Increasing Stringency in Symptom Cluster Research: A Methodological Exploration of Symptom Clusters in Patients With Inoperable Lung Cancer

Ingela Henoch, RN, PhD, Alexander Ploner, PhD, and Carol Tishelman, RN, PhD

Purpose/Objectives: To inductively explore the existence of symptom clusters among a homogenous group of patients with inoperable lung cancer close to diagnosis and to explore if the symptom clusters are consistent when examined with different instruments and analytical methods.

Design: Cross-sectional.

Setting: Lung medicine department at two university hospitals in Sweden.

Sample: 400 patients (52% men, 48% women) newly diagnosed with lung cancer with a mean age of 64.5 years.

Methods: Data were analyzed from various questionnaires, including the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30, the EORTC LC13, and the Symptom Distress Scale. Items in the instruments were adapted to increase their correspondence. Symptom clusters were analyzed with Pearson correlations, cluster analysis, factor analysis, and Cronbach alphas.

Main Research Variables: Symptom clusters.

Findings: Three clusters were found to be notably consistent across instruments and analyses: first, a pain cluster consisting of pain, nausea, bowel issues, appetite loss, and fatigue; second, a mood cluster consisting of mood, outlook, concentration, and insomnia; and third, a respiratory cluster consisting of breathing and cough, with fatigue and appetite loss closely related to more than one cluster in several analysis.

Conclusions: The authors found consistent symptom clusters for a large cohort of patients with lung cancer at a comparable point in their cancer trajectory, across different measurement tools and statistical methods.

Implications for Nursing: The symptom cluster consistency for patients with lung cancer is an important finding because the relevance of symptom cluster research is questionable if consistency is lacking across data collection and analysis approaches. Achieving consistency is possible in symptom cluster research across instruments and analysis methods if instrument items are comparable.

Patients with cancer can experience a variety of symptoms, such as pain, fatigue, nausea, dyspnea, and sleep disturbances. Although several symptoms often occur in conjunction, research traditionally has focused on single symptoms. In 2004, Miaskowski, Dodd, and Lee argued that the new frontier of symptom research is the study of symptom clusters. A symptom cluster was defined by Dodd, Miaskowski, and Paul (2001) as three or more concurrent symptoms that are interrelated, although Kim, McGuire, Tulman, and Barsevick (2005) argued that two or more symptoms are sufficient to constitute a cluster if other criteria are met. The criteria involve the cluster symptoms occurring together in stable combinations relatively independently of other symptom constellations and that relationships among symptoms within a cluster should be stronger than with symptoms outside the cluster (Kim et al.).

In perusing the literature, the authors of this article found two main approaches used to determine the existence of symptom clusters. One approach is to inductively determine the cluster empirically; another is to investigate the existence of a predetermined symptom cluster formulated on the basis of previous research or clinical experience (Miaskowski, Aouizerat, Dodd, & Cooper, 2007). Fan, Filipczak, and Chow (2007) conducted a literature review of empirically derived symptom clusters commonly occurring in patients with cancer. After reviewing 13 studies, only one cluster, consisting of gastrointestinal symptoms, occurred consistently (in six of seven studies of patients with heterogeneous cancers), and no consistent symptom clusters were found in patients with lung or breast cancer (Fan et al.). On the other hand, when Barsevick (2007) examined scientific literature for occurrence of a predetermined cluster of fatigue, insomnia, pain, and depression in patients with cancer, she found that, regardless of method, various combinations of these symptoms formed a cluster.

This lack of consistency in the literature may not only be related to whether symptom clusters are predefined or empirically determined, but also to differences in

statistical strategies for empirically distinguishing and defining symptom clusters.

Beck (2004) stated that gaps in symptom cluster research can be found on conceptual, methodological, and analytical levels. The conceptual level is about the manner in which symptom clusters are defined. Methodological issues include, for example, whether symptoms should be measured with unidimensional instruments assessing several symptoms or by several instruments, each focusing on more than one dimension of the same symptom. The analytical level relates to the best manner of statistically determining the existence of a symptom cluster (Beck).

Barsevick, Whitmer, Nail, Beck, and Dudley (2006) recommended that homogenous samples, with all subjects at the same disease stage, are best used to investigate symptom clusters. Longitudinal explorations also have been recommended because symptom clusters may be dynamic constructs, which change over time in patients with cancer (Barsevick et al.; Kirkova & Walsh, 2007).

Given the lack of consensus and gaps in symptom cluster research to date, the current study was conducted to attempt to offset weaknesses in the existing literature. The authors first critically reviewed the symptom cluster literature to delineate the statistical approaches most commonly used to empirically determine symptom clusters. They then applied some of the statistical methods commonly used in the literature to examine symptom clusters in a relatively homogenous sample of 400 patients with nonresectable lung cancer (LC) close to diagnosis, using data generated by two widely used assessment instruments at the same time point. The primary aim of this study is, therefore, to determine if clusters are consistent when examined with different symptom assessment instruments and analytical methods in a sample which is relatively homogeneous in terms of diagnosis, prognosis, and time point in disease trajectory.

