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"Symptom Clusters in Oncology Outpatients: Stability and Consistency Across a Cycle of Chemotherapy"

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Abstract

Objectives: Improved understanding of the stability and consistency of symptom clusters across time, symptom dimensions, and cancer diagnoses will lead to refinements in symptom assessments and management, and provide direction for mechanistic studies. Study purposes were to describe the occurrence, severity, and distress of 38 symptoms; evaluate the stability and consistency of symptom clusters across a cycle of chemotherapy, three symptom dimensions, and four distinct cancer types; and identify common and distinct symptom clusters.

Methods: Oncology outpatients (n=1329) completed the Memorial Symptom Assessment Scale prior to their next cycle of chemotherapy (T1), one week after chemotherapy (T2), and two weeks after chemotherapy (T3). Symptom clusters were identified using exploratory factor analysis using unweighted least squares. GEOMIN rotated factor loadings with absolute values ≥0.40 were considered meaningful. Clusters were stable if they were identified across each time point and/or dimension. Clusters were consistent if the same two or three symptoms with the highest factor loadings were identified across each time point and/or dimension.

Results: Patients reported 13.9 (±7.2) symptoms at T1, 14.0 (±7.0) at T2, and 12.2 (±6.8) at T3. Psychological, weight gain, gastrointestinal, and respiratory clusters were stable across time and dimensions. Only the psychological, weight gain, and respiratory clusters were consistent across time and dimensions.

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Conclusion: Given the stability of the psychological, weight gain, and gastrointestinal clusters across cancer diagnoses, symptoms within these clusters need to be routinely assessed. However, respiratory and hormonal clusters are unique to specific cancer types and the symptoms within these clusters are variable.

Keywords

cancer; chemotherapy; factor analysis; symptom clusters

INTRODUCTION

Over the past 20 years, research on symptom clusters in oncology patients has increased exponentially.[1] However, whether symptom clusters change over time or differ based on the dimension of the symptom experience (i.e., occurrence, severity, distress) warrant additional consideration. In a systematic review of 23 studies that evaluated for symptom clusters in patients receiving chemotherapy,[1] 43.5% were longitudinal. Only four of these studies evaluated for symptom clusters across two or more symptom dimensions.[2–5] An improved understanding of the stability and consistency of symptom clusters will lead to refinements in symptom assessments and management, as well as provide direction for mechanistic studies.

Of the five longitudinal studies that evaluated for symptom clusters in patients with various types of cancer receiving chemotherapy,[6–10] three used severity to identify the clusters,[8–10] one used distress,[6] and one did not report on the dimension.[7] Across these five studies, the number of clusters ranged from three to seven. While a gastrointestinal cluster was identified across four studies,[6–9] no symptoms were consistent across studies and time points. Of the four studies that identified a psychological cluster,[7–10] anxiety- and depression-related symptoms (e.g., worry, feeling sad) were consistently identified across studies and time points. These inconsistencies are due to variability in the number of symptoms evaluated; symptom dimensions used; timing of symptom assessments; and statistical methods used. Because of these differences, the stability and consistency of clusters requires additional investigation. In our cross-sectional study of symptom clusters in patients with heterogeneous types of cancer,[11] we identified five symptom clusters that were stable across occurrence, severity, and distress in the week prior to chemotherapy. Based on comparisons with our previous analyses of specific types of cancer (i.e., breast,[5] gastrointestinal,[12] gynecological,[13] lung[4]), we identified three symptom clusters that were common across all four cancer diagnoses (i.e., psychological, gastrointestinal, weight gain or change) and two clusters that were unique to specific types of cancer (i.e., hormonal for breast[5] and gynecological[13] cancer; respiratory for gynecological[13] and lung[4] cancer). Given the stability of these five clusters across three symptom dimensions, we suggested that a single dimension can be used to identify these clusters.

However, an unanswered question is whether these common and distinct clusters remain stable over time. While we previously reported on the stability of symptom clusters across a single cycle of chemotherapy in patients with breast,[5] gastrointestinal,[2] gynecological,[14] and lung[4] cancer using two or more symptom dimensions, we have not evaluated for symptom

clusters over time using the total sample. A comparison of the stability and consistency of symptom clusters across the specific cancer diagnoses to the total sample may provide additional evidence for the existence of common and distinct symptom clusters in oncology patients.

Therefore, the study purposes were to describe the occurrence, severity, and distress of 38 symptoms across a cycle of chemotherapy and evaluate the stability and consistency of symptom clusters over time and across symptom dimensions. In addition, an evaluation of common and distinct symptom clusters across the total sample and the four distinct types of cancer (i.e., breast,[5] gastrointestinal,[2] gynecological,[14] lung[4]) was done.

METHODS

Patients and settings

This analysis was planned as part of a larger study funded by the National Cancer Institute.[2 4 5 14] 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 six times over two cycles of chemotherapy. Data from the first three assessments were used in these analyses. Assessments took place in the week prior to patients' second or third cycle of chemotherapy (T1), approximately one week after chemotherapy (T2), and approximately two weeks after chemotherapy (T3). Medical records were reviewed for disease and treatment information. The study was approved by the Committee on Human Research at the University of California, San Francisco and Institutional Review Board at each of the study sites.

Instruments

Patients completed a demographic questionnaire, Karnofsky Performance Status (KPS) scale,[15] and Self-Administered Comorbidity Questionnaire.[16] Toxicity of each patient's chemotherapy regimen was rated using the MAX2 index.[17 18]

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.[19] Six common symptoms were added: hot flashes, chest tightness, difficulty breathing, abdominal cramps, increased appetite, and weight gain. Using the valid and reliable MSAS,[19] 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 and distress were rated using four- and five-point Likert scales, respectively.

