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The symptom burden of cancer: evidence for a core set of cancer-related and treatment-related symptoms from the Eastern Cooperative Oncology Group's Symptom Outcomes and Practice Patterns Study

Charles S. Cleeland, PhD¹, Fengmin Zhao, PhD², Victor T. Chang, MD³, Jeff A. Sloan, PhD⁴, Ann M. O'Mara, PhD⁵, Paul B. Gilman, MD⁶, Matthias Weiss, MD⁷, Tito R. Mendoza, PhD¹, Ju-Whei Lee, PhD², and Michael J. Fisch, MD, MPH⁸

¹Department of Symptom Research, The University of Texas MD Anderson Cancer Center, Houston, TX

²Department of Biostatistics & Computational Biology, Dana-Farber Cancer Institute, Boston, MA

³VA New Jersey Health Care System/Rutgers UMDNJ, East Orange, NJ

⁴Department of Health Sciences Research, Mayo Clinic College of Medicine, Rochester, MN

⁵Community Oncology and Prevention Trials Research Group, Division of Cancer Prevention, National Cancer Institute, Bethesda, MD

⁶Main Line Hematology/Oncology Associates, Lankenau Cancer Center, Wynnewood, PA

⁷Marshfield Clinic, Marshfield, WI

⁸Department of General Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Abstract

BACKGROUND—A set of common cancer-related and treatment-related symptoms has been proposed for quality-of-care assessment and clinical research. Using data from a large, multicenter, prospective study, we assessed effects of disease site and stage on the percentages of patients rating these proposed symptoms as moderate to severe.

METHODS—The severity of 13 symptoms proposed to represent “core” oncology symptoms was rated by 3106 ambulatory patients with cancer of the breast, prostate, colon/rectum, or lung, regardless of disease stage or phase of care; 2801 patients (90%) repeated the assessment 4–5 weeks later.

RESULTS—At the initial assessment, approximately one third of the patients reported 3 symptoms in the moderate-to-severe range; 11 of the 13 symptoms were rated as moderate to severe by at least 10% of all patients and 6 by at least 20% of those in active treatment. Fatigue/tiredness was the most-severe symptom, followed by disturbed sleep, pain, dry mouth, and numbness/tingling. More lung cancer patients and patients in active treatment reported moderate-to-severe symptoms. Percentages of symptomatic patients increased by disease stage, less-

Correspondence: Charles S. Cleeland, PhD, Department of Symptom Research, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Unit 1450, Houston, TX 77030, USA, Tel: 713-745-3470; Fax: 713-745-3475; ccleeland@mdanderson.org.

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adequate response to therapy, and declining performance status. Percentages of patients reporting moderate-to-severe symptoms were stable across both assessments.

CONCLUSIONS—These results support a core set of moderate-to-severe symptoms common across outpatients with solid tumors that can guide consideration of progression-free survival as a trial outcome and that should be considered in clinical care and in assessments of quality of care and treatment benefit.

Keywords

symptoms; symptom assessment; cancer; symptom management; M. D. Anderson Symptom Inventory; MDASI

INTRODUCTION

The control of disease-related and treatment-related symptoms is an integral component of cancer care, and symptom reduction is essential for patients with advanced disease. Substantial research has described the prevalence and severity of cancer-related pain and has identified factors associated with its expression and the adequacy of its treatment.^{1–3} However, cancer patients often rate other symptoms, including fatigue, poor appetite, and disrupted sleep, as equally or even more distressing^{4,5}; reducing or delaying the onset of such symptoms would be a significant treatment benefit. Similarly, progression-free survival is becoming a standard endpoint in oncology, yet the critical association between symptoms and progression-free survival is difficult to estimate because the symptomatic status of patients who progress has not been well defined.

