Title
Stress and Symptom Burden in Oncology Patients During the COVID-19 Pandemic

Journal
Journal of Pain and Symptom Management, 60(5)

ISSN
0885-3924

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Publication Date
2020-11-01

DOI
10.1016/j.jpainsymman.2020.08.037

Peer reviewed

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Journal Pre-proof

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PII: S0885-3924(20)30724-7

DOI: https://doi.org/10.1016/j.jpainsymman.2020.08.037

Reference: JPS 10626

To appear in: *Journal of Pain and Symptom Management*

Received Date: 30 July 2020

Revised Date: 24 August 2020

Accepted Date: 28 August 2020

Please cite this article as: Miaskowski C, Paul SM, Snowberg K, Abbott M, Borno H, Chang S, Chen LM, Cohen B, Hammer MJ, Kenfield SA, Kober KM, Levine JD, Pozzar R, Rhoads KF, Van Blarigan EL, Van Loon K, STRESS AND SYMPTOM BURDEN IN ONCOLOGY PATIENTS DURING THE COVID-19 PANDEMIC, *Journal of Pain and Symptom Management* (2020), doi: https://doi.org/10.1016/j.jpainsymman.2020.08.037.

STRESS AND SYMPTOM BURDEN IN ONCOLOGY PATIENTS DURING THE COVID-19 PANDEMIC

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Running head: Stress and symptoms during COVID-19

Word count:
Number of tables:
Number of figures:
Number of references:

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ABSTRACT

Context - No information is available on oncology patients' level of stress and symptom burden during the COVID-19 pandemic. We evaluated for differences in demographic and clinical characteristics, levels of social isolation and loneliness, and the occurrence and severity of common symptoms between oncology patients with low versus high levels of COVID-19 and cancer-related stress. In addition, we determined which of these characteristics were associated with membership in the high stressed group.

Methods – Patients were ≥18 years of age; had a diagnosis of cancer; and were able to complete an online survey.

Results - Of the 187 patients in this study, 31.6% were categorized in the stressed group (Impact of Event Scale –Revised (IES-R score of ≥24)). Stressed group's IES-R score exceeds previous benchmarks in oncology patients and equates with probable PTSD. In this stressed group, patients reported occurrence rates for depression (71.2%), anxiety (78.0%), sleep disturbance (78.0%), evening fatigue (55.9%), cognitive impairment (91.5%), and pain (75.9%). Symptom severity scores equate with clinically meaningful levels for each symptom.

Conclusions – We identified alarmingly high rates of stress and an extraordinarily high symptom burden among cancer patients, exceeding those previously benchmarked in this population and on par with non-cancer patients with PTSD. Given that the COVID19 pandemic will likely impact cancer care for an indefinite period of time, clinicians must exhibit increased vigilance in their assessments of patients' level of stress and symptom burden. Moreover, an increase in referrals to appropriate supportive care resources must be prioritized for high risk patients.

Key words: symptoms, stress, cancer, loneliness, social isolation, COVID-19

INTRODUCTION

A cancer diagnosis and its treatments are stressful experiences for most patients.[1,2] The corona virus disease 2019 (COVID-19) pandemic and associated mitigation procedures have imposed additional stress. Emerging evidence suggests that fear of infection, concerns regarding the efficacy of COVID-19 treatments, the negative impact of various mitigation procedures (e.g., social isolation), and economic uncertainty are associated with higher levels of perceived stress in the general population.[3-8] In addition, oncology patients may experience higher levels of stress if they perceive themselves to be at increased risk for contracting the disease[9,10] and for serious adverse events if they become infected with COVID-19.[10-12] Furthermore, the social distancing procedures and restrictions in access to care may increase patients' fears and concerns about receiving cancer treatments and disease recurrence.[13-15]

While the types and the duration of stressors can vary, a significant amount of variability exists in individuals' cognitive, emotional, and neurobiological responses to stress.[16] A growing body of evidence from the general population suggests that these inter-individual differences in responses to stress contribute to higher rates and severity of both psychological and physical symptoms. Surprisingly, research on the association between stress and symptom burden in oncology patients is limited.