Literature Review

The review was limited to studies aimed at empirically determining new symptom clusters published before 2008. Literature was obtained using the search terms *symptom cluster* and *cancer* via PubMed and CINAHL®, with reference lists also examined for potentially relevant studies. An overview of designs, samples, research instruments, methods, analysis approaches, and resulting clusters of symptoms used in published studies meeting inclusion criteria is presented in Table 1. Seven articles reporting inductive empirical explorations to distinguish symptom clusters were found. Studies aiming to explore outcomes of symptom clusters, rather than distinguish the clusters themselves, have been excluded. The authors acknowledge that some studies cited here had additional aims (e.g., exploring antecedents to symptom clusters), but additional discussion of these aims is beyond the scope of this article.

Most studies were conducted with patients with varied cancer diagnoses, with one study based exclusively on women with three different stages of breast cancer. Two studies are based on patients with LC: Sarna and Brecht (1997) examined dimensions of symptoms in women with advanced LC whereas Gift, Jablonski, Stommel, and Given (2004) used data from patients in different LC stages.

Among the seven studies empirically exploring new symptom clusters, the same symptom assessment instrument was only used twice: Chen and Lin (2007) and Chen and Tseng (2006) used the M.D. Anderson Symptom Inventory.

In general, correlations (Chen & Lin, 2007; Chow, Fan, Hadi, & Filipczak, 2007), factor analysis or principal component analysis (Chen & Lin; Chen & Tseng, 2006; Chow et al.; Gift et al., 2004; Sarna & Brecht, 1997), and internal consistency measured by Cronbach alpha (Chow et al.; Gift et al.) have been used in different constellations to explore symptom clusters. Cluster analysis (Bender, Ergyn, Rosenzweig, Cohen, & Sereika, 2005; Walsh & Rybicki, 2006) also has been used to a lesser extent. Chow et al. were unique in using 50% random samples to validate the clusters they derived, although some of the differences in loadings inside and outside clusters were small (i.e., appetite loaded 0.5 inside its primary cluster and 0.45 with another fatigue-related cluster). Chen and Lin and Chen and Tseng used t tests to validate the empirically derived symptom clusters.

The levels of the factor loadings that qualify a symptom for inclusion in a cluster vary between the reviewed studies, ranging from 0.3–0.55. Hazard Munro (2001) argued that a difference of at least 0.2 between an item's highest loading and its next highest loading may be an appropriate criterion for including an item in a factor, although such criteria are seldom applied in published symptom cluster research. Communalities refer to the portion of item variance accounted for by the various factors and provide an indication of the significance of an item. In the reviewed studies using factor analysis, a specific symptom was included in the cluster with which it had highest factor loading. In two of the studies, factor loadings outside cluster and communalities are presented (Chow et al., 2007; Gift et al., 2004). No predetermined criteria for level of factor loadings, communalities, or Cronbach alpha have been stated in any of the reviewed studies. Factor or principal component analysis and Cronbach alpha also have been used in combination with testing to discriminate between correlations within and outside the cluster in three studies (Chen & Tseng, 2006; Chow et al.; Gift et al.). Although Kim et al. (2005) stated that the relationship within the cluster should be stronger than outside the cluster, no

criterion for appropriate correlation between clusters is stated in any of the articles reviewed.

The lack of consensus in how to measure and analyze symptom clusters makes it impossible to determine whether the clusters found in the studies would be consistent in patients with the same diagnosis at the same stage. The extent to which the reported clusters are dependent on stage of disease, time point, or type of