Studies have identified various symptoms as commonly occurring and attributable both to the disease itself and to the toxicities of cancer therapy,^{6,7} and there is great interest in having a set of “core” symptoms to guide oncology research⁶ and clinical care.⁸ A panel of symptom-assessment experts from the Center for Medical Technology Policy (CMTF) developed recommendations for a core set of common cancer-related and treatment-related symptoms to be included in adult oncology clinical-effectiveness studies, especially studies of patients having advanced disease or undergoing aggressive therapy.⁹ The concept of a core set of symptoms is supported by systematic reviews of studies with large patient samples (both inpatients and outpatients) and various disease sites.^{4,5} The CMTF panel identified 12 common symptoms that affect patients to a meaningful degree: anorexia, anxiety, constipation, depression, diarrhea, dyspnea, fatigue, insomnia, nausea, pain, neuropathy, and vomiting.

In 2002, a National Institutes of Health State of the Science panel¹⁰ called for more data on the occurrence and treatment of pain, depression, and fatigue in adequately powered prospective studies. In response to this call, the Eastern Cooperative Oncology Group (ECOG) designed the large, multisite Symptom Outcomes and Practice Patterns (SOAPP) study to characterize common treatment-related and disease-related symptoms in oncology outpatient practice and to identify the relative influence of factors such as disease site, disease stage, disease status, active treatment, and performance status on patients' symptomatic status. Outpatients with cancers of high prevalence (breast, colorectal, prostate, lung) were selected for the study.

We analyzed SOAPP data to characterize the prevalence of the core symptoms proposed by the CMTF panel at moderate-to-severe levels across the 4 disease sites and to examine clinical characteristics that influence symptom severity. We hypothesized that symptoms would be substantially more-severe in patients with progressive disease, later-stage cancer, or worse performance status. We also expected that, due to treatment toxicities, symptoms

would be worse for patients currently receiving cancer therapy and that more patients with lung cancer would report severe symptoms, compared with patients in the other 3 disease groups.

METHODS

Participants

From March 3, 2006 to May 19, 2008, 3123 outpatients with invasive breast, colorectal, prostate, or lung cancer enrolled in the SOAPP study at any point in the trajectory of their care. Patients were registered at 38 ECOG-affiliated institutions, including 6 academic sites and 32 community clinics. To reduce selection bias, each site devised an ECOG-approved recruitment algorithm that was not biased toward symptom-management issues. Eligible patients were 18 years of age, willing to complete the follow-up survey, and judged by the study screener to have adequate cognitive function to complete study surveys.

The protocol was approved by the Institutional Review Boards at each registering institution. The protocol and case-report forms are accessible at www.ecogsoapp.org.

Procedures

Patients were recruited at check-in for their clinic appointments and provided written informed consent upon enrollment. Basic clinical and demographic information, including disease stage, current treatment, disease status, and ECOG performance status (ECOG PS), was then collected by study staff, before the clinician's visit. ECOG PS is a physician-rated measure of functional ability, ranging from 0 (fully functional) to 4 (completely disabled).¹¹

Symptom assessment was completed at the initial visit and at a follow-up visit 28–35 days later. Patients were asked to complete all questionnaire items according to their experience during the preceding 24 hours. Patients who were too ill to complete the follow-up questionnaire were given the option to mail the forms to the treating clinic by day 42 after the initial visit.

Symptom Assessment

Patients reported symptom intensity using an expanded version of the 19-item M. D. Anderson Symptom Inventory (MDASI).¹² Symptoms are rated “at their worst” on an 11-point numeric scale ranging from 0 (“not present”) to 10 (“as bad as you can imagine”) in the previous 24 hours. For the SOAPP study, diarrhea, constipation, sore mouth, rash, hair loss, and coughing were added to the 13 MDASI symptoms. Of these, diarrhea and constipation comprised the 2 remaining proposed core symptoms from the CMTP panel.

