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Journal

Journal of Pain and Symptom Management, 58(2)

ISSN

0885-3924

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Publication Date

2019-08-01

DOI

10.1016/j.jpainsymman.2019.04.035

Peer reviewed

HHS Public Access

Author manuscript

J Pain Symptom Manage. Author manuscript; available in PMC 2020 August 01.

Published in final edited form as:

J Pain Symptom Manage. 2019 August ; 58(2): 224–234. doi:10.1016/j.jpainsymman.2019.04.035.

Symptom Clusters in Patients with Gastrointestinal Cancers Using Different Dimensions of the Symptom Experience

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Abstract

Background: Patients with gastrointestinal (GI) cancers undergoing chemotherapy (CTX) experience multiple co-occurring symptoms.

Objectives: The aim of this study was to describe the occurrence, severity, and distress of 38 symptoms and to identify symptom clusters based on three symptom dimensions (i.e., occurrence, severity and distress) in patients with GI cancers receiving CTX (n=399). We compared whether the numbers and types of symptom clusters differed based on the dimension of the symptom experience used to create the clusters.

Methods: A modified version of the Memorial Symptom Assessment Scale was used to assess the occurrence, severity and distress of 38 symptoms prior to the initiation of the patient's next dose of CTX. Exploratory factor analysis was used to determine the symptom clusters.

Results: These patients experienced 13.0 (+7.1) symptoms prior to their second or third dose of CTX. For all three symptom dimensions,four symptom clusters were identified, namely psychological distress, CTX-related, GI, and weight change. The number and types of symptom clusters were relatively similar using all three symptom dimensions. However, some variability was found in the specific symptoms within each of the clusters.

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Conflict of interest: The authors have no conflicts of interest to declare.

Conclusions: Our findings suggest that patients with GI cancers experience multiple cooccurring symptoms. Consistent with previous studies of patients with a variety of cancer diagnoses, psychological and GI clusters are common. Clinicians need to assess for and tailor interventions for these symptom clusters.

Keywords

symptoms; symptom clusters; gastrointestinal cancer; chemotherapy; exploratory factor analysis

INTRODUCTION

Gastrointestinal (GI) cancers account for 20% of new cancer cases and 15% of cancer deaths worldwide.[1] While treatment for GI cancers depends on the specific type of cancer and stage of the disease, the majority of patients will undergo surgery, radiation therapy, and/or chemotherapy (CTX).[2,3] Patients with GI cancer experience a variety of multiple, co-occurring symptoms as a result of their disease and its treatment.[4] For example, in a study of patients with colorectal cancer (n=104),[5] the average number of symptoms on the Memorial Symptom Assessment Scale (MSAS) was 10.3 and the most common symptoms were: numbness/tingling in the hands/feet (64%), lack of energy (62%), feeling drowsy (49%), difficulty sleeping (46%), nausea (45%), worrying (44%), shortness of breath (43%), and dry mouth (42%). In another study of 397 patients with a variety of GI cancers who were evaluated one week after CTX,[6] the mean number of MSAS symptoms was 12.5. The co-occurrence of multiple symptoms in cancer patients is associated with decrements in functional status and quality of life (QOL), as well as an increase in mortality.[7]

One promising approach to examine multiple co-occurring symptoms is to evaluate for symptom clusters.[8] An evaluation of symptom clusters in patients with GI cancer may assist with the identification of “sentinel” symptom clusters, symptoms that share a common underlying mechanism, as well as the development of more effective interventions.[8] Across various types of GI cancer, only six studies have evaluated for symptom clusters.[9–14] Across these six studies, two evaluated patients with pancreatic cancer,[9,14] two evaluated patients with hepatocellular carcinoma,[10,11] one evaluated patients with esophageal cancer,[12] and one compared symptom clusters in younger versus older survivors with colorectal cancer.[13] The instruments used to create the symptom clusters were highly variable in terms of the number of symptoms evaluated (i.e., 6[13] to 19[11]) and were primarily cancer diagnosis specific (e.g., FACT-Hepatobiliary Questionnaire[10,11,14]). The majority of these studies used exploratory factor analysis (EFA)[11,14] or principal component analysis (PCA)[10,12,13] to identify the symptom clusters. Across these six studies, while the number of symptom clusters ranged from one[9] to five,[14] no common symptom cluster was identified.[9–14] While these studies provide information on symptom clusters in a select number of GI cancers, given their limitations, particularly the use of disease specific instruments, it is difficult to compare findings across symptom cluster studies that used more generic instruments (e.g., MSAS,[15] MD Anderson Symptom Inventory [MDASI][16]).

Patients are often diagnosed with multiple GI cancers simultaneously (e.g., colon and rectum)[17] and have cancer metastases across multiple GI organs.[17] For example, in one

study,[18] approximately 30% of the patients with GI cancers had at least two multiple metastatic and malignant tumors in the digestive system. None of the studies of symptom clusters in patients with GI cancers[9–14] included a more heterogeneous sample of patients in terms of GI cancer diagnoses; none of these studies compared symptom clusters based on multiple dimensions of the symptom experience (i.e., occurrence, severity, and distress); and none of these studies evaluated for symptom clusters in patients undergoing CTX. Therefore, the purposes of this study, in a sample of patients with GI cancer undergoing CTX (n = 399), were to describe the occurrence, severity, and distress of 38 symptoms and to identify whether the number and types of symptom clusters differed based on the symptom dimensions (i.e., occurrence, severity, distress) used to create the clusters.