Table 1. Research on Determination of New Symptom Clusters

Study	Design and Sample Size	Diagnosis	Instruments	Data Analysis	Details of Analysis	Symptom Clusters
Bender et al., 2005	Cross-sectional, pooled analysis of three studies (N = 154)	Breast cancer	–	Cluster analysis of 13 symptoms	Hierarchical cluster analysis of binary symptom variables within each study	Fatigue, cognitive impairment, and mood issues
Chen & Lin, 2007	Cross-sectional (N = 321)	Heterogeneous cancer diagnoses	MDASI	Factor analysis, Pearson correlation, and t test	Factor loadings within clusters: 0.59–0.93; correlations between clusters: 0.48–0.72	Detailed in Chen & Tseng, 2006
Chen & Tseng, 2006	Cross-sectional (only baseline data) (N = 151)	Heterogeneous cancer diagnoses	MDASI and HADS	Factor analysis, t test, and Cronbach alpha	Factor loadings within clusters: 0.437–0.656; Cronbach alpha: 0.65–0.88; correlations between clusters: 0.43–0.55	Pain, fatigue, sleep disturbances, lack of appetite, and drowsiness; nausea and vomiting; and distress and sadness
Chow et al., 2007	Longitudinal (N = 518)	Heterogeneous cancer diagnoses	ESAS	Spearman correlation, principle component analysis, and Cronbach alpha	Factor loadings within clusters: 0.55–0.9; factor loadings outside clusters: 0.02–0.42; communalities: 0.55–0.83; Cronbach alpha: 0.61–0.81	Fatigue, pain, drowsiness, and sense of well-being; anxiety and depression; and shortness of breath, nausea, and appetite
Gift et al., 2004	Cross-sectional (N = 220)	Lung cancer	Physical Symptom Experience of the SF-36®	Factor analysis and Cronbach alpha	Eight variables had communalities greater than 0.3. Of these, seven symptoms had factor loadings greater than 0.4, which constituted the cluster; Cronbach alpha: 0.73; mean interitem correlation: 0.28	Nausea, fatigue, weakness, appetite loss, weight loss, altered taste, and vomiting
Sarna & Brecht, 1997	Cross-sectional (N = 60)	Lung cancer	SDS (used as a Likert scale)	Factor analysis	Factor loadings within clusters: 0.55–0.91	Nausea (frequency and intensity) and appetite; pain (frequency and severity) and appearance; insomnia, breathing, and cough; bowel and outlook; and concentration and fatigue
Walsh & Rybicki, 2006	Cross-sectional (N = 922)	Heterogeneous cancer diagnoses	–	Cluster analysis of 38 symptoms	Hierarchical cluster analysis with average linkage method	Easy fatigue, weakness, anorexia, lack of energy, dry mouth, early satiety, weight loss, and taste change; sleep issues, depression, and anxiety; dizzy spells, dyspepsia, belching, and bloating; nausea and vomiting; dyspnea, cough, hoarseness, and dysphagia; edema and confusion; and pain and constipation

ESAS—Edmonton Symptom Assessment Scale; HADS—Hospital Anxiety and Depression Scale; MDASI—M.D. Anderson Symptom Inventory; SDS—Symptom Distress Scale

instrument used to measure the symptoms also is unclear. To compensate for the use of inconsistent methods of measurement and analysis, heterogeneous samples, and different time points along disease trajectory, the current study was conducted among patients newly diagnosed with inoperable LC, with symptom clusters examined using two commonly used instruments and analyzed in manners described in the reviewed literature.

Methods

Participants and Setting

The data are derived from a longitudinal research project of 400 adults with newly diagnosed inoperable LC, consecutively recruited through the lung medicine departments of two university hospitals (Lovgren et al., 2007; Tishelman et al., 2005), which are the primary centers for treatment of LC in Stockholm, Sweden. The study presented here is based on data from the first interview with each patient conducted about one month after diagnosis ($\overline{X}$ = 31 days, SD = 27).

Procedure

After providing informed consent, eligible patients completed a battery of instruments, including the Symptom Distress Scale (SDS), the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30, and the EORTC LC13. For this study, only items on the SDS (McCorkle & Quint-Benoliel, 1983), the EORTC QLQ-C30, and the EORTC LC13 (Aaronson et al., 1993; Bergman, Aaronson, Ahmedzai, Kaasa, & Sullivan, 1994), which assess the same symptoms, were deemed relevant. All data were collected in the presence of a research nurse at a venue determined by the patient.

Instruments

The SDS was developed originally by McCorkle and Young (1978) to measure symptoms in adult patients with cancer. Although the scale was intended to measure symptom distress, SDS measures occurrence in terms of intensity and frequency from symptoms, rather than distress per se, as additional research has differentiated these constructs (Tishelman, Petersson, Degner, & Sprangers, 2007; Wells & Ridner, 2008). The instrument was later revised and expanded to reflect symptoms patients with LC experience (McCorkle & Quint-Benoliel, 1983). In the current study, 11 of the 15 items on the Swedish version of the visual analog scale are used (i.e., those that correspond to EORTC items, such as appetite, concentration, fatigue, insomnia, mood, nausea, outlook, pain, bowel function, breathing, and cough). The items are scored by measuring the distance from the beginning of the scale to the mark made by the patient across the 10 cm VAS line, therefore yielding a score of 0–10 for each item, with higher scores indicating greater symptomatology. Cronbach alpha varied across time points in the main project from 0.84–0.88 (Tishelman et al., 2005), comparing well with previous English versions reporting alpha scores between 0.7–0.92 (McCorkle, Cooley, & Shea, 1998).

EORTC QLQ-C30 and EORTC LC13: In the current study, 11 of the 30 items of the EORTC QLQ-C30 (v.3.0), a cancer-specific, health-related, quality-of-life questionnaire (Aaronson et al., 1993), are used: fatigue, pain, bowel issues, nausea, appetite loss, dyspnea, cough, mood, outlook, concentration, and insomnia. The 13-item, LC-specific EORTC LC13 module (Bergman et al., 1994), also was administered, but only the item assessing cough was used in this article.

Four response options are employed in EORTC instruments: 1, not at all; 2, a little; 3, quite a bit; and 4, very much. Scores are linearly transformed to 0–100 scales (Aaronson et al., 1993). Higher scores represent higher levels of functioning and symptomatology. Although items do not distinguish among intensity, frequency, or severity of issues, mean scores are interpreted as reflecting intensity of functioning and symptoms. The EORTC QLQ-C30 and EORTC LC13 have been found to yield adequate levels of reliability and validity in Swedish patients with LC (Nicklasson & Bergman, 2007).

