3 with four symptoms was named the *nutritional* cluster. Factor 4 with four symptoms was named the *psychological* cluster. Factor 5 with four symptoms was named the *epithelial* cluster.<sup>9</sup>

A five-factor solution was found for the T3 assessment (Table 7). Factor 1 with five symptoms was named the *sickness behavior* cluster. Factor 2 with nine symptoms was named the *lung cancer-specific* cluster. Factor 3 with 13 symptoms was named the *epithelial/GI* cluster. Factor 4 with five symptoms was named the *psychological* cluster. Factor 5 with three symptoms was named the *nutritional* cluster.

#### Similarities and Differences in the Number and Types of Symptom Clusters

As shown in Table 8, for the occurrence dimension, the number of symptom clusters was five for all three time points. Across the three occurrence assessments, four of the symptom clusters were the same, namely, sickness behavior, lung cancer specific, psychological, and nutritional. Although an epithelial/GI cluster occurred at T1 and T3, the epithelial symptom cluster was identified at T2.

For the severity dimension, the number of symptom clusters ranged from four to five. Across the three severity assessments, three of the symptom clusters were the same, namely, lung cancer specific, psychological, and nutritional. The sickness behavior cluster was identified for the T2 and T3 assessments. Although the epithelial/GI cluster was found at T1 and T3, the epithelial cluster was only identified at T2.

#### Agreement in the Types of Symptoms Within Each Symptom Cluster

Table 8 presents a summary of the percentage agreement among the symptoms across the

Table 2  
Exploratory Factor Analysis<sup>a</sup> Using Ratings of Symptom Occurrence for the Week Before the Next Cycle of Chemotherapy (T1, N = 145)

| Symptom <sup>b</sup>                      | Factor 1                          | Factor 2                             | Factor 3                      | Factor 4                      | Factor 5                    |
|---|-----------------------------------|--------------------------------------|-------------------------------|-------------------------------|-----------------------------|
|   | Sickness Behavior Symptom Cluster | Lung Cancer—Specific Symptom Cluster | Psychological Symptom Cluster | Epithelial/GI Symptom Cluster | Nutritional Symptom Cluster |
| Abdominal cramps                          | 0.144                             | 0.034                                | 0.222                         | <b>0.443</b>                  | 0.129                       |
| Constipation                              | -0.091                            | 0.154                                | -0.019                        | <b>0.627</b>                  | 0.021                       |
| Difficulty concentrating                  | 0.364                             | -0.066                               | <b>0.517</b>                  | -0.045                        | 0.102                       |
| Feeling drowsy                            | <b>0.564</b>                      | 0.187                                | 0.298                         | -0.064                        | -0.170                      |
| Lack of energy                            | <b>1.021</b>                      | 0.081                                | 0.025                         | 0.004                         | -0.273                      |
| Nausea                                    | 0.269                             | 0.032                                | 0.108                         | <b>0.476</b>                  | -0.091                      |
| Sweats                                    | 0.148                             | 0.013                                | 0.014                         | <b>0.430</b>                  | 0.296                       |
| Vomiting                                  | -0.105                            | 0.217                                | 0.179                         | 0.278                         | 0.112                       |
| Chest tightness                           | 0.297                             | 0.399                                | 0.042                         | 0.203                         | 0.000                       |
| Cough                                     | 0.280                             | <b>0.504</b>                         | 0.076                         | 0.023                         | 0.074                       |
| Difficulty breathing                      | 0.060                             | <b>0.772</b>                         | <b>0.407</b>                  | 0.006                         | -0.038                      |
| Shortness of breath                       | 0.037                             | <b>0.469</b>                         | 0.368                         | 0.101                         | 0.119                       |
| Feeling bloated                           | -0.167                            | 0.074                                | <b>0.548</b>                  | 0.231                         | 0.138                       |
| Feeling irritable                         | 0.086                             | -0.053                               | <b>0.525</b>                  | 0.372                         | -0.027                      |
| Feeling nervous                           | 0.385                             | 0.017                                | <b>0.505</b>                  | -0.053                        | 0.243                       |
| Feeling sad                               | 0.148                             | -0.361                               | <b>0.601</b>                  | 0.225                         | -0.020                      |
| Problems with sexual interest or activity | <b>0.467</b>                      | -0.349                               | 0.132                         | 0.031                         | 0.158                       |
| Worrying                                  | -0.021                            | -0.297                               | <b>0.925</b>                  | 0.088                         | -0.006                      |
| Increased appetite                        | -0.077                            | -0.116                               | 0.027                         | 0.023                         | <b>1.056</b>                |
| Lack of appetite                          | -0.003                            | -0.206                               | 0.049                         | <b>0.814</b>                  | - <b>0.470</b>              |
| Weight gain                               | 0.046                             | 0.037                                | 0.070                         | -0.148                        | <b>0.783</b>                |
| Weight loss                               | 0.380                             | -0.058                               | - <b>0.620</b>                | <b>0.717</b>                  | 0.004                       |
| Changes in skin                           | -0.051                            | 0.122                                | 0.094                         | <b>0.714</b>                  | -0.029                      |
| Hair loss                                 | <b>0.565</b>                      | 0.004                                | -0.314                        | 0.264                         | 0.275                       |
| I do not look like myself                 | 0.061                             | 0.042                                | 0.175                         | <b>0.543</b>                  | 0.003                       |
| Mouth sores                               | 0.206                             | 0.027                                | 0.310                         | 0.136                         | 0.295                       |
| Dizziness                                 | <b>0.413</b>                      | 0.174                                | 0.032                         | 0.239                         | 0.132                       |
| Dry mouth                                 | 0.316                             | <b>0.438</b>                         | 0.049                         | 0.140                         | 0.001                       |
| Pain                                      | <b>0.456</b>                      | 0.226                                | -0.075                        | 0.232                         | -0.061                      |
| Swelling of arms or legs                  | 0.033                             | <b>0.483</b>                         | -0.068                        | 0.302                         | 0.002                       |
| Change in the way food tastes             | -0.253                            | 0.108                                | -0.018                        | <b>0.852</b>                  | 0.021                       |
| Difficulty sleeping                       | 0.132                             | -0.134                               | 0.356                         | 0.026                         | 0.041                       |
| Numbness/tingling in hands/feet           | 0.312                             | 0.028                                | -0.125                        | 0.355                         | 0.166                       |
| Total number of symptoms                  | 6                                 | 5                                    | 8                             | 9                             | 3                           |

Factor loadings  $\geq 0.40$  are in bold.

