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Journal

Supportive Care in Cancer, 30(8)

ISSN

0941-4355

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Publication Date

2022-08-01

DOI

10.1007/s00520-022-07125-z

Peer reviewed

HHS Public Access

Author manuscript

Support Care Cancer. Author manuscript; available in PMC 2024 January 17.

Published in final edited form as:

Support Care Cancer. 2022 August ; 30(8): 6889–6899. doi:10.1007/s00520-022-07125-z.

Symptom Clusters in Outpatients with Cancer Using Different Dimensions of the Symptom Experience

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Abstract

Purpose: Relatively few studies have evaluated for symptom clusters across multiple dimensions. It is unknown whether the symptom dimension used to create symptom clusters influences the number and types of clusters that are identified. Study purposes were to describe ratings of occurrence, severity, and distress for 38 symptoms in a heterogeneous sample of oncology patients (n=1329) undergoing chemotherapy; identify and compare the number and types of symptom clusters based on three dimensions (i.e., occurrence, severity, and distress); and identify common and distinct clusters.

Methods: A modified version of the Memorial Symptom Assessment Scale was used to assess the occurrence, severity, and distress ratings of 38 symptoms in the week prior to patients' next cycle of chemotherapy. Symptom clusters for each dimension were identified using exploratory factor analysis.

Results: Patients reported an average of 13.9 (±7.2) concurrent symptoms. Lack of energy was both the most common and severe symptom while "I don't look like myself" was the most

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Authors' Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Dr. Miaskowski, Dr. Cooper, and Dr. Paul. The first draft of the manuscript was written by Ms. Harris and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Availability of Data and Material

Available with reasonable request.

Ethics Approval

The study procedures were approved by the Committee on Human Research at the University of California, San Francisco and the Institutional Review Board at each of the study sites. This study was performed in accordance with the ethnical standards as laid down in the 1964 Helsinki Declaration.

Consent to Participate

Informed consent was obtained from all individual participants included in this study.

distressing. Psychological, gastrointestinal, weight gain, respiratory, and hormonal clusters were identified across all three dimensions. Findings suggest that psychological, gastrointestinal, and weight gain clusters are common while respiratory and hormonal clusters are distinct.

Conclusions: Psychological, gastrointestinal, weight gain, hormonal, and respiratory clusters are stable across occurrence, severity, and distress in oncology patients receiving chemotherapy. Given the stability of these clusters and the consistency of the symptoms across dimensions, use of a single dimension to identify these clusters may be sufficient. However, comprehensive and disease-specific inventories need to be used to identify distinct clusters.

Keywords

cancer; chemotherapy; symptoms; symptom clusters

INTRODUCTION

Patients receiving chemotherapy report between 10 [1] to 14.5 [2] concurrent symptoms. While these data fostered symptom clusters' research [3, 4], progress in this area of scientific inquiry is limited by multiple unanswered questions [5–7]. One question is whether the symptom dimension (i.e., occurrence, severity, distress) impacts the number and types of symptom clusters that are identified. As highlighted in one systematic review of symptom clusters in patients receiving adjuvant chemotherapy [7], less than half of the 23 studies evaluated for symptom clusters across two or more symptom dimensions. A second question that warrants investigation is the determination of which clusters are common and distinct across various types of cancer [5]. The answers to these questions will guide clinical assessments and inform mechanistic-based studies.

Nine cross-sectional studies evaluated for symptom clusters in heterogeneous samples receiving chemotherapy [8–16]. Six studies used a single symptom dimension to identify the clusters [8–10, 12, 15, 16], two used two or more dimensions [11, 13], and one did not report the dimension used in the analysis [14]. Across these nine studies, the number of clusters varied from three to eight. While a psychological cluster was the only common one across seven of these studies [8–10, 12, 13, 15, 16], none of them contained the same symptoms. This variability in both the types of clusters and symptoms within the clusters is related to heterogeneity in the symptom inventories used; number of symptoms evaluated; timing of the assessments; and statistical methods used. Because of these differences, one cannot determine if the number and types of symptom clusters vary based on the dimensions used to create the clusters. In addition, these data suggest that the only common cluster, in samples with heterogeneous types of cancer, is a psychological one.