Because one aim of the current study was to explore whether the symptom clusters would be consistent with different instruments used at the same time point, the authors used only the variables found in the SDS, EORTC QLQ-C30, and the EORTC LC13, with item comparability determined through Pearson correlations between instruments. In general, correlations were highest for items designed to measure the same symptoms. The items in the EORTC QLQ-C30 were used at item level to enhance correspondence with SDS (e.g., EORTC depression corresponds with SDS mood, EORTC worry with SDS outlook, EORTC concentration with SDS concentration, EORTC pain with SDS pain intensity, EORTC nausea with SDS nausea intensity, EORTC dyspnea with SDS breathing). Because the SDS fatigue item correlated higher with the EORTC fatigue scale than with the individual EORTC fatigue items, the scale was used for analysis. Items were omitted if overlap in assessment existed. Items were adjusted to allow comparison (i.e., the constipation and diarrhea items in EORTC were recalculated as a composite item to correspond to SDS symptom bowel function).

Statistical Analyses

According to Kim et al. (2005), items included in a symptom cluster should be better correlated with symptoms within the cluster than with items outside the cluster, in this case determined through Pearson correlations.

Cluster analysis with average linkage between groups was conducted with all items and scales to explore if a

different approach would lead to substantially different results. Because the subsequent factor analysis also is based on correlations (Hazard Munro, 2001), Pearson correlations were used as a distance measure in cluster analysis.

Factor analysis was used most commonly to identify symptom clusters in the literature. Therefore, in the current study, the authors present factor analysis with principal components analysis as extraction method and Varimax rotation of the resulting factor scores for this purpose. In line with Chow et al. (2007), the authors used random selections of 50% of the sample to verify stability in clusters derived from the factor analysis. Symptom clusters derived from factor analysis were examined for internal consistency with Cronbach alpha. All statistical calculations were performed using SPSS® (v.15.0) for Windows®.

Results

Demographic and medical characteristics of patients are presented in Table 2. This sample deviated from nonparticipants and the patient population in that the participants were younger and survived longer (Tishelman et al., 2005).

Correlations

To examine the existence of symptom clusters, Pearson correlations were calculated, with statistically significant relationships found between most items, as shown in Tables 3 and 4. Table 3 includes items from the EORTC in which two groups of symptoms could be regarded as symptom clusters. The first was bowel, pain, nausea, appetite loss, and fatigue (called "pain cluster"), with a median correlation of 0.34 for symptoms within the cluster (range 0.3–0.54) and median correlation of 0.21 among symptoms outside the cluster (range 0.02–0.45). The second cluster consisted of insomnia, mood, concentration, and outlook (called "mood cluster"), with median within cluster correlation of 0.33 (range 0.28–0.68) and outside the cluster of 0.19 (range 0.07–0.37).

Table 4 presents correlations for the symptoms based on SDS, which formed three clusters: a pain cluster, with median correlations within the cluster of 0.33 (range 0.24–0.49) and outside of 0.21 (range 0.11–0.44); a mood cluster, with median correlation within the cluster of 0.34 (range 0.25–0.53) and outside of 0.21 (range 0.06–0.33); and a third cluster based on correlation of 0.46 between breathing and cough (called respiratory cluster) and of 0.21 outside (range 0.06–0.44). Fatigue, although included in the pain cluster, correlated above 0.3 with the mood and respiratory clusters in both instruments.

Cluster Analysis

Hierarchical cluster analysis with Pearson correlations are presented in the dendrograms in Figures 1 and 2. In the first cluster analysis, symptoms from EORTC (see Figure 1) resulted in only one tight cluster of mood and outlook. A fairly tight relationship also was found between fatigue and appetite. Although the relationships were not very close, some trends could be distinguished in the cluster analysis: mood, outlook, concentration, and insomnia were separated from other symptoms, as were dyspnea and cough. Bowel function, nausea, pain, appetite, and fatigue showed some separation from other symptoms. The findings are fairly consistent with those from the correlations.

Symptoms from the SDS were included in the second cluster analysis (see Figure 2). The analysis shows a similar pattern as for EORTC items, with mood and outlook well separated from other symptoms. Mood, outlook, concentration, and insomnia are linked together, as are nausea, bowel function, and pain. Fatigue and appetite were closely related to one another, as were breathing and cough.

A mood cluster consisting of mood, outlook, concentration, and insomnia could be distinguished in both instruments. A respiratory cluster with dyspnea and cough, and a pain cluster consisting of pain, bowel issues, and nausea, also could be seen in both instruments. Appetite and fatigue are closely related to each other in both instruments and are related to the pain cluster in EORTC and the respiratory cluster in SDS.