Data analysis

Descriptive statistics and frequency distributions were calculated using Statistical Package for Social Sciences Version 27 (IBM Corporation, Armonk, NY). To identify the symptom clusters, exploratory factor analysis (EFA) was done using MPlus Version 8.6.[20]

Factor loadings were considered meaningful if the loading was ≥0.40.[20] Factors were adequately defined if at least two symptoms had loadings of ≥0.40.[21] Items were allowed to cross-load if they fell within our preset criteria of ≥0.40. While tetrachoric correlations were used to create the matrix of associations for the occurrence items, polychoric correlations were used for the severity and distress ratings.[20] Simple structures for the EFAs were estimated using the method of unweighted least squares with geomin (i.e., oblique) rotation.[20]

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). 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 was over 90% and the estimation failed to converge.

Factor solutions were estimated for two through five factors. Factor solution with the greatest interpretability and clinical meaningfulness was selected given that it met the criteria set for evaluating simple structure. Clusters were named based on the symptoms with the highest factor loadings and the majority of the symptoms in the cluster.

Evaluation of stability and consistency

To evaluate the stability of symptom clusters across time and/or dimensions, previous work by our group[2 4 5 11–14 22 23] and others[3 6 24] used the Kirkova and Walsh criteria.[25] They suggested that for a cluster to be considered stable, at least 75% of the symptoms in the cluster should be present including the prominent and most important symptom (i.e., symptom with the highest factor loading). This method has some limitations. First, while the term “stability” was used to describe these criteria, its definition and use within symptom cluster research are inconsistent.[1] This lack of consensus has led to the subjective application of these criteria. Second, a cutoff of 75% agreement is somewhat arbitrary and is applied inconsistently. Finally, in order to assess percent agreement, multiple calculations are needed. These considerations make the interpretation of results, within and across studies, challenging.

Given these limitations, we propose the following terminology and criteria to clarify this component of symptom cluster research. The term *stability* is used to describe whether or not the same clusters are identified over time, across symptom dimensions, and/or study samples.[11] In contrast, *consistency* is used to describe whether the specific symptoms within a cluster remain the same across these conditions. For a cluster to be considered consistent, the two or three symptoms with the highest factor loadings must be present across all time points and/or symptom dimensions. This evaluation of consistency builds on previous work

that evaluated for “core sets of symptoms” that occurred consistently over time (p.98).[6] Given that a symptom cluster must contain a minimum of two symptoms,[26] a minimum of the same two symptoms with the highest factor loadings should be applied to clusters with only two or three symptoms. For clusters with four or more symptoms, a minimum of the same three symptoms with the highest factor loadings must be present across all time points and/or dimensions to be considered consistent.

This appraisal of consistency has multiple strengths. First, by requiring the symptoms with the highest factor loadings to be consistent across each assessment, a rank-based method is utilized to prioritize symptoms with the highest factor loadings. Given that the threshold for a minimum factor loading is still being determined and that symptoms with a lower score may negatively skew the results, this method improves upon the previous method. Second, these criteria can be rapidly applied and easily interpreted.

RESULTS

Demographic and clinical characteristics

Characteristics of the patients were reported previously.[11] In brief, of the 1329 patients in the total sample, 77.8% were female, 69.9% were White, 60.4% reported a mean household annual income of ≥$70,000, and had a mean age of 57.3 (±12.3) years (Table 1). 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).

Symptom prevalence and characteristics

Mean number of symptoms was 13.9 (±7.2) at T1, 14.0 (±7.0) at T2, and 12.2 (±6.8) at T3. Across the three assessments, lack of energy had the highest occurrence rate (Table 2). The most severe symptoms were hair loss at T1 and problems with sexual interest or activity at T2 and T3. The most distressing symptoms were: “I don’t look like myself” at T1, “I don’t look like myself” and problems with sexual interest or activity at T2, and problems with sexual interest or activity at T3.

Symptom clusters over time

At T1, a five-factor solution was selected for the occurrence, severity, and distress EFAs (Table 3). Psychological, weight gain, respiratory, gastrointestinal, and hormonal clusters were identified across all three dimensions. At T2, a four-factor solution was selected for the occurrence, severity, and distress EFAs. Psychological, weight gain, respiratory, and gastrointestinal clusters were identified across all three dimensions. At T3, a five-factor solution was selected for the occurrence, severity, and distress EFAs. Psychological, weight gain, respiratory, gastrointestinal, and body image clusters were identified using occurrence and severity. Using distress, psychological, weight gain, respiratory, gastrointestinal, and hormonal clusters were identified. The stability (Table 4) and consistency (Table 5) of each of these clusters is reported next.

Psychological cluster

Psychological cluster, comprised of five (T1 for severity) to nine (T2 and T3 for occurrence) symptoms, was stable across all three times and dimensions. For all three dimensions, worrying had the highest factor loading across all three times.

Symptoms within the psychological cluster were consistent across times and dimensions. Worrying, feeling sad, and feeling nervous had the highest factor loadings across times and dimensions.

Weight gain cluster

Weight gain cluster, comprised of two (T1 for occurrence, severity, and distress; T3 for severity and distress) to three (T2 for occurrence, severity, and distress) symptoms, was stable across all three times and dimensions. For all three dimensions, weight gain had the highest factor loading across all three times.

Weight gain cluster was comprised of two or three symptoms. Given that only two symptoms with the highest factor loadings needed to be present and weight gain and increased appetite had the highest factors loadings across times and dimensions, this cluster is consistent.

Gastrointestinal cluster

Gastrointestinal cluster, comprised of six (T3 for occurrence and severity) to 11 (T1 for occurrence) symptoms, was stable across all three times and dimensions. While lack of appetite had the highest factor loading at T1 for occurrence, severity, and distress and at T2 and T3 for distress, nausea had the highest factor loading at T2 and T3 for occurrence and severity.

Regarding the consistency of symptoms over time, none of the clusters met the criteria for consistency. For occurrence, only two symptoms were consistent across times. None of the symptoms were consistent across time for severity. For distress, only one symptom was consistent over time.

Regarding the consistency of symptoms across dimensions, this cluster met the criteria for consistency only at T2. At T1, only two symptoms were consistent across dimensions. At T3, only one symptom was consistent.