<sup>a</sup>Extraction method: Unweighted least squares. Rotation method: Geomin (oblique) rotation.

<sup>b</sup>Five symptoms present in  $<20\%$  of patients did not meet our criteria for inclusion in the EFA: diarrhea, difficulty swallowing, hot flashes, itching, and problems with urination.

occurrence and severity dimensions and across time. For the sickness behavior cluster, although no symptom was included in all the EFAs, lack of energy and feeling drowsy loaded on four of the five EFAs. For the lung cancer—specific cluster, the three symptoms that were included in all six EFAs were cough, difficulty breathing, and shortness of breath. For the psychological cluster, the three symptoms that were included in all six of the EFAs were feeling nervous, feeling sad, and worrying. For the nutritional cluster, the two symptoms that were found in all the EFAs were increased appetite and weight gain. For the epithelial/GI cluster, the symptoms that were included in the four EFAs were sweats, lack of appetite, changes in skin, “I do not look like myself,” and change in the way food tastes. For the epithelial cluster, the symptoms that were common were “I do not look like myself” and mouth sores.

## Discussion

This study is the first to evaluate for changes over time in the number and types of symptom clusters in patients with lung cancer who received CTX, using occurrence rates and severity ratings. A total of six clusters were identified across the two dimensions and the three assessments. However, only three of these clusters remained relatively stable (i.e., lung cancer specific, psychological, and nutritional). The epithelial/GI and epithelial clusters varied by time, but not by dimension. Except for severity at T1, the sickness behavior cluster was found across all dimensions at T2 and T3. Our findings suggest that most of the symptom clusters remained relatively stable over time, regardless of the dimensions used to create the clusters. The remainder of the discussion will describe the variability in the specific symptoms within

Table 3  
Exploratory Factor Analysis<sup>a</sup> Using Ratings of Symptom Occurrence for One Week After the Administration of Chemotherapy<sup>b</sup> (T2, N = 145)

| Symptom <sup>c</sup>                      | Factor 1                          | Factor 2                             | Factor 3                      | Factor 4                    | Factor 5                   |
|---|-----------------------------------|--------------------------------------|-------------------------------|-----------------------------|----------------------------|
|   | Sickness Behavior Symptom Cluster | Lung Cancer–Specific Symptom Cluster | Psychological Symptom Cluster | Nutritional Symptom Cluster | Epithelial Symptom Cluster |
| Abdominal cramps                          | <b>0.560</b>                      | −0.006                               | 0.241                         | −0.063                      | 0.307                      |
| Constipation                              | <b>0.438</b>                      | −0.359                               | −0.060                        | 0.128                       | 0.256                      |
| Difficulty concentrating                  | <b>0.498</b>                      | 0.022                                | <b>0.445</b>                  | −0.147                      | 0.074                      |
| Feeling drowsy                            | <b>0.768</b>                      | 0.028                                | 0.003                         | 0.003                       | −0.146                     |
| Lack of energy                            | <b>0.766</b>                      | 0.165                                | 0.154                         | 0.036                       | 0.004                      |
| Nausea                                    | <b>0.869</b>                      | −0.319                               | −0.035                        | 0.095                       | −0.108                     |
| Sweats                                    | <b>0.416</b>                      | 0.160                                | 0.071                         | −0.027                      | 0.328                      |
| Vomiting                                  | <b>0.600</b>                      | −0.029                               | 0.032                         | 0.033                       | −0.040                     |
| Chest tightness                           | 0.255                             | <b>0.601</b>                         | −0.012                        | 0.089                       | 0.098                      |
| Cough                                     | 0.185                             | <b>0.608</b>                         | −0.234                        | −0.025                      | −0.002                     |
| Difficulty breathing                      | 0.011                             | <b>0.934</b>                         | 0.023                         | 0.022                       | −0.028                     |
| Shortness of breath                       | 0.070                             | <b>0.900</b>                         | 0.080                         | 0.140                       | −0.039                     |
| Feeling bloated                           | 0.230                             | −0.001                               | <b>0.433</b>                  | 0.019                       | 0.246                      |
| Feeling irritable                         | −0.163                            | 0.175                                | <b>0.803</b>                  | 0.036                       | −0.021                     |
| Feeling nervous                           | 0.387                             | 0.177                                | <b>0.663</b>                  | 0.021                       | −0.064                     |
| Feeling sad                               | 0.269                             | 0.059                                | <b>0.571</b>                  | 0.174                       | 0.020                      |
| Problems with sexual interest or activity | 0.093                             | −0.022                               | <b>0.526</b>                  | −0.073                      | 0.029                      |
| Worrying                                  | 0.323                             | −0.058                               | <b>0.744</b>                  | −0.021                      | 0.003                      |
| Increased appetite                        | 0.056                             | 0.359                                | −0.002                        | − <b>0.841</b>              | −0.025                     |
| Lack of appetite                          | 0.289                             | 0.044                                | 0.056                         | <b>0.709</b>                | 0.028                      |
| Weight gain                               | −0.033                            | 0.356                                | −0.021                        | − <b>0.867</b>              | 0.214                      |
| Weight loss                               | 0.020                             | 0.177                                | −0.128                        | <b>0.526</b>                | 0.385                      |
| Changes in skin                           | 0.030                             | −0.201                               | 0.311                         | −0.051                      | <b>0.795</b>               |
| Hair loss                                 | 0.136                             | 0.051                                | −0.216                        | 0.242                       | <b>0.428</b>               |
| “I do not look like myself”               | −0.145                            | −0.063                               | 0.288                         | 0.098                       | <b>0.693</b>               |
| Mouth sores                               | 0.001                             | 0.131                                | −0.049                        | 0.046                       | <b>0.643</b>               |
| Dizziness                                 | 0.224                             | −0.015                               | 0.266                         | −0.153                      | 0.226                      |
| Dry mouth                                 | 0.398                             | 0.202                                | −0.003                        | 0.099                       | 0.128                      |
| Pain                                      | 0.386                             | 0.287                                | −0.067                        | −0.020                      | 0.125                      |
| Swelling of arms or legs                  | −0.182                            | 0.285                                | 0.041                         | −0.038                      | 0.344                      |
| Change in the way food tastes             | −0.079                            | 0.180                                | 0.302                         | 0.205                       | 0.288                      |
| Difficulty sleeping                       | 0.392                             | 0.104                                | 0.148                         | −0.117                      | 0.011                      |
| Numbness/tingling in hands/feet           | 0.274                             | 0.279                                | 0.002                         | −0.119                      | 0.349                      |
| Total number of symptoms                  | 8                                 | 4                                    | 7                             | 4                           | 4                          |