In this report we focus on 13 of the 19 symptoms assessed in the SOAPP study: the 12 symptoms suggested by the CMTP group⁹ (fatigue [MDASI fatigue/tiredness], insomnia [MDASI disturbed sleep], pain, anxiety [MDASI distress], neuropathy [numbness/tingling], dyspnea [MDASI shortness of breath], anorexia [MDASI lack of appetite], depression [MDASI sadness], constipation, diarrhea, nausea, and vomiting), plus xerostomia (MDASI dry mouth), which systematic reviews reported as highly prevalent.^{4,5}

Statistical Analysis

Descriptive statistics present estimates of the prevalence of moderate-to-severe symptoms across disease sites (breast, colorectal, prostate, lung) and in the presence of other variables, including current therapy (yes/no), ECOG PS (0, 1, 2–4), disease status (complete remission, partial remission, stable disease, progressive disease), and disease stage (no evidence of disease [NED], locoregional, metastatic, locoregional/metastatic). Chi-square tests were

used for subgroup comparisons. Chi-square test for trend was used to test the overall trend of change in percentage of moderate-to-severe symptoms by change in disease stage, disease status, and ECOG PS. No adjustment was made for multiple comparisons. All *P* values were 2-sided and *P* < .05 was considered statistically significant. STATA 11.2 software was used for all data analysis.¹³

We defined a moderate-to-severe symptom as 5 on the MDASI's 0–10 scale, on the basis of results from various studies, primarily of cancer-related pain. "Pain at its worst" rated as 5 causes disproportionately greater interference with function, as measured in cancer patients^{14,15} and community samples.¹⁶ Although the cutpoint used to delineate "moderate to severe" has varied somewhat across studies and even among symptoms, ranging from 4–6, we reasoned that using 5 across the board would be a simplifying compromise that offered analytical consistency across all symptoms.

RESULTS

Of 3123 patients enrolled, 3106 completed the initial MDASI and were included in our analysis. The sample included 1544 (50%) patients with breast cancer, 718 (23%) with colorectal cancer, 320 (10%) with prostate cancer, and 524 (17%) with lung cancer (Table 1). The median age was 61 years. The sample was predominantly white (86%), non-Hispanic (90%), and female (70%). The median time from initial cancer diagnosis to study registration was 1.2 years; 2299 patients (74%) were receiving cancer treatment. At the follow-up assessment, 2801 patients completed the MDASI; retention rates were 90% for breast, 93% for colorectal, 90% for prostate, and 87% for lung.

Symptom Severity at Initial Assessment

By Disease Site—By disease site, the percentages of patients rating 3 core symptoms as moderate to severe ranged from 28%–47% (Table 2). Overall, 11 of the 13 symptoms were rated as moderate to severe by 10% of all patients (Table 3). Vomiting was rated as moderate or severe by <4% of patients. Fatigue/tiredness was the most prevalent moderate-to-severe symptom in each of the cancer groups, ranging from 31% in breast cancer to 46% in lung cancer.

Patients with lung cancer were the most symptomatic group, with almost half rating 3 symptoms as moderate to severe (Table 2). Compared with patients in the other disease groups, a higher percentage of patients with lung cancer reported moderate-to-severe fatigue/tiredness, disturbed sleep, pain, dry mouth, distress, shortness of breath, lack of appetite, sadness, constipation, and nausea (all *P* < .05; Table 3). Additionally, 28% of lung cancer patients rated at least 5 of the 13 symptoms as moderate or severe, compared with 17% of the breast, 19% of the colorectal, and 15% of the prostate cancer patients (*P* < .001 for all 3 pairwise comparisons).

By Treatment Status—More than a third of patients currently receiving treatment reported 3 moderate-to-severe symptoms (Table 2). Grouped by treatment status, >20% of patients reported moderate-to-severe fatigue/tiredness and disturbed sleep; percentages were significantly higher for patients receiving treatment (both *P* < .001; Table 3). Significantly more patients receiving treatment also reported moderate-to-severe nausea, lack of appetite, dry mouth, sadness, vomiting, diarrhea, and constipation (all *P* < .05). Prior systemic therapy was associated with increased pain (16.1% versus 21.4%, *P* < .001) and numbness/tingling (15.1% versus 21.6%, *P* < .001).

