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The Validity and Utility of the M. D. Anderson Symptom Inventory in Patients With Breast Cancer: Evidence From the Symptom Outcomes and Practice Patterns Data From the Eastern Cooperative Oncology Group

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Abstract

The M. D. Anderson Symptom Inventory assesses the severity and impact of multiple symptoms related to cancer and its treatment. Psychometric analysis of data from a national multicenter study of 1544 patients with breast cancer showed the M. D. Anderson Symptom Inventory to be a valid, reliable, sensitive symptom-assessment instrument that can enhance descriptive and clinical studies of symptom status in this patient population.

Background—The M. D. Anderson Symptom Inventory (MDASI) is a psychometrically validated patient-reported outcome measurement that assesses the severity and impact of multiple symptoms related to cancer and its treatment. With the MDASI, patients rate 13 common “core” symptoms and 6 items that reflect symptom interference with functioning. Several MDASI modules (core symptom and interference items plus additional symptoms specific to a particular cancer type or treatment modality) have been developed. Although the original MDASI validation study encompassed various cancer types, the instrument's psychometric properties have not been examined in a homogenous sample of patients with breast cancer in a national multicenter study.

Materials and Methods—We performed a secondary analysis of data from an Eastern Cooperative Oncology Group study to establish the reliability, validity, and sensitivity of the

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MDASI in a large sample of patients with breast cancer (n = 1544), 78% of whom were receiving treatment. The instrument was administered twice, approximately 1 month apart.

Results—Internal consistency and test-retest reliability were adequate, with Cronbach's values 0.85 and intraclass correlations = 0.76 for all subscales. Known-group validity was evaluated by using performance status, tumor response, and disease stage. Sensitivity to change in patient-reported quality of life was established.

Conclusion—The MDASI is a valid, reliable, and sensitive symptom-assessment instrument that can enhance descriptive and clinical studies of symptom status in patients with breast cancer. Future studies might include cognitive debriefing and qualitative interviews to identify additional disease-specific items for inclusion in a MDASI breast cancer module.

Keywords

Eastern Cooperative Oncology Group; M. D. Anderson Symptom Inventory; Patient-reported outcome; Symptom assessment; Validation

Introduction

Breast cancer and its treatments produce multiple symptoms that significantly distress patients and impair function.¹ For patients with advanced disease, symptom reduction is a primary goal of therapy. Therapy-induced symptoms may cause delays during treatment or lead to premature treatment termination, and residual treatment-related symptoms often complicate posttreatment rehabilitation. Assessing symptoms is important during active treatment^{2,3} and in survivorship⁴; gaining an understanding of the patient's experience of and perspective on the benefits of treatment also requires that symptoms be assessed. Symptoms (and variants, such as symptom severity and symptom threshold levels) have been shown in randomized clinical trials to differ between intervention and control groups.^{5,6} Symptom assessment should thus be a required component of cancer clinical trials.⁷ Because effective symptom management requires effective symptom assessment, treatment teams must ensure that the symptom assessment tool being used is valid, reliable, and sensitive to change in the patient's clinical status.

Studies conducted in patients with breast cancer have used a variety of symptom assessment tools, some of which were created specifically for use in the breast cancer population and some of which were not. In the latter category are the Memorial Symptom Assessment Scale (MSAS)⁸ and the Therapy-Related Symptom Checklist.⁹ Other studies have used combinations of instruments, such as the MSAS with the Functional Assessment of Cancer Therapy-Breast (FACT-B),¹⁰ or the Breast Cancer Prevention Trial Symptom Checklist with the Short Form 36.¹¹⁻¹³ Of the measurement instruments created for breast oncology practice, perhaps the 2 most widely used questionnaires are the FACT-B¹⁴ and the EORTC QLQ-BR23 (European Organisation for Research and Treatment of Cancer breast-cancer-specific quality-of-life [QOL] questionnaire).¹⁵