Factor loadings  $\geq 0.40$  are in bold.

<sup>a</sup>Extraction method: Unweighted least squares. Rotation method: Geomin (oblique) rotation.

<sup>b</sup>Reprinted with permission from reference 9.

<sup>c</sup>Five symptoms present in <20% of patients did not meet our criteria for inclusion in the EFA: diarrhea, difficulty swallowing, hot flashes, itching, and problems with urination.

each cluster and compare our findings to previous reports.

### Lung Cancer–Specific Cluster

A lung cancer–specific cluster was identified in all six EFAs. The number of symptoms in this cluster ranged from four to nine. Cough, difficulty breathing, and shortness of breath were identified across all dimensions and time points. Chest tightness was identified across all time points for severity and at T2 and T3 for occurrence. In three studies of symptom clusters in patients with lung cancer,<sup>3,7,10</sup> some type of respiratory cluster was identified. Direct comparisons of the specific symptoms within the lung cancer–specific cluster are not possible because of the different symptom measures used (i.e., Symptom Distress Scale [SDS]<sup>3,7</sup> and M.D. Anderson Symptom Inventory [MDASI]<sup>10</sup>).

However, across these four studies, cough, difficulty breathing, and shortness of breath were the common symptoms. This consistent finding highlights the clinical importance of this symptom cluster in patients with lung cancer. Additional support for the clinical significance of this cluster is the fact that in one study,<sup>31</sup> a higher incidence of respiratory symptoms on initial presentation of lung cancer is associated with a poorer prognosis. In addition, respiratory symptoms interfere with patients' ability to perform routine activities and maintain an acceptable quality of life.<sup>32</sup>

### Psychological Cluster

In our study, a psychological cluster was identified across all six EFAs. The total number of symptoms ranged from four to eight. Feeling nervous, feeling sad, and worrying were present in both dimensions and across all six time points. In addition, feeling

Table 4  
Exploratory Factory Analysis<sup>a</sup> Using Ratings of Symptom Occurrence for Approximately Two Weeks After the Administration of Chemotherapy (T3, N = 145)

| Symptom <sup>b</sup>                      | Factor 1                          | Factor 2                             | Factor 3                      | Factor 4                      | Factor 5                    |
|---|-----------------------------------|--------------------------------------|-------------------------------|-------------------------------|-----------------------------|
|   | Sickness Behavior Symptom Cluster | Lung Cancer–Specific Symptom Cluster | Epithelial/GI Symptom Cluster | Psychological Symptom Cluster | Nutritional Symptom Cluster |
| Abdominal cramps                          | 0.013                             | 0.068                                | <b>0.579</b>                  | 0.338                         | 0.068                       |
| Constipation                              | −0.062                            | 0.102                                | 0.390                         | 0.083                         | 0.237                       |
| Difficulty concentrating                  | <b>0.641</b>                      | 0.034                                | 0.009                         | 0.394                         | 0.088                       |
| Feeling drowsy                            | <b>0.518</b>                      | 0.069                                | <b>0.488</b>                  | 0.004                         | −0.206                      |
| Lack of energy                            | <b>0.729</b>                      | −0.039                               | 0.360                         | 0.041                         | −0.099                      |
| Nausea                                    | 0.001                             | 0.176                                | <b>0.220</b>                  | <b>0.535</b>                  | −0.290                      |
| Sweats                                    | 0.018                             | 0.266                                | <b>0.451</b>                  | 0.208                         | 0.011                       |
| Vomiting                                  | −0.089                            | 0.246                                | 0.078                         | <b>0.624</b>                  | −0.141                      |
| Chest tightness                           | 0.087                             | <b>0.827</b>                         | 0.013                         | 0.200                         | 0.093                       |
| Cough                                     | <b>0.426</b>                      | <b>0.459</b>                         | −0.008                        | 0.056                         | 0.018                       |
| Difficulty breathing                      | 0.366                             | <b>0.794</b>                         | −0.057                        | 0.095                         | −0.057                      |
| Shortness of breath                       | 0.367                             | <b>0.631</b>                         | 0.105                         | −0.016                        | 0.034                       |
| Feeling bloated                           | 0.046                             | −0.189                               | <b>0.518</b>                  | 0.296                         | 0.084                       |
| Feeling irritable                         | 0.117                             | −0.105                               | 0.274                         | <b>0.522</b>                  | 0.080                       |
| Feeling nervous                           | 0.260                             | −0.027                               | −0.047                        | <b>0.735</b>                  | 0.022                       |
| Feeling sad                               | 0.150                             | 0.074                                | 0.023                         | <b>0.771</b>                  | −0.088                      |
| Problems with sexual interest or activity | 0.082                             | −0.344                               | <b>0.561</b>                  | 0.180                         | 0.051                       |
| Worrying                                  | −0.013                            | −0.110                               | −0.008                        | <b>1.001</b>                  | −0.054                      |
| Increased appetite                        | −0.065                            | 0.147                                | 0.026                         | 0.063                         | <b>0.889</b>                |
| Lack of appetite                          | −0.203                            | −0.017                               | <b>0.559</b>                  | 0.209                         | − <b>0.420</b>              |
| Weight gain                               | −0.057                            | −0.022                               | <b>0.407</b>                  | −0.021                        | <b>0.866</b>                |
| Weight loss                               | −0.259                            | <b>0.451</b>                         | 0.285                         | −0.015                        | −0.357                      |
| Changes in skin                           | −0.113                            | 0.157                                | <b>0.589</b>                  | 0.085                         | −0.033                      |
| Hair loss                                 | −0.055                            | −0.010                               | <b>0.460</b>                  | −0.066                        | 0.049                       |
| I do not look like myself                 | −0.297                            | 0.056                                | <b>0.518</b>                  | 0.304                         | 0.052                       |
| Mouth sores                               | 0.078                             | −0.025                               | <b>0.682</b>                  | −0.124                        | 0.025                       |
| Dizziness                                 | 0.333                             | − <b>0.468</b>                       | <b>0.889</b>                  | 0.017                         | −0.026                      |
| Dry mouth                                 | 0.395                             | 0.237                                | 0.368                         | −0.197                        | −0.109                      |
| Pain                                      | 0.284                             | <b>0.406</b>                         | 0.294                         | −0.045                        | 0.123                       |
| Swelling of arms or legs                  | 0.107                             | 0.181                                | 0.234                         | −0.124                        | 0.013                       |
| Change in the way food tastes             | −0.365                            | 0.078                                | <b>0.624</b>                  | −0.024                        | −0.042                      |
| Difficulty sleeping                       | 0.182                             | 0.103                                | 0.015                         | 0.183                         | 0.119                       |
| Numbness/tingling in hands/feet           | −0.014                            | 0.351                                | 0.209                         | 0.250                         | −0.023                      |
| Total number of symptoms                  | 4                                 | 7                                    | 13                            | 6                             | 3                           |