METHODS

Patients and Settings

This analysis is part of a larger study, funded by the National Cancer Institute, that evaluated the symptom experience of oncology outpatients receiving CTX.[19] Eligible patients were >18 years of age; had a diagnosis of breast, lung, GI, or gynecological cancer; had received CTX within the preceding four weeks; were scheduled to receive at least two additional cycles of CTX; 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. For this analysis, from a total sample of 1,343 patients, 399 patients with a GI cancer (e.g., colon, rectal, esophagus, stomach) were evaluated.

Procedures

Eligible patients were approached by a research staff member in the infusion unit, following their first or second cycle of CTX, to discuss participation in the study. Written informed consent was obtained from all patients. Depending on the length of their CTX cycle, patients completed questionnaires in their home and returned them in a postage paid envelope, a total of 6 times over two cycles of CTX. Data from the enrollment assessment (symptoms in the week prior to their second or third cycle of CTX; namely recovery from the previous cycle [T1]) were used in these analyses. Medical records were reviewed for disease and treatment information. The parent study was approved by the Committee on Human Research at the University of California, San Francisco and by the Institutional Review Board at each of the study sites.

Instruments

A demographic questionnaire obtained information on age, gender, ethnicity, marital status, living arrangements, education, employment status, and income. Karnofsky Performance Status (KPS) scale was used to evaluate patients' functional status.[20] Patients rated their functional status using the KPS scale that ranged from 30 (I feel severely disabled and need to be hospitalized) to 100 (I feel normal; I have no complaints or symptoms).[21,22] Self-Administered Comorbidity Questionnaire (SCQ) was used to evaluate 13 common medical conditions.[23] The total SCQ score ranges from 0 to 39. The SCQ has well established validity and reliability.[24,25]

A modified version of the MSAS was used to evaluate the occurrence, severity, and distress of 38 symptoms commonly associated with cancer and its treatment. Given that the 32-item MSAS was not revised since its publication in 1994,[15] six additional symptoms that are common in oncology patients were assessed: hot flashes, chest tightness, difficulty breathing, abdominal cramps, increased appetite, and weight gain. Using the MSAS, patients were asked to indicate whether they had experienced each symptom in the past week (i.e., symptom occurrence). If they had experienced the symptom, they were asked to rate its severity and distress. Symptom severity was measured using a 4-point Likert scale (i.e., 1 = slight, 2 = moderate, 3 = severe, 4 = very severe). Symptom distress was measured using a 5-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 is well established in studies of oncology inpatients and outpatients.[15]

Data Analyses

Data were analyzed using the Statistical Package for the Social Sciences Version 23,[26] STATA Release 15,[27] and MPlus Version 7.3.[28] Descriptive statistics and frequency distributions were calculated for the demographic and clinical characteristics, as well as symptom occurrence rates and severity and distress ratings.

To identify the symptom clusters, EFAs were done for the dichotomous (i.e., occurrence) and ordinal (i.e., severity and distress) items. Factor analysis is a generic term used for several procedures that aim to identify whether correlations between a set of observed variables can be explained by a few latent, unobserved variables (i.e., factors).[29] While it is more common to describe the results of an EFA as “factors”, the “factors” in the current study are referred to as symptom clusters.[30,31] All of the EFAs were done using MPlus because the program provides appropriate estimation for dichotomous and ordinal items.[28]

For the EFA, factor loadings were considered meaningful if the loading was ≥ 0.40.[28] In addition, factors were considered to be adequately defined if at least two items (i.e., symptoms) had loadings (i.e., structure coefficients following rotation) of ≥0.40.[29] While it is common to require that each item load strongly on only one factor, in this study, items that loaded on two factors (i.e., cross loaded) and fell within our pre-set criteria of ≥0.40, were retained and used to define both factors (i.e., the symptom clusters). The cross loading of symptoms on more than one factor may be beneficial in the interpretation of potential causal mechanisms, especially when oblique rotation is employed.[29,32]

In order to have sufficient variation and covariation to perform the EFAs, only symptoms that were present in >20% and <80% of the patients were included in these analyses. Based on these criteria, for each of the EFAs, 29 out of the 38 MSAS symptoms were used. Nine symptoms on the MSAS (i.e., hot flashes, shortness of breath, mouth sores, chest tightness, difficulty breathing, swelling of arms or legs, difficulty swallowing, problems with urination, vomiting) were excluded from the analyses due to insufficient variation in the occurrence of these symptoms.