These instruments were designed within the conceptual framework of health-related QOL, however, and, although many QOL measures include symptom items, they are not necessarily symptom instruments per se. For example, the Breast Cancer Prevention Trial Symptom Scales¹⁶ assess adverse effects associated with the treatment and prevention of breast cancer, and a FACT-Breast Symptom Index, derived from the FACT-B,¹⁷ measures the 6 most important breast-cancer-related symptoms. Given its brevity, however, the FACT-Breast Symptom Index may not include target symptoms of interest, depending on the research question at hand. Further, instruments that are specific to breast cancer may not allow for comparison of symptoms across disease sites, an important consideration in light

of a September 2011 call from the National Cancer Institute Symptom Management and Quality of Life Steering Committee to identify a standard set of core patient-reported symptoms to be assessed in National Cancer Institute sponsored clinical trials in patients with cancer.¹⁸

The M. D. Anderson Symptom Inventory (MDASI)¹⁹ assesses the severity and impact of multiple symptoms related to cancer and its treatment. A systematic review of 21 symptom-assessment tools identified as appropriate for clinical use indicated that the MDASI has several advantages over other measures.²⁰ First, the MDASI assesses 13 symptoms most commonly experienced by patients with any type of cancer, which suggests that the MDASI is comprehensive yet brief enough to avoid patient burden. Second, along with the severity of common cancer-related symptoms, the MDASI also assesses how much these symptoms interfere with daily functioning. Third, the MDASI 0-10 numerical scale is readily understood (even by less-educated patients), is very easy to translate into other languages, and is readily adaptable for electronic administration, such as via telephone or computer.

Although the MDASI and its core symptom items were shown to be valid and reliable in a large sample of oncology outpatients,¹⁹ to our knowledge no study has demonstrated how the core symptom items of the MDASI perform psychometrically in a large breast-cancer-specific patient population accrued from centers across the United States. Thus, the goal of this secondary analysis was to establish the reliability, validity, and sensitivity of the MDASI by using data derived from the Eastern Cooperative Oncology Group (ECOG) Symptom Outcome and Practice Patterns study, a nationwide, multicenter project that included a large sample of patients with breast cancer. A unique feature of this study was the collection of MDASI data at 2 time points, baseline and the next follow-up visit, which allowed us to assess the stability of symptom reporting and changes in symptom reporting related to patient perceptions of changes in QOL.

Materials and Methods

Study Participants

From March 3, 2006, to May 19, 2008, outpatients with breast cancer were enrolled from 37 ECOG-affiliated institutions, including 5 academic centers and 32 community clinics. Patients treated in academic centers were enrolled from breast-cancer-specific clinics, whereas community oncology patients were enrolled from general oncology clinics. To reduce selection bias, each site devised a prespecified recruitment algorithm that was approved by the coordinating center. Approved algorithms were feasible for the specific site but not biased with regard to symptom-management issues. Patients were enrolled at any point in the trajectory of their care. Participants were at least 18 years old, had a diagnosis of breast cancer, were willing to complete the follow-up survey, and were judged by the study screener to have cognitive function adequate for completing study surveys. The protocol was approved by the institutional review boards at each participating site. All participants provided written informed consent.

Study Procedures

Patients were recruited when they checked in for their appointments. Basic clinical and demographic information, including cancer treatment history and current therapies, was collected before the clinician visit. Patients completed the MDASI and global QOL items at this initial visit and at a follow-up visit 28-35 days later. Each patient was asked to read the instructions at the beginning of each questionnaire and to complete all items in terms of his or her experience during the time frame specified on the form. Reasons for incomplete forms were documented on an Assessment Compliance Form. Patients who could not complete the

follow-up questionnaire because of acute illness were given the option to mail the forms to the treating clinic by day 42.

Survey Measures

The MDASI—Patients reported symptom intensity and functional interference by using the MDASI. Symptoms (pain, fatigue, nausea, disturbed sleep, emotional distress, shortness of breath, difficulty remembering, lack of appetite, drowsiness, dry mouth, sadness, vomiting, and numbness or tingling) were rated at their worst in the previous 24 hours on a scale from 0-10, with 0 representing “not present” and 10 representing “as bad as you can imagine.” For this study, an additional 6 symptom items (diarrhea, constipation, mouth sores, skin rash, hair loss, and coughing) deemed to be important as exploratory were included. Patients also rated the degree to which symptoms interfered with various aspects of life during the past 24 hours. Each interference item (general activity, mood, work [including both work outside the home and housework], relations with other people, walking ability, and enjoyment of life) was rated on a 0-10 scale, with 0 representing “did not interfere” and 10 representing “interfered completely.”¹⁹