Respiratory cluster

Respiratory cluster, comprised of four symptoms, was stable across all three times and dimensions. For all three dimensions, difficulty breathing had the highest factor loading across all three times.

Symptoms within the respiratory cluster were consistent across all three times and dimensions. Difficulty breathing, shortness of breath, and chest tightness had the highest factor loadings across times and dimensions.

Hormonal cluster

Hormonal cluster was stable across all three dimensions at T1 and was identified using distress at T3. It was comprised of two symptoms. When this cluster was identified, hot flashes had the highest factor loading. Symptoms within the hormonal cluster were consistent across dimensions only at T1.

Body image cluster

Body image cluster was identified at T3 using severity and distress. It was comprised of three symptoms. When this cluster was identified, changes in skin had the highest factor loading. Given the lack of stability of the body image cluster across times and dimensions, its consistency was not evaluated.

DISCUSSION

This study is the first to provide a detailed characterization of the symptom burden of oncology patients across a cycle of chemotherapy and present an approach to characterize both the stability and consistency of symptom clusters across time and dimensions. In terms of symptom burden, patients reported an average of 13 symptoms across the three assessments. This finding suggests that symptoms persist across an entire cycle of chemotherapy and patients enter the next cycle with a high symptom burden.

The remainder of the Discussion describes the stability (Table 4) and consistency (Table 5) of each cluster, compares these clusters with our previous findings in patients with breast,[5] gastrointestinal,[2] gynecological,[14] and lung[4] cancers, and places our findings in the context of the extant literature.

Psychological cluster

Consistent with our previous studies of patients with breast,[5] gastrointestinal,[2] gynecological,[14] and lung[4] cancers, in the current study, a psychological cluster was stable and consistent over time and symptom dimensions. Of note, across all five studies, worrying and feeling sad were the consistent symptoms for the majority of the EFAs. Because worrying and feeling sad are two of the most common symptoms associated with a psychological cluster,[1 27] one can hypothesize that these two symptoms may represent core or sentinel symptoms within this cluster. Given that anxiety and depressive symptoms occurred in 38% and 46% of patients undergoing chemotherapy, respectively, it is imperative to routinely assess for these symptoms and initiate interventions and/or referrals to psychological support services.

Weight gain cluster

Named nutrition or weight change clusters in our patients with gastrointestinal,[2] gynecological,[14] and lung[4] cancers, and weight gain in the total sample, this cluster was stable across times and dimensions. However, across these four studies, the symptoms in this cluster were not consistent. Furthermore, in our patients with breast cancer,[5] this cluster was neither stable nor consistent. Similarly, in two studies of patients with acute myelogenous

leukemia[3] and breast cancer,[24] while a nutritional or weight cluster was stable across time, the cluster was not consistent.

These findings suggest that the relationships among symptoms associated with nutritional status are dynamic. Differences in chemotherapy regimens, specific types of cancer and/or disease stage, comorbid conditions, and/or concurrent medications may contribute to this variability. An additional consideration is the specific nutritional symptoms on the symptom assessment instrument. For example, while the MSAS includes the items “weight loss” and “lack of appetite,” for our studies, weight gain and increased appetite were added. This cluster is an example of how the specific symptoms on an inventory may allow for the identification of different symptom clusters based on the type of cancer (e.g., weight gain in women with breast cancer[24]) and/or stage of disease (e.g., cachexia in patients with lung cancer[28]).

Gastrointestinal cluster

Because a gastrointestinal cluster is one of the most common symptom clusters,[1 27] it is not surprising that it was identified across each cancer type and the total sample.[2 4 5 14] However, its stability and consistency were highly variable across time, dimensions, and cancer types. For example, in the total sample, across dimensions at T1, lack of appetite and weight loss were the two consistent symptoms. However, across dimensions at T2, weight loss, nausea, and vomiting were the consistent symptoms. Across dimensions at T3, only nausea was consistent.

The dynamic nature of this cluster is consistent with previous reports. For example, in three studies[6 8 9] that evaluated for symptom clusters across two or more cycles of chemotherapy, while stable, the gastrointestinal cluster was not consistent. Additional research is warranted to examine how the gastrointestinal cluster evolves during chemotherapy.

Respiratory cluster

In the total sample, the respiratory cluster was stable and consistent across times and dimensions. However, this cluster was identified only in patients with gynecological[14] and lung[4] cancers which suggests it may be cancer-specific. Across the breast,[5] lung,[4] and total samples, difficulty breathing was the only consistent symptom. Given that respiratory symptoms may arise from different mechanisms (e.g., bronchial lesions in lung cancer, ascites in gynecological cancer), this inconsistency has some clinical validity. Given that 26.9% of the entire sample reported shortness of breath at enrollment and that it persisted over time, suggests that it warrants evaluation and management across all cancer types.

Hormonal cluster—While the hormonal cluster was identified in the entire sample, it was only identified in our previous studies of women with breast[5] and gynecological[14] cancers. While this cluster was stable across times and dimensions in these previous studies,[5 14] for the entire sample, it was only stable across dimensions at T1. When this cluster was identified, hot flashes and sweats were the consistent symptoms. These findings suggest that a hormonal cluster is unique to specific cancer types. Evidence from studies of women with

breast cancer receiving chemotherapy support our findings. For example, in three studies,[6 24 29] a vasomotor cluster was stable over time and hot flashes and sweats were the consistent symptoms.

Body image cluster

While a body image cluster was not identified across our previous studies of individual cancer types,[2 4 5 14] the symptoms in this cluster were found in an epithelial cluster. However, the stability and consistency of this cluster varied across times, dimensions, and cancer types. For example, in the entire sample, changes in skin, "I don't look like myself," and change in the way food tastes comprised the body image cluster. In our other studies, symptoms unique to specific cancer types were: hair loss and itching for breast[5] and gastrointestinal[2] cancers, and mouth sores for breast[5] and lung[4] cancers. This variability may be due to differences in the type of chemotherapy received, cycle length, and/or prior treatments. Despite these differences, a body image or epithelial cluster is stable across cancer types. Of note, change in the way food tastes and "I don't look like myself" were two of the most common, severe, and distressing symptoms reported by patients across a cycle of chemotherapy. By providing education and management strategies prior to and throughout chemotherapy,[30] clinicians can help patients manage and cope with these symptoms.