For the EFA using the dichotomous occurrence items, tetrachoric correlations were used to create the matrix of associations.[28] For the EFAs using the ordinal 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 geomin rotation method was used to create the best fit for the model. Adopting this rotational method provided an improved representation of how the factors were correlated and improved the interpretability of each factor solution.[28] The unweighted least squares estimator (ULSMV: unweighted least squares parameter estimates with standard errors and a mean and variance adjusted chi-square test using a full weight matrix[28]) was selected in order to achieve more reliable results because the scales for the MSAS items are dichotomous (i.e., occurrence) and ordinal (i.e., severity and distress).

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 (i.e., occurrence), a severity score of zero was assigned. The EFA for distress was done using distress ratings that included a 0 (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 six factors. After examining all of the factor solutions, the factor solution with the greatest interpretability and clinical meaningfulness was selected, given that it met the criteria set for evaluating simple structure (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. The name of the symptom cluster was based on the majority of the symptoms in the cluster.

Differences in number and types of symptom clusters

To evaluate the percentage agreement among the symptoms within the same cluster using occurrence, severity, and distress ratings, we used the criteria proposed by Kirkova and Walsh.[33] In their paper, they suggested that to be in agreement with each other, at least 75% of the symptoms in the clusters should be present including the prominent and most important symptom, namely the symptom with the greatest weight from the factor analyses. By way of example, percentage agreement for the psychological symptom cluster, that consisted of a total of 12 symptoms across all three dimensions, was calculated as follows for the occurrence dimension: 8 symptoms/12 symptoms × 100 = 66.7% agreement.

RESULTS

Demographic and Clinical Characteristics

The demographic and clinical characteristics of the patients are summarized in Table 1. Of the total sample of 399 patients, 54.9% were male, 63.2% were married or partnered, 68.7% were White, and had a mean age of 57.9±11.8 years. The majority of patients were well educated (16.0 ±3.0 years), non-smokers (69.4%), and exercised on a regular basis (65.9%). In terms of clinical characteristics, the patients had an average of 2.3±1.3 comorbid conditions; a KPS score of 80.7±12.5; were 1.4±2.8 years from their cancer diagnosis

(median = 0.4 years); and had received 1.4±2.8 prior cancer treatments. The most common GI cancer diagnoses were colon (46.4%), rectal (20.1%), and pancreatic (18.5%). While the majority of the patients were receiving adjuvant CTX, 8.5% were receiving neoadjuvant CTX. On average, patients reported 13.0±7.1 symptoms on the MSAS prior to their next cycle of CTX.

Symptom Ratings

The occurrence, severity, and distress ratings for the 38 MSAS symptoms are summarized in Table 2. The six symptoms that occurred in >50% of the patients were: lack of energy (79.7%), numbness or tingling in hands/feet (62.2%), difficulty sleeping (60.7%), pain (59.4%), feeling drowsy (57.1%), and nausea (50.9%).

In terms of the severity ratings, mean scores were calculated in two ways (i.e., with and without zeros). In the “with zeros” analyses, all 399 patients were included and those patients who did not report the symptom were assigned a severity score of zero. When zeros were included in the calculation of the mean severity scores, scores ranged from 0.16±0.6 (swelling of arms or legs) to 1.62±1.0 (lack of energy). In the “without zeros” analyses, only those patients who reported each symptom were included and had severity scores that could range from 1 to 4. When zeros were not included in the mean severity scores, the scores ranged from 1.38±0.5 (cough) to 2.39±1.0 (problems with sexual interest or activity). As shown in Table 2, in the “with zeros” analysis, none of the symptoms had a mean severity score of ≥2.0. In contrast, when zero was not included in the analysis, the symptoms that had a mean severity score of ≥2.0 included: problems with sexual interest or activity (2.39±1.0), change in the way food tastes (2.10±0.8), and lack of energy (2.03±0.7). In terms of the symptom distress ratings, the mean distress scores ranged from 0.75±1.1 (increased appetite) to 1.77±1.1 (“I don’t look like myself”; Table 2).

Symptom Clusters Based on Symptom Occurrence

The EFA for symptom occurrence indicated that a 4-factor solution was the best fit for the data (Table 3). Factor 1 with eight symptoms was named the psychological cluster. Factor 2 with eight symptoms was named the CTX-related cluster. Factor 3 with three symptoms was named the GI cluster. Factor 4 with two symptoms was named the weight change cluster.

Symptom Clusters Based on Symptom Severity

For the severity dimension, a 4-factor solution was the best fit for the data (Table 4). Factor 1 with eight symptoms was named the psychological cluster. Factor 2 with eight symptoms was named the CTX-related cluster. Factor 3 with four symptoms was named the GI cluster. Factor 4 with two symptoms was named the weight change cluster.

Symptom Clusters Based on Symptom Distress

For the distress dimension, a 4-factor solution was the best fit for the data (Table 5). Factor 1 with 10 symptoms was named the psychological cluster. Factor 2 with eight symptoms was named the CTX-related cluster. Factor 3 with two symptoms was named the weight change cluster. Factor 4 with two symptoms was named the GI cluster.