By Disease Stage, Disease Status, and ECOG PS—Overall, the percentage of patients reporting each symptom as moderate to severe increased as disease stage worsened (Table 4). However, more than 20% of patients with NED reported moderate-to-severe fatigue/tiredness and disturbed sleep.

A similar pattern of increasing symptom severity was noted when patients were characterized by disease status and ECOG PS (Table 4). Higher percentages of patients with stable or progressive disease reported moderate-to-severe levels for all symptoms, compared with patients with complete response (all $P < .05$). Patients with ECOG PS = 2 were highly symptomatic. The percentages of patients with ECOG PS = 1 reporting moderate-to-severe symptoms were significantly greater than the percentages of patients with ECOG PS = 0 reporting moderate-to-severe symptoms ($P < .001$ for all 13 symptoms).

Symptom Severity at Follow-Up

In the aggregate, severity ratings made by patients at the follow-up visit were similar to those at the initial assessment, even though many individual patients did show change in symptom ratings between the 2 visits. For all disease sites, the change in proportions of patients reporting moderate-to-severe symptoms was within 5.4%. The largest discrepancy between baseline and follow-up was an increase in patients with lung cancer reporting moderate-to-severe pain. Most of the top 5 symptoms remained consistent over time, in all patients as a group and by disease site, current therapy, disease stage, disease status, and ECOG PS (Table 5).

DISCUSSION

The current study illustrates that cancer patients are at risk for experiencing multiple moderate-to-severe symptoms simultaneously and supports the use of routine clinical screening for a core set of symptoms in addition to pain—especially for patients in active treatment, with diminished performance status, or with metastatic disease.

More than one fourth (prostate) to almost half (lung) of the sample rated 3 core symptoms as moderate to severe. Fatigue/tiredness was rated as moderate to severe by the greatest percentages of patients across the 4 disease groups. Disturbed sleep and pain also were prevalent. Dry mouth, not among the core symptoms proposed by the CMTP,⁹ was among the most-frequent moderate-to-severe symptoms in this study. Numbness/tingling was second in prevalence for patients with colorectal cancer, likely a product of the neurotoxic therapies used to treat this cancer type. Although moderate-to-severe nausea was reported by more than 10% of patients with ECOG PS >0 or metastatic disease, vomiting was rarely reported. Overall, 11 of the 12 CMTP symptoms (excluding vomiting) were rated as moderate or severe by 10% of at least 1 of the disease groups, suggesting that they are candidates for routine clinic screening.

Although individual patients demonstrated improvement or worsening of their symptoms between the initial and follow-up assessments, the overall percentages of patients reporting moderate-to-severe symptoms for each disease group and by disease stage, disease status, and ECOG PS were quite stable between the 2 assessments. The stability of the ratings supports the representativeness of the selected symptoms and their ordering by severity.

Expectations for associations of greater symptom burden with more-advanced disease, poor response to therapy, poor performance status (ECOG PS = 2), and lung cancer were supported by the data. Less-expected was the substantial symptomatic difference between patients with ECOG PS = 1 (ambulatory, able to carry out light work) and those with ECOG PS = 0 (fully active). At least 20% of patients with ECOG PS = 1 reported moderate-to-

severe levels for 9 of the 13 symptoms, as opposed to only 2 symptoms (fatigue/tiredness and disturbed sleep) for those with ECOG PS = 0. This suggests that performance status may need to be included as a stratification or eligibility factor, in addition to disease status and stage, in trials where change in symptom status is a variable of interest. In contrast to results from previous studies,^{1,17} we found no differences in symptom severity by gender (data not shown).