MDASI ratings can be averaged into several subscale scores: mean core (13 core symptom items only), mean core symptoms plus any additional symptom items, and mean interference (6 interference items only). A more-sensitive characterization of symptoms may use a subset of the most-severe symptoms reported by that group. Symptom items may be used individually or in subsets without summary scoring if specified a priori. Specific symptom items can also be used if prespecified as part of the expected outcome.²¹

The interference items can further be separated into mean activity-related interference (WAW [work, general activity, and walking ability]) and mean mood-related interference (REM [relations with people, enjoyment of life, and mood]).²² Our previous studies have shown that a rating of 5 or higher (on a 0-10 numeric rating scale) for pain and for fatigue indicates a moderate-to-severe symptom that significantly impairs daily functioning.^{22,23} This cut point was used to determine moderate-to-severe symptom levels in this study.

Global QOL—The global QOL item asked patients to rate their QOL as excellent, good, fair, poor, or very poor. At follow-up, patients were also asked how they would characterize the change in their global QOL since their last visit: much better, better, the same, worse, or much worse. By using global QOL as an anchor, we described the smallest symptom score difference that represents the minimal clinically significant difference or minimally important difference about which patients care.

Statistical Analysis

All statistical analyses were conducted by using Statistical Analysis Software version 9.2 (SAS Institute, Cary, NC). Means (SD) and 95% confidence limits (CL) were computed for all symptoms and subscales. Statistical significance was set by using a 2-tailed level of 0.05.

Reliability of the MDASI—Reliability refers to the extent to which the items in a scale are consistently measuring the same concept. Cronbach coefficient levels were computed to estimate the internal consistency reliability of baseline and follow-up values for 4 MDASI subscales: the core symptom subscale (13 MDASI symptom items), the interference subscale (6 interference items), and the WAW and REM interference subscales. The criterion for good internal-consistency reliability requires a Cronbach value of 0.70 or higher. To evaluate test-retest reliability, we calculated the intraclass correlations (ICC) of the 4 subscales between the baseline and follow-up MDASI administrations by using 2-way

analysis of variance ($ICC = [\text{mean square}_{\text{patient}} - \text{mean square}_{\text{error}}] / \text{mean square}_{\text{patient}}$). Although the test-retest occurred approximately 30 days apart, we expected that most of these outpatients would report stable symptoms.

Construct Validity of the MDASI—Construct validation requires demonstrating that the instrument measures the underlying construct(s) it is intended to measure. Various methods of establishing construct validity can be used, such as quantifying the instrument's ability to distinguish among groups known to be clinically different (known-group validity), factor analysis, and a multitrait—multimethod matrix. We performed factor analysis of baseline data to determine the underlying constructs that the 13 core MDASI items measure, and we conducted independent-sample *t* tests of ECOG performance status, tumor response, and cancer stage to demonstrate known-group validity. Differences in mean symptom scores among groups were considered clinically meaningful if ≥ 0.5 SD.²⁵⁻²⁷

Criterion Validity of the MDASI—Criterion, or concurrent, validity refers to the extent to which an instrument is related to another instrument that measures a similar, but not the same, concept.²⁴ To show concurrent validity, we used the area under the receiver operating characteristics (ROC) curve to demonstrate the relationship between baseline MDASI subscale scores and QOL ratings (dichotomized as excellent or good vs. fair, poor, or very poor). An ROC area of 1.0 represents a perfect test; an ROC area of 0.5 represents a worthless test. A rough guide for classifying the accuracy of a diagnostic test is the traditional academic point system: 0.90-1.00, excellent (A); 0.80-0.90, good (B); 0.70-0.80, fair (C); 0.60-0.70, poor (D); < 0.60 , fail (F).²⁸

Sensitivity of the MDASI—Sensitivity is defined as the ability of an instrument to detect change in outcome when such change is expected. At follow-up, the patients indicated whether their global QOL had changed since the baseline visit: much better, 1; better, 2; nearly the same, 3; worse, 4; or much worse, 5. We also computed the change in MDASI subscale scores between baseline and follow-up. Bar graphs are used to illustrate the relationship among changes in symptom severity and symptom interference by change in patient-reported QOL.

One way of considering meaningful changes is to use an anchor-based approach. We used an anchor item administered at follow-up. The patients were asked whether their global QOL had improved, worsened, or remained the same since their last visit. Symptom subscale change scores within each of the groups defined by this anchor item represent the minimally important differences for the MDASI.