Factor loadings  $\geq 0.40$  are in bold.

<sup>a</sup>Extraction method: Unweighted least squares. Rotation method: Geomin (oblique) rotation.

<sup>b</sup>Five symptoms present in <20% of patients did not meet our criteria for inclusion in the EFA: diarrhea, difficulty swallowing, hot flashes, itching, and problems with urination.

irritable was identified in five of six EFAs. Although none of the previous studies used the MSAS, our findings are consistent with four reports of symptom clusters in patients with lung cancer.<sup>3,7,10,11</sup> Two of these studies used the SDS<sup>3,7</sup> and two used the MDASI.<sup>10,11</sup> Although the specific psychological symptoms on these three instruments are rather disparate, sad was the psychological symptom that was common across all five studies. This finding is of particular interest because the prevalence rate for depressive symptoms in patients with lung cancer ranges from 9% to 53%.<sup>33</sup> In addition, in a study that reported on the incidence of depression in patients with the four most common cancers in the U.S.,<sup>34</sup> lung cancer ranked first. Given this consistent finding, clinicians need to screen for psychological symptoms and recommend efficacious interventions such as

cognitive-based therapy, mindfulness training, and participation in support groups.<sup>35</sup>

#### Nutritional Cluster

A nutritional cluster, which included the common symptoms of increased appetite and weight gain, was identified across both dimensions and all six EFAs. Of note, lack of appetite was identified in five of the six EFAs and weight loss was included in three of the six EFAs. The fact that none of the previous studies identified a nutritional cluster in patients with lung cancer may be related to differences in the symptoms that were assessed; for example, in the two studies that used the SDS,<sup>3,7</sup> which assesses appetite (i.e., I have my normal appetite to I cannot stand the thought of food), this symptom loaded on a GI distress cluster<sup>3</sup> or on a pain cluster.<sup>7</sup> In the two studies that used

Table 5  
Exploratory Factory Analysis<sup>a</sup> Using Ratings of Symptom Severity for the Week Before the Next Cycle of Chemotherapy Administration (T1, N = 145)

| Symptom <sup>b</sup>                      | Factor 1                             | Factor 2                      | Factor 3                      | Factor 4                    |
|---|--------------------------------------|-------------------------------|-------------------------------|-----------------------------|
|   | Lung Cancer—Specific Symptom Cluster | Epithelial/GI Symptom Cluster | Psychological Symptom Cluster | Nutritional Symptom Cluster |
| Abdominal cramps                          | 0.129                                | 0.384                         | 0.187                         | 0.177                       |
| Constipation                              | 0.046                                | <b>0.528</b>                  | 0.072                         | 0.204                       |
| Difficulty concentrating                  | 0.281                                | 0.126                         | 0.383                         | 0.122                       |
| Feeling drowsy                            | <b>0.679</b>                         | -0.038                        | 0.238                         | -0.165                      |
| Lack of energy                            | <b>0.621</b>                         | 0.215                         | 0.039                         | -0.227                      |
| Nausea                                    | 0.336                                | <b>0.453</b>                  | 0.004                         | -0.022                      |
| Sweats                                    | 0.016                                | <b>0.447</b>                  | -0.014                        | <b>0.428</b>                |
| Vomiting                                  | 0.295                                | 0.172                         | -0.009                        | 0.159                       |
| Chest tightness                           | <b>0.557</b>                         | 0.145                         | -0.066                        | 0.133                       |
| Cough                                     | <b>0.584</b>                         | 0.043                         | -0.014                        | 0.056                       |
| Difficulty breathing                      | <b>0.835</b>                         | -0.023                        | 0.038                         | -0.048                      |
| Shortness of breath                       | <b>0.730</b>                         | 0.042                         | 0.040                         | 0.056                       |
| Feeling bloated                           | 0.045                                | 0.249                         | <b>0.404</b>                  | 0.238                       |
| Feeling irritable                         | 0.098                                | 0.362                         | <b>0.453</b>                  | 0.082                       |
| Feeling nervous                           | 0.282                                | -0.028                        | <b>0.491</b>                  | 0.351                       |
| Feeling sad                               | -0.019                               | 0.141                         | <b>0.702</b>                  | -0.069                      |
| Problems with sexual interest or activity | 0.097                                | -0.021                        | 0.262                         | 0.265                       |
| Worrying                                  | -0.047                               | 0.073                         | <b>0.911</b>                  | -0.006                      |
| Increased appetite                        | -0.347                               | 0.043                         | 0.044                         | <b>0.984</b>                |
| Lack of appetite                          | -0.012                               | <b>0.815</b>                  | 0.109                         | - <b>0.508</b>              |
| Weight gain                               | -0.171                               | -0.075                        | 0.019                         | <b>0.879</b>                |
| Weight loss                               | 0.038                                | <b>0.740</b>                  | - <b>0.443</b>                | 0.028                       |
| Changes in skin                           | -0.042                               | <b>0.790</b>                  | 0.048                         | -0.039                      |
| Hair loss                                 | 0.177                                | 0.340                         | -0.196                        | 0.263                       |
| I do not look like myself                 | -0.018                               | <b>0.597</b>                  | 0.190                         | 0.017                       |
| Mouth sores                               | 0.056                                | 0.224                         | 0.252                         | 0.399                       |
| Dizziness                                 | <b>0.403</b>                         | 0.261                         | 0.029                         | 0.187                       |
| Dry mouth                                 | 0.354                                | 0.336                         | 0.052                         | 0.024                       |
| Pain                                      | <b>0.454</b>                         | 0.280                         | -0.076                        | 0.036                       |
| Swelling of arms or legs                  | 0.281                                | 0.317                         | -0.228                        | -0.029                      |
| Change in the way food tastes             | -0.160                               | <b>0.894</b>                  | -0.076                        | -0.064                      |
| Difficulty sleeping                       | 0.189                                | -0.085                        | <b>0.470</b>                  | -0.011                      |
| Numbness/tingling in hands/feet           | 0.114                                | 0.374                         | -0.021                        | 0.233                       |
| Total number of symptoms                  | 8                                    | 8                             | 7                             | 4                           |