Our use of a fixed cutpoint of 5 to define a moderate-to-severe symptom is a potential limitation. Others have suggested that different symptoms may become moderate to severe at different ratings on a 0–10 scale.¹⁸ Practice guidelines for the management of cancer-related pain, fatigue, and distress¹⁹ suggest that these symptoms are moderate when rated as 4. It is not our intention to indicate that symptoms rated <5 are not clinically significant and do not warrant clinical care; we chose a cutpoint of 5 because it was not likely to exclude patients with significant symptoms. More research on cutpoints for severity ratings across symptoms is needed.

Second, we did not factor in comorbid conditions (such as arthritis or cardiovascular disease) that may have contributed to symptom burden. However, it is likely that any such comorbid conditions would have equally affected the cancer-free (NED) patients in this sample, >10% of whom rated 7 of the 13 symptoms as moderate or severe (Table 4). Similarly, we purposely made no attempt to attribute symptoms to treatment or disease, because making such attribution is difficult at best and unreliable at worst.^{6,20}

Finally, we restricted our investigation to the 12 core symptoms recommended by the CMTP expert panel⁹ and 1 additional symptom, dry mouth, that was shown as prevalent in 2 extensive systematic reviews.^{4,5} The SOAPP data were generally consistent with the systematic reviews and support the CMTP core symptom list with the exception of vomiting, which was rarely reported even by the patients with the most-advanced disease. In addition, the high percentage of patients reporting moderate-to-severe dry mouth suggests that it is a candidate for inclusion in a core list. MDASI symptoms not identified as prevalent by either the CMTP panel or the systematic reviews, and therefore not included in our analysis, were drowsiness and difficulty remembering. These symptoms were rated as moderate to severe by 22.9% and 17.2% of patients in the SOAPP sample, respectively, indicating that they also may warrant inclusion in a core list. It is possible that other symptoms not contemplated here could be prevalent at moderate-to-severe levels in patients with cancer. Future studies may resolve such discrepancies; notwithstanding, we believe that the 12 symptoms corroborated in this report form a reliable representation of symptom burden that would aid quality-of-care evaluations and clarify the patient's perspective on the symptomatic consequences of disease progression.

It is increasingly routine to have patients rate pain on a 0–10 scale at clinic visits. Adding a limited number of core symptoms would not appreciably increase patient burden. Doing so might capture symptoms that are even more-distressing than pain and could provide clinical teams with more-robust information to understand the patient within the context of cancer care—especially if high levels of symptoms are documented and trigger an evaluation and management plan.⁸

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TABLE 1

Patient Demographic and Disease Characteristics (N = 3106)

Variable	n	%
Age (median, range)	61	18–93
Years since cancer diagnosis (median, range) (n = 51 missing)	1.2	0.0–52.3
Sex		
Women	2170	69.9
Men	936	30.1
Race (n = 37 missing)		
White	2648	86.3
Black	364	11.9
Others	57	1.8
Ethnicity (n = 249 missing)		
Hispanic	285	10.0
Non-Hispanic	2572	90.0
ECOG PS (n = 15 missing)		
0	1755	56.8
1	1105	35.8
2–4	231	7.5
Disease site		
Breast	1544	49.7
Colorectal	718	23.1
Prostate	320	10.3
Lung	524	16.9
Disease status (n = 20 missing)		
Complete remission	1157	37.5
Partial remission	147	4.8
Stable disease	1336	43.3
Progressive disease	446	14.5
Disease stage (n = 11 missing)		
NED	1332	43.0
Locoregional	589	19.0
Metastatic	959	31.0
Locoregional + metastatic	215	7.0
Patient currently receive therapy		
No	807	26.0
Yes	2299	74.0
Prior systemic therapy (n = 1 missing)		
No	1195	38.5
Yes	1910	61.5

Variable	n	%
Prior radiation therapy (n = 27 missing)		
No	1782	57.9
Yes	1297	42.1
Type of institution		
Academic	303	9.8
CCOP	2214	71.3
MB-CCOP	589	19.0

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; NED, no evidence of disease; CCOP, Community Clinical Oncology Program; MBCCOP, Minority-Based Community Clinical Oncology Program.