Results

Patient Demographic and Clinical Characteristics

Demographic and clinical characteristics of the patient cohort ($n = 1544$) are summarized in Table 1. The sample primarily comprised non-Hispanic white women with an average age of approximately 58 years. Most patients had good ECOG performance status, with no evidence of disease and with a complete response. However, approximately 25% of patients (395/1544) had metastatic or both local and/or regional and metastatic disease, and 10% (157/1544) had disease progression. Approximately 66% (1024/1544) had prior chemotherapy, immunotherapy, or hormonal therapy, and 47% (729/1544) had previous radiation therapy.

Change in Symptom Severity Over Time

At baseline, the overall mean subscale scores for the core and interference subscales were 1.80 and 1.91, respectively (Table 2). The most-severe core symptoms reported were fatigue, disturbed sleep, drowsiness, distress, and difficulty remembering; nausea and vomiting were the least-severe core symptoms reported. Moderate-to-severe levels of pain and fatigue were found for 18% (282/1528) and 31% (473/1509) of patients, respectively. In contrast, 7% (107/1525) and 4% (54/1530) of patients reported moderate-to-severe nausea and vomiting, respectively. Missing data were minimal: at most, 2% (35/1544) for fatigue and much less for most of the other items.

At follow-up, the mean scores for the core and interference subscales were 1.83 and 2.10, respectively (Table 2). Fatigue, disturbed sleep, drowsiness, and distress remained the most-severe symptoms, with difficulty remembering replaced by pain to complete the top 5 symptoms at follow-up. Approximately a third of patients (451/1366) had moderate-to-severe fatigue, and 19% (263/1383) had moderate-to-severe pain at follow-up. Nausea and vomiting remained low, at 8% (110/1372) and 3% (42/1381), respectively.

Psychometric Validation of the MDASI

Internal Consistency Reliability—The MDASI subscales showed good internal consistency reliability (Table 3). Baseline Cronbach coefficient values were 0.91 for the core subscale and 0.85 for the interference subscale. All subscale scores were 0.89 and higher at follow-up.

Test-Retest Reliability—The ICCs of the MDASI core and interference subscales administered approximately 1 month apart were indicative of good test-retest reliability. All values were at least 0.76 (Table 4).

Construct Validity—The factor loadings of the core MDASI items were distributed across 2 factors, shown in Table 5. Nausea, vomiting, and lack of appetite appeared to load on the same underlying factor. The remaining symptoms loaded onto a separate factor.

In our analysis of known-group validity, patients with poor ECOG performance status reported clinically significant higher scores for all of the MDASI subscales (Table 6). Patients with a complete response reported significantly lower MDASI subscale scores than did patients with a partial response or with disease progression. Patients with no evidence of disease reported significantly lower MDASI subscale scores than did patients with both local/regional and metastatic cancer. Effect sizes between these groupings for the MDASI subscales were higher than 0.5. For example, shown in Table 6, an effect size of 0.61 between the good and poor performance status groups for the core symptom subscale is equivalent to a difference of 1.02 in raw unit score (scale of 0-10) given that the SD is approximately 1.67. Note that statistically significant group comparisons at either $P < .01$ or $P < .001$ were not necessarily clinically significant, based on effect sizes.

Criterion Validity—The relationships between the MDASI subscales and patient-reported QOL at baseline are shown in Table 7. As expressed by area under the ROC curves, all the MDASI subscales demonstrated good accuracy, with values of at least 0.80 when compared with dichotomized QOL (excellent or good vs. fair, poor, or very poor).

Sensitivity—When patient-reported QOL remained nearly the same from baseline to follow-up, MDASI symptom items changed only slightly during the same period (Figure 1A). Conversely, when patients reported worse or a much-worse change in QOL, very-large

changes occurred in the MDASI symptom items. Similar concordance was observed for the MDASI symptom interference items (Figure 1B).

Similar observations for the MDASI subscales are shown in Table 8. Change scores for MDASI subscales between baseline and follow-up indicate that patients with worse or much-worse QOL experienced significant increases in symptom severity and interference. Significant decreases were observed for patients with better or much-better QOL at follow-up, whereas changes in the MDASI subscales for patients whose QOL remained nearly the same were not always significant.