While we previously evaluated for symptom clusters across two or more symptom dimensions in patients with breast [17], gastrointestinal [18], gynecological [19], or lung [20] cancer using exploratory factor analysis (EFA), we have not used EFA to evaluate for symptom clusters in the entire sample. In addition, we recently reported on the results of a network analysis (NA) of symptom clusters in the combined sample [13]. A comparison of the number and types of symptom clusters that were identified for each type of cancer diagnosis to those that are identified for the combined sample, as well as a comparison of

findings using different analytic approaches [5], will allow for the generation of hypotheses related to common and unique symptom clusters in oncology patients.

Therefore, the purposes of this study were to describe ratings of occurrence, severity, and distress for 38 symptoms in a heterogeneous sample of oncology patients undergoing chemotherapy and identify and compare the number and types of symptom clusters based on three symptom dimensions (i.e., occurrence, severity, and distress). In addition, an evaluation of common and distinct symptom clusters was done for the total sample compared to four distinct types of cancer (i.e., breast [17], gastrointestinal [18], gynecological [19], lung [20]) and for two different methods (i.e., EFA, NA[13]).

METHODS

Patients and Settings

This analysis is part of a larger study that evaluated symptom clusters in oncology outpatients receiving chemotherapy [13, 17–20]. Eligible patients were ≥18 years of age; had a diagnosis of breast, lung, gastrointestinal, or gynecologic cancer; had received chemotherapy within the preceding four weeks; were scheduled to receive at least two additional cycles of chemotherapy; were able to read, write, and understand English; and gave written informed consent. Patients were recruited from two Comprehensive Cancer Centers, one Veteran's Affairs hospital, and four community-based oncology programs. Of the 1343 patients enrolled, 1329 patients had complete Memorial Symptom Assessment Scale (MSAS) data.

Procedures

Eligible patients were approached during their first or second cycle of chemotherapy and provided written informed consent. Patients completed questionnaires in their home and returned them in a postage paid envelope, six times over two cycles of chemotherapy. Data from the enrollment assessment (symptoms in the week before the patient's second or third cycle of chemotherapy) were used in these analyses. Medical records were reviewed for disease and treatment information. This study was approved by the Committee on Human Research at the University of California, San Francisco.

Instruments

Patients completed a demographic questionnaire, Karnofsky Performance Status (KPS) scale [21], and Self-Administered Comorbidity Questionnaire [22]. Toxicity of each patient's chemotherapy regimen was rated using the MAX2 index [23, 24].

A modified version of the 32-item MSAS was used to evaluate the occurrence, severity, and distress of 38 common symptoms associated with cancer and its treatment [25]. Six common symptoms were added: hot flashes, chest tightness, difficulty breathing, abdominal cramps, increased appetite, and weight gain. Using the MSAS, patients reported whether they had experienced each symptom in the past week. If they had experienced the symptom, they were asked to rate its severity and distress. Severity was measured using a four-point Likert scale (i.e., 1 = slight, 2 = moderate, 3 = severe, 4 = very severe). Distress was measured

using a five-point Likert scale (i.e., 0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much). The validity and reliability of the MSAS are well established [25].

Data Analysis

Descriptive statistics and frequency distributions were calculated for the demographic and clinical characteristics, as well as symptom occurrence rates and severity and distress ratings using the Statistical Package for the Social Sciences Version 27 (IBM Corporation, Armonk, NY). EFA was used to identify symptom clusters using Mplus Version 8.6 [26].

For the EFA, factor loadings were considered meaningful if the loading was ≥0.40 [26]. In addition, factors were considered to be adequately defined if at least two items (i.e., symptoms) had loadings of ≥0.40 [27]. Items were allowed to load on two factors (i.e., cross-load) if they fell within our preset criteria of ≥0.40. For the EFA of the occurrence items, tetrachoric correlations were used to create the matrix of associations [26]. For the EFAs of the severity and distress ratings, polychoric correlations were used to create the matrix of associations. The simple structure for the occurrence, severity, and distress EFAs were estimated using the method of unweighted least squares with geomin (i.e., oblique) rotation. The unweighted least squares estimator was selected to achieve more reliable results with the dichotomous (i.e., occurrence) and ordinal (i.e., severity, distress) items [26].