These findings are limited by several considerations. Among our previous studies of patients with breast[5] and lung[4] cancer, only two symptom dimensions (i.e., occurrence, severity) were used to identify symptom clusters. Therefore, an evaluation of the stability and consistency of clusters using distress ratings are needed. In addition, our sample was primarily White and well-educated, which limits the generalizability of our findings. Finally, given that this study was the first to evaluate the consistency of symptoms within clusters using a new approach, this method warrants evaluation in future studies.

CONCLUSION

In the most recent state of the science report,[26] an expert panel identified stability of symptoms within a cluster as one of the key characteristics of a symptom cluster. However, our findings suggest that while a specific cluster may be stable across time, dimensions, and/or cancer type, its consistency may vary. These findings support our hypothesis that stability and consistency are two distinct but related characteristics of symptom clusters. While various terms have been used to describe the stability of symptom clusters and the symptoms within them (e.g., stable,[26] prominent,[25] core sets of symptoms[6]), these terms were applied inconsistently. Our proposed method to evaluate the stability and consistency of clusters has the potential to advance symptom cluster research and provide direction for mechanistic studies.

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Key Messages Box:

What is already known on this topic?

- Stability is a characteristic of symptom clusters
- Psychological and gastrointestinal clusters are stable across cancers

What this study adds

- Stability and consistency are distinct but related characteristics of symptom clusters
- Respiratory and hormonal clusters are unique to some cancers

How this study might affect research, practice, or policy

- Findings will allow for a more robust evaluation of the stability and consistency of symptom clusters across studies
- Findings will lead to refinements in symptom assessments and management

Summary of study implications –

This study provides details on a new method to evaluate both the consistency and stability of symptom clusters within and across different types of cancer and time. In addition, findings suggest that psychological, gastrointestinal, and weight gain clusters need to be evaluated across all types of cancer.

Table 1.

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

Characteristic	**Mean**	**SD**
Age (years)	57.3	12.3
Education (years)	16.2	3.0
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)	2.0	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	1.0
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	22.0
Care of adult responsibilities (% yes)	95	7.9
Currently employed (% yes)	462	35.1
Income		
< $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	25.0
Only CTX, surgery, or RT	543	42.0
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	61.0
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

Abbreviations: CTX, chemotherapy; MSAS, Memorial Symptom Assessment Scale; NK-1, neurokinin 1; RT, radiation therapy; SD, standard deviation

Table 2.

Occurrence Rates and Severity and Distress Ratings for Symptoms Over One Cycle of Chemotherapy in Patients with Cancer