In terms of psychological symptoms, in a meta-analysis of studies that focused on the prevalence of COVID-19 related stress and anxiety in the general population,[7] 29.6% of individuals surveyed reported high levels of stress, 31.9% reported anxiety, and 33.7% reported depression. While often studied together as psychological distress,[17,18] depression occurs in 15% to 30% of oncology patients and anxiety in 30% to 50%.[19,20] In three recent studies that evaluated psychological symptoms in oncology patients during the COVID-19 pandemic,[21-23] occurrence rates for depression and anxiety ranged from 9.3%[21] to 31.0%[23] and from 8.9%[21] to 36.0%,[23] respectively. The wide range in occurrence rates may be related to the instruments and clinically meaningful cut-off scores that were used to dichotomize the samples.

Less is known about the impact of the COVID-19 pandemic on physical symptoms. While fatigue occurs in 60% to 90% of oncology patients,[24] recent evidence suggests that higher levels of stress correlated with increased fatigue in oncology patients undergoing chemotherapy.[25] Sleep disturbance is reported by 30% to 88% of oncology patients.[26,27] While findings from preclinical and clinical studies suggest that stress has a negative impact on the sleep-wake cycle,[28,29] no data are available on the relationship between stress and sleep disturbance in oncology patients. Similarly while increased stress can exacerbate chronic pain,[30,31] less is known about this relationship in cancer patients. Our study was the first to report significant levels of stress in patients with chemotherapy-induced peripheral neuropathy.[32] In another study that assessed both combat and cancer-related post traumatic stress disorder (PTSD) in Veterans with oral-digestive cancers,[33] patients with both types of stress had an 8.49 times higher odds of experiencing chronic pain. Finally, cancer-related cognitive impairment (CRCI) occurs in 75% of oncology patients[34] and has been associated with increased levels of stress.[35,36] In terms of the relationships between physical symptoms and COVID-19, in one study of patients with breast cancer,[21] 12.9% of women reported moderate and 4.0% reported severe insomnia. In another study of patients with heterogeneous cancer diagnoses,[22] higher levels of fatigue and pain were associated with higher risk for mental disorders.

The loneliness and social isolation imposed by COVID-19 “stay-at-home” orders are additional sources of stress.[37,38] While not extensively studied in oncology patients,[39] loneliness and social isolation are associated with a higher symptom burden,[40] poorer health, and higher all-cause mortality in older adults.[41]

Given the paucity of research on the associations between COVID-19 and cancer-related stress and the severity of common symptoms in oncology patients, we evaluated for differences in demographic and clinical characteristics, levels of social isolation and loneliness, and the occurrence and severity of common symptoms between oncology patients with low

versus high levels of COVID-19 and cancer-related stress. In addition, we determined which demographic, clinical, symptom, and stress characteristics were associated with membership in the high stressed group. We hypothesized that patients in the high stressed group would have a higher symptom burden and higher levels of social isolation and loneliness.

METHODS

Sample and settings

Patients were recruited from a registry of individuals who participated in our previous National Cancer Institute funded studies (CA187160, CA212064, CA151692). Potential participants received an email with a brief explanation of the study and a link that directed them to the study's enrollment page. This study was exempt from requiring written informed consent by the Institutional Review Board at the University of California, San Francisco. Patients were included if they: were ≥18 years of age; were able to read, write, and understand English; had a diagnosis of cancer; and were able to complete the survey online.

Survey administration

Emails were sent to potential participants beginning May 27, 2020. Patients who received the survey link were asked to complete the survey within two weeks. One email reminder was sent 14 days after the initial request. Patients were asked to answer all of the survey questions in relationship to their experiences in the past 14 days. The entire survey took ~60 minutes to complete. All of the instruments were completed online using the Research Electronic Data Capture (REDCap) system.[42,43] Responses as of July 10, 2020 are presented in this paper.