The EFA for severity was done using severity ratings that included a zero (i.e., 0, 1, 2, 3, 4). If the patient indicated that they did not have the symptom, a severity score of zero was assigned. The EFA for distress was done using distress ratings that included a zero (did not have the symptom) and the original ratings shifted from 1 (not at all) to 5 (very much). The initial EFA analyses were done using severity and distress ratings that did not include zero (i.e., 1, 2, 3, 4, 5). However, the pairwise missingness (i.e., 1-covariance coverage for each of the item pairs) was over 90% and the estimation failed to converge.

Factor solutions were estimated for two through five factors. The factor solution with the greatest interpretability and clinical meaningfulness was selected given that it met the criteria set for evaluating simple structure (i.e., size of item loadings, number of items on a factor). Then, each factor solution was examined to determine a clinically appropriate name for the symptom cluster. Clusters were named based on the symptoms with the highest factor loadings and the majority of the symptoms within the cluster.

Differences in Number and Types of Clusters

To evaluate percent agreement among the symptoms within the same cluster using occurrence, severity, and distress ratings, previous studies by our group [17–20, 28–31] and others [32, 33] used the criteria proposed by Kirkova and Walsh [34]. They suggested that to be in agreement with each other, at least 75% of the symptoms in the cluster should be present including the prominent and most important symptom (i.e., symptom with the largest factor loading).

While Kirkova and Walsh [34] used the term “stability” to describe these criteria, the definition and use of stability within symptom cluster research is inconsistent [7] and has led to the subjective application of these criteria. Therefore, in this study, the term *stability*

is used to describe whether or not the same clusters are identified across dimensions and/or studies. In contrast, *consistency* is used to describe whether the specific symptoms within a cluster remain the same across symptom dimensions (i.e., percent agreement among the symptoms within the cluster).

RESULTS

Demographic and Clinical Characteristics

Of the 1329 patients in this study, 77.8% were female, 69.9% were White, 64.4% were married or partnered, and had a mean age of 57.3 (±12.3) years (Table 1). While the majority (60.4%) reported a mean household annual income of ≥$70,000, only 35.1% were currently employed. Most patients were well-educated (16.2 ±3.0 years), exercised on a regular basis (70.9%), and had never smoked (64.7%). Patients had 2.4 (±1.4) comorbid conditions and an average KPS score of 80.1 (±12.4). On average, patients reported 13.9 (±7.2) concurrent symptoms before their second or third cycle of chemotherapy.

Symptom Prevalence

Lack of energy was the most common symptom (Table 2). Mean severity ratings were calculated in two ways (i.e., with and without zeros). When zeros were included in the calculation, lack of energy was the most severe symptom. In the “without zeros” analyses, hair loss was rated as the most severe symptom. “I don’t look like myself” was the most distressing symptom.

Occurrence Clusters

Five-factor solution was selected for the occurrence EFA (Table 3). Psychological cluster had six symptoms and worrying had the highest factor loading. Gastrointestinal cluster had 11 symptoms and lack of appetite had the highest factor loading. Weight gain cluster had two symptoms and weight gain had the highest factor loading. Hormonal cluster had two symptoms and hot flashes had the highest factor loading. Respiratory cluster had four symptoms and difficulty breathing had the highest factor loading.

Severity Clusters

Five-factor solution was selected for the severity EFA (Table 3). Psychological cluster had five symptoms and worrying had the highest factor loading. Gastrointestinal cluster had 10 symptoms and lack of appetite had the highest factor loading. Weight gain cluster had two symptoms and weight gain had the highest factor loading. Hormonal cluster had two symptoms and hot flashes had the highest factor loading. Respiratory cluster had four symptoms and difficulty breathing had the highest factor loading.