Factor loadings  $\geq 0.40$  are in bold.

<sup>a</sup>Extraction method: Unweighted least squares. Rotation method: Geomin (oblique) rotation.

<sup>b</sup>Five symptoms present in <20% of patients did not meet our criteria for inclusion in the EFA: diarrhea, difficulty swallowing, hot flashes, itching, and problems with urination.

the MDASI, which assess for lack of appetite, this symptom loaded on a general symptom cluster<sup>6</sup> and on a cluster named “pattern 3” that included drowsiness, fatigue, dry mouth, sleep disturbance, and distress.<sup>5</sup> Finally, in a study that used the Physical Symptom Experience tool,<sup>4</sup> weight loss and loss of appetite were part of a general symptom cluster. Although an explanation for weight gain and increased appetite in the nutritional cluster are not readily apparent, weight loss and malnutrition are prevalent problems in patients with lung cancer that can have a negative impact on an individual’s ability to tolerate treatment and on survival.<sup>36</sup> Given the significance of this problem, clinicians need to assess for decreases in appetite and weight loss on a routine basis and provide nutrition counseling.

### Epithelial/GI Cluster

Our epithelial/GI cluster included symptoms associated with changes in the skin, hair, and oral mucosa that occur as a result of CTX’s action on rapidly dividing cells. Although not identified at the T2 assessment, the common symptoms that were included in the other four EFAs were sweats, lack of appetite, changes in the skin, “I don’t look like myself,” and change in the way food tastes. Although none of the previous studies reported an epithelial/GI cluster, four studies reported a GI cluster.<sup>3,5,6,11</sup> Across these four studies, the two common symptoms were nausea and vomiting. In one of the studies that used the SDS,<sup>3</sup> the appearance symptom loaded only on the emotional and physical suffering cluster. It should be noted that the MDASI does not assess for any

Table 6  
Exploratory Factor Analysis<sup>a</sup> Using Ratings of Symptom Severity for One Week After the Administration of Chemotherapy<sup>b</sup> (T2, N = 145)