Instruments

Demographic and clinical characteristics – Patients completed demographic and clinical questionnaires, Karnofsky Performance Status (KPS) scale,[44] and Self-Administered Comorbidity Questionnaire (SCQ).[45]

Stress measure – The 22-item Impact of Event Scale-Revised (IES-R) was used to measure COVID-19 and cancer-related stress.[46] Patients rated each item based on how distressing each potential difficulty was for them during the past 14 days "with respect to their cancer and its treatment and the COVID-19 pandemic". Each item was rated on a 0 to 4 Likert scale. Three mean subscale scores were created that evaluated levels of perceived intrusion, avoidance, and hyperarousal. A total IES-R score was created by summing the responses to the 22 items and can range from 0 to 88. A total IES-R score of $\geq$24[47] indicates clinically meaningful post-traumatic symptomatology and scores of $\geq$33 indicate probable PTSD.[48,49] The IES-R has been used to assess COVID-19 specific stress in the general population in China,[50] in the Chinese workforce,[51] in health care workers,[52] in psychiatric patients,[53] and in oncology patients.[21-23]

Additional measures of stress included the Perceived Stress Scale (PSS, general stress),[54,55] the Connor Davidson Resilience Scale (CDRS, resilience),[56] and the Comprehensive Score for Financial Toxicity (COST, financial stress).[57]

Loneliness and social isolation - UCLA Loneliness Scale assesses an individual's subjective feelings of loneliness and social isolation.[58-60] A score of 36.0 represents a normative value for the general population.[61] Social Isolation Scale (SIS) evaluates an individual's perceptions of connectedness and belongingness.[62] A score of between 10 and 15 suggests that an individual is at risk for social isolation and a score of $\leq$9 indicates social isolation.

Symptom measures – To assess the occurrence and severity of the most common symptoms associated with cancer and its treatment, patients completed: Center for Epidemiological Studies-Depression scale (CES-D),[63] Spielberger State-Trait Anxiety Inventories (STAI-S, STAI-T),[64] General Sleep Disturbance Scale (GSDS),[65] Lee Fatigue Scale (LFS, which assessed levels of morning and evening fatigue and morning and evening energy),[66] Attentional Function Index,[67] and Brief Pain Inventory.[68]

Data analysis

Data were downloaded from REDCap[42,43] into the Statistical Package for the Social Sciences Version 27 (IBM Corporation, Armonk, NY). Descriptive statistics were generated for sample characteristics and study measures. Using the IES-R total score, patients were dichotomized into the stressed (i.e., ≥24) and non-stressed (i.e., <24) groups.[48,49] To determine symptom occurrence rates, symptoms were dichotomized based on clinically meaningful cut-off scores for each of the symptom measures. Between group differences were evaluated using Independent sample t-tests, Chi Square analyses, and Mann Whitney U tests. Multiple logistic regression analysis was used to evaluate for predictors of stress group membership. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 627 emails were sent, 250 patients began the survey (39.9% response rate), and 187 provided complete information (29.8% completion rate). The characteristics of the total sample and the two stress groups are presented in Table 1.

Demographic and clinical characteristics

Of these 187 patients, 31.6% (n=59) were categorized in the stressed group. Compared to the non-stressed group, the stressed group had a higher number of comorbidities, a higher comorbidity burden, were fewer years from their cancer diagnosis, were more likely to report a diagnosis of depression, and had a lower functional status score (all p<.05, Table 1).

Stress, social isolation, and loneliness scores

Compared to the non-stressed group, the stressed group had significantly higher scores for general stress, intrusion, avoidance, hyper-arousal, and loneliness. In addition, they had lower scores (indicating worse outcomes) for resilience, social isolation, and financial toxicity (Table 2).

Symptom scores

As shown in Table 3, compared to the non-stressed group, the stressed group had significantly higher occurrence rates for all of the symptoms except decrements in evening

energy. In addition, compared to the non-stressed group, the stressed group had significantly higher scores for depressive symptoms, trait and state anxiety, sleep disturbance, and morning and evening fatigue. In addition, they had lower scores (indicating a higher level of symptom severity) for morning and evening energy and attentional function (Table 2).

Factors associated with stressed group membership

In the logistic regression analysis, clinical characteristics (i.e., time since cancer diagnosis, SCQ score, KPS score), stress scores (i.e., PSS, UCLA Loneliness scale, SIS, CDRS, COST), and symptom severity scores (i.e., CES-D, STAI-T, STAI-S, GSDS, morning and evening fatigue, morning energy, AFI, presence of pain) that were significantly different between the two stress groups in the bivariate analyses were included in the model. While the number of comorbidities and the proportion of patients with a diagnosis of depression were significantly different between the two stress groups, they were not included in the analysis because the total SCQ and CES-D scores were used in the logistic regression.

