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An Examination of Distress, Sleep, and Fatigue in Metastatic Breast Cancer Patients

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Abstract

Objective—Few studies have used rapid screening instruments to document the prevalence of distress among metastatic breast cancer patients. This study used the one-item Distress Thermometer (DT) to assess distress in this population. Anxiety and depressive symptoms, sleep problems, fatigue, and mental health service use were assessed for patients who met the cutoff on the DT for probable distress (score ≥ 4).

Methods—A total of 173 metastatic breast cancer patients rated their distress on the DT. Respondents who met study eligibility criteria ($n = 90$), including a score > 4 on the DT, completed a telephone survey one week later that assessed anxiety, depressive symptoms, sleep problems, and fatigue. Associations of study outcomes with demographic and medical characteristics were computed.

Results—Sixty percent of the 173 patients met the cutoff for probable distress on the DT. Meeting this cutoff was not associated with age, ethnicity, time since diagnosis, or medical treatments. The majority (61%) of respondents who were classified as distressed on the DT reported clinically significant anxiety or depressive symptoms one week later. On average, these patients also showed significant fatigue and sleep disturbance, with 70% reporting decrements in sleep quality. Only 29% of patients with significant anxiety or depressive symptoms accessed mental health services.

Conclusions—Results point to a high prevalence of distress, sleep problems, and fatigue across demographic and medical subgroups of metastatic breast cancer patients. A rapid one-item screening tool may be used to identify patients with a potential need for psychosocial assessment and intervention.

Keywords

metastatic breast cancer; oncology; sleep; fatigue; psychological distress; mental health services

As women live for months or years with metastatic breast cancer, they face a growing dependence on health care professionals and significant others, cognitive and physical decline, and their own mortality. Metastatic breast cancer is considered incurable, with a median survival time of 2 to 4 years following diagnosis [1]. As patients cope with increased physical symptoms, frequent medical appointments, and relational and existential concerns, a substantial minority experience psychological morbidity [2–6]. For example, over 40% of metastatic breast cancer patients were found to have a DSM-IV psychiatric disorder [3–4]. Almost one-third met the criteria for a depressive disorder, whereas 6% met the criteria for

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an anxiety disorder [3–4]. Similar rates of anxiety and depression have been found in other advanced cancer patient samples; 6% to 8.2% have met the criteria for an anxiety disorder and 14% to 31% have met the criteria for a depressive disorder [7]. Younger advanced cancer patients, including those with metastatic breast cancer, have shown higher rates of depressive disorders [3–4, 8]. Medical treatment variables have not been associated with depressive or anxiety disorders in metastatic breast cancer patients, but have been associated with distress in other advanced cancer populations [3–4, 8].

Depression, cancer, and anti-cancer therapies contribute to the high prevalence of sleep disturbance and fatigue in advanced cancer patients [9–12]. Over 60% of metastatic breast cancer patients reported one or more types of sleep disturbance [12–13], and worsening depression was associated with the greatest number of negative changes in sleep patterns relative to other predictors (pain and life stress) [12]. In heterogeneous samples of advanced cancer patients, fatigue, pain, and psychological distress have predicted sleep disturbance [11, 13–14]. Fatigue, defined as a subjective sense of tiredness or weakness [15], is experienced by many patients who undergo cancer treatment [16]. One study found that over half of metastatic breast cancer patients reported high levels of fatigue [17]. Fatigue reduces physical and psychological well-being [10, 16, 18] and is often one of the key reasons for patients' discontinuation of anti-cancer therapy [19].

To date, little research has documented the degree of fatigue and sleep problems among distressed women with metastatic breast cancer. In addition, distress has been evaluated using structured clinical interviews and questionnaires that are not easily administered and scored in routine clinical practice. To our knowledge, this study is the first to use the single-item Distress Thermometer (DT) [20] to assess the prevalence of distress among metastatic breast cancer patients. Knowledge of the frequency of distress in this population based on a rapid screening tool and further characterization of the nature of distress and its predictors could inform clinical care. Prior research with a variety of cancer populations has found that 43% to 61% of patients report clinically significant distress (score ≥ 4) on the DT [21–24], and younger age and functional impairment have generally been associated with greater distress [21–23].