Symptoms[a]	Occurrence Rates % (n)			Severity Ratings with Zeros[b] Mean (SD)			Severity Ratings without Zeros[c] Mean (SD)			Distress Ratings[d] Mean (SD)		
	Time 1*	Time 2	Time 3	Time 1	Time 2	Time 3	Time 1	Time 2	Time 3	Time 1	Time 2	Time 3
Lack of energy	83.2 (1106)	86.2 (1091)	81.0 (1000)	1.67 (1.0)	1.91 (1.1)	1.64 (1.1)	2.02 (0.7)	2.23 (0.8)	2.04 (0.7)	1.79 (1.1)	1.98 (1.1)	1.75 (1.1)
Difficulty sleeping	69.1 (918)	68.2 (864)	64.3 (793)	1.38 (1.1)	1.37 (1.1)	1.25 (1.2)	2.01 (0.8)	2.04 (0.8)	1.99 (0.8)	1.79 (1.1)	1.76 (1.1)	1.72 (1.1)
Pain	60.4 (803)	65.9 (834)	60.9 (751)	1.14 (1.1)	1.30 (1.1)	1.15 (1.1)	1.92 (0.7)	2.00 (0.8)	1.94 (0.7)	1.77 (1.1)	1.92 (1.1)	1.74 (1.1)
Feeling drowsy	60.3 (801)	65.2 (825)	53.4 (659)	1.04 (1.0)	1.17 (1.1)	0.90 (1.0)	1.75 (0.7)	1.84 (0.7)	1.74 (0.7)	1.16 (1.1)	1.28 (1.1)	1.14 (1.0)
Hair loss	54.8 (728)	49.6 (628)	47.3 (584)	1.35 (1.5)	1.13 (1.4)	1.04 (1.4)	2.49 (1.1)	2.34 (1.1)	2.27 (1.1)	1.88 (1.3)	1.89 (1.4)	1.81 (1.3)
Numbness/tingling in hands/feet	52.2 (694)	53.9 (682)	50.3 (621)	0.94 (1.1)	0.99 (1.1)	0.91 (1.1)	1.84 (0.8)	1.89 (0.8)	1.87 (0.8)	1.52 (1.2)	1.57 (1.2)	1.56 (1.2)
Worrying	52.1 (692)	47.5 (601)	43.5 (537)	0.94 (1.1)	0.85 (1.0)	0.77 (1.0)	1.85 (0.7)	1.82 (0.7)	1.81 (0.8)	1.63 (1.0)	1.61 (1.0)	1.57 (1.1)
Difficulty concentrating	51.9 (690)	56.0 (709)	51.7 (638)	0.79 (0.9)	0.91 (1.0)	0.80 (0.9)	1.55 (0.6)	1.64 (0.7)	1.60 (0.7)	1.48 (1.1)	1.48 (1.1)	1.36 (1.0)
Change in the way food tastes	49.4 (656)	55.4 (701)	45.9 (567)	1.04 (1.2)	1.19 (1.3)	0.89 (1.2)	2.12 (0.9)	2.19 (0.9)	2.00 (0.9)	1.72 (1.3)	1.86 (1.2)	1.61 (1.2)
Nausea	47.5 (631)	58.5 (741)	41.0 (506)	0.82 (1.0)	1.06 (1.1)	0.69 (1.0)	1.76 (0.8)	1.86 (0.8)	1.74 (0.8)	1.65 (1.1)	1.84 (1.1)	1.61 (1.1)
Feeling sad	46.0 (612)	45.3 (573)	39.0 (481)	0.77 (1.0)	0.76 (1.0)	0.66 (1.0)	1.71 (0.7)	1.73 (0.7)	1.74 (0.7)	1.50 (1.1)	1.59 (1.0)	1.51 (1.0)
Dry mouth	45.4 (603)	44.3 (561)	33.7 (416)	0.77 (1.0)	0.76 (1.0)	0.58 (0.9)	1.73 (0.8)	1.77 (0.8)	1.77 (0.8)	1.23 (1.1)	1.24 (1.1)	1.25 (1.1)
Constipation	43.5 (578)	46.3 (586)	33.5 (414)	0.84 (1.1)	0.89 (1.1)	0.63 (1.0)	1.98 (0.8)	1.97 (0.8)	1.94 (0.8)	1.70 (1.2	1.70 (1.1)	1.65 (1.1)
Feeling irritable	41.3 (549)	43.8 (554)	40.9 (505)	0.69 (1.0)	0.73 (1.0)	0.66 (0.9)	1.70 (0.7)	1.71 (0.7)	1.66 (0.7)	1.46 (1.0)	1.50 (1.0)	1.43 (1.0)
Lack of appetite	41.3 (549)	50.1 (634)	37.0 (456)	0.78 (1.1)	0.98 (1.1)	0.67 (1.0)	1.92 (0.8)	2.00 (0.8)	1.87 (0.8)	1.28 (1.1)	1.39 (1.1)	1.28 (1.2)
Feeling nervous	38.0 (505)	31.4 (397)	26.3 (324)	0.59 (0.9)	0.49 (0.8)	0.42 (0.8)	1.62 (0.7)	1.63 (0.7)	1.65 (0.7)	1.41 (1.0)	1.48 (1.0)	1.46 (1.1)
“I don’t look like myself”	37.9 (503)	40.2 (509)	38.5 (475)	0.80 (1.2)	0.84 (1.2)	0.77 (1.1)	2.15 (0.9)	2.16 (1.0)	2.04 (0.9)	1.98 (1.2)	1.98 (1.2)	1.90 (1.2)
Changes in skin	36.3 (482)	37.8 (478)	32.7 (403)	0.68 (1.0)	0.69 (1.0)	0.59 (1.0)	1.91 (0.8)	1.87 (0.8)	1.86 (0.8)	1.64 (1.2)	1.60 (1.2)	1.58 (1.2)
Feeling bloated	33.1 (440)	31.1 (394)	27.1 (334)	0.58 (0.9)	0.56 (0.9)	0.47 (0.9)	1.79 (0.7)	1.85 (0.8)	1.79 (0.7)	1.54 (1.1)	1.60 (1.1)	1.55 (1.0)
Cough	32.6 (433)	28.9 (366)	28.8 (355)	0.45 (0.8)	0.42 (0.8)	0.44 (0.8)	1.42 (0.6)	1.53 (0.7)	1.59 (0.7)	1.02 (1.1)	1.17 (1.1)	1.28 (1.1)
Hot flashes	31.8 (423)	29.7 (376)	26.7 (329)	0.58 (1.0)	0.54 (1.0)	0.48 (0.9)	1.87 (0.8)	1.89 (0.8)	1.89 (0.8)	1.42 (1.2)	1.49 (1.2)	1.49 (1.1)
Dizziness	31.3 (416)	32.7 (414)	24.2 (299)	0.46 (0.8)	0.49 (0.8)	0.36 (0.7)	1.51 (0.7)	1.54 (0.7)	1.53 (0.7)	1.24 (1.0)	1.34 (1.0)	1.34 (0.9)
Sweats	31.2 (415)	28.6 (362)	22.8 (281)	0.53 (0.9)	0.49 (0.9)	0.40 (0.9)	1.77 (0.8)	1.77 (0.8)	1.84 (0.8)	1.29 (1.1)	1.30 (1.1)	1.42 (1.1)
Problems with sexual interest/activity	29.9 (397)	26.7 (338)	25.7 (317)	0.71 (1.2)	0.64 (1.2)	0.62 (1.2)	2.47 (1.0)	2.49 (0.9)	2.49 (1.0)	1.87 (1.3)	1.98 (1.3)	2.00 (1.3)
Diarrhea	29.6 (393)	28.4 (360)	25.8 (318)	0.54 (1.0)	0.52 (0.9)	0.46 (0.9)	1.87 (0.8)	1.88 (0.8)	1.84 (0.8)	1.46 (1.1)	1.53 (1.1)	1.51 (1.1)