| Symptom <sup>c</sup>                      | Factor 1                          | Factor 2                             | Factor 3                    | Factor 4                      | Factor 5                   |
|---|-----------------------------------|--------------------------------------|-----------------------------|-------------------------------|----------------------------|
|   | Sickness Behavior Symptom Cluster | Lung Cancer–Specific Symptom Cluster | Nutritional Symptom Cluster | Psychological Symptom Cluster | Epithelial Symptom Cluster |
| Abdominal cramps                          | <b>0.572</b>                      | 0.013                                | −0.102                      | 0.037                         | 0.226                      |
| Constipation                              | <b>0.441</b>                      | −0.230                               | 0.072                       | −0.049                        | 0.183                      |
| Difficulty concentrating                  | <b>0.509</b>                      | 0.010                                | 0.010                       | 0.307                         | 0.125                      |
| Feeling drowsy                            | <b>0.667</b>                      | 0.117                                | 0.139                       | −0.027                        | −0.081                     |
| Lack of energy                            | <b>0.775</b>                      | 0.135                                | 0.197                       | 0.010                         | 0.007                      |
| Nausea                                    | <b>0.709</b>                      | −0.189                               | 0.193                       | −0.059                        | −0.068                     |
| Sweats                                    | <b>0.629</b>                      | 0.130                                | −0.066                      | −0.135                        | 0.159                      |
| Vomiting                                  | <b>0.543</b>                      | 0.033                                | −0.079                      | −0.044                        | −0.092                     |
| Chest tightness                           | 0.254                             | <b>0.643</b>                         | −0.018                      | −0.023                        | 0.032                      |
| Cough                                     | 0.114                             | <b>0.670</b>                         | −0.109                      | −0.017                        | −0.212                     |
| Difficulty breathing                      | −0.083                            | <b>0.948</b>                         | 0.004                       | 0.203                         | 0.032                      |
| Shortness of breath                       | 0.128                             | <b>0.806</b>                         | 0.044                       | 0.217                         | −0.026                     |
| Feeling bloated                           | <b>0.430</b>                      | −0.110                               | −0.090                      | 0.069                         | 0.358                      |
| Feeling irritable                         | 0.004                             | 0.156                                | −0.008                      | <b>0.674</b>                  | 0.225                      |
| Feeling nervous                           | <b>0.429</b>                      | 0.234                                | −0.008                      | <b>0.469</b>                  | −0.036                     |
| Feeling sad                               | <b>0.408</b>                      | 0.047                                | 0.141                       | <b>0.653</b>                  | 0.006                      |
| Problems with sexual interest or activity | <b>0.555</b>                      | −0.267                               | −0.169                      | 0.108                         | 0.012                      |
| Worrying                                  | <b>0.482</b>                      | −0.079                               | −0.025                      | <b>0.668</b>                  | 0.069                      |
| Increased appetite                        | 0.194                             | 0.088                                | − <b>0.845</b>              | 0.012                         | 0.000                      |
| Lack of appetite                          | 0.323                             | 0.076                                | <b>0.723</b>                | 0.025                         | 0.119                      |
| Weight gain                               | 0.027                             | 0.205                                | − <b>0.843</b>              | −0.102                        | 0.211                      |
| Weight loss                               | 0.054                             | 0.349                                | <b>0.524</b>                | −0.158                        | 0.262                      |
| Changes in skin                           | −0.004                            | −0.078                               | 0.032                       | 0.026                         | <b>0.889</b>               |
| Hair loss                                 | 0.137                             | 0.157                                | 0.197                       | −0.244                        | 0.238                      |
| “I do not look like myself”               | −0.046                            | −0.026                               | 0.107                       | 0.129                         | <b>0.752</b>               |
| Mouth sores                               | 0.079                             | 0.125                                | −0.032                      | −0.307                        | <b>0.535</b>               |
| Dizziness                                 | <b>0.489</b>                      | 0.038                                | −0.190                      | 0.039                         | 0.133                      |
| Dry mouth                                 | <b>0.407</b>                      | 0.227                                | 0.068                       | −0.031                        | 0.118                      |
| Pain                                      | <b>0.432</b>                      | 0.219                                | 0.103                       | 0.171                         | −0.082                     |
| Swelling of arms or legs                  | − <b>0.453</b>                    | <b>0.438</b>                         | −0.003                      | 0.005                         | <b>0.448</b>               |
| Change in the way food tastes             | 0.190                             | 0.012                                | 0.242                       | 0.104                         | 0.339                      |
| Difficulty sleeping                       | 0.313                             | 0.178                                | −0.065                      | 0.229                         | 0.164                      |
| Numbness/tingling in hands/feet           | 0.071                             | 0.284                                | −0.137                      | 0.111                         | 0.296                      |
| Total number of symptoms                  | 17                                | 5                                    | 4                           | 4                             | 4                          |

Factor loadings  $\geq 0.40$  are in bold.

<sup>a</sup>Extraction method: Unweighted least squares. Rotation method: Geomin (oblique) rotation.

<sup>b</sup>Reprinted with permission from reference 9.

<sup>c</sup>Five symptoms present in <20% of patients did not meet our criteria for inclusion in the EFA: diarrhea, difficulty swallowing, hot flashes, itching, and problems with urination.

symptoms related to changes in appearance, hair loss, or changes in skin. However, in two studies that used the MSAS to assess symptom clusters in patients with other cancer diagnoses,<sup>37,38</sup> a cluster that contained the symptoms “I don’t look like myself,” changes in skin, and change in the way food tastes was identified. The presence of these symptoms across three studies suggests that they warrant additional evaluation in patients with heterogeneous cancer diagnoses.

#### Sickness Behavior Cluster

We identified a sickness behavior cluster in both dimensions and across all time points, except for severity at T1. The three most common symptoms were lack of energy, difficulty concentrating, and feeling drowsy. Although this cluster was not identified in previous studies of patients with lung cancer,<sup>3,4,6,10</sup> it is a common symptom cluster in a number of studies of

oncology patients undergoing active treatment.<sup>39</sup> Additional studies are needed to confirm the presence of this symptom cluster in patients with lung cancer.

#### Epithelial Cluster

Our epithelial cluster was only identified at the T2 timepoint for both dimensions. Similar to the epithelial/GI cluster, changes in skin, “I do not look like myself,” and mouth sores were the three common symptoms across the two EFAs. Although it is not entirely clear why this cluster was identified only at the T2 assessment, in other studies of patients with breast, ovarian, or heterogeneous cancer diagnoses that used the MSAS,<sup>37,39–41</sup> a body image–related symptom cluster was identified that included these three symptoms. Additional research is needed to confirm the presence of this cluster and how it

Table 7  
Exploratory Factor Analysis<sup>a</sup> Using Ratings of Symptom Severity for Approximately Two Weeks After the Administration of Chemotherapy (T3, N = 145)