Distress Clusters

Five-factor solution was selected for the distress EFA (Table 3). Psychological cluster had six symptoms and worrying had the highest factor loading. Gastrointestinal cluster had nine symptoms and lack of appetite had the highest factor loading. Weight gain cluster had two symptoms and weight gain had the highest factor loading. Hormonal cluster had

two symptoms and hot flashes had the highest factor loading. Respiratory cluster had four symptoms and difficulty breathing had the highest factor loading.

Stability and Consistency

Five stable clusters were identified across all three symptom dimensions (Table 3). Across all five clusters, the symptom with the highest factor loading was the same across all three dimensions. In terms of consistency, for psychological cluster, consistency ranged from 83.3% (severity) to 100% (occurrence, distress). For gastrointestinal cluster, consistency ranged from 75.0% (distress) to 91.7% (occurrence). For weight gain, hormonal, and respiratory clusters, consistency was 100% across the three dimensions.

DISCUSSION

Findings from this study provide new information on the occurrence, severity, and distress of 38 symptoms in a large, heterogeneous sample of oncology patients. In the week prior to their second or third cycle of chemotherapy, patients reported on average 13.9 symptoms. Consistent with previous studies of patients receiving chemotherapy, lack of energy was the most common and severe symptom [8, 9, 15]. However, as noted previously [18, 19, 35], the most common symptoms are not always the most distressing. Hair loss was rated as the most severe symptom when zeros were not included in the mean severity scores, while “I don’t look like myself” was the most distressing. Based on these findings, to have a more complete picture of the impact of individual symptoms, multiple dimensions of the symptom experience warrant evaluation.

Using findings from the literature, as well as our previous EFAs for breast [17], gastrointestinal [18], gynecological [19], and lung [20] cancers, and our NA for the entire sample [13], the remainder of this discussion describes the common and distinct symptom clusters (Table 4).

Psychological Cluster

Consistent with two reviews that reported that a psychological cluster was one of the most common clusters in patients receiving chemotherapy [6, 7], this cluster was identified across all three symptom dimensions. Therefore, it is not surprising that a psychological cluster was identified in our previous studies of four types of cancer [17–20] as well as in our NA [13]. In this cluster, the most consistent symptoms across dimensions, cancer types, and analytic methods were: worrying, feeling sad, feeling nervous, and feeling irritable. Taken together, these findings suggest that a psychological cluster is stable across various cancer types and can be identified using any symptom dimension. Given its stability, psychological symptoms need to be routinely assessed in all oncology patients.

Gastrointestinal Cluster

Across studies of patients receiving chemotherapy [6, 7], a gastrointestinal cluster was identified repeatedly using ratings of occurrence, severity, and distress. Given chemotherapy affects rapidly dividing cells, its impact on the gastrointestinal tract results in a constellation of symptoms [36]. While nausea, vomiting, and diarrhea are the most consistent symptoms

within this cluster [6, 7], in the current study, lack of appetite, weight loss, nausea, change in the way food tastes, vomiting, difficulty swallowing, diarrhea, abdominal cramps, and dry mouth were consistent across the three dimensions.

When compared with our previous studies of individual types of cancer [17–20], as well as the NA of the total sample [13], the names of this cluster, as well as the specific symptoms were not consistent. For example, abdominal cramps was the only symptom that was consistent across these studies and dimensions. In addition, the “gastrointestinal” cluster identified in patients with gynecological or lung cancer included multiple symptoms related to the epithelium (e.g., changes in skin, itching). This variability has a number of plausible explanations, including: differential effects of specific chemotherapy regimens on the gastrointestinal mucosa; differential effects of the cancer itself (e.g., colon cancer versus breast cancer) on the gastrointestinal tract; differential perceptions of a specific symptom in terms of its severity versus its distress; and/or variations in the relationships among various symptoms that are associated with specific types of cancer (e.g., feeling bloated in gastrointestinal cancers). Despite these variations, given the identification of a gastrointestinal cluster across multiple independent samples [8, 9, 12, 32, 33, 37–39], this cluster can be considered stable. Additional research is warranted to determine the specific factors that contribute to subtle variations in the consistency of symptoms within this cluster.