Agreement in the Types of Symptoms within Each Symptom Cluster

Table 6 presents a summary of the percentage agreement among the symptoms within each cluster across the occurrence, severity, and distress dimensions. For the psychological symptom cluster, the total number of symptoms ranged from 8 to 10 and the percent agreement ranged from 66.7% to 83.3%. The seven symptoms that were included in the occurrence, severity, and distress clusters were: lack of energy, difficulty concentrating, feeling nervous, feeling drowsy, feeling sad, worrying, and feeling irritable.

For the CTX-related symptom cluster, the total numbers of symptoms was 8 and the percent agreement was 80%. The six symptoms that were included in the occurrence, severity, and distress clusters were: itching, lack of appetite, weight loss, change in the way food tastes, changes in skin, and dizziness.

For the GI symptom cluster, the total numbers of symptoms ranged from 2 to 4 and the percent agreement ranged from 40% to 80%. Only abdominal cramps was included in the occurrence, severity and distress clusters.

For the weight change symptom cluster, the total number of symptoms was 2 and the percent agreement was 100%. The two symptoms that were included were: increased appetite and weight gain.

DISCUSSION

This study is the first to provide detailed information on the symptom experience of patients with GI cancers, and to evaluate for differences in symptom clusters derived using occurrence rates, as well as severity and distress ratings. These patients reported an average of 13 symptoms in the week prior to their second or third cycle of CTX. The most common and severe symptom was lack of energy and the most distressing symptom was “I don’t look like myself”. Consistent with previous reports in patients with breast[19,34,35] and lung[36] cancer, for all three symptom dimensions, the same four symptom clusters (i.e., psychological, CTX-related, GI, weight change) were identified and the symptoms within each cluster were relatively similar. The remainder of this discussion will place these findings within the context of the extant literature.

Psychological Symptom Cluster

While a psychological symptom cluster was reported in previous studies of patients with breast,[19,35,37] lung,[36,38] and heterogeneous cancer diagnoses,[16,39–44] it was found in only three of the six studies of symptom clusters in patients with GI cancers.[11,13,14] Across the four symptom cluster studies in GI cancers (i.e., our study and the other three[11,13,14]), anxiety and depression were the two consistent symptoms. However, in other studies that used the MSAS,[45–47] worrying, feeling sad, feeling nervous, feeling irritable, difficulty in concentrating, lack of energy, and feeling drowsy were the common symptoms in the psychological cluster. The lack of a psychological cluster in the remaining three GI studies[9,10,12] is most likely related to variations in instruments used to assess symptoms. Given the relatively high rates of depression (i.e., 21%[48] to 31%[49]) and anxiety(17%)[48] in

patients with GI cancers, future studies should include these symptoms on GI cancer specific assessment instruments (e.g., FACT-Hepatobiliary Questionnaire).

CTX-related Symptom Cluster

While none of the previous studies of symptom clusters in patients with specific GI cancers identified a CTX-related symptom cluster,[9–14] this cluster was identified in a previous study that evaluated for age differences in symptom clusters in patients with a variety of cancer diagnoses.[45] Given that the previous studies of GI patients did not evaluate for symptom clusters during CTX,[9–14] it is not surprising that a CTX-related cluster was not identified. Patients with GI cancers often receive CTX regimens that contain oxaliplatin, 5-fluouracil and/or irinotecan.[50,51] The most common adverse effects associated with these agents include nausea, lack of appetite, change in the way food tastes, and weight loss.[52] In the current study, across all symptom dimensions, nausea (50.9%), change in the way food tastes (49.9%) and dry mouth (44.4%) were the most prevalent symptoms within the CTX-related cluster. In a previous study of patients with pancreatic cancer,[14] nausea and change in the way food tastes were included in the gustatory (i.e., change in taste, dry mouth) or a discomfort (i.e., nausea) symptom cluster. In another study of patients with hepatocellular cancer,[10] loss of appetite, nausea, and change in taste loaded on the pain-appetite symptom cluster and itching was included in the itching-constipation cluster. In three studies of patients with breast cancer,[35,37,53] lack of appetite, nausea, and change in the way food tastes loaded on a GI symptom cluster.

A surprising and not readily explained finding in our study is that while numbness/tingling in hands/feet loaded on a CTX-related symptom cluster in studies of patients with breast cancer[19] and heterogeneous cancer diagnoses,[54] this symptom did not load on any of our symptom clusters. In terms of the other two symptoms in the CTX-related cluster, patients in our study reported relatively high distress rating for both ”I don’t look like myself” and hair loss. In a previous study of patients with ovarian cancer,[47] these two symptoms loaded on a “body image distress symptom cluster.” These inconsistent findings may be related to differences in the symptom assessment measures, patients’ cancer diagnoses, specific CTX regimens administered, and the method used to create the symptom clusters.

GI Symptom Cluster

While a GI symptom cluster was identified across all three symptom dimensions in our study, abdominal cramps was the only consistent symptom. In numerous studies of patients with breast,[19,35,37,53] lung,[36,38] and heterogeneous cancer diagnoses,[55] a GI symptom cluster was identified and nausea and vomiting were the most common symptoms in these studies. However, a GI symptom cluster was identified in only three studies of patients with GI cancers.[10,11,14] In two of these studies,[10,14] diarrhea was the symptom that was consistent with our findings. In another study of patients with GI cancers,[11] nausea was the consistent symptom in the GI cluster.