Percentages of Patients Reporting Moderate-to-severe Symptoms at Initial Assessment, by Number of Symptoms Reported

TABLE 2

Number of Moderate-to-severe Symptoms Reported ^a	Disease Site ^b				Current Therapy ^c	
	Breast (n = 1544)	Colorectal (n = 718)	Prostate (n = 320)	Lung (n = 524)	No (n = 807)	Yes (n = 2299)
0	47.0	43.7	43.1	30.5	51.2	40.2
3	30.1	31.6	27.8	47.1	27.2	35.2
5	17.0	18.5	15.3	28.1	14.5	20.7
7	8.5	9.1	7.2	14.9	7.1	10.5

^aCategories are not mutually exclusive; columns may total >100%.

^bCompared with the other disease types (Chi-square test), a greater percentage of patients with lung cancer reported (a) 3 moderate-to-severe symptoms ($P < .001$ for all 3 pairwise comparisons), (b) 5 moderate-to-severe symptoms ($P < .001$ for all 3 pairwise comparisons), and (c) 7 moderate-to-severe symptoms ($P < .001$ for all 3 pairwise comparisons).

^cCompared with patients not undergoing treatment (Chi-square test), a greater percentage of patients receiving treatment reported (a) 3 moderate-to-severe symptoms ($P < .001$), (b) 5 moderate-to-severe symptoms ($P < .001$), and (c) 7 moderate-to-severe symptoms ($P < .005$).

TABLE 3
Percentages of Patients Reporting Moderate-to-severe Symptoms at Initial Assessment, by Disease Site and Current Therapy

Symptom ^a	Disease Site ^b				Current Therapy ^c		Total (n = 3106)
	Breast (n = 1544)	Colorectal (n = 718)	Prostate (n = 320)	Lung (n = 524)	No (n = 807)	Yes (n = 2299)	
Fatigue/tiredness	31.3	32.9	35.5	46.1	26.7	37.4	34.6
Disturbed sleep	27.5	23.0	25.6	31.0	22.1	28.5	26.9
Pain	18.5	18.5	17.5	24.3	17.7	19.9	19.4
Dry mouth	19.1	15.7	15.9	26.4	14.4	20.9	19.2
Distress	18.9	17.9	13.5	23.4	16.6	19.7	18.9
Numbness/tingling	16.9	25.8	15.8	18.4	17.1	19.8	19.1
Shortness of breath	10.4	11.4	16.1	33.9	14.3	15.5	15.2
Lack of appetite	11.9	17.3	11.1	27.1	11.7	17.0	15.6
Sadness	16.1	14.1	14.5	20.9	13.4	17.3	16.3
Constipation	11.4	11.0	12.4	19.9	9.5	14.1	12.9
Diarrhea	8.9	15.8	8.8	9.4	7.9	11.5	10.5
Nausea	7.0	10.0	4.7	10.7	5.0	9.2	8.1
Vomiting	3.5	3.5	1.6	3.7	1.8	3.9	3.4

^a The 5 most-prevalent symptoms for each column are presented in bold face. Of the 3106 patients who completed the initial assessment, the percentages of patients with missing values for a given symptom ranged from 0.7% to 2.4%.

^b A higher percentage of patients with lung cancer patients reported moderate-to-severe fatigue/tiredness, disturbed sleep, pain, dry mouth, distress, shortness of breath, lack of appetite, sadness, constipation, and nausea, compared with other patients combined (all $P < .05$, Chi-square test).

^c A higher percentage of patients in active therapy reported moderate-to-severe fatigue/tiredness, disturbed sleep, nausea, lack of appetite, dry mouth, sadness, vomiting, diarrhea, and constipation than did patients not currently receiving therapy (all $P < .05$, Chi-square test).