Weight Gain Cluster

In the current study, a weight gain cluster was identified that included weight gain and increased appetite across all three symptom dimensions. However, across previous studies with heterogeneous cancer types [10, 13, 15, 16], as well as in our own studies with specific cancer diagnoses [17–20], this cluster was highly variable both in terms of stability and consistency. For example, in a study of patients with hematologic malignancies [10], lack of appetite, taste changes, and nausea were included in an appetite cluster. In another study of older cancer patients with a variety of solid tumors [15], lack of appetite, change in the way food tastes, constipation, weight loss, and “I do not look like myself” were identified as a nutrition cluster. In our work [13, 17–20], weight gain was the only consistent symptom across cancer types, analytic methods, and dimensions.

Variability, in both stability and consistency, across studies may be due to differences in the types of chemotherapy received, medications patients are taking, and/or the location of tumors in or near the digestive system. Another factor that may contribute to variability is the symptom assessment instrument that was used. In our [13, 17–20] and one of the aforementioned studies [10], modified versions of the MSAS were used that included multiple symptoms related to appetite and nutrition. Studies that use an instrument with fewer symptoms will not be able to identify a weight- or nutrition-related cluster. Given that changes in nutritional status can lead to a variety of comorbidities (e.g., diabetes) [40], comprehensive nutritional assessments are a vital component of cancer care.

Respiratory Cluster

Respiratory cluster, that included difficulty breathing, shortness of breath, chest tightness, and cough, was found across all three dimensions. In our previous studies, a respiratory

cluster was identified in the total sample using NA [13] and in patients with gynecological [19] and lung [20] cancer across two or more dimensions; but not in patients with breast [17] or gastrointestinal [18] cancers. In addition, across two studies that evaluated for symptom clusters in a heterogeneous sample [15, 38], only one identified a respiratory cluster [38]. The inconsistent identification of this cluster suggests that it may be unique to certain cancer types. These differences may be related to tumor locations and/or conditions that are more common to specific diagnoses (e.g., ascites, pleural effusion).

Hormonal Cluster

Hormonal cluster was identified that included hot flashes and sweats across all three symptom dimensions. In another study that compared symptom clusters that were identified in younger (<60 years) and older (≥60 years) patients receiving chemotherapy [15], a hormonal cluster was identified in only the younger group. The identification of this cluster in younger patients supports the hypothesis that this cluster may emerge during/following cancer treatments that induce menopause [41, 42].

In addition, this cluster may be unique to specific cancer diagnoses. For example, a type of hormonal cluster (i.e., menopausal, vasomotor) was identified in women with breast [39] and ovarian [43] cancer. In addition, among our previous analyses [13, 17–20], a hormonal cluster was identified in the total sample using NA, and in women with breast [17] and gynecological [19] cancer across two or more symptom dimensions. Across all symptom dimensions within these three studies [13, 17, 19], hot flashes and sweats were consistent. Of note, studies that do not use disease-specific or comprehensive symptom inventories will not be able to identify this distinct cluster in patients with breast or gynecological cancers, and perhaps in men with prostate cancer.

Comparison with Network Analysis

Identification of psychological, gastrointestinal, weight gain or nutritional, hormonal, and respiratory clusters using EFA is consistent with our previous NA of the total sample [13]. For both analyses, the symptoms within the psychological, hormonal, and respiratory clusters were relatively consistent across all three symptom dimensions. While both studies identified a gastrointestinal cluster, this cluster was only identified using distress in the NA. While both analytic approaches use measures of correlation to identify clusters, they differ in key ways. In our previous NA [13], symptom clusters were identified using the Walktrap algorithm and all symptoms within the network were retained regardless of the strength of the relationship between and among symptoms. For the EFAs, because the symptoms needed to have a factor loading ≥0.40, 13 to 15 symptoms did not load on one or more clusters. The advantages and disadvantages of various analytic methods need to be explored in future studies with large samples.