As shown in Table 4, the overall model was significant (X^2=85.20, p<.001). Three variables were significant in the final model (i.e., length of time since cancer diagnosis, PSS score, and occurrence of pain). Patients who were a shorter time from their cancer diagnosis; had a higher level of general stress; and who reported the occurrence of pain were more likely to be in the stressed group.

DISCUSSION

Consistent with a prevalence rate of 29.6% for high levels of COVID-19 related stress in the general population,[7] 31.6% of our patients were categorized into the stressed group. While the IES-R score of 18.6 for the total sample was below the clinically meaningful cut-point, patients in our stressed group had a mean score of 36.9 ($\pm$10.1; range 24 to 60) which is alarmingly high and consistent with probable PTSD.[48] It should be noted that, while the majority of the patients in the current study were female, White, well-educated, had an annual income of $\geq$\$60,000, had completed their cancer treatment, and had a high functional status, the IES-R

cut-off score used in this study was established with war Veterans,[48] earthquake survivors,[47] and survivors of the Tokyo Metro sarin gas attack.[47] By way of comparison, in our study of patients receiving chemotherapy prior to COVID-19,[69] IES-R scores ranged from 15.4 (±12.1) to 27.9 (±13.8). In addition, in two recent studies of oncology patients during the COVID-19 pandemic, IES-R total scores ranged from 19.7[23] to 28.2.[21] Taken together, these findings indicate that during this COVID-19 pandemic, oncology patients are experiencing a clinically meaningful level of stress that exceeds previously reported benchmarks and equates with probable PTSD.

In addition to the COVID-19 and cancer-related stress measure, patients completed a measure of general stress (i.e., PSS). For the total sample, their PSS score slightly exceeded the clinically meaningful cut-point score of ≥14.0 (i.e., 14.6 (±7.3)) and was significantly higher in the stressed group (i.e., 20.2 (±6.7)). In the study mentioned above of patients receiving chemotherapy,[69] PSS scores ranged from 8.5 (±4.5) to 25.4 (±6.7). During these particularly stressful times, that include the stressors associated with the pandemic as well as societal and political challenges, the use of a general measure of stress captures additional information on patients' experiences.

Consistent with the known associations between COVID-19 mitigation procedures and heightened levels of loneliness in the general population,[70] it is not surprising that patients in our stressed group reported higher levels of social isolation and loneliness. While our sample did not meet the clinically meaningful cut-point for social isolation, the loneliness score for the total sample was above the clinically meaningful cut-point. Finally, given the economic consequences of the COVID-19 pandemic[71] and the financial toxicity associated with cancer and its treatment,[72] it is not surprising that the stressed group reported more financial concerns. Given that the majority of the patients in this study had a relatively high annual income, additional research is needed on the added stress of the COVID-19 pandemic on patients with fewer economic and health care resources.

The population-based studies that evaluated for associations between COVID-19 related stress and symptoms assessed anxiety and depression. As noted in a recent systematic review of these studies,[7] the prevalence rates for COVID-19 related anxiety and depression were 31.9% and 33.7%, respectively.[7] In addition, in studies of oncology patients during COVID-19, occurrence rates for depression and anxiety ranged from 9.3%[21] to 31.0%[23] and from 8.9%[21] to 36.0%,[23] respectively. While for our total sample, the rate of depression was comparable (i.e., 39.8%), our rates for trait (59.1%) and state (48.4%) were considerably higher.[7] Reasons for these differences may include the measures used to evaluate the symptoms; differences in sample characteristics; and/or various additional stressors not evaluated in the questionnaires (e.g., access to care, sociopolitical stress). However, it is notable that in studies of oncology patients prior to the COVID-19 pandemic, rates of depression and anxiety ranged from 15% to 30% and 30% to 50%, respectively.[19,20] In addition, in the current sample, between group differences in the severity of both anxiety and depression represent not only statistically significant but clinically meaningful differences (d=1.07 for state anxiety to d=1.38 for depression). In addition, the CES-D scores of the patients in the stressed group (i.e., 22.4 ($\pm$9.8)) suggest the need for a clinical evaluation of depression.