| Symptom <sup>b</sup>                      | Factor 1                          | Factor 2                             | Factor 3                      | Factor 4                      | Factor 5                    |
|---|-----------------------------------|--------------------------------------|-------------------------------|-------------------------------|-----------------------------|
|   | Sickness Behavior Symptom Cluster | Lung Cancer–Specific Symptom Cluster | Epithelial/GI Symptom Cluster | Psychological Symptom Cluster | Nutritional Symptom Cluster |
| Abdominal cramps                          | 0.238                             | 0.138                                | <b>0.541</b>                  | 0.154                         | 0.015                       |
| Constipation                              | 0.048                             | −0.021                               | <b>0.543</b>                  | 0.046                         | 0.236                       |
| Difficulty concentrating                  | <b>0.629</b>                      | <b>0.418</b>                         | −0.091                        | 0.043                         | 0.007                       |
| Feeling drowsy                            | 0.223                             | <b>0.415</b>                         | 0.214                         | 0.120                         | −0.135                      |
| Lack of energy                            | 0.292                             | <b>0.586</b>                         | 0.074                         | −0.056                        | −0.162                      |
| Nausea                                    | 0.014                             | 0.234                                | 0.196                         | <b>0.525</b>                  | −0.120                      |
| Sweats                                    | −0.043                            | 0.285                                | <b>0.455</b>                  | 0.212                         | 0.032                       |
| Vomiting                                  | 0.005                             | 0.155                                | −0.028                        | <b>0.771</b>                  | 0.027                       |
| Chest tightness                           | − <b>0.418</b>                    | <b>0.745</b>                         | −0.004                        | 0.233                         | 0.136                       |
| Cough                                     | −0.126                            | <b>0.595</b>                         | −0.004                        | 0.134                         | −0.157                      |
| Difficulty breathing                      | 0.078                             | <b>0.898</b>                         | −0.094                        | −0.012                        | −0.042                      |
| Shortness of breath                       | 0.055                             | <b>0.764</b>                         | 0.094                         | −0.107                        | 0.111                       |
| Feeling bloated                           | 0.328                             | 0.039                                | <b>0.467</b>                  | 0.096                         | 0.225                       |
| Feeling irritable                         | <b>0.452</b>                      | 0.013                                | 0.366                         | 0.173                         | −0.004                      |
| Feeling nervous                           | <b>0.425</b>                      | 0.026                                | −0.007                        | <b>0.566</b>                  | 0.026                       |
| Feeling sad                               | 0.328                             | 0.017                                | 0.077                         | <b>0.701</b>                  | −0.159                      |
| Problems with sexual interest or activity | 0.355                             | −0.104                               | <b>0.483</b>                  | 0.010                         | 0.073                       |
| Worrying                                  | 0.322                             | −0.049                               | 0.109                         | <b>0.733</b>                  | −0.019                      |
| Increased appetite                        | −0.029                            | 0.054                                | 0.032                         | 0.015                         | <b>0.855</b>                |
| Lack of appetite                          | 0.050                             | 0.016                                | <b>0.661</b>                  | 0.046                         | −0.370                      |
| Weight gain                               | 0.013                             | 0.022                                | 0.327                         | −0.036                        | <b>0.854</b>                |
| Weight loss                               | −0.333                            | 0.236                                | <b>0.617</b>                  | −0.007                        | − <b>0.446</b>              |
| Changes in skin                           | 0.001                             | 0.059                                | <b>0.662</b>                  | 0.044                         | −0.038                      |
| Hair loss                                 | 0.006                             | 0.089                                | <b>0.419</b>                  | 0.012                         | −0.050                      |
| I do not look like myself                 | −0.046                            | −0.125                               | <b>0.604</b>                  | 0.339                         | 0.111                       |
| Mouth sores                               | 0.193                             | −0.024                               | <b>0.736</b>                  | −0.278                        | 0.008                       |
| Dizziness                                 | <b>0.434</b>                      | 0.094                                | <b>0.562</b>                  | −0.097                        | 0.028                       |
| Dry mouth                                 | 0.052                             | <b>0.448</b>                         | 0.309                         | −0.149                        | −0.084                      |
| Pain                                      | −0.079                            | <b>0.530</b>                         | 0.175                         | 0.067                         | 0.052                       |
| Swelling of arms or legs                  | −0.056                            | 0.083                                | 0.202                         | 0.052                         | −0.053                      |
| Change in the way food tastes             | −0.190                            | −0.095                               | <b>0.831</b>                  | 0.018                         | −0.069                      |
| Difficulty sleeping                       | 0.279                             | 0.210                                | −0.038                        | 0.299                         | 0.053                       |
| Numbness/tingling in hands/feet           | −0.024                            | 0.296                                | 0.245                         | 0.093                         | 0.093                       |
| Total number of symptoms                  | 5                                 | 9                                    | 13                            | 5                             | 3                           |

Factor loadings  $\geq 0.40$  are in bold.

<sup>a</sup>Extraction method: Unweighted least squares. Rotation method: Geomin (oblique) rotation.

<sup>b</sup>Five symptoms present in <20% of patients did not meet our criteria for inclusion in the EFA: diarrhea, difficulty swallowing, hot flashes, itching, and problems with urination.

changes over time and in relation to treatments that are known to affect body image.

Several limitations warrant consideration. Patients were enrolled before their second or third cycle of CTX. Therefore, the number and types of symptom clusters may vary if the patients were enrolled before the initiation of CTX. In addition, we were unable to use symptom distress, another important dimension of the symptom experience, to identify symptom clusters and compare our results using occurrence and severity ratings. When we evaluated the symptom distress ratings, not enough patients with each symptom were available to allow for accurate estimation. Finally, five symptoms with occurrence rates <20% were omitted from the EFAs, so their contribution to the various symptom clusters could not be determined.

Despite these limitations, our findings suggest that three symptom clusters (i.e., lung cancer specific, psychological, and nutritional) were relatively stable across both symptom dimensions and time. The other clusters that were less consistent and stable over time (i.e., sickness behavior, epithelial/GI, epithelial) warrant confirmation in independent samples.

Given that the science of symptom clusters is still its infancy,<sup>2,42</sup> additional research is required to determine the stability of symptom clusters across symptom dimensions and across time. Future studies need to include the phenotypic characterization of symptom clusters, as well as an evaluation of the mechanisms that underlie symptom clusters. Novel analytic techniques, such as network analysis,<sup>43,44</sup> will provide new insights into the stability of symptom clusters with and across dimensions and time.

Table 8  
 Summary of Symptom Clusters Over Time Using Occurrence Rates and Severity Ratings