A number of limitations warrant consideration. Because our previous studies of patients with breast [17] and lung [20] cancer used only two symptom dimensions (i.e., occurrence, severity) to identify symptom clusters, our evaluation of the stability and consistency of clusters using distress warrants additional research. Given the study's cross-sectional design, additional research needs to determine which clusters remain stable across dimensions,

cancer diagnoses, and/or time. Given that the occurrence and severity of symptoms may be influenced by specific chemotherapy drugs, additional research is warranted on the stability and consistency of symptom clusters across different chemotherapy regimens. While these findings suggest that respiratory and hormonal clusters are distinct clusters that occur with specific types of cancer, the proportions of patients with a gynecological (i.e., 17.5%) or lung (i.e., 11.7%) cancer were relatively small. In addition, our sample was primarily White and well-educated, which limits the generalizability of our findings.

CONCLUSION

Our findings suggest that psychological, gastrointestinal, weight gain, hormonal, and respiratory clusters are stable across occurrence, severity, and distress prior to the start of the next cycle of chemotherapy. Given the stability of these clusters across dimensions and the consistency of the symptoms within the clusters, they can be identified using any dimension of the symptom experience. However, for any single symptom, multiple dimensions of the symptom experience warrant evaluation to assess its full impact on a patient.

In addition, these findings suggest that gastrointestinal, psychological, and nutrition or weight change clusters are common across cancer types. Given the stability of these clusters across diagnoses, future research should explore whether these clusters share common biological mechanisms. Furthermore, additional research is needed to evaluate whether these clusters remain stable over time and across other cancer treatments (e.g., radiation therapy, surgery). Conversely, hormonal and respiratory clusters may be unique to specific cancer types. Symptoms within these distinct clusters need to be assessed in patients with breast, gynecological, or lung cancer in the clinical and research settings.

Funding

This work was supported by a grant from the National Cancer Institute (NCI, CA134900). Ms. Harris is supported by a grant from the American Cancer Society and the National Institute of Nursing Research of the National Institutes of Health (T32NR016920). The content is solely the responsibilities of the authors and does not necessarily represent the official views of the National Institutes of Health. Dr. Miaskowski is an American Cancer Society Clinical Research Professor.

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Table 1.

Demographic and Clinical Characteristics of the Patients (n=1329)

Characteristic	Mean	SD
Age (years)	57.3	12.3
Education (years)	16.2	3
Body mass index (kilograms/meters squared)	26.2	5.7
Karnofsky Performance Status score	80.1	12.4
Number of comorbidities out of 13	2.4	1.4
Self-administered Comorbidity Questionnaire score	5.5	3.2
Time since cancer diagnosis (years)	2	3.9
Time since diagnosis (median)	0.42	
Number of prior cancer treatments (out of 9)	1.6	1.5
Number of metastatic sites including lymph node involvement (out of 9)	1.2	1.2
Number of metastatic sites excluding lymph node involvement (out of 8)	0.8	1
MAX2 Index of Chemotherapy Toxicity score (0 to 1)	0.17	0.08
Mean number of MSAS symptoms (out of 38)	13.9	7.2
	n	(%)
Gender		
Female	1033	77.8
Male	295	22.2
Ethnicity		
White	917	69.9
Black	95	7.2
Asian or Pacific Islander	161	12.3
Hispanic, Mixed, or Other	139	10.6
Married or partnered (% yes)	843	64.4
Lives alone (% yes)	283	21.6
Child care responsibilities (% yes)	286	22
Care of adult responsibilities (% yes)	95	7.9
Currently employed (% yes)	462	35.1
Income		

Characteristic	Mean	SD
< $30,000	219	18.4
$30,000 to < $70,000	252	21.2
$70,000 to < $100,000	199	16.7
≥ $100,000	520	43.7
Exercise on a regular basis (% yes)	922	70.9
Current or history of smoking (% yes)	462	35.3
Type of cancer		
Breast	534	40.2
Gastrointestinal	407	30.6
Gynecological	233	17.5
Lung	155	11.7
Type of prior cancer treatment		
No prior treatment	323	25
Only CTX, surgery, or RT	543	42
CTX and surgery, or CTX and RT, or surgery and RT	257	19.9
CTX and surgery and RT	169	13.1
Cycle length	558	42.1
14 days	671	50.6
21 days	97	7.3
28 days		
Emetogenicity of the chemotherapy regimen		
Minimal/low	259	19.5
Moderate	810	61
High	258	19.4
Antiemetic regimen		
None	92	7.1
Steroid alone or serotonin receptor antagonist alone	265	20.4
Serotonin receptor antagonist and steroid	618	47.7
NK-1 receptor antagonist and two other antiemetics	321	24.8

Table 2.