Table 2. Patient Characteristics

Characteristic	$\bar{X}$	SD
Age (years)	64.5	10.4
Characteristic	**n**	**%**
Gender		
Male	209	52
Female	191	48
Education		
Elementary school (9 years)	185	46
High school (12 years)	75	19
Academic (more than 12 years)	128	32
Missing data	12	3
Civil status		
Married or cohabiting	254	64
Living alone	142	35
Missing data	4	1
Lung cancer histology		
Non-small cell lung cancer	339	85
Small cell lung cancer	56	14
Other	5	1
Disease stage		
I	11	3
II	19	4
IIIA	35	9
IIIB	78	19
IV	164	41
Unclassified tumor	23	6
Missing data	70	18

N = 400

Table 3. Pearson Correlations Between Items in the European Organisation for Research and Treatment of Cancer Questionnaires

Variable	Pain	Nausea	Appetite Loss	Fatigue	Insomnia	Mood	Concentration	Outlook	Dyspnea	Coughing
Bowel	0.304[a]	0.336[a]	0.338[a]	0.331[a]	0.127	0.088	0.214	0.156	0.169	–0.017
Pain	–	0.316[a]	0.34[a]	0.505[a]	0.262	0.193	0.306	0.171	0.23	0.113
Nausea	–	–	0.427[a]	0.386[a]	0.126	0.184	0.258	0.227	0.161	0.149
Appetite loss	–	–	–	0.535[a]	0.241	0.203	0.306	0.171	0.259	0.232
Fatigue	–	–	–	–	0.277	0.254	0.372	0.158	0.448	0.283
Insomnia	–	–	–	–	–	0.306[b]	0.317[b]	0.275[b]	0.155	0.187
Mood	–	–	–	–	–	–	0.35[b]	0.682[b]	0.234	0.145
Concentration	–	–	–	–	–	–	–	0.371[b]	0.121	0.177
Outlook	–	–	–	–	–	–	–	–	0.172	0.06
Dyspnea	–	–	–	–	–	–	–	–	–	0.281

[a] Pain symptom cluster
[b] Mood symptom cluster

Factor Analysis

Factor analysis was conducted with individual items and the fatigue scale from the EORTC (see Table 5) and individual items from the SDS (see Table 6). In both the EORTC and SDS, three almost identical clusters were found. EORTC included a pain cluster consisting of bowel issues, nausea, pain, appetite loss, and fatigue; a mood cluster with outlook, mood, concentration, and insomnia; and a respiratory cluster with cough and dyspnea. Fatigue showed high loadings in the first and third factors. These three clusters also were found in the SDS, although in different order, with insomnia, appetite, and fatigue loading on more than one factor (see Table 6).

To clarify correspondence in symptom clusters across instruments, a graph of each cluster is presented in Figure 3, with the SDS factor loadings on the y-axis and the EORTC factor loadings on the x-axis. The correspondence between items on both instruments is demonstrated by the linear distribution of symptoms in all three factors. Figure 3a indicates that bowel function, pain, and nausea compose a clear cluster, with appetite and fatigue closely related. Figure 3b presents the mood cluster, with concentration and insomnia showing somewhat lower factor loadings. Figure 3c shows the respiratory cluster, with moderately high loadings, particularly for fatigue, appetite, and insomnia.

Three additional factor analyses were conducted with both the EORTC and SDS using random selections of 50% of the original sample, which resulted in clusters similar to those in the full data set to a high degree. Concentration, in addition to fatigue, appetite loss, and insomnia, loaded on more than one factor (data not shown).

Cronbach alpha ranged from 0.44–0.71 for each factor (see Tables 5 and 6). In both instruments, the highest alpha was found for the mood cluster and the lowest for the respiratory cluster.

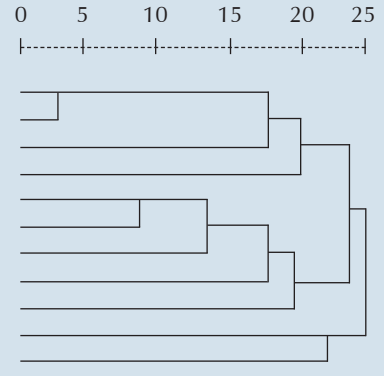
Discussion

Consistent symptom clusters were found for a large cohort of patients, with LC at a comparable point in their cancer trajectory, across different measurement tools and

Table 4. Pearson Correlations Between Items in the Symptom Distress Scale

Variable	Pain	Nausea	Appetite	Fatigue	Insomnia	Mood	Concentration	Outlook	Breathing	Cough
Bowel	0.33[a]	0.365[a]	0.37[a]	0.291[a]	0.207	0.219	0.308	0.162	0.2	0.176
Pain	–	0.304[a]	0.243[a]	0.396[a]	0.235	0.187	0.143	0.106	0.241	0.146
Nausea	–	–	0.338[a]	0.317[a]	0.168	0.29	0.217	0.193	0.206	0.202
Appetite	–	–	–	0.491[a]	0.331	0.318	0.148	0.18	0.269	0.313
Fatigue	–	–	–	–	0.28	0.306	0.243	0.159	0.443	0.369
Insomnia	–	–	–	–	–	0.406[b]	0.265[b]	0.252[b]	0.231	0.243
Mood	–	–	–	–	–	–	0.444[b]	0.533[b]	0.221	0.225
Concentration	–	–	–	–	–	–	–	0.254[b]	0.123	0.162
Outlook	–	–	–	–	–	–	–	–	0.062	0.071
Breathing	–	–	–	–	–	–	–	–	–	0.455[c]

[a] Pain symptom cluster
[b] Mood symptom cluster
[c] Respiratory symptom cluster



Note. Selected symptoms are from the European Organisation for Research and Treatment of Cancer QLQ-C30 and LC13.