Secondary objectives of this study were to characterize the degree of elevated anxiety and depressive symptoms, sleep problems, and fatigue among metastatic breast cancer patients who met the cutoff on the DT for probable distress (score ≥ 4) [22]. In addition, we examined associations between study outcomes and demographic variables, medical factors, and mental health service use. Predictors of mental health service use and meeting the criteria for significant anxiety or depressive symptoms were analyzed separately. Study participants were completing assessments in the context of a randomized clinical trial on the health effects of expressive writing. We present data collected prior to randomization and intervention.

Methods

Participants and Procedures

Women with Stage IV breast cancer were recruited from Memorial Sloan-Kettering Cancer Center (MSKCC) for an expressive writing intervention trial. All study procedures were approved by the MSKCC institutional review board. Permission to contact patients was sought from their oncologists, and letters of invitation and consent forms were mailed to women approved for contact. Patients provided consent for study participation and completed a screening interview via telephone. Inclusion requirements for the screening interview were: (1) at least 18 years of age; (2) English fluency; and (3) regular visits to an oncologist at MSKCC. Following screening, patients were excluded from study participation

if they: (1) had severe cognitive impairment assessed with the Short Portable Mental Status Questionnaire [25]; (2) engaged in expressive writing on a daily basis; and (3) did not meet the established cutoff (score = 4) for probable distress on the DT [22]. Those who met study eligibility criteria completed a baseline telephone interview approximately one week after the screening assessment that included measures of anxiety, depression, sleep, fatigue, and functional status. Participants received a \$25 money order for their time. All measures reported here were completed before the completion of the any part of the writing intervention.

Measures

General distress—The Distress Thermometer (DT) [20] was used to assess patients' distress during the past week on a scale from 1 (*no distress at all*) to 10 (*the worst distress imaginable*). Among cancer patients, a cutoff score of 4 on the DT yielded optimal sensitivity and specificity [22].

Depressive symptoms—The reliable and valid Center for Epidemiologic Studies—Depression scale (CES-D) [26] was used to assess depressive symptoms during the past week. Each of the 20 items (e.g., “I felt sad”) was rated on a 4-point scale from 0 (*rarely or none of the time [less than 1 day]*) to 3 (*most or all of the time [5–7 days]*).

Anxiety symptoms—Participants completed the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A) [27]. Each of the 7 items assesses anxiety symptoms during the past week. A sample item is “I feel tense or ‘wound up’” with four response options ranging from “not at all” to “most of the time.” The HADS has strong data supporting its validity and reliability, including data from advanced breast cancer patients [28–29].

Sleep disturbance—The Pittsburgh Sleep Quality Index (PSQI) [30] was used to assess habitual sleep disturbances during the past month. The 19-item PSQI yields a total habitual sleep disturbance score and 7 subscale scores including Subjective Sleep Quality, Sleep Latency, Sleep Duration, Habitual Sleep Efficiency, Sleep Disturbances, Use of Sleeping Medications, and Daytime Dysfunction. Research with cancer patients has supported the reliability and construct validity of the PSQI [31–32].

Fatigue—The Functional Assessment of Chronic Illness Therapy Fatigue subscale (FACIT-F) [33] assessed cancer-related fatigue during the past 7 days. The FACIT-F consists of 13 items (e.g., “I have energy”) that are rated on 5-point scales from 0 (*not at all*) to 4 (*very much*). Higher scores indicate less fatigue. The FACIT-F has predicted group differences in hemoglobin level and performance status among cancer patients [33–34].