Interestingly, abdominal cramps and feeling bloated were included in the GI cluster in our study, as well as in a study of patients with hepatocellular carcinoma[10] and two studies of patients with breast cancer.[19,45] These two symptoms may be associated with the GI cancers

themselves and/or occur as a result of CTX-induced changes in the gut microbiome.[56] In addition, these symptoms may be related to decreases in GI motility associated with various CTX agents (e.g., cisplatin, oxaliplatin).[2] While loperamide is a non-analgesic agonist that acts at the 8-opioid receptor and is a first line therapy for CTX-related diarrhea,[57] the most common side effects associated with this drug include severe constipation, abdominal cramps, and bloating.[58] Given that, in our study, diarrhea and constipation loaded on the GI cluster depending on the symptom dimension that was used to create the cluster, interventions to manage this symptom cluster need to be tailored to individual patients.

Weight Change Symptom Cluster

For the weight change symptom cluster, increased appetite and weight gain were found in all three EFAs. None of the studies of patients with GI cancers identified a weight change cluster.[9–14] However, in our previous report of patients with breast cancer from this sample, while a weight change cluster was identified at the same assessment as this analysis,[59] only weight gain was the consistent within this symptom cluster. Of note, in the patients with breast cancer, weight gain loaded negatively on the weight change cluster. While only 22.8% of our patients with GI cancer reported weight gain and 24.6% reported increased appetite, the underlying reasons for this symptom cluster are not known. Additional research is warranted to confirm this distinct symptom cluster.

Several limitations warrant consideration. The heterogeneity in the patients' GI cancer diagnoses (e.g., colorectal, liver, pancreatic), CTX agents used, and various types of previous cancer treatments could influence the numbers and types of symptom clusters. In addition, because of its cross-sectional design, changes in symptom clusters during and after CTX need to be evaluated.

In summary, four symptom clusters (i.e., psychological, CTX-related, GI, weight change) were identified in patients with GI cancers prior to their second or third cycle of CTX. Across all three symptom dimensions, the symptoms within each cluster were relatively stable. This finding suggests that patients may not be able to distinguish between the dimensions of severity and distress or that the Likert scales did not provide an adequate range of scores to detect these differences. Future studies of symptom clusters in patients with GI cancers need to evaluate the stability of symptom clusters over time. If these symptom clusters persist, tailored interventions that address each symptom cluster need to be designed and evaluated (e.g., nutritional counseling for the weight change cluster). Finally, the underlying mechanisms for the various symptom clusters need to be determined.

Acknowledgments

Disclosures: This study was funded by a grant from the National Cancer Institute (NCI, CA134900). Dr. Miaskowski is an American Cancer Society Clinical Research Professor and is funded by a K05 award from the NCI (CA168960), Dr. Han is funded by a NCI Training Program in Biobehavioral Cancer Prevention and Control (CA092408).

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Table 1.

Demographic and Clinical Characteristics of Patients with GI cancers (n=399)

Characteristic	**Mean**	**(SD)**
Age (years)	57.9	(11.8)
Education (years)	16.0	(3.0)
Body mass index (kilograms/metered squared)	25.8	(5.3)
Karnofsky Performance Status score	80.7	(12.5)
Number of comorbidities out of 13	2.3	(1.3)
Self-administered Comorbidity Questionnaire score	5.4	(2.9)
Time since cancer diagnosis (years)	1.4	(2.8)
Time since diagnosis (median)	0.4	
Number of prior cancer treatments (out of 9)	1.4	(1.3)
Number of metastatic sites including lymph node involvement (out of 9)	1.5	(1.1)
Number of metastatic sites excluding lymph node involvement (out of 8)	0.9	(1.0)
Mean number of MSAS symptoms (out of 38)	13.0	(7.1)
	n	%
Gender		
Female	180	(45.1)
Male	219	(54.9)
Ethnicity		
White	274	(68.7)
Black	36	(9.0)
Asian or Pacific Islander	46	(11.5)
Hispanic, Mixed, or Other	43	(10.8)
Married or partnered (% yes)	252	(63.2)
Lives alone (% yes)	74	(18.5)
Child care responsibilities (% yes)	81	(20.3)
Care of adult responsibilities (% yes)	27	(6.8)
Currently employed (% yes)	133	(33.3)
Income		
< $30,000	73	(18.4)
$30,000 to < $70,000	69	(17.4)
$70,000 to < $100,000	61	(15.3)
> $100,000	155	(38.8)
Exercise on a regular basis (% yes)	263	(65.9)
Current or history of smoking (% yes)	122	(30.6)
Receiving neoadjuvant chemotherapy (% yes)	34	(8.5)
Type of prior cancer treatment		
No prior treatment	113	(28.3)
Only surgery, CTX, or RT	149	(37.3)

Characteristic	Mean	(SD)
Surgery & CTX, or surgery & RT, or CTX & RT	85	(21.3)
Surgery & CTX & RT	42	(10.5)
GI cancer diagnoses		
Colon	185	(46.4)
Rectal	80	(20.1)
Pancreatic	74	(18.5)
Esophageal	21	(5.3)
Gastric	19	(4.8)
Gall blander/bile duct	10	(2.5)
Liver	6	(1.5)
Small intestine	6	(1.5)
Anal	5	(1.3)
Other	25	(6.3)

Abbreviations: CTX = chemotherapy; GI = gastrointestinal; MSAS = Memorial Symptom Assessment Scale, RT = radiation therapy, SD = standard deviation

Table 2.