Figure 1. Cluster Analysis Between Groups With Pearson Correlation as Method Using Average Linkage Between Groups With Rescaled Distance Cluster

statistical methods. This is an important finding, as the relevance of symptom cluster research is questionable if a lack of consistency across data collection and analysis approaches exist.

Instruments

Two instruments were used in these analyses. When comparing the results from the EORTC instruments with the SDS, the clusters derived were notably stable. In both instruments, fatigue loaded on more than one factor with similar findings for appetite and insomnia. One approach to this lack of clarity might be to set a threshold to discriminate factor loadings between clusters, which was not done in any of the reviewed articles. Another approach, which the authors feel is preferable, would be to consider clinical relevance. It may be that symptoms such as fatigue, appetite loss, and insomnia may be influential in more than one cluster. These symptoms may well affect patients in different ways, depending on their etiology, characteristics, and meaning to the individual.

None of the articles described in Table 1 used the EORTC instrument and only Sarna and Brecht (1997) used the SDS, albeit in a different language and version. Despite such differences, the authors found one SDS cluster similar to Sarna and Brecht's proposed cluster of breathing, cough, and insomnia. In the current study, cough and breathing constituted a stable cluster, whereas insomnia loaded on more than one factor. Numerous potential explanations exist for differences in results. The authors included only some items to ensure comparability with EORTC and had nearly equal numbers of men and women, as opposed to Sarna and Brecht's single-sex sample. Sarna and Brecht also divided their sample into more- or less-severe symptom score, which might well lead to different factor solutions.

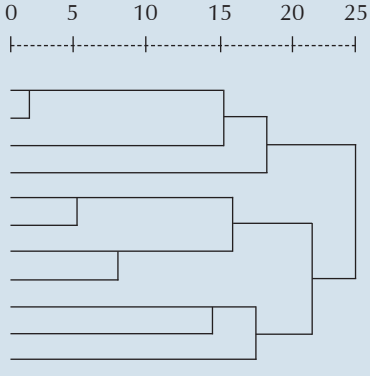
Analysis Strategies

The authors have not tried to reproduce exactly all the statistical methods used in the articles listed in Table 1. Instead, the authors have chosen three methods that are frequently used in symptom cluster research and cover a wide range of statistical sophistication. On the elementary and purely descriptive level, correlations within and between clusters are compared, as in Chen and Tseng (2006). On a more general level, hierarchical clustering are used, as in Walsh and Rybicki (2006), offering a range of different groupings of symptoms but no easy quantification of the strength of the relationship between individual symptoms and symptom clusters. Finally, factor analysis is employed as in Chow et al. (2007), which expresses the relationship between the underlying latent shared factors and the original symptoms via the factor loadings shown in Tables 5 and 6.

Exploratory techniques such as cluster analysis and factor analysis come in countless variants, which are not always clearly distinguished in the literature. Again, the authors have not attempted to be comprehensive, but have instead chosen, arguably, the most common variants: average linkage for hierarchical clustering and principal component extraction with varimax rotation for factor analysis. The authors also have chosen to use ordinary Pearson correlations throughout as a measure of similarity for symptom occurrence because the choice is common and because it facilitates comparison and reduces artificial variability introduced by using different statistical techniques.

Empirically Derived Symptom Clusters

To summarize the substantive findings, three relatively consistent clusters were found in all analyses and with both instruments: a pain cluster, a mood cluster, and a



Note. Selected symptoms are from the Symptom Distress Scale.

Figure 2. Cluster Analysis Between Groups With Pearson Correlation as Method Using Average Linkage Between Groups With Rescaled Distance Cluster

Table 5. Factor Analysis of the European Organisation for Research and Treatment of Cancer Items at First Interview

Symptom Cluster	Component 1[a]	2[b]	3[c]	Communality
Pain				
Bowel issues	0.74	0.053	–0.157	0.575
Nausea	0.673	0.15	0.053	0.477
Pain	0.632	0.164	0.187	0.462
Appetite loss	0.66	0.122	0.321	0.553
Fatigue	0.646	0.147	0.509	0.697
Mood				
Outlook	0.094	0.878	–0.054	0.783
Mood	0.047	0.862	0.125	0.762
Concentration	0.367	0.543	0.119	0.443
Insomnia	0.162	0.483	0.282	0.34
Respiratory				
Coughing	–0.024	0.074	0.808	0.659
Dyspnea	0.209	0.126	0.657	0.491

N = 386

[a] Cronbach alpha is 0.66; explained variance is 18.9%.