TABLE 4

Percentages of Patients Reporting Moderate-to-severe Symptoms at Initial Assessment, by Disease Stage, Disease Status, and Performance Status

Symptom ^a	Disease Stage ^{b,c}				Disease Status ^{b,d}				ECOG PS ^{b,e}			
	NED (n = 1332)	LR (n = 589)	Mets (n = 959)	LR + Mets (n = 215)	CR (n = 1157)	PR (n = 147)	SD (n = 1336)	PD (n = 446)	0 (n = 1755)	1 (n = 1105)	2-4 (n = 231)	
Fatigue/tiredness	24.7	38.4	42.3	52.9	23.9	44.0	39.6	45.4	23.9	44.8	67.7	
Disturbed sleep	23.2	27.6	30.5	30.8	22.8	28.8	28.8	30.6	20.6	33.6	41.9	
Pain	14.0	16.6	25.7	31.5	13.9	17.9	20.9	29.6	11.5	26.2	46.0	
Dry mouth	14.7	20.7	22.6	28.8	14.6	21.5	19.9	28.6	12.1	26.1	39.4	
Distress	16.2	20.7	19.2	29.9	15.3	18.9	20.5	22.8	12.8	25.5	31.7	
Numbness/tingling	15.6	14.6	25.5	24.3	15.4	22.8	19.6	26.6	13.2	25.0	35.2	
Shortness of breath	9.7	18.4	18.4	26.3	9.2	18.5	17.7	22.1	7.8	22.7	34.2	
Lack of appetite	8.5	18.9	21.4	25.8	8.0	16.7	18.6	26.0	8.1	22.3	40.3	
Sadness	14.0	17.9	17.2	22.0	13.6	15.1	17.1	21.4	11.2	21.9	27.6	
Constipation	8.8	13.9	16.2	20.8	8.4	11.1	15.3	18.1	8.3	17.0	26.9	
Diarrhea	8.6	11.5	11.3	16.7	8.1	8.2	12.5	11.8	7.2	14.9	14.5	
Nausea	5.4	8.4	11.1	11.2	5.4	9.6	9.5	10.5	4.6	11.7	16.8	
Vomiting	2.0	3.8	4.9	3.3	1.9	4.8	3.8	5.0	1.8	5.1	5.7	

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; NED, no evidence of disease; LR, locoregional; Mets, metastatic cancer; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease.

^aThe 5 most-prevalent symptoms for each column are presented in bold face. Of the 3106 patients who completed the initial assessment, the percentages of patients with missing values for a given symptom ranged from 0.7% to 2.4%.

^bChi-square test for trend showed an increasing percentage of moderate-to-severe symptoms for all 13 symptoms by increasing disease stage (all $P < .001$), disease status (all $P < .001$), and ECOG PS (all $P < .0001$).

^cCompared with patients with NED (Chi-square test), (1) a higher percentage of patients with metastatic disease (metastatic and locoregional/metastatic categories combined) reported moderate-to-severe levels for all 13 symptoms (all $P < .05$), and (2) a higher percentage of patients with locoregional disease reported having moderate-to-severe fatigue/tiredness, nausea, disturbed sleep, distress, shortness of breath, lack of appetite, dry mouth, sadness, vomiting, diarrhea, and constipation (all $P < .05$).

^dCompared with patients who achieved complete response (Chi-square test), (1) a higher percentage of patients with stable or progressive disease reported having moderate-to-severe levels of all 13 symptoms (all $P < .001$), and (2) a higher percentage of patients with partial response reported moderate-to-severe fatigue/tiredness, nausea, shortness of breath, lack of appetite, dry mouth, vomiting, and numbness/tingling (all $P < .05$).