Symptom Occurrence Rates, Severity and Distress Ratings for Symptoms at the Time of Enrollment (n=399)

Symptoms[a]	Occurrence		Severity Ratings without Zero[b]		Rank order	Severity Ratings with Zero[c]		Rank order	Distress Ratings[d]		Rank order
	%	n	Mean	SD		Mean	SD		Mean	SD	
Lack of energy	79.7	318	2.03	0.7	3	1.62	1.0	1	1.72	1.1	3
Numbness or tingling in hands/feet	62.2	248	1.95	0.8	7	1.20	1.1	3	1.62	1.1	9
Difficulty sleeping	60.7	242	1.99	0.7	4	1.21	1.1	2	1.73	1.3	2
Pain	59.4	237	1.90	0.7	11	1.12	1.1	4	1.72	1.1	3
Feeling drowsy	57.1	228	1.78	0.7	16	1.01	1.0	6	1.14	1.0	28
Nausea	50.9	203	1.81	0.7	15	0.90	1.1	7	1.68	1.1	4
Change in the way food tastes	49.9	199	2.10	0.8	2	1.05	1.2	5	1.61	1.2	10
Worrying	47.1	188	1.82	0.7	14	0.85	1.0	10	1.52	0.9	15
Difficulty concentrating	44.6	178	1.56	0.6	24	0.69	0.9	13	1.49	1.0	17
Dry mouth	44.4	177	1.75	0.7	17	0.77	1.0	11	1.20	1.2	27
Lack of appetite	44.1	176	1.98	0.8	5	0.88	0.8	8	1.42	1.0	19
Constipation	43.9	175	1.99	0.8	4	0.87	1.1	9	1.67	1.2	5
Feeling sad	40.9	163	1.69	0.6	19	0.69	0.9	13	1.37	1.0	23
Hair loss	40.4	161	1.95	0.9	7	0.77	1.1	11	1.58	1.1	11
Diarrhea	38.3	153	1.97	0.8	6	0.75	1.1	12	1.65	1.1	6
Feeling irritable	36.3	145	1.60	0.7	22	0.57	0.9	16	1.33	1.2	24
Changes in skin	32.6	130	1.91	0.8	10	0.62	1.0	15	1.61	1.1	10
Weight loss	30.1	120	1.78	0.8	16	0.53	0.9	19	1.38	1.1	22
Feeling bloated	29.8	119	1.87	0.8	12	0.55	0.9	17	1.65	1.3	6
Abdominal cramps	28.3	113	1.94	0.8	8	0.54	0.9	18	1.63	1.0	8
Feeling nervous	28.3	113	1.64	0.7	21	0.46	0.8	21	1.40	0.9	21
Dizziness	27.8	111	1.55	0.7	25	0.43	0.8	22	1.28	1.1	25
Problems with sexual interest or activity	27.1	108	2.39	1.0	1	0.63	1.2	14	1.64	1.1	7
“I don’t look like myself’	25.6	102	1.92	0.7	9	0.48	0.9	20	1.77	1.1	1
Sweats	24.8	99	1.75	0.8	17	0.42	0.8	23	1.12	1.2	29

Symptoms[a]	Occurrence		Severity Ratings without Zero[b]		Rank order	Severity Ratings with Zero[c]		Rank order	Distress Ratings[d]		Rank order
	%	n	Mean	SD		Mean	SD		Mean	SD	
Increased appetite	24.6	98	1.76	0.6	16	0.42	0.8	23	0.75	1.1	32
Cough	23.6	94	1.38	0.5	27	0.32	0.6	26	0.83	1.0	31
Weight gain	22.8	91	1.56	0.6	24	0.35	0.7	25	0.87	1.3	30
Itching	21.1	84	1.83	0.8	13	0.38	0.8	24	1.44	1.0	18
Mouth sores	19.0	76	1.74	0.8	18	0.32	0.7	26	1.41	1.2	20
Shortness of breath	18.3	73	1.59	0.6	23	0.29	0.7	28	1.54	1.1	13
Hot flashes	17.8	71	1.82	0.7	14	0.32	0.8	26	1.23	1.1	26
Difficulty swallowing	16.8	67	1.81	0.8	5	0.30	0.7	27	1.77	1.2	1
Vomiting	15.3	61	1.82	0.9	14	0.28	0.7	29	1.73	1.1	2
Difficulty breathing	14.8	59	1.67	0.7	20	0.24	0.6	31	1.56	1.2	12
Problems with urination	14.0	56	1.83	0.6	13	0.25	0.7	30	1.68	1.2	4
Chest tightness	12.8	51	1.39	0.5	26	0.17	0.5	32	1.33	1.2	24
Swelling of arms or legs	8.5	34	1.97	0.8	6	0.16	0.6	33	1.53	1.1	14

Abbreviation: SD = standard deviation

[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: 1 = slight, 2 = moderate, 3 = severe, 4 = very severe.