[b] Cronbach alpha is 0.58; explained variance is 18.4%.

[c] Cronbach alpha is 0.62; explained variance is 18.3%.

Note. Principal component analysis was the extraction method and varimax with Kaiser normalization was the rotation method. Cronbach alphas for the derived factors excluding items loading on more than one factor are shown.

respiratory cluster. In the reviewed literature, only Walsh and Rybicki (2006) included pain and bowel issues (constipation) in a cluster. A cluster consisting of mood and outlook is similar to the anxiety and depression cluster found by Chow et al. (2007) and the distress and sadness cluster reported by Chen and Tseng (2006). Cough only was included in two studies and was clustered with breathing (Sarna & Brecht, 1997; Walsh & Rybicki). These similarities are notable despite the marked differences in measurement methods, sample choice, and analysis approaches cited.

In factor and cluster analyses, results distinguish between physical symptoms (i.e., pain and respiratory clusters) and psychological symptoms (i.e., mood cluster). Although it is well recognized that disease and symptoms have effects on mood, the findings do not lend support to the use of a predetermined cluster of breathlessness, fatigue, and anxiety (Chan, Richardson, & Richardson, 2005). Although Dodd, Miaskowski, and Lee (2004) stated that the symptoms in a cluster must not share the same etiology, the authors did not find the breathlessness mood cluster expected from the literature (Henoch, Bergman, Gustafsson, Gaston-Johansson, & Danielson, 2008; Tanaka, Akechi, Okuyama, Nishiwaki, & Uchitomi, 2002). This raised the question of the relation between statistically derived symptom clusters and their relevance to patients' experiences. One explanation might be that this analysis concerns concurrent symptoms close to diagnosis, and that relationships between breathlessness and mood may be causal later in the illness trajectory. The diagnosis and initial adaptation to a changed life situation might be the most salient events affecting mood in this group of patients.

Fatigue and appetite appear to have an intermediate role with high loadings in pain and respiratory clusters. Fatigue correlated highly with symptoms in all clusters. Chow et al. (2007) also found that fatigue loaded on more than one factor, and Chen and Lin (2007) found this to be the case with appetite. In the reviewed literature, fatigue was clustered with different sets of symptoms (e.g., pain [Chen & Tseng, 2006; Chow et al.], drowsiness [Chen & Tseng; Chow et al.], sense of well-being [Chow et al.], nausea [Gift et al., 2004], weakness [Gift et al.; Walsh & Rybicki, 2006], appetite loss [Chen & Tseng; Gift et al.], weight loss [Gift et al.; Walsh & Rybicki], altered taste [Gift et al.; Walsh & Rybicki], vomiting [Gift et al.], sleep disturbances [Chen & Tseng], concentration [Sarna & Brecht, 1997], anorexia [Walsh & Rybicki], lack of energy [Walsh & Rybicki], dry mouth [Walsh & Rybicki], early satiety [Walsh & Rybicki], cognitive impairment [Bender et al., 2005], mood issues [Bender et al.]). This suggests that fatigue and appetite loss may be general consequences of many symptoms or contribute to the experience of other symptoms in manners needing additional clarification.

Table 6. Factor Analysis of the Symptom Distress Scale Items at First Interview

Symptom Cluster	Component 1[a]	2[b]	3[c]	Communality
Pain				
Bowel issues	0.174	0.744	0.048	0.586
Nausea intensity	0.194	0.676	0.096	0.503
Pain intensity	0.021	0.684	0.172	0.498
Appetite	0.211	0.479	0.439	0.467
Fatigue	0.153	0.461	0.599	0.595
Mood				
Outlook	0.781	0.055	–0.041	0.615
Mood	0.823	0.136	0.207	0.738
Concentration	0.615	0.238	0.038	0.437
Insomnia	0.522	0.119	0.369	0.422
Respiratory				
Cough	0.104	0.037	0.791	0.638
Breathing	0.031	0.139	0.785	0.637

N = 388

[a] Cronbach alpha is 0.66; explained variance is 18.9%.

[b] Cronbach alpha is 0.58; explained variance is 18.4%.

[c] Cronbach alpha is 0.62; explained variance is 18.3%.

Note. Principal component analysis was the extraction method and varimax with Kaiser normalization was the rotation method. Cronbach alphas for the derived factors excluding items loading on more than one factor are shown.

