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

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### Abstract

**Context:** Lung cancer patients 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 lung cancer patients (n=145) who were receiving chemotherapy were to 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 to 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 were relatively stable across both dimensions and across time (i.e., lung cancer specific, psychological, nutritional). Two additional clusters varied by time but not by symptom dimension (i.e., epithelial/gastrointestinal, epithelial). A sickness behavior cluster was identified at each assessment with the exception of the week before CTX using only the severity dimension.

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**Conclusion:** Findings provide insights into the most common symptom clusters in lung cancer patients undergoing CTX. Most common symptoms within each cluster appear to be relatively stable across the two dimensions, as well as across time.

### Keywords

symptoms; symptom clusters; lung cancer; chemotherapy; exploratory factor analysis; symptom occurrence; symptom severity

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## INTRODUCTION

Lung cancer patients have an extremely high symptom burden that negatively effects 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 management of symptoms in this vulnerable group of patients.<sup>2</sup>

In the first study of symptom clusters in lung cancer patients,<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 distress, respiratory distress, malaise).

Since this publication in 1997, eight studies have evaluated for symptom clusters in lung cancer patients. Four of these studies,<sup>4-7</sup> along with Sarna and Brecht's paper,<sup>3</sup> were summarized in a systematic review by Chen and colleagues.<sup>8</sup> Three additional studies,<sup>11</sup> including one from our research team,<sup>11</sup> were published following the systematic review. While across these eight studies, the number of symptom clusters 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>3,7,9,11</sup> with cough being the most common symptom. Finally, a gastrointestinal (GI) symptom cluster was identified in four studies,<sup>3,5,6,10</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 utilized to identify the symptom clusters. Of note, except for our own study,<sup>11</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>11</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' third or fourth cycle of CTX. Across both dimensions, five relatively similar symptom clusters were identified (i.e., sickness behavior, lung cancer specific, psychological, nutritional, 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 lung cancer patients were identified, this study expands on our previous analysis with this sample.<sup>11</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: evaluate for differences in the number and types of symptom clusters at three time points (i.e., in the week prior to the next cycle of CTX, approximately one week after CTX administration, approximately two weeks after CTX administration) using ratings of occurrence and severity and 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, that 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 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, out of 2,234 patients approached, 1,343 consented to participate (60.1% response rate). The major reason for refusal was being overwhelmed with cancer treatment. In the current analysis, only lung cancer patients (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 4-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 prior to the third or fourth 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>23–25</sup> Factors were considered to be adequately defined if at least two symptoms had loadings of  $\geq 0.40$ .<sup>18</sup> While 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 pre-specified criteria of  $\geq 0.40$ . The cross loading of symptoms may be beneficial in the interpretation of potential causal mechanisms.<sup>20,26–28</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>23,29</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>23,30</sup> The unweighted least squares estimator<sup>23,27</sup> was selected in order 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 of 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>31</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; NB: for each of the EFAs the specific symptoms within each cluster are found on Tables 2 through 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 3 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>11</sup>

A five factor solution was found for the T3 assessment (Table 4). Factor 1 with four symptoms was named the *sickness behavior* cluster. Factor 2 with seven symptoms was named the *lung cancer specific* cluster. Factor 3 with thirteen 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 seventeen 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>11</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 thirteen 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. While 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. While 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 occurrence and severity dimensions and across time. For the sickness behavior cluster, while no symptom was included in all of 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 of 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, 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 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 lung cancer patients,<sup>3,7,9</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,<sup>3,7</sup> M.D. Anderson Symptom Inventory (MDASI)<sup>9</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 lung cancer patients. Additional support for the clinical significance of this cluster is the fact that in one study,<sup>32</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>33</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 irritable was identified in five of six EFAs. While none of the previous studies used the MSAS, our findings are consistent with four reports of symptom clusters in lung cancer patients.<sup>3,7,9,10</sup> Two of these studies used the Symptom Distress Scale (SDS)<sup>3,7</sup> and two used the MDASI.<sup>9,10</sup> While 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>34</sup> In addition, in a study that reported on the incidence of depression in patients with the four most common cancers in the United States,<sup>35</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>36</sup>

### **Nutritional Cluster**

A nutritional cluster, that included the common symptoms of increased appetite and weight gain, was identified across both dimensions and all six of the 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 lung cancer patients 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 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> Lastly, 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. While an explanation for weight gain and increased appetite in the nutritional cluster are not readily apparent, weight loss and malnutrition are prevalent problems in lung cancer patients that can have a negative impact on an individual’s ability to tolerate treatment and on survival.<sup>37</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. While 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. While none of the previous studies reported an epithelial/GI cluster, four studies reported a GI cluster.<sup>3,5,6,10</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 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>38,39</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. While this cluster was not identified in previous studies of lung cancer patients,<sup>3,4,6,9</sup> it is a common symptom cluster in a number of studies of oncology patients undergoing active treatment.<sup>40</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. While it is not entirely clear why this cluster was identified only at the T2 assessment, in other studies of patients with breast, ovarian, or heterogenous cancer diagnoses that used the MSAS,<sup>38,40–42</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 changes over time and in relation to treatments that are known to effect body image.