Functional impairment—Trained research assistants administered the Australia-modified Karnofsky Performance Status Scale (AKPS) [35] to assess functional impairment. This scale has been found to be valid for use with cancer patients and was more predictive of survival at the lower end of the scale than the original Karnofsky Performance Scale [35]. Evidence of the validity of a telephone-administered Karnofsky Performance Scale has been documented [36].

Socio-demographic and medical variables—Participants reported their socio-demographic data and use of mental health services (e.g., counseling) and cancer support groups. Medical information, including their date of diagnosis and medical treatments, was obtained from chart review.

Statistical Analyses

Data were analyzed with SPSS statistical software (version 18.0; SPSS, Chicago, IL, USA). First, descriptive statistics were computed to characterize the demographic and medical characteristics and psychological adjustment, sleep, and fatigue of the study sample. Second, correlations between study outcomes (general distress, depressive symptoms, anxiety, sleep disturbance, and fatigue) and demographic and medical variables were calculated. Variables that were significantly correlated with mental health service use were entered into a logistic regression predicting that outcome. Simultaneous predictor entry was used. Finally, a discriminant function analysis was conducted to determine which patient characteristics differentiated those who met the criteria for clinically meaningful anxiety or depressive symptoms from those who did not.

Results

Patient Characteristics

A total of 521 breast cancer patients were identified by MSKCC medical records for this study, and permission was granted to contact 83% of the patients (see Figure 1). Of the 405 patients who were potentially eligible for this study (e.g., fluent in English), 173 (43%) completed the screening assessment. Respondents were significantly younger (58.1 ± 11.5 vs. 61.4 ± 13.0 years, respectively; $p < .01$) and more proximal to diagnosis (4.0 ± 3.2 vs. 5.0 ± 5.1 years, respectively; $p < .05$) than nonrespondents. Ethnicity and medical treatment variables (i.e., receipt of chemotherapy, surgery, hormonal therapy, and radiation) did not differ between respondents and nonrespondents. Sixty percent of respondents met the cutoff (≥ 4) for probable distress on the DT [22] (95% CI = 52% to 67%) and 58% of respondents were eligible for the intervention trial. Reasons for ineligibility included obtaining a score less than 4 on the DT (39%) or engaging in expressive writing on a daily basis (2%). When comparing those who obtained scores of 4 or higher on the DT to those who scored below this cutoff, no differences emerged with regard to age, ethnicity, time since diagnosis, and medical treatments.

Of the 101 patients who were eligible for this study, 90 (89%) completed the baseline assessment. The majority of participants were Caucasian, married, and well-educated (see Table 1). The average time since diagnosis of Stage IV breast cancer was 4 years, and most participants had received chemotherapy or hormonal therapy. A minority of participants reported current use of mental health services such as counseling (23%) and cancer support group attendance (17%).

Descriptive Statistics on Study Outcomes

Table 2 displays means, standard deviations, and alphas for study variables. Sixty-one percent had scores above the cutoffs of 16 on the CES-D or 8 on the HADS-A (95% CI = 50% to 71%), indicating significant symptoms of depression or anxiety, respectively [26, 28]. Twenty-nine percent of women who met the cutoffs for depression or anxiety reported current use of mental health services and 18% reported current cancer support group attendance.

Examination of the Global Sleep Quality index showed that 70% of the patients had scores greater than the cutoff score of 5 (95% CI = 59% to 79%), indicating significant decrements in sleep quality. Mean scores on the subscales of the PSQI were generally comparable to those reported for heterogeneous cancer patient samples [31]. Analysis of individual PSQI items and component scores revealed that the average time to sleep onset (i.e., sleep latency) was 32 minutes ($SD = 35$), with 60% of patients reporting a sleep latency greater than 15 minutes. The mean sleep duration was 7.0 hours per night ($SD = 1.6$) with 18% sleeping less

than 6 hours per night. Forty-four percent had habitual sleep efficiency scores less than 85%, and 29% described the quality of their sleep as “fairly bad” or “very bad.” The mean level of fatigue (32.0) on the FACIT-fatigue scale differed from the population mean (43.6) by more than one standard deviation [37], suggesting that patients, on average, experienced significant fatigue. In addition, 12% reported extreme fatigue (95% CI = 6% to 21%), defined as a score greater than 2 standard deviations below the population mean [37]. Finally, Karnofsky scores suggested that most participants were able to carry out their daily activities and experienced moderate physical symptoms.