The results of this study extend the findings of previous studies of COVID-19 stress,[7] by evaluating the impact of this added stress on the occurrence and severity of physical symptoms in oncology patients. In the previous study of patients with breast cancer who were evaluated during COVID-19,[21] only 12.9% of women reported moderate and 4.0% reported severe insomnia. In contrast, nearly 60% of the total sample and 78% of the stressed group reported clinically meaningful levels of sleep disturbance. The severity of sleep disturbance reported by the stressed group (i.e., GSDS score of 60.1) is comparable to that of permanent shift workers[65] or parents of newborn infants.[73] Consistent with the very high level of sleep disturbance in these patients, the occurrence rates for and severity of morning fatigue, as well as decrements in morning and evening energy represent clinically meaningful levels of all three symptoms.

Previous work from our research team demonstrated that while morning and evening fatigue, as well as morning and evening energy are associated with depression, they are distinct symptoms.[74-76] While CRCI occurs in 75% of oncology patients,[34] 91.5% of the patients in the stressed class reported clinically meaningful decrements in cognitive function. Finally, while fewer patients in the non-stressed group (54.4%) compared to the stressed group (75.9%) reported pain, both groups reported pain severity scores in the moderate to severe range that had a moderate impact on their functional activities.[77] Taken together, these findings demonstrate an extremely strong relationship between COVID-19 and cancer-related stress and a significant symptom burden. While this relationship was stronger in the stressed group, the occurrence rates and severity of symptoms in the non-stressed group are clinically meaningful, higher than normative data, and warrant immediate assessment and management.

In terms of the regression analysis, shorter time since the cancer diagnosis, higher levels of general stress (i.e., higher PSS scores), and the occurrence of pain were significant predictors of membership in the stressed group. While in a recent systematic review,[78] no association was found between time since cancer diagnosis and PTSD, this non-modifiable characteristic may be used to identify higher risk patients. It is interesting to note that patients with higher scores on our measure of general stress, were more likely to be in the stressed group. This finding suggests that stressors other than those related to COVID-19 and cancer (e.g., social unrest, family stress) can contribute to the overwhelming stress reported by the patients in our sample.

Of note, pain was the only symptom associated with membership in the stressed group. Consistent with previous reports,[32,33] patients with pain were 5.02 times more likely to be in the stressed group. Sixty-one percent of the total sample and 75.9% of the stressed group reported this symptom. The most common causes of non-cancer pain were low back pain (20.7%) and arthritis (24.5%). In terms of cancer pain, 16.0% reported chronic post-surgical pain and 19.7% reported chemotherapy-induced peripheral neuropathy. Given that the severity of and level of

interference from pain were relatively high in both groups, effective management of this symptom (e.g., cognitive behavioral therapy[79]) is warranted.

While this study provides new information on the significant impact of COVID-19 and cancer-related stress on oncology patients,[80] several limitations warrant consideration. Given that the majority of the patients were well-educated women with breast cancer, the generalizability of our findings to men or patients with other cancer diagnoses warrant confirmation in future studies. Given that the majority of our patients were White, had health insurance (97.7%), and reported annual incomes of >$60,000, we may be significantly under-estimating the impact of the stress associated with this pandemic, particularly among individuals who are socioeconomically disadvantaged. Expansion of this research to underserved populations is needed to inform planning and implementation of appropriate interventions to decrease stress and symptom burden. Longitudinal studies are needed to assess the relationships among changes over time in stress and symptom burden as the COVID-19 pandemic evolves.

In conclusion, we identified alarmingly high rates of stress and an extraordinarily high symptom burden among cancer patients in the COVID-19 pandemic, exceeding those previously benchmarked in this patient population and on par with non-cancer patients with PTSD. Given that the COVID19 pandemic and the ensuing economic downturn will likely impact cancer care for an indefinite period of time, clinicians must exhibit increased vigilance in their assessments of oncology patients' level of stress and symptom burden. In addition, clinicians need to educate patients on the benefits of using simple strategies (e.g., relaxation exercises, stress reduction techniques) to manage stress and decrease symptoms.[15] Equally important, an increase in referrals to appropriate supportive care resources (e.g., online peer support groups, exercise therapy, psycho-oncology, symptom management services) must be prioritized for high risk patients. At the institutional level, we recommend that supportive care services increase; that patients have increased access to these services using telehealth approaches; and that

concerted efforts be made to provide these services to our most vulnerable and underserved patients. Future research should identify additional factors that contribute to heightened stress levels and increased symptom burden among cancer patients and how these factors may vary with race, socioeconomic status, and other important social determinants of health.