Occurrence Rates and Severity and Distress Ratings for Symptoms Prior to Chemotherapy

Symptoms[a]	Occurrence Rates[b]		Severity Ratings with Zeros[c]		Severity Ratings without Zeros[d]		Distress Ratings[e]	
	n	%	Mean	SD	Mean	SD	Mean	SD
Lack of energy	1106	83.2	1.67	1.01	2.02	0.72	1.79	1.14
Difficulty sleeping	918	69.1	1.38	1.13	2.01	0.76	1.79	1.11
Pain	803	60.4	1.14	1.10	1.92	0.73	1.77	1.10
Feeling drowsy	801	60.3	1.04	1.01	1.75	0.70	1.16	1.05
Hair loss	728	54.8	1.35	1.49	2.49	1.12	1.88	1.34
Numbness/tingling in hands/feet	694	52.2	0.94	1.09	1.84	0.81	1.52	1.18
Worrying	692	52.1	0.94	1.06	1.85	0.74	1.63	1.04
Difficulty concentrating	690	51.9	0.79	0.90	1.55	0.64	1.48	1.07
Change in the way food tastes	656	49.4	1.04	1.23	2.12	0.89	1.72	1.26
Nausea	631	47.5	0.82	1.04	1.76	0.81	1.65	1.12
Feeling sad	612	46.0	0.77	0.97	1.71	0.71	1.50	1.06
Dry mouth	603	45.4	0.77	1.00	1.73	0.75	1.23	1.12
Constipation	578	43.5	0.84	1.12	1.98	0.83	1.70	1.17
Feeling irritable	549	41.3	0.69	0.95	1.70	0.72	1.46	1.03
Lack of appetite	549	41.3	0.78	1.07	1.92	0.79	1.28	1.11
Feeling nervous	505	38.0	0.59	0.88	1.62	0.68	1.41	0.98
“I don’t look like myself”	503	37.8	0.80	1.18	2.15	0.93	1.98	1.22
Changes in skin	482	36.3	0.68	1.03	1.91	0.81	1.64	1.19
Feeling bloated	440	33.1	0.58	0.93	1.79	0.73	1.54	1.07
Cough	433	32.6	0.45	0.75	1.42	0.62	1.02	1.08
Hot flashes	423	31.8	0.58	0.98	1.87	0.81	1.42	1.16
Dizziness	416	31.3	0.46	0.79	1.51	0.69	1.24	0.98
Sweats	415	31.2	0.53	0.92	1.77	0.78	1.29	1.09
Problems with sexual interest or activity	397	29.9	0.71	1.24	2.47	0.98	1.87	1.28
Diarrhea	393	29.6	0.54	0.95	1.87	0.81	1.46	1.13
Shortness of breath	357	26.9	0.44	0.82	1.67	0.71	1.51	1.04

Symptoms[a]	Occurrence Rates[b]		Severity Ratings with Zeros[c]		Severity Ratings without Zeros[d]		Distress Ratings[e]	
	n	%	Mean	SD	Mean	SD	Mean	SD
Increased appetite	344	25.9	0.44	0.83	1.75	0.68	0.91	1.11
Weight gain	337	25.4	0.39	0.76	1.58	0.70	1.37	1.33
Weight loss	335	25.2	0.38	0.76	1.56	0.71	0.96	1.17
Itching	330	24.8	0.41	0.82	1.71	0.74	1.28	1.07
Abdominal cramps	299	22.5	0.40	0.84	1.87	0.75	1.61	1.08
Mouth sores	278	20.9	0.34	0.76	1.70	0.74	1.46	1.06
Difficulty breathing	265	19.9	0.32	0.72	1.64	0.72	1.63	1.13
Chest tightness	237	17.8	0.27	0.64	1.54	0.67	1.42	1.00
Swelling of arms or legs	194	14.6	0.27	0.74	1.91	0.83	1.62	1.16
Problems with urination	187	14.1	0.24	0.68	1.79	0.80	1.51	1.21
Difficulty swallowing	183	13.8	0.23	0.66	1.73	0.82	1.64	1.15
Vomiting	164	12.3	0.21	0.66	1.80	0.90	1.74	1.18

Table 3.