For patients whose overall QOL worsened, the mean increases in MDASI subscale scores (1.12 for the core symptom subscale, 2.43 for the mean activity-related interference subscale, and 2.03 for the mean mood-related interference subscale) (Table 8) can be considered minimally important differences on the MDASI 0-10 scale. Similarly, for patients whose overall QOL improved, reductions of 0.31, 0.26, and 0.22 points for the mean core symptom, activity-related, and mood-related subscales, respectively, can be considered minimally important differences. For the 5 most severe symptoms and for patients whose overall QOL worsened, fatigue showed the largest increase at 2.15, followed by distress at 1.63, disturbed sleep at 1.02, drowsiness at 1.12, and hair loss at 0.76.

Discussion

In this article, we evaluated the use of the core items of the MDASI in a large, national, multicenter cohort of patients with breast cancer. The results provide strong psychometric evidence that support the use of the MDASI in this patient population and expand the generalizability of the psychometric properties of the MDASI beyond the original validation sample of a heterogeneous group of cancer patients in a single tertiary cancer center.

Demonstrating the psychometric properties of an instrument was once limited to providing evidence of reliability and validity. With the issuance of US Food and Drug Administration guidance on the use of patient-reported outcomes in labeling claims, additional demonstrations of an instrument's validity and adequacy have increasingly become standard, including the ability to detect change and inclusion of patient input. As shown here, the MDASI core symptom and interference subscales demonstrated high test-retest reliability between baseline and a 1-month follow-up, and acceptable internal consistency reliability; its subscales were sensitive to changes in patient-reported QOL, as demonstrated by statistically and clinically significant change in symptom severity and interference from baseline to follow-up.

We have also provided estimates of the clinically minimally important difference in MDASI subscale scores for patients whose condition worsened and for patients whose condition improved. It is possible for the minimally important difference to be larger than a difference that is statistically significant, especially in studies that involve large samples; in other words, statistically significant but not clinically significant results may be of little practical importance.

We have developed several modules of the MDASI, such as the MDASI-Lung Cancer,²⁹ MDASI-Brain Tumor,³⁰ and MDASI-Heart Failure,³¹ that contain additional items specific to the condition. The current study is not a module validation, however, because the 6 additional symptom items were not derived by using qualitative interviews of patients with breast cancer, as suggested in the US Food and Drug Administration guidelines for developing patient-reported outcomes assessment tools. Three additional symptom items, hot flashes, vaginal dryness, and decrease in sexual interest and/or activity, were shown to

be more severe in patients with breast cancer who were receiving anastrozole treatment.³² These items may be useful for developing a breast cancer module of the MDASI.

Data collected with the MDASI, as opposed to disease-specific symptom scales, eg, the Breast Cancer Prevention Trial Symptom Scale, can be used to compare symptom prevalence and severity across cancer types, necessary for epidemiologic studies and clinical trials that may include patients with different types of cancers. Unlike other breast cancer assessment tools, such as the FACT-B and EORTC QLQ-BR23, the MDASI is based on the concept of symptom burden rather than health-related QOL. Thus, the study of symptom burden, a concept akin to tumor burden but dictated primarily by symptom severity and its impact, allows for comparison of symptoms across cancer types.

Several studies have recommended including multiple symptoms as outcomes in clinical practice to improve care quality³³⁻³⁵ and in cancer clinical trials to better understand the benefits of cancer therapies from the patient's point of view.^{2,7,36-38} In a previous study,³⁹ we found minimal linguistic and cultural effect on symptom reports, which suggests that we may be able to pool symptom outcomes from various countries, as is typical of large international and multicenter clinical trials.

Conclusion

This study validated the core items of the MDASI for use in patients with breast cancer and demonstrated its sensitivity to clinical outcomes. Further research is needed to determine additional symptoms that are salient to the disease and its treatment through qualitative interviews and to conduct cognitive debriefing on the symptoms identified in the interviews. The core MDASI is a valid, reliable, and sensitive instrument for assessing the severity of symptoms and their interference in the daily functioning of patients with breast cancer. Because validation is an ongoing process, these new data provide additional evidence that shows the psychometric properties of the MDASI in quantifying the symptom burden of patients with cancer.