Symptoms[a]	Occurrence Rates % (n)			Severity Ratings with Zeros[b] Mean (SD)			Severity Ratings without Zeros[c] Mean (SD)			Distress Ratings[d] Mean (SD)		
	Time 1*	Time 2	Time 3	Time 1	Time 2	Time 3	Time 1	Time 2	Time 3	Time 1	Time 2	Time 3
Shortness of breath	26.9 (357)	24.9 (315)	21.7 (268)	0.44 (0.8)	0.41 (0.8)	0.36 (0.8)	1.67 (0.7)	1.71 (0.7)	1.70 (0.7)	1.51 (1.0)	1.51 (1.1)	1.50 (1.0)
Increased appetite	25.9 (344)	20.5 (260)	23.0 (284)	0.44 (0.8)	0.35 (0.8)	0.38 (0.8)	1.75 (0.7)	1.78 (0.7)	1.72 (0.7)	0.91 (1.1)	1.05 (1.2)	0.98 (1.2)
Weight gain	25.4 (337)	20.6 (260)	20.9 (258)	0.39 (0.8)	0.31 (0.7)	0.32 (0.7)	1.58 (0.7)	1.58 (0.7)	1.64 (0.8)	1.37 (1.3)	1.51 (1.4)	1.55 (1.4)
Weight loss	25.2 (335)	26.2 (332)	21.1 (260)	0.38 (0.8)	0.39 (0.7)	0.31 (0.7)	1.56 (0.7)	1.53 (0.7)	1.56 (0.8)	0.96 (1.2)	1.02 (1.1)	1.05 (1.2)
Itching	24.8 (330)	21.1 (267)	19.7 (243)	0.41 (0.8)	0.35 (0.8)	0.32 (0.7)	1.71 (0.7)	1.72 (0.7)	1.72 (0.7)	1.28 (1.1)	1.40 (1.1)	1.31 (1.0)
Abdominal cramps	22.5 (299)	26.9 (340)	19.0 (235)	0.40 (0.8)	0.49 (0.9)	0.34 (0.8)	1.87 (0.8)	1.91 (0.8)	1.89 (0.8)	1.61 (1.1)	1.67 (1.1)	1.64 (1.1)
Mouth sores	20.9 (278)	21.1 (267)	20.3 (251)	0.34 (0.8)	0.35 (0.8)	0.34 (0.8)	1.70 (0.7)	1.74 (0.8)	1.69 (0.8)	1.46 (1.1)	1.47 (1.1)	1.46 (1.1)
Difficulty breathing	19.9 (265)	17.4 (220)	14.9 (184)	0.32 (0.7)	0.28 (0.7)	0.23 (0.6)	1.64 (0.7)	1.74 (0.7)	1.68 (0.7)	1.63 (1.1)	1.63 (1.1)	1.56 (1.1)
Chest tightness	17.8 (237)	16.5 (209)	11.8 (145)	0.27 (0.6)	0.25 (0.7)	0.18 (0.6)	1.54 (0.7)	1.61 (0.7)	1.65 (0.6)	1.42 (1.0)	1.50 (1.0)	1.54 (1.0)
Swelling of arms or legs	14.6 (194)	13.3 (168)	13.8 (170)	0.27 (0.7)	0.23 (0.7)	0.24 (0.7)	1.91 (0.8)	1.82 (0.9)	1.82 (0.8)	1.62 (1.2)	1.56 (1.2)	1.59 (1.2)
Problems with urination	14.1 (187)	14.8 (187)	11.8 (145)	0.24 (0.7)	0.25 (0.7)	0.20 (0.6)	1.79 (0.8)	1.73 (0.8)	1.79 (0.8)	1.51 (1.2)	1.53 (1.2)	1.71 (1.2)
Difficulty swallowing	13.8 (183)	15.6 (198)	12.2 (151)	0.23 (0.7)	0.26 (0.7)	0.21 (0.6)	1.73 (0.8)	1.75 (0.8)	1.76 (0.8)	1.64 (1.2)	1.60 (1.1)	1.63 (1.2)
Vomiting	12.3 (164)	14.5 (184)	9.0 (111)	0.21 (0.7)	0.25 (0.7)	0.15 (0.5)	1.80 (0.9)	1.82 (0.8)	1.79 (0.8)	1.74 (1.2)	1.68 (1.3)	1.76 (1.2)

Abbreviation: SD = standard deviation;

*Orientation column in rank order

Timing of symptom assessments: Time 1 = prior to the initiation of next cycle of chemotherapy (i.e., recovery from the first or second cycle of chemotherapy), Time 2 = approximately one week after chemotherapy (i.e., acute symptoms), Time 3 = approximately two weeks after chemotherapy (i.e., potential nadir).

[a]Symptoms from the Memorial Symptom Assessment Scale with the addition of the following six symptoms: chest tightness, difficulty breathing, increased appetite, hot flashes, abdominal cramps, weight gain.

[b]Severity ratings with zeros: 0 = did not have the symptoms, 1 = slight, 2 = moderate, 3 = severe, 4 = very severe.

[c]Severity ratings without zeros: 1 = slight, 2 = moderate, 3 = severe, 4 = very severe.

[d]Distress ratings: 0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much.

Table 3.

Number and Types of Symptoms within Each Symptom Cluster Over a Cycle of Chemotherapy Using Ratings of Occurrence, Severity, and Distress[a]

Symptom Cluster	Symptoms	Time 1			Time 2			Time 3		
		Occurrence	Severity	Distress	Occurrence	Severity	Distress	Occurrence	Severity	Distress
Psychological	Worrying	**0.864**	**0.866**	**0.875**	**0.859**	**0.858**	**0.874**	**0.906**	**0.856**	**0.874**
	Feeling sad	**0.855**	**0.850**	**0.872**	**0.831**	**0.848**	**0.816**	**0.823**	**0.845**	**0.868**
	Feeling nervous	**0.744**	**0.750**	**0.760**	**0.682**	**0.682**	**0.701**	**0.788**	**0.749**	**0.766**
	Feeling irritable	0.626	0.569	0.574	0.670	0.680	0.646	0.652	0.650	0.682
	Difficulty concentrating	0.549	0.517	0.560	0.621	0.545	0.558	0.659	0.596	0.587
	“I don’t look like myself”	0.458	–	0.427	0.591	0.627	0.553	0.422	–	0.590
	Problems with sexual interest or activity	–	–	–	0.510	0.413	0.456	0.467	–	–
	Difficulty sleeping	–	–	–	0.444	–	–	0.436	0.425	–
	Lack of energy	–	–	–	0.403	–	0.429	0.574	0.441	0.469
	Sweats	–	–	–	–	–	0.416	–	–	–
	Total number of symptoms	6/10	5/10	6/10	9/10	7/10	9/10	9/10	7/10	7/10
Weight gain	Weight gain	**0.921**	**0.875**	**0.914**	**0.875**	**0.858**	**0.923**	**0.824**	**0.818**	**0.912**
	Increased appetite	**0.785**	**0.746**	**0.736**	**0.711**	**0.695**	**0.708**	**0.666**	**0.664**	**0.724**
	Lack of appetite	–	–	–	−0.494	−0.498	−0.443	–	–	–
	Feeling bloated	–	–	–	–	–	–	0.416	–	–
	Total number of symptoms	2/4	2/4	2/4	3/4	3/4	3/4	3/4	2/4	2/4
Gastrointestinal	Lack of appetite	**0.784**	**0.774**	**0.770**	**0.691**	**0.687**	**0.691**	**0.669**	0.622	**0.762**
	Weight loss	**0.679**	**0.658**	**0.680**	0.443	0.459	0.537	0.579	0.592	**0.690**
	Nausea	**0.663**	0.624	0.612	**0.867**	**0.766**	**0.610**	**0.873**	**0.735**	**0.693**
	Change in the way food tastes	0.612	**0.690**	**0.677**	–	–	0.498	–	–	0.481
	Vomiting	0.546	0.538	0.525	**0.735**	**0.738**	**0.638**	**0.777**	0.639	0.686
	Difficulty swallowing	0.513	0.517	0.503	0.411	0.478	0.566	–	–	0.442
	Abdominal cramps	0.455	0.472	0.444	0.465	0.531	0.511	0.569	**0.666**	0.583
	Diarrhea	0.433	0.483	0.455	0.479	0.549	0.501	0.634	**0.688**	0.634
	Dry mouth	0.431	0.472	0.474	0.492	0.424	0.483	–	–	–