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

Disclosures - Dr. Miaskowski is an American Cancer Society Clinical Research Professor. Dr. Van Blarigan is funded by CA197077. Dr. Kenfield is funded by the Helen Diller Family Chair in Population Science for Urologic Cancer.

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Table 1 - Differences in demographic, clinical, and behavioral characteristics between the stress groups

Characteristic	Total Sample n=187	Non-stressed group 68.4% (n=128)	Stressed group 31.6% (n=59)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Demographic and Clinical Characteristics				
Age (years)	63.3 (10.9)	63.0 (12.4)	62.8 (10.5)	t=0.41, p=.680
Number of people in your household including yourself	1.9 (0.9)	2.0 (0.9)	1.9 (0.9)	t=0.49, p=.624
Body mass index (kg/m^2)	26.3 (5.4)	26.5 (5.8)	25.9 (4.4)	t=0.71, p=.476
Karnofsky Performance Status score	92.8 (9.1)	93.7 (9.1)	90.7 (8.9)	t=2.14, p=.033
Number of comorbidities	1.6 (1.4)	1.4 (1.4)	2.0 (1.4)	t=-2.53, p=.012
Self-administered Comorbidity Questionnaire score	3.2 (3.0)	2.7 (2.8)	4.1 (3.1)	t=-3.06, p=.003
Time since cancer diagnosis (years)	9.7 (6.9)	10.9 (7.4)	7.2 (4.6)	U, .001
Time since cancer diagnosis - median	8.1	8.7	6.4	
Number of previous cancer treatments	3.0 (1.0)	3.1 (1.0)	2.9 (0.9)	t=1.64, p=.103
Number of current cancer treatments	0.3 (0.5)	0.3 (0.5)	0.3 (0.5)	t=-0.19, p=.851
	% (n)	% (n)	% (n)	
Female (% yes)	97.9 (183)	97.7 (125)	98.3 (58)	FE, p=1.000
Living arrangements				X^2=0.46, p=.496
Private home or apartment	99.5 (186)	99.2 (127)	100.0 (59)	
Assisted living facility	0.0 (0)	0.0 (0)	0.0 (0)	
Other	0.5 (1)	0.8 (1)	0.0 (0)	
Lives alone (% yes)	29.9 (56)	30.5 (39)	28.8 (17)	FE, p=.865
Married/partnered (% yes)	61.5 (115)	60.2 (77)	64.4 (38)	FE, p=.630
Race/ethnicity				FE, p=.838
White	82.4 (154)	82.8 (106)	81.4 (48)	
Non-White	17.6 (33)	17.2 (22)	18.6 (11)	
Highest level of education				U, p=.107
High school	2.7 (5)	3.1 (4)	1.7 (1)	
Some college	19.9 (37)	22.0 (28)	15.3 (9)	
College graduate	25.8 (48)	27.6 (35)	22.0 (13)	
Some graduate school	15.1 (28)	13.4 (17)	18.6 (11)	
Advanced degree	36.5 (68)	33.9 (43)	42.4 (25)	
Currently employed (% yes)	40.3 (75)	41.7 (53)	37.3 (22)	FE, p=.631