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Clinical Practice Points

- The MDASI is a psychometrically validated patient-reported outcome measurement that assesses the severity and impact of multiple symptoms related to cancer and its treatment. The MDASI should be useful in screening for major symptoms in clinical practice.
- This study demonstrated the psychometric properties and utility of the MDASI in a large multicenter study of outpatients with breast cancer. Psychometric analysis of the MDASI administered twice to a sample of 1544 patients with breast cancer showed that the MDASI had excellent reliability, met validity requirements, and was sensitive to change in this patient group. We also provided estimates of the minimally important difference in MDASI subscale scores, which may facilitate interpretation of the scores.
- In conclusion, the MDASI is a valid, reliable, and sensitive symptom-assessment instrument that can enhance descriptive and clinical studies of symptom status in patients with breast cancer. These new results add to the growing validation dossier related to the use of the MDASI and increase our confidence in continued use of the tool.

Figure 1. Sensitivity of the MDASI. (A) Change in Severity for 19 MDASI Symptoms by Patient-Reported Change in QOL. (B) Change in Severity for 6 MDASI Interference Items by Patient-Reported Change in QOL. Abbreviations: MDASI = M.D. Anderson Symptom Inventory; QOL = quality of life.

Table 1
Patient Demographic and Disease Characteristics at Baseline (n = 1544)

Variable	
Median (range) age, years	57.9 (17.9-91.5)
Sex, no. (%)	
Women	1541 (99.8)
Men	3 (0.2)
Race, no. (%)	
Unknown	16 (1.0)
White	1330 (86.1)
Black	171 (11.1)
Asian	18 (1.2)
Native Hawaiian	1 (0.1)
Native American	7 (0.5)
Indian	1 (0.1)
Ethnicity, no. (%)	
Unknown	114 (7.4)
Hispanic or Latino	122 (7.9)
Non-Hispanic	1304 (84.5)
Patient refused	2 (0.1)
Institution refused	2 (0.1)
ECOG performance status, no. (%)	
Unknown	9 (0.6)
0	1048 (67.9)
1	414 (26.8)
2	73 (4.7)
Disease stage, no. (%)	
Unknown	7 (0.5)
NED	901 (58.4)
Local/regional	241 (15.6)
Metastatic	348 (22.5)
Local/regional and metastatic	47 (3.0)
Tumor response, no. (%)	
Unknown	11 (0.7)
Complete response	806 (52.2)
Partial response	45 (2.9)
Stable	525 (34.0)
Progression	157 (10.2)
Previous chemotherapy, immunotherapy, or hormonal therapy, no. (%)	1024 (66.3)
Previous radiation therapy, no. (%)	729 (47.2)

Variable	
Currently receiving cancer treatment, no. (%)	1203 (77.9)

Abbreviations: ECOG = Eastern Cooperative Oncology Group; NED = no evidence of disease.

Table 2
Prevalence, Severity, and Percentage Missing of Individual MDASI Symptoms and Subscales at Baseline and Follow-Up (n = 1544)

	Mean (SD)	95% CL	% Moderate to Severe ^a	% No Symptom ^a	% Missing ^b
Baseline					
MDASI symptom					
Fatigue	3.14 ± 2.89		30.6	24.3	2.3
Disturbed sleep	2.69 ± 2.98		27.2	36.1	1.0
Drowsiness	2.33 ± 2.68		21.4	36.0	0.9
Distress	2.04 ± 2.66		18.8	43.5	1.0
Difficulty remembering	2.01 ± 2.41		17.0	37.2	0.8
Dry mouth	1.96 ± 2.77		18.8	50.1	1.4
Pain	1.91 ± 2.72		18.3	52.7	1.0
Sadness	1.82 ± 2.60		16.0	48.3	0.7
Numbness/tingling	1.82 ± 2.75		16.7	52.9	0.8
Shortness of breath	1.28 ± 2.19		10.3	60.8	0.8
Lack of appetite	1.26 ± 2.35		11.7	66.6	1.3
Nausea	0.83 ± 1.91		7.0	75.9	1.2
vomiting	0.35 ± 1.45		3.5	91.2	0.9
Diarrhea	0.96 ± 2.10		8.8	72.8	0.5
Constipation	1.33 ± 2.44		11.3	64.4	1.5
Mouth sores	0.49 ± 1.52		4.0	85.3	0.5
Skin rash	0.60 ± 1.74		5.7	83.4	0.9
Hair loss	2.30 ± 3.66		22.3	61.0	0.9
Coughing			7.9	67.3	0.6
MDASI subscale					
Core	1.80 ± 1.73	1.71, 1.89			6.7
Interference	1.91 ± 2.27	1.80, 2.02			2.1
WAW	2.17 ± 2.61	2.04, 2.30			1.4
REM	1.65 ± 2.18	1.54, 1.76			1.3
Follow-up					