Relations of Study Outcomes to Patient Characteristics

Correlations between the measures of psychological adjustment, sleep, fatigue, and functional status are shown in Table 3. Moderate to strong correlations were found between the measures, except that functional status was unrelated to anxiety and general distress. Next, correlations were computed between study outcomes and demographic variables, time since diagnosis, medical treatment variables (i.e., chemotherapy, radiation, hormonal therapy, surgery), and use of mental health services and cancer support groups. Younger women had higher levels of anxiety ($r = -.22, p < .05$), and greater medical comorbidities were associated with greater depressive symptoms ($r = .21, p < .05$), greater fatigue ($r = -.26, p < .05$), and poorer sleep quality ($r = .21, p < .05$). Current use of mental health services was correlated with more depressive symptoms ($r = .31, p < .01$), anxiety ($r = .28, p < .01$), and fatigue ($r = -.34, p < .01$). In a logistic regression analysis, these three variables correctly classified 81% of the sample with regard to mental health service use, $\chi^2(3, n = 90) = 13.61, p < .01$, and only fatigue uniquely predicted service use ($\beta = -.06, p < .05$). Cancer support group use was unrelated to depressive symptoms, anxiety, and fatigue. None of the other univariate correlations between study outcomes and patients’ demographic and medical characteristics were statistically significant.

Finally, we conducted a discriminant function analysis to determine which patient characteristics distinguished those who met the clinical cutoffs on the CES-D or HADS-A from those who did not. We included seven variables that had significant univariate relationships with CES-D or HADS-A scores: age, number of comorbidities, distress on the DT, fatigue, sleep quality, functional status, and mental health service use. Table 4 shows variables entered into the discriminant analysis, average differences between the two groups, and the standardized discriminant function coefficients for the seven variables. The overall Wilks’ lambda was significant, $\Lambda = .80, \chi^2(7, n = 90) = 18.54, p < .05$, with a canonical correlation of .44. Univariate F tests yielded significant results for four of the seven predictors. Higher distress on the DT, greater fatigue, worse sleep quality, and functional impairment were all related to clinically meaningful levels of anxiety or depressive symptoms. Using the discriminant function, 71.1% of patients were correctly classified as to whether they had significant anxiety or depressive symptoms or not.

Discussion

A high prevalence of distress was found among metastatic breast cancer patients who completed a screening interview for an expressive writing trial, with 60% meeting the criterion for probable distress on the DT. Using this measure, Graves and colleagues [21] found a similar prevalence of distress (62%) among patients being seen in a lung cancer clinic. Another study documented a lower rate of distress (43%) based on the DT criterion in a heterogeneous sample of cancer patients [22]. In the present sample, distress was correlated with symptoms of depression, anxiety, fatigue, and sleep disturbance. Meeting the criterion for probable distress on the DT was not associated with age, ethnicity, time since diagnosis, and medical treatments. The lack of relationship between distress and medical variables is similar to previous findings [21–22]. Although younger age has generally been

associated with greater distress among cancer patients [38], age has shown mixed associations with DT scores [21–22, 24].

Over 60% of women who were classified as distressed on the DT showed clinically meaningful levels of anxiety or depressive symptoms one week later. Greater distress on the DT, reduced sleep quality, greater fatigue, and worse functional status were all related to meeting clinical criteria for anxiety or depressive symptoms. These results are consistent with prior research [10–12, 18] and suggest that sleep hygiene and symptom management should be integrated into mental health care. The prevalence of sleep disturbance in this sample (70%) is slightly higher than that reported for metastatic breast cancer patients who participated in group psychotherapy trials (63–64%) [12–13]. Greater functional impairment and medical comorbidities were associated with poorer sleep quality and higher levels of fatigue and depressive symptoms, suggesting that patients with greater disability may be especially vulnerable to depression. Greater fatigue, the most bothersome symptom for many cancer patients [9], was correlated with mental health service use. Given the low rate of mental health service use (29%) among patients with significant anxiety or depressive symptoms, developing accessible interventions, such as telephone and Internet-based counseling, is an important direction for future research.