Annual household income				
<$20,000	5.0 (8)	4.7 (5)	5.8 (3)	
$20,000 to $59,000	24.5 (39)	24.3 (26)	25.0 (13)	U, p=.957
$60,000 to $100,000	22.0 (35)	23.4 (25)	19.2 (10)	
>$100,000	48.5 (77)	47.6 (51)	50.0 (26)	
Chronic conditions (% yes)				
Heart disease	8.2 (15)	7.1 (9)	10.5 (6)	FE, p=.561
High blood pressure	28.1 (52)	24.2 (31)	36.8 (21)	FE, p=.110
Lung disease	5.5 (10)	4.8 (6)	7.0 (4)	FE, p=.505
Diabetes	4.3 (8)	5.5 (7)	1.8 (1)	FE, p=.438
Ulcer or stomach disease	3.3 (6)	4.0 (5)	1.7 (1)	FE, p=.667
Kidney disease	1.6 (3)	1.6 (2)	1.8 (1)	FE, p=1.000
Liver disease	1.7 (3)	2.4 (3)	0.0 (0)	---
Anemia or blood disease	2.2 (4)	2.4 (3)	1.8 (1)	FE, p=1.000
Depression	25.7 (47)	15.0 (19)	50.0 (28)	FE, p<.001
Osteoarthritis, degenerative arthritis	28.8 (53)	27.8 (35)	31.0 (18)	FE, p=.727
Back pain	32.6 (59)	29.8 (37)	38.6 (22)	FE, p=.306
Rheumatoid arthritis	4.0 (7)	5.0 (6)	1.8 (1)	FE, p=.437
Cancer diagnosis				
Breast cancer	80.6 (149)	80.3 (102)	81.0 (47)	
Gastrointestinal	3.2 (6)	2.4 (3)	5.2 (3)	
Lung	0.5 (1)	0.8 (1)	0.0 (0)	X^2=6.60, p=.360
Malignant melanoma	0.5 (1)	0.8 (1)	0.0 (0)	
Gynecological	4.9 (9)	3.1 (4)	8.6 (5)	
Prostate	0.5 (1)	0.8 (1)	0.0 (0)	
Multiple cancer types or other	9.8 (18)	11.8 (15)	5.2 (3)	
Presence of metastatic disease (% yes)	24.7 (45)	23.2 (29)	28.1 (16)	FE, p=.579
Currently receiving cancer treatment (% yes)	26.2 (49)	25.8 (33)	27.1 (16)	FE, p=.859

Abbreviations: kg = kilograms, m^2 = meters squared, SD = standard deviation, U = Mann Whitney U

Table 2 - Differences in stress and symptom scores between the stress groups

Characteristic*	Total Sample n=187	Non-stressed group 68.4% (n=128)	Stressed group 31.6% (n=59)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Stress scores				
IES-R - Total score (≥24)	18.6 (14.8)	10.2 (6.9)	36.9 (10.1)	t=-18.43, p<.001
IES-R – Intrusion subscale	0.9 (0.8)	0.4 (0.4)	1.8 (0.6)	t=-15.56, p<.001
IES-R – Avoidance subscale	0.8 (0.7)	0.5 (0.5)	1.5 (0.5)	t=-13.22, p<.001
IES-R – Hyper-arousal subscale	0.8 (0.8)	0.4 (0.4)	1.7 (0.7)	t=-13.92, p<.001
Perceived Stress Scale (≥14.0)	14.6 (7.3)	12.0 (6.1)	20.2 (6.7)	t=-8.20, p<.001
Connor Davidson Resilience Scale	29.9 (6.4)	31.4 (5.8)	26.6 (6.5)	t=5.07, p<.001
Social Isolation Scale (≤9 is social isolation; 10-15 at risk for social isolation)	23.3 (4.1)	24.0 (3.7)	21.8 (4.7)	t=3.15, p=.002
UCLA Loneliness Scale (≥36)	37.5 (10.8)	35.0 (9.3)	42.8 (11.9)	t=-4.82, p<.001
Comprehensive Score for Financial Toxicity	31.3 (10.1)	32.4 (9.8)	29.1 (10.7)	t=2.04, p=.043
Symptom scores				
Center for Epidemiological Studies – Depression (≥16)	14.5 (10.0)	10.8 (7.7)	22.4 (9.8)	t=-8.02, p<.001
Trait anxiety (≥31.8)	36.0 (10.7)	32.5 (8.5)	43.4 (11.3)	t=-6.60, p<.001
State anxiety (≥32.2)	34.5 (12.6)	30.6 (10.3)	42.7 (13.2)	t=-6.22, p<.001
General Sleep Disturbance Scale (≥43.0)	50.2 (21.4)	45.6 (19.7)	60.1 (21.8)	t=-4.54, p<.001
Morning fatigue (≥3.2)	3.4 (2.5)	2.8 (2.3)	4.8 (2.4)	t=-5.50, p<.001
Evening fatigue (≥5.6)	5.0 (2.2)	4.6 (2.1)	5.7 (2.2)	t=-3.09, p=.002
Morning energy (≤6.2)	5.0 (2.4)	5.4 (2.4)	4.1 (2.2)	t=3.65, p<.001
Evening energy (≤3.5)	2.8 (2.1)	2.9 (2.2)	2.6 (1.9)	t=0.77, p=.441
Attentional Function Index (< 5 = low cognitive function, 5 to 7.5 = moderate cognitive function, >7.5 = high cognitive function)	6.7 (1.7)	7.2 (1.6)	5.6 (1.6)	t=6.29, p<.001
Types of pain None Only non-cancer pain Only cancer pain Both non-cancer and cancer pain	 38.8 (71) 14.8 (27) 25.1 (46) 21.3 (39)	 45.6 (57) 10.4 (13) 24.8 (31) 19.2 (24)	 24.1 (14) 24.1 (14) 25.9 (15) 25.9 (15)	X^2=10.61, p=.014 0>1
Worst pain intensity score	6.6 (2.2)	6.8 (2.0)	6.3 (2.5)	t=1.17, p=.245