	Mean (SD)	95% CL	% Moderate to Severe ^a	% No Symptom ^a	% Missing ^b
MDASI symptom					
Fatigue	3.34 ± 2.88		34.5	20.3	11.5
Disturbed sleep	2.51 ± 2.78		23.2	34.1	10.9
Drowsiness	2.39 ± 2.62		22.3	33.0	10.4
Distress	2.12 ± 2.67		18.9	40.0	10.6
Pain	2.01 ± 2.72		19.2	48.8	10.4
Difficulty remembering	1.94 ± 2.37		15.1	36.6	10.4
Sadness	1.88 ± 2.61		16.3	46.4	10.4
Numbness/tingling	1.84 ± 2.63		16.8	47.9	10.6
Dry Mouth	1.79 ± 2.69		16.3	51.3	10.8
Shortness of breath	1.35 ± 2.23		11.7	58.6	10.5
Lack of appetite	1.32 ± 2.32		12.8	63.1	10.8
Nausea	0.89 ± 2.01		7.9	75.4	11.1
Vomiting	0.34 ± 1.31		3.0	90.1	10.6
Diarrhea	0.94 ± 2.00		7.9	71.2	10.6
Constipation	1.40 ± 2.52		12.8	63.3	10.6
Mouth sores	0.43 ± 1.35		2.9	84.4	10.4
Skin rash	0.58 ± 1.59		4.4	81.1	10.6
Hair loss	2.35 ± 3.63		23.5	58.5	10.8
Coughing	1.01 ± 2.04		8.7	68.2	10.5
MDASI subscale					
Core	1.83 ± 1.71	1.74, 1.92			15.6
Interference	2.10 ± 2.39	1.97, 2.23			11.8
WAW	2.41 ± 2.72	2.27, 2.55			11.3
REM	1.78 ± 2.31	1.66, 1.90			11.0

Abbreviations: CL = confidence limit; MDASI = M. D. Anderson Symptom Inventory; REM = mood-related interference items (relations with people, enjoyment of life, and mood); WAW = activity-related interference items (work, general activity, and walking ability).

^aPercentage of patients who answered the question.

^bPercentage of missing responses from all 1544 patients.

Table 3
Internal Consistency Reliability of the MDASI at Baseline and Follow-Up

MDASI Subscale	No. Items	Cronbach Coefficient	
		Baseline (n = 1537)	Follow-up (n = 1385)
Core symptoms	13	0.91	0.91
Interference	6	0.85	0.89
WAW	3	0.89	0.91
REM	3	0.85	0.89

Abbreviations: MDASI = M. D. Anderson Symptom Inventory; REM = mood-related interference items (relations with people, enjoyment of life, and mood); WAW = activity-related interference items (work, general activity, and walking ability).

Table 4
Test-Retest Reliability of the MDASI Administered Approximately 30 Days Apart (n = 1385)

MDASI Subscale	No. Items	Intraclass Correlation
Core symptoms	13	0.82
Interference	6	0.78
WAW	3	0.77
REM	3	0.76

Abbreviations: MDASI = M. D. Anderson Symptom Inventory; WAW = activity-related interference items (work, general activity, and walking ability); REM = mood-related interference items (relations with people, enjoyment of life, and mood).

Table 5
Construct Validity of the MDASI: Baseline Factor Loadings of the Core Symptom Items
(n = 1441)^a

MDASI Symptom	Factor 1, General Severity	Factor 2, Gastrointestinal
Fatigue	0.750	0.299
Distress	0.715	0.242
Sadness	0.702	0.240
Drowsiness	0.683	0.298
Disturbed sleep	0.640	0.261
Difficulty remembering	0.615	0.119
Dry mouth	0.595	0.275
Pain	0.587	0.321
Shortness of breath	0.546	0.282
Numbness	0.513	0.254
Nausea	0.226	0.874
Vomiting	0.162	0.672
Lack of appetite	0.459	0.518

Bold values indicates the items loaded on Factor 1 and Factor 2.