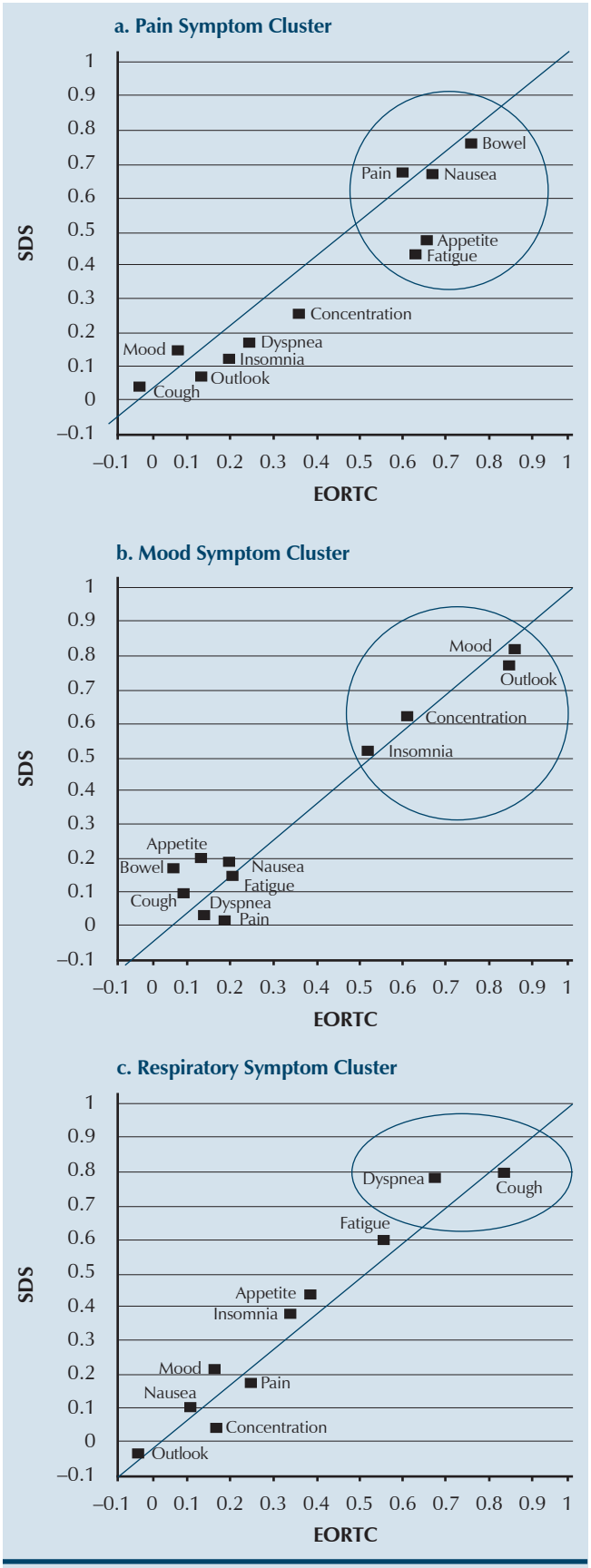


Figure 3. Scatter Plot of the Factor Loadings From Factor Analysis of the European Organisation for Research and Treatment of Cancer (EORTC) Scale and the Symptom Distress Scale (SDS)

Implications for Nursing

Oncology healthcare providers are aware that symptoms often cluster simultaneously in patients with cancer, with a rapidly increasing body of knowledge indicating that these clusters are not random occurrences. In this article, the authors have shown that the pain, mood, and respiratory clusters were stable across instruments and analyses in this relatively homogenous patient group. Fatigue, appetite loss, insomnia, and concentration were all found to be related to more than one symptom cluster. The characteristics of these symptoms should be further examined in relation to the more demarcated symptom clusters. Nurses and other healthcare professionals should be observant that these symptoms may have different etiologies and may be interrelated with a variety of symptoms in different clusters.

The authors found that factor analysis based on Pearson correlations extracted highly consistent symptom clusters from the matched items of two different measurement tools. Given the wider range of interpretation and inference compared to the other methods employed in this article, the authors suggest that factor analysis is the most suitable tool for the empirical exploration of potential symptom clusters.

Symptom cluster research is still in its infancy, with additional research needed before this area has direct clinical relevance. Two major issues that will need to be addressed are the consistency of symptom clusters over time as well as the consequences of symptom clusters on patients' experiences. Additional applied research is needed to guide evidence-based management of all symptoms in a symptom cluster. A pronounced need exists to foster congruence in measurements and analyses to build a consistent body of knowledge to aid in alleviating symptom-related suffering for patients with cancer.

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Ingela Henoch, RN, PhD, is a postdoctoral fellow at Karolinska Institutet, Institution of Learning, Informatics, Management, and Ethics, Medical Management Centre in Stockholm, Sweden, and researcher in the Research Unit of the Bräcke Diakoni Foundation in Göteborg, Sweden; Alexander Ploner, PhD, is a researcher in the Department of Medical Epidemiology and Biostatistics at Karolinska Institutet; and Carol Tishelman, RN, PhD, is a professor of nursing at Karolinska Institutet, Institution of Learning, Informatics, Management, and Ethics, Medical Management Centre, with affiliations with the University of Manchester, School of Nursing, Midwifery, and Social Work in Manchester, UK, and Sjukhem Foundation Research and Development Unit/Palliative Care in Stockholm. No financial relationships to disclose. Henoch can be reached at ingela.henoch@ki.se, with copy to editor at ONFEditor@ons.org. (Submitted August 2008. Accepted for publication February 22, 2009.)

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