| Symptom Cluster                           | Symptoms Within the Cluster               | Occurrence               |       |       | Severity       |       |       |       |
|---|---|--------------------------|-------|-------|----------------|-------|-------|-------|
|   |   | T1                       | T2    | T3    | T1             | T2    | T3    |       |
| Sickness behavior symptom cluster         | Lack of energy                            | ●                        | ●     | ●     | Not identified | ●     |       |       |
|   | Problems with sexual interest or activity | ●                        |       |       |                | ●     |       |       |
|   | Hair loss                                 | ●                        |       |       |                |       |       |       |
|   | Dizziness                                 | ●                        |       |       |                | ●     | ●     |       |
|   | Dry mouth                                 |                          |       |       |                | ●     |       |       |
|   | Abdominal cramps                          |                          | ●     |       |                | ●     |       |       |
|   | Constipation                              |                          | ●     |       |                | ●     |       |       |
|   | Difficult concentrating                   |                          | ●     | ●     |                | ●     | ●     |       |
|   | Nausea                                    |                          | ●     |       |                | ●     |       |       |
|   | Sweats                                    |                          | ●     |       |                | ●     |       |       |
|   | Vomiting                                  |                          | ●     |       |                | ●     |       |       |
|   | Cough                                     |                          |       | ●     |                |       |       |       |
|   | Feeling bloated                           |                          |       |       |                | ●     |       |       |
|   | Feeling drowsy                            | ●                        | ●     | ●     |                | ●     |       |       |
|   | Feeling irritable                         |                          |       |       |                |       | ●     |       |
|   | Feeling nervous                           |                          |       |       |                | ●     | ●     |       |
|   | Feeling sad                               |                          |       |       |                | ●     |       |       |
|   | Worrying                                  |                          |       |       |                | ●     |       |       |
|   | Pain                                      | ●                        |       |       |                | ●     |       |       |
|   | Swelling of arms or legs                  |                          |       |       |                | ●     |       |       |
| Chest tightness                           |   |                          |       |       |                | ●     |       |       |
| Percent agreement                         |   | 28.6%                    | 38.1% | 19.0% | 0.0%           | 81.0% | 23.8% |       |
| Lung cancer-specific symptom cluster      | Cough                                     | ●                        | ●     | ●     | ●              | ●     | ●     |       |
|   | Difficulty breathing                      | ●                        | ●     | ●     | ●              | ●     | ●     |       |
|   | Shortness of breath                       | ●                        | ●     | ●     | ●              | ●     | ●     |       |
|   | Dry mouth                                 | ●                        |       |       |                | ●     | ●     |       |
|   | Swelling of arms or legs                  | ●                        |       |       |                |       | ●     |       |
|   | Chest tightness                           |                          | ●     | ●     | ●              | ●     | ●     |       |
|   | Weight loss                               |                          |       | ●     | ●              |       |       |       |
|   | Dizziness                                 |                          |       | ●     | ●              |       |       |       |
|   | Pain                                      |                          |       | ●     | ●              |       | ●     |       |
|   | Difficulty concentrating                  |                          |       |       |                |       | ●     |       |
|   | Feeling drowsy                            |                          |       |       |                |       | ●     |       |
|   | Lack of energy                            |                          |       |       |                |       | ●     |       |
|   | Percent agreement                         |                          | 41.6% | 33.3% | 58.3%          | 66.7% | 41.7% | 75.0% |
|   | Psychological symptom cluster             | Difficulty concentrating | ●     | ●     |                |       |       |       |
| Difficulty breathing                      |   | ●                        |       |       |                |       |       |       |
| Feeling bloated                           |   | ●                        | ●     |       | ●              |       |       |       |
| Feeling irritable                         |   | ●                        | ●     | ●     | ●              | ●     |       |       |
| Feeling nervous                           |   | ●                        | ●     | ●     | ●              | ●     | ●     |       |
| Feeling sad                               |   | ●                        | ●     | ●     | ●              | ●     | ●     |       |
| Worrying                                  |   | ●                        | ●     | ●     | ●              | ●     | ●     |       |
| Weight loss                               |   | ●                        |       |       | ●              |       |       |       |
| Problems with sexual interest or activity |   |                          | ●     |       |                |       |       |       |
| Vomiting                                  |   |                          |       | ●     |                |       | ●     |       |
| Nausea                                    |   |                          |       | ●     |                |       | ●     |       |
| Difficulty sleeping                       |   |                          |       |       |                |       |       |       |
| Percent agreement                         |   |                          | 66.7% | 58.3% | 50.0%          | 58.3% | 33.3% | 41.7% |

(Continued)

Table 8  
Continued

| Symptom Cluster                             | Symptoms Within the Cluster               | Occurrence     |                |                | Severity       |                |                |
|---|---|----------------|----------------|----------------|----------------|----------------|----------------|
|   |   | T1             | T2             | T3             | T1             | T2             | T3             |
| Nutritional symptom cluster                 | Increased appetite                        | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Sweats                                    | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Lack of appetite                          | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Weight gain                               | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Weight loss                               | ●              | ●              | ●              | ●              | ●              | ●              |
| Epithelial/gastrointestinal symptom cluster | Percent agreement                         | 60.0%          | 80.0%          | 60.0%          | 80.0%          | 80.0%          | 60.0%          |
|   | Abdominal cramps                          | ●              | Not identified | ●              | ●              | Not identified | ●              |
|   | Constipation                              | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Nausea                                    | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Sweats                                    | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Lack of appetite                          | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Weight loss                               | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Changes in skin                           | ●              | ●              | ●              | ●              | ●              | ●              |
|   | I do not look like myself                 | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Change in the way food tastes             | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Mouth sores                               | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Hair loss                                 | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Feeling drowsy                            | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Feeling bloated                           | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Weight gain                               | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Dizziness                                 | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Problems with sexual interest or activity | ●              | ●              | ●              | ●              | ●              | ●              |
| Epithelial symptom cluster                  | Percent agreement                         | 56.3%          | 0.0%           | 81.3%          | 50.0%          | 0.0%           | 81.3%          |
|   | Changes in skin                           | Not identified | ●              | Not identified | Not identified | ●              | Not identified |
|   | Hair loss                                 | ●              | ●              | ●              | ●              | ●              | ●              |
|   | "I do not look like myself"               | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Mouth sores                               | ●              | ●              | ●              | ●              | ●              | ●              |
|   | Swelling of arms and legs                 | ●              | ●              | ●              | ●              | ●              | ●              |
| Total number of symptom clusters            | Percent agreement                         | 0.0%           | 80.0%          | 0.0%           | 0.0%           | 80.0%          | 0.0%           |
|   |   | 5              | 5              | 5              | 4              | 5              | 5              |

By way of example, percentage agreement for the sickness behavior symptom cluster at T1 using the results for the occurrence dimension was calculated as follows:  $(6 \text{ [total number of symptoms]} / 21 \text{ [total number of possible symptoms in the sickness behavior cluster]}) \times 100 = 28.6\%$ .

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