Limitations of this study include the cross-sectional design, reliance on self-report measures, and the self-selected nature of the sample. Younger age and shorter time since diagnosis were associated with a greater likelihood of participation in this study; however, these response biases were relatively small in magnitude. Results may not necessarily generalize to the larger population of metastatic breast cancer patients, as accrual efforts were linked to participation in an expressive writing trial. Higher distress may have been associated with greater interest in expressive writing. On the other hand, participation in psychosocial research has been associated with lower distress among advanced cancer patients [39]. In addition to respondent bias, patients at this cancer center were primarily Caucasian and well-educated. Future research should examine distress among metastatic breast cancer patients with greater socioeconomic and ethnic diversity. Finally, we only administered measures of psychological adjustment, sleep, fatigue, and functional status to those with scores of 4 or higher on the DT. Although this clinical cutoff has been established with heterogeneous cancer patient samples [22], the sensitivity and specificity of this cutoff has not been examined among metastatic breast cancer patients. Further research is needed to determine the most appropriate clinical cutoff on the DT for metastatic breast cancer patients and to examine other variables that may contribute to distress (e.g., social context variables, other physical symptoms) in this population.

The present findings have important implications for future research and clinical practice. First, results suggest that the DT may be used to identify distressed metastatic breast cancer patients and point to high levels of distress, fatigue, and sleep problems across demographic and medical subgroups. Second, these problems tended to co-occur, suggesting that interventions may be most effective if they target both physical and psychological symptoms. Third, results suggest that the majority of metastatic breast cancer patients with high levels of distress are not receiving mental health services, despite their availability at this comprehensive cancer center. Research efforts are needed to identify barriers to seeking professional support and to develop interventions that are tailored to the needs and preferences of this chronically ill population. A Cochrane review indicated that cognitive-behavioral and supportive-expressive group psychotherapy only resulted in short-term psychological benefits for women with metastatic breast cancer [40]. Novel home-based interventions are needed to promote well-being, as patients with functional impairment were more likely to experience depressive symptoms. Finally, the impact of adherence to NCCN guidelines for distress management (e.g., routine screening followed by referral to mental

health professionals) on patient outcomes deserves further research attention [41–42]. In the face of incurable and protracted illness, optimizing symptom management and quality of life are central goals of health care.

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Catherine Mosher is now at Indiana University-Purdue University Indianapolis in the Department of Psychology.