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Symptom Cluster	Symptoms	Time 1			Time 2			Time 3		
		Occurrence	**Severity**	**Distress**	**Occurrence**	**Severity**	**Distress**	**Occurrence**	**Severity**	**Distress**
	Constipation	0.430	–	–	–	–	–	–	–	0.401
	Dizziness	0.404	–	–	–	0.421	0.407	–	–	–
	Mouth sores	–	–	–	–	–	–	–	–	–
	Lack of energy	–	–	–	0.454	–	–	–	–	–
	Total number of symptoms	11/13	10/13	9/13	9/13	9/13	10/13	6/13	6/13	9/13
Respiratory	Difficulty breathing	**1.037**	**1.032**	**1.035**	**0.971**	**0.972**	**0.958**	**0.965**	**0.974**	**0.964**
	Shortness of breath	**0.716**	**0.763**	**0.741**	**0.821**	**0.846**	**0.843**	**0.856**	**0.845**	**0.863**
	Chest tightness	**0.689**	**0.614**	**0.628**	**0.677**	**0.618**	**0.617**	**0.710**	**0.610**	**0.644**
	Cough	0.457	0.430	0.427	0.466	0.438	0.429	0.483	0.440	0.437
	Total number of symptoms	4/4	4/4	4/4	4/4	4/4	4/4	4/4	4/4	4/4
Hormonal	Hot flashes	**0.883**	**0.907**	**0.920**	Not identified					0.843
	Sweats	**0.670**	**0.728**	**0.647**						0.799
	Total number of symptoms	2/2	2/2	2/2						2/2
Body image	Changes in skin	Not identified						0.595	0.582	Not identified
	"I don't look like myself"							0.461	0.558	
	Change in the way food tastes							0.461	0.496	
	Total number of symptoms							3/3	3/3	

[a]Extraction method: unweighted least squares. Rotation method: Geomin (oblique) rotation.

Timing of symptom assessments: Time 1 = prior to the initiation of next cycle of chemotherapy (i.e., recovery from the first or second cycle of chemotherapy), Time 2 = approximately one week after chemotherapy (i.e., acute symptoms), Time 3 = approximately two weeks after chemotherapy (i.e., potential nadir).

For total number of symptoms, the numerator represents the number of symptoms identified at the corresponding time point according to the corresponding dimension of the symptom experience. The denominator represents the total number of symptoms identified across all time points and according to all dimensions of the symptom experience.

Not identified = This symptom cluster was not identified at the corresponding time point according to the corresponding dimension of the symptom experience. − = Factor loadings for these symptoms were <0.40.

Bold font indicates the highest factor loading.

Table 4.

Comparison of Stability of Symptom Clusters Across the Total Sample and Individual Cancer Types Using Ratings of Occurrence, Severity, and Distress

Symptom dimension	Symptom cluster	Total Sample (n=1329)			Breast[a] (n=534)			GI[b] (n=399)			GYN[c] (n=232)			Lung[d] (n=145)		
		T1	T2	T3	T1	T2	T3	T1	T2	T3	T1	T2	T3	T1	T2	T3
Occurrence	Psychological	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
	GI	●	●	●	●	●	●	●			●	●	●			
	Epithelial/GI													●		●
	Epithelial				●	●	●		●	●					●	
	Body image			●												
	Nutritional					●	●							●	●	●
	Weight change				●			●	●	●	●	●	●			
	Weight gain	●	●	●												
	Respiratory	●	●	●							●	●	●			
	Lung CA-specific													●	●	●
	Hormonal	●			●	●	●				●	●	●			
	CTX related							●	●	●						
	Sickness behavior				●									●	●	●
Severity	Psychological	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
	GI	●	●	●	●	●	●	●				●	●			
	GI/epithelial										●					
	Epithelial/GI													●		●
	Epithelial				●	●	●		●	●					●	
	Body image			●												
	Nutritional					●	●							●	●	●
	Weight change				●			●	●	●	●	●	●			
	Weight gain	●	●	●												
	Respiratory	●	●	●							●	●	●			
	Lung CA-specific													●	●	●
	Hormonal	●			●	●	●				●	●	●			
	CTX neuropathy					●										
	CTX related							●	●	●						
	Sickness behavior				●										●	●
Distress	Psychological	●	●	●	NA			●	●	●		●	●	NA		
	Psychological/GI										●					
	GI	●	●	●				●				●	●			
	GI/epithelial										●					
	Epithelial								●	●						
	Weight change							●	●	●	●	●	●			