Mean pain interference score	3.2 (2.2)	2.9 (2.1)	3.6 (2.2)	t=-1.63, p=.105

*Clinically meaningful cutoff scores are in parentheses

Abbreviations: IES-R = Impact of Event Scale-Revised, SD = standard deviation

Table 3 – Differences in symptom occurrence rates between the stress groups

Symptom occurrence	Total Sample n=187	Non-stressed group 68.4% (n=128)	Stressed group 31.6% (n=59)	Statistics
Depression	39.8	25.4	71.2	FE, p<.001
Trait anxiety	59.1	48.8	81.4	FE, p<.001
State anxiety	48.4	34.6	78.0	FE, p<.001
Sleep disturbance	59.7	51.2	78.0	FE, p<.001
Morning fatigue	45.9	38.6	72.9	FE, <.001
Evening fatigue	40.5	33.3	55.9	FE, p=.004
Decrements in morning energy	69.2	62.7	83.1	FE, p=.006
Decrements in evening energy	67.7	66.9	69.5	FE, p=.866
Decrements in cognitive function	68.3	57.5	91.5	FE, p<.001
Pain	61.2	54.4	75.9	FE, p=.006

Abbreviations: FE = Fischer's Exact test, IES-R = Impact of Event Scale-Revised

Table 4 - Multiple Logistic Regression Analysis Predicting Stress Group Membership (n = 169)

Predictor	Odds Ratio	95% CI	p-value
Karnofsky Performance Status score	1.06	1.00, 1.13	.072
Self-administered Comorbidity Questionnaire score	1.15	0.97, 1.35	.102
Time since cancer diagnosis in years	0.92	0.85, 0.99	.028
Perceived Stress Scale score	1.13	1.01, 1.27	.033
Connor Davidson Resilience Scale score	0.97	0.87, 1.09	.646
Social Isolation Scale score	0.95	0.80, 1.12	.518
UCLA Loneliness Scale score	0.96	0.90, 1.04	.329
Comprehensive Score for Financial Toxicity	1.04	0.98, 1.10	.171
Center for Epidemiological Studies Scale score	1.11	1.00, 1.25	.062
Trait anxiety score	1.00	0.90, 1.11	.995
State anxiety score	0.99	0.92, 1.06	.737
General Sleep Disturbance Scale score	0.98	0.95, 1.02	.294
Lee Fatigue Scale – morning fatigue score	1.34	0.94, 1.89	.102
Lee Fatigue Scale – evening fatigue score	0.94	0.71, 1.25	.686
Lee Fatigue Scale – morning energy score	1.22	0.92, 1.61	.172
Attentional Function Index score	0.72	0.47, 1.11	.140
Occurrence of pain	5.02	1.64, 15.4	.005
Overall model fit: df = 17, $X^2 = 85.2$, $p < 0.001$			

Abbreviations: CI = confidence interval, df = degrees of freedom