[c] Severity ratings: 0 = did not have the symptom, 1 = slight, 2 = moderate, 3 = severe, 4 = very severe.

[d] Distress ratings: 1 = not at all, 2 = a little bit, 3 = somewhat, 4 = quite a bit, 5 = very much.

Table 3.

Exploratory Factory Analysis Using Ratings of Symptom Occurrence at the Time of Enrollment (n=399)

Symptoms	Factor 1	Factor 2	Factor 3	Factor 4
	Psychological Symptom Cluster	Chemotherapy-related Symptom Cluster	Gastrointestinal Symptom Cluster	Weight change Symptom Cluster
Lack of energy	**0.463**	0.307	0.135	−0.128
Difficulty concentrating	**0.712**	0.057	0.023	−0.079
Feeling nervous	**0.822**	0.030	−0.113	−0.011
Feeling drowsy	**0.404**	0.365	−0.014	−0.036
Feeling sad	**0.863**	−0.039	−0.017	−0.016
Worrying	**0.895**	−0.213	0.115	−0.001
Feeling irritable	**0.642**	0.080	0.095	0.025
Dry mouth	0.084	**0.451**	−0.039	0.121
Nausea	0.025	**0.464**	0.330	−0.056
Itching	0.048	**0.489**	−0.174	0.337
Lack of appetite	−0.162	**0.844**	0.083	−0.147
Weight loss	−0.022	**0.617**	0.059	−0.220
Change in the way food tastes	0.035	**0.466**	0.035	0.158
Changes in skin	**0.420**	**0.500**	−0.232	0.047
Dizziness	0.073	**0.504**	0.094	0.121
Feeling bloated	0.072	0.083	**0.689**	0.126
Abdominal cramps	0.052	−0.001	**0.734**	0.159
Constipation	0.011	0.302	**0.431**	−0.116
Increased appetite	−0.061	0.047	0.094	**0.836**
Weight gain	−0.005	−0.139	0.024	**0.962**
Pain	0.310	−0.034	0.268	0.061
Cough	0.231	0.268	−0.138	0.141
Numbness/tingling in hands/feet	0.147	0.185	0.086	0.020
Difficulty sleeping	0.254	0.265	0.109	0.084
Diarrhea	0.006	0.207	0.341	0.145

Symptoms	Factor 1	Factor 2	Factor 3	Factor 4
	Psychological Symptom Cluster	**Chemotherapy-related Symptom Cluster**	**Gastrointestinal Symptom Cluster**	**Weight change Symptom Cluster**
Sweats	0.333	0.051	0.169	0.187
Problems with sexual interest or activity	0.341	0.177	0.065	0.077
Hair loss	0.105	0.320	0.000	0.190
“I don’t look like myself’	0.241	0.272	−0.007	0.121

Rotation method: Geomin (oblique) rotation.

Bold fonts indicate factor loading for symptom was > 0.40.

Table 4.

Exploratory Factory Analysis Using Ratings of Symptom Severity at the Time of Enrollment (n=399)

Symptoms	Factor 1	Factor 2	Factor 3	Factor 4
	Psychological Symptom Cluster	Chemotherapy-related Symptom Cluster	Gastrointestinal Symptom Cluster	Weight change Symptom Cluster
Lack of energy	**0.498**	0.218	0.151	−0.248
Difficulty concentrating	**0.716**	0.052	0.009	−0.107
Feeling nervous	**0.775**	−0.062	0.006	0.045
Feeling drowsy	**0.458**	0.271	0.033	−0.124
Feeling sad	**0.845**	−0.064	−0.057	0.030
Worrying	**0.800**	−0.105	0.063	0.025
Feeling irritable	**0.528**	0.094	0.175	0.040
Problems with sexual interest or activity	**0.428**	0.149	−0.006	−0.044
Dizziness	0.051	**0.507**	0.137	0.035
Weight loss	−0.019	**0.582**	0.027	−0.278
Lack of appetite	−0.073	**0.768**	0.079	−0.260
Itching	0.061	**0.466**	−0.033	0.295
Hair loss	−0.039	**0.443**	0.026	0.177
Change in the way food tastes	0.029	**0.606**	0.029	0.100
“I don’t look like myself’	0.241	**0.418**	−0.122	0.089
Changes in skin	0.347	**0.586**	−0.249	0.006
Nausea	0.104	0.305	**0.404**	−0.140
Feeling bloated	0.034	0.102	**0.616**	0.154
Diarrhea	0.018	0.035	**0.561**	0.065
Abdominal cramps	0.035	−0.072	**0.858**	0.004
Constipation	0.108	0.321	0.200	−0.164
Increased appetite	−0.038	0.022	0.297	**0.785**
Weight gain	0.050	−0.003	0.101	**0.871**
Cough	0.185	0.295	−0.098	0.119
Dry mouth	0.157	0.269	0.192	0.049