Abbreviation: MDASI = M. D. Anderson Symptom Inventory.

^aThe 2-factor structure was supported by eigenvalues of 6.2 and 1.2 for the first 2 factors and 0.8 for a third.

Table 6
Known-Group Validity of the MDASI: Comparison of Baseline Symptom and Interference Subscale Scores by ECOG Performance Status, Tumor Response, and Disease Stage

	No. Patients	Mean (SD)	Diff	Effect Size
MDASI Core Symptoms Subscale				
ECOG performance status				
Good (0)	1044	1.48 ± 1.52	1.02 ^a	0.61
Poor (1)	485	2.50 ± 1.94		
Tumor response				
Complete response ^b	806	1.52 ± 1.61		
Partial response	45	2.35 ± 2.20	0.83 ^c	0.50
Stable	522	1.99 ± 1.77	0.47 ^a	0.28
Progression	154	2.48 ± 1.79	0.96 ^a	0.59
Disease stage				
NED ^d	900	1.53 ± 1.61		
Local/regional	239	2.01 ± 1.96	0.48 ^a	0.28
Metastatic	346	2.28 ± 1.70	0.75 ^a	0.46
Local/regional and metastatic	46	2.6 2 ± 1.89	1.09 ^a	0.67
MDASI Interference Subscale				
ECOG performance status				
Good (0)	1043	1.46 ± 1.97	1.42 ^a	0.65
Poor (1)	486	2.88 ± 2.56		
Tumor response				
Complete response ^b	806	1.47 ± 2.03		
Partial response	45	2.51 ± 2.56	1.04 ^c	0.50
Stable	522	2.26 ± 2.38	0.79 ^a	0.36
Progression	154	2.88 ± 2.48	1.41 ^a	0.67
Disease stage				
NED ^d	900	1.51 ± 2.07		
Local/regional	238	2.24 ± 2.40	0.73 ^a	0.34
Metastatic	346	2.59 ± 2.41	1.08 ^a	0.50
Local/regional and metastatic	47	2.96 ± 2.47	1.45 ^a	0.69

Abbreviations: Diff = for categories with 2 groups, the difference in the means between the 2 groups, and for categories with several groups, the difference in the means between the group and its reference group; ECOG = Eastern Cooperative Oncology Group; MDASI = M. D. Anderson Symptom Inventory; NED = no evidence of disease.

^aSignificant at $P < .001$.

^bComplete response was the reference group for tumor response.

^cSignificant at $P < .01$.

^dNED was the reference group for disease stage.

Table 7
Criterion Validity of the MDASI: Area Under the ROC Curve for MDASI Subscales Compared With QOL at Baseline (n = 1534)

MDASI Subscale	Overall QOL ^a
Core Symptoms	0.80
Interference	0.82
WAW	0.80
REM	0.81

Abbreviations: MDASI = M. D. Anderson Symptom Inventory; QOL = quality of life; REM = mood-related interference items (relations with people, enjoyment of life, and mood); ROC = receiver operating curve; WAW = activity-related interference items (work, general activity, and walking ability).

^aDichotomized: excellent or good vs. fair, poor, or very poor.

Table 8
Sensitivity of the MDASI: Change in MDASI Subscales Compared With Changes in QOL, From Baseline to Follow-Up

Overall QOL at Follow-up	MDASI Subscale			
	Core Symptom	Interference	WAW	REM
	Mean (SD) Change	Mean (SD) Change	Mean (SD) Change	Mean (SD) Change
Much better/better (n = 422)	-0.31 ± 1.44 ^a	-0.24 ± 2.04 ^a	-0.26 ± 2.38 ^a	-0.22 ± 2.04 ^a
Nearly the same (n = 825)	0.07 ± 1.09	0.18 ± 1.57 ^a	0.27 ± 1.88 ^a	0.08 ± 1.58
Worse/much worse (n = 124)	1.12 ± 1.70 ^a	2.22 ± 2.49 ^a	2.43 ± 2.82 ^a	2.03 ± 2.63 ^a

Abbreviations: MDASI = M. D. Anderson Symptom Inventory; QOL = quality of life; REM = mood-related interference items (relations with people, enjoyment of life, and mood); WAW = activity-related interference items (work, general activity, and walking ability).

^aSignificant at $P < .001$.