Several limitations warrant consideration. Patients were enrolled prior to their second or third cycle of CTX. Therefore, the number and types of symptom clusters may vary if the patients were enrolled prior to 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. Lastly, 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>2,43</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, like network analysis,<sup>44,45</sup> will provide new insights into the stability of symptom clusters with and across dimensions and time.

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**Table 1.**

Demographic and clinical characteristics of lung cancer patients receiving CTX (n = 145) \*

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	

Characteristic	N (%)
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 day	4 (3.5)
21 day	124 (85.5)
28 day	16 (11.0)
Mean number of MSAS symptoms (out of 38, SD)	14.3 (7.1)

Abbreviations: 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.

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**Table 2.**

Exploratory factor analysis<sup>a</sup> using ratings of symptom occurrence for the week prior to 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<sup>c</sup></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



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
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

<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, problems with urination.

<sup>c</sup>Factor loadings 0.40 are in bold.

**Table 3.**

Exploratory factor analysis<sup>d</sup> using ratings of symptom occurrence for one week after the administration of chemotherapy\* (T2, 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	Nutritional Symptom Cluster	Epithelial Symptom Cluster	Sickness Behavior Symptom Cluster	Lung Cancer-Specific Symptom Cluster	Psychological Symptom Cluster	Nutritional Symptom Cluster	Epithelial Symptom Cluster
Abdominal cramps	<b>0.560<sup>c</sup></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	-0.841	-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	-0.867	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>					

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	Nutritional Symptom Cluster	Epithelial Symptom Cluster
"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

<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, problems with urination.

<sup>c</sup>Factor loadings 0.40 are in bold.

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Table 4.

Exploratory factor 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<sup>c</sup></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	0.220	<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

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
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

<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, problems with urination.

<sup>c</sup>Factor loadings 0.40 are in bold.

**Table 5.**

Exploratory factor analysis<sup>a</sup> using ratings of symptom severity for the week prior to 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

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
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

<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, problems with urination.

<sup>c</sup>Factor loadings >0.40 are in bold.



**Table 6.**

Exploratory factor analysis<sup>d</sup> using ratings of symptom severity for one week after the administration of chemotherapy\* (T2, 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	Nutritional Symptom Cluster	Psychological Symptom Cluster	Epithelial Symptom Cluster	Sickness Behavior Symptom Cluster	Lung Cancer-Specific Symptom Cluster	Nutritional Symptom Cluster	Psychological Symptom Cluster	Epithelial Symptom Cluster
Abdominal cramps	<b>0.572<sup>c</sup></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	-0.845	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	-0.843	-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					

Symptom <sup>b</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
"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

<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, problems with urination.

<sup>c</sup>Factor loadings 0.40 are in bold.

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**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

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
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

<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, problems with urination.

<sup>c</sup>Factor loadings 0.40 are in bold.

**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	●	●	●		●	
	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	●				●	●

Symptom Cluster	Symptoms Within the Cluster	Occurrence			Severity		
		T1	T2	T3	T1	T2	T3
	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%
	Difficulty concentrating	●	●				
Psychological Symptom Cluster	Difficulty breathing	●					
	Feeling bloated	●	●		●		
	Feeling irritable	●	●	●	●	●	
	Feeling nervous	●	●	●	●	●	●
	Feeling sad	●	●	●	●	●	●
	Worrying	●	●	●	●	●	●
	Weight loss	●			●		
	Problems with sexual interest or activity		●				
	Vomiting			●			●
	Nausea			●			●
Nutritional Symptom Cluster	Difficulty sleeping				●		
	Percent agreement	66.7%	58.3%	50.0%	58.3%	33.3%	41.7%
	Increased appetite	●	●	●	●	●	●
	Sweats				●		
	Lack of appetite	●	●	●	●	●	●
	Weight gain	●	●	●	●	●	●
	Weight loss		●			●	●
	Percent agreement	60.0%	80.0%	60.0%	80.0%	80.0%	60.0%

Symptom Cluster	Symptoms Within the Cluster	Occurrence			Severity		
		T1	T2	T3	T1	T2	T3
Epithelial/Gastrointestinal Symptom Cluster	Abdominal cramps	●	NO	●		NOT	●
	Constipation	●	TI		●	DE	●
	Nausea	●	DE		●	NT	
	Sweats	●	NT	●	●	FI	●
	Lack of appetite	●	FI		●	ED	●
	Weight loss	●	ED		●		●
	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						●	
Percent agreement		56.3%	0.0%	81.3%	50.0%	0.0%	81.3%
Epithelial Symptom Cluster	Changes in skin		●			●	
	Hair loss		●			●	
	"I do not look like myself"		●		NOT IDENTIFIED	●	NOT IDENTIFIED
	Mouth sores		●			●	
	Swelling of arms and legs					●	
Percent agreement		0.0%	80.0%	0.0%	0.0%	80.0%	0.0%
Total number of symptom clusters		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 (total number of symptoms)/21 (total number of possible symptoms in the sickness behavior cluster) x 100 = 28.6%.