Symptom dimension	Symptom cluster	Total Sample (n=1329)			Breast[a] (n=534)			GI[b] (n=399)			GYN[c] (n=232)			Lung[d] (n=145)		
		T1	T2	T3	T1	T2	T3	T1	T2	T3	T1	T2	T3	T1	T2	T3
	Weight gain	●	●	●												
	Respiratory	●	●	●							●	●	●			
	Hormonal	●		●							●	●	●			
	CTX related							●	●	●						

Abbreviations: CA = cancer; CTX = chemotherapy; GI = gastrointestinal; GYN = gynecological; NA = dimension not assessed

[a] Sullivan CW, Leutwyler H, Dunn LB, et al. Stability of symptom clusters in patients with breast cancer receiving chemotherapy. J Pain Symptom Manage. 2018;55(1):39–55. https://doi.org/10.1016/j.jpainsymman.2017.08.008

[b] Han CJ, Reding K, Cooper BA, et al. Stability of symptom clusters in patients with gastrointestinal cancers receiving chemotherapy. *J Pain Symptom Manage*2019;58(6):989–1001. https://doi.org/10.1016/j.jpainsymman.2019.07.029

[c] Pozzar RA, Hammer MJ, Cooper BA, et al. Stability of symptom clusters in patients with gynecologic cancer receiving chemotherapy. *Cancer Nurs*[Preprint]. September 23, 2021. https://doi.org/10.1097/NCC.0000000000000988

[d] Russell J, Wong ML, Mackin L, et al. Stability of symptom clusters in patients with lung cancer receiving chemotherapy. *J Pain Symptom Manage*2019;57(5):909–922. https://doi.org/10.1016/j.jpainsymman.2019.02.002

Table 5.

Consistency of Symptoms within Each Symptom Cluster Over Time and Across Dimensions of the Symptom Experience for the Total Sample

Symptom cluster	Time point	Occurrence	Severity	Distress	Symptom agreement over time[a]
Psychological	Time 1	Worrying	Worrying	Worrying	3 of 3
		Feeling sad	Feeling sad	Feeling sad	
		Feeling nervous	Feeing nervous	Feeling nervous	
	Time 2	Worrying	Worrying	Worrying	3 of 3
		Feeling sad	Feeling sad	Feeling sad	
		Feeling nervous	Feeling nervous	Feeling nervous	
	Time 3	Worrying	Worrying	Worrying	3 of 3
		Feeling sad	Feeling sad	Feeling sad	
		Feeling nervous	Feeling nervous	Feeling nervous	
Symptom agreement across dimensions[b]		3 of 3	3 of 3	3 of 3	
Weight gain	Time 1	Weight gain	Weight gain	Weight gain	2 of 2
		Increased appetite	Increased appetite	Increased appetite	
		-	-	-	
	Time 2	Weight gain	Weight gain	Weight gain	2 of 2
		Increased appetite	Increased appetite	Increased appetite	
		Lack of appetite	Lack of appetite	Lack of appetite	
	Time 3	Weight gain	Weight gain	Weight gain	2 of 2
		Increased appetite	Increased appetite	Increased appetite	
		Feeling bloated	-	-	
Symptom agreement across dimensions		2 of 2	2 of 2	2 of 2	
Gastrointestinal	Time 1	Lack of appetite	Lack of appetite	Lack of appetite	2 of 3
		Weight loss	Change in the way food tastes	Weight loss	
		Nausea	Weight loss	Change in the way food tastes	
	Time 2	Nausea	Nausea	Lack of appetite	3 of 3
		Vomiting	Vomiting	Vomiting	
		Lack of appetite	Lack of appetite	Nausea	
	Time 3	Nausea	Nausea	Lack of appetite	1 of 3
		Vomiting	Diarrhea	Nausea	
		Lack of appetite	Abdominal cramps	Weight loss	
Symptom agreement across dimensions		2 of 3	0 of 3	1 of 3	
Respiratory	Time 1	Difficulty breathing	Difficulty breathing	Difficulty breathing	3 of 3
		Shortness of breath	Shortness of breath	Shortness of breath	

Symptom cluster	Time point	Occurrence	Severity	Distress	Symptom agreement over time[a]
		Chest tightness	Chest tightness	Chest tightness	
	Time 2	Difficulty breathing	Difficulty breathing	Difficulty breathing	3 of 3
		Shortness of breath	Shortness of breath	Shortness of breath	
		Chest tightness	Chest tightness	Chest tightness	
	Time 3	Difficulty breathing	Difficulty breathing	Difficulty breathing	3 of 3
		Shortness of breath	Shortness of breath	Shortness of breath	
		Chest tightness	Chest tightness	Chest tightness	
Symptom agreement across dimensions		3 of 3	3 of 3	3 of 3	
Hormonal	Time 1	Hot flashes	Hot flashes	Hot flashes	2 of 2
		Sweats	Sweats	Sweats	
		-	-	-	
	Time 2	NI	NI	NI	NA
	Time 3	NI	NI	Hot flashes	NA
				Sweats	
Symptom agreement across dimensions		NA	NA	NA	
Body image	Time 1	NI	NI	NI	NA
	Time 2	NI	NI	NI	NA
	Time 3	Changes in skin	Changes in skin	NI	NA
		“I don’t look like myself”	“I don’t look like myself”		
		Change in the way food tastes	Change in the way food tastes		
Symptom agreement across dimensions		NA	NA	NA	

Timing of symptom assessments: Time 1 = prior to the initiation of next cycle of chemotherapy (i.e., recovery from the first or second cycle of chemotherapy), Time 2 = approximately one week after chemotherapy (i.e., acute symptoms), Time 3 = approximately two weeks after chemotherapy (i.e., potential nadir).

[a]Calculated as the number of symptoms out of two or three that were identified across the three time points

[b]Calculated as the number of symptoms out of two or three that were identified across the three symptom dimensions (i.e., occurrence, severity, distress)

NA = Symptom agreement was not assessed.

NI = This symptom cluster was not identified.

− = Only two symptoms were identified at a dimension and/or time point.