^eFor all 13 symptoms, a higher percentage of patients with ECOG PS > 0 had moderate-to-severe symptoms than did patients with ECOG PS = 0 ($P < .001$ for ECOG PS = 2–4 vs. 0 and ECOG PS = 1 vs. 0, Chi-square test). Compared with patients with ECOG PS = 1, a higher percentage of patients with ECOG PS = 2–4 had moderate-to-severe pain, fatigue/tiredness, nausea, disturbed sleep, shortness of breath, lack of appetite, dry mouth, numbness/tingling, and constipation (all $P < .05$, Chi-square test).

TABLE 5

Percentages of Patients Reporting Moderate to Severe Symptoms at Follow-Up Assessment

Symptom ^a	Disease Site				Current Therapy		Disease Stage				Disease Status				ECOG PS			Total (n = 2801)
	Breast (n = 1389)	Colorectal (n = 666)	Prostate (n = 289)	Lung (n = 457)	No (n = 704)	Yes (n = 2097)	NED (n = 1211)	LR (n = 520)	Mets (n = 867)	LR + Mets (n = 193)	CR (n = 1053)	PR (n = 134)	SD (n = 1216)	PD (n = 380)	0 (n = 1610)	1 (n = 984)	2-4 (n = 194)	
Fatigue/tiredness	34.5	31.8	31.1	50.6	27.4	39.0	28.1	39.1	43.1	47.3	27.5	45.5	38.9	47.6	28.0	44.0	63.0	36.1
Disturbed sleep	23.2	22.9	21.7	28.4	21.3	24.7	21.4	27.9	23.2	29.6	21.1	28.6	25.2	24.9	19.1	28.2	39.6	23.8
Pain	19.2	16.0	17.0	29.7	16.2	21.2	14.3	21.7	24.8	28.1	13.5	23.1	23.2	26.1	13.8	25.3	42.2	19.9
Dry mouth	16.3	15.5	15.3	22.4	13.8	18.1	13.9	19.0	18.3	25.1	13.2	22.6	17.3	24.4	12.1	22.9	27.1	17.0
Distress	18.9	18.6	18.3	20.1	17.2	19.5	16.8	19.5	20.1	26.5	16.2	20.3	19.3	24.3	14.4	23.0	35.4	19.0
Numbness/tingling	16.8	25.6	16.7	21.3	17.9	20.2	16.9	17.6	23.3	26.2	16.4	22.6	20.0	26.5	14.5	24.9	34.9	19.6
Shortness of breath	11.6	12.1	14.9	32.4	14.7	15.7	11.0	18.8	18.0	22.5	10.4	17.4	17.7	21.6	10.1	20.8	32.1	15.5
Lack of appetite	12.8	15.3	9.4	25.7	11.4	16.4	9.4	18.4	19.4	23.7	8.7	21.1	17.5	23.1	9.6	20.6	33.3	15.1
Sadness	16.3	15.6	13.9	19.7	13.9	17.3	14.4	18.2	16.1	26.6	14.0	17.9	16.4	21.8	12.4	20.7	28.9	16.5
Constipation	12.8	10.9	10.5	20.4	9.5	14.6	10.4	15.2	15.1	18.7	9.9	12.8	15.3	16.9	10.4	16.2	23.4	13.3
Diarrhea	7.9	15.7	6.9	8.4	7.6	10.5	7.5	12.1	11.5	8.9	6.6	11.2	11.5	11.9	7.9	13.0	8.9	9.7
Nausea	7.9	10.3	2.4	11.3	4.6	9.8	5.7	11.3	9.4	13.7	6.0	9.7	9.7	10.7	6.7	10.5	12.6	8.5
Vomiting	3.0	4.7	1.4	4.9	2.8	3.8	2.2	5.2	4.4	4.3	2.1	4.5	3.8	6.4	1.9	5.4	6.8	3.6

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; NED, no evidence of disease; LR, locoregional; Mets, metastatic cancer; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease.

^aThe 5 most-prevalent symptoms for each column are presented in bold face. Of the 2801 patients who completed the follow-up assessment, the percentages of patients with missing values for a given symptom ranged from 1.1% to 3.6%.