Comparison of Symptom Clusters Prior to Initiation of Chemotherapy Using Ratings of Occurrence, Severity, and Distress[a]

Cluster	Symptoms	Occurrence	Severity	Distress
Psychological symptom cluster	Worrying	0.864	0.866	0.875
	Feeling sad	0.855	0.850	0.872
	Feeling nervous	0.744	0.750	0.760
	Feeling irritable	0.626	0.569	0.574
	Difficulty concentrating	0.549	0.517	0.560
	“I don’t look like myself”	0.458	–	0.427
	Total number of symptoms in this cluster	6/6	5/6	6/6
Gastrointestinal symptom cluster	Lack of appetite	0.784	0.774	0.770
	Weight loss	0.679	0.658	0.680
	Nausea	0.663	0.624	0.612
	Change in the way food tastes	0.612	0.690	0.677
	Vomiting	0.546	0.538	0.525
	Difficulty swallowing	0.513	0.517	0.503
	Abdominal cramps	0.455	0.472	0.444
	Diarrhea	0.433	0.483	0.455
	Dry mouth	0.431	0.472	0.474
	Constipation	0.430	–	–
	Dizziness	0.404	–	–
	Mouth sores	–	0.420	–
	Total number of symptoms in this cluster	11/12	10/12	9/12
Weight gain symptom cluster	Weight gain	0.921	0.875	0.914
	Increased appetite	0.785	0.746	0.736
	Total number of symptoms in this cluster	2/2	2/2	2/2
Hormonal symptom cluster	Hot flashes	0.883	0.907	0.920
	Sweats	0.670	0.728	0.647
	Total number of symptoms in this cluster	2/2	2/2	2/2
Respiratory symptom cluster	Difficulty breathing	1.037	1.032	1.035
	Shortness of breath	0.716	0.763	0.741
	Chest tightness	0.689	0.614	0.628
	Cough	0.457	0.430	0.427
	Total number of symptoms in this cluster	4/4	4/4	4/4

Table 4.

Comparison of Symptom Clusters Across Cancer Types and Analytic Methods Using Ratings of Occurrence, Severity, and Distress

Symptom dimension	Symptom cluster	EFA n=1329	NA[a] n=1328	Breast[b] n=534	GI[c] n=399	GYN[d] n=232	Lung[e] n=145
Occurrence	Psychological	X	X	X	X	X	X
	GI	X		X	X	X	
	Epithelial/GI						X
	Epithelial			X			
	Nutritional		X				X
	Weight change			X	X	X	
	Weight gain	X					
	Hormonal	X	X	X		X	
	Respiratory	X	X			X	
	Lung CA-specific						X
	CTX related		X		X		
	Sickness behavior			X			X
	Pain and abdominal		X				
Severity	Psychological	X	X	X	X	X	X
	GI	X		X	X		
	GI/epithelial					X	
	Epithelial/GI						X
	Epithelial			X			
	Nutritional		X				X
	Weight change			X	X	X	
	Weight gain	X					
	Hormonal	X	X	X		X	
	Respiratory	X	X			X	
	Lung CA-specific						X
	CTX related		X		X		
	Sickness behavior			X			
Distress	Psychological	X	X	Not assessed	X		Not assessed
	Psychological/GI					X	
	GI	X	X		X		
	GI/epithelial					X	
	Epithelial		X				
	Nutritional		X				
	Weight change				X	X	
	Weight gain	X					
	Hormonal	X	X			X	

Symptom dimension	Symptom cluster	EFA n=1329	NA[a] n=1328	Breast[b] n=534	GI[c] n=399	GYN[d] n=232	Lung[e] n=145
	Respiratory	X	X			X	
	CTX related		X		X		