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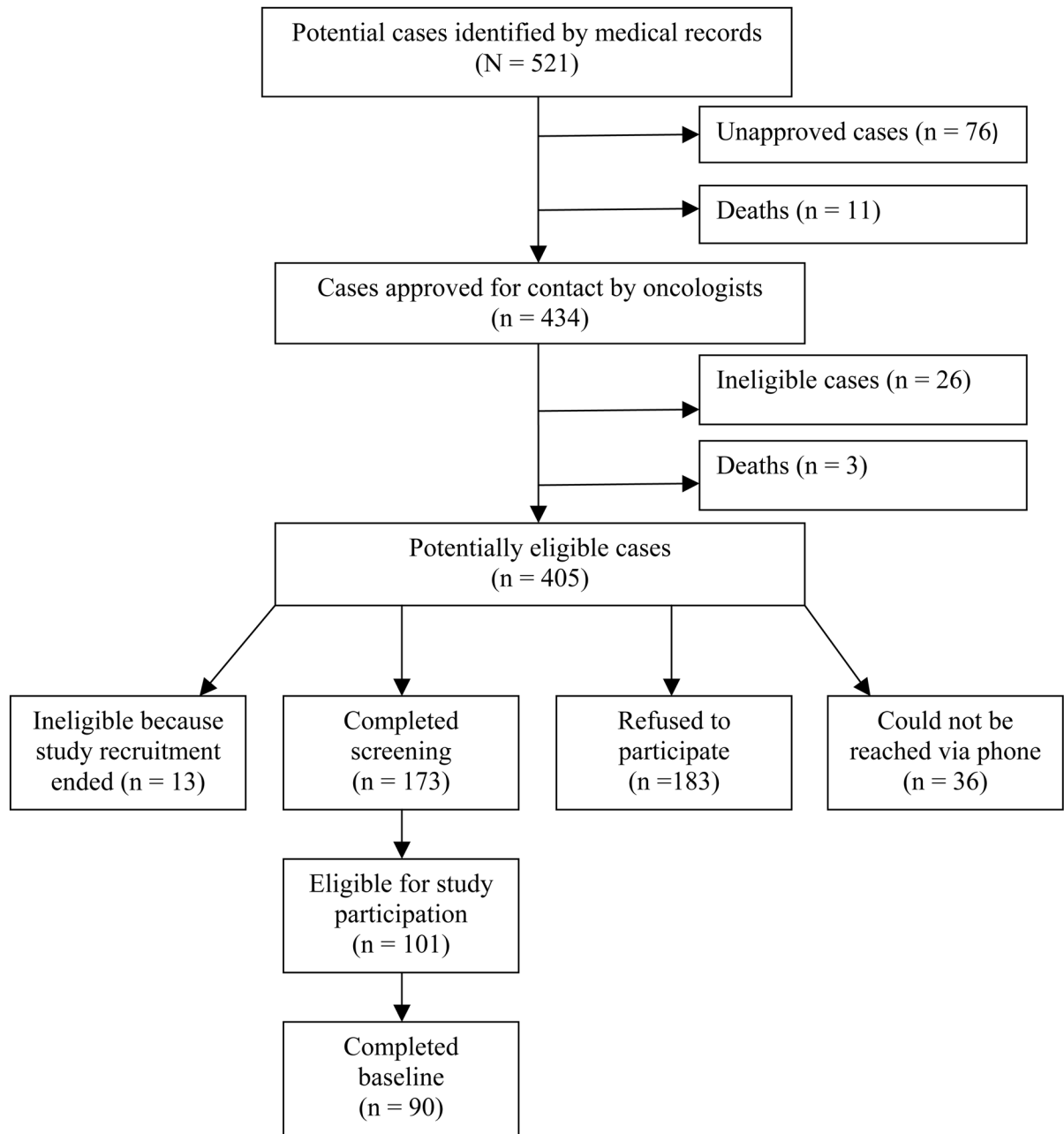


Figure 1.
Study Schema

Table 1Sample Characteristics ($N = 90$)

Characteristic	No.	%
<i>Age, years</i>		
Mean		57.9
SD		11.9
<i>Race</i>		
Caucasian	71	78.9
African American	7	7.8
Hispanic	6	6.7
Other	6	6.7
<i>Education</i>		
12 years	12	13.3
Some college	22	24.4
College or graduate degree	56	62.2
<i>Employment Status</i>		
Employed	31	34.4
Not employed	59	65.6
<i>Marital Status</i>		
Married or marriage equivalent	61	67.8
Not married	29	32.2
<i>No. of comorbid conditions</i>		
Mean		1.4
SD		1.4
<i>Time since diagnosis of Stage IV breast cancer, years</i>		
Mean		4.4
SD		3.2
<i>Chemotherapy</i>		
Yes	83	92.2
No	7	7.8
<i>Hormonal therapy</i>		
Yes	75	83.3
No	15	16.7
<i>Radiation</i>		
Yes	58	64.4
No	32	35.6
<i>Breast cancer-related surgery</i>		
Yes	75	83.3
No	15	16.7
<i>Type of surgery (n = 75)</i>		
Mastectomy	36	48.0
Lumpectomy	21	28.0

Characteristic	No.	%
Both surgeries	15	20.0
Other	1	1.3
Missing	2	2.7
<i>Current mental health service use</i>		
Yes	21	23.3
No	69	76.7
<i>Current cancer support group attendance</i>		
Yes	15	16.7
No	75	83.3

SD = standard deviation.