Symptoms	Factor 1	Factor 2	Factor 3	Factor 4
	Psychological Symptom Cluster	**Chemotherapy-related Symptom Cluster**	**Gastrointestinal Symptom Cluster**	**Weight change Symptom Cluster**
Difficulty sleeping	0.361	0.195	0.081	0.081
Numbness/tingling in hands/feet	0.241	0.068	0.190	−0.077
Pain	0.282	0.056	0.267	0.003
Sweats	0.314	0.108	0.159	0.151

Rotation method: Geomin (oblique) rotation.

Bold fonts indicate factor loading for symptom was > 0.40.

Table 5.

Exploratory Factory Analysis Using Ratings of Symptom Distress at the Time of Enrollment (n=399)

Symptoms	Factor 1	Factor 2	Factor 3	Factor 4
	Psychological Symptom Cluster	Chemotherapy-related Symptom Cluster	Weight change Symptom Cluster	Gastrointestinal Symptom Cluster
Difficulty concentrating	**0.767**	−0.030	−0.083	0.037
Feeling nervous	**0.707**	−0.060	0.047	0.001
Feeling sad	**0.760**	0.041	0.084	−0.137
Worrying	**0.959**	−0.166	0.040	−0.102
Feeling irritable	**0.618**	0.071	−0.013	0.119
Lack of energy	**0.552**	0.252	−0.235	0.051
Feeling drowsy	**0.488**	0.240	−0.099	0.079
Difficulty sleeping	**0.407**	0.140	0.030	0.095
Pain	**0.459**	0.109	0.002	0.117
Sweats	**0.502**	0.031	0.093	0.075
Dizziness	0.093	**0.564**	0.031	0.022
Change in the way food tastes	0.046	**0.559**	0.058	0.052
Lack of appetite	−0.041	**0.807**	−0.246	−0.030
Weight loss	−0.010	**0.602**	−0.233	0.048
Itching	−0.089	**0.516**	0.263	0.024
“I don’t look like myself’	0.187	**0.537**	0.059	−0.207
Changes in skin	0.268	**0.622**	0.034	−0.293
Hair loss	0.020	**0.449**	0.118	0.100
Increased appetite	−0.004	0.050	**0.779**	0.241
Weight gain	0.050	−0.018	**0.929**	0.001
Diarrhea	0.064	0.063	0.087	**0.620**
Abdominal cramps	0.289	−0.029	0.024	**0.621**
Constipation	0.297	0.279	−0.135	0.089
Cough	0.066	0.322	0.075	0.028
Dry mouth	0.081	0.344	0.113	0.205

Symptoms	Factor 1	Factor 2	Factor 3	Factor 4
	Psychological Symptom Cluster	**Chemotherapy-related Symptom Cluster**	**Weight change Symptom Cluster**	**Gastrointestinal Symptom Cluster**
Nausea	0.252	0.367	−0.133	0.262
Numbness/tingling in hands/feet	0.321	0.150	−0.046	0.156
Feeling bloated	0.356	0.103	0.126	0.358
Problems with sexual interest or activity	0.384	0.278	−0.016	−0.170

Rotation method: Geomin (oblique) rotation.

Bold fonts indicate factor loading for symptom was > 0.40.

J Pain Symptom Manage. Author manuscript; available in PMC 2020 August 01.

Table 6.

Summary of Symptom Clusters Using Occurrence Rates and Severity and Distress Ratings

Symptom Cluster	Symptoms within the Cluster	Occurrence	Severity	Distress
Psychological	Lack of energy	•	•	•
	Difficulty concentrating	•	•	•
	Feeling nervous	•	•	•
	Feeling drowsy	•	•	•
	Feeling sad	•	•	•
	Worrying	•	•	•
	Feeling irritable	•	•	•
	Problems with sexual interest or activity		•	
	Changes in skin	•		
	Difficulty sleeping			•
	Pain			•
	Sweats			•
	Percent agreement (n=12)	66.7	66.7	83.3
Chemotherapy-related	Dry mouth	•		
	Nausea	•		
	Itching	•	•	•
	Lack of appetite	•	•	•
	Weight loss	•	•	•
	Change in the way food tastes	•	•	•
	Changes in skin	•	•	•
	Dizziness	•	•	•
	Hair loss		•	•
	“I don’t look like myself’		•	•
	Percent agreement (n=10)	80.0	80.0	80.0
Gastrointestinal	Feeling bloated	•	•	
	Abdominal cramps	•	•	•
	Constipation	•		

Symptom Cluster	Symptoms within the Cluster	Occurrence	Severity	Distress
	Nausea		•	
	Diarrhea		•	•
	Percent agreement (n=5)	60.0	80.0	40.0
Weight change	Increased appetite	•	•	•
	Weight gain	•	•	•
	Percent agreement (n=2)	100.0	100.0	100.0