Table 2Descriptive Statistics for Study Variables ($N = 90$)

Variable	<i>M</i>	<i>SD</i>	α
Distress Thermometer	6.02	1.72	
Center for Epidemiologic Studies-Depression Scale	17.51	9.52	.87
Anxiety subscale of the Hospital Anxiety and Depression Scale	7.31	4.28	.84
FACIT-fatigue scale	32.00	10.85	.92
Pittsburgh Sleep Quality Index			
Subjective Sleep Quality	1.26	0.84	
Sleep Latency	1.48	1.00	
Sleep Duration	0.63	0.88	
Habitual Sleep Efficiency	0.86	1.12	
Use of Sleeping Medications	1.23	1.37	
Daytime Dysfunction	1.08	0.80	
Sleep Disturbances	1.59	0.69	.69
Global Sleep Quality	8.12	3.95	.67
Karnofsky Performance Status	79.11	8.95	

FACIT = Functional Assessment of Chronic Illness Therapy. *M* = mean. *SD* = standard deviation. The distress thermometer was administered at screening, whereas all other measures were administered at baseline.

Table 3

Correlations among Study Variables (N= 90)

Study Variable	1	2	3	4	5	6
1. Distress Thermometer	—	.43 ^{***}	.38 ^{***}	-.29 ^{**}	.31 ^{**}	-.15
2. CES-D			.67 ^{***}	-.59 ^{***}	.48 ^{***}	-.40 ^{***}
3. HADS-Anxiety				-.30 ^{**}	.42 ^{***}	-.16
4. FACIT-fatigue					-.51 ^{***}	.55 ^{***}
5. Global Sleep Quality						-.33 ^{**}
6. Karnofsky Performance Status						

^{**} $p < .01$.

^{***} $p < .001$. CES-D = Center for Epidemiologic Studies—Depression Scale. HADS = Hospital Anxiety and Depression Scale. FACIT = Functional Assessment of Chronic Illness Therapy. Higher scores on the FACIT-fatigue indicate less fatigue, and higher Global Sleep Quality scores indicate worse sleep quality.

Table 4

Means, Standard Deviations, Analyses of Variance (ANOVA), and Standardized Discriminant Function Coefficients for Predictors of Anxiety and Depressive Symptoms

Variable	No significant anxiety or depressive symptoms			Significant anxiety or depressive symptoms			ANOVA <i>F</i>	Standardized coefficient
	<i>M</i>	<i>SD</i>		<i>M</i>	<i>SD</i>			
Age	59.97	12.17		56.55	11.60		1.80	.18
No. of comorbid conditions	1.23	1.26		1.49	1.54		.71	.04
Distress Thermometer	5.43	1.42		6.40	1.79		7.35**	-.36
FACIT-fatigue	37.26	8.20		28.65	11.07		15.65***	.59
Global Sleep Quality	6.63	3.32		9.07	4.05		8.91**	-.25
Karnofsky Performance Status	81.71	9.23		77.45	8.44		5.07*	.10
Current mental health service use	.14	.36		.29	.46		2.64	-.10

* $p < .05$.

** $p < .01$.

$p < .001$. $N = 90$. M = mean. SD = standard deviation. FACIT = Functional Assessment of Chronic Illness Therapy. Higher scores on the FACIT-fatigue indicate less fatigue, and higher Global Sleep Quality scores indicate worse sleep quality. Current mental health service use dummy coded (0 = no; 1 = yes).